The ongoing COVID-19 pandemic has revealed the fragility of our societies and economies, stressing the urgent need to improve our relationship with the natural world. Early studies projected that air pollution increases the likelihood, vulnerability and severity of succumbing to COVID-19. The World Health Organization, in collaboration with other international organizations, is supporting research to verify such findings and to urgently address the need to improve the quality of the air we breathe.

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Air quality and health impacts in the Eastern Mediterranean Region: an eye on COVID-19

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Air quality is intimately linked to human activities, climate, atmosphere and ecosystems. Many of the anthropogenic contributors to air pollution are also sources of greenhouse gases including CO2 and other short-lived climate pollutants, such as Ozone and black carbon, which greatly contribute to the climate change phenomenon and its adverse effects on human health. Unfortunately, fragile and dry ecosystems prevailing in most of our countries in the Eastern Mediterranean Region may be implicated for exacerbation of this air pollution and climate change dilemma even more severely.

Air pollution sources in the Region differ significantly from those in other parts of the world, in part due to the arid nature and high prevalence of natural dust, as well as the widespread practice of biomass and solid waste burning. More than 50% of air pollutants were reported to come from natural sources, while the other half is blamed on the transportation sector, energy production, industrial emissions, agricultural operations, wastes open burning practices, and household use of unclean fuels for cooking, heating ad lighting (1).

From photochemical smog and dust hanging over our cities, to the prefiltration of kitchen and secondhand tobacco smoke inside the homes, air pollution poses a major threat to public health. More than 90% of the people living in our urban areas are exposed to air pollutants levels that exceed World Health Organization (WHO) guideline limits for health protection (2). Children, women, older people and outdoor workers, among other vulnerable groups, are at greater risks as they are subjected to higher levels of air pollution. The combined effects of ambient and household air pollution are causing approximately 500 000 premature deaths every year in the Region (3). This is largely a result from increased morbidity and mortality attributed to stroke, heart disease, chronic obstructive pulmonary disease, lung cancer, asthma and acute respiratory infections.

Air quality management policies and actions are still far below the optimal levels that control air pollution in the Region due to the following major gaps and challenges: poor environmental monitoring and reporting mechanisms; poor commitment; poor coordination between the different related sectors; weak health surveillance systems, and lack of heath based

standards in almost all countries of the Region (4).

Living in a healthy environment is an integral human right, and it is the responsibility of governments to provide clean air to their citizens to breathe safely. There are numerous options available to national governments and local authorities on know-how to support actions to improve air quality. Some of these options are designed to make sure that capacity and processes are built up to enable decision-makers to recognize where air pollution comes from and what emission rates and atmospheric concentrations are, and what actions are to be taken in order to reduce air pollution and exposure levels. Although institutional capacities are limited in this regard, there are still numerous WHO resources available to help countries understand their air pollution problems and identify priority actions and interventions to protect public health and the surrounding environment in which we live.

While controlling the natural sources of air pollution is perhaps difficult and may need long-term mitigation, curtailing other man-made sources is relatively feasible and can be done immediately. cost effective interventions are readily available, yielding health gains and co-benefits surpassing necessary investments. Fortunately, indoor air pollution is a problem for which we know the solutions. All countries where many people still cook using biomass and other dirty fuels, such as kerosene, can develop programmes to improve access to clean energy sources, fuels and technologies. Secondhand smoke, as well as other sources of indoor air pollution such as incense and candles burning, should be minimized or even eliminated, especially in well-insulated living environments with air conditioning and restricted ventilation.

In order to meet the WHO guideline levels for safe, healthy ambient air quality, countries must address the major sources of air pollution in different contexts and resource settings. These may include: development of evidence on health impacts of natural air pollution (dust and sea salt particulate matter), including relevant mitigation interventions to be enhanced and used in the development of national air quality standards and management; rapidly phase out health-harmful subsidies for dirty fuels and polluting industries and introduce penalties for polluters and/or taxes on pollution; adopt and strictly enforce emissions standards for all pollutants

in all relevant sectors, including industry, energy, transport, waste and agriculture; redirect investment to health promotion, accessible alternatives including clean transport, renewable energy and/or to provide universal health coverage; improve housing conditions and ensure access to clean energy sources for indoor cooking, heating and lighting; and include air quality measures In urban, rural and transport planning at city, regional and national level, including measures to encourage modal shift and active mobility, noting the additional benefits to health, wellbeing and reduction of health inequalities (5).

To help our Member States focus their actions on the most efficient way to prevent and reduce the pollution risks and adverse health effects, WHO has identified the key air pollutants with negative impacts on people's health. WHO is continuously reviewing and analyzing the accumulated scientific evidence and relying on upon experts' opinion and advice to draw tangible conclusions on the level of risk due to indoor and outdoor air pollution. WHO has been providing technical support at country-level on best practices to both reduce air pollution and mitigate public health effects. Special attention should be given to reducing emissions of short-lived climate pollutants, as this can provide health benefits in three key ways: 1) directly from reduced air pollution and related ill-health; 2) indirectly from reduced ozone and black carbon effects on extreme weather and agricultural production (adversely affecting food security); and 3) from other types of health benefits that are not associated with air pollution, but may accrue as a result of certain mitigation actions, such as improved diets or more opportunities for safe active travel and enhanced physical activity.

The WHO Regional Centre for Environmental Health Action (WHO/CEHA) in Amman, Jordan, has developed and commenced the implementation of a regional plan of action on air pollution and health in the Eastern Mediterranean Region for 2017–2022 (3). The plan of action takes into consideration the regional context, including climate and local air pollutants, availability of monitoring data and the status of national surveillance systems and policies for controlling air pollution. The plan is linked to relevant targets of the Sustainable Development Goals (SDGs) and also considers developments as opportunities for synergies at global and regional levels, including the Paris Agreement on Climate Change (2015) (6), Marrakech Declaration on Health, Environment and Climate Change (2016) (7), the Arab Strategy on Health and Environment 2017–2030 (8), and the regional work priorities for the WHO Eastern Mediterranean Region (9).

The ongoing COVID-19 pandemic has revealed, like never before, the fragility of our societies and economies, stressing the urgent need to improve our relationship with the natural world. Early studies projected that air pollution increases the likelihood, vulnerability and severity of succumbing to COVID-19. WHO in collaboration with other international organizations are supporting research to verify such findings and to answer several important questions such as: do air conditioning and ventilation systems increase the risk of virus transmission? If so, how can this be managed? Can we use air conditioning in the context of COVID-19? Can fans and indoor air circulation be used safely in indoor spaces and how can ventilation reduce the risk of contracting COVID-19 in transportation facilities? All of these questions and worries are giving us yet another good reason to urgently improve the quality of the air we breathe. On the other hand, COVD-19 lockdowns and other public health precautionary measures have provided clear evidence that high levels of air pollution can be readily reduced, not necessarily through banning human activities, but through healthy and wise socioeconomic recovery, controlling industrial and transportation emissions, and utilizing clean and green fuels, energies, planning and technologies.

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COVID-19 during the crisis in the Syrian Arab Republic

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In December 2019, an unknown cause of pneumonia was announced in Wuhan, China (1). The pathogen was later identified as severe acute respiratory syndrome corona-virus 2 (SARS-CoV-2), and the disease was named coronavirus 2019 (COVID-19) by the World Health Organization (WHO). On 30 January 2020, the WHO announced (COVID-19) as a Public Health Emergency of International Concern (PHEIC). However, as a result of the rapid spread of the disease worldwide, COVID-19 outbreak was announced as a global pandemic on March 11 (2). Until 24 August 2020, about 23,311,719 laboratory-confirmed cases of COVID-19, including 806,410 deaths, have been reported globally (3).

The pandemic had severe health and economic impacts globally, which were even worse in low-income countries. For instance, Syria, which has suffered from a 9-year war, was classified as a high-risk area according to the global risk assessment by WHO even before reporting the first confirmed case (4). This high-risk estimation was due to, among other reasons, the large number of vulnerable people, the religious tourism, fragile health system, and limited resources (4).

As of March 2020, the Syrian authorities started to take strict measures at harbors, land- border crossing points and Damascus International Airport, including temperature measurement and checking travel history to detect any suspected cases of COVID-19, and finally traveling was banned unless for certain humanitarian or trade exemptions (5). Moreover, starting from 24 March 2020, a night curfew was imposed in addition to further measures like reducing the number of workers in the public institutions as well as suspension of universities, schools, and institutes (6).

The first case of COVID-19 in Syria was reported on 22 March 2020 for a traveler from another country (6), while the first confirmed death was reported on 29 March 2020 (7). However, COVID-19 cases started to increase significantly after 26 May 2020 when some precautionary measures were lifted, such as the curfew, the travel ban between and within governorates, and universities and institutions suspension (8). As of 20 August 2020, the Syrian Ministry of Health has confirmed (2008) cases of COVID-19, including (82) deaths and (460) recoveries (9). The majority of reported cases are in Damascus and Aleppo, followed by rural Damascus and Latakia. To notice, these official numbers were doubled within three weeks, which indicates that community transmission is widespread. Moreover, there is a concern that the actual number of cases is much higher than the reported ones due to poor testing capacity that results in many asymptomatic or mild cases to remain undiagnosed (9).

According to published data, 76 COVID-19 cases were among healthcare workers as of 20 August 2020, the majority of these cases are in Damascus. Moreover, it is estimated that one in five cases in north-east Syria is of healthcare worker. An estimation that raises the urgent need for providing more personal protective equipments (PPE) for healthcare workers (9).

Several factors were hypothesized to explain the relatively low-reported number of COVID-19 cases in Syria especially between March and May 2020 (10); In our opinion, firstly, the few numbers of tests being conducted due to the low numbers of diagnostics kits and equipped laboratories. Secondly, the lack of transportation movement between Syria and the rest of the world. Finally, the precautionary measures that were taken early in March. However, the situation was significantly deteriorated later which might indicate the lack of preventive measures at the individual and community level, as well as the impact of the undetected cases on the subsequent prevalence.

The nine years of conflict In Syria caused a deterioration of Syria's health system, by the end of December 2019, and out of 113 public hospitals assessed by WHO, only 50% (57) were fully functioning and 43%(49) were damaged. Syrian hospitals are still suffering from a shortage and/or malfunction of medical devices and equipment, and there is a shortage of beds at varying degrees across all governorates (11). An estimated capacity to manage a maximum number of 6,500 patients all over the country is reported. This capacity varies widely across Syria (12), and the medical devices are overburdened by increased numbers of people in safe areas (11).

Several factors make the epidemiological situation more critical In Syria; around 80% of the population live in poverty, thus home quarantine measures could have severe consequences for the population (12). Social And economical impacts of COVID-19 are likely to exacerbate existing substantial humanitarian needs across the country (13). In addition, internationally recommended measures are unlikely to be enforceable or effective in areas where overcrowding

are rife (12), especially in Damascus/Rural Damascus, Aleppo and Homs (13), as well as other areas including Deir-Ez-Zor, where conflict may be ongoing making sample collection more challenging (13). SARS-CoV-2 could spread rapidly through affected populations, particularly among those in the most vulnerable groups (12).

More challenges face the Syrian health system, for example, the poor surveillance system and lack of a standardized method for reporting infections (14). Moreover, numbers of qualified healthcare workers at the frontline of healthcare provision are insufficient and in continuous threat due to lack of PPE. Thus, they are particularly vulnerable not only to the risk of infection but also to ethical challenges posed by the current situation, including difficult triage and resource allocation decisions (12,13). .

In conclusion, we think that there is a crucial need for a comprehensive and evidence-based health plan in Syria in coordination with non-governmental organizations and community bodies to improve detecting, monitoring, and tracking of cases in order to improve hospitals' capacities, and to manage received aids fairly and prudently.

Acknowledgement

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Use of complementary and alternative therapies in infants under 3 months in Jordan

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Abstract

Background: The use of complementary and alternative medicine in infants to maintain health and treat illnesses is popular in Jordan. No guidelines or regulations govern their use.

Aims: This study explored mothers' knowledge and use of complementary and alternative therapies for infants younger than 3 months in Jordan and their reasons for using these remedies.

Methods: This was a cross-sectional study of a convenience sample of mothers of babies born in 2015 in Jordan. Data were collected using a questionnaire posted on six Facebook groups that target mothers in Jordan. Mothers were asked about their use of several complementary and alternative therapies for different conditions.

Results: Of 1028 questionnaires received, 520 were included in the analysis. Most mothers (81.3%) were 18–29 years old and had a university degree (78.3%). Most knew about the use of the complementary and alternative medicines for bloating/colic but had never used them. Of the medicines used for bloating/colic, aniseed was most often used (by 70.2% of mothers). Aniseed was also used by 60.8% of mothers to help their baby sleep and by 48.1% for constipation. The main reasons for using these remedies were availability at home (60.4%) and social acceptability of their use (55.4%). The main sources of information about these medicines were older female relatives (78.1%) and social media (56.0%).

Conclusions: The use of complementary and alternative medicines for babies is common in Jordan. Efforts are needed to increase awareness among mothers of the risks, side-effects and efficacy of complementary and alternative therapies in infants.

Keywords: complementary therapies, infants, neonates, mothers, Jordan

Introduction

The use of complementary and alternative medicine for the treatment of diseases has a long tradition worldwide *(1)*. According to the World Health Organization, traditional medicine is defined as, "the sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness" *(2)* whereas complementary and alternative medicine is defined as, "A broad set of health care practices that are not part of that country's own tradition or conventional medicine and are not fully integrated into the dominant health-care system" *(2)*. Complementary and alternative medicine may include using herbs, prayers and spiritual healing, aromatherapy, special food, massage and body movement, cupping, vitamins, relaxation techniques and acupuncture *(1)*.

The prevalence of the use of complementary and alternative medicine in children in Europe is 52% *(3)*. One in every nine children in the United States of America (USA) has been given some type of complementary and alternative therapy *(4)*. The use of complementary and alternative medicine is considerably higher in children with special health care needs: the use of such medicine is most common in children with asthma *(5)*, epilepsy *(6)*, attention-deficit hyperactivity disorder *(7)*, autism *(8)*, cerebral palsy *(9)*, cystic fibrosis *(10)*, inflammatory bowel disease *(11)*, anaemia and juvenile rheumatoid arthritis *(12)*. Despite its wide use, complementary and alternative medicine has risks, especially as laws and regulations on its use are generally lacking *(13)*. In addition, parents often do not report the use of complementary and alternative medicine to the paediatrician *(3)*. As a result, research done in conventional medical settings may not have sufficiently described the use of complementary medicine in young children *(14)*. Therefore, research on the use of complementary and alternative medicine in children in the general population using representative samples are needed.

In Jordan, the use of complementary and alternative medicine, including herbs, is popular during infancy to help treat mild and severe illnesses. Several studies

have reported the use of complementary and alternative medicine in children in Jordan: in paediatric patients (aged more than 1 year) at a neurology clinic (15); in children with cancer (16,17); by parents to manage illnesses of their children younger than 12 years (2); as traditional care practice for newborns (1–4 weeks) (18); and as traditional practice in infants in rural areas (19). To our knowledge, no studies in Jordan have looked into the use of complementary and alternative medicine in babies up to 3 months of age. The aims of this study therefore were to explore mothers' reasons for using traditional, complementary and alternative therapies for their babies in the first three months of life, and the sources of information on the use of such therapies.

Methods

Study design and sample

This was a cross-sectional study conducted in 2015 in Jordan. A convenience sample of Jordanian mothers of infants born in 2015 in Jordan was recruited. The exclusion criteria were: (i) incomplete questionnaires; (ii) questionnaires completed twice by the same mother with twin infants; and (iii) questionnaires completed by mothers whose infants were born in years other than 2015 or in a country outside Jordan.

We chose the age group 0–3 months because babies at this early stage depend on milk as their primary source of nutrition.

Data collection

We used a questionnaire to assess different traditional, complementary and alternative medicine practices. We reviewed scientific literature and articles in local magazines and newspaper as the first step in developing the questionnaire. We posted a short survey on traditional practices/remedies used by mothers for their children on Facebook groups dedicated to motherhood and childhood in Jordan. We included all the complementary and alternative medicine products reported by the mothers who completed the survey in our questionnaire. The research committee at the school of pharmacy in Isra University, which includes professors of medicine, biology and pharmacy, reviewed the questionnaire and provided feedback. The questionnaire was developed and distributed in Arabic.

To ensure face and content validity of the questionnaire, it was also reviewed by two independent faculty members at Isra University with doctorates in clinical pharmacy. We rephrased some items for clarity based on the comments of the reviewers.

The questionnaire had four sections that explored: (i) mothers' knowledge and use of traditional remedies for colic and bloating; (ii) mothers' use of traditional practices for the treatment or prevention of other baby ailments; (iii) mothers' reasons for using these treatments; and (iv) mothers' sources of information on these complementary and alternative treatments.

The final version of the questionnaire was posted online to six Facebook groups that target mothers in Jordan with their permission: moms to be Jordan (https://www.facebook.com/groups/397387487039655/); mommy to be (https://www.facebook.com/groups/mommytobesecretgroup); smart mama (https://www.facebook.com/groups/481735031997763/); breastfeeding in Jordan (https://www.facebook.com/groups/breastfeedinginjordan/); Jordanian mamaz in the United Arab Emirates (https://www.facebook.com/groups/803574686387943/); and babies food (https://www.facebook.com/groups/babiesfood/). The questionnaire was live online for a week in January 2017 and data were collected using Survey Monkey (San Mateo (CA), USA).

Statistical analysis

We transferred data from Survey Monkey to *Excel* and translated them into English. We used descriptive statistics to describe the demographic characteristics of the responders, and the chi-squared test to examine differences between groups for categorical variables. We considered a *P*-value of less than 0.05 as statistically significant. We used *SPSS*, version 24 for statistical analyses.

Ethical considerations

The Scientific Committee in the Faculty of Pharmacy of Isra University (Amman, Jordan) approved the study.

The questionnaire was anonymous. Mothers were informed that their data was confidential and that the study would neither harm nor help them directly, and that the results would be a valuable addition to the field of paediatrics. Information about the participating mother's age (< 18, 18–29, 30–39 and ≥ 40 years), educational level, city of residence and health insurance was collected for statistical analyses.

Results

Response rate

Of the 1028 submitted questionnaires, we included 520 in the analysis. We excluded questionnaires that were incompletely filled, and questionnaires filled by mothers who gave birth before or after 2015 and who gave birth outside Jordan.

The total number of newborns in Jordan in 2015 was 198 018 (Jordanian statistics department, 2015) (20). A sample size of 383 provides a 95% confidence level to provide statistically meaningful data with an alpha level of 0.05. Our final sample size (520) therefore provides 95.7% power.

Characteristic of the mothers

None of the mothers was younger than 18 or older than 40 years: 423 (81.3%) were 18–29 years old and 97 (18.7%) were 30–39 years. Most of the mothers were residents of Amman (315; 60.6%), while 64 (12.3%) were from Zarqa and 52 (10.0%) were from Irbid. Only 41 (7.9%) mothers had less than secondary school education, while 366 (70.4%) had a bachelor degree. The demographic characteristics of the mothers are shown in Table 1.

Table 1 Demographic characteristics of the study sample, Jordan

Characteristic	No. (%) (*n* = 520)
Mother's age (years)	
18–29	423 (81.3)
30–39	97 (18.7)
Residence	
Amman	315 (60.6)
Zarqa	64 (12.3)
Irbid	52 (10.0)
Balqaa	23 (4.4)
Aqaba	13 (2.5)
Other in Jordan	30 (5.8)
Outside Jordan	23 (4.4)
Medical insurance	
Not insured	128 (24.6)
Governmental insurance	150 (28.8)
Through UNRWA	15 (2.9)
Private insurance	200 (38.5)
Two types of insurance	27 (5.2)
Educational level	
Secondary school or less	41 (7.9)
Professional (skills) training only	5 (1.0)
Diploma in medical field	20 (3.8)
Diploma in non-medical field	47 (9.0)
Bachelor degree in medical field	82 (15.8)
Bachelor degree in non-medical field	284 (54.6)
Postgraduate degree in medical field	32 (6.2)
Postgraduate degree in non-medical field	9 (1.7)

UNRWA: United Nations Relief and Works Agency for Palestine Refugees in the Near East.

Baby colic and bloating

Table 2 shows the mothers' use of complementary and alternative medicine for treating their babies' colic or bloating. Most participants were aware of the reported use of these complementary and alternative medicine for baby colic and bloating but had never used them. Of the complementary and alternative medicines used for bloating and colic, the most frequently used one was aniseed (used by 70.2%), cumin (36.7%), chamomile (34.8%), sage (27.3%), mint (26.2%) and fennel (26.0%).

About half of the mothers were not aware of teucrium. Most of the mothers were familiar with mint (69.8%), sage (69.4%), fennel (64.0%) and cumin (59.6%) even though they had never used them to treat colic or bloating (Table 2).

Minor diseases in infants

Complementary and alternative medicines used to treat some conditions in babies in the first 3 months of their lives are shown in Table 3. Most mother did not use any complementary or alternative medicines to treat baby jaundice, nappy rash, cough, eye problems, diarrhoea, or colds. However, almost a quarter of the mothers used a mix of rock candy with water (24.4%) or date extract (22.7%) to treat jaundice. Just over a quarter (26.5%) of the mothers used starch mixed with grease or oil to treat nappy rash. Two fifths of the mothers massaged their babies with sesame oil to treat a cough and 29.4% used bitter tea to treat eye inflammation. As regards other conditions, over half the mothers (60.8%) used aniseed as a sedative to help the baby sleep for a long time and 48.1% used this plant to treat constipation. Almost all the mothers (90.4%) used olive oil for body massaging for overall well-being while 2.7% used castor oil for massage.

Table 2 Mothers' knowledge and use of complementary and alternative medicine for treating colic or bloating in their babies

Treatment used: English name (scientific name)	Used it for colic, No. (%)	Used it for bloating, No. (%)	Used it for colic and bloating, No. (%)	Know about it but never used it, No. (%)	Didn't know that it was used for colic and bloating, No. (%)	Don't know this product, No. (%)
Anise (*Pimpinella anisum*)	28 (5.4)	196 (37.7)	141 (27.1)	149 (28.7)	5 (1.0)	1 (0.2)
Chamomile (*Matricaria chamomilla*)	18 (3.5)	56 (10.8)	107 (20.6)	316 (60.8)	21 (4.0)	2 (0.4)
Wall germander (*Teucrium chamaedrys*)	16 (3.1)	0 (0.0)	3 (0.6)	234 (45.0)	26 (5.0)	241 (46.3)
Thyme (*Thymus vulgaris*)	3 (0.6)	1 (0.2)	7 (1.3)	439 (84.4)	63 (12.1)	7 (1.3)
Fennel (*Foeniculum vulgare*)	3 (0.6)	94 (18.1)	38 (7.3)	333 (64.0)	36 (6.9)	16 (3.1)
Caraway (*Carum carvi*)	2 (0.4)	25 (4.8)	15 (2.9)	396 (76.2)	63 (12.1)	19 (3.7)
Cumin (*Cuminum cyminum*)	4 (0.8)	145 (27.9)	42 (8.1)	310 (59.6)	18 (3.5)	1 (0.1)
Mahaleb or St Lucie cherry (*Prunus mahaleb*)	0 (0.0)	11 (2.1)	7 (1.3)	345 (66.3)	69 (13.3)	88 (16.9)
Sage (*Salvia officinalis*)	92 (17.7)	18 (3.5)	32 (6.2)	361 (69.4)	16 (3.1)	1 (0.2)
Mint (*Mentha spicata*)	29 (5.6)	63 (12.1)	44 (8.5)	363 (69.8)	20 (3.8)	1 (0.2)
Orange blossom water	17 (3.3)	67 (12.9)	34 (6.5)	354 (68.1)	43 (8.3)	5 (1.0)

Sources of information

The participants' mothers and mothers-in-law were the main sources of information about complementary and alternative medicine (78.1%), while 56.0% depended on information published on social media (Figure 1). Participants with a lower education level (less than a bachelor degree) versus those with a higher education level (bachelor degree or higher) tended to ask either a relative (64/113 (56.6%) versus 163/407 (40.1%); P = 0.002), or their doctor or pharmacist or someone working in health care (59/113 (52.2%) versus 140/407 (34.4%); P = 0.001). Younger mothers were more likely to be influenced by social media in their decision to use complementary and alternative medicine: 252 (59.6%) mothers aged 18–29 years versus 39 (40.2%) mothers aged 30 years or more (P = 0.001).

Benefits of complementary and alternative medicine

Most mothers (419/520; 80.6%) reported that they had used complementary and alternative medicine to treat themselves. About half of the mothers (249; 47.9%) believed that complementary and alternative medicines could harm their infant, while (411; 79.0%) believed that their infants had benefitted from complementary and alternative medicines. These beliefs were associated with a higher education level – more mothers with a bachelor or postgraduate degree believed that complementary and alternative medicines could have harmful effects: 218/407 (53.6%) mothers with a bachelor or postgraduate degree versus 38/113 (33.6%) of those with less than a bachelor degree (P < 0.001). More educated mothers also thought that their child had not benefitted from these medicines: 93/407 (22.8%) mothers with bachelor or postgraduate degree versus 16/113 (14.2%) mothers with less than a bachelor degree (P = 0.045). Only 17/520 (3.3%) mothers reported that their infants had experienced side-effects when using complementary and alternative medicine.

Reasons for use

The most common reasons for using complementary and alternative medicine in infants were the availability of these medicines at home (60.4%), because these medicines are known and used in the community (55.4%) and because conventional medicines may cause side-effects (50.0%). The results are presented in Figure 2. The belief that complementary and alternative medicines give better results than conventional medicines and that the latter can harm their children was significantly more common in mothers of a lower education level: 59/113 (52.2%) of mothers whose education level was less than bachelor degree versus 139/407 (34.2%) mothers with a bachelor or postgraduate degree (P < 0.001).

Discussion

Our study shows that mothers use complementary and alternative medicine for treatment or prevention of various baby ailments during the first 3 months of life. Chiefly, they tend to use different complementary and alternative therapies for treating their babies' colic and

Table 3 **Mothers' use of complementary and alternative medicines to treat various conditions in their babies in the first 3 months of their lives**

Complementary and alternative medicines used for:	No. (%) (n = 520)
Treatment of jaundice	
Mix of rock candy with grease	14 (2.7)
Mix of rock candy with water	127 (24.4)
Date extract	118 (22.7)
Chain of garlic	82 (15.8)
Full-fat cow's milk	7 (1.3)
Treatment of nappy rash	
Starch slurry	57 (11.0)
Starch mixed with grease or oil	138 (26.5)
Banana peels	1 (0.2)
Treatment of cough	
Drinking sesame oil	109 (21.0)
Massaging sesame oil	208 (40.0)
Black caraway	13 (2.5)
Radish extract	6 (1.2)
Treatment of eye inflammation	
Drops of breast milk	100 (19.2)
Compresses of bitter tea	153 (29.4)
Honey spreads	5 (1.0)
Treatment of diarrhoea	
Starch	56 (10.8)
Rice water	128 (24.6)
Treatment of cold symptoms	
Onion juice	8 (1.5)
Home-made salty water as nasal drops	39 (7.5)
Other practices	
Aniseed to treat constipation	250 (48.1)
a long time	51 (9.8)
Aniseed to help the baby sleep for a long time	316 (60.8)
Washing the baby with salted water	151 (29.0)
Massaging with olive oil	470 (90.4)
Massaging with castor oil	14 (2.7)

bloating problems. The use of such therapies for infantile colic is perhaps because this condition is known to have many causes and evidence is limited on an effective treatment for managing it (21).

We know that aniseed is widely used during infancy in Jordan because it soothes a crying baby by reducing colic and bloating pain. Our results showed that most mothers preferred to use aniseed for this purpose. In fact, it has been previously documented that mothers in Jordan frequently give their neonates bottles of boiled herbs containing aniseed and sage (18). In addition, in traditional Iranian medicine, fennel and aniseed were used to treat symptoms of colic (22). Aniseed has been shown to have sedative and antispasmodic properties (23). It has also been shown that the essential oil of aniseed reduces spasms of the gastrointestinal tract, and extract of aniseed increases milk production of lactating mothers and reduces the gastrointestinal problems of their infants
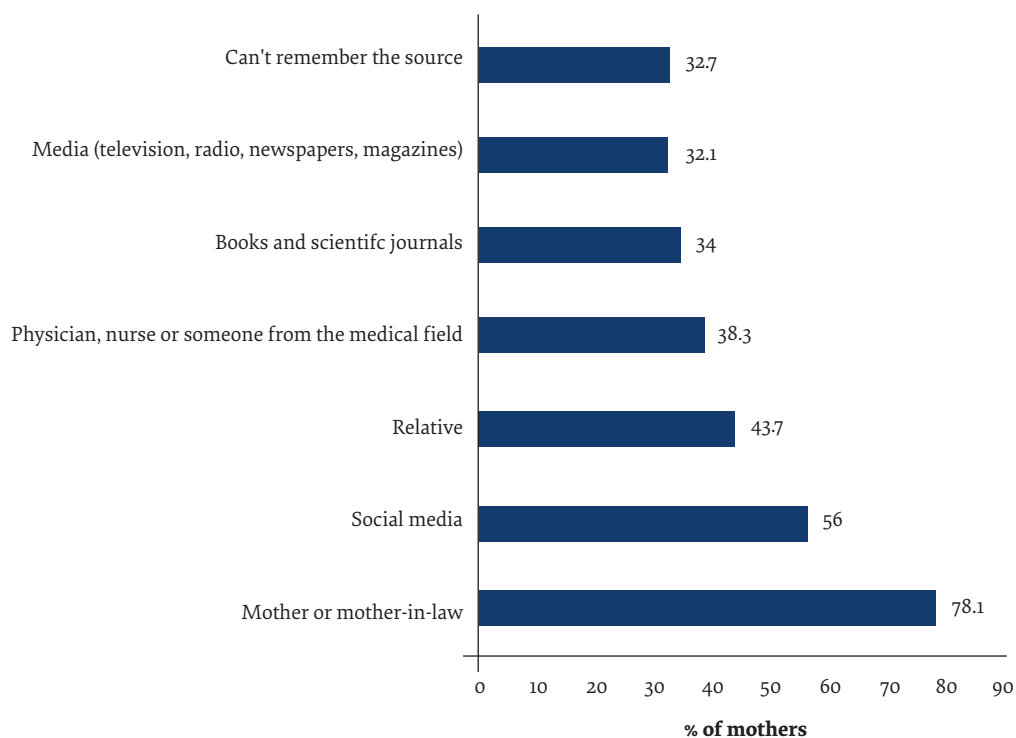
(24). Nevertheless, caution is needed while using aniseed in neonates and infants because it might have some toxic effects (25). This toxic effect is attributed to the fact that aniseed contains anethole in the essential oil which may cause neurological symptoms (26). Therefore, awareness campaigns are needed to educate the community about the possible side-effects of aniseed.

Our results also show that the other traditional colic remedy that is often used is massaging with olive oil, which has been reported to be used extensively in Jordan (18,19).

Many of the common complementary and alternative medicine used traditionally were not familiar to most of our participants. Nevertheless, we know from our initial short survey on general traditional practices by mothers that these practices are used by older Jordanian generations and by some young mothers. In particular, these include massaging with olive oil and putting a necklace of garlic to treat jaundice. We believe it is important to document these practices and to conduct scientific research on the validity and rationale of their use, especially as many of them are not reported in the literature.

The average of total reading hours per year in the Jordanian population is only 50 hours, according to the 2016 Arab reading index (27). As Jordanian people rarely read, they get their information from other sources that might not be reliable. According to our results, mothers depend on relatives and social media for their information on remedies for childhood ailments. Our data is consistent with previous findings in Jordan that showed

that mothers and mothers-in-law are the first source of information on questions about early infancy (18). For participants in our study, mothers, mothers-in-law and elderly contacts were the main source of information about complementary and alternative medicine. In fact, the care of a newborn baby is primarily a maternal duty in Jordan; most new mothers choose to spend at least 40 days after delivery at the home of their parents or their husband's parents, if they do not already live within an extended family. Indeed, mothers in our study who lived outside Jordan preferred to give birth in Jordan so as to spend time with their mothers after delivery.

Social media was the second most important source of information about complementary and alternative medicine. This finding might be linked to the fact that most of our participants were 18–29 years old and lived in Amman, the capital of Jordan. According to reports of the Jordanian telecommunication regulatory commission, the percentage penetration rates of mobile telephones and Internet use in the Jordanian population in 2015 were 145% and 48.4%, respectively (28). This finding suggests that some Jordanians have multiple mobile telephones and SIM cards, which makes social media highly available and accessible.

The two main reasons for the mothers gave for using complementary and alternative therapies were their availability in the house and their acceptance within society. Herbal medicine is widely used in Jordan (29), and most of the products mentioned in the questionnaire are available in all Jordanian households.

Although complementary and alternative therapies

Figure 2 Mothers' reasons for using complementary and alternative medicine
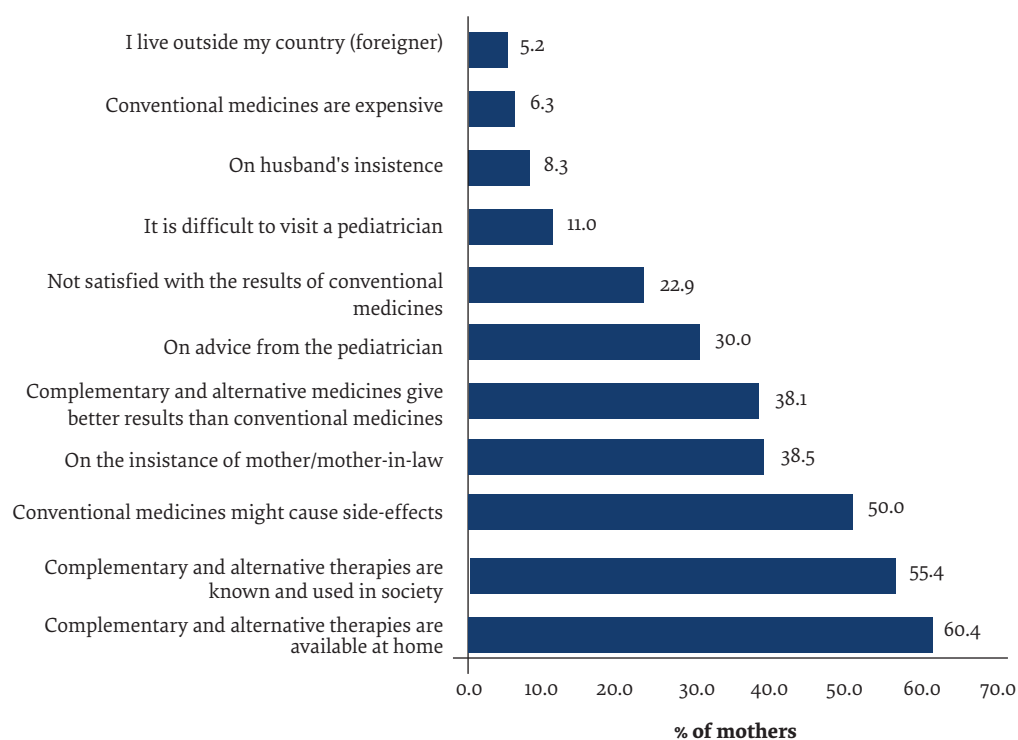
appear to be safe and are recommended as alternatives for treatments *(30)*, it has been reported that Chinese herbal medicine might have side-effects *(31)*. We found that the third most common reason for using complementary and alternative medicine was the fear of side-effects from conventional drugs which concurs with another study *(32)*. Furthermore, parents often choose to give their children natural health products because they believe that these products are safe *(33)*. Most mothers in our study thought that their babies benefited from complementary and alternative medicine, and many said that these medicines gave better results than conventional drugs. Our results show that most of the mothers also used complementary and alternative medicine for themselves. Therefore, we think that awareness campaigns are needed to educate people about the possible side-effects of complementary and alternative medicine and that they should not be preferred to visiting the paediatrician or using conventional drugs.

The findings from our study will help increase the knowledge of parents and of paediatricians, nurses, midwives, pharmacists and health care providers in Jordan who should be well informed about complementary and alternative medicine therapies used in infancy so they can recommend their use or not. Our study has some limitations. Our sample was a convenience sample so may not be representative of all Jordanian mothers. In addition, the questionnaire only reached mothers who were capable of accessing the Internet and social media, and who were members of the Facebook groups where we posted the questionnaire.

Given that mothers' use of complementary and alternative therapies for their infants younger than 3 months is high in Jordan, and that evidence on the safety and efficacy of these products in infants is lacking, we recommend the following: (i) promote awareness of the risks, side-effects and efficacy of the use of both complementary and alternative therapies and conventional medicines in infants; (ii) Educate current and future mothers on dealing with health conditions in infants and the importance of seeking medical information from valid and reliable scientific sources, e.g. doctors, pharmacists and other health care professionals; and (iii) Conduct more research on complementary and alternative therapies to build evidence of their efficacy and possible toxicity so guidelines can be set for their safe and effective use.

Acknowledgement

Utilisation de traitements complémentaires et alternatifs chez les nourrissons de moins de trois mois en Jordanie

Résumé

Contexte : L'utilisation de médicaments complémentaires et alternatifs chez les nourrissons pour maintenir leur santé et traiter les maladies est populaire en Jordanie. Aucune directive ou réglementation ne régit leur utilisation.

Objectifs : La présente étude a analysé les connaissances des mères et leur recours aux traitements complémentaires et alternatifs chez les nourrissons de moins de trois mois en Jordanie, ainsi que les raisons pour lesquelles elles utilisent ces remèdes.

Méthodes : Il s'agissait d'une étude transversale portant sur un échantillon de commodité de mères de bébés nés en 2015 en Jordanie. Les données ont été recueillies à l'aide d'un questionnaire publié sur six groupes Facebook ciblant les mères en Jordanie. Les mères ont été interrogées sur leur utilisation de plusieurs traitements complémentaires et alternatifs pour différentes affections.

Résultats : Sur les 1028 questionnaires reçus, 520 ont été inclus dans l'analyse. La plupart des mères (81,3 %) étaient âgées de 18 à 29 ans et détenaient un diplôme universitaire (78,3 %). Beaucoup d'entre elles connaissaient l'utilisation des médicaments complémentaires et alternatifs pour le traitement des ballonnements/coliques mais ne les avaient jamais utilisés. Parmi les médicaments utilisés pour le traitement des ballonnements/coliques, l'anis était le plus souvent utilisé (par 70,2 % des mères). L'anis était également utilisé par 60,8 % des mères pour aider leur bébé à dormir et par 48,1 % pour la constipation. Les principales raisons de l'utilisation de ces remèdes sont la disponibilité à domicile (60,4 %) et l'acceptabilité sociale de leur utilisation (55,4 %). Les principales sources d'information sur ces médicaments étaient les femmes plus âgées membres de la famille (78,1 %) et les médias sociaux (56,0 %).

Conclusions : L'utilisation de médicaments complémentaires et alternatifs chez les nourrissons est courante en Jordanie. Des efforts doivent être déployés pour sensibiliser les mères aux risques, aux effets secondaires et à l'efficacité des traitements complémentaires et alternatifs chez les nourrissons.

استخدام العلاجات التكميلية والبديلة للرضع الأقل من 3 أشهر في الأردن

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الخلاصة

الخلفية: يحظى استخدام الطب التكميلي والبديل مع الرُّضَّع بغرض الحفاظ على الصحة وعلاج الأمراض بشعبية في الأردن، غير أنه لا توجد مبادئ توجيهية أو لوائح تحكم استخدامه.

الأهداف: هدفت هذه الدراسة إلى استكشاف معرفة الأمهات بالعلاجات التكميلية والبديلة واستخدامهن لها مع الرضع الذين تقل أعمارهم عن 3 أشهر في الأردن وأسباب استخدام تلك العلاجات.

طرق البحث: هذه دراسة مقطعية لعينة عشوائية من أمهات الأطفال الذين وُلدوا في عام 2015 في الأردن. وجُمعت البيانات باستخدام استبيان نُشر على ست مجموعات على الفيسبوك تستهدف الأمهات في الأردن. وسُئلت الأمهات عن استخدامهن لعدة علاجات تكميلية وبديلة لحالات مختلفة.

النتائج: من بين 1028 استبياناً مُستكملاً، أُدرجَ 520 استبياناً في التحليل. وتراوحت أعمار معظم الأمهات (81.3 ٪) بين 18 و29 عاماً، كما كُنَّ حاصلات على درجة جامعية (78.3 ٪). وكانت لدى أغلبيتهن معرفة باستخدام الأدوية التكميلية والبديلة المعالجة لانتفاخ البطن/ المغص، لكنهن لم يستخدمنها قط. ومن بين الأدوية المستخدمة لعلاج انتفاخ البطن/ المغص، كان الينسون هو الأكثر استخداماً (من قبل 70.2 ٪ من الأمهات). كما استخدمت 60.8 ٪ من الأمهات الينسون لمساعدة أطفالهن على النوم، و48.1 ٪ لعلاج لإمساك. وكانت الأسباب الرئيسية لاستخدام تلك العلاجات هي توافرها في المنزل (60.4 ٪) ومقبولية استخدامها من الناحية الاجتماعية (55.4 ٪). وكانت المصادر الرئيسية للحصول على معلومات حول تلك الأدوية هن القريبات الأكبر سناً (78.1 ٪)، ووسائل التواصل الاجتماعي (56.0 ٪).

الاستنتاجات: يشيع استخدام الأدوية التكميلية والبديلة للرضع في الأردن. ويلزم بذل جهود لإذكاء وعي الأمهات بمخاطر العلاجات التكميلية والبديلة وآثارها الجانبية وفعاليتها بالنسبة للرضع.

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Human resources for health density and its associations with child and maternal mortality in the Islamic Republic of Iran

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Abstract

Background: The Family Physician and Social Protection Scheme for Iranian rural inhabitants was launched in June 2005 to improve physician density. To our knowledge, a comprehensive study of the impact of the Scheme on mortality-related health indicators has not been conducted.

Aims: To investigate the effects of health workforce density on maternal, neonatal, infant and under-5 mortality rates in rural areas of the Islamic Republic of Iran between 2005 and 2011.

Methods: We built mixed-effects Poisson regression models including mortality measures as response variables and physician and behvarz (community-based health worker) densities as independent variables, using data from the Iranian Vital Horoscope tool, annual Households Income and Expenditure Survey, and DTARH software. We also included population sizes, age of inhabitants, rate of urbanization, years of schooling, and wealth index in each district, as well as effect of time, as covariates.

Results: Physician density was significantly associated with child mortality rates (1.5%, 1.1% and 63.5% decrease in neonatal, under-5 and maternal mortality with a 1-unit increase in physician density per 1000 individuals). In the model built for infant mortality rate, physician density and behvarz densities were not significantly associated with this measure.

Conclusions: Improving the distribution of family physicians was associated with lower child and maternal mortality. Improvements in behvarz densities were not associated with decrements in these rates, which probably calls for improvement in access to more professional health services and facilities.

Keywords: child mortality, family physicians, infant mortality, Islamic Republic of Iran, maternal mortality.

