Factors associated with tuberculosis diagnosis and treatment delays in Middle East and North Africa: a systematic review

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Abstract

Background: Political instability, economic sanctions and substandard quality of health care negatively affect tuberculosis (TB) control in the Middle East and North Africa (MENA) region.

Aims: We aimed to elucidate factors contributing to delays in TB diagnosis and treatment in MENA countries.

Methods: Two reviewers independently appraised eligible articles identified through comprehensive searching and extracted data which were subjected to meta-analysis.

Results: Delays in TB diagnosis were associated with older age and low income [(OR = 1.49; 95% CI: 1.31–1.70) and (OR = 1.26; 95% CI: 1.09–1.45)] respectively (n = 17 studies). Being female was associated with patient delay and health system delay [(OR = 1.24; 95% CI: 1.02–1.50) and (OR = 1.68; 95% CI: 1.18–2.38)] respectively. Knowledge and perception of TB, having employment and low levels of crowding were each protective against patient delay. The GRADE system rated the evidence as of low quality.

Conclusion: This review provides evidence for facilitators and barriers to TB diagnosis and health system delays. For successful TB control in the MENA region, TB awareness and interventions targeting the elderly and those from lower-income settings, particularly directed at gender differences, are essential.

Keywords: Tuberculosis case finding, delayed diagnosis, tuberculosis control, Middle East and North Africa, health care-seeking behaviour, delivery of health care

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Introduction

Tuberculosis (TB) remains a major global health problem (1). In 2015, an estimated 4.3 million cases were neither detected nor treated in national TB programmes globally (1).

A diagnostic delay of two months will result in transmission of TB to an average of 8 contacts (2) and within a year, this number will increase eight to 15 persons; the increase would be even higher in settings of overcrowding and higher social capital (3). Furthermore, delays between admission and initiation of treatment will result in the exposure to TB of an average of 23.9 health care workers (4). Therefore, to curb TB transmission and reduce poor disease outcomes and adverse social and economic consequences, timely diagnosis and prompt initiation of anti-TB treatment is vital (5).

Reasons for delayed TB diagnosis can be attributed to both patients and the health care system (6). Patients may delay in seeking help while the health care system may delay in suspecting TB and initiating relevant investigations. Delays, and ultimately TB control, are affected by patient factors such as sociodemographic characteristics, stigmatization effects of TB, fear of high individual expenses, symptoms on presentation and health care factors such as absence of a refined TB suspicion index, infrastructure and organization of the health system (7).

The World Bank's description of the Middle East and North Africa (MENA) region covers the 21 members of the Arab League, plus the Islamic Republic of Iran, Israel and Turkey (8). The MENA region is challenged with delayed detection of TB, which negatively affects treatment and control in the region (9). Factors in the region that have destabilized health care delivery are political instability and economic sanctions. Health care resources are thus stretched beyond control, and the quality of health care service delivery deteriorated to a level that can be described as "below standard" (9).

There is a scarcity of systematic reviews addressing TB diagnostic and treatment delays (10). Furthermore, these reviews included older studies, are applicable to high HIV prevalence settings, and specifically did not include diagnostic and treatment delays in MENA countries.

We conducted a systematic review to address this paucity of data. We wished to evaluate the evidence regarding factors associated with TB diagnostic and treatment delays in the MENA region. Successful identification of such factors may actually lead to interventions which may ultimately increase effective TB control.

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Methods

Protocol

The review protocol has been published in the PROSPE-RO International Prospective Register of systematic reviews, (http://www.crd.york.ac.uk/PROSPERO) registration number CRD42015023337.

Search methods for identification of studies

This systematic review adheres to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRIS-MA) guidelines 2009 (11). We searched MEDLINE using combinations of the following keywords: TB, tuberculosis, mycobacterium, patient delay, health seeking delay, care-seeking delay, health system delay, health facility delay, health provider delay, diagnosis delay, total delay and treatment delay. Key terms (factors or enablers and barriers) that did not provide new articles were excluded from the final search strategy. Search strategies incorporated both medical subject headings (MeSH) and freetext terms using controlled vocabularies applicable to databases. Published and unpublished articles, irrespective of language used, were interrogated up to June 2015.

Electronic searches were carried out on the following published databases: Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, PubMed, CINAHL, Psychlnfo and Scopus. Grey literatures were searched using Index Medicus for the Eastern Mediterranean Region (IMEMR), (Africa-wide) allied health and Google scholar. In addition, we searched conference proceedings and reference lists of relevant articles.