Introduction

In 2015, the Millennium Development Goals (MDGs) were replaced by the more detailed Sustainable Development Goals (SDGs) to create a framework for ending poverty, protecting the planet, and ensuring prosperity for all by 2030. The third goal of the SDGs addresses health-related obstacles in the path to sustainable development, and calls for improving maternal and child mortality rates, as well as universal health coverage (UHC) and access to healthcare services, such as vaccination and family planning (1,2). UHC is defined as the availability of quality essential primary health services to all people, which necessitates promoting insurance coverage, increasing the extent of primary health services covered by insurance, and improving inequalities in the availability of these services (3). The provision of access to a trained and motivated health workforce, including community-based health workers (known as behvarzes in the Islamic Republic of Iran), midwives, and family physicians (FPs), is known a critical step in improving UHC in low- and high-income societies (4).

In 2004, the Joint Learning Initiative proposed that training a motivated health workforce, improving work environments for these workers, fair distribution of health human resources, and implementing health strategies designed to meet the health needs of each society lie at the centre of shaping sustainable health systems in all countries (5). Several studies have shown the roles of human resources in improving health outcomes, ranging from prevention and management of noncommunicable diseases (NCDs) to lowering maternal, neonatal and under-5-year mortality rates (6,7).

In rural regions of the Islamic Republic of Iran, the smallest health facility, which is part of the primary healthcare network, is known as the health house. Each health house is staffed by at least 1 community-based health worker (behvarz), who is selected form residents of the same village and is trained for 2 years. Health houses provide primary health services, including vaccinations, prenatal and postnatal primary healthcare, growth monitoring, and management of common infections. Patients with more severe conditions that cannot be managed in health houses are referred to rural health

centres to be visited by rural FPs (*6*).

The Family Physician and Social Protection Scheme was launched in June 2005 for rural inhabitants to improve physician density in areas covered by the scheme (*8*). We conducted the present nationally representative study to investigate the effects of health workforce density, including FPs and behvarzes, on maternal mortality rate (MMR), neonatal mortality rate (NMR), infant mortality rate (IMR), and under-5-year mortality rate (U5MR) in rural areas of the Islamic Republic of Iran between 2005 and 2011.

Methods

Data collection

Data used in this cross-sectional study were collected from multiple sources. Annual numbers of deaths, including MMR (number of pregnancy-related maternal deaths per 100 000 live births), NMR (number of neonatal deaths per 1000 live births), IMR (number of infant deaths per 1000 live births) and U5MR (number of under-5-year deaths per 1000 live births), in each district, as well as data on live births were collected from the Iranian Vital Horoscope tool. This tool was designed to record vital events such as births, deaths and family planning activities in rural areas. It consists of a paper sheet that is kept pinned to the wall at the health house. These data were used to calculate MMR, NMR, IMR and U5MR.

Data on numbers of inhabitants, residents' mean age, rate of urbanization, average years of schooling, and wealth status in each district were collected from surveys and census data, including the annual Households Income and Expenditure Survey (HIES), which were performed by the Statistical Center of Iran. The Wealth Index (WI) is a reduced-dimension measure of a household's cumulative living standards. We used principal component analysis (PCA) and created a WI based on the national HIES. PCA was performed on 14 assets including: home area; number of rooms; type of materials used for home construction; type of fuel used for home heating; ownership of washing machines, freezers, vacuum cleaners, personal computers, mobile phones, telephones and cars; and kitchens, bathrooms and access to mains gas. The values ranged between -4 and +4. After calculating wealth at household level, it was averaged at district level, and the exact values were used in the analyses.

Regional data on years of schooling were unified using the recommended International Standard Classification of Education 1976. The numbers of FPs and behvarzes in each district were gathered from the DTARH software (used in primary healthcare system surveys in the Islamic Republic of Iran). We calculated regional FP and behvarz densities (number per 1000 inhabitants of each area).

Ethical approval

This study was a reanalysis of the available data and was approved by the Ethics Committee of Tehran University of Medical Sciences.

Statistical analysis

We built 4 mixed-effects Poisson regression models using the response variables MMR, NMR, IMR and U5MR. We included FP and Behvarz densities as our independent variables. We also included natural logarithm of population size, mean age of inhabitants, rate of urbanization, average years of schooling, and WI in each district, in addition to the effect of time as covariates. The general form of the mixed-effects Poisson regression models was as follows:

$$log(Y_i) = \alpha + \beta_1 PD + \beta_2 BD + \beta_3 MA + \beta_4 YS + \beta_5 WI + \beta_6 UR + \beta_7 TIME + \beta_7 log_{POP} + b_{0i} + \varepsilon_{ij}$$

$$\varepsilon_{ij} N(0, \sigma^2)$$

$$b_{0i} N(0, \sigma_{b0}{}^2)$$

Where Y, PD, BD, MA, YS, WI, UR, $TIME$ and log $\_POP$ represent our response variables: physician density, behvarz density, regional mean age of inhabitants, regional years of schooling, WI, urbanization rate, years and logarithm of population size in each area, respectively. b_{0i} and ε_{ij} Are the random intercept and error terms, respectively, which were independent.

The analyses were carried out using SAS version 9.2 (SAS Institute, Cary, NC, USA), and maps were prepared using the open source R software, version 3.1.2, and the 'maptools' and 'SDMTools' (Species Distribution Modeling Tools) packages. $P < 0.05$ was assumed to be statistically significant.

Results

MMR, NMR, IMR and U5MR in the Islamic Republic of Iran decreased between 2005 and 2011 (Table 1), and almost in all rural districts over the years of the study (Figure 1). However, inequalities in FP and behvarz densities in these areas were evident, and both of these measures were lowest in the central parts of the country between 2005 and 2011 (Figure 2).

Upon investigating the associations between the covariates and NMR in rural areas, physician density, WI, population size, and mean age of inhabitants were significantly associated with NMR (Table 2). The models showed that a 1-unit increase in FP per 1000 individuals resulted in a 1.5% decrease in NMR per 1000 live births. However, behvarz density failed to show such associations with NMR. Our analysis of the associations between covariates and IMR showed that WI, population size, and mean age of inhabitants were significantly associated with IMR. However, FP and behvarz densities were not significantly associated with IMR. Our analysis of the association between covariates and U5MR showed that FP density, WI, mean age of inhabitants, urbanization, and population size were significantly associated with U5MR. A 1-unit increase in physician density per 1000 individuals was evaluated to cause a 1.1% decrease in

Table 1 Maternal and child mortality rates in the Islamic Republic of Iran 2005–2011

Mortality rate	2005	2011
Neonatal mortality rate per 1000 live births	14.66 (13.98–15.34)	10.45 (9.87–11.02)
Infant mortality rate per 1000 live births	20.48 (19.62–21.34)	15.21 (14.41–16.01)
Under-5-year mortality rate per 1000 live births	24.44 (23.48–25.39)	18.65 (17.70–19.60)
Maternal mortality rate per 1000 live births	0.29 (0.20–0.37)	0.26 (0.19–0.32)

The data are presented with 95% confidence intervals.

U5MR per 1000 live births. However, the association with behvarz density was not significant. In the model built for assessing the effects of the covariates on MMR, physician density, population size, and mean age of inhabitants were significantly associated with MMR. A 1-unit increase in physician density per 1000 individuals was evaluated to cause a 63.5% decrease in U5MR per 1000 live births.

Discussion

An increase in FP density was significantly associated with decrements in NMR, U5MR and MMR but there was no significant association between FP density and IMR. The data failed to show any significant association between behvarz density and child mortality rates. The data also showed the effects of several socioeconomic variables, including average wealth status and size of the population, on child and maternal mortality.

The effects of health workforce density on health measures have been studied thoroughly in other countries. In a study from Brazil, Sousa et al. showed that an increase of 1 nurse professional and 1 physician per 1000 individuals reduced NMR by 3.8% and 2.3%, respectively (9). Fernandes et al. studied the determinants of child mortality in Mozambique and observed that the overall health workforce density and the density of specialized nurses for child and maternal care were strongly associated with NMR. However, their findings did not support the contributing role of improving physician density in decreasing infant mortality (10). In contrast, in a cross-country study, Anand and Bärnighausen did show significant associations between physician density and infant mortality (11). These results show that improving accessibility to specialized child and maternal care, such as services provided by physicians and nurse professionals, is more effective in

Figure 1 Child mortality rates in rural areas of the Islamic Republic of Iran in 2011. Neonatal (A), infant (B), and under-5-year (C) mortality rates are shown in these maps using 5 colours, corresponding to quintiles of values
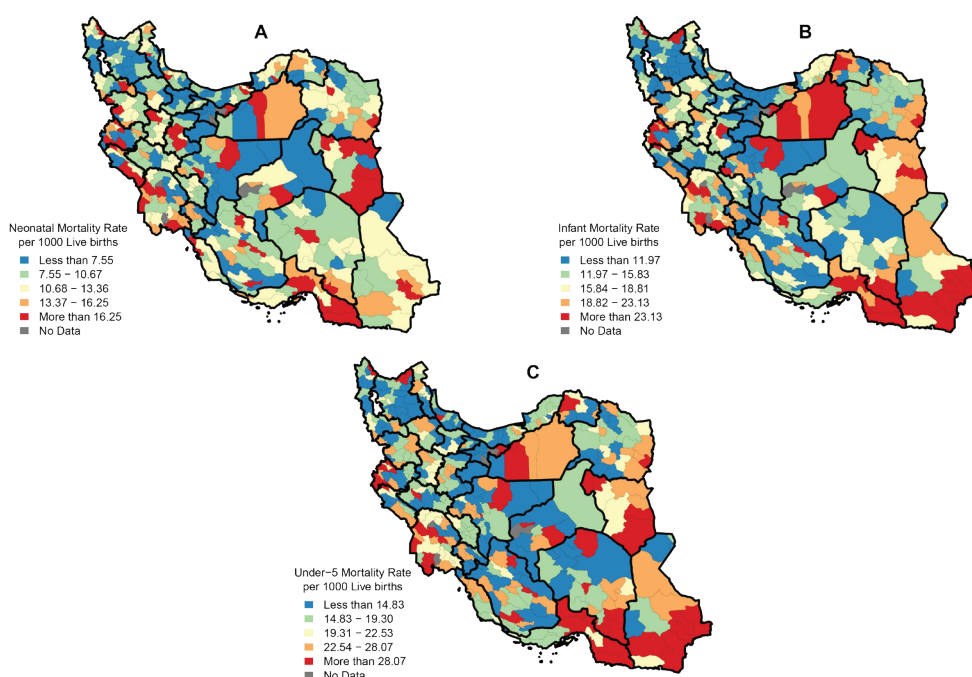
Figure 2 Health workforce density in rural areas of the Islamic Republic of Iran in 2011. Density of family physicians (A) and behvarzes (B) are shown in these maps using 5 colours, corresponding to quintiles of values

Density of Physicians per 1000 Populations
- Less than 0.21
- 0.21 – 0.26
- 0.27 – 0.30
- 0.31 – 0.38
- More than 0.38
- No Data

Density of Behvarz per 1000 Populations
- Less than 1.20
- 1.20 – 1.41
- 1.42 – 1.73
- 1.74 – 2.13
- More than 2.13
- No Data
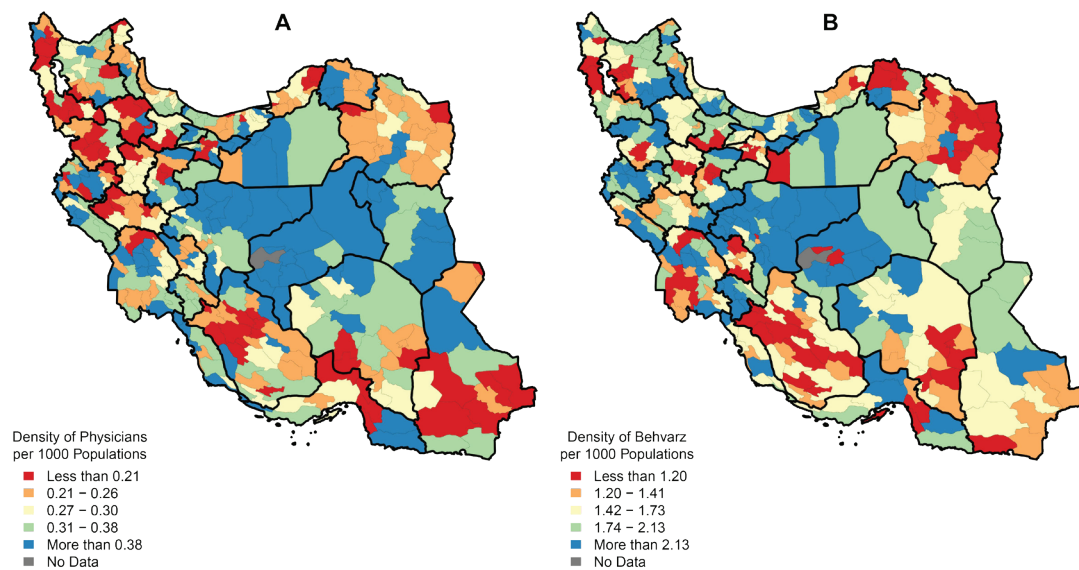
decreasing neonatal and infant mortality than improving the density of community health workers who provide primary health services (10). The differing results of Fernandes et al. on the effects of FP density on IMR (11) may have stemmed from different mortality profiles during this period in Mozambique (when diseases like malaria and those emerging against the background of human immunodeficiency virus infection caused most U5M) and the inability of FPs to manage these cases (12). Similar to infant mortality, there are controversial results about the effects of human resource density on U5MR. We observed a significant association between physician density and U5MR, which may have been due to diseases prevalent in children aged < 5 years and the health services provided by FPs. In the Islamic Republic of Iran, U5MR is mainly due to common diseases like diarrhoea, neonatal sepsis, measles, injuries, prematurity, and acute respiratory infection (12,13), which can be managed by FPs at rural health centres.

MMR showed a significant decline from 1990 to 2015 in the Islamic Republic of Iran, thereby achieving the fifth MDG to reduce MMR by 75% (12). As a result, MMR was estimated to be zero in 79% of the rural districts in our study. Based on our findings, FPs and behvarz densities significantly affected MMR, albeit in different directions. We showed that, although improving FP density was associated with decreased MMR, improvements in behvarz density was associated with MMR deterioration. Previous studies have shown that reducing MMR is more complex and more dependent on strengthening the health system infrastructure to provide inhabitants with health services and facilities such as blood transfusion, ultrasonography, and diagnostic curettage (14,15).

We investigated the association between economic status (through WI) and mortality rates. Improved financial status significantly contributed to decreases in

child mortality rates. Several studies have indicated the impact of economic status on child mortality rates (16, 17). Naderimagham et al. conducted a study to evaluate the effects of the FP programme and social factors on mortality rates in the Islamic Republic of Iran from 1995 to 2011 using time-series analysis, and found that residents' wealth status was significantly associated with reductions in child mortality rates (16). Moreover, a National Family Health Survey in India showed that ≥ 9 years of school education was associated with decreases in child mortality (17).

In addition to the factors in the present study, other variables have been shown to affect mortality rates, such as: breastfeeding promotion, delivery by trained individuals, kangaroo mother care, regular prenatal care, providing supplements for pregnant women, and implementing clinical practice guidelines at all levels of health care (13,16).

This is believed to be the first study to evaluate the effects of health workforce density on infant, child and maternal mortality rates at a national level in the Islamic Republic of Iran. However, our study had several limitations. First, we did not have data on causes of death among children. Hence, our findings cannot be confirmed by reviewing the question of whether the reported decreases in child mortality were due to causes that could be managed by FPs. Second, we had to exclude urban areas from the study, since the Family Physician and Social Protection Scheme was launched only in rural areas. As a result, our findings cannot be generalized to urban areas, where decreasing mortality measures perhaps require a more complex approach. Third, we did not have access to data on distribution of midwives. Earlier reports have shown that maternal mortality decreases with improvement in access to health professionals with midwifery skills (18,19). However, the unavailability of this

Table 2 Association of health workforce density and socioeconomic variables with maternal and child mortality rates

Variable	NMR per 1000 live births		IMR per 1000 live births		U5MR per 1000 live births		MMR per 100 000 live births	
	(No. of observations 2199)		(No. of observations 2199)		(No. of observations 2199)		(No. of observations 2169)	
	b	P	b	P	b	P	b	P
Physician density per 1000 individuals	-0.01482 (-0.02, -0.001)	0.0317	-0.00714 (-0.01, 0.002)	0.1271	-0.01052 (-0.01, -0.001)	0.0246	-0.6350 (-1.11, -0.15)	0.0092
Behvarz density per 1000 individuals	0.00005 (-0.01, 0.01)	0.9932	-0.00033 (-0.008, 0.007)	0.9364	-0.00201 (-0.009, 0.005)	0.6052	0.1313 (0.22, 0.24)	0.0203
Wealth index	-0.05012 (-0.07, -0.02)	<0.0001	-0.05029 (-0.06, -0.03)	<0.0001	-0.04813 (-0.06, -0.03)	<.0001	-0.1019 (-0.22, 0.02)	0.1041
Years of schooling	0.004190 (-0.02, 0.02)	0.7402	-0.00864 (-0.02, 0.01)	0.4243	-0.00603 (-0.02, 0.01)	0.5402	0.1636 (0.01, 0.3)	0.0284
Size of population	-0.09803 (-0.13, -0.06)	<0.0001	-0.1063 (-0.13, -0.07)	<.0001	-0.1175 (-0.14, -0.08)	<0.0001	-0.1811 (-0.35, -0.006)	0.0422
Mean age of population	-0.02812 (-0.03, -0.01)	<0.0001	-0.03739 (-0.04, -0.02)	<0.0001	-0.03714 (-0.04, -0.02)	<0.0001	-0.09913 (-0.15, -0.04)	0.0004
Urbanization rate	-0.03901 (-0.18, 0.10)	0.6036	-0.09470 (-0.22, 0.03)	0.1468	-0.1271 (-0.24, -0.009)	0.0345	0.2897 (-0.39, 0.97)	0.4091
Time effect	-0.04658 (-0.05, -0.03)	<0.0001	-0.03880 (-0.04, -0.03)	<0.0001	-0.03392 (-0.03, -0.02)	<0.0001	-0.01895 (-0.06, 0.02)	0.4368

IMR = number of infant deaths per 1000 live births; MMR = number of pregnancy-related maternal deaths per 100 000 live births; NMR = number of neonatal deaths per 1000 live births; U5MR = number of under-5-year deaths per 1000 live births.

information at a national level (with comparable quality) limited the opportunity to evaluate the hypothesis that increased midwife density can reduce maternal and child mortality.

The Iranian health system stands 104th among 188 worldwide in the path to sustainable development, based on a report published by the Global Burden of Diseases 2015 SDG collaborators (*2*). That study showed that the Iranian health system had reached targets related to lowering MMR, U5MR and NMR, although it still had to tackle burdens caused by road injuries, unsafe sources of water, partner violence, and unacceptable sanitation and hygiene among people. Their estimate showed that 85.9% of the Iranian population is covered by interventions related to UHC, and efforts are needed to improve public access to quality essential health services. Moreover, with the ageing of populations, countries like the Islamic Republic of Iran are expected to experience an increasing burden due to NCDs (*20,21*). The launching of the Family Physician and Social Protection Scheme has successfully contributed to reducing child and maternal mortality rates. However, with the transition in disease profiles, improvements in the Scheme are needed to provide patients with the care necessary for NCDs, and to decrease inequality in access to services.

Densité des ressources humaines pour la santé et son association avec la mortalité infanto-maternelle en République islamique d'Iran

Résumé

Contexte: Le système de médecins de famille et de protection sociale pour les habitants des zones rurales iraniennes a été lancé en juin 2005 pour améliorer la densité des médecins. À notre connaissance, l'impact de ce système sur les indicateurs de santé liés à la mortalité n'a pas fait l'objet d'une étude exhaustive.

Objectifs : Étudier les effets de la densité de personnels de santé sur les taux de mortalité maternelle, néonatale, infantile et des enfants de moins de cinq ans dans les zones rurales de la République islamique d'Iran entre 2005 et 2011.

Méthodes: Nous avons construit des modèles de régression de Poisson à effets mixtes, intégrant des mesures de la mortalité en tant que variables de réponse, des densités de médecins et de behvarz (agents de santé communautaires) en tant que variables indépendantes, en utilisant des données de l'outil iranien Vital Horoscope, de l'enquête annuelle sur les revenus et les dépenses des ménages et du logiciel DTARH. Nous avons également inclus la taille de la population, l'âge des habitants, le taux d'urbanisation, les années de scolarité et l'indice de richesse dans chaque district, ainsi que l'effet du temps, en tant que covariables.

Résultats : La densité de médecins était fortement associée aux taux de mortalité de l'enfant (baisse de 1,5 %, 1,1 % et 63,5 % de la mortalité maternelle, néonatale et des moins de cinq ans lors d'une augmentation d'une unité de la densité de médecins pour 1000 personnes). Dans le modèle établi pour le taux de mortalité infantile, la densité de médecins et les densités de behvarz n'étaient pas associées de manière significative à cette mesure.

Conclusions : L'amélioration de la répartition des médecins de famille est associée à une baisse de la mortalité infantile et maternelle. Les progrès en matière de densité de behvarz n'étaient pas associés à des baisses de ces taux, ce qui nécessite probablement une amélioration de l'accès à des services et installations de santé plus professionnels.

كثافة الموارد البشرية في مجال الصحة وما يرتبط بها من وفيات الأطفال والأمهات في جمهورية إيران الإسلامية

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الخلاصة

الخلفية: بدأ تنفيذ برنامج طبيب الأسرة والحماية الاجتماعية لسكان الريف الإيرانيين في يونيو/ حزيران 2005 لتحسين كثافة الأطباء. وعلى حد علمنا، لم تُجرَ دراسة شاملة لأثر البرنامج على المؤشرات الصحية المرتبطة بالوفيات.

الأهداف: هدفت هذه الدراسة إلى دراسة آثار كثافة القوى العاملة (في مجال الصحة) على معدلات وفيات الأمهات، وحديثي الولادة، والرضع، والأطفال دون سن الخامسة في المناطق الريفية في جمهورية إيران الإسلامية بين عامي 2005 و2011.

طرق البحث: وضعنا نماذج التحوُّف المتعددة الآثار لبراسون، مشتملة على مقاييس الوفيات كمتغيرات الاستجابة، وكثافة الأطباء والعاملين في مجال صحة المجتمع كمتغيرات مستقلة، باستخدام بيانات مستمدة من أداة المرصاد الحياتي الإيراني، والمسح السنوي لدخل وإنفاق الأسر المعيشية، وبرنامج DTARH. كما أدرجنا حجم السكان، وأعمارهم، ومعدل التحضر، وسنوات الدراسة، ومؤشر الثروة في كل منطقة، بالإضافة إلى تأثير الوقت، كمتغيرات مشتركة.

النتائج: ارتبطت كثافة الأطباء بشكل كبير بمعدلات وفيات الأطفال (انخفاض بنسب 1.5 ٪ و1.1 ٪ و63.5 ٪ في وفيات حديثي الولادة، والأطفال دون سن الخامسة، والأمهات، مع زيادة في كثافة الأطباء بمقدار وحدة واحدة لكل 1000 شخص). وفي النموذج الذي وُضع لمعدل وفيات الرضع، لم تكن كثافة الأطباء وكثافة العاملين في مجال صحة المجتمع مرتبطتين بشكل كبير بهذا المقياس.

الاستنتاجات: كان هناك ارتباط بين تحسين توزيع أطباء الأسرة وبين انخفاض معدلات وفيات الأطفال والأمهات. ولم ترتبط التحسينات في كثافة العاملين في مجال صحة المجتمع بتراجع تلك المعدلات، الأمر الذي ربما يدعو إلى تحسين فرص الحصول على خدمات ومرافق صحية أكثر مهنية.

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Diagnostic and treatment delays in breast cancer in association with multiple factors in Pakistan

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Abstract

Background: Breast cancer has the highest incidence rate among all types of cancer worldwide. There is strong evidence that delay in presentation to an oncologist may lead to a decrease in survival.

Aims: This study explores factors causing diagnostic and treatment delays among the breast cancer patients enrolled in Jinnah Hospital, Lahore, from 2016 to 2018.

Methods: Data from 372 patients were collected, including tumour characteristics, first symptoms, knowledge and experience of breast cancer, first visit to a doctor, etc. We calculated the patient, physician, treatment, system and total delay intervals.

Results: Breast cancer cases showed longer mean patient delay in older women (> 50 years) in comparison with younger women. Women with painless lump as the initial symptom showed the longest delay with median total delay 280 days (25th and 75th percentiles 140 and 410 days respectively). Initial symptoms were correlated with total delay ($P = 0.036$). Educated women showed shorter delay in treatment compared with illiterate women ($P = 0.068$). Rural residence showed significant delay ($P = 0.007$). Lump size showed correlation with delay ($P = 0.039$). Patients with low household income (< Rs 10 000) had greater delay in diagnosis ($P = 0.027$) and actively employed women showed shorter delay ($P < 0.0001$). Unmarried women were diagnosed earlier than married ($P < 0.001$).

Conclusions: Women showed delay in presentation due to lack of resources and lack of awareness about the disease. They presented late due to fear of surgery and chemotherapy. Using traditional treatment methods leads to diagnosis of the disease at more advanced stages.

Keywords: breast cancer, time delays, socioeconomic factors, Pakistan

Introduction

Breast cancer has the highest incidence rate among all types of cancer worldwide (1): the age standardized rate per 100 000 for breast cancer diagnosis was 46.3 in 2018. The rate for the developed countries was reported to be 75.2 in comparison to 32.8 for the developing countries. The International Agency for Research on Cancer reported breast cancer as the second most common cancer, with 11.6% of the total 18.1 million cancer cases in 2018 (2). Cancer is the leading barrier to increased life expectancy in the 21st century. There is strong evidence that delay in presentation to an oncologist may lead to a decrease in survival (3). These results highlight the need for research regarding awareness of the early warning signs of breast cancer in Pakistani women (4). Most breast cancers begin in the breast lobules or in the ducts of the breast, for which the most common sign is a painless lump (5). Breast cancer mortality can be reduced with early detection and improvements in the health care system (6).

The worldwide survival rates for breast cancer exhibit large variations across the globe from the developed to the developing countries. Indicators of 5-year survival rates from the developed part of the world include: America (83.2%), Australia (80.7%), Japan (81.6%) and Sweden (80.0%). In the developing countries, Algeria (38.8%) Brazil (58%), Gambia (12%) and India (52.1%) have noticeably low survival rates among diagnosed cases (7).

Delay is found between the the appearance of the first symptoms and time of diagnosis and initiation of treatment in women who have breast cancer. Early diagnosis and treatment within 30 days is beneficial for patients and helps to increase survival rates (8). Delay between the appearance of symptoms and presentation to an oncologist depends on the patient's behaviour and beliefs (9).

Long waiting times can lead to advancement and complications in the disease process. Li et al. studied Chinese breast cancer patients and associated the longer detection to treatment time interval with rural residence, low education level and older age (10). Nonavailability of early detection programmes increases delay in the detection of breast cancer at a curable stage. Pakistani oncologists follow the TNM staging developed by American Joint Committee on Cancer. The stage at

diagnosis indicates the expected prognosis. In a recent study in Pakistan, Gulzar et al. reported that 88.8% of breast cancer patients were diagnosed late and 59.0% at an advanced stage (11). The study associates 81.1% of delays to ignorance, painless lump and scarce financial resources. Lopes et al. in Brazil observed 102 days delay in diagnosis and 57 days delay in treatment of breast cancer (12). The study described low education as a main cause for late diagnosis. A study from Mali observed patient interval to report breast cancer of 4.8 months, diagnostic interval 0.9 months and treatment interval 1.3 months (13). They concluded that working women living in capital had shorter delay time in comparison to housewives and those living in rural areas. Maghous et al. reported delay in 70.1% patients due to personal reasons and 13.9% due to medical facility reason for Moroccan women (14). They recommended the training of medical practitioners and improving the awareness of general public about breast cancer to early detection of cancer. Jaiswal et al. found presentation to diagnostic time interval of 23 days and other treatment times within the published limits except time for radiotherapy at Denver hospital Colorado (15). They associated longer than median time intervals with ethnicity, language, stage, method of presentation and surgical treatment.

There are multiple factors to be focused on including growth rate of tumour, misunderstandings about cancer, age at detection, awareness in women and heath policy while addressing the core issue of early cancer detection. Breast cancer treatment has several sequential processes: surgery, chemotherapy and radiation therapy. Traditionally in Pakistan, mammography and biopsy are the choices for detection. Long waiting times in the diagnosis process can be reduced to increase patient comfort. Biopsy, consultation, surgical and patient-perceived wait times are some factors which increase the system delay in breast cancer treatment (16). Women with family history of breast cancer had greater awareness of breast cancer and experienced greater fear about the symptoms in comparison with women without any family history (17).

The main objectives of this study were to determine the number of women with breast cancer who experienced delay in diagnosis and to determine causes of late presentation and the factors that contribute to system delay and overall wait time at the beginning of treatment among breast cancer patients enrolled at Jinnah Hospital, Lahore during 2016–2018 using quantitative strategies.

Methods

Ethics

This study was carried out at Jinnah Hospital, Lahore, and was approved by the hospital ethical committee. The questionnaire and consent forms were designed in the local language, Urdu, for better communication. The consent form was prepared according to the guidelines of the ethical committee. The guidelines of the Helsinki Declaration were followed in conducting this research work.

The consent forms were signed by the participants to accept the use of their medical records and interview data.

Participants

Data were collected during the 2 years January 2016–January 2018. Over this period, a total of 428 breast cancer patients were enrolled in Jinnah Hospital, Lahore. Those women who met the following criteria were included in the research:

- diagnosed case of biopsy-proven breast cancer
- understand Urdu
- visited Allam Iqbal Medical College/Jinnah Hospital for treatment
- complete records were available for them
- agreed to provide consent for participation in research.

Total population sampling allowed deep insight to study the factors involved in delay for the treatment and diagnosis of cancer. This is a method through which we included all the patients fulfilling our criteria and excluded those who did not meet the criteria. Total population sampling decreases the guesswork in research and provides a complete picture of the factors causing delays. From the 428 breast cancer patients attending during the study period, 372 fulfilled our inclusion criteria and the remaining 56 patients were excluded: 7 with benign lumps, 11 for noncooperative behaviour, 5 who had other cancers, 7 who were unable to answer the questions (for any reason), 6 who were mentally not able, 8 who did not agree to sign the consent form and 12 for whom information was missing on initial breast symptom and dates. The majority of related work utilized the whole population as the sample (12–14,18).

Women with self-detected or imaging-detected (mammogram or MRI) symptoms were included. All the patients were informed about the purpose of the study. We identified patients and took their medical history from the hospital medical records along with the date of admission and the date of surgery. When the patients were unable to provide the date of initiation of their symptoms, they were asked to provide the month and then the date was estimated as 15th of that month. The date of first consultation with a doctor was obtained from the receipt provided by the doctor to the patient. Each interview took 15–25 minutes but some took longer due to illiteracy and a socially complex environment. The interviews were conducted independently by trained staff. Information was collected about patient's tumour characteristics, first symptoms, experiences with a breast problem, their knowledge about breast cancer, first visit to a doctor, number of health care facility visits before the diagnosis, sociodemographic information, age, marital status, residential status, education, profession, monthly household income, comorbidities, tumour stage, history of breast disease and family history of breast cancer. We used the strategy to define the stage of the disease, I, II, III and IV. The patients were divided into 5 groups according to age (21–30, 31–40, years, etc.). Data on education level,

residential status and monthly household income were also collected.

Data

We categorized the delay into 4 types: patient delay, physician delay, system delay and treatment delay. Patient delay was defined as the time from the first appearance of symptoms to the first visit to a hospital. Physician delay was defined as the time from first consultation to diagnosis of the disease. Referral delay (period between first consultations with the health care provider to first referral to hospital) was considered a part of physician delay. The time from biopsy to surgery, from surgery to onset of chemotherapy or from biopsy to onset of chemotherapy and time from surgery to onset of radiotherapy were defined as system delay. Treatment delay comprised the time between the diagnosis of cancer to the start of treatment.

Questions were asked of the patients to determine the causes of late presentation such as: Were you using alternative/traditional medicine? Did you not have enough money to pay the hospital bills? Did you present late due to the lump being small and painless? We calculated the patient delay, physician delay, treatment delay, system delay and total delay intervals and determined the median and 25th and 75th percentiles among different groups of patients for the comparison of multiple factors. The percentile methods help in the comparison of health indicators in the environment.

Statistics

We used *SPSS* software for statistical analysis. The Pearson correlation and Chi-squared were used to determine the relationships between variables. Significance was set as $P < 0.05$.

Results

Delay

Characteristics of the participants are illustrated in Table 1. A total of 372 women were interviewed; all were residents of Punjab province; 81.7 were married. Age at the time of diagnosis was 20–68 years, 33.0% were in the range 41–50 years. Half the women reported painless lump as the initial symptom.

Table 2 shows patient delay, referral delay and oncologist delay. Different age groups show different patient delay, the shortest patient delay, median 40 days, was found in young women (11–20 years) and the longest patient delay, median 152 days was found in the age group from 51–60 years. Women with painless lump as their initial symptom showed the longest delay with median total delay 280 days. Lump size is also a significant factor in association with delay, patients with lump size 1–5 mm presented with median 244 days total delay, Q_{25} (136 days) and Q_{75} (382 days), longer than patients with lump size > 5mm.

Table 1 Characteristics of breast cancer patients (*n* = 372), Lahore, 2016–2018

Factors	No. (%)
Age at diagnosis (years)	
11–20	18 (4.8)
21–30	56 (15.0)
31–40	84 (22.5)
41–50	123 (33.0)
51–60	62 (16.6)
61–70	29 (7.8)
Initial symptoms	
Painless lump/tumour	189 (50.0)
Change in breast	48 (13.0)
Discharge/bleeding	33 (8.9)
Lump under arm	47 (12.6)
Dimpling	23 (6.1)
Rash	32 (8.6)
Cancer detection	
Self-detected	143 (38.4)
Exam detected	91 (24.5)
Imaging detected (mammogram or magnetic resonance imaging)	138 (37.1)
Education	
Illiterate	162 (43.5)
Primary	43 (11.5)
Middle	22 (6.0)
Metric	72 (19.3)
Intermediate	34 (9.1)
Bachelor	23 (6.1)
Masters	16 (4.3)
Family history of breast cancer	
Yes	64 (17.2)
No	308 (82.8)
Active employment	
Yes	87 (23.3)
No	285 (76.7)
Monthly household income (Pakistan rupees)ᵃ	
< 10000	84 (22.5)
10000–20000	62 (16.6)
21000–30000	65 (17.4)
31000–40000	78 (21.0)
41000–50000	53 (14.2)
>50000	30 (8.0)
Marital status	
Married	304 (81.7)
Unmarried	68 (18.3)
Lump size (mm)	
1–5	164 (44.0)
6–10	83 (22.3)
11–20	81 (21.7)
21–30	26 (6.9)
31–50	18 (4.8)

Table 1 **Characteristics of breast cancer patients (*n* = 372), Lahore, 2016–2018 (*concluded*)**

Factors	No. (%)
Tumour stage on diagnosis	
Stage I	75 (20.1)
Stage II	128 (34.4)
Stage III	102 (27.4)
Stage IV	67 (18.0)
First start self-treatment	
Yes	132 (35.5)
No	240 (64.5)
Place of residence	
Village	103 (27.7)
Town	93 (25.0)
Tehsil	57 (15.3)
District	68 (18.2)
Division	51 (13.7)
Menopausal status	
Premenopausal	128 (34.4)
Postmenopausal	244 (65.6)
Comorbid conditions	
None	257 (69.0)
≥ 1	115 (31.0)
First consultation	
Health worker or nurse	142 (38.1)
Doctor clinic	124 (33.3)
Private hospital	34 (9.1)
Government hospital	72 (19.2)

ª1 US$ = 139.9 Rs.

A difference was found between married and unmarried women in regard to in total delay. The unmarried women showed short patient delay compared with married women, however physician and system delay were almost the same. Educated women showed a shorter delay in treatment compared with illiterate women. Working women faced shorter physician and system delay. Women who were dependent on their family showed longer patient delay compared with those who were independent.

We combined the referral and oncologist delay into a single term physician delay (Table 3). System delay and treatment delay are also shown in Table 3. There was a significant difference in total delay time among the women according to their area of residence. Patients from villages and small towns showed longer patient delay and faced longer physician and system delay compared with those who lived in cities (Tables 2,3). Women from villages also showed total delay higher than in cities with median 276 days; 25th and 75th percentiles were 163 and 370 days respectively, (Table 4). Household income was an important factor.

Patients with low household income (< 10 000 rupees) showed longer delays in diagnosis and treatment (Table 3); we found that most of these patients had started

treatment with nonmedical traditional methods. Patients with household income > 50 000 rupees faced shorter physician and system delay and had a shorter total delay in treatment (Table 4).

Factors associated with delay

The association between multiple factors and delays was calculated using the Pearson correlation (*r*). For initial symptoms, $r = 0.847$ ($P = 0.036$), i.e. there is a strong association between delay and symptoms initially noticed (Table 5). Residence was also associated with delays: $r = 0.965$ ($P = 0.007$). There was a correlation between monthly income and delay ($r = 0.86$, $P = 0.027$). Delay has a correlation $r = 0.896$ with lump size ($P = 0.039$). Education was also correlated with delay ($r = 0.7195$), but this was not statistically significant ($P = 0.068$). Age was not strongly associated with delay ($P = 0.322$).

Chi-squared test results associating total delay with active employment, menopause status and marital status are shown in Table 6. For marital status chi-squared was 49.917, and this was statistically significant ($P < 0.001$). Actively employed women had significantly shorter delay times: chi-squared was 21.588 ($P < 0.001$). For menopause status, chi-squared was 2.731, but this was not statistically significant ($P = 0.098$).

Discussion

This research work has revealed that women with breast cancer in Pakistan presented with significant delays, which leads to a high mortality rate. Although it is important to research delays in breast cancer patients, limited related studies are conducted in Pakistan. Our research reported 65% patients had a delay of more than median 90 days in Lahore in comparison with a study conducted by Habibullah et al. in Karachi with 50% women (*19*). Gulzar et al. reported 92.8% of patients with initial symptom of painless lump in comparison to 50% in our study (*11*); painless lump was an important factor for delay in both studies. The common causes reported in patients in previous studies were lack of awareness and lack of knowledge related to breast cancer. This leads to diagnosis at later stages and consequently to lower survival rates. Grossie et al. in a study in Mali reported median time to visit first medical advice was 144 days (*13*). Kitano et al. researched treatment delay among 18% of breast cancer patients in Tokyo (*20*).

Our study has highlighted multiple factors responsible for the delays in breast cancer patients at Lahore, Pakistan. Multiple causes are recognized in the process of diagnosis and treatment of breast cancer. The women considered their breast changes temporary and harmless, in addition painless lump made them feel relaxed. The general public remains ignorant about these important signs and symptoms of breast cancer, which can lead to death due to negligence. The low literacy among our sample lead to ignorance and caused the other factors of delay to emerge. The cultural beliefs made it difficult for the population to realize the importance of women's education. This study emphasizes the fact that

Table 2 Patient, physician and oncologist delay in breast cancer patients, Lahore, 2016–2018

Characteristic	No.	Patient delay (days)			Referral delay (days)			Oncologist delay (days)		
		Median	25th	75th	Median	25th	75th	Median	25th	75th
Overall	372	255	120	345	16	7	24	7	4	14
Age (years)										
11–20	18	40	24	70	10	6	18	5	3	11
21–30	56	60	30	165	12	7	21	4	2	9
31–40	84	126	45	216	16	9	30	6	3	12
41–50	123	115	64	184	15	9	32	5	2	10
51–60	62	152	90	224	12	5	24	8	5	14
61–70	29	146	84	173	20	11	36	7	3	15
Initial symptoms										
Painless lump/tumour	189	180	105	325	24	8	38	6	2	12
Change in breast	48	124	63	186	16	5	24	7	4	16
Discharge/bleeding	33	135	74	215	14	8	25	8	3	16
Lump under arm	47	90	45	120	15	6	28	6	2	10
Dimpling	23	135	85	180	9	4	21	5	2	9
Rash	32	75	30	105	12	7	25	8	3	14
Menopausal status										
Premenopausal	158	135	60	205	18	7	28	9	4	16
Postmenopausal	214	165	90	255	16	5	24	12	5	20
Marital status										
Married	304	225	145	300	18	12	30	8	3	15
Unmarried	68	180	105	230	15	8	21	7	2	11
Education										
Illiterate	162	240	135	320	14	5	22	9	4	16
Primary	43	225	120	270	15	6	28	7	3	12
Middle	22	165	75	210	12	5	20	8	5	14
Metric	72	180	90	240	16	9	30	7	4	15
Intermediate	34	115	60	195	18	10	28	6	2	12
Bachelor	23	60	25	135	14	5	24	8	3	16
Masters	16	45	30	90	11	6	20	5	2	10
Household income (Rs/month) [a]										
< 10000	84	270	135	330	22	12	38	8	4	16
10000–20000	62	240	120	315	20	9	36	8	3	14
21000–30000	65	195	105	280	12	7	24	6	2	10
31000–40000	78	165	90	225	9	4	20	9	4	14
41000–50000	53	120	90	180	11	5	25	7	4	12
> 50000	30	75	30	105	8	3	15	6	3	10
Area of residence										
Village	103	285	150	360	25	10	40	10	4	18
Town	93	225	120	320	18	7	30	10	6	15
Tehsil	57	180	115	280	15	6	24	8	5	16
District	68	150	90	210	10	4	18	6	3	10
Division	51	105	75	165	5	2	12	6	4	12
Active employment										
Yes	87	120	90	195	12	7	21	8	5	14
No	285	240	150	345	18	11	32	12	5	18
Lump size (mm)										
1–5	164	255	120	330	12	5	32	9	4	12
6–10	83	210	105	300	9	4	20	8	3	16
11–20	81	120	75	205	11	6	21	6	2	11
21–30	26	105	60	135	14	6	30	5	2	7
31–50	18	45	15	60	18	7	32	3	2	6

[a]1 US$ = 139.9 Rs.

Table 3 Physician, treatment and system delay in breast cancer patients, Lahore, 2016–2018

Characteristic	No.	Physician delay (days)			Treatment delay (days)			System delay (days)		
		Median	25th	75th	Median	25th	75th	Median	25th	75th
Overall	372	24	15	42	26	12	44	30	14	58
Age (years)										
11–20	18	15	9	28	14	5	21	20	8	32
21–30	56	16	8	30	16	6	28	28	10	40
31–40	84	24	12	40	24	12	40	30	12	54
41–50	123	20	11	42	20	7	32	26	11	58
51–60	62	20	10	34	26	10	30	24	9	38
61–70	29	18	13	28	12	4	21	22	6	30
Initial symptoms										
Painless lump/tumour	189	30	10	50	30	13	40	40	12	64
Change in breast	48	23	8	40	22	7	34	28	8	46
Discharge/ bleeding	33	22	11	41	24	11	38	26	7	42
Lump under arm	47	21	8	38	28	12	44	30	10	40
Dimpling	23	14	6	30	20	7	32	28	8	40
Rash	32	20	10	39	26	11	42	22	7	38
Menopausal status										
Premenopausal	158	27	11	44	30	12	45	30	14	52
Postmenopausal	214	28	10	40	32	15	48	26	16	60
Marital status										
Married	304	26	15	45	26	12	46	26	12	45
Unmarried	68	22	10	38	20	8	32	25	11	38
Education										
Illiterate	162	23	9	36	29	9	41	36	11	56
Primary	43	22	13	40	24	12	40	32	12	54
Middle	22	20	10	34	23	9	32	29	10	50
Metric	72	24	13	44	25	14	38	34	12	58
Intermediate	34	24	12	40	20	8	30	26	13	38
Bachelor	23	18	10	36	16	6	28	20	8	32
Master	16	16	8	30	12	4	21	16	7	28
Household income (Rs/month) [a]										
< 10000	84	28	16	46	30	12	46	42	12	64
10000–20000	62	30	12	42	26	12	38	38	10	60
21000–30000	65	18	9	34	22	8	36	34	14	52
31000–40000	78	18	8	36	24	10	32	30	12	46
41000–50000	53	16	9	35	18	7	28	26	10	40
> 50000	30	14	6	25	16	5	22	18	8	26
Area of residence										
Village	103	35	14	58	26	12	48	42	14	62
Town	93	28	12	45	28	15	46	38	12	56
Tehsil	57	16	7	28	26	11	40	32	11	52
District	68	12	6	26	22	9	36	28	8	40
Division	51	10	5	24	16	6	22	22	7	32
Active employment										
Yes	87	20	11	35	18	12	30	24	9	38
No	285	26	12	44	24	16	44	36	15	60
Lump size (mm)										
1–5	164	21	8	44	28	12	42	30	12	62
6–10	83	17	6	36	22	10	38	32	15	54
11–20	81	16	8	32	20	8	32	24	10	42
21–30	26	12	5	28	18	8	26	18	10	36
31–50	18	8	3	18	12	5	20	10	6	28

[a]1 US$ = 139.9 Rs.

Table 4 Total delay in breast cancer patients, Lahore, 2016–2018

Characteristic	No.	Total delay (days)		
		Median	25th	75th
Total	372	310	160	430
Age (years)				
11–20	18	85	40	150
21–30	56	120	55	230
31–40	84	180	80	310
41–50	123	185	90	270
51–60	62	210	114	314
61–70	29	190	106	270
Initial symptoms				
Painless lump/tumour	189	280	140	410
Change in breast	48	200	80	305
Discharge/bleeding	33	205	75	285
Lump under arm	47	160	70	240
Dimpling	23	132	92	206
Rash	32	120	63	192
Menopausal status				
Premenopausal	158	264	150	345
Postmenopausal	214	286	174	330
Marital status				
Married	304	315	260	416
Unmarried	68	214	95	324
Education				
Illiterate	162	282	163	368
Primary	43	270	106	320
Middle	22	190	84	276
Metric	72	228	127	308
Intermediate	34	130	73	285
Bachelor	23	116	68	194
Masters	16	96	59	137
Household income (Rs/month) [a]				
< 10000	84	330	264	412
10000–20000	62	283	196	365
21000–30000	65	245	143	336
31000–40000	78	228	106	312
41000–50000	53	185	94	278
> 50000	30	124	65	186
Area of residence				
Village	103	276	163	370
Town	93	243	146	335
Tehsil	57	184	78	246
District	68	172	65	208
Division	51	152	60	186
Active employment				
Yes	87	178	87	214
No	285	285	194	358
Lump size (mm)				
1–5	164	244	136	332
6–10	83	218	145	280
11–20	81	160	84	238
21–30	26	126	58	173
31–50	18	64	42	86

[a]1 US$ = 139.9 Rs.

Table 5 Correlation between selected factors and total delay among breast cancer patients (*n* = 372), Lahore, 2016–2018

Factor	Correlation (*r*)	*P*-value
Area of residence	0.965	0.007
Lump size	0.897	0.039
Income per month	0.8617	0.027
Initial symptoms	0.847	0.036
Education	0.7197	0.068
Age	0.491	0.322

education can significantly reduce delays. Less-educated patients cannot effectively decide about their health issues in a proper time period. Jassem et al. studied delays in 12 countries and noted that higher education was associated with less delay (*21*). The perception among a population that cancer is incurable and treatment is not available makes the life of breast cancer victims shorter. Both ignorance and illiteracy lead to the presentation of disease at later stages. It is important in developing countries like Pakistan to identify high risk patients in a timely manner and to treat new cases with curative intent.

A cohort study from the United States of America reported financial problems caused self-delay in 17% of breast cancer patients below 40 years of age (*22*). Our study shows low income per month is highly correlated with delay in treatment. Low financial status prioritizes health at a low level in comparison with other essentials of everyday life. We found that employed women underwent less delay in comparison with unemployed women. Other research has found employment to be a barrier in the process of diagnosis and treatment of breast cancer (*23*). Employment is the characteristic of educated and self-dependent women: employed women take their own decisions and face fewer social and cultural barriers. Homemakers are financially and culturally dependent on husbands or family heads and face more delays. Dianatinasab et al. also found that, among Iranian women, employed breast cancer patients faced fewer delays (*24*).

Our research points out that unmarried women with breast cancer are detected early in comparison to married women. Married women may fear of divorce and remarriage of the husband as in our society cancer is also suspected as being a contiguous disease. So a married woman may decide not to pursue a diagnosis even if she suspects initial symptoms of breast cancer.

A majority of the Pakistani population resides in rural areas. Our study demonstrated that rural breast cancer patients have multiple delays in comparison with those from urban areas. Rural residents have no direct approach to cancer centres and also their awareness level is not good. They also have to travel long distances to approach medical facilities. Rural culture and social values also prohibit women from discussing their disease with others. Other studies from developing countries have reported women living in rural areas encountering long delays (*13,14,18*). The health care system in Pakistan is not strong enough to cater to patients at grass roots level. Cancer days are observed to increase awareness among the public but their impact is limited.

There is a requirement for continuous awareness programmes to make the population aware about their health concerns. Early detection can reduce the mortality rate and the burden on health facilities: mammography plays a vital role in screening programmes (*25*). Developing countries have limited resources and the population mostly depends on the government medical care system. In most of the developing countries infrastructure for screening and early detection of breast cancer do not exist even though early detection can decrease the burden of incurable breast cancer patients on the health care facilities. Due to the lack of a social security system, people are reluctant to accept the cost of health facilities in Pakistan; there is no breast cancer screening programme and the cost of mammography is high. An awareness of breast self-examination and making people realize that cancer is curable at the early stages may reduce delays and reduce the mortality rate.

Conclusion

The women included in this study showed delay in presentation due to lack of resources and lack of awareness about the disease. There is a strong need to create awareness about the disease among women from rural areas and there is need to develop cancer care centres in primary health care departments so that diagnosis of the disease can be made possible at early stage.

Table 6 Association between selected factors and total delay among breast cancer patients, Lahore, 2016–2018

Factor	Chi square	*P*-value
Menopause status	2.731	0.098
Active employment	21.588	< 0.001
Marital status	48.917	< 0.001

Retards de diagnostic et de traitement du cancer du sein liés à de multiples facteurs au Pakistan

Résumé

Contexte : Le cancer du sein a le taux d'incidence le plus élevé parmi tous les types de cancer dans le monde. Il existe des preuves solides montrant que le retard de consultation d'un oncologue peut entraîner une diminution de la survie.

Objectifs : La présente étude explore les facteurs causant des retards de diagnostic et de traitement chez les patientes atteintes de cancer du sein admises à l'hôpital Jinnah de Lahore entre 2016 et 2018.

Méthodes : Les données de 372 patientes ont été recueillies ; elles comprenaient notamment les caractéristiques de la tumeur, les premiers symptômes, les connaissances et l'expérience en matière du cancer du sein, la première consultation chez un médecin, etc. Nous avons calculé les intervalles en matière de retard pour le patient, le médecin, le système et les intervalles totaux.

Résultats : Les cas de cancer du sein montraient un retard moyen plus important chez les femmes âgées (plus de 50 ans) que chez les femmes plus jeunes. Les femmes ayant un nodule indolore comme symptôme initial affichaient le retard le plus long avec un total médian de 280 jours (25e et 75e percentiles, 140 et 410 jours respectivement). Les symptômes initiaux étaient corrélés au retard total (*p* = 0,036). Les femmes éduquées montraient un retard de traitement plus court que les femmes analphabètes (*p* = 0,068). Le retard était significatif pour les femmes vivant en milieu rural (*p* = 0,007). La taille du nodule révélait une corrélation avec le retard (*p* = 0,039). Les patients dont le revenu du ménage est faible (< 10 000 roupies) présentaient un retard de diagnostic plus important (*p* = 0,027) et les femmes actives affichaient un retard plus court (*p* < 0,0001). Les femmes célibataires étaient diagnostiquées plus tôt que les femmes mariées (*p* < 0,001).

Conclusions : Les femmes tardaient à consulter un médecin en raison du manque de ressources et de sensibilisation à la maladie, de la peur de la chirurgie et de la chimiothérapie. L'utilisation de méthodes de traitement traditionnelles permet de diagnostiquer la maladie à des stades plus avancés.

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تأخر تشخيص سرطان الثدي وعلاجه واقتران ذلك بعوامل متعددة في باكستان

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الخلاصة

الخلفية: يُظْهِر سرطان الثدي أعلى معدل للإصابة من بين جميع أنواع السرطان في جميع أنحاء العالم. وهناك دلائل قوية على أن تأخُّر العرض على طبيب الأورام قد يؤدي إلى تدني فرص البقاء على قيد الحياة.

الأهداف: هدفت هذه الدراسة إلى اكتشاف العوامل التي تسبب تأخُّر التشخيص والعلاج في صفوف مريضات سرطان الثدي المقيدات في مستشفى جنة في لاهور في الفترة من 2016 وحتى 2018.

طرق البحث: جُمِعت بيانات من 372 مريضة، شملت خصائص الورم، والأعراض الأولية، والمعرفة بسرطان الثدي والخبرة في التعامل معه، وأول زيارة للطبيب، وغير ذلك. كما قمنا بحساب إجمالي فترات التأخر بالنسبة للمريض، والطبيب، والعلاج، والنظام بأكمله.

النتائج: أظهرت حالات سرطان الثدي ارتفاعاً في متوسط التأخير في صفوف المريضات الأكبر سناً (أكثر من 50 عاماً) مقارنة بالنساء الأصغر سناً. أما النساء اللاتي يعانين من كُتَل غير مؤلمة تُعتبر العَرَض الأول للمرض، فقد أظهرن أطول مدة تأخير مع متوسط تأخير إجمالي بلغ 280 يوماً (25 و75 شريحة مئوية و140 و410 يوماً على التوالي). وكان هناك ارتباط بين الأعراض الأولية وإجمالي فترة التأخير (P = 0.036). وأظهرت النساء المتعلمات تأخراً أقل في الحصول على العلاج مقارنة بالنساء الأميات (P = 0.068). وأظهرت المقيمات في الريف تأخراً كبيراً (P = 0.007). وأظهر حجم كتلة الورم ارتباطاً بالتأخير (P = 0.039). أما المريضات من ذوات الدخل الأسري المنخفض (أقل من 10000 روبية) فكان التأخير لديهن أكبر بالنسبة للتشخيص (P = 0.027) كما أظهرت النساء اللاتي يعملن بنشاط تأخيراً أقل (P < 0.0001). وشُخِّصت النساء غير المتزوجات في وقت أبكر من المتزوجات (P < 0.0001).

الاستنتاجات: أظهرت النساء تأخراً في العرض على الأطباء بسبب نقص الموارد وقلة الوعي بالمرض. وكان السبب في تأخرهن عن زيارة الطبيب هو الخوف من الجراحة والمعالجة الكيميائية. ويؤدي استخدام طرق العلاج التقليدية إلى تشخيص المرض في مراحل أكثر تقدماً.

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Trends in premature mortality in the Islamic Republic of Iran: probability of dying between ages 30 and 70 years

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Abstract

Background: The burden of noncommunicable diseases (NCDs) is a major challenge facing the whole world. Around 15 million premature deaths due to NCDs occur in people aged 30–70 years annually.

Aims: Mortality data based on death registration systems and population data were used to estimate proposed mortality statistics in the Islamic Republic of Iran.

Methods: Various criteria and methods were used to assess the quality of mortality data. The probability of dying among those aged 30–70 years for all causes and for NCDs was calculated using the life table method.

Results: The mortality rate in the population aged 30–69 years was 343.12 (per 100 000 persons) in 2006 and decreased to 240.62 in 2016 in both sexes. The probability of dying due to NCDs was 21.36% in 2006 and declined to 14.95% in 2016 for both sexes.

Conclusions: The number of premature deaths due to NCDs have decreased over the last decade. We predict that this reduction will continue and the country will meet the targets of the WHO NCD action plan by 2025 and also the targets of the Sustainable Development Goals for reducing premature deaths by 2030. However, the morbidity and burden of NCDs are still public health concerns in the country. Due to advancements in health care technologies and also the aging population, these concerns will impose greater costs on the health system. Hence, prevention programmes for NCDs should be an urgent priority for Iranian health policy.

Keywords: probability of dying, mortality rate, vital statistics, noncommunicable diseases, Iran

Introduction

The burden of noncommunicable diseases (NCDs), including cardiovascular diseases (CVDs), cancers, diabetes and chronic respiratory diseases, is among the major challenges worldwide in the current century: NCDs accounted for 72.3% of deaths in 2016 (*1*). Around 15 million premature deaths due to NCDs in people aged 30–69 years occur every year worldwide (*2*). Remarkably, low-income and lower-middle-income countries with half of the premature NCDs deaths have more problems than developed countries. Additionally, within countries, poor people suffer more from NCDs.

This multidimensional health problem is determined by various factors such as low socioeconomic situation, international marketing, trade in health-harming products, urbanization, demographic transition, and changes in lifestyle (*3*).

The Islamic Republic of Iran, a middle-income country, has faced considerable social, economic and demographical transitions over the past 4 decades. Although, general health outcomes have improved considerably, there was a significant and uniform shift from communicable, maternal, neonatal, and nutritional (CMMN) conditions to NCDs from 1990 to 2010 (*4,5*).

It seems that the country will face a 35% increase in burden of disease and injury over the next 2 decades, mainly due to aging or demographic and epidemiological changes. In this regard, communicable diseases (except HIV/AIDS) will have less contribution and on the other hand NCDs will play a significant role (*6,7*).

Shahraz et al. estimated the population health and burden of disease profile for the Islamic Republic of Iran among 20 countries in the region, from Afghanistan to Lebanon and Qatar, between 1990 and 2010 (*4*). They used classic global burden of disease metrics, and indicated the ranking of the countries. Overall health outcomes, life expectancy at birth and age-standardized death rate improved considerably in the Islamic Republic of Iran from 1990 to 2010. Additionally, the results showed that the burden of communicable, maternal, neonatal, and nutritional conditions sharply declined compared with that of NCDs. The Islamic Republic of Iran ranked 13th in health-adjusted life expectancy and 12th in age-standardized death rate.

In 2011, international agencies such as the UN and WHO targeted reducing premature deaths due to NCDs, and announced the list of all countries which were planning to control NCDs. According to this agenda,

the target indicator is to decrease by 25% the probability of dying due to 4 NCDs (CVD, diabetes, cancer, and chronic respiratory disease) in individuals aged 30–70 years by 2025 (8,9). In addition, in 2015 the UN General Assembly formally released the 2030 programme for the Sustainable Development Goals (SDGs), which incorporated an arrangement of 17 strong new global goals and 169 particular targets. The plan additionally incorporates reducing by 33% premature mortality due to NCDs from the current level (10).

The aim of this paper was to estimate the probability of dying between ages 30 and 69 years for all-cause mortality and for 4 NCDs from 2006 to 2016 in the Islamic Republic of Iran.

Methodology

Data source

We used mortality data based on death registration systems and population data in order to estimate proposed mortality statistics. The cause of death data were gathered from the Ministry of Health and Medical Education. We also used all-cause mortality data from the National Organization for Civil Registration for 2006–2016. As the data quality (considering cause of death from the National Organization for Civil Registration) was not acceptable, these data were only used to estimate total mortality statistics and also the completeness of the death registration system (11).

We obtained population data according to sex and 5-year age groups via the Statistical Center of Iran. These data (for 2006, 2011 and 2016) were based on census data; estimated data were used for intercensual years (2007–2010 and 2012–2015). The method for population projection was the cohort component method based on information on the structure of the population (12). The *People* software package was used; this required data and information on population structure, fertility, mortality, sex ratio and migration. These were obtained using various data sources and reports such as birth and death registries from the National Organization for Civil Registration, the Ministry of Health and Medical Education and the Statistical Center of Iran (12,13).

Statistical methods

Various criteria and methods were used to assess the quality of mortality data. We reviewed the missing data for age and sex information. Unknown sex- and age-related deaths were redistributed among cause–sex–age groups. We reviewed the quality of information on cause of death. One of the key criteria for checking the data quality of cause of death is the proportion assigned to "ill-defined or non-specific codes", known as "misclassification" of cause of death (14,15). We redistributed deaths in the category symptoms, signs and ill-defined conditions proportionally to all well-defined causes except injury (16).

In this study we defined cause of death codes based on the International Classification of Diseases (ICD) system as: CVDs (ICD-10 codes I00–I99), cancers (ICD-10 codes C00–C97), diabetes (ICD-10 codes E10–E14), and chronic respiratory disease (ICD-10 codes J30–J98) (17–20).

In order to estimate the unconditional probability of dying due to all causes and to NCDs between ages 30 and 69 years, the life table method was used. In the first step, we calculated age-specific death rates in 5-year age groups (e.g. 30–34, 65–69) (18,21).

$_5M_x$ = deaths among persons aged x to x+5 during a given year/ population x to x+5 at the mid-point of the same year   [1]

In the second step, we calculated probability of dying in each 5-year age range between 30 and 70 years.

$$_5q_x = 5{*}5Mx/1+(2.5{*}5Mx)$$ [2]

The above formula is derived from the assumption that deaths are linearly distributed throughout the year (18).

In the next step, we calculated probability of survival in each 5-year age group between 30 and 69 years.

$$_5p_x = 1- {}_5q_x$$ [3]

And in the final step, we calculated the unconditional probability of dying from age 30 to 69 years.

$$_{40}q_{30} = 1 - \prod^{60} {}_5p_x$$ [4]

Correction for underreporting of deaths

Generally, data from death registration systems have the drawback of underreporting. To correct for this limitation, various statistical and demographical methods have been developed. We used the new method presented by Adair and Lopez, which is based on the mixed effects model for predicting completeness of data from death registration system (22). The model for predicting completeness is based on the relationship between registered crude death rate (Reg CDR), the true level of child mortality rate ($_5q_0$), registered child mortality rate (Reg $_5q_0$), and population age structure (percentage of population 65 years old and above (%Pop 65i). Data on the registered crude death rate were obtained from the National Organization for Civil Registration. We also used child mortality data estimated from the UN Inter-agency Group as the true level of child mortality (22,23). The models are:

$$logit(C_i^{All}) = \beta_0 + RegCDR_i^2 * \beta_1 + RegCDR_i * \beta_2$$
$$+ \%Pop65_i * \beta_3 + \ln(5q0)_i * \beta_4$$ [5]
$$+ C_i^{5q0} * \beta_5 + Year * \beta_6 + e_i + \gamma$$

Completeness of Registration of All ages

$$C_i^{5q0} = \frac{Reg\,5q0}{5q0}$$

Completeness of Registration of $_5q_0$

In the above model e, is an error term, i is calendar year, and γ is a random effect and β_0 to β_6 are the coefficient. In the study by Adair and Lopez, all random effects of countries were presented in the appendices (*22*). We also had personal communication with them and they sent us an *Excel* template which contained all model coefficients (Adair T, personal communication, 15 August 2018).

Average annual rate of decline

As probability of dying from age 30 to age 70 years ($_{40}q_{30}$) was estimated for each year during 2006 to 2016, we next estimated the average annual rate of decline applying regressing log probability of death for each year:

$$\ln(_{40}q_{30})=a+b*year \qquad [6]$$

This generated a coefficient (b) separately for males, females and both sexes, from which we calculated the relative decline as follows:

$$\text{Annual average change } _{40}q_{30}=1\text{-}e^{b} \qquad [7]$$

We can use this annual average change in 40^q30 to compare the mortality risk of 4 NCDs between men and women on the same basis (*18*). We also predicted the trends for probability of dying for each year over the period 2017–2025. To do this, using the parameters obtained from Model [6], the trend for probability of dying was predicted.

Results

In 2006, about 129 668 (46.5%) deaths occurred in people aged 30–69 years in the Islamic Republic of Iran. This increased to 137 267 deaths in 2016.

Table 1 shows the proportion of adult deaths (30–69 years) due to NCDs for each sex during 2006–2016. In general, the proportion of NCD deaths was greater in females than in males. In 2006, these proportions were 75.92% and 60.88% respectively, and 74.73% and 65.69% respectively in 2016.

The trend in the mortality rate for people aged 30–70 years during 2006–2016 is shown in Table 2. Overall, the rates for males are nearly double the rates for females over this period. The all-cause mortality rates per 100 000 for males and females were 673.47 and 371.47 in 2006; these decreased to 450.69 and 263.56 in 2016. All-cause mortality rates per 100 000 population were 518.39 in 2006 and 348.82 in 2016 for both sexes. It can be seen that mortality rates due to NCDs were higher in males than in females and also that they decreased considerably over the study period. The NCD mortality rates per 100 000 population were 410.01 for males and 282.01 for females in 2006, decreasing to 296.04 and 196.97 respectively in 2016. These rates were 343.12 in 2006 and 240.62 in 2016 for both sexes.

Table 1 **Proportion of deaths from noncommunicable diseases in the Iranian population aged 30–69 years, 2006–2016**

Year	Sex		
	Male (%)	Female (%)	Both (%)
2006	60.88	75.92	66.17
2007	63.12	77.32	68.29
2008	62.07	76.78	67.48
2009	62.57	75.44	67.22
2010	61.81	76.67	67.15
2011	63.94	76.76	68.69
2012	65.13	76.39	69.25
2013	65.49	75.40	69.13
2014	69.60	76.66	72.19
2015	67.12	76.57	70.55
2016	65.69	74.73	68.98

Table 3 shows the 2 most important mortality statistics: the probability of dying due to all causes and the probability of dying due to NCDs in individuals aged 30–69 years. Both indicators were higher in males than females; all indicators decreased over the study period. The probability of all-causes death was 33.28% and 22.27% for males and females respectively in 2006, declining to 24.38% and 15.63% respectively in 2016. The probability of dying was 27.75% in 2006 and decreased to 19.61% in 2016 for both sexes. The probability of dying due to NCDs was 24.63% and 18.35% in 2006 and fell to 18.24% and 12.39% in 2016 for males and females respectively. This index was 21.36% in 2006 and fell to 14.95% in 2016 for both sexes.

Next, we calculated the average annual rate of decline of 40^q30 over the period 2006–2016 using a re-creation model of ln 40^q30. Regression analysis showed that the annual average rate of decline of 40^q30 for males in this period was 2.8% for all causes (Table 4). The annual average rate of decline of 40^q30 for females in this period was 3.4% based on Ministry of Health and Medical Education data for all causes. The annual average rate of decline of 40^q30 for both sexes in this period was 3.3% based on Ministry of Health and Medical Education data for all causes. The annual average rate of decline of 40^q30 for males over this period was 2.3% considering the 4 main NCDs as cause of death (using Ministry of Health and Medical Education data). This value was 3.7% for females considering the 4 main NCDs as cause of death (using Ministry of Health and Medical Education data). The annual average rate of decline of 40^q30 for both sexes over this period was 3.2% considering the 4 main NCDs as cause of death (using Ministry of Health and Medical Education data). Table 4 shows the predictor variables of the regression model for predication annual average reduction such as regression coefficient, *F*-ratio, *P*-value, and R^2. All predictor variables were statistically significant ($P < 0.05$).

Table 2 **All-cause mortality and noncommunicable diseases (NCDs) mortality in the Iranian population aged 30–69 years, 2006–2016**

Year	All causes of mortality (No. per 100 000)			NCD mortality (No. per 100 000)		
	Male	Female	Total	Male	Female	Total
2006	673.47	371.47	518.39	410.01	282.01	343.12
2007	590.09	342.82	464.99	372.48	265.07	317.56
2008	592.33	339.54	459.89	367.63	260.70	310.32
2009	581.80	332.00	453.45	364.05	250.47	304.82
2010	563.74	313.69	435.69	348.46	240.52	292.58
2011	524.16	311.50	418.49	335.13	239.11	287.46
2012	501.58	296.25	395.80	326.66	226.31	274.10
2013	482.53	283.13	377.59	315.99	213.48	261.04
2014	481.45	284.07	370.45	335.08	217.78	267.42
2015	463.23	268.24	355.96	310.92	205.39	251.12
2016	450.69	263.56	348.82	296.04	196.97	240.62

Figure 1 shows the trends for the probability of dying due to NCDs in the population aged 30–69 years for both sexes using observed data (2006–2016) and predicated data (2006–2025). From the observed data, which were corrected for underreporting and misclassification, the probability of dying from NCDs for both sexes declined from 21.36% in 2006 to 14.95% in 2016. From the predicted model, this indicator was 21.23% in 2006 and is estimated to fall to 11.4% in 2025.

Discussion

Our results showed that mortality due to the 4 leading NCDs was a public health concern in the Islamic Republic of Iran over the last decade. Total deaths due to NCDs increased in the Iranian population aged 30–69 years from 69 072 in 2006 to 90 281 in 2016. Although the total number of deaths increased, the unconditional probability of dying due to NCDs in this age group decreased from 21.3% in 2006 to 14.95% in 2016; we predicted that it would

Table 3 **Probability of dying due to all-causes and noncommunicable diseases (NCDs) in Iranian males and females aged 30–69 years, 2006–2016**

Year	All causes of death			4 main NCDs as cause of death		
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)
2006	33.28	22.27	27.75	24.63	18.35	21.36
2007	30.31	20.84	25.60	22.91	17.37	20.07
2008	30.65	20.71	25.49	22.98	17.18	19.86
2009	30.49	20.05	25.19	22.78	16.38	19.43
2010	29.67	19.09	24.31	22.14	15.75	18.81
2011	27.91	18.62	23.31	21.16	15.34	18.22
2012	27.08	17.67	22.22	20.65	14.44	17.35
2013	26.44	17.03	21.46	20.09	13.76	16.65
2014	26.20	16.97	20.96	20.56	13.80	16.61
2015	25.22	15.85	20.05	19.22	12.87	15.60
2016	24.38	15.63	19.61	18.24	12.39	14.95

Table 4 **Regression analysis showing average annual rate of decline for cause of death, [all causes and 4 main noncommunicable diseases (NCDs)]**

Cause of death	Alpha	Beta	1-exp (Beta)	F	P-value	R²
All causes						
Male	42.979	−0.029	0.028	217.445	< 0.05	0.96
Female	51.795	−0.035	0.034	742.592	< 0.05	0.988
Total	50.031	−0.034	0.033	525.541	< 0.05	0.983
4 main NCDs						
Male	36.786	−0.024	0.023	123.325	< 0.05	0.939
Female	55.922	−0.038	0.037	617.047	< 0.05	0.987
Total	48.42	−0.033	0.032	452.049	< 0.05	0.983

fall to 11.40% in 2025.

This paper is the first comprehensive attempt to estimate different statistics for premature deaths based on various data available in the country. Usually, data from death registration systems have 2 limitations: underreporting and misclassification. There are various indirect demographic methods, such as the death distribution method, which can be used to correct mortality data for underreporting (*22*). Using these methods requires 2 assumptions: a stable population and closed to migration. In light of the demographic changes in the Islamic Republic of Iran over the last 4 decades, we therefore used new methods in order to correct underreporting of deaths. Misclassification is another challenge considering data on cause of death based on registration. We used the distribution method to correct ill-defined or non-specific codes for cause of death.

We found that the probability of dying due to 4 main groups of NCDs in the Iranian population aged 30–69 years decreased during 2006–2016. From WHO estimates, the probability of dying from NCDs was 17.3% in 2012, decreasing to 14.8% in 2015; this result is similar to our findings (*24,25*).

Our findings also showed that, excepting the premature death rate from diabetes, which increased (11.0 per 100 000 in 2006 and 16.7 in 2016), death rates from the other 3 NCDs (cancer, CVD and chronic respiratory disease) decreased between 2006 and 2016. These patterns of reduction for 3 groups of diseases and increasing for diabetes were noted in the WHO report and also the Global Burden of Disease study (*26,27*). In addition, incidences of these 4 diseases were 171.7 for cancer, 877.0 for CVDs, 450 for diabetes and 486 for chronic respiratory disease per 100 000 in 2006 and 210.6 for cancer, 879.3 for CVDs, 594.7 for diabetes and 505.3 for chronic respiratory disease per 100 000 in 2016. Hence, the incidence of CVDs did not increase considerably over the study period. However, morbidity and mortality increased for diabetes. This could be the result of socioeconomic and lifestyle changes in the Islamic Republic of Iran over the past 2 decades.

Among the 4 groups of diseases, CVD had the highest mortality rate, and as a result, this showed the greatest decrease during the study period. Therefore, CVD might have been responsible for the greatest contribution to reducing the probability of death (mortality) from NCDs.

Figure 1 **Trends in probability of dying (%) due to noncommunicable diseases in the population aged 30–69 years based on observed and predicated data, Islamic Republic of Iran, 2006–2025**
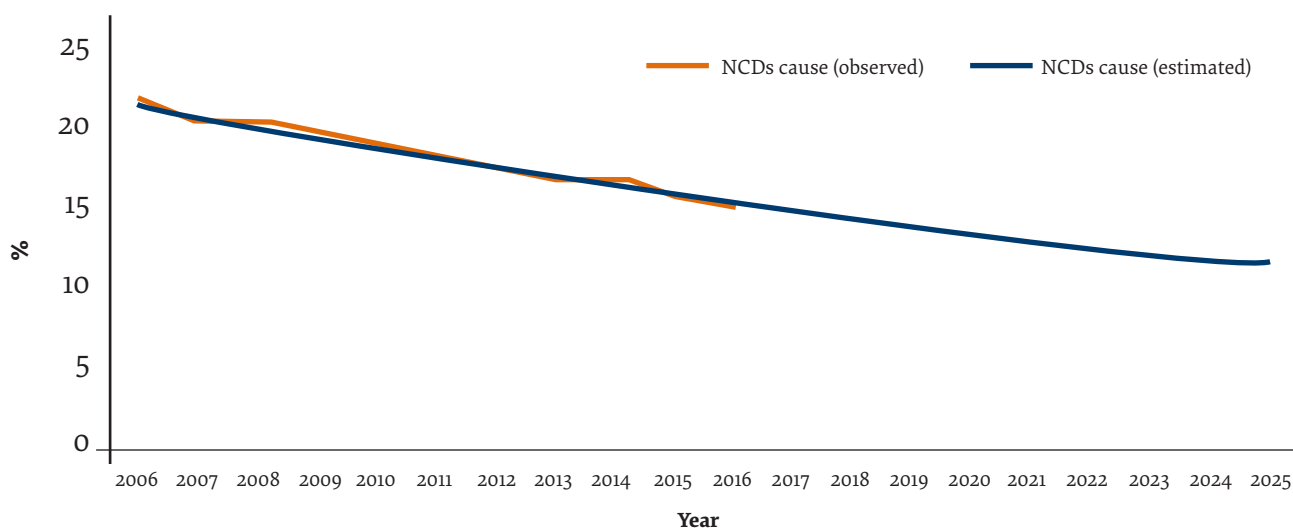
Considering the significant improvements in access and continuous improvements in diagnosis and treatment of CVDs, the case-fatality for CVDs has decreased significantly (*28*).

According to a WHO report, at least 80% of premature heart disease, stroke and type 2 diabetes, and 40% of cancers can be prevented through interventions aimed at several risk factors, such as healthy diet, regular physical activity and avoidance of tobacco products (*29*).

In the context of international attempts, including the improvement of health service delivery based on universal health coverage, a memorandum of understanding was signed in 2015 between the Ministry of Health and Medical Education and other relevant ministries (aimed at the prevention and control of NCDs) (*7,30*). This document was planned to implement various programmes to prevent NCDs and related risk factors by 2025. Additionally, to provide universal health coverage, the Ministry of Health and Medical Education launched a transformation plan in 2014. Service packages delivered in the primary health care units were revised based on the WHO Package of Essential Noncommunicable Disease Interventions (known as IrPEN); these packages are currently available at primary health care units (*31,32*).

The information system for mortality and cause of death is a key component in monitoring and assessment of health interventions to prevent and reduce the NCDs and related risk factors. During the last decade, the cause of death registration system was improved in the Islamic Republic of Iran (*24*). Using multiple data sources for capturing cause of death information increased the completeness of the data. Using the detailed ICD-10 coding system has also improved the quality of cause of death data, particularly for females. An urgent priority for public health policy is focusing on better diagnosis of cause of death through the issuing of death certificates by physicians of adult mortality.

Although we attempted a comprehensive assessment of trends and levels of premature death due to NCDs, this research had several limitations. First, mortality data for 2 provinces (Tehran until 2014 and Isfahan 2007–2010) were not available in Ministry of Health and Medical Education data; thus, we assumed that their patterns for cause of death were the average of all other provinces. Second, the Statistical Center of Iran estimated population data for age and sex were used for the intercensual years. Third, in this study we corrected the cause of death data for garbage and ill-defined codes using a simple proportional distribution method.

In conclusion, premature deaths due to NCDs have decreased over the last decade in the Islamic Republic of Iran. We predicted that this reduction would continue and that the country will meet the targets of the WHO NCD action plan for 2025 and also the SDGs targets to reduce premature deaths by 2030. The improvements in curative services along with the aging population will impose more costs on the health system. Hence, a prevention programme for NCDs should be an urgent priority in Iranian health policy (*29,33*).

Tendances en matière de mortalité prématurée en République islamique d'Iran : probabilité de décès entre 30 et 70 ans

Résumé

Contexte : La charge des maladies non transmissibles (MNT) constitue un défi majeur pour le monde entier. Chaque année, près de 15 millions de décès prématurés dus à des maladies non transmissibles se produisent chez des personnes âgées entre 30 et 70 ans.

Objectifs : Des données sur la mortalité fondées sur les systèmes d'enregistrement des décès et des données obtenues en population ont été utilisées pour estimer les statistiques de mortalité proposées en République islamique d'Iran.

Méthodes : Divers critères et méthodes ont été utilisés pour évaluer la qualité des données sur la mortalité. La probabilité de décès parmi les 30-70 ans , toutes causes confondues et pour les maladies non transmissibles, a été calculée à l'aide de la méthode de la courbe de survie.

Résultats : Le taux de mortalité dans la population âgée de 30 à 69 ans était de 343,12 (pour 100 000 personnes) en 2006 et a régressé à 240,62 en 2016 pour les deux sexes. La probabilité de décéder des suites de maladies non transmissibles était de 21,36 % en 2006 et a diminué pour atteindre 14,95 % en 2016 pour les deux sexes.

Conclusions : Le nombre de décès prématurés dus aux MNT a diminué au cours de la dernière décennie. Nous prévoyons que cette baisse se poursuivra et que le pays atteindra les cibles du plan d'action de l'OMS pour la lutte contre les maladies non transmissibles à l'horizon 2025 ainsi que les cibles des objectifs de développement durable visant à réduire les décès prématurés d'ici 2030. Toutefois, la morbidité et le fardeau des MNT continuent à être une source de

préoccupation pour la santé publique dans le pays. En raison des progrès des technologies en matière de soins de santé et de vieillissement de la population, ces préoccupations entraîneront des coûts plus élevés pour le système de santé. Les programmes de prévention des maladies non transmissibles devraient donc constituer une priorité urgente de la politique de santé iranienne.

اتجاهات الوفيات المبكرة في جمهورية إيران الإسلامية: احتمال الوفاة بين 30 و70 عاماً

الهه كاظمى، اردشير خسروى، سعيده آغا محمدي، محمد شريعتى، حسين كاظمينى

الخلاصة

الخلفية: يمثل عبء الأمراض غير السارية تحدياً كبيراً يواجه العالم بأسره. وتحدث نحو 15 مليون وفاة مبكرة جرّاء الإصابة بالأمراض غير السارية في صفوف الأشخاص الذين تتراوح أعمارهم بين 30 و70 عاماً سنوياً.

الأهداف: هدفت هذه الدراسة إلى استخدام بيانات الوفيات المستمدة من نُظُم تسجيل الوفيات والبيانات السكانية لتقدير الإحصاءات المُقترحة للوفيات في جمهورية إيران الإسلامية.

طرق البحث: استُخدمت معايير وأساليب مختلفة لتقييم جودة بيانات الوفيات. وتم حساب احتمال الوفاة الناجمة عن جميع الأسباب وعن الامراض غير السارية في صفوف من تتراوح أعمارهم بين 30 و70 عاماً باستخدام طريقة جدول الحياة.

النتائج: كان معدل الوفيات في صفوف السكان الذين تتراوح أعمارهم بين 30 – 69 سنة 343.12 (لكل 100000 شخص) في عام 2006، وانخفض إلى 240.62 في عام 2016 لكلا الجنسين. وبلغ احتمال الوفاة الناجمة عن الأمراض غير السارية 21.36٪ في عام 2006، وانخفض إلى 14.95٪ في عام 2016 لكلا الجنسين.

الاستنتاجات: انخفض عدد الوفيات المبكرة الناجمة عن الأمراض غير السارية على مدار العقد الماضي. ونتنبأ باستمرار هذا الانخفاض، وسيفي البلد بالغايات الواردة في خطة عمل منظمة الصحة العالمية بشأن الأمراض غير السارية بحلول عام 2025، وكذلك أهداف التنمية المستدامة للحد من الوفيات المبكرة بحلول عام 2030. ومع ذلك، فلا تزال الأمراض غير السارية وعبؤها من الشواغل الصحية العامة السائدة في البلد. وبسبب التقدم في تكنولوجيات الرعاية الصحية وكذلك شيخوخة السكان، ستفرض تلك الشواغل تكاليف أكبر على النظام الصحي. ومن ثم، ينبغي أن تكون برامج الوقاية من الأمراض غير السارية أولوية عاجلة للسياسة الصحية الإيرانية.

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Impact of government budget on health prepayment levels: evidence from OECD countries

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Abstract

Background: Health prepayment, a key indicator under the Sustainable Development Goals monitoring framework, is strongly associated with household financial protection; however, the impact of government health budget on the level of prepayment has rarely been discussed.

Aims: To address the following research questions. (1) Does a higher government health budget translate into higher prepayment rates in the healthcare financing system? (2) What are the effects of government health budget on public prepayment and private prepaid plans? (3) What are the heterogeneities between groups of countries with different income levels and public health prepayment systems?

Methods: Analysis of panel co-integration, impulse response function, and variance decomposition were conducted in 34 Organisation for Economic Co-operation and Development (OECD) members for the period 1995–2016.

Results: Government health budget has a long-running equilibrium relationship with the level of public and total prepayment. However, a stable relationship could not be confirmed with private prepaid plans. Moreover, government health budget played a significant positive role in explaining the fluctuations in the total and public prepayments over a long time, that is, 51 and 37 periods, respectively. Considering differences between groups of countries, the impacts are greater for those with higher income levels and more public-dominated health-financing systems.

Conclusions: Government health budget has a long-time relationship with the levels of both total prepaid expenditure and public prepayment. By contrast, it does not systematically crowd out private prepaid plans.

Keywords: government health budget, healthcare financing, OECD, private prepaid plan, public prepayment

Introduction

Globally, health care remains important but expensive. Good health and well-being is the third of 17 global Sustainable Development Goals launched by the United Nations in 2015 with approximately 10.0% of global gross domestic product (GDP) dedicated to health that year. Between 2000 and 2015, average annual real growth rate of the global health economy was 4.0% compared with 2.8% for the overall global economy (1). Health accounts for a large proportion of the GDP and government budget of the world's top 10 economies (Figure 1).

Prepayment of healthcare financing[1] is crucial to ensure that all individuals have access to effective public and personal healthcare at affordable prices. A high level of prepayment, especially through public financing via a tax-based system, social health insurance scheme, or mixed system, positively affects the fairness of the payment distribution burden. Additionally, public financing spreads financial risks more strategically and

subsidises poorer people. The degree of risk sharing in a health financing organization positively affects its health system attainment (2). In contrast, healthcare financing systems with high out-of-pocket (OOP) payments create problems of access, particularly for vulnerable groups including low-income populations.

Considerable research has examined the determinants of prepayment levels in terms of both public prepayment and private prepaid plans (Appendix). For public prepayment, these factors include economic growth, Wagner's law, demographic heterogeneity, political legitimacy, and capitalism. In particular, the important stewardship role that the government can play may facilitate the transition to higher levels of prepayment even in slower-growing countries (3). The public prepaid financing system is an important tool for the ruling party to ease conflict among different social classes and maintain political power. To safeguard its legitimate status, the system can be improved as political opposition

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[1] According to the World Health Organization definition, prepayment refers to the health expenditure excluding out-of-pocket payments. Public prepayment includes transfers from government domestic revenue and social insurance contributions (from employers and employees). Private prepayment refers to the fund collected by private health insurance.

Figure 1 Large proportion of gross domestic product and budget expenditure on health for world's top 10 economies (2016)
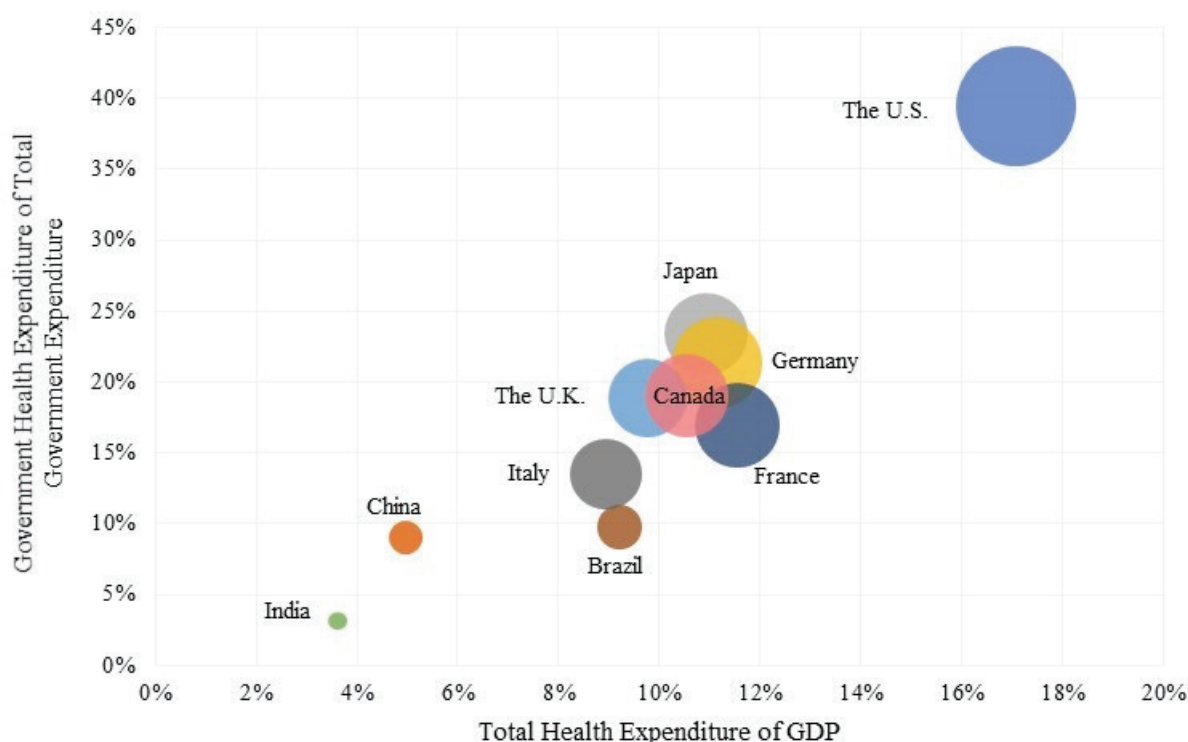
The size of each bubble represents the health expenditure per capita of the country. Ranking of national economies is provided by International Monetary Fund's World Economic Outlook for 2019. Since economies of different levels of development are compared, the health expenditure and out-of-pocket expenditure per capita is calculated in PPP int. $ (purchasing power of national currencies against USD).

Source: World Health Organization, 2019.

intensifies (*4*). For private prepayment, in addition to traditional socioeconomic and political demand factors including income (*5–7*), population ageing (*8,9*), education levels (*10,11*), and employment status (*12*), various other factors can explain the growth of private prepaid plans.

For instance, the longer waiting lists for National Health Service treatment in the United Kingdom of Great Britain and Northern Ireland have been associated with more purchases of private health insurance (PHI) (*13*). The service quality gap between public and private prepaid

Table 1 Panel co-integration tests of prepayment, public and private financing

Methods	Y	Y_1	Y_1
Pedroni (1999) Panel v-Stat.	−0.251814(0.5994)	1.220125(0.1112)	−0.969307(0.8338)
Pedroni (1999) Panel ρ-Stat.	−3.082017(0.0010)	−4.371516(0.0000)	−0.385095(0.3501)
Pedroni (1999) Panel pp-Stat.	−3.546204(0.0002)	−5.230357(0.0000)	−0.891136(0.1864)
Pedroni (1999) Panel ADF-Stat.	−2.879510(0.0020)	−4.653091(0.0000)	−1.576539(0.0575)
Pedroni (1999) Group ρ-Stat.	−0.284915(0.3879)	−0.934630(0.1750)	3.359792(0.9996)
Pedroni (1999) Group pp-Stat.	−5.128860(0.0000)	−5.939829(0.0000)	0.205246(0.5813)
Pedroni (1999) Group ADF-Stat.	−4.828542(0.0000)	−5.594431(0.0000)	−0.817908(0.2067)
Kao (1999) ADF t-Stat.	−2.853071(0.0022)	−5.389342(0.0000)	−2.646904(0.0041)
Johansen Fisher Fisher Stat. (from trace test)	137.3(0.0000)	134.5(0.0000)	131.4(0.0000)
Johansen Fisher Fisher Stat. (from max-eigen test)	108.1(0.0014)	104.7(0.0006)	100.5(0.0014)

We report no intercept or trend results for Pedroni (1999) and Johansen Fisher tests. Panel v-Stat refers to panel variance statistic. Panel ρ-Stat refers to panel ρ statistic. Panel pp-Stat refers to Panel Phillips–Perron (PP) statistic. Panel ADF-Stat refers to panel augmented Dickey–Fuller statistic. Group ρ-Stat refers to group ρ statistic, a type of group mean panel cointegration statistics. Group pp-Stat refers to group Phillips–Perron statistic. Group ADF-Stat refers to group augmented Dickey–Fuller statistic. ADF t-Stat refers to augmented Dickey–Fuller t-Statistic based on cointegration test proposed by Kao (1999). Fisher Stat (from trace test) refers to trace statistics based on Johansen co-integration test. Fisher Stat (from max-eigen test) refers to maximum eigenvalue statistics based on Johansen co-integration test.

Figure 2 Effect of government health budget on the level of health prepayment
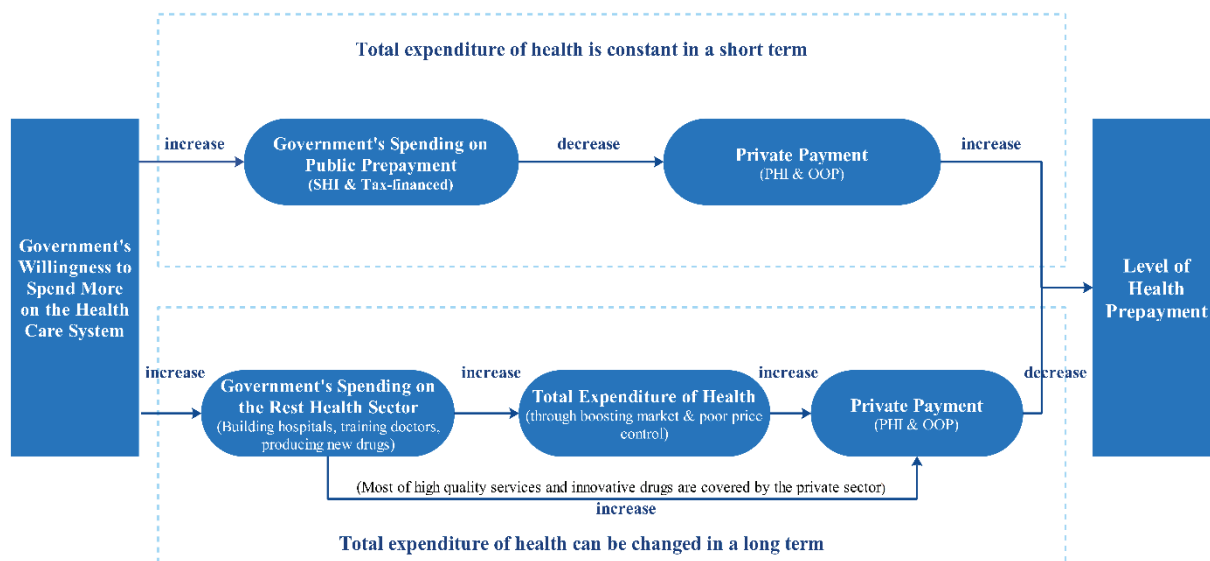
plans could also drive demand for PHI (*14*).

Government health budget influences prepayment levels through at least 2 channels (Figure 2). On the one hand, if the overall health expenditure remains constant in the short term, then when the government increases its expenditures in the health sector, the spending will partially go to the public prepaid system (social health insurance, tax-financed) and may cover a certain proportion of originally private spending, that is, private prepaid plans and OOP payments. Consequently, the level of prepayment increases (*15*). On the other hand, government spending on health may increase total expenditure in the health sector, thus driving long-term prepayment levels in the opposite direction (*16*). The increased government expenditure on health can also be used to build hospitals, train doctors and nurses, and produce innovative drugs, thus promoting the overall development of the health sector and boosting the market (*17,18*). Compared with necessary medical services, high-tech equipment and services offered by well-educated employees are more expensive, while price regulation and control of premium healthcare packages are not always easy, particularly in a private-dominated system (*19*). Therefore, these conditions may boost total healthcare expenditure and private spending, including PHI and OOP costs. Hence, the prepayment level decreases simultaneously. Moreover, since public prepaid plans normally cover basic pharmaceutical services and drugs, most high-quality services and innovative drugs are paid for by private financing packages (e.g., private insurers and patients). Thus, these examples indicate that government budgetary increases in the health sector may have various impacts on public and private financing.

The aim of this study was to evaluate how such government health budgets operate in various economies.

Methods

Empirical model

To measure the long-term relationship between the level of healthcare prepayment and government health budget, we established a panel vector autoregressive (PVAR) model:

$$Z_{it} = b\,Z_{it-1} + a_i + g_t + e_{it} \quad (1)$$

In Model (1), Z_{it} is a vector of two variables (*Y*, *X*). *Y* denotes the prepaid expenditure on health (total health expenditure excluding OOP expenses) as a ratio to GDP. We divide healthcare prepayment into public prepayment (Y_1) and private prepaid plans (Y_2), with both expressed as a percentage of GDP. *X* represents government expenditure on health as a share of total government expenditure, α_i represents the country-specific effects, γ_t the time effects, β the coefficient matrix, and ε_{it} the error term. The subscripts *i* and *t* denote country and year, respectively. This model includes only first-order lags, which are included based on the Bayesian information criterion.

In any dynamic model including lags of the dependent variables, inclusion of fixed effects creates biased coefficients because individual effects are correlated with the regressors. To mitigate this, our PVAR estimation routine follows the methods proposed by Love and Zicchino (*20*), using forward mean-differencing, also referred to as the Helmert procedure (*21*). Accordingly, all variables are transformed into deviations from forward means. This transformation preserves the orthogonality between transformed variables and lagged regressors, which allows us to use lagged regressors as instruments for the generalized method of moments estimation. The time effects are removed by subtracting the means of each variable calculated per country.

Figure 3 Comparison of variables (X, Y, Y$_1$, Y$_2$) among Organisation for Economic Co-operation and Development (OECD) members (1995–2016)

X:General government expenditure on health as a percentage of total government expenditure
Y:Total prepayment as a percentage of GDP
Y1:Public prepayment as a percentage of GDP
Y2:Private prepayment as a percentage of GDP
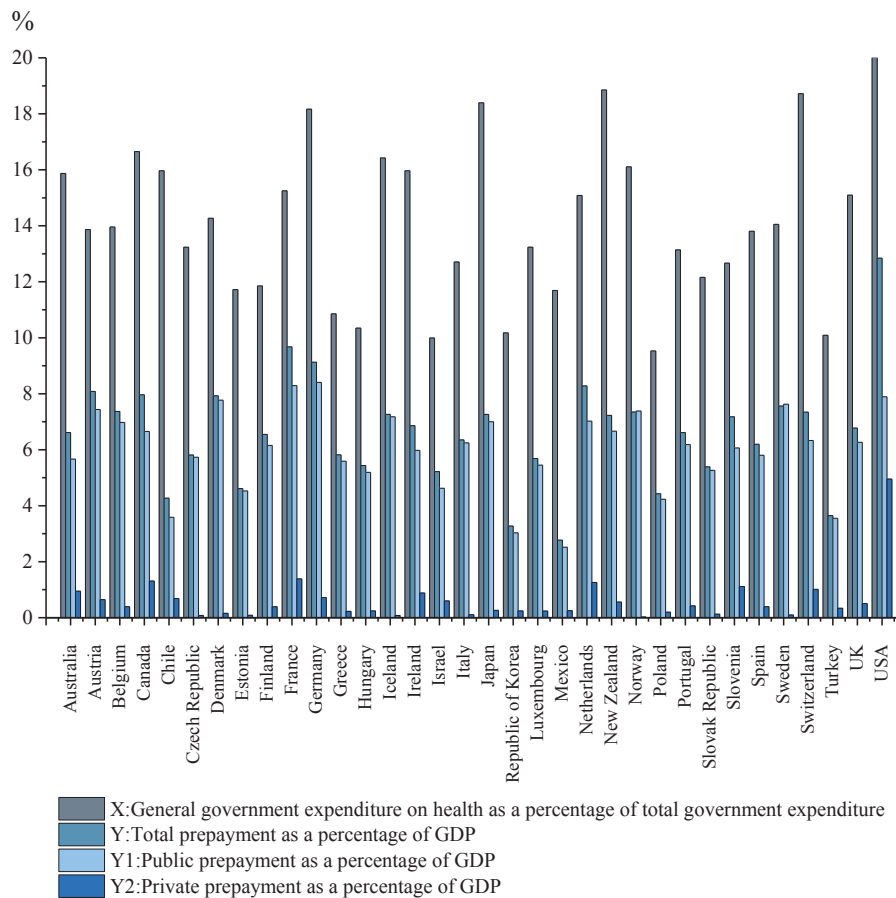
The PVAR methodology combines the traditional VAR approach, which treats all the variables in the system as endogenous, with the panel-data approach, which allows for unobserved individual heterogeneity (*20*). However, PVAR estimates are seldom interpreted by themselves. In practice, the impact of exogenous changes in each endogenous variable on other variables in the PVAR system is of interest. The prime benefit of this approach is evaluating the reaction of one variable to the innovations in another variable in the system, while holding all other shocks at 0 using impulse response functions (*22*). The impulse response function describes the evolution of the variable of interest along a specified time horizon after a shock in a given moment. Based on the equation of PVAR model, it captures the correlations between the present and future values of all endogenous variables because of its lagged specification. In this iterative process, any shock to 1 variable will have an effect on the values of other variables at the time of the shock and over subsequent periods. This feature allows one to trace the transmission of a single shock within a system and, thus, makes it a useful tool in the assessment of economic policies. Additionally, the PVAR system can measure the percentage variation in 1 variable that is explained by the

shock to another variable accumulated over time, that is, variance decomposition.

Impulse response functions and forecast-error variance decompositions are conducted to investigate the dynamic effects of government's willingness to fund on the level of health prepayment. Accordingly, we can measure the impact of a shock in government's willingness to fund on the level of health prepayment and the percentage variance in health prepayment levels that are attributable to innovations in government's willingness to fund, respectively.

Panel data

We used the panel annual data of the 34 OECD member countries over the period 1995–2016, obtained mainly from the World Health Organization Global Health Observatory data and the OECD library. Figure 3 compares the variables among the countries. However, we excluded Norway, Sweden and Turkey because of missing values of private prepaid plans as a ratio of private health expenditure. Thus, we restricted our sample of the indicators Y_1 and Y_2 to 31 members. Additionally, the data series of *X* was selected to match different panel data when analysing its relationship with Y, Y_1 and Y_2 separately.

Figure 4 Heterogeneity among 34 Organisation for Economic Co-operation and Development member countries
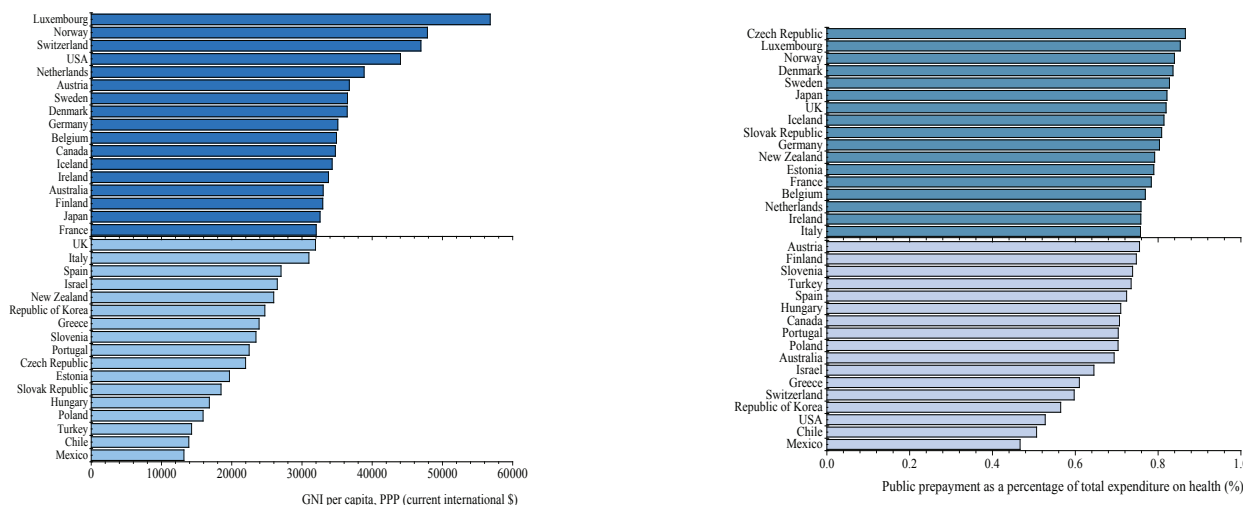
Results

Overall effects

Panel cointegration analysis

We first conducted unit root tests to examine whether the panel variables were stationary. Six best-known panel stationarity test methods were used, including the LLC (unit root tests for panel data proposed by Levin et al., 2002) (*23*), Breitung (*24*), IPS (unit root tests for panel data proposed by Im et al., 2003) (*25*), and 2 Fisher-type (*26, 27*) tests. The results showed that all the variables, Y, Y_1, Y_2 and X, were stationary after the first difference was taken, which simply means that the panel data variables were consistent with the *AR(1)* process (Appendix Table 2).

Subsequently, Pedroni (*28*), Kao (*29*) and Johansen Fisher panel cointegration tests were applied to examine whether long-term cointegration relationships existed between the level of health prepayment and a government's willingness to fund it, that is (Y, X), (Y_1, X), and (Y_2, X). Table 1 indicates that the tests' results of indicators (Y, X) and (Y_1, X) rejected the null hypothesis of no cointegration at the 5% significance level. However, most of the test results for the indicators (Y_2, X) did not reject the null hypothesis.

Shock and fluctuation analysis by impulse responses and variance decompositions

To investigate further the response of the level of health prepayment to the shock of government health budget, impulse response functions were constructed. Appendix Figure 1 illustrates the impulse responses of Y in 34 countries and Y_1 and Y_2 in 31 countries to 1 standard deviation (SD) shock of X. Y positively responded to the shock of X, and this effect lasted for 51 periods. The impulse response of Y expanded rapidly and peaked at 0.08 in the 10th period before declining gradually until

it approaches 0 in the 51st period. A similar pattern emerged in the impulse response of Y_1 to the shock of X, which increased dramatically to 0.016 in the 4th period before decreasing steadily to 0 in the 37th period. In contrast, the response curve of Y_2 immediately approached 0 in the first several periods and remained flat thereafter. Appendix Table 5 shows that the percentages of variations in Y and Y_1 explained by X reached their peaks at 13.7% in the 51st period and 13.7% in the 37th period, respectively, while X explained only at most 2.3% of the variation in Y_2 in the 96th period, which was lower than that of Y and Y_1.

Heterogeneity by country: income variance and prepayment variance

To analyse whether heterogeneity by country mattered in the context of our study, we divided the 34 OECD members into groups by income levels and prepayment systems. Figure 4A represents the income differences among the members based on gross national income (GNI) per capita, while Figure 4B represents the public prepayment differences using public prepayment as a percentage of total expenditure on health. The sample was divided by the medians of the 2 factors. First, through the average ranking of GNI per capita from 1995 to 2016 for the 34 countries, we identified the median income to be US$ 31 974.09; Group A and Group B represented the panel above and below this median, respectively. The country with the highest GNI per capita was Luxembourg at US$ 56 800 and the lowest was Mexico at US$ 13 197.27. Second, using the median of public prepayment as a percentage of total expenditure on health for the 34 countries, 17 countries (Group C) exceeded this median (i.e., 75.63%) while the rest were classified in Group D. Among them, the Czech Republic had the highest (86.59%) and Mexico the lowest (46.67%) public dominance.

As shown in Appendix Tables 3–6, the results of unit root tests and panel cointegration tests for subgroups were the same as those with the full sample panel. All the variables were first-order stationary. (Y, X) and (Y_1, X) were cointegrated but (Y_2, X) were not.

The result of particular interest was the difference in impulse responses between subgroups. Appendix Figure 2 reports that a 1 SD shock in X of Group B had shorter and weaker impacts on Y than that of Group A (i.e., peaks at 0.004, lasting for 27 periods compared with peaks at 0.023, lasting for 48 periods). Similar features were found in Y_1: Group A had greater response intensity and longer duration (i.e., peaks at 0.038, lasting for 42 periods compared with peaks at 0.009, lasting for 35 periods). By contrast, the responses of Y_2 to shock in X were close to 0 for both Groups A and B. According to the results of variance decomposition, the proportions of variations in Y and Y_1 attributed to X were higher in Group A (Appendix Table 6).

Concerning the sample grouped by public dominance, the above patterns still existed. For instance, Appendix Figure 3 shows that the impulse response of Y_1 was stronger in Group C (i.e., peaks at 0.03 compared with 0.009). It is also worth noting that the percentage of variation in Y_1 that could be explained by the shock of X in Group C was larger than in Group D (i.e., remained stable at 22.7% compared with 8.5% in the 33rd period) (Appendix Table 7).

Discussion

For all OECD members, when a government highly prioritizes healthcare (i.e., the ratio of government expenditure on health to total government expenditure increases), the prepaid fund raised by social health insurance and/or tax increases greatly. Thus, the public prepayment level improves the total prepayment level simultaneously. Moreover, this effect is sustainable and persists in the short term because policies tend to have lagged effects. Compared to the positive effects, government health budgets have no effect on private prepaid plans, potentially because individuals purchase PHI according to their own health status, income level, and risk preferences, which are not directly affected by government health budgets.

The empirical results demonstrate that for countries with higher GNI per capita, the government health budget has greater and longer impacts on the public prepayment level. The income level of a country is related to its overall fiscal capacity and its government's decisions regarding the share of public spending to allocate to the health sector (30). In higher-income countries, government budget prioritization for health plays a more important role in the public health financing system. Appendix Figure 4 shows that the government health expenditure as a ratio of total government expenditure of higher-income countries is higher than that of less-high-income countries, on average. That is, governments of higher-income countries are willing to give greater priority to health in their limited budgets. Due to this prioritization, government fiscal expansion in health drives a greater

increase in public health prepayment over a longer period of time.

Regarding differences between the 2 groups categorized based on public prepayment, we found that in countries with more public-dominated health-financing systems, the public and total health prepayment levels responded more strongly to the shock of government health budgets. Government health budgets made a greater contribution to the variation in the level of public health prepayment in these countries. These results make economic sense. When the share of health prepayment that is channelled from the public sector increases, the policy transmission mechanism is less obstructed and more effective. For instance, it is typical that public health financing dominates in Northern Europe, including Norway and Sweden, which are reputed for their nearly universal health coverage and low OOP payment per capita. It is suggested that financial protection improves as reliance on public prepayment increases.

Another interesting point is that in the less-public-dominated group, lower-income countries, such as Mexico and Turkey, tend to have weaker fiscal capacity to finance health prepayments. Thus, government health budgets play a limited role in public health prepayment, leading to weaker financial protection for citizens. However, despite an increase in income levels, government health budgets do not necessarily have a greater impact on public prepayment levels. The extent of financial protection of individuals is closely associated with the proportion of public prepayment. For instance, the public sector is less dominant in the health financing system of the USA, accompanied by the highest OOP payment per capita worldwide, although the US government spends the most on health among the world's top 10 economies.

There are important lessons to be learned from the OECD countries for policy-makers seeking to adjust the role of government expenditure on health; specifically, policy choices should be based on the comparison of impacts on different financing sources (i.e., public and private). Our findings show that the increase in government health expenditure ratio has positive impacts on public and total prepayment levels, but little impact on the level of private prepaid plans. A health system that relies mainly on high levels of government funding and a high share of prepayment sources in overall health spending generally provides better and more equitable access to services and financial protection. Therefore, strengthening government health budgets is essential for increasing public health prepayment, which is a key factor for achieving the Sustainable Development Goal for health. However, government budget prioritization has not been fully tapped in lower-income countries, leaving room for more investments in health (30). Based on the group comparisons, low-income countries require greater attention to prioritizing health in government budgets and better exploiting them to increase health prepayment levels. Additionally, the dynamic relationship between government health budget and the level of

health prepayment indicates that policy implementations may have delayed effects, which should be considered in policy decision-making.

However, there were several limitations to the present study. Due to data unavailability, the direct and indirect effects of government health budgets on the level of health prepayment could not be distinguished. For example, government expenditure on health can influence the health prepayment through direct transfers to health-financing schemes or indirectly, by improving individuals' incentives to purchase public/private health insurance. There may also have been a methodological limitation since the PVAR model was less theory based compared to traditional structural models, while other factors that may affect health payment levels were not included in the model. We leave such considerations for future research.

Conclusion

This study shows that government health budgets have a long-term equilibrium relationship with and play a significant role in explaining the fluctuations in the level of public and total prepayment. By contrast, government health expenditure does not systematically crowd out private prepaid plans and contributes little to explaining their variations.

Impact du budget de l'État sur les niveaux de prépaiement pour les soins de santé : données probantes des pays membres de l'OCDE

Résumé

Contexte : Le prépaiement pour les soins de santé, un indicateur clé du cadre de suivi des objectifs de développement durable, est fortement associé à la protection financière des ménages ; toutefois, l'impact du budget public de la santé sur le niveau de prépaiement a rarement été examiné.

Objectifs : Répondre aux questions de recherche suivantes. 1) Une augmentation du budget public de la santé se traduit-elle par des taux de prépaiement plus élevés dans le système de financement des soins de santé ? 2) Quels sont les effets du budget public de la santé sur le prépaiement public et les systèmes privés de prépaiement ? 3) Quelles sont les hétérogénéités entre les groupes de pays ayant des niveaux de revenu et des systèmes de prépaiement de santé différents ?

Méthodes : Pour la période 1995-2016, 34 membres de l'Organisation de coopération et de développement économiques (OCDE) ont procédé à une analyse de la co-intégration des panels, de la fonction de réponse impulsive et de la décomposition des variances.

Résultats : Le budget public de la santé est depuis longtemps en équilibre avec le niveau des prépaiements publics et totaux. Cependant, une relation stable n'a pas pu être confirmée avec les systèmes privés de prépaiement. En outre, le budget de la santé a joué un rôle positif important en expliquant les fluctuations de l'ensemble des prépaiements et des prépaiements publics sur une longue période, c'est-à-dire 51 et 37 périodes, respectivement. Compte tenu des différences entre groupes de pays, les impacts sont plus importants pour ceux dont les niveaux de revenu sont plus élevés et dont les systèmes de financement de la santé sont plus à dominante publique.

Conclusions : Le budget public de la santé est lié depuis longtemps aux niveaux du total des dépenses prépayées et des prépaiements publics. En revanche, il ne permet pas de supplanter systématiquement les systèmes privés de prépaiement.

أثر الميزانية الحكومية على مستويات الدفع المسبق في مجال الصحة: دلائل مستمدة من بلدان منظمة التعاون والتنمية في الميدان الاقتصادي

ينج تشانج، جاك فانيست، وينكينج بان، ليوي تشانج

الخلاصة

الخلفية: يرتبط الدفع المسبق للحصول على الخدمات الصحية، وهو مؤشر رئيسي في إطار رصد أهداف التنمية المستدامة، بصورة وثيقة بالحماية المالية للأسر؛ غير أنه من النادر أن تجري مناقشة تأثير الميزانية الحكومية للصحة على مستويات الدفع المسبق.

الأهداف: هدفت هذه الدراسة إلى الرد على الأسئلة البحثية التالية: (1) هل يُترجَم ارتفاع مخصصات الميزانية الحكومية للصحة إلى ارتفاع معدلات الدفع المسبق في نظام تمويل الرعاية الصحية؟ (2) ما هي آثار الميزانية الحكومية للصحة على خطط الدفع المسبق العامة وخطط الدفع المسبق الخاصة؟ (3) ما هي أوجه التفاوت بين مجموعات البلدان المختلفة من حيث مستويات الدخل ونُظم الدفع المسبق في مجال الصحة العامة؟

طرق البحث: أجري تحليل تآلف المجموعة، ووظيفة الاستجابة الاندفاعية، وتحليل التفكك التبايني في 34 عضواً في منظمة التعاون والتنمية في الميدان الاقتصادي خلال الفترة من 1995 وحتى 2016.

النتائج: هناك علاقة طويلة الأمد ومتوازنة بين الميزانية الحكومية للصحة ومستوى الدفع المسبق العام وإجمالي الدفع المسبقٍ. ومع ذلك، لم يتسن تأكيد وجود علاقة مستقرة مع خطط الدفع المسبق الخاصة. وعلاوة على ذلك، فقد أدت الميزانية الحكومية للصحة دوراً إيجابياً هاماً في تفسير التقلبات في إجمالي الدفع المسبق والدفع المسبق العام على مدى فترة طويلة بلغت 51 و 73 دورةٍ على التوالي. وبالنظر إلى الاختلافات بين مجموعات البلدان، فإن الآثار المترتبة تكتسي أهمية أكبر بالنسبة للبلدان التي لديها مستويات دخل أعلى ونُظم تمويل صحي يهيمن عليها القطاع العام أكثر من أي قطاع آخر.

الاستنتاجات: هناك علاقة ممتدة بين الميزانية الحكومية للصحة ومستويات إجمالي الإنفاق المدفوع مقدماً والدفع المسبق العام على حد سواء. وعلى العكس من ذلك، فإن الميزانية الحكومية لا تتنافس مع خطط الدفع المسبق الخاصة.

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Development and psychometric testing of a Gastric Cancer Behavioural Risk Assessment Inventory (GC-BRAI)

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Abstract

Background: Gastric cancer (GC) is one of the most common cancers worldwide. There is no disease-specific tool for GC risk assessment in research and practice settings within the Iranian sociocultural context.

Aims: To develop and assess the psychometric properties of the Gastric Cancer Behavioral Risk Assessment Inventory (GC-BRAI) in GC patients in Northwest Islamic Republic of Iran.

Methods: Face-to-face interviews were performed on a convenient sample of 175 GC patients and a purposive sample of 350 matched non-GC patients as a control group. Exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) were performed to appraise the structure validity of GC-BRAI and examine its possible latent constructs.

Results: The designed instrument with its 5 latent factors indicated acceptable internal consistency (0.72), reliability (0.99) and fit indices (χ^2/degrees of freedom = 2.24, root mean square error of approximation = 0.049, adjusted goodness of fit index = 0.91 and root mean square residual = 0.085). The identified components were specific nutritional behaviours, typical daily diet, routine heartburn-causing behaviours or foods in diet, daily use of rice and smoked foods, and tobacco smoking/alcohol consumption, which all indicated a significant association (P= 0.0001) with high-risk of GC.

Conclusions: GC-BRAI can be considered a feasible tool to measure individual GC risk and a reliable data collection instrument in tailor-made risk reduction interventional programmes.

Keywords: gastric cancer, health behaviour, psychometrics, questionnaire design

Introduction

Cancer is among the leading causes of death worldwide after cardiovascular disease and the second most prominent cause of death in less-developed countries (*1,2*). Gastric cancer (GC) ranks among the top causes of cancer-related deaths worldwide, with ~1 million new cases detected annually and an estimated 783 000 (8.2%) deaths (*3,4*). Almost 75% of new cases of GC occur in developing countries (*5,6*). In the Islamic Republic of Iran, GC is the leading cause of cancer mortality in men and the second main cause in women. The reported standardized incidence rate of GC for Iranian men and women is 19.6 and 10.0 per 100 000 population, respectively (*7*). Although GC-induced mortality has declined significantly in most developed countries over the past few decades, it is still high in some Asian, Eastern European and South American countries (*8,9*). During the past few years, the incidence and mortality of GC have increased in the Islamic Republic of Iran (*10*), and GC has become the second most common malignancy after lung cancer and the leading cause of cancer deaths (*11*). GC is the most prevalent cancer among Iranian men and the third most common among women (*12*). The highest incidence of cancer has been reported in the north and northwest of the country,

mainly in the Gilan, Mazandaran, Golestan, Ardabil and East Azarbaijan Provinces (*13*).

Previous studies have shown that modifications in diet and food preparation methods can reduce GC incidence (*14*). Based on empirical research evidence, behavioural risk factors currently are important determinants of GC (*15*). GC prevention strategies, therefore, are focused on behavioural changes (*16*).

GC is a multifaceted disease and a wide range of environmental and genetic factors could play a role in its distribution (*17*). The major reported risk factors for GC include: family history; Helicobacter pylori infection (*18*); dietary habits such as consumption of salt-cured and smoked meat, fried foods, and spicy and nitrate-containing foods; consumption of alcoholic drinks; cigarette smoking; and occupational exposure to heavy metals such as cadmium and lead (*15*). Suggested GC protective measures include daily consumption of adequate servings of green vegetables and fresh fruit, especially citrus fruits with high vitamin C content (*19*).

Several studies have used exploratory factor analysis (EFA) to identify potential dietary risk factors for GC (*20,21*). However, no study has investigated the possible relationship between dietary/nondietary behavioural

patterns and development of GC in Iranian or other Persian-speaking populations. Through classifying individual risk factors into exposure categories and aggregation of these potential risk factors into distinct risk components, the GC risk pathways and behavioural patterns can better be explained. The purported advantages of lifestyle change in prevention of GC mean that targeting modifiable risk factors (e.g., poor dietary habits) is considered essential in interim interventional programmes (21). The main encouragements for the present study were: current trends in the incidence of GC in the Islamic Republic of Iran (13); empirical evidence about the effectiveness of behaviour change on the epidemiological profile of GC (21); and lack of a specific tool to appraise individuals' GC risk pattern. We aimed to develop and psychometrically assess a definitive questionnaire for GC risk assessment that might be applicable for risk stratification and mitigation in research and practice settings.

Methods

Participants

This case–control study consisted of a convenience sample of 175 GC patients and a purposive sample of 350 age- and sex-matched non-GC controls who were admitted to 3 hospitals (Imam Reza, Shahid Ghazi Tabatabai, and Alinasab) with oncology wards in Tabriz, East Azarbaijan Province, Islamic Republic of Iran.

The study was conducted in accordance with the ethical standards in the Declaration of Helsinki, and the Medical Ethics Review Board of Trustees (MERBoT) in Tabriz University of Medical Science approved all of the study procedures (approval number: 5/D/1026302-1397-12-05). Inclusion criteria for cases were diagnosis of GC and age 18–85 years. Inclusion criteria for controls were admission for any disease other than GC and age 18–85 years. The exclusion criterion for GC patients was any type of concurrent cancer due to immunodeficiency. The exclusion criterion for the control group was GC caused by metastasis from an extra-gastrointestinal tract malignancy. The study participants were also excluded if they had any other critical health condition.

The rounded up (to the nearest 5) proportions of the respondents (25% in the controls and 45% in the cases) that reported a high-risk dietary habit (e.g., reusing cooking oil) in the study of Salvador et al. (22) were utilized to decide on the study sample size. To improve precision of estimates, a one-to-many matching approach (2:1 ratio of controls to cases), type 1 error of 0.05 and test power of 0.90 were deemed as prior statistical parameters in STATA version 13 software (StataCorp LP, College Station, TX, USA). Thus, a minimum sample size of 175 subjects per group was estimated to be appropriate to satisfy the statistical significance threshold, although 175 patients were included in the case group and 350 matched individuals in the control group. Face-to-face interviews were conducted for data collection purposes from 9 April 2017 to 20 June 2018. The study participants gave their written informed consent to participate in the study.

Instrument development stages

The item pool was based on an extensive literature search and interviews with relevant healthcare professionals. Thus, 22 items were generated and validity and reliability appraisal procedures were used to assess psychometric properties of the adapted instrument. The preliminary draft of the Gastric Cancer Behavioral Risk Assessment Inventory (GC-BRAI) was sent to 12 healthcare professionals for their comments on face and content validities of the questionnaire, including lucidity of the wording and ability of the items to communicate the messages of interest to potential readers. They were also asked to comment on a 5-point Likert scale about importance, necessity or redundancy of the items. The content validity index and content validity ratio were used to quantitatively validate the designed instrument. The calculated content validity index (0.68) and content validity ratio (0.83) were in the vicinity of the acceptable range (23); therefore, no changes were made to the preliminary draft of the GC-BRAI. A sample of GC and non-GC patients (15 from each group) was approached in the next step to canvass their opinions about the simplicity, clarity and consistency of the items. Minor modifications were made to the items based on these comments.

Reliability of the GC-BRAI

We estimated the test–retest reliability of the scales and Cronbach's α as the measure of internal consistency and intraclass correlation coefficient (ICC) as the reliability index of the constructed tool (60 GC and non-GC patients completed the scale within 30 days). Exploratory factor analysis (EFA) was performed by main factors analysis using Varimax rotation on a randomly selected sample of half of the GC patients (n = 78) and non-GC patients (n = 77) to assess construct validity of the scale. To include an item in EFA, the minimum factor load was assumed to be 0.3. AMOS software was used to evaluate the factor construct and to determine the goodness of fit indices (GFIs).

The scale items' response choices were considered as: not at all (1), rarely (2), sometimes (3), most of the time (4) and always (5). Some of the items were positive statements representing proven preventive impact on GC, that is, Q1, Q2, Q3, Q5, Q12 and Q16; therefore, they were reverse scored so that the higher score implied a high-risk behavioural pattern of GC. Respecting the number of composed scale's items (22), values of the respondents' total score was considered to be in the range of 22–110, with higher score reflecting a higher risk of GC.

Data analysis results for continuous variables was presented as mean (standard deviation) and for categorical variables as numbers and frequencies. Conditional logistic regression analysis was used for data analysis because of the one-to-many matched case–control design, and having a series of observations that were not independent but matched for sex and age. Conditional logistic regression is an extension of logistic regression that allows one to take into account stratification and matching in the data analysis. The data analysis was performed using R version 3.6.1 (survival package).

Results

There were 175 patients with GC in the case group: 118 (67.4%) male and 57 (32.6%) female, with a mean age of 57.03 (12.23) years and mean body mass index (BMI) of 25.72 (4.25) kg/m2. There were 350 controls: 236 (67.4%) male and 114 (32.6%) female, with a mean age of 57.03 (12.21) years and mean BMI of 24.9 (2.96) kg/m2. BMI differed significantly between the groups ($P = 0.012$). The approximated Cronbach's α 0.72 and ICC 0.99 represented acceptable internal consistency (24) and reliability of the developed scale (25) over time.

The Kaiser–Meyer–Olkin measure of sampling adequacy (0.771) and Bartlett's test of sphericity (1883.35, df = 231, $P < 0.001$) as preanalysis verification indices to perform factor analysis on the study data were in the vicinity of acceptable ranges (26).

The EFA analysis results demonstrated a 5-factor solution representing that the designed scale's items can be classified effectively into the 5 distinct constructs according to their loadings for the components that together accounted for 47.46% of the total variance (Table 1).

The identified latent components were specific nutritional behaviours, typical daily diet, routine heartburn causing behaviours or foods in diet, daily use of rice and smoked foods, and tobacco smoking and alcohol consumption (Table 2).

To verify the number of factor solutions and give a visual representation of the possible factor solutions, we analysed the scree plot (Figure 1). The plot indicated a levelling off the Eigenvalues after 5 factors were extracted. The first extracted latent variable explained a disproportionate amount of the variability in the data set. However, due to the inherent subjectivity that is involved in interpreting scree plots and considering theoretical cohesion of the other variables, the appropriate number of variables was based on the study data structure.

The prior factor structure of the GC-BRAI, which had been extracted by EFA, was also examined by confirmatory factor analysis (CFA) to verify a good data fit with the hypothesized factorial structure. CFA was conducted on a sample comprising the other half of the GC patients (n = 77) added to the randomly selected sample of non-GC patients ($n = 78$). The $\chi 2$/df ratio = 2.24 ($P < 0.05$), root mean square residual = 0.085, GFI = 0.86,

Table 1 Loadings values for the Gastric Cancer Behavioral Risk Assessment Inventory (GC-BRAI) items

Items		Latent variables				
		1	2	3	4	5
1	Did you generally eat vegetables with meals?	0.778				
2	Did you eat at least two servings of fruit daily?	0.663				
3	Did you eat nuts every day or once every few days?	0.627				
4	Did you eat nuts and fruit at night before going to bed?	0.622				
5	Did you eat soybeans?	0.542				
6	Did you eat fruits like apples and cucumbers with peel?	−0.465				
7	Did you use ready-to-eat meat products like sausage every day or once every few days?		0.742			
8	Did you routinely eat canned foods like tuna fish every day?		0.673			
9	Did you drink bottled water every day?		0.637			
10	Did you generally drink carbonated beverages with meals?		0.636			
11	Did you generally eat your meal with spicy condiments?			0.611		
12	Did you have normal bowel movement every day?			0.594		
13	Did you go to bed immediately after eating on day and/or at night?			0.531		
14	Did you generally eat pickles with meals?			0.523		
15	Did you immediately drink tea after meals?			0.424		
16	Did you routinely use Iranian rice crops in your daily diet?				0.829	
17	Did you routinely use imported rice crops in a daily diet?				0.816	
18	Did you eat smoked rice routinely?				-0.306	
19	Did you drink domestic or homemade alcoholic beverages?					0.724
20	Did you smoke every day?					0.716
21	Did you wake up at night because of heartburn?					0.491
22	Did you smoke hookah at least once every week or every two weeks?					0.491

Table 2 The latent variables' eigenvalues and percentage of explained variance for the Gastric Cancer Behavioral Risk Assessment Inventory (GC-BRAI)

Latent variables	Initial Eigenvalues	% of explained variance	% of cumulative variance
Specific nutritional behaviors	3.72	16.91	16.91
Canned and processed foods in daily diet	2.63	11.98	28.89
Routine heartburn causing behaviors or foods in diet	1.55	7.06	35.95
Daily use of rice and smoked foods	1.31	5.97	41.93
Tobacco smoking and alcohol drinking	1.21	5.52	47.46

root mean square error of approximation = 0.049) and adjusted GFI = 0.91 demonstrated an acceptable model fit with the 5-factor solution (Figure 2). The item-to-factors correlations and the observed correlations among the 5 factors (Figure 2) were significant ($P < 0.05$).

Mean scores of the GC and non-GC patients based on each single item, identified factors and total GC-BRAI scores are shown in Table 3. Except for eating fruits like apples and cucumbers with peel, the identified latent variables and total GC-BRAI scores were significantly lower in non-GC than in GC patients (Table 3). Based on the data in Figure 2 and Table 3, the following could be considered as high-risk behavioural patterns for GC: high-risk nutritional/non-nutritional habits such as eating late at night and before going to bed; not having the recommended portions of fruits and vegetables in the daily diet; frequent inclusion of processed and canned foods in the daily diet; routinely having foods or behaviours that cause heartburn; routine consumption of rice and smoked foods; and regular tobacco smoking and alcohol consumption.

Discussion

Given the lack of a common and intelligible tool for application in research and practice settings to recognize people at greater risk for GC, this study was conducted to design and appraise psychometric properties of GC-BRAI in a sample of GC and non-GC patients in the Islamic Republic of Iran. The data indicated an acceptable validity and reliability of the constructed 22-item tool with 5 dimensions. The initial conceptual factors and items were retrieved through an extensive literature search and a preliminary draft of the developed scale was verified by a panel of experts. The designed instrument confirmed an acceptable internal consistency, reliability and a good fitting measurement model. The GC-BRAI identified 5 latent variables that represented potential GC-causing high-risk lifestyle behaviour.

Figure 1 Scree plot representing the eigenvalues of the extracted variables obtained in a principal-component analysis of the Gastric Cancer Behavioral Risk Assessment Inventory (GC-BRAI).
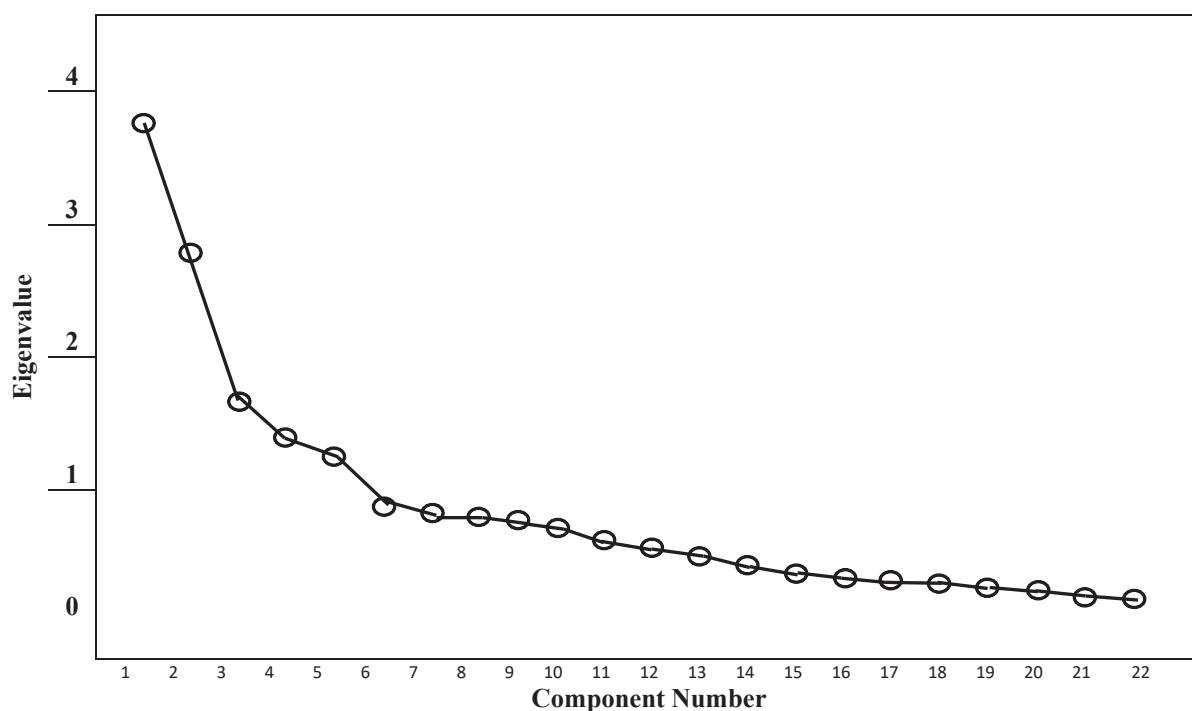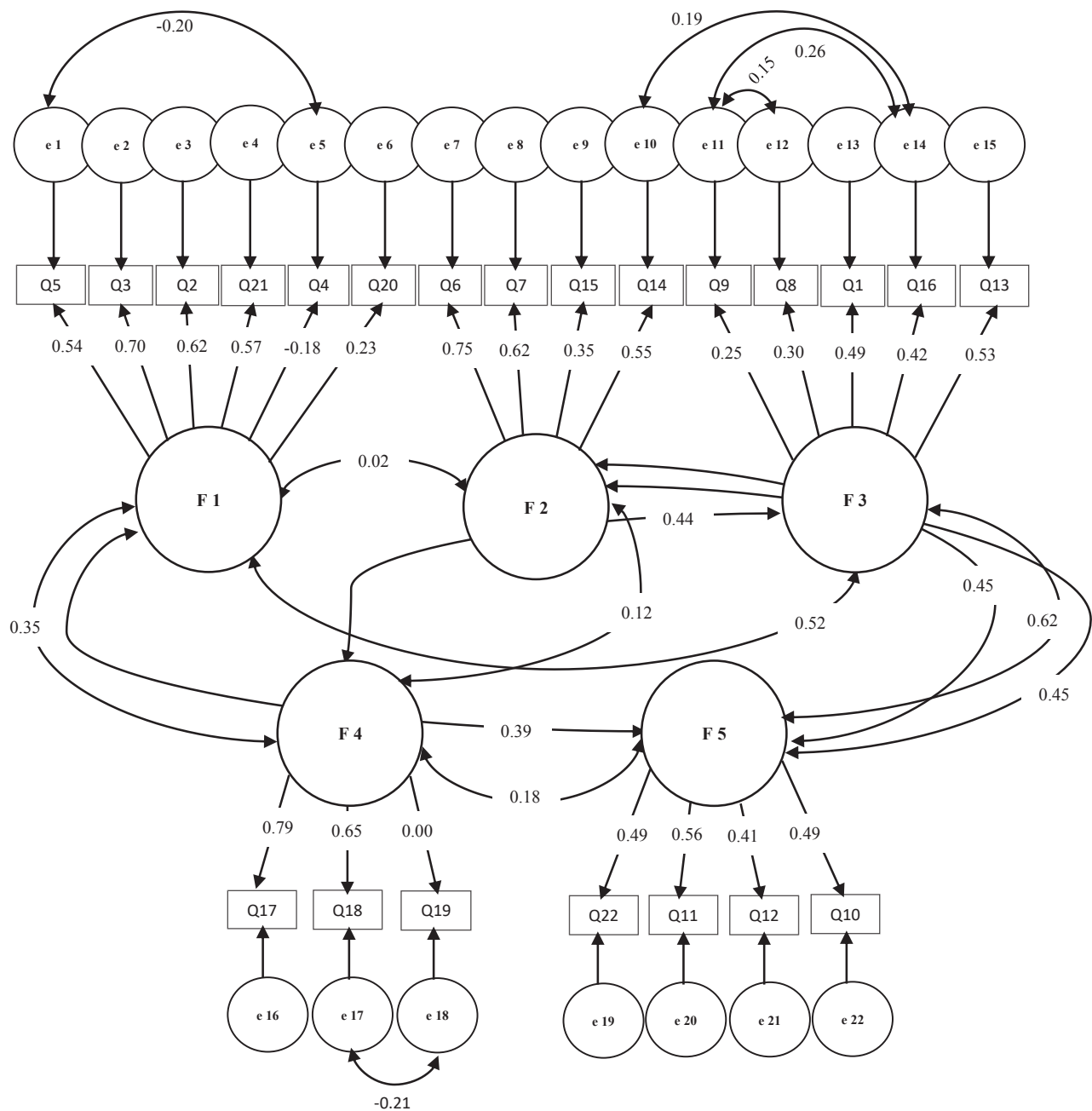
Figure 2 **The path diagram of the identified latent variables in the GC-BRAI verified by the confirmatory factor analysis model.**

F1: Specific nutritional behaviors

F2: Canned and processed foods in daily diet

F3: Routine heartburn causing behaviors or foods in diet

F4: Daily use of rice and smoked foods

F5: Tobacco smoking and alcohol drinking

Our results agree with those reported in the literature. Frequent consumption of salty food, heavy smoking and high alcohol consumption are suggested to increase the risk of GC (27–31). History of gastroesophageal reflux, low fruit and vegetable consumption, intake of nitrites in canned and processed foods, low amounts of nuts and peanut butter consumption are also reported to increase the risk of GC (32–34). All these results provided empirical support for the psychometric soundness and utility of the GC-BRAI.

GC-BRAI is a simple tool for assessing the risk profile for development of GC and could be helpful to healthcare professionals and researchers seeking to identify GC risk of their target groups. The instrument could also be used in assessment of lifestyle as a part of regular health assessment programmes and in health research to assess effectiveness of the GC-targeted interventions,

or to identify important behavioural antecedents of the disease in GC patients. In more tailored applications, GC-BRAI may be used to reveal insights into the level and components of GC risk of individuals.

We made efforts to have a diverse team of researchers in order to collect a range of opinions about the validity of the items in GC-BRAI and its cross-country applicability (35). The study sample consisted only of Iranian GC and non-GC patients, which may restrict the applicability of GC-BRAI in other cultures. Crosscultural differences in daily diet and lifestyle could cause heterogeneous variance in responses. Therefore, universal applicability of the developed tool should be considered with caution given the unrepresentativeness of our study sample. Future research may alleviate these limitations by conducting crosscultural tests of the GC-BRAI on broader and more diverse populations. Reliance on self-reported

Table 3 Mean scores for Gastric Cancer Behavioral Risk Assessment Inventory (GC-BRAI) items and latent variables among the studied GC and non-GC patients.

GC-BRAI Items		Mean (SD)		P
		GC patients (n= 175)	Non GC patients (n= 350)	
1	Did you generally eat vegetables with meals?	3.60 (1.12)	2.75 (1.17)	0.0001
2	Did you eat at least two servings of fruits daily?	3.82 (1.24)	2.75 (1.25)	0.0001
3	Did you eat nuts every day or once every few days?	4.14 (0.90)	3.46 (1.02)	0.0001
4	Did you eat nuts and fruits at nights before going to bed?	2.09 (1.15)	3.04 (1.18)	0.0001
5	Did you eat soybeans?	3.75 (0.89)	3.31 (1.16)	0.0001
6	Did you eat fruits like apples and cucumbers with peel?	3.07 (1.40)	3.18 (1.32)	0.3840
Subscale	Specific nutritional behaviours	18.41 (3.07)	15.48 (2.87)	0.0001
7	Did you use ready-to-eat meat products like sausage every day or once every few days?	2.14 (0.95)	1.73 (0.89)	0.0001
8	Did you routinely eat canned foods like tuna fish every day?	2.53 (0.98)	1.95 (0.94)	0.0001
9	Did you drink bottled water every day?	2.20 (1.11)	1.89 (1.02)	0.007
10	Did you generally drink carbonated beverages with meals?	2.78 (1.21)	2.33 (1.18)	0.0001
Subscale	Canned and processed foods in daily diet	9.66 (2.82)	7.90 (2.75)	0.0001
11	Did you generally eat your meal with spicy condiments?	3.12 (1.18)	2.28 (1.16)	0.0001
12	Did you have normal bowel movement every day?	3.05 (1.06)	3.74 (1.28)	0.0001
13	Did you go to bed immediately after eating on day and/or at night?	3.41 (1.21)	2.46 (1.23)	0.0001
14	Did you generally eat pickles with meals?	3.61 (1.09)	2.88 (1.22)	0.0001
15	Did you immediately drink tea after meals?	4.00 (1.41)	3.00 (1.36)	0.0001
Subscale	Routine heartburn causing behaviours or foods in diet	17.21 (2.96)	14.39 (2.98)	0.0001
16	Did you routinely use Iranian rice crops in your daily diet?	3.26 (1.39)	2.87 (1.31)	0.0050
17	Did you routinely use imported rice crops in a daily diet?	3.40 (1.33)	2.63 (1.33)	0.0001
18	Did you eat smoked rice routinely?	2.44 (1.30)	2.16 (1.20)	0.0170
Subscale	Daily use of rice and smoked foods	9.10 (2.47)	7.68 (2.46)	0.0001
19	Did you drink domestic or homemade alcoholic beverages?	1.29 (0.79)	1.08 (0.45)	0.0001
20	Did you smoke every day?	2.20 (1.66)	1.50 (1.20)	0.0001
21	Did you wake up at night because of heartburn?	2.61 (1.32)	1.68 (1.02)	0.0001
22	Did you smoke hookah at least once every week or every two weeks?	1.80 (1.39)	1.27 (0.78)	0.0001
Subscale	Tobacco smoking and alcohol drinking	7.90 (3.23)	5.55 (2.27)	0.0001
Total GC-BRAI score		64.32 (8.29)	54.14 (7.05)	0.0001

lifestyle behaviour could have been another source of bias in our study. Further research is recommended by adding other sources of measurement when dealing with individual GC antecedents.

Although we collected data through positively and negatively expressed questions, personal reservations to answer a specific questions, for example, about alcohol consumption or smoking, should be considered in the interpretation of the findings. The GC-BRAI items were focused on individual risk factors and probable effects of environmental factors, such as pollutants, food toxicities and psychosocial covariates, were not studied. Inclusion of these variables and examination of the possible pathways between GC and environmental and community level factors is recommended in future studies.

Conclusion

There has been a paucity of research on the behavioural risk factors for GC, which has been partially hampered by the absence of a valid tool to measure individual GC risk. Therefore, GC-BRAI could provide research evidence to be used for prevention of GC. GC-BRAI can be used to measure individual-level GC risk, which justifies its applicability in tailor-made risk reduction interventional programmes. This concise scale could help with research on GC risk assessment and ultimately contribute to prevention or early detection of the disease.

Mise au point et test psychométrique d'un inventaire d'évaluation du risque comportemental de cancer de l'estomac (Gastric Cancer Behavioural Risk Assessment Inventory, GC-BRAI)

Résumé

Contexte : Le cancer de l'estomac est l'un des cancers les plus fréquents dans le monde. Dans le contexte socioculturel iranien, il n'existe pas d'outil spécifique à la maladie pour l'évaluation du risque de cancer de l'estomac dans le cadre de la recherche et de la pratique.

Objectifs : Mettre au point et évaluer les propriétés psychométriques de l'inventaire d'évaluation du risque comportemental de cancer de l'estomac chez les patients atteints de ce type de cancer dans le nord-ouest de la République islamique d'Iran.

Méthodes : Des entretiens en présentiel ont été réalisés sur un échantillon de commodité de 175 patients atteints de cancer de l'estomac et sur un échantillon ciblé de 350 patients appariés non atteints de cancer de l'estomac comme groupe témoin. Une analyse factorielle exploratoire et une analyse factorielle confirmatoire ont été effectuées pour évaluer la validité structurale du GC-BRAI et examiner ses possibles structures latentes.

Résultats : Les résultats de l'analyse factorielle exploratoire et de l'analyse factorielle confirmatoire ont montré que le modèle à cinq facteurs avait des indices d'ajustement acceptables (χ2/degrés de liberté = 2,24, erreur quadratique moyenne d'approximation = 0,049, indice d'ajustement comparatif = 0,86, validité ajustée de l'indice d'ajustement = 0,91, validité de l'indice d'ajustement = 0,93 et résidu quadratique moyen = 0,085). Les éléments identifiés étaient les comportements nutritionnels spécifiques, le régime alimentaire quotidien typique, les comportements ou aliments courants provoquant des brûlures d'estomac, la consommation quotidienne de riz et d'aliments fumés et la consommation de tabac/alcool, qui indiquaient tous une association significative (*p*= 0,0001) avec un risque élevé de cancer de l'estomac.

Conclusions : Le GC-BRAI peut être considéré comme un outil permettant de mesurer le risque individuel lié au cancer de l'estomac et un instrument fiable de collecte de données dans des programmes interventionnels de réduction du risque personnalisés.

إعداد قائمة لتقييم المخاطر السلوكية المرتبطة بسرطان المعدة، وإخضاعها لاختبارات القياس النفسي

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الخلاصة

الخلفية: يعتبر سرطان المعدة من أكثر أنواع السرطان شيوعاً حول العالم. ولا توجد أداة خاصة بمرض معين لتقييم المخاطر المرتبطة بسرطان المعدة في مواقع البحث والممارسات في السياق الاجتماعي والثقافي الإيراني.

الأهداف: هدفت هذه الدراسة إلى تحديد وتقييم خصائص القياس النفسي لقائمة تقييم المخاطر السلوكية المرتبطة بسرطان المعدة في صفوف مرضى سرطان المعدة في شمال غرب جمهورية إيران الإسلامية.

طرق البحث: أُجريت مقابلات وجهاً لوجه مع عينة عشوائية تتكون من 175 مريضاً بسرطان المعدة، وعينة مقصودة متناسبة تتكون من 350 شخصاً غير مريض بسرطان المعدة كمجموعة مرجعية. وأجري التحليل العاملي الاستكشافي والتحليل العاملي التوكيدي لتقييم صلاحية هيكل قائمة تقييم المخاطر السلوكية المرتبطة بسرطان المعدة، واختبار تركيباته الكامنة المحتملة.

النتائج: أشارت الأداة المصممة بعاملها الخامس الكامن إلى تناسق داخلي مقبول (0.72) ، وموثوقية (0.99) ومؤشرات ملائمة (²χ / درجة الحرية = 2.24، ومتوسط الخطأ التربيعي الجذري التقريبي = 0.049، والجودة المعدَّلة لمؤشر الملاءمة = 0.91، ومتوسط الجذر التربيعي المتبقي = 0.085). وكانت المكوِّنات المحددة هي سلوكيات غذائية معيَّنة: النظام الغذائي اليومي المعتاد، والسلوكيات الروتينية أو الأطعمة في النظام الغذائي المسببة للحموضة المعوية، والاستخدام اليومي للأرز والأطعمة المدخنة، وتدخين التبغ / وتعاطي الكحول، وكلها تشير إلى ارتباط كبير (P = 0.0001) مع ارتفاع خطر الإصابة بسرطان المعدة.

الاستنتاجات: يمكن اعتبار قائمة تقييم المخاطر السلوكية المرتبطة بسرطان المعدة أداة مجدية لقياس مخاطر سرطان المعدة الفردية وأداة موثوقة لجمع البيانات في برامج التدخل المصممة خصيصاً للحد من المخاطر.

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Willingness and determinants of participation in public health research: a cross-sectional study in Saudi Arabia

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Abstract

Background: Active participation in health research plays an integral role in the development and implementation of evidence-based health interventions and policies.

Aims: To assess public willingness and determinants of participation in public health research.

Methods: A cross-sectional survey targeting Saudi residents aged > 16 years from the 13 regions of Saudi Arabia, using computer-assisted telephone interviews. We assessed the sociodemographic of participants, participants' involvement in research, their acceptance to participate, barriers hindering their participation, and their willingness to be involved in future health research. Pearson's χ^2 and logistic regression analyses were used to explore determinants.

Results: There were 2512 participants in this study. Three hundred and seventy one (14.8%) confirmed that they had been invited previously to participate in research studies and 271 (73%) accepted the invitation. The majority (92%, n = 2319) of participants were willing to participate in future research. Being a young adult, male, college-educated, and employed were the main factors associated with willingness to participate in health research. Those who had previous experience of participation in health research were 3 times more willing to participate in future health research compared with participants with no prior experience (P < 0.001).

Conclusions: This study highlighted the key determinants of willingness to participate in health research. Most participants had never been invited to participate in health research, but the majority reported a positive attitude towards participation. With rapid health system development nationally and regionally, Saudi participation levels in health research still need improvement.

Keywords: community involvement; medical research; public health; research awareness; research participation

Introduction

Active community participation in research has a positive impact on public health. Engaging community members in the research process empowers them to improve their community health (1,2). The active participation of diverse members of society in research studies ensures that the study sample is representative and the research is relevant to the needs of its target population (3). Community participation is also important for the development and implementation of evidence-based interventions and public health policy that target the community's needs (4). Moreover, public involvement in health research affects community awareness and support for science and research (5,6).

Community participation makes a valuable contribution to health research by fostering the research process and improving the generalization and enhancing the credibility of the results. Insufficient and low recruitment rates of research participants is costly because they delay study completion and increase its expense (7,8). Low research participation can lead to ineffective translation of study findings to meet the target group's needs (3). Likewise, low enrolment in research studies can lead to potential sampling bias and affect the validity of the study and generalization of the results (9,10). However, the public is still not fully aware of the value their participation in research has on enriching and improving health (9).

In Saudi Arabia, there are several challenges associated with conducting health research. One of these is associated with recruiting the target number of research participants. Most studies that investigate health issues in Saudi Arabia are small and target metropolitan cities, such as Riyadh, Jeddah and Dammam (11–15). In a Saudi national survey conducted through telephone interviews, female sample quotas in some regions were difficult to reach (16). Health and clinical studies face challenges in recruiting participants, which is due to research infrastructure, accessibility issues, and the limited number of research data resources (7,17,18).

Rapid development of the health sector and expansion of the population have increased the demand for health research (9,19). Increasing community participation and engagement in research is an integral part of the research process that contributes to health advances and improves quality of life (6,19). This study was conducted

to assess public willingness for and sociodemographic determinants of participation in public health research.

Methods

Study design

This was a self-reported cross-sectional survey conducted between July and August 2017 among Arabic-speaking Saudi residents aged > 16 years. The survey was carried out in the 13 main regions in Saudi Arabia: Riyadh, Jeddah, Abha, Hail, Tabuk, Al-Madinah, Southern Province, Aljouf, AlQassim, Najran, Jazan, Albaha, and Northern Borders. The research was reviewed and approved by the Saudi Food and Drug Authority Ethics Committee (Ethical Approval Number: 190009). Based on the nature of the research and data collected, this study was considered a minimal-to-no-risk survey and participants aged > 16 years were considered as mature minors who were able to provide informed consent to participate. Consent was obtained from all participants prior to recruitment.

Sampling and recruitment methods

Participants were approached through a computer-aided telephone interview (CATI) after a telephone number list was generated from a governmental database. The study used a convenience sampling technique, in which the sample was randomly selected from the telephone numbers without a known probability of selection. Each participant received 3 call attempts before being dropped from the list. Participants were asked via a Web-based CATI to participate in the study voluntarily and verbal informed consent was obtained from all participants. The survey took approximately 10 minutes to complete. All questions had to be answered to be submitted to the CATI database. Therefore, there were no missing data in the dataset.

Questionnaire design

After providing verbal consent, participants were asked about their sociodemographic characteristics, such as age, sex, region of residence, education and employment status. The questionnaire consisted of 4 main components. The first part assessed participants' involvement in research by asking them, "Have you been invited to participate in a scientific health research study in the past?" The second part assessed their acceptance to participate in research studies. The third part asked about barriers that might hinder their participation in research. The final part assessed participants' willingness to be involved in future health research.

Data analysis

Frequencies and percentages with 95% confidence intervals (CIs) were used for descriptive analysis. Cross tabulations with Pearson's χ^2 and logistic regression analyses were used to explore determinants of participation in research. The association was considered statistically significant if P was < 0.05. SPSS version 25 was used for analysis.

Results

A total of 2512 adults participated in this study from the 13 regions of Saudi Arabia; with a response rate of 89.71%. The median age of participants was 35 years (interquartile range 29–42 years), 1669 (66.4%) were male, and 1543 (61.4%) had a bachelor's degree (Table 1).

Only 1371 (4.8%) of the sampled population had been invited previously to participate in research studies, and 271 (73%) reported that they had agreed to participate (Table 2). Most participants (92%, n = 2320) stated that they would be willing to participate in future health research studies. The factors that hindered community participation were low awareness of community participation in research (13%, n = 13), time constraints (4%, n = 4), and absence of financial incentives (4%, n = 4). Most participants (79%, n = 79) reported other factors

Table 1 Sociodemographic characteristics of participants

Sociodemographic characteristics	Mean	Standard deviation
Age (years)	36.34	10.24
	n	*%*
Sex		
Male	1669	66.4
Female	843	33.5
Education		
High school education and below	434	17.3
Diploma education	163	6.5
Bachelor education	1543	61.4
Higher education	372	14.8
Employment		
Employed	1834	73
Unemployed	540	21.5
Student	138	5.5
Nationality		
Saudi	1529	60.8
Non Saudi	983	39.1
Regions		
Riyadh	1352	53.8
Makkah	211	8.4
Madinah	51	2.0
Qasim	35	1.4
Eastern Province	449	17.9
Asir	116	4.6
Tabuk	119	4.7
Hail	116	4.6
Northern Borders	17	0.7
Jizan	14	0.6
Najran	19	0.8
Bahah	8	0.3
Jouf	5	0.2

Table 2 **Assessment items for public participation in health research**

Categories	Levels	n	%	95% CI
Ever received an invitation to participate in health research[a]	Invited	371	14.8	13.42–16.23
	Never invited	2141	85.2	83.77–86.58
Accepted the invitation to participate in research studies[b]	Accepted	271	73	68.18–77.44
	Refused	100	27	22.56–31.82
Factors hinder participation in health research studies[c]	Time constraints	4	4.0	1.29–10.51
	Lack of awareness about research	13	13	7.38–21.56
	Absence of financial incentives	4	4.0	1.29–10.51
	Others	79	79	69.47–86.25
Willingness to participate in future health research[a]	Willing	2319	92.3	91.19–93.32
	Not willing	193	7.7	6.68–8.81

[a]n = 2512; total number of participants.

[b]n = 371; total number of participants who received an invitation.

[c]n = 100; total number of participants who refused to participate.

CI = confidence interval.

as a barrier to their willingness to participate in health research.

After controlling for other sociodemographic factors (age, sex, education and employment), those with prior experience of research, who had participated at least once in any previous health research, were approximately 3 times more likely to be willing to participate in health research compared with participants with no prior experience (95% CI: 1.57–4.95, $P < 0.001$). Those aged ≥ 36 years were less likely to have participated in health research compared with those aged < 36 years (adjusted odds ratio = 0.46, 95% CI: 0.29–0.74; $P < 0.001$) (Table 3). Male participants were more likely than female participants to be willing to participate in health research (adjusted odds ratio = 1.56, 95% CI: 1.12–2.18, $P < 0.01$). Other determinants of willingness to participate in future research were age, education and employment ($P < 0.001$, $P = 0.04$ and $P = 0.02$, respectively).

Discussion

This is one of the first studies to assess public participation in health research in the Middle East and North Africa Region. This study found that about 15% of the total participants had ever been invited to participate in previous health studies. The present level of community involvement in research needs improvement with a high demand for scientific-based health interventions and innovations in the national health system. The Saudi Vision 2030 for healthcare transformation seeks to improve public health by implementation of policies and interventions based on the recommendations of scientific research (20). This urges increased demand for community participation and involvement in health research to achieve a vibrant society and a better health system based on scientific evidence.

We showed that the majority of the study population had positive attitudes toward participation in health research, with a high rate (73%) of acceptance of participation among those who had received a previous research invitation. These findings are similar to other research conducted in the Gulf Cooperation Council countries (9,21). A study conducted in Qatar found that most of the population had never been invited to participate in research, but they reported positive attitudes towards such participation. The favourable attitude toward participation in research will enhance national and regional scientific mobility (15,17).

Despite the challenges associated with recruitment of research participants in Saudi Arabia, most of the participants in our study had a favourable attitude toward research participation. About 92% of participants reported that they would be willing to participate in future health research, which leads us to believe that public willingness is not a limiting factor for participation. Similar findings were found in other studies conducted in Middle Eastern countries that assessed community participation in health and clinical research (9,18,21,22). Some of these studies have found that prior awareness of health research is associated with willingness to participate in future research (9,18). Similarly, this study found that previous participation in health research had a positive impact on willingness to participate in future research.

Previous studies have found that there are challenges in recruiting some groups of participants for health research (9,21). The present study showed that middle-aged and older adults, women, unemployed people, and those with below college education were less likely to be willing to participate in health research. This may lead to underrepresentation of these groups and consequently biased findings in health research (4,9). Having a representative study sample reflects the sociodemographic diversity of the target population, helps strengthen external validity, and improves implementation of health research findings (4,23). Therefore, future research may study the hesitancy, barriers and motivators for participation among these groups.

We found that more male than female participants were willing to participate in health research. Low female

Table 3 Association of sociodemographic factors with public acceptance and willingness to participate in health research

Factors	Levels	n	%	P value	OR	95% CI	P value	AOR	95% CI
Acceptance to participate in health research									
Sex				0.23	1.32	0.84–2.10	0.17	1.45	0.86–2.46
Male	Accepted	149	75.6						
	Refused	48	24.4						
Female	Accepted	122	70.1						
	Refused	52	29.9						
Education				0.42	0.81	0.49–1.35	0.4	0.79	0.46–1.36
Less than college education	Accepted	85	75.9						
	Refused	27	24.1						
College education and above	Accepted	186	71.8						
	Refused	73	28.2						
Employment				0.72	0.92	0. 58–1.47	0.4	1.27	0.72–2.23
Unemployed	Accepted	114	74						
	Refused	40	26						
Employed	Accepted	157	72.4						
	Refused	60	27.6						
Age				0.002	0.48	0.30–0.76	0.001	0.46	0.290.74
≤ 36 years	Accepted	186	78.5						
	Refused	51	21.5						
≥ 36 years	Accepted	85	63.4						
	Refused	49	36.6						
Willingness to participate in future health research									
Sex				< 0.001	1.78	1.32–2.39	< 0.01	1.56	1.12–2.18
Male	Willing	1565	93.8						
	Not willing	104	6.2						
Female	Willing	754	89.4						
	Not willing	89	10.6						
Education				< 0.001	0.57	0.40–0.80	0.04	0.69	0.48–0.99
Less than college education	Willing	384	88.5						
	Not willing	50	11.5						
College education and above	Willing	1935	93.1						
	Not willing	143	6.9						
Employment				< 0.001	0.53	0.39–0.71	0.02	0.66	0.46–0.94
Unemployed	Willing	601	88.6						
	Not willing	77	11.4						
Employed	Willing	1718	93.7						
	Not willing	116	6.3						
Age				< 0.001	1.77	1.31–2.38	< 0.001	1.96	1.44–2.66
≤ 36 years	Willing	1318	94.1						
	Not willing	82	5.9						
≥ 36 years	Willing	1001	90.1						
	Not willing	111	9.9						

AOR = adjusted odds ratio; CI = confidence interval; OR = odds ratio.

participation is a global challenge that has an impact on health research (*24,25*). Male participants represented > 60% of the sample size in several studies conducted to assess different health risk factors in Saudi Arabia (*26–28*). Under-representation of women in health research can lead to undesirable and biased outcomes for the female community in the studied population (*25*). Therefore, increasing female involvement and participation in health research needs to be further investigated.

There are different factors that hinder public participation in health-related research. Offering incentives to participants has commonly been used to increase research participation (*29,30*). However, in our study, only 4% reported that the absences of incentives hindered their participation. A study conducted in Qatar and another in Kuwait found that the most frequently reported barrier to participating in research is time constraints (*9,21*). In the present study, a lack of awareness about research was the most commonly reported barrier. However, we found that factors other than time constraints, awareness about research, and financial incentives affected research participation. Most participants reported other hindrances to their participation in health research, which needs to be investigated further. It is has been reported previously that privacy issues, fear of the study, and participants' confidence in data collectors have impacts on willingness to participate in research (*4,7,31,32*). From the review of literature, participation in research can be increased if participants are contacted by a well-known and highly reputable institution, or if the study is funded by government or charities (*4,31,32*). More research is needed to assess and tackle these issues to improve public participation in health research.

Given the cross-sectional nature of this study, there was no substantial evidence to claim a temporal relationship among factors. Another limitation of this study was that the sample did not reflect the entire Saudi population; therefore, these findings cannot be generalized to the whole community. The study design and sampling method of this study might have resulted in selection bias and favoured data collection from people who had a positive attitude toward participation in research. However, given the high response rate of almost 90%, this study provides a snapshot of the public's willingness to participate in health research in Saudi Arabia. It also highlighted the key sociodemographic determinants of participation in health research. Future nationally representative studies with deeper insights into the barriers and motivators for participation are needed to understand better the predictors and determinants of participation in health research. Future research may also consider collecting data from nonrespondents to discover to what extent they are different from the study sample.

Conclusions

Public participation is an integral part of the research process that contributes to health advances. Our findings have implications at the practice level to improve participation in health research. Although reduced participation rates present challenges in conducting research, we found that participation in health research was viewed favourably by most participants. The results also highlighted the sociodemographic determinants of public participation in health research. Individuals with previous participation in health research have more favourable attitudes toward participation in future health research. With a lack of data on population health nationally and regionally, this study focused on assessing participation at the data collection level. Prospective studies and interventions are recommended to improve community participation from passive to active full engagement in research. This will ensure participants' engagement not only as data points but also to empower them to be stakeholders in planning, designing and conducting research studies.

Étude transversale en Arabie saoudite sur la volonté et les déterminants relatifs à la participation à la recherche en santé publique

Résumé

Contexte : La participation active à la recherche en santé joue un rôle essentiel dans l'élaboration et la mise en œuvre d'interventions et de politiques sanitaires reposant sur des bases factuelles.

Objectifs : Évaluer la volonté du public et les déterminants de sa participation à la recherche en santé publique.

Méthodes : Une enquête transversale ciblant des résidents saoudiens âgés de plus de 16 ans dans les 13 régions d'Arabie saoudite, a été menée au moyen d'entretiens téléphoniques assistés par ordinateur. Nous avons évalué le profil sociodémographique des participants, leur implication dans la recherche, leur acceptation d'y participer, les obstacles qui les empêchent de le faire et leur volonté de participer à une future recherche en santé. Les analyses de régression logistique et du coefficient de correlation de Pearson ont été utilisées pour explorer les déterminants.

Résultats : 2 512 personnes ont participé à cette étude. Trois cent soixante et onze personnes (14,8 %) ont confirmé avoir été préalablement invitées à participer à des études de recherche et 271 (73 %) ont accepté l'invitation. La majorité des participants (92 %, *n* = 2319) étaient prêts à contribuer à des recherches futures. Le fait d'être un jeune homme adulte, d'avoir reçu une éducation universitaire et d'avoir un emploi constituaient les principaux facteurs associés à la volonté de participer à la recherche en santé. Ceux qui avaient déjà participé à des recherches en santé étaient trois fois plus enclins à s'engager dans de futures recherches que ceux qui n'avaient aucune expérience antérieure (*p* < 0,001).

Conclusions : La présente étude a mis en évidence les principaux déterminants de la volonté de participer à la recherche en santé. La plupart des participants n'avaient jamais été invités à prendre part à la recherche en santé, mais la majorité d'entre eux ont fait état d'une attitude positive envers ce type de participation. Avec le développement rapide des systèmes de santé aux plans national et régional, les niveaux de participation saoudiens à la recherche en santé doivent encore être améliorés.

الاستعداد للمشاركة في بحوث الصحة العامة ومحدداتها: دراسة مقطعية في المملكة العربية السعودية

الجوهرة القباني، أماني القحطاني، ناصر بن دحيم

الخلاصة

الخلفية: تؤدي المشاركة النشطة في البحوث الصحية دوراً أساسياً في إعداد وتنفيذ التدخلات والسياسات الصحية المسندة بالدلائل.

الأهداف: هدفت هذه الدراسة إلى تقييم مدى استعداد الجمهور للمشاركة في بحوث الصحة العامة ومحدداتها.

طرق البحث: أجرينا مسحاً مقطعيا استهدف السكان السعوديين الذين تزيد أعمارهم على 16 عاماً في 13 منطقة بالمملكة العربية السعودية، باستخدام مقابلات هاتفية بمساعدة الحاسوب. قمنا بتقييم الحالة الاجتماعية والسكانية للمشاركين، ومشاركة المشاركين في البحوث، وقبولهم بالمشاركة، والعقبات التي تعوق مشاركتهم، واستعدادهم للمشاركة في البحوث الصحية المستقبلية. واستُخدمت تحليلات بيرسون X² والتحوُّف اللوجستي لاستكشاف المحددات.

النتائج: شارك في هذه الدراسة 2512 مشاركاً. وأكد 371 شخصاً (14.8٪) أنهم تلقوا دعوة من قبل للمشاركة في الدراسات البحثية، وقبَل 271 شخصاً (73٪) الدعوة. وكان معظم المشاركين (92٪، العدد = 2319) على استعداد للمشاركة في بحوث مستقبلية. وتمثلت العوامل اَلرئيسية المرتبطة بالاستعداد للمشاركة في البحوث الصحية في كون المشاركين من الشباب، والذكور، والحاصلين على تعليم جامعي، والموظفين. وكان أصحاب الخبرة السابقة في المشاركة في البحوث الصحية أكثر استعداداً بثلاث مرات للمشاركة في بحوث صحية مستقبلية من المشاركين الذين ليست لديهم خبرة سابقة (P<0.001).

الاستنتاجات: سلطت هذه الدراسة الضوء على المحددات الرئيسية للاستعداد للمشاركة في البحوث الصحية. ومعظم المشاركين لم تُوجَّه لهم الدعوة من قبل للمشاركة في البحوث الصحية، ومع ذلك، فقد أبدى أغلبهم موقفاً إيجابياً إزاء المشاركة. ومع التطور السريع للنُّظم الصحية على الصعيدين الوطني والإقليمي، فلا تزال مستويات المشاركة السعودية في البحوث الصحية بحاجة إلى التحسين.

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Decreasing trend in Toxoplasma seroprevalence among pregnant women in Kuwait

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Abstract

Background: Primary toxoplasmosis early in pregnancy may cause fetal pathology. Understanding and documenting serological epidemiology and associated risk factors about Toxoplasma gondii infection is crucial to offering appropriate interventions to prevent such fetal pathology.

Aims: To determine the seroepidemiological status and major risk factors associated with *T. gondii* infection among pregnant women in Kuwait.

Methods: This was an observational cross-sectional multicentre descriptive study. Blood samples and sociodemographic information were collected from 280 pregnant women attending antenatal clinics. The blood samples were screened with VIDAS Toxo-IgG/IgM and SERIONE IgG/IgM and IgG avidity assays to detect T. gondii-specific antibodies.

Results: Overall seroprevalence of *T. gondii* IgG and IgM antibodies among pregnant women was 12.5% and 2.1%, respectively. Only two IgG-positive women had low IgG avidity suggesting acute infection. No significant association was observed between seroprevalence and known risk factors for toxoplasmosis.

Conclusions: This is believed to be the first study of *T. gondii* infection and its associated risk factors among pregnant women in Kuwait. The seroprevalence rate of 12.5% is one of the lowest in the Middle East. There was no significant association between *T. gondii* seroprevalence and known risk factors. This may have been due to the high education level (>94%) among pregnant women that may have changed women's behavior during pregnany, thus minimizing transmission of toxoplasmosis.

Keywords: Kuwait, pregnant women, risk factors, seroprevalence, Toxoplasma gondii

Introduction

Toxoplasmosis is caused by an obligate intracellular opportunistic protozoan parasite, *Toxoplasma gondii*, which has a worldwide distribution, affecting about one third of the human population (*1,2*). Humans are infected by ingesting cysts from undercooked meat, or by consuming water or food contaminated with infectious oocysts (*3*). Approximately 10–15% of infected cases may develop flu-like symptoms; however, *T. gondii* may cause severe consequences in patients with supressed immune systems (*4*).

Serological testing to detect specific anti-*T. gondii* IgG and/or IgM antibodies is the first step in the diagnosis of toxoplasmosis; however, it may be difficult to distinguish between primary and chronic infection by a single test. IgG appears later than IgM and is usually detectable within 1–2 weeks after infection, reaching a peak reached within 3–6 months after acute infection, and remaining detectable throughout life. A second sample within 2–3 weeks showing a 2-fold rise in IgG titre or positive IgM indicates recent/acute infection. A recently introduced IgG avidity test can distinguish between acute and chronic infection within a window of 3 months, and thus gives more reliable information on the status of acute/ chronic infection, which is crucial for management of pregnant women.

Based on serological surveys, the incidence of primary maternal toxoplasma infection ranges from 1 to 8 per 1000 pregnancies in different populations (*5*). Generally, > 80% of pregnant women with acute primary infection do not present with any symptoms. However, the infection may be transmitted to the fetus through the placenta, causing a wide range of serious congenital conditions, especially during the first trimester (*1,6,7*). It is therefore important to detect infection early in pregnancy to prevent congenital fetal infection and minimize the risk of serious congenital conditions (*8,9*).

A number of epidemiological surveys carried out among women of childbearing age have repeatedly shown variation in the prevalence of toxoplasmosis, ranging from 7.5 to 92.5% in different parts of the world: 9–11% in the United States of America (USA) and 9.1–67% in Europe, with France being at the upper end. A decline in seroprevalence of T. gondii infection has been reported recently in the USA and some other developed countries (*10*). A high incidence of seroprevalence of up to 92.5% was reported in Ghana (*11*), but a moderate to low seroprevalence was reported in most South Asian

countries (*12*). A recent systematic review and meta-analysis showed a seroprevalence of 27.8% among Saudi women of reproductive age (*13*), while a higher prevalence of 46.2–64.3% was observed among pregnant women in Yemen (*14*). Although there is a good understanding of the risks of infection transmission among pregnant women, more detailed studies are needed to understand toxoplasmosis among the general population (*15*).

Kuwait is demographically diverse with up to 70% of the total population coming from other parts of the world. Information on the prevalence of toxoplasmosis and its associated risk factors among pregnant women in Kuwait is limited. A retrospective cohort study conducted > 10 years ago reported an incidence of 53.1% for IgG and 13.8% for IgM in Kuwait, but there was no report on the risk factors associated with toxoplasmosis (*16*). The present study aimed to determine the current seroepidemiological status of toxoplasmosis and the major risk factors among pregnant women in Kuwait.

Methods

Study design and population

This was an observational, cross-sectional, multicentre descriptive study. We used online statistical calculators to enter our values for 95% confidence interval, power (80%), margin of error (5%) and population size of 4.1 million individuals. Based on these criteria, the minimum sample size was calculated as 280 on the basis of previously reported incidence of 13.8% of active infection warranting therapeutic intervention (*16*). Kuwait is a small country with no distinction between rural and urban regions; thus, the geographical environment, sociodemographic characteristics and lifestyle of its population are similar throughout the country. Therefore, a systematic random sampling procedure was utilized to enrol pregnant women attending antenatal clinics at 3 major hospitals (Maternity Hospital, Al-Jahra Hospital and Al-Adan Hospital) in Kuwait between October 2017 and February 2019.

Sample and data collection

Venous blood (2.5 ml) was collected in a plain tube from all enrolled women and transported to the Parasitology Laboratory in the Faculty of Medicine, Kuwait University. Sera were collected from the blood and stored at -20°C in small tubes until analysis. Relevant sociodemographic characteristics and exposure to known risk factors were recorded using an approved structured questionnaire mostly with predetermined definitive closed-end answers.

Enzyme immunoassays

A series of immunoassays was carried out on the specimens to detect *T. gondii*-specific IgG and IgM and IgG avidity. All 280 blood specimens were screened for *T. gondii*-specific IgG and IgM antibodies using the recently introduced SERION ELISA classic assay (Institute Virion\Serion GmbH, Würzburg, Germany). Additionally, 100 subsamples were selected randomly and tested for IgG and IgM using VIDAS Toxo-IgG and IgM assays (bioMer-

ieux, Durham, NC, USA) to compare the performance of the SERION and VIDAS assays. All IgG-positive samples were tested for IgG avidity.

Anti-T. gondii IgG and IgM antibody detection by SERION ELISA

T. gondii IgG/IgM antibodies were measured in each blood specimen using the SERION ELISA classic assay. Optical density (OD) was analysed using the SERION software. Each test run included a substrate blank, positive, negative and two standard sera to determine precision and accuracy. The test results for IgG were interpreted as follows: $\leq$ 5 IU/ml, negative; 10–20 IU/ml, equivocal; and > 20 IU/ml, positive. The test results for IgM were interpreted as follows: $\leq$ 100 IU/ml, negative; 100–350 IU/ml, equivocal; and > 350 IU/ml, positive.

IgG avidity-ELISA detection by SERION ELISA classic

The IgG-avidity test distinguished past and newly acquired infections within a window of 3 months and thus gives reliable information on the status of acute/active infection. The test results for IgG avidity index were interpreted as follows: < 45% correlated with acute primary infection; 45–50%, borderline range; and > 50% indicated previous infection.

VIDAS Toxo-IgG, IgM and IgG avidity

Anti-*T. gondii* IgG, IgM and IgG avidity was measured using the fully automated VIDAS instrument. Anti-*T. gondii* IgG or IgM antibodies were analysed following catalysis by conjugated enzyme-labelled mouse monoclonal anti-human IgG or IgM antibodies coated on the plate. OD_{450} was measured and the results were automatically calculated by the VIDAS instrument. To determine IgG avidity, the diluted specimens were added to the VIDAS Toxo-IgG avidity test strips that contained 6 M urea to remove the low-avidity IgG antibodies from their binding sites, while the antibodies with high avidity remained bound to the solid phase. The ratio between the quantity of high-avidity antibodies (test strip) and total antibodies (reference strip) provided an index. A low avidity index < 0.2 indicated acute infection and > 0.25 excluded primary infection within the previous 16 weeks.

Statistical analysis

Data collected from all pregnant women were correlated with their corresponding OD values to determine the risk factors associated with T. gondii infection. Data were coded and analysed using SPSS version 25 software. The c2 and nonparametric tests for $\geq$ 2 independent samples, Mann–Whitney and Kruskal–Wallis tests were used to evaluate the possible differences between various diagnostic assays and risk factors. $P < 0.05$ was considered as statistically significant.

Ethical considerations

All women participating in this study gave written informed consent with strict confidentiality of their data

and test results. All women were informed of their serological status and those with acute infection were advised for immediate consultation with their attending physicians. The study was approved by the Ethical Committee for the Protection of Human Subjects in Research, Kuwait University and the Kuwaiti Ministry of Health, under reference no. 187/2014, which is in agreement with the Code of Ethics of the World Medical Association.

Results

Participant characteristics

The demographic data of all participants are presented in Table 1. Most women were aged 30–39 years (*n* = 151; 53.9%) with a median age of 31.2 years. The interquartile range (Q3–Q1)= 10.548; where (Q1 = 25.309, Q2 =31.221 and Q3 = 35.857). Most women were Kuwaiti nationals (*n* = 188; 67.1%). Most of the non-Kuwaiti women had spent ≥ 7 years in Kuwait. Most women had completed their secondary and higher education (*n* = 264; 94.3%) and 137 (48.9%) were Government employees. Two hundred and five women (73%) were multigravida and 162 (57.9%) had no history of abortion. Most women were in the third trimester (*n* = 123; 43.9%).

Prevalence of IgG and IgM antibodies

A total of 35 (12.5%) specimens were positive for IgG antibodies (Table 2). Thirteen (4.6%) gave an equivocal result and 232 (82.9%) were negative for IgG antibodies. T. gondii-specific IgM antibodies were detected in only 6 (2.1%) women who were also positive for IgG antibodies; one woman each was in the first or second trimester and 4 were in the third trimester. All 35 IgG-positive women were also screened for IgG avidity to determine their infection status. Only 2 women who were IgG+ and IgM+ showed low IgG avidity index, suggesting an acute infection rate of 5.7% among the IgG-positive women and 0.71% among all the enrolled women. Both of these women were in their third trimester. The remaining 33 women had high IgG avidity, indicating chronic infection. Twenty-one of the 35 IgG+ women (60%) and all 6 IgM+ women attended the Maternity Hospital. There was a positive correlation between IgG and IgM antibodies (r = 0.108), and a significant negative correlation between IgG/IgM antibodies and IgG avidity index; r = -0.399 and -0.400, respectively.

The sociodemographic and behavioral risk factors, obstetric and serological status of the 2 women with acute toxoplasmosis are presented in Table 3. Both women had high IgG and IgM antibody titres and low IgG avidity index status, attended the Maternity Hospital and had a history of eating uncooked meat, but their contact with cats was variable.

A total of 100 randomly selected samples were also screened with VIDAS Toxo-IgG, IgM and IgG avidity assays which were used earlier in a retrospective study conducted in Kuwait > 10 years ago (*16*). No significant difference was observed in the sensitivity and specificity of SERIONE and VIDAS assays to detect *T. gondii*-specific

Table 1 Distribution of sociodemographic characteristics for Toxoplasma gondii among pregnant women (n = 280) in Kuwait

Characteristic	No. (%)
Age group (years)	
< 20	9 (3.2)
20–29	105 (37.5)
30–39	151 (53.9)
> 40	15 (5.4)
Country of origin	
Kuwait	188 (67.1)
Gulf Countries	32 (11.4)
Africa	22 (7.9)
India	21 (7.5)
Eastern Mediterranean Region	17 (6.1)
Educational status	
Uneducated	4 (1.4)
Educated	12 (4.3)
Secondary school & above	264 (94.3)
Occupation	
Housewife	85 (30.4)
Private employee	30 (10.7)
Government employee	137 (48.9)
Other	28 (10.0)
Gravidity	
Primigravida	75 (26.8)
Multigravida	205 (73.2)
Gestational period	
First trimester	60 (21.4)
Second trimester	97 (34.6)
Third trimester	123 (43.9)
History of abortion	
No	162 (57.9)
Yes	118 (42.1)
Contact with domestic cats	
No	240 (85.7)
Yes	40 (14.3)
Consumption of undercooked meat	
No	178 (63.6)
Yes	102 (36.4)
Hand washing	
Sometimes	12 (4.3)
Yes	268 (95.7)

IgG and IgM antibodies and IgG avidity index (data not shown).

Risk factors associated with T. gondii IgG-positive pregnant women

Table 4 shows the association of major risk factors with *T. gondii* seropositivity. There was no significant association

Table 2 Seroprevalence of Toxoplasma gondii IgG and IgM antibodies among pregnant women attending antenatal clinics of 3 major hospitals in Kuwait

Hospital	Total cases screened	Seroprevalence	
		IgG (%)	IgM (%)
Maternity	98	21 (21.4%) (P = 0.004)	6.0 (6.1%)
Al-Jahra	68	6 (8.8%)	0
Al-Adan	114	8 (7.0%)	0
Total	280	35 (12.5%)	6 (2.1%)

of any particular age group with seropositivity, although 21 of 35 (60%) seropositive women were aged 30–39 years, and 11 women (31.4%) were aged 20–29 years. Similarly, no significant association was observed between seropositivity and gravidity or history of abortion. Contact with domestic cats and eating undercooked meat showed no significant association with *T. gondii* seropositivity. There was no significant association between *T. gondii* seropositivity and age, occupation and gestational age. However, the site of sample collection (Maternity Hospital) and the country/region of origin (Kuwaiti) were significantly associated with IgG seropositivity (P = 0.004 and P = 0.014, respectively).

Discussion

Understanding the seroepidemiology and associated risk factors for *T. gondii* infection among pregnant women is crucial to offer appropriate interventions to prevent congenital fetal infection. In this study, the overall seroprevalence of *T. gondii* IgG- and IgM-specific antibodies among pregnant women in Kuwait was 12.5% and 2.1%, respectively. These rates were significantly lower than the incidence of 53.1% for IgG and 13.8% for IgM reported earlier by a retrospective cohort study > 10 years ago (16), although different screening assays were used in the 2 studies. We tested 100 randomly selected samples with the SERION and VIDAS assays and there was no significant difference in their sensitivity and specificity to detect *T. gondii*-specific antibodies. Perhaps more awareness through effective health education campaigns and better hygiene may have contributed to the decreasing trend in toxoplasmosis seroprevalence among pregnant women in Kuwait. Surprisingly, the rate reported in the present study was even lower than previously reported in some neighbouring countries. A comprehensive review of seroepidemiological studies of toxoplasmosis among pregnant women in the Middle East showed a wide range of rates from 24.1% in Jazan Province, Saudi Arabia (17) to 82.6% in Beirut, Lebanon (18) (Table 5). A recent systematic review and meta-analysis of > 13 000 Saudi women of childbearing age and a meta-analysis of 43 Iranian studies among pregnant women showed an overall toxoplasmosis seroprevalence of 27.8% and 41.3%, respectively (13,19). Similarly, several prior studies in other countries across the Middle East reported higher rates of *T. gondii* seroprevalence in pregnant women and/or those of childbearing age: including 47.0% in Jordan (20), 46.2% in Yemen (14), 38.0% in Riyadh, Saudi Arabia (8), 35.1% in Qatar (21) and 33.7% in Egypt (22).

This variation in prevalence between countries within a region may be attributed to differences in socioeconomic status, geographic conditions and hygienic practices. Currently, the seroprevalence and potential risk factors for *T. gondii* infection are not fully understood. Therefore,

Table 3 Sociodemographic and behavioral risk factors, obstetric and serological status of 2 women with acute Toxoplasma gondii infection

Factors	Case 1	Case 2
Sociodemographic factors		
Age	23 years	27 years
Nationality	Lebanese	Armenian
Resident in Kuwait	> 10 years	> 7 years
Education status	High school	High school
Obstetric history		
Gestational age	Third trimester	Third trimester
Gravity	Primigravida	Primigravida
History of abortion	Yes	No
Behavioral factors		
Contact with domestic cats	Yes	No
Eating undercooked meat	Yes	Yes
Hand washing	Yes	Yes
Serological status		
IgG	137.065 IU/ml (2.094)	95.497 IU/ml (1.187)
IgM	1205.252 IU/ml	2347.776 IU/ml
IgG avidity status	Low, 32%	Low, 43%

OD_{450} = optical density at 450 nm.

Table 4 Nonparametric analysis of risk factors associated with Toxoplasma gondii IgG seropositivity among pregnant women (n = 280) in Kuwait

Variables	Positive (n = 35)	Negative (n = 245)	P
	n (%)	n (%)	
Age groups (years)			
< 20	0	9 (100)	
20–29	11 (10.5)	94 (89.5)	0.290
30–39	21 (13.9)	130 (86.1)	
> 40	3 (20.0)	12 (80.0)	
Nationality			
Kuwaiti	16 (8.5)	171 (91.5)	0.014 *
Non-Kuwaiti	19 (20.4)	74 (79.6)	
Gravidity			
Primigravida	10 (13.3)	65 (86.7)	0.799
Multigravida	25 (12.2)	180 (87.8)	
History of abortion			
No	17 (10.5)	145 (89.5)	0.234
Yes	18 (15.3)	100 (84.7)	
Contact with domestic cats			
No	31 (12.9)	209 (87.1)	0.606
Yes	4 (10.0)	36 (90.0)	
Eating undercooked meat			
No	25 (14.0)	153 (86.0)	0.302
Yes	10 (9.8)	92 (90.2)	
Hand washing			
Sometimes	3 (25.0)	9 (75.0)	0.178
Yes	32 (11.9)	236 (88.1)	

Significant risk factor for T. gondii infection.

understanding the variation in prevalence of *T. gondii* infection in a geographically close area, like the Gulf Region, is important for infection prevention and control.

In this study, seropositivity to toxoplasmosis started in women aged 20–29 years (31.4%), increased to 60% at age 30–39 years, and then decreased among those aged > 40 years. However, there was no significant association between seroprevalence and the older age group. In contrast to the current study, a number of studies from various regions and a recent review of studies documenting potential risk factors related to seroepidemiological status of *T. gondii* infection in several Arab and African countries showed a significant association between *T. gondii* seropositivity and ageing (*17,23–25*). The possible reason for this association is still not clear. In countries with moderate to high endemicity, lack of awareness of potential risk factors may predispose older people to toxoplasmosis and they then usually maintain a steady level of anti-*T. gondii* antibodies throughout life. However, in this study, we detected a low level of seropositivity (12.5%) to toxoplasmosis and little or no exposure to risk factors. Therefore, it was not surprising to detect lower seropositivity among pregnant women in the older age group.

Additionally, other risk factors associated with toxoplasmosis (i.e., area of residence, contact with domestic cats, cultural practices and economic status) have been reported in previous studies. A systematic review and meta-analysis reported a significant association between toxoplasmosis and age, contact with cats and gestational age among Iranian women of child bearing age (*26*). However, we did not find a significant association between toxoplasmosis and most of these known risk factors. In agreement with our study, several studies have reported no significant association between toxoplasmosis and all or some of the reported risk factors (*13,27,28*). This may be because of similar geographical environment and sociodemographic charactersitics, and particular lifestyles, culture and traditions prevailing in this part of the world.

We did not find evidence of any specific control measures or health education campaigns by health officials in Kuwait to prevent transmission of *T. gondii*. However, we believe that several factors may have been responsible for the current decreasing trend of toxoplasmosis seroprevalence in Kuwait. Kuwait is a small country with an economically affluent society and well-organized, highly developed infrastructure

Table 5 Seroprevalence of Toxoplasma gondii IgG and IgM antibodies among pregnant women in the Eastern Mediterranean Region

Country	No. of cases	IgG positivity n (%)	IgM positivity n (%)	Assay	Refs
Riyadh, Saudi Arabia	2176	825 (38.0)	NA	ELISA	(8)
Saudi Arabia	13 597	(27.8)[a]	NA	ELISA	(13)
Taiz, Yemen	359	166 (46.2)	12 (3.3)	ELISA	(14)
Jazan, Saudi Arabia	195	39 (20.1)	12 (6.2)	ELISA	(17)
Beirut, Lebanon	2456	2029 (82.6)	46 (1.8)	ELISA	(18)
Islamic Republic of Iran[b]	22 644	(41.3)	(4.0)	ELISA	(19)
Jordan	280	133 (47.0)	NA	IFA	(20)
Qatar	823	289 (35.1)	43 (5.2)	ELISA	(21)
Egypt	364	(33.7)	NA	ELISA	(22)
Hebron, Palestine	204	57 (27.9)	36 (17.6)	EIA	(28)
Kuwait	224	119 (53.1)	31 (13.8)	VIDAS	(16)
Kuwait	280	35 (12.5)	6 (2.1)	VIDAS ELISA	This study

[a]Pooled estimation for T. gondii prevalence using a systematic review and meta-analysis of 20 studies.

[b]Pooled estimation for T. gondii prevalence using systematic review and meta-analysis of 43 studies.

IFA = immunofluorescence assay; NA = not available.

and health facilities throughout the country, providing timely diagnosis and treatment. Importantly, > 94% of the pregnant women in this study had a higher education level that may have changed their behavior during pregnany, thus minimizing transmission of *T. gondii*. A recent multicentre survey on toxoplasmosis among pregnant women in Poland showed that higher education level was significantly associated with better knowledge of toxoplasmosis (29).

There were limitations to our study and other confounding factors in comparing our results with other studies, including small sample size, and differences in assay systems and demographic characteristics. We enrolled a small sample of 280 pregnant women and their demographic characteristics may partially explain the disparity with the prevalence rate of 53.1% reported in 2002–2003. However, we believe that differences in assay systems and location of the study population do not account for significant differences in the seropositivity rate between the 2 studies. There was no significant difference in the sensitivity and specificity of SERION and VIDAS assays when testing 100 blood samples.

Furthermore, compared with the earlier study, 92 non-Kuwaiti pregnant women were enrolled in our study but > 83% of these women had been residing in Kuwait for > 7 years. Additionally, the sociodemographic characteristics and lifestyle of the population of Kuwait are similar throughout the country.

Conclusion

We detected a significantly lower *T. gondii* seroprevalence rate of 12.5% among pregnant women in Kuwait compared with 53.1% reported > 10 years ago. This overall seroprevalence rate is one of the lowest among pregnant women in the Middle East. We did not find a significant association between *T. gondii* seroprevalence and the known risk factors. However, a higher education level among pregnant women (> 94%) may have changed women's behavior during pregnany, thus minimizing transmission of infection. This study is important because it is believed to be the first to study the characteristics of *T. gondii*-seropositive pregnant women in Kuwait. Further surveys are needed to investigate the factors related to the decreasing trend of *T. gondii* seropositivity in Kuwait.

Acknowledgement

Tendance à la baisse de la séroprévalence de la toxoplasmose chez les femmes enceintes au Koweït

Résumé

Contexte : La toxoplasmose primaire au début de la grossesse peut provoquer une pathologie fœtale. Il est essentiel de comprendre et de documenter l'épidémiologie sérologique et les facteurs de risque associés à l'infection à *Toxoplasma gondii* afin de pouvoir proposer des interventions appropriées pour prévenir ladite pathologie fœtale.

Objectifs : Déterminer le statut séroépidémiologique et les principaux facteurs de risque associés à l'infection à *T. gondii* chez les femmes enceintes au Koweït.

Méthodes : Il s'agissait d'une étude observationnelle transversale, multicentrique et descriptive. Des échantillons de sang et des informations socio-démographiques ont été recueillis auprès de 280 femmes enceintes consultant dans les dispensaires de soins prénatals. Les échantillons de sang ont été analysés au moyen des tests d'avidité VIDAS Toxo-IgG/IgM et SERIONE IgG/IgM et IgG pour détecter les anticorps spécifiques de *T. gondii*.

Résultats : La séroprévalence globale des anticorps de la classe des IgG et IgM de *T. gondii* chez la femme enceinte était respectivement de 12,5 % et 2,1 %. Seules deux femmes positives pour les IgG avaient une faible avidité des IgG évoquant la présence d'une infection aiguë. Aucune association significative n'a été observée entre la séroprévalence et les facteurs de risque connus de toxoplasmose.

Conclusions : Il s'agit apparemment de la première étude sur l'infection à *T. gondii* et ses facteurs de risque associés chez les femmes enceintes au Koweït. Le taux de séroprévalence de 12,5 % est l'un des plus faibles au Moyen-Orient. Il n'y avait pas d'association significative entre la séroprévalence de *T. gondii* et les facteurs de risque connus. Cela peut être dû au niveau d'éducation élevé (supérieure à 94 %) chez les femmes enceintes, qui peut avoir modifié le comportement des femmes pendant la grossesse, minimisant ainsi la transmission de la toxoplasmose.

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اتجاه تنازلي لحالات الانتشار المصلي للمقوسة في صفوف النساء الحوامل في الكويت

نورا الشمري، جمشيد إقبال

الخلاصة

الخلفية: قد تسبب الإصابة بداء المقوسات الأوَّلي في وقت مبكر من الحمل أمراضاً للجنين. وتمسُّ الحاجة إلى فهم وتوثيق الخصائص الوبائية المصلية وعوامل الخطر المرتبطة بعدوى المقوسة الجوندية لتقديم التدخلات المناسبة للوقاية من مثل تلك الأمراض التي تصيب الأجنة.

الأهداف: هدفت هذه الدراسة إلى تحديد الحالة المصلية الوبائية وعوامل الخطر الرئيسية المرتبطة بعدوى المقوسة الجوندية في صفوف النساء الحوامل في الكويت.

طرق البحث: هذه دراسة رصدية مقطعية متعددة المراكز. حيث أُخذت عينات الدم والمعلومات الاجتماعية والسكانية من 280 امرأة حاملاً من اللواتي يراجعن عيادات الرعاية السابقة للولادة. كما تم تحري عينات الدم باستخدام مقايسات VIDAS للأجسام المضادة IgM /IgG–Toxo وكذلك مقايسات SERIONE للأجسام المضادة IgG /IgM/IgG avidity للكشف عن الأجسام المضادة المحددة للمقوسة الجوندية.

النتائج: كان الانتشار المصلي الكلي لـ IgG, IgM للمقوسة الجوندية في صفوف النساء الحوامل 12.5 ٪ و 2.1 ٪ على التوالي. وكانت هناك امرأتان إيجابيتيْن لـ IgG للأجسام المضادة من مجموعة IgG لديها انخفاض في الرغابة المناعية للأجسام المضادة من مجموعة IgG، مما يشير إلى وجود عدوى حادة. ولم يُلاحظ وجود ارتباط ذي دلالة بين الانتشار المصلي وعوامل الخطر المعروفة لداء المقوسات.

الاستنتاجات: يُعتقد أن هذه هي الدراسة الأولى لعدوى المقوسة الجوندية وعوامل الخطر المرتبطة بها في صفوف النساء الحوامل في الكويت. ويُعدُّ معدل الانتشار المصلي البالغ 12.5 ٪ من أدنى المعدلات في الشرق الأوسط. ولم يكن هناك ارتباط يُعتد به بين معدل الانتشار المصلي للمقوسة الجوندية وعوامل الخطر المعروفة. وقد يُعزى ذلك إلى ارتفاع المستوى التعليمي (أكثر من 94 ٪) في صفوف النساء الحوامل، وهو ما يُرجح أن يكون قد غيَّر من سلوك النساء أثناء الحمل، وقلل بذلك من سريان داء المقوسات إلى الحد الأدنى.

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Estimated and projected prevalence of tobacco smoking in males, Eastern Mediterranean Region, 2000–2025

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Abstract

Background: Three global reports published by the World Health Organization (WHO) report trends in the prevalence of tobacco smoking from 2000 to 2025 based on data from national surveys.

Aims: The is study aimed to: (i) compare current and projected prevalence rates of tobacco smoking presented in these reports for males ≥ 15 years in countries of the Eastern Mediterranean Region; and (ii) assess changes in the prevalence rates in the context of changes in tobacco monitoring and control policies in these countries.

Methods: Regional and country-level data on tobacco smoking were extracted from the trend reports. Percentage point differences between the estimated prevalence of tobacco smoking in 2010 and the projected prevalence in 2025 were calculated for countries with available data. Data on implementation of national surveys and policies on tobacco use were obtained from relevant WHO reports.

Results: In the latest trend report (2019), the prevalence of male current tobacco smoking is projected to decrease by less than 2 percentage points in the Region (from 33.1% in 2010 to 31.2% in 2025). The projections for male tobacco smoking for 2025 in the 2019 report are more encouraging than in the 2015 report in seven of the eight countries of the Region. For five of these seven countries, implementation of tobacco monitoring and tobacco control policies improved over the same period.

Conclusions: Countries of the Region need to conduct additional national tobacco-use surveys to improve the accuracy of prevalence estimates and projections. Such data can help guide policy-makers to implement policies to control tobacco smoking.

Key words: tobacco smoking, prevalence, male, Eastern Mediterranean Region

Introduction

Tobacco is one of the leading preventable causes of morbidity and premature mortality in the world and contributed to 8 million deaths globally in 2017 *(1)*. About 80% of these deaths occurred in developing countries. In 2013, the World Health Assembly endorsed the World Health Organization's (WHO) Global Monitoring Framework for Noncommunicable Diseases (NCDs) and an associated voluntary global target of a 30% relative reduction in tobacco use worldwide in people aged 15 years and older by 2025 (with 2010 levels as the baseline) *(2)*.

Updated data on tobacco use are necessary to identify key gaps in policies on tobacco control. To overcome this challenge, WHO and the US Centers for Disease Control and Prevention have developed a number of surveys designed to track tobacco use among young people (13–15 years) and adults for implementation at the country level *(3)*. These surveys include the global youth tobacco survey, global adult tobacco survey and STEPwise surveillance of NCD risk factors survey.

WHO published three global reports, in 2015, 2018 and 2019 *(4–6)*, that track trends in the prevalence of tobacco smoking from 2000 to 2025 based on data from national surveys. These WHO trend reports are companions to the two-yearly WHO report on the global tobacco epidemic *(7)*. This two-yearly report provides the opportunity to compare developments in tobacco control policies with the prevalence projections given in the trend reports.

We aimed to review and compare regional and country projections on the prevalence of current tobacco smoking given in the WHO trend reports. We highlight how the projected prevalence of tobacco smoking in the WHO Eastern Mediterranean Region has changed over time and in the context of globally recognized targets for reduction in tobacco use. We consider the data from the trend reports in the context of the implementation of country-level surveillance systems and the implementation of national tobacco control policies. This approach provides a relevant and detailed insight into current and future tobacco smoking in the Region and the likely effect of improved monitoring efforts and policy changes on projected prevalence rates. It also allows specific recommendations to be made for both future tobacco use surveillance systems and tobacco control policy-making.

Methods

The three WHO trends reports contain globally comparable national estimates for tobacco smoking prevalence for the years 2000–2025. In these reports these estimates are summarized into global and regional prevalence estimates and projections. For the projection analysis, the reports use data from nationally representative surveys of tobacco use (or tobacco smoking) published since 1990. The full details of the method for producing trend estimates and projections is described in the trend reports themselves *(4–6)*. In the 2015 trend report, eight countries of the Region had sufficient survey data for projections to be made. In the 2018 and 2019 trend reports, 14 countries had sufficient data for projections to be made.

We focused on tobacco smoking because it is the indicator used in all three trend reports (unlike tobacco use). Tobacco smoking is also by far the most common form of tobacco use in the Region *(6)*. We calculated the projected percentage point increases in tobacco smoking between 2000 and 2025 for the Region overall by sex, and by country for males. We only reviewed current male tobacco smoking because male smokers make up most smokers in the Region *(6)* and some concerns exist about the reliability of data for current female tobacco smoking. In all cases, we calculated the projected percentage point increase for current tobacco smoking between 2000 and 2025 by subtracting the estimated current tobacco smoking prevalence in 2000 from the projected prevalence in 2025. We compared country-level results from the 2015 and 2019 trend reports to assess changes between the reports in the projected percentage point increase for current male tobacco smoking between 2000 and 2025.

We assessed changes between the 2015 and 2019 reports in country-level projected percentage point increases for current male tobacco smoking and the extent to which tobacco use was monitored nationally. We obtained data on implementation of national tobacco surveys from the WHO Report on the Global Tobacco Epidemic and the trend reports *(4,6,7)*. We also assessed changes in national tobacco control policies between 2015 and 2019. We obtained information on these policy changes from the WHO reports on the global tobacco epidemic for 2015 and 2019. We used progress in the implementation of any WHO "demand-reduction" MPOWER measure as the metric: protect people from tobacco smoke; offer help to quit tobacco use; warn about the dangers of tobacco; enforce bans on tobacco advertising, promotion and sponsorship; and raise taxes on tobacco *(7,8)*. The demand-reduction MPOWER measures are the five policy recommendations included in the WHO MPOWER package that have been shown to reduce the prevalence of tobacco use when implemented (i.e. all of the MPOWER measures except the monitoring measure) *(7)*.

Results

In the latest trend report of 2019 *(6)*, decreases in overall tobacco smoking rates are projected in all WHO Regions. The smallest decrease is expected in the Eastern Mediterranean Region, where the overall tobacco smoking prevalence is projected to drop from 18.3% in 2010 to 16.3% in 2025, if current tobacco control efforts continue. This equates to an 11% relative reduction in overall tobacco smoking prevalence. For men, who make up most of all smokers in the Region, the prevalence of current tobacco smoking is projected to decrease by less than 2 percentage points from 33.1% in 2010 to 31.2% in 2025.

Unlike the 2019 trend report, both the 2015 and 2018 reports projected an increase in overall tobacco smoking prevalence in the Eastern Mediterranean Region between 2010 and 2025 (of 5 percentage points in the 2015 report and less than 1 percentage point in the 2019 report) *(4,5)*. All three WHO trend reports projected that the Region was unlikely to achieve a 30% relative reduction in the prevalence of tobacco smoking by the year 2025 *(4–6)*.

For country-level projections of the prevalence of male current tobacco smoking in the 2015 trend report (Table 1), the rates in all but one country were projected to increase in percentage points between 2000 and 2025. This ranged from 9.9 percentage points in Pakistan to 68.8 percentage points in Bahrain. Only in the Islamic Republic of Iran was the prevalence tobacco smoking projected to decrease, by 8.2 percentage points.

For country-level projections of the prevalence of male current tobacco smoking in the 2019 trend report (Table 2), the rates in four countries were projected to increase in percentage point terms (Egypt, Lebanon, Oman and Saudi Arabia). All of these increases were less than 4 percentage points, with the highest increase projected for Oman (3.7 percentage points). The prevalence rates in the remaining 10 countries were projected to decrease. These ranged from a decrease of 2.1 percentage points for Bahrain to a decrease of 27.4 percentage points for Tunisia.

Of the eight countries for which trend projections were calculated in both reports (Bahrain, Egypt, Islamic Republic of Iran, Lebanon, Morocco, Oman, Pakistan and Saudi Arabia), all but one country (Islamic Republic of Iran) saw a decline in the projected percentage point increase for current male tobacco smoking between 2000 and 2025 (Table 1 and Table 2). For three of these seven countries, this decline in the projected increase between 2000 and 2025 was enough to take the country from a projected increase in the prevalence of current male tobacco smoking in the 2015 trend report to a projected decrease in the 2019 report. For the remaining four countries, the prevalence of current male tobacco smoking was still projected to increase in percentage points between 2000 and 2025 in the 2019 report, but to a lesser extent than in the 2015 report.

Of the six countries for which the projection was only done in the 2019 report, all were projected to see a percentage point decrease in the prevalence of current male tobacco smoking between 2000 and 2025.

Over the same period as the three trend reports (2015–

Table 1 Estimated and projected tobacco smoking among males ≥ 15 years in the WHO Eastern Mediterranean Region, by country, 2000 and 2025

Country [a]	Estimated prevalence of tobacco smoking in males, 2000 (%)	Projected prevalence of tobacco smoking in males, 2025 (%)	Absolute percentage point difference [b]
Bahrain	18.4	87.2	68.8
Egypt	34.2	62.9	28.7
Islamic Republic of Iran	26.7	18.5	−8.2
Lebanon	34.4	57.1	22.7
Morocco	34.0	57.6	23.6
Oman	12.8	33.3	20.5
Pakistan	35.2	45.1	9.9
Saudi Arabia	21.1	36.1	15.0

[a]*Other countries of the Region were either not included in the report because their profiles were yet to be finalized (Djibouti, Jordan, Qatar, Syrian Arab Republic, Tunisia, United Arab Emirates), or no data were available.*

[b]*A negative value indicates a projected decrease in the prevalence between 2000 and 2025.*

Source: WHO trend report, 2015 (4).

2019), country-level tobacco use surveys and surveillance systems have been implemented in several countries of the Region. As noted above, the projection was done for six more countries in the 2018 and 2019 trend reports than in the 2015 report *(4–6)*. This increase indicates that many more countries now have more robust data on tobacco use and smoking, of the kind that allows useful trend projections to be calculated.

Of the countries for which the projected percentage point increase in the prevalence of tobacco smoking in males between 2000 and 2025 decreased between the 2015 and 2019 trend reports (as described above), the number of national surveys on adult smoking since 2000, which are used to calculate country-specific trends, increased in five of these countries: Egypt (from five to six surveys), Lebanon (from four to five), Morocco (from four to five), Oman (from two to three) and Pakistan (from three to five) *(4,6,7)*. The number of such surveys stayed the same in Bahrain and Saudi Arabia.

Of the seven countries for which the projected percentage point increase in the prevalence of smoking in males between 2000 and 2025 decreased between the 2015 and 2019 trend reports (as described above), five improved their performance for at least one of the five "demand-reduction" MPOWER measures between 2015 and 2019 *(7,8)*. Bahrain and Pakistan improved their performance for one measure each, Egypt and Oman improved their performance for two measures each and Saudi Arabia improved its performance for four measures.

Discussion

In seven countries of the Eastern Mediterranean Region, the 2019 trend report show more encouraging projections to 2025 for the prevalence of current male tobacco smoking compared with the 2015 trend report. It is reasonable to suppose that this improved outlook is at least in part due to improved monitoring which provides a more accurate picture of actual current tobacco use. The cut-off points for national tobacco surveys used as data points by

the 2015 and 2019 trend reports (the years 2014 and 2018, respectively) differed by only about 4 years, making it unlikely that policy change was solely responsible for the reduction actual tobacco use.

Nevertheless, considering changes in the country-level projections in the 2015 and 2019 trend reports in the context of implementation of tobacco control policies is still important. It is likely that for many of the countries that have more encouraging projections in the 2019 trend report than in the 2015 report, their improved tobacco control policies have played a key role, including in Bahrain, Egypt, Oman, Pakistan and Saudi Arabia. In general, many countries moved forward with MPOWER policy strengthening between 2015 and 2019, including for the monitoring measure *(7,8)*.

Despite this progress, a number of countries have not achieved any legal policy improvement since the publication of the 2015 trend report and the 2015 edition of the WHO Report on the Global Tobacco Epidemic *(7,8)*. These countries include some that have more encouraging projections in the 2019 trend report than the 2015 report; as noted above, this is likely due to improvements in monitoring. Other countries in the Region have moved backwards with respect to key tobacco control policies since 2015 or have implemented only moderate policy changes, such as banning tobacco use in some, but not all, public places, which are substantially less likely to have an effect on reducing the prevalence of tobacco smoking *(7)*.

The above situation and the fact that none of the countries in the Region, except one (Islamic Republic of Iran), is projected to achieve the target of a 30% relative reduction in tobacco use by 2025 *(6)* are symptoms of the following factors. First, a steady and systematic approach to moving forward with tobacco control across the Region as a whole is lacking *(9)*, and countries regularly make retrogressive changes to their tobacco control policies, even while other positive policy changes are being made

Table 2 Estimated and projected tobacco smoking among males ≥ 15 years in the WHO Eastern Mediterranean Region, by country, 2000 and 2025

Country [a]	Estimated current male tobacco smoking, 2000 (%)	Projected current male tobacco smoking, 2025 (%)	Absolute percentage point difference [a]
Bahrain	36.6	34.5	−2.1
Egypt	40.3	42.6	2.3
Islamic Republic of Iran	25.9	18.3	−7.6
Iraq	38.1	33.5	−4.6
Kuwait	41.0	36.7	−4.3
Lebanon	40.2	41.4	1.2
Morocco	39.0	23.4	−15.6
Oman	13.6	17.3	3.7
Pakistan	37.2	27.6	−9.6
Qatar	26.2	23.9	−2.3
Saudi Arabia	23.3	25.4	2.1
Tunisia	64.2	36.8	−27.4
United Arab Emirates	35.7	28.5	−7.2
Yemen	35.5	24	−11.5

[a]Other countries of the Region were excluded because no data were available.
[a]A negative value indicates a projected decrease in prevalence between 2000 and 2025.
Source: WHO trend report, 2019 (6).

(7,10). Second, in many cases a multisectoral approach is missing (2). Third, a comprehensive approach to tobacco control is often lacking, with policy-makers selecting certain policies to implement and not others, which is not effective in reducing the prevalence of smoking (11). Fourth, the humanitarian emergencies in many countries of the Region are affecting progress across the whole Region, as recently indicated in a report of the WHO Framework Convention on Tobacco Control (FCTC) to the FCTC Conference of Parties (12). Individually, these countries are unable to move forward in tobacco control and they also make it harder for other countries in the Region to continue to improve.

As outlined in the trend results, considerable gender differences in tobacco smoking exist in the Region. Research suggests that this difference is attributable to the social stigma attached to smoking among women in countries of the Region (13). The standardized survey methods call for family visits to collect data on smoking behaviour. In the presence of male members of the family, women may be reluctant to reveal their true smoking behaviour and are therefore more likely to underreport smoking than their male counterparts because of sociocultural factors (14).

The prevalence of smoking among adolescent women is notably higher than among adult women (15). This difference could be the result of less underreporting by this younger population because of increased openness about smoking (14). It could also reflect some bias related to the fact that adolescent girls who are not in school are excluded from the school-based surveys. Another reason for the difference may be the relative anonymity of the data collection process among the adolescent population. Respondents of adult surveys, where data are typically collected in the home, may feel anonymity is less assured. The prevalence of smoking of all types of tobacco products among young people in the Region can reach 42% in boys and 31% in girls (15). These rates include waterpipe smoking, which is in fact more popular among young people than cigarettes (15).

External factors such as religious beliefs might also play an important role in influencing smoking behaviour in the Region. However, the effect of such factors on tobacco use has not been sufficiently studied (16).

Our study has some limitations. Of all WHO Regions, the Eastern Mediterranean Region has the lowest level of coverage of national surveys that monitor smoking. Since 2013, only 15 of the 22 countries of the Region have completed a nationally representative survey of adults that measures some form of tobacco use, and made these results public (6). Three countries (Afghanistan, Libya and Sudan) have no results in the WHO trend reports because they have done only one survey to date, while at least two surveys are needed to calculate a trend. Somalia is among the six countries globally that have produced no nationally representative data on tobacco use among adults (5).

Other indicators of tobacco use, such as smokeless tobacco use, waterpipe use and cigarette use by children aged 13–15 years, were not projected in the trend reports. Despite the fact that Parties to the WHO are required to monitor all forms of tobacco use, some have technical and logistic problems in implementing the recommended surveys. Of the 181 Parties to the FCTC, only 76 countries regularly monitor all types of tobacco use in both their

adult and child populations, which accounts for only 40% of the world's population (5). Data on the use of electronic nicotine delivery systems, including electronic cigarettes, are just beginning to be collected.

The reliance of all tobacco use surveys on self-reporting of tobacco use is another limitation, especially if various cultural factors make it likely that tobacco use is underreported. According to one study that compared estimates of the prevalence of smoking produced from self-reported data against the estimates based on measured smoking biomarkers, self-reported smoking often results in underreporting, so much so that the true smoking figures can be underestimated by up to 47% (17).

Recommendations

Compared to a high (≥ 95%) probability of a decline in smoking prevalence for most countries in the American, European and Western Pacific regions of WHO for both men and women, the possibility of an increase in prevalence of smoking in the Eastern Mediterranean Region is high, especially among men (6). With the uncertain decline of smoking rates in the Region, and the slow pace of implementation of tobacco control measures in many countries, the economic burden attributed to tobacco-related diseases could increase (18). This situation will in turn prevent most countries in the Region from achieving a 30% reduction in tobacco use by 2025 and undermine attempts to progress the goals of universal health coverage (19). Continued monitoring is essential to inform and sensitize decision-makers from the Region about this public

health epidemic, the socioeconomic burdens caused by tobacco use, and the growing use among young people and females that had not been anticipated (18).

Incomplete data is one of the greatest challenges; some countries of the Region have not conducted a national survey for over a decade. In addition, some surveys do not provide sufficient detail, such as tobacco use by age. Efforts to monitor tobacco use with cost-effective solutions should be considered, such as inclusion of tobacco questions within other surveys that countries already implement (20).

Solutions to the problem of underreporting could include ensuring respondents have privacy when completing the survey. Another solution would be to manually identify individuals who are likely to have misreported, such as women during pregnancy, and ignore or correct their testimony, e.g. by identifying current smoking using cotinine blood tests or exhaled breath carbon monoxide monitors (21). Governments should take underreporting into consideration in their policy-making as long as it continues.

Data on the nature and scale of the tobacco epidemic should be used to implement targeted and effective policies to reduce its use, including the "demand-reduction" MPOWER measures (7). All countries of the Region could do more to strengthen and improve implementation of these proven measures.

Estimations et projections de la prévalence du tabagisme chez les hommes dans la Région de la Méditerranée orientale pour la période 2000-2025

Résumé

Contexte : Trois rapports mondiaux publiés par l'Organisation mondiale de la Santé (OMS) rendent compte des tendances en matière de prévalence du tabagisme entre 2000 et 2025 sur la base de données issues d'enquêtes nationales.

Objectifs : L'étude a pour objectifs : i) de comparer les taux de prévalence actuels et prévus du tabagisme présentés dans ces rapports pour les hommes âgés de 15 ans et plus dans les pays de la Région de la Méditerranée orientale ; et ii) d'évaluer les évolutions des taux de prévalence dans le contexte des changements apportés aux politiques de surveillance et de lutte antitabac dans ces pays.

Méthodes : Les données régionales et nationales sur le tabagisme ont été extraites des rapports concernant les tendances. Les différences de points de pourcentage entre la prévalence estimée du tabagisme en 2010 et la prévalence prévue pour 2025 ont été calculées pour les pays pour lesquels des données étaient disponibles. Les données relatives à la mise en œuvre des enquêtes nationales et des politiques de lutte antitabac ont été tirées des rapports pertinents de l'OMS.

Résultats : Dans le dernier rapport sur les tendances (2019), il est prévu que la prévalence du tabagisme chez les hommes devrait baisser de moins de deux points de pourcentage dans la Région de la Méditerranée orientale (de 33,1 % en 2010 à 31,2 % en 2025). Les projections dans le rapport de 2019 concernant le tabagisme chez les hommes pour l'année 2025 sont plus encourageantes que celles du rapport de 2015 dans sept des huit pays de la Région qui sont inclus dans les deux rapports. La mise en œuvre de politiques de surveillance et de lutte antitabac s'est améliorée dans cinq de ces sept pays au cours de la même période.

Conclusion : Les pays de la Région doivent mener des enquêtes nationales supplémentaires pour améliorer l'exactitude des estimations et des projections de la prévalence. De telles données peuvent aider à guider les responsables de l'élaboration des politiques dans la mise en œuvre de politiques positives pour lutter contre le tabagisme.

معدل الانتشار التقديري والمتوقع لتدخين التبغ في صفوف الذكور، إقليم شرق المتوسط، من 2000 إلى 2025

هبة فؤاد، أليسون كومار، رندة حمادة، فاطمة العوا، زي شن، تشارلز فريزر

الخلاصة

الخلفية: رصدت ثلاثة تقارير عالمية نشرتها منظمة الصحة العالمية اتجاهات معدل انتشار تدخين التبغ من عام 2000 إلى عام 2025 استناداً إلى البيانات المستمدة من المسوحات الوطنية.

الأهداف: هدفت هذه الدراسة إلى: (1) مقارنة معدلات الانتشار الحالية والمتوقعة لتدخين التبغ والواردة في تلك التقارير للذكور الذين تتراوح أعمارهم بين 15 أو أكثر في بلدان إقليم شرق المتوسط؛ (2) تقييم التغيرات في معدلات الانتشار في سياق التغيرات التي تطرأ على سياسات رصد التبغ ومكافحته في تلك البلدان.

طرق البحث: استُخرجت بيانات إقليمية وقُطرية بشأن تدخين التبغ من تقارير الاتجاهات. وتم احتساب فروق النقاط المئوية بين معدل الانتشار التقديري لتدخين التبغ في عام 2000 ومعدل الانتشار المتوقع في عام 2025 بالنسبة للبلدان التي تتوافر بشأنها البيانات. وأُخِذت البيانات حول تنفيذ المسوحات والسياسات الوطنية بشأن تعاطي التبغ من التقارير ذات الصلة الصادرة عن منظمة الصحة العالمية.

النتائج: يتوقع أحدث تقرير اتجاهات (2019) أن ينخفض المعدل الحالي لتدخين التبغ بين الذكور بنسبة تقل عن نقطتيْن مئويتيْن في إقليم شرق المتوسط (من 33.1 ٪ في 2010 إلى 31.2 ٪ في 2025). وجاءت التوقعات الخاصة بتدخين التبغ بين الذكور لعام 2025 في تقرير عام 2019 مُشجِّعة أكثر من تقرير عام 2015 في سبعة من بين ثمانية بلدان وردت معلومات عنها في كلا التقريريْن. وخلال نفس الفترة الزمنية، تحسَّن تنفيذ سياسات رصد التبغ ومكافحته على حد سواء في خمسة بلدان من تلك البلدان السبعة.

الاستنتاج: ينبغي أن تُجري بلدان الإقليم مسوحات وطنية إضافية لتحسين دقة تقديرات معدل الانتشار وتوقعاته. ويمكن أن تساعد تلك البيانات في توجيه راسمي السياسات لتنفيذ سياسات إيجابية لمكافحة تدخين التبغ.

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Reporting immunization coverage inequalities in Pakistan

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Abstract

Background: Immunization coverage in Pakistan is unequally distributed. Understanding the current status of reporting of immunization coverage inequalities in Pakistan can help to identify gaps and opportunities for strengthened monitoring and reporting.

Aims: To assess the published literature on immunization coverage inequality measurement and reporting in Pakistan.

Methods: We performed a literature search in PubMed in April 2019 to obtain articles reporting inequalities in immunization coverage in Pakistan. A data extraction rubric was applied to collate information about data sources, immunization indicators and dimensions of inequality.

Results: We included 42 studies in our analysis. Most studies reported data from household surveys or research studies. Dimensions of inequality reflected geography (primarily provinces/territories), economic status, place of residence, education level, sex and occupation. District-level comparisons were featured in 5 studies that were subnational in scope.

Conclusions: Expanded monitoring at district level is warranted as a major way forward in characterizing immunization inequalities in Pakistan.

Keywords: Pakistan, inequality, immunization coverage

Introduction

Despite recent national improvements to immunization coverage in Pakistan (*1*), the country has not yet realized the full benefits of immunization. The reasons why Pakistan trails behind in terms of immunization can be traced to political, geographical and sociocultural forces, which are experienced differently throughout the country (*2,3*). As a result, Pakistan has high levels of immunization coverage inequality, with marked differences according to parental education, household economic status, subnational region and other factors (*4,5*).

Health inequality monitoring methods can be used to measure and track immunization coverage differences between subgroups within a target population (*6,7*). Inequality monitoring can help to identify where immunization coverage inequalities exist, and the characteristics of disadvantaged subgroups. Among other factors, the inequality monitoring process is premised on data availability and the identification of population subgroups that reflect relevant (and actionable) dimensions of inequality.

A comprehensive overview of how inequality monitoring efforts have assessed immunization coverage in Pakistan is warranted to characterize the current scope of monitoring, reveal gaps in monitoring, and indicate opportunities to strengthen and expand monitoring. Here, we report the results of a systematic survey of published literature about immunization coverage inequality in Pakistan between 2000 and 2019, with a focus on data sources and dimensions of inequality. The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

Methods

Two of the authors performed a systematic literature on PubMed (Medline) in April 2019. The search strategy used Boolean operators, Medical Subject Headings terms and title/abstract keywords to search for articles on Pakistan and immunization. Filters were applied to refine the search criteria according to language (English) and date (after 2000) of publication. The search results were screened in 2 stages: first by title and abstract, and then by full text. The following inclusion criteria were applied: (1) full text of article available online; (2) article pertained to humans; (3) article reported immunization coverage for Pakistan; (4) article contained disaggregated data for immunization coverage in Pakistan; (5) article stated the data source; and (6) article reported monitoring of immunization coverage according to demographic, sociocultural or geographic factors, or other perceived sources of systemic discrimination. Articles that evaluated the impact of an intervention or trial were not included. A data extraction rubric was used to extract key information from articles included at the full-text review stage. The rubric collected standardized and freeform information, including: publication details, target population, data sources, immunization indicators, disaggregation criteria and

population subgroups. Both authors contributed to article screening and data extraction, and incongruities were resolved through discussion and consensus. Detailed information about the search strategy and data extraction rubric is available from the authors upon request.

Results

Characteristics of included articles

The literature search yielded 42 relevant articles (Table 1). The included articles were published in international (*n* = 28), regional (*n* = 6) or national (*n* = 8) journals, and predominantly reported on the national population (*n* = 24) or geographically determined subnational populations (*n* = 15). The majority of articles were original research studies (*n* = 31), followed by reports (*n* = 8) and reviews (*n* = 3). A complete list of included articles is available in Appendix 1. The articles reported coverage of single vaccines, including polio (*n* = 17), diphtheria, tetanus, and pertussis (*n* = 7), measles (*n* = 7) and hepatitis B (*n* = 5), or coverage of multiple vaccines (*n* = 13).

Data sources

The data used to measure inequalities in immunization coverage were sourced from international or national household surveys (*n* = 16) or collected as part of a research study (*n* = 16), with 10 additional articles reporting World Health Organization/United Nations Children's Fund (WHO/UNICEF) modelled estimates based on official country estimates. Household survey sources included 2 prominent international surveys: the Pakistan Demographic and Health Survey (PDHS) (*n* = 11) and the Multiple Indicator Cluster Surveys (MICS) (*n* = 1). While articles using PDHS data were national in scope, the PDHS excludes certain geographical areas [e.g. the 2012–2013 PDHS did not include Azad Jammu and Kashmir (Pakistan-administered Kashmir) and Federally Administered Tribal Areas]. Since 2010, MICS has been

conducted on a rotating basis by province/territory. The article using MICS data reported on subnational populations in Balochistan and Punjab. Other household surveys included the Pakistan Social and Living Standards Measurement (*n* = 4), Pakistan Integrated Household Survey (or Pakistan Integrated Economic Survey) (*n* = 3), Expanded Programme on Immunization surveys (*n* = 2), National Nutrition Survey (*n* = 1) and Maternal and Child Health Program Indicator Survey (*n* = 1). Articles that reported data collected as part of a research study (*n* = 16) all represented populations within specific provinces or territories: Sindh (*n* = 7), Khyber Pakhtunkhwa (*n* = 6), Balochistan (*n* = 1), Azad Jammu and Kashmir (*n* = 1) and multiple provinces (Sindh, Khyber Pakhtunkhwa and Punjab) (*n* = 1).

Dimensions of inequality

Over half of the articles disaggregated immunization coverage by subnational region (*n* = 25). Other major dimensions of inequality included: economic status (*n* = 18), rural–urban place of residence (*n* = 18), education level (*n* = 16), sex (*n* = 15) and occupation (*n* = 9). Of the 25 articles that reported subnational region as a dimension of inequality, data were most often disaggregated by provinces and territories (*n* = 20). These articles drew from WHO/UNICEF estimates (*n* = 10), PDHS (*n* = 5) or national household surveys (*n* = 5), and were national in scope. Five articles, subnational in scope, reported district or subdistrict inequalities in coverage (Table 2).

Discussion

This literature review demonstrates the scope of immunization inequality reporting in Pakistan. Although many studies were national in scope, some geographical regions were not covered by major household surveys and thus not reported in the studies. It is a concern that conflict-affected and unstable areas are not included in regular data collection, as they are also areas where vac-

Table 1 Articles excluded at literature search and review stages

Stage of search/review	Reason for exclusion (no. of articles)	No. of articles
Titles identified through database searching		1231
Applied filter: articles published since 2000	Articles published outside of specified timeframe (*n*=184)	1047
Duplicates removed	(*n*=192)	855
Applied filter: articles published in English	Articles published in Spanish (*n*=5), Danish (*n*=2), French (*n*=2), Japanese (*n*=2), Dutch (*n*=1), German (*n*=1), Serbian (*n*=1) or Swedish (*n*=1)	840
Removed items catalogued as "Species: other animals" for content unrelated to humans	Article did not contain information about human subjects [a] (*n*=103)	734
Title and abstract review	Articles did not contain information about human subjects; did not report immunization coverage for Pakistan; did not contain disaggregated data for Pakistan; did not disaggregate data by relevant demographic, socioeconomic, cultural, or geographic factors (*n*=650)	87
Full-text review	Article did not report immunization coverage for Pakistan (*n*=40) Article did not disaggregate data by relevant demographic, socioeconomic, cultural, or geographic factors (*n*=3) Full text of article was not available (*n*=2)	42

[a]These titles were reviewed for potentially relevant articles, and one article was retained.

Table 2 Articles that reported subnational regional inequality in immunization coverage at district or subdistrict levels

First author (ref)	Title of article	Data source	Study location	Subnational regions
Cockcroft (14)	One size does not fit all: local determinants of measles vaccination in 4 districts of Pakistan	Research study	Sindh, Punjab and North West Frontier province [a]	Select districts: Khairpur, Haripur, Khanewal, Sialkot
Imran (11)	Routine immunization in Pakistan: comparison of multiple data sources and identification of factors associated with vaccination	MICS	Balochistan and Punjab	District groups within Balochistan and districts within Punjab
Khowaja (18)	Routine EPI coverage: subdistrict inequalities and reasons for immunization failure in a rural setting in Pakistan	Research study	Matiari district, Sindh	Matiari district talukas and union councils
Riaz (19)	Reasons for nonvaccination and incomplete vaccinations among children in Pakistan	Research study	Sindh	Select districts: Karachi, Hyderabad, Matriari, Jamshoro, Thatta, Sujawal, Tando Muhammad Khan, Tando Allah Yar
Siddiqi (20)	Ethnic disparities in routine immunization coverage: a reason for persistent poliovirus circulation in Karachi, Pakistan?	Research study	Periurban Karachi	Communities: Baldia, BinQasim, Gadap, Gulberg, Gulshan, Jamshed, Kemari, Korangi, Landhi, Liaqatabad, Lyari, Malir, New Karachi, North Nazimabad, Orangi, Saddar, Shah Faisal, SITE

[a]now known as Khyber Pakhtunkhwa.

EPI = Expanded Programme on Immunization; MICS = Multiple Indicator Cluster Surveys.

cine-preventable diseases are likely to be more prevalent or problematic. The transmission of wild poliovirus, for instance, originates from regions, including Federally Administered Tribal Areas, where surveillance systems are suboptimal and immunization activities, routinely compromised (8).

The results indicate a reliance on household survey and research data, with low use of data from administrative sources (records from routine encounters with the health system, which are taken into account in the WHO/UNICEF modelled estimates). Administrative data have important potential for inequality monitoring, as they can provide timely information gathered from all members of a population, with high geographical precision. The quality of administrative data, however, relies on accurate and coordinated reporting systems as well as denominator estimates (typically generated through censuses) (9). Unfortunately, Pakistan's health information system lacks capacity (10), and therefore immunization coverage estimates derived from this system tend to be discrepant from survey-derived estimates (11).

Given the decentralization of the health system in Pakistan since 2011 – which devolved national responsibilities to provincial and district-level officials, raising equity concerns (10,12) – and the practical importance of area-based inequality monitoring (13), geographical monitoring is particularly important to close coverage gaps. To date, published inequality analyses conducted at the district or subdistrict level are small in number, and appear to be primarily undertaken for specific research purposes rather than as part of routine inequality monitoring. Notably, however, coverage estimates within districts of the same province were variable, and thus provincial data did not necessarily reflect the situation within a particular district (14). No study included in this analysis reported district-level inequalities across the entire country.

A wider survey of publicly available grey literature (i.e., published online by the Government of Pakistan Ministry of National Health Services, Regulation and Coordination, and organizations involved in promoting immunization) presented some district-level disaggregation of immunization coverage, although detailed background documents about these analyses were not readily available (15,16). Consultations with national and international immunization experts have revealed that immunization data at a district level (aligning with national administrative units) were preferred by country-level immunization experts, and that small-area estimations were ranked as a top research priority (17). Participants in that consultation, however, also noted the costly nature of collecting data with district-level granularity, and cited quality and logistical complexities.

Overall, the results of this preliminary analysis suggest an international and national interest in monitoring immunization inequalities in Pakistan, with a predominant focus on geographically defined inequalities (noting that other dimensions are also

monitored). Expanded monitoring at district level is a major way forward in characterizing immunization inequalities and targeted responses, and should be pursued on a national scale, especially including geographical areas that are less well represented in prominent data sources. Additionally, further studies are warranted to expand upon the methods used in this preliminary analysis, including multiple databases and handsearching of relevant unindexed journals. The results of this analysis draw attention to the continued need for regular inequality monitoring of immunization coverage as a central part of national efforts to ensure the full benefits of immunization for all.

Rapport sur les inégalités en matière de couverture vaccinale au Pakistan

Résumé

Contexte : La couverture vaccinale au Pakistan est inégale. Comprendre la situation actuelle concernant la notification des inégalités en matière de couverture vaccinale au Pakistan peut aider à identifier les lacunes et les possibilités de renforcement du suivi et de la notification.

Objectifs : Évaluer la littérature publiée sur la mesure et la notification concernant les inégalités liées à la couverture vaccinale au Pakistan.

Méthodes : Nous avons réalisé une recherche de littérature dans PubMed en avril 2019 pour obtenir des articles signalant des inégalités dans la couverture vaccinale au Pakistan. Une grille d'extraction des données a été utilisée pour recueillir des informations sur les sources de données, les indicateurs de vaccination et les dimensions des inégalités.

Résultats : Nous avons inclus 42 études dans notre analyse. La plupart des études ont fourni des données issues d'enquêtes auprès des ménages ou d'études de recherche. Les dimensions de l'inégalité reflètent la géographie (principalement les provinces/territoires), le statut économique, le lieu de résidence, le niveau d'études, le sexe et la profession. Des comparaisons au niveau des districts ont été présentées dans cinq études de portée infranationale.

Conclusions : Un suivi étendu au niveau des districts est nécessaire pour permettre une meilleure caractérisation des inégalités en matière de vaccination au Pakistan.

التبليغ بأوجه التفاوت في التغطية بالتحصين في باكستان

نيكول بيرجن، جريس زو، كاثرين كيركبي

الخلاصة

الخلفية: يتسم توزيع التغطية بالتحصين في باكستان بعدم التكافؤ. ويمكن أن يساعد فهم الوضع الحالي للتبليغ بأوجه التكافؤ في التغطية بالتحصين في باكستان في تحديد الثغرات والفرص المتاحة لتعزيز الرصد والتبليغ.

الأهداف: هدفت هذه الدراسة إلى تقييم الأدبيات المنشورة حول قياس التفاوت في التغطية بالتحصين والتبليغ به في باكستان.

طرق البحث: أجرينا استعراضاً للمؤلفات باستخدام برنامج PubMed في أبريل/ نيسان 2019 للحصول على مقالات أبلغت بعدم التكافؤ في التغطية بالتحصين في باكستان. وطُبِّقت إرشادات استخراج البيانات لجمع المعلومات حول مصادر البيانات، ومؤشرات التحصين، وأبعاد عدم التكافؤ.

النتائج: أدرجنا 42 دراسة في تحليلنا. وأبلغت معظم الدراسات عن بيانات مستمدة من مسوحات منزلية أو دراسات بحثية. واتضحت أبعاد عدم التكافؤ في الجغرافيا (بصورة أولية المقاطعات/ الأقاليم)، والوضع الاقتصادي، ومكان الإقامة، ومستوى التعليم، ونوع الجنس، والمهنة. وظهرت مقارنات على مستوى المناطق في 5 دراسات تمت على نطاق دون وطني.

الاستنتاجات: هناك ما يبرر إجراء رصد موسع على مستوى المناطق بوصفه سبيلاً رئيسياً للمضي قدماً في تحديد خصائص أوجه عدم التكافؤ في التحصين في باكستان.

Appendix 1 Articles included in the review (n = 42)

Authors	Article title	Year published	Journal	Article type	Population
Alexander JP et al.	Progress and peril: poliomyelitis eradication efforts in Pakistan, 1994–2013.	2018	J Infect Dis	Research	National
Asif M et al.	Hepatitis B vaccination coverage in medical students at a medical college of Mirpurkhas.	2011	J Pak Med Assoc	Research	Professional group
Attaullah S et al.	Prevalence of HBV and HBV vaccination coverage in healthcare workers of tertiary hospitals of Peshawar, Pakistan.	2011	Virology J	Research	Professional group
Batool S, Ahmed AM.	Achievements of healthcare services vis a vis the MDG targets: Evidence from Pakistan.	2017	J Pak Med Assoc	Research	National
Bugvi AS et al.	Factors associated with nonutilization of child immunization in Pakistan: evidence from the Demographic and Health Survey 2006–2007.	2014	BMC Public Health	Research	National
CDC	Progress toward poliomyelitis eradication – Pakistan, January 2012–September 2013.	2013	MMWR Morb Mortal Wkly Rep	Report	National
CDC	Progress toward poliomyelitis eradication – Afghanistan and Pakistan, January 2010–September 2011.	2011	MMWR Morb Mortal Wkly Rep	Report	National
CDC	Progress toward poliomyelitis eradication – Afghanistan and Pakistan, 2009.	2010	MMWR Morb Mortal Wkly Rep	Report	National
CDC	Progress toward poliomyelitis eradication – Afghanistan and Pakistan, 2008.	2009	MMWR Morb Mortal Wkly Rep	Report	National
Cockcroft A et al.	One size does not fit all: local determinants of measles vaccination in four districts of Pakistan.	2009	BMC Int Health Hum Rights	Research	Subnational
Farag NH et al.	Progress toward poliomyelitis eradication – Afghanistan and Pakistan, January 2013 –August 2014.	2014	MMWR Morb Mortal Wkly Rep	Report	National
Farag NH et al	Progress toward poliomyelitis eradication – Pakistan, January 2014–September 2015.	2015	MMWR Morb Mortal Wkly Rep	Report	National
Hasan Q et al.	A review of EPI progress in Pakistan towards achieving coverage targets: present situation and the way forward.	2010	East Mediterr Health J	Review	National
Hosseinpoor AR et al.	State of inequality in diphtheria–tetanus–pertussis immunisation coverage in low-income and middle-income countries: a multicountry study of household health surveys.	2016	Lancet Global Health	Research	National
Hsu C et al.	Progress toward poliomyelitis eradication – Pakistan, January 2017–September 2018.	2018	MMWR Morb Mortal Wkly Rep	Report	National
Hsu CH et al.	Progress toward poliomyelitis eradication – Pakistan, January 2015–September 2016.	2016	MMWR Morb Mortal Wkly Rep	Report	National
Husain S, Omer SB.	Routine immunization services in Pakistan: seeing beyond the numbers.	2016	East Mediterr Health J	Review	National
Imran H et al.	Routine immunization in Pakistan: comparison of multiple data sources and identification of factors associated with vaccination.	2018	Int Health	Research	Subnational
Imran W et al.	What is causing high polio vaccine dropout among Pakistani children?	2018	Public Health	Research	National
Khan MT et al.	Maternal education, empowerment, economic status and child polio vaccination uptake in Pakistan: a population based cross sectional study.	2017	BMJ Open	Research	National
Khowaja AR et al.	Parental awareness and coverage of mass measles vaccination drive 2011: cross-sectional survey in the metropolitan city of Karachi, Pakistan.	2015	Asia Pac J Public Health	Research	Subnational

Appendix 1 Articles included in the review (n = 42) (concluded)

Authors	Article title	Year published	Journal	Article type	Population
Khowaja AR et al.	Routine EPI coverage: subdistrict inequalities and reasons for immunization failure in a rural setting in Pakistan.	2015	Asia Pac Journal of Public Health	Research	Subnational
Kols A et al.	Provincial differences in levels, trends, and determinants of childhood immunization in Pakistan.	2018	East Mediterr Health J	Research	National
Malik SM, Ashraf N.	Equity in the use of public services for mother and newborn child health care in Pakistan: a utilization incidence analysis.	2016	Int J Equity Health	Research	National
Mitchell S et al.	Equity and vaccine uptake: a cross-sectional study of measles vaccination in Lasbela District, Pakistan.	2009	BMC Int Health Hum Rights	Research	Subnational
Murtaza F et al.	Determinants of nonimmunization of children under 5 years of age in Pakistan.	2016	J Fam Commun Med	Research	National
Naeem M et al.	Coverage and causes of missed oral polio vaccine in urban and rural areas of Peshawar.	2011	J Ayub Med Coll Abbottabad	Research	Subnational
Naeem M et al.	Coverage and causes of missed Haemophilus influenzae type B vaccination in urban and rural areas of Peshawar.	2011	J Ayub Med Coll Abbottabad	Research	Subnational
Naeem M et al.	Coverage and factors associated with tetanus toxoid vaccination among married women of reproductive age: a cross sectional study in Peshawar.	2010	J Ayub Med Coll Abbottabad	Research	Subnational
Naeem M et al.	Factors associated with low hepatitis B vaccination; a user and provider perspective study in Peshawar.	2011	J Pak Med Assoc	Research	Subnational
Noh JW et al.	Factors affecting complete and timely childhood immunization coverage in Sindh, Pakistan; A secondary analysis of cross-sectional survey data.	2018	PLOS one	Research	Subnational
Owais A et al.	Pakistan's expanded programme on immunization: an overview in the context of polio eradication and strategies for improving coverage.	2013	Vaccine	Review	National
Raza O et al.	Differential achievements in childhood immunization across geographical regions of Pakistan: analysis of wealth-related inequality.	2018	Int J Equity Health	Research	National
Rehman SU et al.	Coverage and predictors of routine immunization among 12–23 months old children in disaster affected communities in Pakistan.	2017	Int J Health Sci	Research	Subnational
Riaz A et al.	Reasons for non-vaccination and incomplete vaccinations among children in Pakistan.	2018	Vaccine	Research	Subnational
Shah M et al.	Resistance of polio to its eradication in Pakistan.	2011	Virology J	Research	National
Shaikh S et al.	Coverage and predictors of vaccination among children of 1-4 years of age in a rural sub-district of Sindh.	2010	J Coll Physicians Surg Pak	Research	Subnational
Siddiqi N et al.	Assessment of EPI (expanded program of immunization) vaccine coverage in a peri-urban area.	2007	J Pak Med Assoc	Research	Subnational
Siddiqui NT et al.	Ethnic disparities in routine immunization coverage: a reason for persistent poliovirus circulation in Karachi, Pakistan?	2014	Asia Pac J Public Health	Research	Subnational
Singh PK, Parsuraman S.	Sibling composition and child immunization in India and Pakistan, 1990–2007.	2014	World J Pediatrics	Research	National
Yousafzai MT et al.	Hepatitis B vaccination among primary health care workers in Northwest Pakistan.	2014	Int J Health Sci	Research	Professional group
Zaidi SM et al.	Coverage, timeliness, and determinants of immunization completion in Pakistan: evidence from the Demographic and Health Survey (2006–07).	2014	Hum Vaccin Immunother	Research	National

CDC = Centers for Disease Control and Prevention; HBV = hepatitis B virus.

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Cutaneous leishmaniasis as an increasing threat for Iranian travellers attending religious ceremonies

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Abstract

Background: The Islamic Republic of Iran is one of the most important endemic foci of cutaneous leishmaniasis in the world. Annually, a large number of Iranian Shia pilgrims travel to Iraq from this area in order to participate in one of their most important religious ceremonies. This trip has coincided with the seasonal activity of sand flies in recent years. So, cutaneous leishmaniasis could be a serious threat for pilgrims on these trips.

Aims: To report cases of cutaneous leishmaniasis among Iranian Shia pilgrims attending a religious ceremony in Iraq during 2017.

Methods: Sixteen patients were referred to our laboratory in the Department of Parasitology and Mycology at Qazvin University of Medical Sciences. Dermal scrapings and stained slides prepared of skin lesions were used to morphological diagnosis. DNA extraction and PCR amplification were optimized to identification of *Leishmania* species.

Results: All of the patients were infected with cutaneous leishmaniasis in microscopic survey. *L. major* was detected by molecular approach. The number of lesions observed in patients were 1 (31%), 2 (25%), and ≥ 3 (44%).

Conclusions: Since a large number of Shia Muslims participate in the annual religious ceremonies, serious measures must be taken to prevent the disease.

Introduction

Leishmaniasis is an important parasitic disease with a diverse spectrum of clinical syndromes, such as cutaneous leishmaniasis (CL), and visceral leishmaniasis (VL) (1). Some cutaneous lesions can be self-healing. CL considered as an important public health problem when the lesions are presented for a long period, with persistent ulcers, and secondary bacterial infections causing heavy treatment cost and complications of drug therapy (2–4). Etiologic agent of CL is species of *leishmania* genus, an obligate intracellular protozoan parasite of mononuclear phagocytes in vertebrate hosts (5). Up to now, more than 30 species of *Leishmania* have been detected, At least 20 species of parasite can be infected humans (6,7). Female phlebotomine sand flies are vector of the parasite in tropical and subtropical regions. CL are distributed about 95% in South and Central America, Mediterranean, Middle East and Central Asia (8,9). The disease was reported from more than 98 countries in the world, in which the most important endemic foci in old world including; Afghanistan, Algiers, Islamic Republic of Iran, Saudi Arabia and Syria, and in the new world, Brazil, Colombia and Peru countries (10,11). CL is common in Islamic Republic of Iran with both shape of Anthroponotic Cutaneous Leishmaniasis (ACL) and Zoonotic Cutaneous Leishmaniasis (ZCL), caused by *Leishmania tropica* and *Leishmania major*, respectively (12). Up to now, CL is endemic in 17 provinces of 31 provinces of Islamic Republic of Iran, with the majority of ZCL (11). In spite of, the prevalence of human parasitic infections, especially soil transmitted helminthes have remarkably decreased in Islamic Republic of Iran (13), but ZCL is expanding in the country and new foci of infection have been reported in recent years (14–19). It seems that migrating rodent reservoirs to new areas is a possible major cause of wide spreading of CL in Islamic Republic of Iran. Annually, about 20,000 of new cases of CL are recorded in the country, in which the real number of patients are multiplied estimated (20). Also, CL epidemic have been reported from Islamic Republic of Iran in the recent decades (21,22).

Residents of non-endemic areas of CL in Islamic Republic of Iran are the population at risk for this disease when travel to endemic areas during seasonal activity of sand flies. Ilam province is one of the 31 provinces of Islamic Republic of Iran, and also the province is one of important endemic foci of CL that is located in west of Islamic Republic of Iran and in the neighborhood of

Iraq. Mehran is a county in west of the province and categorized as hyper endemic areas of CL in the country (*14,23–25*). This county is the shortest departure way from Islamic Republic of Iran to Karbala city in Iraq. Karbala is a holy city for Shia Muslims, in which a large number of individuals travel to this city for participate in one of the most magnificent religious ceremonies called Arbaeen Husayni. In next years, this massive pilgrimage trip will be coincide with peak seasonal activities of sand flies, therefore, there is an increasing risk of CL for people who will be participating in the pilgrimage tripe.

Methods

The cross-sectional study was performed from January to April 2018. Sixteen patients were referred to laboratory of Parasitology and Mycology at Qazvin University of Medical Sciences, Qazvin, Islamic Republic of Iran. Except for a woman from Qazvin (a non-endemic region for CL) who was among the pilgrims to Karbala, the rest of patients were from Bus Company employees of Qazvin city. These people were responsible for transferring of pilgrims from Mehran to border regions of Islamic Republic of Iran and Iraq. The place of sleep and rest of these people was located in a building on the outskirts of the city of Mehran where they had been stayed for 20 days. Mehran is a city in Ilam province located in west of Islamic Republic of Iran.

Microscopic surveys were used to through of patients. Initially, cutaneous lesions were disinfected by 70% ethanol. Two to three smears were prepared of each lesion. The smears were fixed with methanol and then stained by Giemsa stain. The slides were surveyed under light microscopy to found *Leishman* bodies (amastigotes) at 1000× magnification.

DNA extraction was performed by obtained slides of the patients. The immersion oil on each smear was cleaned with xylol, and then the entire smear was scraped into a 1.5 ml microcentrifuge tube. DNA of the smear was extracted by blood and tissue Kit, Qiagen (QIAamp DNA mini kit) according to the manufacturer's recommended protocol. PCR was performed, targeting the kDNA pattern of *leishmania*, *L. major* / 615 base pair (bp) and for *L. tropica* / 744 bp, by specific primers. Conventional PCR was carried out in a 25 µl total reaction volume. The reaction containing, 5 µM of template DNA, 0.1 µM of each primer and MgCl2 (0.5 to 4 µM) (*26*). Negative and positive controls were used to monitoring all of reactions. After electrophoresis, The PCR product was stained by ethidium bromide and specific bands were seen under UV light.

Ethics approval and consent to participate

The local ethics committee ruled that no formal ethics approval was required in this particular case. The cost of testing was free for the patients. The results of the tests were provided to the patients and they were introduced to university medical center for treatment.

Photographs were taken from the patients' wounds with their oral permission. Written consent of the patient's face in the figure 3 was considered in the consent form.

Results

Leishmania bodies were microscopically diagnosed in all 16 patients referred to our laboratory (Figure 1). The microscopic results were confirmed by molecular approach; therefore, *L. major* species was detected among all specimens (Figure 2). The age range of patients was 28-60 years. The incubation periods of CL in our patients were not definitely cleared, but the onset of the first signs of disease (boil) appeared two weeks to two months after departure from the area and arrival to the mentioned habitat, however, an incubation time of almost 6 months was observed in one patient. A maximum of six lesions was observed in one patient. Frequency distribution for the number of lesions were one wound (31%; 5/16), two wounds (25%; 4/16), and three and more (44%; 7/16). A rare case of CL was seen in a patient who had two ulcers, one in the upper eyelid, and another in the middle and front of the neck (Figure 3). Surprisingly, a patient had self-medication by burning lesions with the heat of cigarette (Figure 4). Only one of the patients was female pilgrim who had returned from the pilgrimage ceremony in Karbala. None of the patients had previous history of CL.

Discussion

Traveling to endemic areas of vector-borne diseases is a risk factor for people who travel from non-endemic areas. CL is a sand flies-borne disease which has been reported among travelers entered the endemic foci of this protozoan parasitic disease (*26–30*). In our study, these infections occurred among the bus company employees who were responsible for transporting the Arbaeen pilgrims from Mehran to the border areas between Islamic Republic of Iran and Iraq and vice versa. The location for the deployment of these people was in a building in the margin of Mehran city where it is considered as an important endemic focus of ZCL in the west of Islamic Republic of Iran (*23*).

Figure 1 *Leishmania tropica* **amastigotes in an intact macrophage (red arrow) and extracellular (blue arrow) from a skin lesion of a traveler who infected with the parasite in Islamic Republic of Iran-Iraq border. (Magnification x1000)**
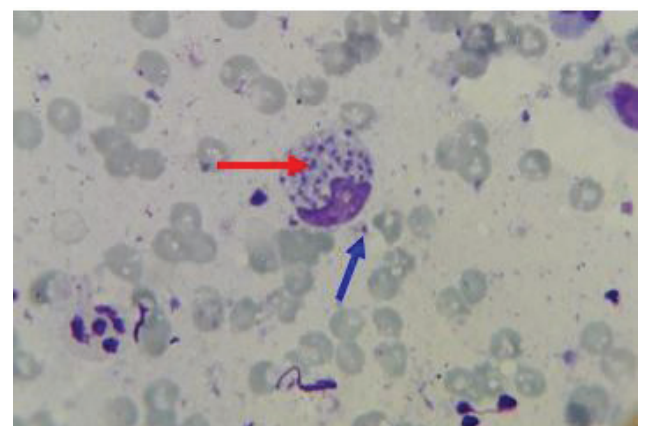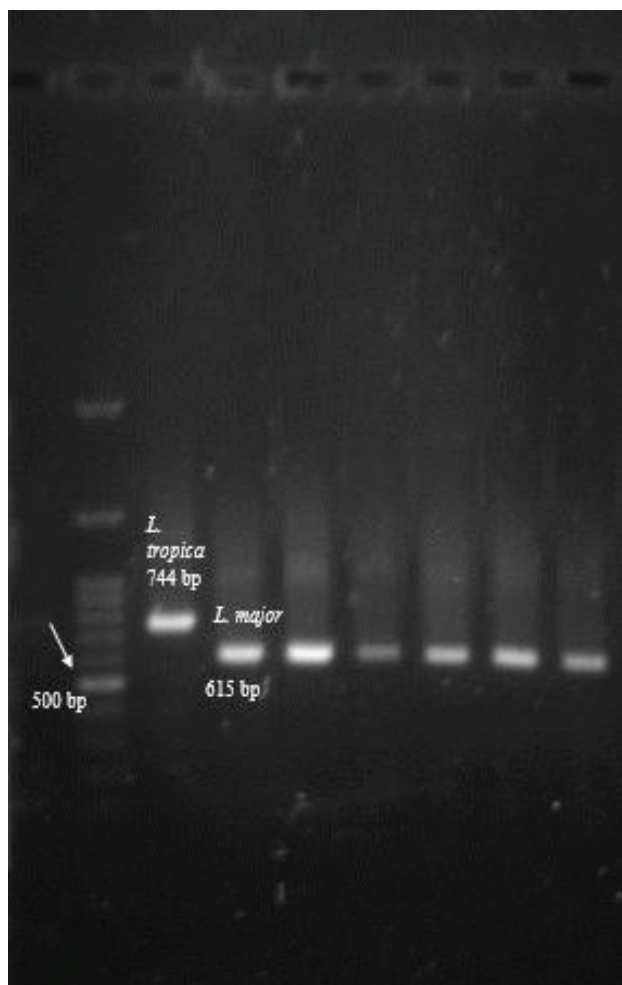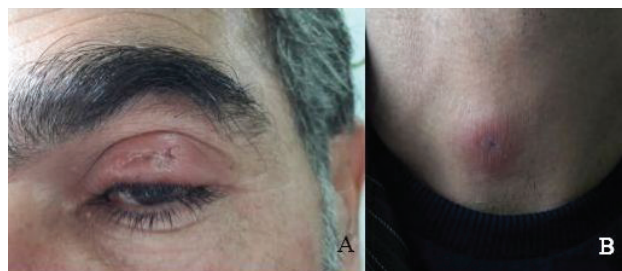
Figure 2 **Gel electrophoresis of PCR product from the patients were referred to laboratory of Parasitology and Mycology at Qazvin University of Medical Sciences, Qazvin, Islamic Republic of Iran. Marker 100bp, *L. major* with 615bp, *L. tropica* with 744bp**

Figure 3 **Cutaneous leishmaniasis caused by *L. major* in a patient who travel from a non-endemic area to an endemic area of Ilam province located in west of Islamic Republic of Iran. He had two ulcers, A; one in the upper eyelid, B; another ulcer in the middle and front of the neck**

The patient gave written consent to use the photograph of his face.

religious travelers are called pilgrims. One of the most holy cities to the Muslims is Karbala city in Iraq, in which the region is the burial ground of the third Imam of the Shiites (Imam Husayn). One of the most important days to commemorate Imam Husayn is the 40th day after his martyrdom known as Arbaeen. Around this time, massive crowd of Shia Muslims travel to Karbala every year (*31*). Mehran is the shortest way to the Iranian pilgrims and most pilgrims go to Karbala from this route. In 2017, the transfer of some Iranian pilgrims to entrance place of Islamic Republic of Iran-Iraq border region was carried out by the employees of the Bus Company of Qazvin. The pilgrims were settled in a building around the city of Mehran where it was neighboring the rodent habitat and

Figure 4 **Cutaneous leishmaniasis caused by *L. major* at the foot of a patient who travel from a non-endemic area to an endemic area of Ilam province located in west of Islamic Republic of Iran. He had done a self-medication by burning lesions with the heat of cigarette**

In the present study, *L. major* was the only species of Leishmania genus which was isolated from the patients and identified by PCR amplification, a finding similar to the results reported in a previous study (*23*). The findings indicated that, the area is a ZCL foci in Islamic Republic of Iran and also showed that human infections with Leishmania have zoonotic origin in this region. Reservoirs of the parasite in west of Islamic Republic of Iran are rodents family of Gerbilidae, such as *Rhombomys opimus*, *Meriones libycus*, *Tatera indica* and *Nesokia indica*, as well as *T. indica* which is categorized as a main reservoir (*28,29*). *Phelobotumus Papatasi* was introduced as a major vector to leishmania in the region and neighboring regions (*30*).

Evidences showed that the CL is increasing in the Mehran area in the recent years (2016) in 92 patients (*23*). It could be a potential risk for Iranian religious travelers who are eager to participate in Arbaeen Husayni ceremony in Iraq in future years. This ceremony is one of the most important religious programs of Shia Muslims. The Muslims are greatly eager to travel to these areas. The

vectors of leishmaniasis. Therefore, they were at risk of CL. A total number of sixteen individuals were referred to our laboratory. Other patients may have been referred to other laboratories or had small lesions and preferred not to visit a doctor for their treatment.

In this study, only one of the patients was among Arbaeen pilgrims. All patients were free of immune deficiency and lived in Qazvin which is considered as a non-endemic region for CL. However, the number of pilgrims was much higher than the persons involved in transportation. Probably, low frequency of CL among the pilgrims is related to the short-term stop of few hours in comparison to one-month stay of staff in the area, so the pilgrims were at lower risk of sand fly bite.

It seems that the risk of CL will be an increasing threat for Iranian people involved in Arbaeen ceremony in future years, even CL could be threat to the pilgrims with short-term inhabitancy, because this religious trip will gradually coincide with the peak biting activity of sand flies in the study area. The ceremony is based on lunar months with 354 days in a year (355 days in the third year), whereas it is 365 days in a year according to solar (Shamsi) and AD calendars. Therefore, annual Arbaeen ceremony will occur 10 days earlier than the previous year, based on Shamsi and AD calendars. The ceremony was held on November 9, 2017 and will be held in 2018 on October 30th. The second peak activity of sand flies in the west of Islamic Republic of Iran is around the end of summer to early autumn, so it is predicted that if essential preventive measures are not established within the next years, an outbreak of CL may occur. The eagerness of Shia Muslims for the religious trip is to that extent that even the risk of this parasitic disease cannot discourage the Muslims from travelling to these areas.

We conclude that CL has an increasing risk for Iranian pilgrims who would be participating in Arbaeen pilgrimage trips in the future years. Therefore, it is recommended that the health care providers take serious preventive measures for the coming years in order to secure good health condition of pilgrims. The study recommend that providing insect repellents can be useful to prevent CL infection among travelers for safe journeys in the future.

Acknowledgement

La leishmaniose cutanée : une menace croissante pour les voyageurs iraniens qui se rendent en Iraq pour assister à une cérémonie religieuse

Résumé

Contexte : La République islamique d'Iran est l'un des plus importants foyers d'endémie de leishmaniose cutanée (LC) au monde. Chaque année, un grand nombre de pèlerins chiites iraniens se rendent en Iraq depuis cette région afin de participer à une de leurs cérémonies religieuses les plus importantes. Ces dernières années, ce voyage a coïncidé avec l'activité saisonnière des phlébotomes. La LC pourrait donc représenter une grave menace pour les personnes qui entreprennent ce pèlerinage.

Objectifs : Signaler les cas de LC chez les pèlerins chiites iraniens ayant assisté à une cérémonie religieuse en Iraq en 2017.

Méthodes : Seize patients ont été orientés vers notre laboratoire au département de parasitologie et de mycologie de l'Université des Sciences médicales de Qazvin. Des prélèvements obtenus par grattage et des colorations de lames préparées à partir de lésions cutanées ont été utilisés pour le diagnostic morphologique. L'extraction d'ADN et l'amplification génique ont été optimisées pour l'identification des espèces du genre Leishmania.

Résultats : Une infection par des *Leishmania* a été diagnostiquée au microscope chez tous les patients. *L. major* a été détecté par approche moléculaire. Le nombre de lésions observées chez les patients était de 1 (31 %), 2 (25 %) et supérieure ou égale à 3 (44 %).

Conclusions : Puisqu'un grand nombre de musulmans chiites participent aux cérémonies religieuses annuelles, des mesures sérieuses doivent être prises pour prévenir la maladie.

داء الليشمانيات الجلدي كتهديد متزايد للمسافرين الإيرانيين الذين يحضرون المراسم الدينية في العراق

مهرزاد سرايي، بى بى راضيه حسيني فراش، الهام حاجى عليلو

الخلاصة

الخلفية: تُعد جمهورية إيران الإسلامية واحدة من أهم البؤر الموطونة بداء الليشمانيات الجلدي في العالم. ويسافر كلَّ عام عددٌ كبيرٌ من الحجاج الشيعة الإيرانيين إلى العراق من هذه المنطقة للمشاركة في أحد أهم الاحتفالات الدينية لديهم. وقد تزامنت هذه الرحلة مع النشاط الموسمي لذباب الرمل في السنوات الأخيرة. لذا، يمكن أن يكون داء الليشمانيات الجلدي تهديداً خطيراً للحجاج أثناء هذه الرحلة.

الأهداف: هدفت هذه الدراسة إلى الإبلاغ عن حالات الإصابة بداء الليشمانيات الجلدي في صفوف الحجاج الشيعة الإيرانيين الذين يحضرون احتفالاً دينياً في العراق خلال عام 2017.

طرق البحث: أُحيل ستة عشر مريضاً إلى مختبرنا في قسم علم الطفيليات وعلم الفطريات في جامعة قزوين للعلوم الطبية. واستُخدم كشط الجلد والشرائح الملونة المعدَّة من الآفات الجلدية للتشخيص المورفولوجي. وتحقَّقت الاستفادة المثلى من استخلاص الحمض الريبي النووي المنزوع الأوكسجين وتفاعل البوليميراز المتسلسل لتحديد أنواع الليشمانيا.

النتائج: شُخِّصت أجسام الليشمانيا مجهرياً لدى جميع المرضى. واكتُشفت الليشمانيا الكبيرة من خلال النهج الجُزيئي. ولقد بلغ عدد الآفات التي لوحظت في المرضى 1 (٪31) و2 (٪25) و 3 ≤ (٪44). كما شوهدت 6 آفات بحد أقصى في مريض واحد.

الاستنتاجات: يبدو أن داء الليشمانيات سيكون خطراً محتملاً على الحُجاج الإيرانيين الذين سيشاركون في رحلات الحج في السنوات المقبلة. ونظراً لمشاركة عدد كبير من المسلمين الشيعة في الاحتفالات الدينية السنوية، يجب اتخاذ تدابير جادة للوقاية من المرض.

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Consultative meeting to discuss ways to promote the use of seasonal influenza vaccine among high-risk groups in the Eastern Mediterranean Region[1]

Introduction

Influenza is a major cause of morbidity and mortality worldwide. Each year, seasonal influenza causes up to 650 000 deaths and millions of people are hospitalized (1). Moreover, influenza pandemics can have a major impact on health and society as a whole. A sustainable seasonal influenza programme or policy not only reduces the disease burden but strengthens health systems and leads to better pandemic preparedness (1). Since it is conducted annually, seasonal influenza vaccination allows countries to develop, practice and refine vaccine approval, distribution and delivery plans, each year. Increasing national, regional and global efforts to expand the use of seasonal vaccines provides economic and public health benefits today, while developing systems for pandemic response in the future.

The importance of influenza vaccination has been highlighted in World Health Assembly resolution WHA56.19 on prevention and control of influenza pandemics and annual epidemics (2003) (2), the Global Action Plan for Influenza Vaccines (2006–2016) (3), the Pandemic Influenza Preparedness Framework (2011) (4) and World Health Assembly resolution WHA70(10) on Review of the Pandemic Influenza Preparedness Framework (2017) (5).

The capacity of countries in the WHO Eastern Mediterranean Region in surveillance and pandemic planning has greatly increased over the past decade. However, the Region continues to have some of the lowest rates of vaccine utilization globally. The countries of the Region are highly diverse with respect to their influenza vaccination programmes: some have high-quality robust annual programmes, some have small programmes they wish to expand, while others have yet to introduce the vaccine.

To address these issues a one-day consultative meeting was held in Casablanca, Morocco on 19 November 2019 (6) to discuss ways to promote the use of seasonal influenza vaccine among high-risk groups in the Eastern Mediterranean Region. The meeting focused on identifying challenges and opportunities for the introduction and expansion of influenza vaccination policies and programmes in the Region.

The objectives of the meeting were to:

- review the current landscape of influenza vaccination in the Region;
- review ongoing initiatives related to influenza vaccination and preparedness that are relevant to seasonal vaccination programme development;
- discuss key challenges to influenza vaccination programme growth in the Region;
- discuss tools and approaches to accelerating the creation of an evidence base for the development of national vaccine policies; and
- identify opportunities for regional collaboration to expand influenza prevention in the Region.

Summary of discussions

Despite the expansion of vaccine use globally, vaccines are still underused in many low- and middle-income countries, and in many countries that have vaccination policies, vaccine programmes remain weak. Political and technical challenges to vaccine expansion persist. These include negative perceptions of the relative value, affordability and availability of vaccines, regulatory obstacles, a need for national policies and a lack of operational plans to implement programmes.

In addition to these challenges, vaccine expansion can be technically difficult due to lack of information on disease burden, lack of an infant-focus among target groups and the need to deliver the programme annually, as well as difficulties in measuring impact, communicating value, matching supply and demand and integrating seasonal influenza vaccination into routine immunization programmes.

Recommendations

To WHO

- Creating a mechanism for regional cooperation towards greater influenza prevention and control through increased use of influenza vaccine;
- supporting countries in the Region with adequate

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[1] This summary is extracted from the Summary report on the One day consultative meeting to discuss ways to promote the use of seasonal influenza vaccine among high-risk groups in the Eastern Mediterranean Region, Casablanca, Morocco, 16 November 2019 (https://applications.emro.who.int/docs/WHOEMCSR286E-eng.pdf?ua=1).

epidemiological and laboratory surveillance data to conduct seasonal influenza burden estimation studies in support of better public health decision-making on seasonal influenza vaccine introduction; and

- ensuring the availability of appropriate influenza vaccination campaign materials translated into local languages in all countries of the Region.

To Member States

- Increasing the national evidence base by conducting influenza disease burden estimation studies and developing appropriate policy briefs;

- improving access to vaccination through introduction

of policies on vaccination implementation by nurses, mobile teams and at pharmacies;

- increasing communication messages about influenza vaccines through campaigns, social media or other platforms, ensuring that communications are targeted at high-risk groups;

- reducing the price of influenza vaccination through national subsidies or by participating in regional pooled procurement; and

- advocating for a more effective partnership between the public and private sectors to promote seasonal influenza vaccine uptake and improve coverage rates.

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Dr Mohamed Helmy Wahdan

1933-2020

The World Health Organization (WHO) deeply regrets the recent loss of Dr Mohamed Helmy Wahdan, who died on 24 December, 2020. A great leader in the world of public health, Dr Wahdan was born on 18 August 1933 in Egypt, received his bachelor degree in medicine and surgery from Ain Shams University, Egypt (1958), and doctoral degree in epidemiology from the London School of Hygiene and Tropical Medicine, United Kingdom (1963). Professor Wahdan held a number of academic positions including Lecturer of Public Health, Faculty of Medicine, Alexandria University, Egypt (1964-1969), Associate Professor of Epidemiology (1969-1974), and Professor of Epidemiology and Vice Dean of the High Institute of Public Health, Alexandria University (1975-1979). One of his most important research outcomes was proving the effectiveness of meningococcal meningitis vaccine, a disease that was killing thousands of people at that time.

Dr Wahdan joined the WHO Regional Office for the Eastern Mediterranean in 1979 and served the Eastern Mediterranean Region for more than three decades as a well-recognized expert in the field of communicable disease prevention and control. He had sound judgement and great wisdom, whose insight was sought by many Member States and WHO colleagues. As Director of Communicable Diseases at the Regional Office, Dr Wahdan set the agenda and strategies for control of communicable diseases in the Region and beyond. In recognition of his significant expertise, he was appointed as the Assistant Regional Director and then as Special Adviser to the Regional Director until his retirement during 2012.

While Dr Wahdan helped in the eradication of small pox globally and limiting the spread of HIV/AIDS in the Region, his most enduring legacy is his outstanding contribution to the polio eradication initiative. He established a robust polio eradication infrastructure. This included setting tailored strategies that contributed to national health policies and plans in complex countries such as Afghanistan, Iraq, Pakistan, Somalia, Sudan (including South Sudan) and Yemen. Dr Wahdan was also instrumental in ensuring the elimination of the endemic polio in Egypt, Iraq, Somalia, Sudan, the Syrian Arab Republic and Yemen. Under his leadership, the Region became free of polio, with the exception of Afghanistan and Pakistan.

In honor of his outstanding work, Dr Wahdan received multiple awards, most notably the Jacques Parisot Foundation Medal, awarded by the Thirty-first World Health Assembly for best research in Public Health. Ultimately, Dr Wahdan's legacy will be the lasting inspiration for all those who worked with and learned from him.

الدكتور محمد حلمي وهدان

1933-2020

فقدت منظمة الصحة العالمية رائدًا عظيمًا في عالم الصحة العامة، الأستاذ الدكتور محمد حلمي وهدان، في 24 ديسمبر/ كانون الأول 2020. ولد دكتور وهدان في 18 أغسطس/ آب 1933 في مصر، وحصل على بكالوريوس الطب والجراحة (جامعة عين شمس، 1958) والدكتوراه في علم الوبائيات (كلية لندن للصحة وطب المناطق الحارة، 1963). وعمل محاضرًا للصحة العامة، في كلية الطب، جامعة الإسكندرية (1964–1969)، ثم أستاذًا مشاركًا في علم الوبائيات (1969–1974)، ثم أستاذًا في علم الوبائيات ووكيلًا للمعهد العالي للصحة العامة، جامعة الإسكندرية (1975–1979). وكان من أهم نتائج أبحاثه إثبات فعالية لقاح التهاب السحايا للمكورات السحائية والذي كان الدرع الواقي من المرض الذي كان يقتل آلاف الأشخاص في ذلك الوقت.

انضم الدكتور وهدان إلى المكتب الإقليمي لمنظمة الصحة العالمية لشرق المتوسط في عام 1979 ولأكثر من ثلاثة عقود ظل خبيرًا مشهودًا له في الوقاية من الأمراض السارية ومكافحتها. وتمتع بالرأي السليم والحكمة السديدة، والتمس مساعدته العديد من الدول الأعضاء والزملاء في منظمة الصحة العالمية. وبصفته مدير إدارة الأمراض السارية بالمكتب الإقليمي، وضع الدكتور وهدان خططًا واستراتيجيات لمكافحة الأمراض السارية في الإقليم وخارج الإقليم. واعترافًا بخبرته الكبيرة، عُيِّن مساعدًا للمدير الإقليمي ثم مستشارًا خاصًا للمدير الإقليمي حتى تقاعده في عام 2012.

ومع أن الدكتور وهدان ساهم في القضاء على الجدري من العالم، والحد من انتشار فيروس العوز المناعي البشري/ الإيدز في اقليم شرق المتوسط، إلا أن إرثه المرموق كان في مساهمته البارزة في مبادرة استئصال شلل الأطفال في الإقليم. فقد أنشأ بنيةً أساسيةً قويةً لاستئصال شلل الأطفال، ووضع استراتيجيات مصممةً خصيصًا للحضور الفاعل للمنظمة على المستوى القطري؛ مما ساهم في السياسات والاستراتيجيات والخطط الصحية الوطنية في بلدان ذات أحوال معقدة مثل أفغانستان والعراق وباكستان والصومال والسودان (بما في ذلك جنوب السودان) واليمن. فكان له دور فعَّال في استئصال شلل الأطفال المتوطن في مصر والعراق والصومال والسودان والجمهورية العربية السورية واليمن؛ وتحت قيادته أصبح الإقليم خاليًا من شلل الأطفال، ما عدا أفغانستان وباكستان.

وتكريمًا لأعماله المتميزة، حصل الدكتور وهدان على العديد من الجوائز. وكان أول من حصل على ميدالية مؤسسة جاك باريزوت التي منحتها منظمة الصحة العالمية/ جمعية الصحة العالمية الحادية والثلاثون لأفضل بحث في الصحة العامة. سيظل الدكتور وهدان مصدر إلهام دائم لكل من عمل معه وتعلّم منه.

رحم الله الدكتور وهدان وأدخله فسيح جناته وانا لله وانا اليه راجعون

Dr Fahad Liaquat

1981-2020

The World Health Organization (WHO) deeply regrets the loss of its colleague Dr Fahad Liaquat, District Surveillance Officer, Khyber District in Pakistan, who passed away 31 December 2020, and was 39 years old. Dr Fahad joined the polio programme in 2016, and worked tirelessly to protect Pakistani children from polio, in a strategically important district of the country. During the COVID-19 outbreak response, Dr Fahad played an important role by making sure that communities and clinicians were educated about COVID-19 symptoms and prevention measures. His work contributed to ensuring suspected cases of COVID-19 were identified. Colleagues always remember him as a devoted individual who was committed to saving lives and advance public health. He knew the challenges and risks that are inherent in WHO work, but continued regardless, always putting the greater good first and remains an example to us all.
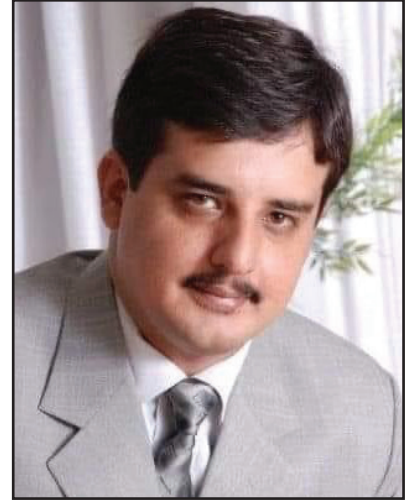
الدكتور فهد لياقت

2020-1981

تنعي منظمة الصحة العالمية ببالغ الحزن والأسى وفاة الزميل الدكتور فهد لياقت، مسؤول الترصّد على مستوى المناطق في منطقة خيبر في باكستان، الذي وافته المنية في 31 ديسمبر / كانون الأول 2020، عن عمر يناهز 39 عامًا. وقد انضم الدكتور فهد إلى برنامج استئصال شلل الأطفال في عام 2016، وعمل بلا كلل من أجل وقاية الأطفال الباكستانيين من شلل الأطفال في منطقة ذات أهمية استراتيجية في البلاد. وخلال الاستجابة لفاشية كوفيد-19، أدّى الدكتور فهد دورًا مهمًا إذ كان حريصًا على توعية المجتمعات المحلية والأطباء السريريين بأعراض كوفيد-19 وتدابير الوقاية منه. وساهم عمله في ضمان اكتشاف الحالات الـمُشتبَه في إصابتها بكوفيد-19. وسيبقى الدكتور فهد حاضراً في أذهان زملائه بإخلاصه والتزامه بإنقاذ الأرواح والنهوض بالصحة العامة. لقد أدرك الدكتور فهد التحديات والمخاطر المتأصلة في عمل المنظمة، لكنه وبغض النظر عن ذلك واصَل عمله واضعًا الصالح العام في المقام الأول دومًا، وسيظل – رحمة الله عليه – مثالًا نحتذي به جميعًا.

Eastern Mediterranean Health Journal reviewers' panel, 2020

The Eastern Mediterranean Health Journal extends sincere thanks to the following experts for their generous and invaluable assistance in the review of papers considered for publication during 2020.

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Arranged in alphabetical order according to the family name

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2. Papers submitted for publication to the EMHJ should conform with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (http://www.icmje.org/icmje-recommendations.pdf) of the International Committee of Medical Journal Editors (ICMJE).

3. **Ethical considerations / clearances:** Where applicable, a statement must be included indicating approval for the study was granted by the ethics committee/institutional review board of the relevant institution. The reference and institution granting ethical clearance must be clearly mentioned in the manuscript. Authors are expected to have reviewed articles already published by EMHJ relating to their research articles topic. Authors should verify where appropriate that all persons on whom research has been carried out have given their voluntary, informed, written consent, and where participants (living or dead) were unable to give such consent, that surrogate consent was obtained. Authors may be asked to supply such consent forms. Conflicts of interest: Authors will be asked to provide details of any competing interests and funding. Please see the ICMJE Recommendations. For clinical trials, a statement should be included reflecting national/international clinical trial registration, including name of registry, registration number and date.

4. **Reporting guidelines:** EMHJ encourages and recommends authors to adhere to the best research protocols available and follow established reporting guidelines. Reporting guidelines are available at the EQUATOR Network (http://www.equator-network.org/). The key guidelines for research in the field of public health are: CONSORT (guidelines for reporting randomized trials); STROBE (guidelines for reporting observational studies); PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses); STARD (Standards for Reporting of Diagnostic Accuracy); COREQ (Consolidated criteria for reporting qualitative research); CARE (guideline for clinical case report) as well as the COCHRANE handbook (for systematic reviews of interventions). Links to these sites and other useful resources are available under "Useful resources for authors and reviewers" (http://www.emro.who.int/emh-journal/links/).

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7. Abstracts of papers accepted for publication will be translated into all three languages. To ensure the correct spelling of authors' names to accompany the Arabic abstract, authors writing in English or French but whose mother tongue is written using Arabic characters should provide their full names in Arabic script along with transliterations in English or French.

8. Manuscripts should be prepared in word processed format (preferably Microsoft Word) double-spaced, single column, preferably using Times New Roman script, font size 12.

9. All papers considered for publication will be peer reviewed. The Editorial Board reserves the right to accept or reject any paper based on the reviewers' comments, scientific rigor and suitability for the journal. Papers are accepted on the understanding that they are subject to statistical and editorial revision as deemed necessary, including abridgement of the text and omission of tabular or graphic material.

10. **Topics:** The subject of the paper should pertain to public health or a related biomedical or technical subject within the field of interest of the WHO, and should have particular relevance to the Eastern Mediterranean Region.

11. The title of the paper should be as concise as possible, preferably not more than 15 words. All authors should have made material contribution to the design, analysis or writing of the study and have approved the final version submitted. No change in authorship will be permitted after the paper has been accepted for publication and any change before this must be agreed by all authors listed. Authors may be asked to verify their contribution. Names of other contributors may be included in the acknowledgements. Please see the ICMJE Recommendations for authorship and contributorship.

12. **Structured abstracts:** Submissions should include a structured abstract in this format: Background; Aims; Methods; Results; and Conclusion. The structure can be flexible if a paper warrants it and a justification offered by the author at submission.

13. **Research articles:** Papers reporting original research findings should follow this format: Background, aims; Methods; Results; Discussion and Conclusion. The text of Research articles and Reports should not exceed 3000 words (excluding references). A structured abstract should not exceed 250 words (see note 12). The maximum number of references permitted is 35 and must include DOIs if available. The number of tables and figures should not exceed 5.

Research data should ideally be no more than 5 years old.

14. **Review articles:** (i.e. critical assessments of research on topics of relevance to public health in the Region). These should contain sections dealing with objectives, sources, methods of selection, compilation and interpretation of data and conclusions. The text should not exceed 3000 words (excluding the accompanying abstract, references, tables and figures), and should be accompanied by an abstract of not more than 250 words (see note 12). The number of tables and figures should not exceed 5. Authors are expected to have reviewed articles already published by EMHJ relating to their research topic, and cite where appropriate.

15. **Reports:** (i.e. papers reporting on projects of public health relevance to the Eastern Mediterranean Region). Manuscript specifications (length, references, tables/figures) are the same as a research article, but abstract length should not exceed 150 words. Authors are expected to have reviewed articles already published by EMHJ relating to their research topic, and cite where appropriate.

16. **Short research communications:** Articles which do not constitute a complete research study but are of particular relevance or importance to public health issues in the Region may be considered for publication. The text should not exceed 1500 words (excluding references), and should be accompanied by a structured abstract (see note 12) of not more than 150 words. The number of tables and figures should not exceed 3, and no more than 35 references. Research data should ideally be no more than 5 years old.

17. **Commentaries:** (i.e. papers reporting on research/issues of public health relevance to the Eastern Mediterranean Region). Manuscript specifications (references, tables/figures) are the same as a short research communication, but maximum length is 1000 words. The abstract (unstructured) for submissions purposes should not exceed 150 words, and the abstract should mirror the 1st paragraph of the submission. Authors are expected to have reviewed articles already published by EMHJ relating to their research topic, and cite where appropriate.

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19. **Letters to the Editor:** Letters commenting on published articles are welcome. Letters will be sent to the authors of the original article for their comments, and these will be published along with the letter. The text of letters should not exceed 500 words.

20. **Editorials:** Editorials are commissioned; unsolicited submissions are not normally received. If commissioned, editorial length is 800 words and supported by 8–10 references. Authors are expected to have reviewed articles already published by EMHJ relating to their research topic, and cite where appropriate.

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Book:
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Journal article:
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Document:
Al-Itneen M, ed. The principles of uncertainty. Geneva: World Health Organization; 1985 (WHO/DOC/537).
Thesis
Smith S. Use of healthcare services by the elderly with the introduction of technical innovations. London: Drake University; 2013.
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Child growth standards. Geneva: World Health Organization; 2006 (http://www.who.int/childgrowth/en/, accessed 8 October 2008).

22. Figures and tables with appropriate captions should each be on a separate page and numbered sequentially with Arabic numerals. Each figure and table must be referred to in the text. Where appropriate, sources should be given. If any figures, tables or other materials have been copied from other sources, authors have the sole responsibility for securing the necessary permission. In order to avoid layout problems in final production, tables and figures should be limited as far as possible. Figures must be supplied in a format which can be edited, preferably Microsoft Excel format, and figures derived from data must be accompanied by those data, e.g. Excel data sheet, to enable redrawing if necessary. Photographs and illustrations should also be sent as separate files. The preferred format is JPG or TIFF; resolution should be minimum 300 dpi.

23. Submissions that do not comply with these guidelines will be returned to the authors for correction before being considered for publication.

٦. تقديم الأبحاث: يمكن تقديم الأبحاث الأصلية المكتوبة باللغة العربية أو الإنجليزية أو الفرنسية للنظر فيها وذلك من خلال نظام التقديم عبر الإنترنت الخاص بالمجلة الصحية لشرق المتوسط. ويمكن الاطلاع على التعليمات حول تقديم مخطوط البحث عبر نظام التقديم على الإنترنت والدخول على ذلك النظام على موقع المجلة الصحية لشرق المتوسط على الإنترنت، وهو (http://www.emro.who.int/emh/emh-journal/ authors) ثم الضغط على أيقونة Editorial Manager.

٧. سوف تُترجم ملخصات الأبحاث التي قُبِلت للنشر إلى اللغات الثلاث، ومن أجل ضمان الكتابة الصحيحة لأسماء المؤلفين في سياق الملخص بالعربية، فإن على المؤلفين الذين كتبوا بحوثهم بالإنجليزية أو الفرنسية ولكن لغتهم الأم تكتب بالحروف العربية أن يكتبوا أسماءهم بالحروف العربية مع مقابلاتها باللغة الإنجليزية أو بالفرنسية.

٨. يجب إعداد المخطوطة باستخدام برامج معالجة الكلمات (ويفضل برنامج ميكروسوفت – وورد) وأن تكتب بفواصل مضاعفة بين الأسطر وفي عمود واحد ويفضل استخدام الخط Times New Roman وأن يكون حجم الخط ١٢.

٩. تخضع جميع الأبحاث التي تقدم للنشر لمراجعة الزملاء، وتحتفظ هيئة التحرير بحق قبول أو رفض أي ورقة استناداً إلى الملاحظات التي يبديها المراجعون، وإلى السلامة العلمية، وإلى ملاءمة البحث للمجلة. ومن المتفق عليه أن قبول الأبحاث يستند إلى مراجعتها إحصائياً وتحريرياً وفق ما تقتضيه الحاجة، ويتضمن ذلك اختصار النص وحذف بعض الجداول أو الرسوم البيانية.

١٠. المواضيع يجب أن يكون موضوع البحث له صلة بالصحة العامة أو بأي مادة تقنية أو طبية حيوية في مجال يحظى باهتمام منظمة الصحة العالمية وله أهمية خاصة لإقليم شرق المتوسط.

١١. ينبغي لعنوان البحث أن يكون مختصراً على قدر المستطاع، ويفضل ألا يزيد على ١٥ كلمة. وينبغي لجميع المؤلفين أن يكونوا قد أسهموا مساهمة مادية في تصميم الدراسة أو تحليلها أو كتابتها، وأن يكونوا قد وافقوا على النسخة النهائية المقدمة. ولن يسمح بأي تغيير في ما يتعلق بتأليف الورقة بعد قبولها للنشر، كما يجب أن يحظى كل تغيير على موافقة مسبقة من جميع المؤلفين المذكورة أسماؤهم. وقد يطلب من المؤلفين إثبات إسهاماتهم، كما يمكن إدراج أسماء مساهمين آخرين في عبارات الشكر، ويُرجَى النظر في توصيات حول السلوكيات والإبلاغ والتحرير والنشر للأعمال العلمية في المجلات الطبية حول التأليف والإسهام.

١٢. الملخصات: يجب أن تحتوي الأبحاث المقدمة على ملخص منظم على النحو التالي: معلومات أساسية، والأهداف، والطرق، والنتائج، والاستنتاجات. ومن الممكن أن يكون التنظيم مرناً إذا اقتضى البحث ذلك، وساق المؤلف تبريرا لذلك وقت تقديم البحث.

١٣. مقالات البحوث: يجب أن تتقيد الأبحاث التي تتضمن الإبلاغ عن نتائج أصلية بالتنسيق التالي: المعلومات الأساسية، والأهداف، والطرق، والنتائج، والمناقشة، والاستنتاجات. ويجب ألا تتجاوز مقالات البحوث والتقارير ٣٠٠٠ كلمة (دون أن يتضمن ذلك المراجع). ويجب ألا يتجاوز الملخص المنظم ٢٥٠ كلمة (انظر البند ١٢). أما العدد الأقصى المسموح به للمصادر والمراجع فهو ٣٥ مصدراً

١. ينبغي للأبحاث المقدَّمة للنشر في المجلة الصحية لشرق المتوسط ألا تكون قد نشرت أو قُبِلت للنشر أو تكون محلاً للنظر في نشرها في مكان آخر. ويحتفظ المكتب الإقليمي لمنظمة الصحة العالمية لشرق المتوسط بجميع حقوق إعادة إنتاج المواد التي تُنشر في المجلة الصحية لشرق المتوسط أو إعادة نشرها.

٢. ينبغي للأبحاث المقدَّمة للنشر في المجلة الصحية لشرق المتوسط أن تلبِّي التوصيات حول السلوكيات والإبلاغ والتحرير والنشر للأعمال العلمية في المجلات الطبية التي أصدرتها اللجنة الدولية لمحرري المجلات الطبية.

٣. اعتبارات البُعد الأخلاقي: بحسب الاقتضاء يجب إرفاق البحث المقدَّم للنشر في المجلة الصحية لشرق المتوسط بما يفيد الموافقة على الدراسة من جانب لجنة الأخلاقيات/ مجلس المراجعة المؤسسية في المؤسسة ذات الصلة بالبحث، كما يجب على المؤلفين التأكد، حيثما كان ذلك مناسباً، من أن جميع الأشخاص الذين شملهم البحث قد قدموا موافقة كتابية طوعية مستنيرة، وعندما يتعذر ذلك على المشاركين في البحث (سواءً الأحياء منهم أو الأموات)، يجب على المؤلفين الحصول على موافقة بديلة. وقد يُطلب من المؤلفين تقديم نماذج هذه الموافقات. تضارب المصالح: سيطلب من المؤلفين تقديم معلومات تفصيلية حول أي تضارب في المصالح وحول التمويل. يُرجَى الاطلاع على توصيات حول السلوكيات والإبلاغ والتحرير والنشر للأعمال العلمية في المجلات الطبية.

٤. دلائل إرشادية حول إعداد التقارير: تشجع المجلة الصحية لشرق المتوسط المؤلفين وتوصيهم بالالتزام بأفضل بروتوكولات البحوث المتاحة، واتباع الدلائل الإرشادية المعتمدة في إعداد التقارير، ويمكن الاطلاع على الدلائل الإرشادية حول كتابة التقارير على شبكة EQUATOR (http://www.equator-network.org). وتتمثَّل الدلائل الإرشادية الرئيسية للبحوث في ميدان الصحة العامة فيما يلي: المعايير المجمّعة لكتابة التقارير حول الدراسات (CONSORT) وهي الدلائل الإرشادية لإعداد التقارير حول الدراسات المعشّاة، وSTROBE وهي الدلائل الإرشادية حول كتابة التقارير للدراسات المعتمدة على الملاحظة، والمكونات المفضلة في كتابة تقارير المراجعات المنهجية والتحليل البعدي PRISMA ومعايير إعداد التقارير حول الدقة التشخيصية STARD، والمعايير المجمّعة لكتابة التقارير حول البحوث النوعية COREQ، وكتيب كوكرين COCHRANE (للمراجعات المنهجية للتدخلات). والروابط إلى تلك المواقع وغيرها من المصادر المفيدة متاحة على الرابط "المصادر المفيدة للمؤلفين والمراجعين" (http://www.emro.who.int/emh-journal/links).

٥. وفقاً لتوصيات منظمة الصحة العالمية وتوصيات اللجنة الدولية لمحرري المجلات الطبية، فإن المجلة الصحية لشرق المتوسط تطلب تسجيل الدراسات السريرية (الإكلينيكية) في سجل للدراسات العامة كشرط للنظر في نشرها، ويُوصَى المؤلفون بالتسجيل في أحد سجلات الدراسات السريرية المشهود لها من قِبَل منظمة الصحة العالمية واللجنة الدولية لمحرري المجلات الطبية، وتتوافر هذه السجلات على البوابة الدولية لسجل الدراسات السريرية (http://www.who.int/ictrp/en).

ومرجعاً، مع ضرورة أن تتضمن معرفات الوثائق الرقمية (DOI) إن وجدت، كما يجب ألا يتجاوز عدد الجداول والأشكال ٥.

١٤.مقالات المراجعة: وهي تقييمات دقيقة للبحوث حول المواضيع ذات الصلة بالصحة العامة في الإقليم. وينبغي لهذه المقالات أن تضم فقرات تتعلق بالأهداف والمصادر وطرق اختيار البيانات وتجميعها وتفسيرها والاستنتاجات. وينبغي للنص ألا يزيد عن ٣٠٠٠ كلمة (ولا يتضمن ذلك ما يرافقه من ملخص ومراجع وجداول وأشكال)، كما يجب أن يرفق بملخص لا يتجاوز ٢٥٠ كلمة (انظر البند ١٢)، وألا يتجاوز عدد الجداول والأشكال ٥.

١٥.التقارير: وهي تقارير أعدت حول مشاريع ذات صلة بالصحة العامة في إقليم شرق المتوسط، وتتطابق مواصفات المخطوطات (من حيث الطول والمراجع والجداول والأشكال) مع ما هو مطلوب بالنسبة لمقالات البحث.

١٦.مراسلات قصيرة: يمكن النظر في نشر مقالات لا تضم دراسة بحثية كاملة، ولكنها ذات صلة أو أهمية خاصة فيما يتعلق بقضايا الصحة العامة في الإقليم. وينبغي للنص ألا يتجاوز ١٥٠٠ كلمة (ولا يتضمن ذلك ما يرافقه من ملخص ومراجع وجداول وأشكال)، كما يجب أن يرفق بملخص منظم لا يزيد عن ١٥٠ كلمة (انظر البند ١٢)، أما عدد الجداول والأشكال فيجب ألا يزيد عن ٣ جداول وأشكال.

١٧.تقارير حالات: لا ينظر للنشر إلا في تقارير حالات ذات طبيعة غير معتادة. وينبغي للنص أن يتضمن مقدمة وتقريراً عن الحالة أو الحالات ومناقشة لها. وينبغي للنص ألا يزيد على ١٥٠٠ كلمة، وأن يكون عدد المراجع في حده الأدنى، والملخص لا يزيد عن ١٥٠ كلمة (انظر البند ١٢).

١٨.رسالة إلى المحرر: إن الرسائل التي تتضمن تعليقاً على المقالات المنشورة هي موضع ترحيب، وترسل هذه الرسائل إلى مؤلفي المقالة الأصلية للتعليق عليها، ثم تنشر تلك التعليقات مع الرسائل. ويجب ألا يتعدى التعليق ٥٠٠ كلمة.

١٩.المراجع: يجب أن يقتصر الاقتباس من الأعمال المنشورة على المراجع الأساسية والمحدَّثة. ويجب ترقيم هذه المنشورات على نحو منفصل وفق ظهورها في النص مع استخدام أرقام عربية متتابعة، مثلً (٨ – ٥، ١). ويجب عرض هذه المراجع في شكل قائمة مرقمة على صفحة منفصلة بعد قسم المناقشة، وينبغي للمراجع أن تتضمن العناصر التالية، وفق المقتضى: اسم المؤلف ولقبه وعنوان الورقة أو الكتاب باللغة الأصلية مع ترجمته؛ وينبغي لمقالات البحث أن تتضمن الاسم المختصر للمجلة مع رقم المجلد وحدود الصفحات. وينبغي للكتب وغيرها من النصوص أن تتضمن مكان النشر (المدينة ثم البلد)، واسم الناشر

(تجاري أم مؤسسة)، وتاريخ النشر. وينبغي للنصوص التي اقتصر نشرها على الإنترنت أن تتضمن العنوان الإلكتروني للصفحة المقتبسة وتاريخ الدخول عليها آخر مرة. وينبغي للنصوص التي لا يزيد عدد المؤلفين لها عن ٦ مؤلفين أن يذكر أسماء جميع المؤلفين، أما النصوص التي يزيد عدد المؤلفين لها على ٦ مؤلفين، فتُذكر أسماء المؤلفين الستة الأوائل متبوعة بكلمة "وزملاؤهم". (برجاء مراجعة النص الإنجليزي لأمثلة الأنماط التي يفضَّل اتباعها في المجلة الصحية لشرق المتوسط).

٢٠.الأشكال والجداول المشفوعة بشروحات ملائمة، ينبغي لكل منها أن يكون في صفحة مستقلة، وأن تُعطى أرقاماً متتالية بأعداد عربية. ويجب الإشارة في النص لكل شكل ولكل جدول. ويجب توضيح المراجع حيثما كان ملائماً. وإذا ما نسخ المؤلفون أي شكل أو جدول أو مادة أخرى من مراجع أخرى، فإنهم يتحملون وحدهم المسؤولية عن تأمين الإذن اللازم للقيام بذلك. وبغية تفادي مشكلات التنسيق في مرحلة الإخراج النهائي، يجب الاقتصار على أقل عدد ممكن من الجداول ومن الأشكال.

٢١. ويجب تقديم الأشكال في صيغة قابلة للتعديل، ويفضل (ميكروسوفت – إكسل)، كما أن الأشكال المستخلصة من البيانات يجب أن تُرفق بها تلك البيانات، مثلاً صفحة إكسل للبيانات، حتى يصبح بالإمكان إعادة إنتاجها عند الضرورة. كما يجب إرسال الصور الفوتوجرافية والرسومات التوضيحية في ملفات منفصلة، ويفضل أن تكون في شكل ملفات JPG أو TIFF، كما يجب أن يكون الوضوح بدرجة لا تقل عن ٣٠٠ نقطة لكل بوصة.

٢٢.ستُعاد الأبحاث المقدمة التي لا تلتزم بالدلائل الإرشادية المذكورة إلى المؤلفين من أجل تصحيحها قبل النظر في نشرها.

٢٣.التعليقات: (ويقصد بها الورقات التي تقدم معلومات عن الأبحاث/ قضايا الصحة العامة ذات الأهمية لإقليم شرق المتوسط). ومواصفات المخطوط (الطول، والمراجع، والجداول/الأشكال) هي ذاتها التي تنطبق على المراسلات القصيرة، غير أنه -ولأغراض تتعلق بالورقات المُقدَّمة- لا ينبغي أن يتجاوز الملخص (غير المنظم) ١٥٠ كلمة، وينبغي أن يتطابق الملخص مع الفقرة الأولى من الورقة المقدمة.

المقالات الافتتاحية: يجري التعاقد مع أحد الأشخاص لكتابة المقالات الافتتاحية؛ وعادة ما تُرفض المقالات التي تُقدَّم دون طلب. وفي حال التعاقد على كتابتها، تحتوي المقالة الافتتاحية على ٨٠٠ كلمة، وتدعمها ٨-١٠ مراجع.

1. Les articles soumis pour publication à *La Revue de Santé de la Méditerranée orientale* ne doivent pas avoir été publiés, avoir été acceptés pour publication dans d'autres revues ou être en cours d'examen par d'autres revues. Le Bureau régional de l'Organisation mondiale de la Santé (OMS) pour la Méditerranée orientale se réserve tous les droits de reproduction et de republication des matériels qui paraissent dans *La Revue de Santé de la Méditerranée orientale.*

2. Les articles soumis pour publication à *La Revue de Santé de la Méditerranée orientale* doivent être conformes aux Recommandations pour la conduite, la présentation, la rédaction et la publication des travaux de recherche soumis à des revues médicales (http://www.icmje.org/recommendations/translations/french2015.pdf) de l'*International Committee of Medical Journal Editors* (Comité international des éditeurs de revues médicales, ICMJE).

3. **Considérations éthiques** : Le cas échéant, une déclaration devra être incluse, indiquant que le Comité d'éthique ou le Comité d'examen institutionnel de l'organisme concerné a donné son accord à l'étude. Les auteurs doivent vérifier, le cas échéant, que toutes les personnes sur lesquelles la recherche porte ont donné leur consentement volontaire et informé par écrit et que si certains participants (en vie ou décédés) n'ont pas pu le donner, un consentement de substitution a été obtenu. Il peut être demandé aux auteurs de fournir ce type de formulaire de consentement. Conflits d'intérêts : Il sera demandé aux auteurs de préciser tout conflit d'intérêts et financement. Veuillez vous reporter aux recommandations de l'ICMJE.

4. **Directives de présentation** : La Revue de Santé de la Méditerranée orientale encourage les auteurs à respecter les meilleurs protocoles de recherche disponibles et leur recommande de suivre les directives de présentation établies. Les directives de présentation sont disponibles sur le site Web du réseau EQUATOR (http://www.equator-network.org/). Les principales directives pour la recherche en santé publique sont les suivantes : directives CONSORT (essais randomisés) ; directives STROBE (études observationnelles) ; directives PRISMA (revues systématiques et méta-analyses) ; directives STARD (normes de présentation de rapports concernant l'exactitude de diagnostic) ; critères COREQ (recherche qualitative) ; directives CARE (publication de cas cliniques) et le manuel COCHRANE (pour les revues systématiques des interventions). Les liens vers ces sites Web et d'autres ressources utiles sont disponibles sous la rubrique « Ressources à l'intention des auteurs et des réviseurs » à l'adresse suivante : http://www.emro.who.int/fr/emh-journal/links/.

5. Suite aux recommandations de l'OMS et de l'ICMJE, *La Revue de Santé de la Méditerranée orientale* impose comme condition de publication que les essais cliniques soient enregistrés auprès du registre public des essais cliniques. Il est recommandé aux auteurs d'enregistrer leurs essais dans un des registres des essais cliniques certifiés par l'OMS et l'ICMJE disponibles dans la base de données du Système d'enregistrement international des essais cliniques (http://www.who.int/ictrp/fr/).

6. **Soumission** : Les articles originaux rédigés en anglais, arabe ou en français peuvent être soumis pour examen en utilisant notre système en ligne. Les instructions relatives à la soumission d'un manuscrit en utilisant le système en ligne sont disponibles en anglais sur notre site Web accessibles à l'adresse suivante : http://www.emro.who.int/emh-journal/authors/, et en cliquant sur « Editorial Manager ».

7. Les résumés des articles acceptés pour publication seront traduits dans les trois langues. Pour assurer que les noms des auteurs soient correctement écrits dans les résumés en arabe, les auteurs rédigeant en anglais ou en français mais dont la langue maternelle s'écrit en caractères arabes doivent fournir leur nom complet en écriture arabe avec une translittération de leur nom en anglais ou en français.

8. Les manuscrits doivent être préparés en format traitement de texte (Microsoft Word, de préférence), avec double interlignage, mise en page d'une seule colonne, police Times New Roman, taille de caractère 12.

9. Tous les articles dont la publication est envisagée seront revus par des pairs. Le Comité de rédaction se réserve le droit d'accepter ou de refuser tout article, sur la base des commentaires des réviseurs, de la rigueur scientifique et de la pertinence de l'article pour La Revue. Les articles sont acceptés sous réserve de la révision statistique et rédactionnelle dont ils feront l'objet, comme jugé nécessaire, ce qui peut amener à abréger le texte et à supprimer certaines données présentées sous forme de tableaux ou de graphiques.

10. **Sujets** : Le sujet de l'article doit concerner la santé publique ou un autre sujet biomédical ou technique connexe faisant partie du champ d'intérêt de l'OMS, et se rapporter plus particulièrement à la Région de la Méditerranée orientale ou revêtir une importance particulière pour celle-ci.

11. Le titre de l'article doit être aussi concis que possible, et de préférence ne pas dépasser 15 mots. Tous les auteurs devraient avoir apporté une contribution importante à la conception, à l'analyse ou à la rédaction de l'étude et avoir approuvé la version finale soumise. Aucun changement dans les noms des auteurs ne sera autorisé après l'acceptation de l'article pour publication; avant cette acceptation, tout changement doit être accepté par l'ensemble des auteurs figurant dans la liste. Une vérification de leur contribution peut être demandée aux auteurs. Les noms d'autres contributeurs peuvent être inclus

dans les remerciements. À ce sujet, veuillez vous reporter aux *ICMJE recommendations for authorship and contributorship* [Recommandations de l'ICMJE relatives à la qualité d'auteur et de contributeur].

12. **Résumés structurés** : Les articles soumis devraient inclure un résumé structuré organisé selon les titres suivants : Contexte ; Objectifs ; Méthodes ; Résultats ; et Conclusion. La structure peut être ajustée selon les besoins de l'article et si l'auteur fournit une justification au moment de la soumission.

13. **Articles de recherche** : Les articles présentant des résultats de recherche originale devront suivre le format suivant : Contexte ; Objectifs ; Méthodes ; Résultats ; Analyse ; Discussion et Conclusion. Le texte des articles et des rapports de recherche ne doit pas excéder 3 000 mots (références exclues). Un résumé structuré ne doit pas dépasser 250 mots (voir paragraphe 12). Le nombre maximal de références autorisées est de 35 et les identifiants d'objet numérique (DOI) doivent être inclus le cas échéant. Le texte ne doit pas comporter plus de cinq tableaux ou figures.

14. **Articles d'analyse** : il s'agit d'évaluations critiques d'études de recherche sur des sujets pertinents concernant la santé publique dans la Région. Ils doivent être composés de paragraphes traitant des objectifs, des sources, des méthodes de sélection, de la compilation et de l'interprétation des données et des conclusions. Le texte ne doit pas excéder 3000 mots (résumé, références, tableaux et figures exclus) et doit être accompagné d'un résumé de 250 mots au maximum (voir paragraphe 12). Le nombre maximal de tableaux et de figures autorisé est de 5.

15. **Rapports** : il s'agit d'articles présentant des projets pertinents de santé publique dans la Région de la Méditerranée orientale. Le format des manuscrits (longueur, références, tableaux et figures) est le même que pour les articles de recherche mais la longueur des résumés ne doit pas excéder 150 mots.

16. **Brèves communications de recherche** : Les articles ne constituant pas une étude de recherche complète, mais présentant un intérêt ou revêtant une importance particulière pour les questions de santé publique dans la Région peuvent être examinés pour publication. Le texte ne doit pas excéder 1 500 mots (références exclues) et doit être accompagné d'un résumé de 150 mots au maximum. Le nombre maximal de tableaux et de figures est de 3.

17. **Commentaires :** (par ex. les articles rendant compte de la recherche/des questions pertinentes pour la santé publique dans la Région de la Méditerranée orientale). Les spécifications des manuscrits (références, tableaux/figures) sont les mêmes que pour une brève communication de recherche, mais le texte ne doit pas excéder 1000 mots au maximun. Le résumé (non structuré) ayant pour objectif d'être soumis à proposition ne devrait pas dépasser 150 mots ; ce résumé doit refléter le contenu du premier paragraphe de la soumission.

18. **Études de cas** : Seules les études de cas inhabituels seront examinées pour publication. Le texte doit comprendre une introduction, un exposé du/des cas et une discussion. Il ne doit pas excéder 1 500 mots et le nombre de références doit être minimal. Il n'est pas nécessaire de fournir un résumé.

19. **Lettres à la rédaction** : Les lettres commentant des articles publiés sont les bienvenues. Elles seront envoyées aux auteurs de l'article afin qu'ils fournissent leurs commentaires, qui seront publiés aux côtés de la lettre. Le texte des lettres ne doit pas dépasser 500 mots.

20. **Editoriaux :** Les éditoriaux sont réalisés sur commande ; les soumissions non sollicitées ne sont généralement pas acceptées. Lorsqu'ils font l'objet d'une commande, les éditoriaux comprennent 800 mots et huit à dix références.

21. **Références** : Les citations dans le texte de travaux publiés doivent être limitées aux références essentielles récentes. Elles doivent être numérotées séparément à l'aide de chiffres arabes indiqués entre crochets, par exemple (1,5-8). Les références doivent figurer sous forme de liste numérotée sur une page séparée après la partie « Discussion ». Elles doivent contenir les éléments suivants, selon le cas : nom(s) et initiales du ou des auteurs ; titre de l'article ou de l'ouvrage dans sa langue originale ainsi que sa traduction ; pour les articles de recherche, le nom abrégé de la revue ainsi que le numéro du volume et les pages concernées ; pour les ouvrages et autres textes, le lieu de publication (ville et pays) et le nom de la maison d'édition (commerciale ou institutionnelle) ; la date de publication et l'identifiant d'objet numérique (DOI) ; pour les textes publiées exclusivement sur Internet, l'URL exact de la page citée et la date du dernier accès. Lorsque les textes comptent moins de six auteurs, tous les auteurs doivent être nommés. Lorsque les textes comptent plus de six auteurs, seul les noms des six premiers auteurs sont mentionnés, suivis de « et al. ». Exemples du style préféré de La Revue :

Livre :

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Article de revue :

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Document :

Al-Itneen M, ed. The principles of uncertainty. Geneva, World Health Organization, 1985 (WHO/DOC/537).

Thèse :

Smith S. Use of healthcare services by the elderly with the introduction of technical innovations.

London: Drake University; 2013.

Texte Web :

Child growth standards. Geneva, World Health Organization, 2006 (http: //www. who. int/ childgrowth/en/, consulté le

8 octobre 2008).

22. Les figures et les tableaux accompagnés des légendes appropriées doivent être placés chacun sur une feuille séparée, numérotés en chiffres arabes selon leur ordre. Chaque figure et chaque tableau doivent être référencés dans le texte, et le cas échéant, les sources doivent être indiquées. Si des figures, tableaux ou d'autres matériels ont été copiés d'autres sources, les auteurs portent l'entière responsabilité d'obtenir les autorisations nécessaires. Afin d'éviter les problèmes de mise en page lors de la production finale, le nombre de tableaux et de figures doit être aussi limité que possible. Les figures doivent être fournies dans un format permettant les modifications, de préférence Microsoft Excel, et celles qui sont établies à partir de données doivent être accompagnées de ces données, sur une fiche technique Excel par exemple, pour permettre une recomposition, le cas échéant. Les photographies et illustrations doivent être envoyées dans des fichiers séparés. Les formats préférés sont JPG et TIFF, et la résolution des images doit être de 300 dpi au minimum.

23. Les manuscrits ne respectant pas ces directives seront renvoyés à leurs auteurs pour correction avant d'être examinés en vue de la publication.

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