Observational studies (case-control, cross-sectional and population-based) were considered for review. Studies which reported patient and health system delays in patients diagnosed with, or suspected of, pulmonary TB (PTB) were included. Andersen's behavioural model of health care utilization was used to classify factors regarded as primary outcomes for the study (12). These factors were defined as predisposing factors (factors influencing the initial performance of behaviour); enabling factors (factors making it possible for individuals to enact their behaviour) and need factors (factors following behaviour enactment and influence continued behaviour). Secondary outcomes were: magnitude of patient delay (defined as time interval from onset of TB symptoms to first visit of any health provider), health system delay (defined as time interval from the first health provider visit to initiation of treatment) and total delay, which includes both patient and health system delays (defined as time interval from onset of TB symptoms to initiation of treatment).

Data collection and analysis

Selection of studies and data extraction

Two reviewers (DE and EP) independently screened titles and abstracts of all identified articles to select potential eligible studies; reviewed full texts of potentially eligible studies; nominated the final set of articles for inclusion into the review; extracted data using a standardized data extraction form and reviewed risk of bias. A third reviewer (ME or LA) facilitated disagreements regarding study selection and data extraction.

Assessment of risk of bias

We noticed a 2-study design, a descriptive phase and an analysis phase, in 12/20 studies. In these studies the descriptive phase, a cross-sectional design, was used to determine the extent of delay while during the analysis phase, a nested case-control design, patient delay was compared to the median time of delay. The quality of these studies was assessed based on results from the analysis phase. Two authors used the Newcastle-Ottawa Quality Assessment Scale for case-control studies (13) to assess the risk of bias in these 12 studies.

Cross-sectional and descriptive surveys were assessed according to an assessment tool by Hoy et al. (14) as adapted by Werfalli et al. (15). This adapted assessment tool allows for allocation of a composite score to assist with relative comparison between studies.

Data analysis and synthesis

The results of each study were expressed as an odds ratio (OR) with the corresponding 95% confidence interval (CI) for dichotomous data. Studies that compared similar types of outcomes were grouped to get feasible results on an overall estimate of effect. Random effects meta-analysis was used due to heterogeneity in study results. Prevalence of TB delay from different studies was pooled in a meta-analysis using *Review Manager*, 5.3.

Assessment of heterogeneity and subgroup analysis

Statistical heterogeneity between the study results were examined using the χ^2 test for homogeneity (with significance defined at the alpha-level of 10%) and quantified using the I-squared statistic. The χ^2 test for subgroup differences was used to test for subgroup interactions.

Grading the quality of evidence

We used *GRADEpro* software to appraise limitations to validity in terms of the quality of evidence on the 12/20 observational studies pooled in the meta-analysis.

Results

Study flow and description of studies

Full-text evaluations were performed on 32 articles, of which 12 were deemed unsuitable for inclusion in the review (Figure 1) (references available from corresponding author upon request). Reasons for exclusion were: in 2 studies participants did not meet the inclusion criteria; in 2 other studies participants were not from the MENA countries; and in the last 8 studies the outcomes measures did not address TB delay.

The 20 studies included in this systematic review were published between 2001 and 2015; 18 had a cross-sectional study design while 2 were nested case-control studies. Participants included in the studies ranged from TB



324 studies identified and screene

• 303 from electronic databases and trail registrices

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- 20 from hand searchin lg
- 1 from contact with authc or

Excluded studies

- 58 duplicates
- 234 based on title and abstract

32 studies: conducted full text reviev



- 2 participants did not meet inclusion criteria
- 2 participants were not from MENA region
- 8 outcome measures not related to TB delay

20 studies from MENA countries included in systematic review: 6 Iran [18,26,27,28,32,33] 5 Turkey [17,19,29,30,34] 2 Yemen [20,35] 2 Syria [21,31] 2 Sudan [22,23] 1 Jordan [16] 1 Morocco [24] 1 multi-country [25] (Iraq, Islamic Republic of Iran, Egypt, Somalia)

suspects (1 study) (16), smear negative and smear positive PTB patients (2 studies) (17,18)) and only new smearpositive patients (17 studies) (19–35). Almost all studies used a consecutive method of sampling and sample sizes ranged from 50 to 5702. Male sex was dominant in all of the studies and the majority were conducted in both urban and rural settings (detailed characteristic of studies included in the systematic review available upon request). Sixteen studies assessed both sources of delay; 4 assessed only patient delay while 2 assessed total delay without any demarcation between patient and health system delay. Seventeen studies measured the duration of patient delay, of which only 10 analysed the factors attributed to this period (16,22,27,28,30–35). Out of 15 studies that measured the duration of health system delay, 6 analysed at least 1 factor associated with this period (22,23,26,32,34,35).

Assessment of risk of bias

We found 11 studies had a low risk of bias (*16,19–25a–25d*), 7 had a moderate risk of bias (*17,26–31*) and 5 had a high risk of bias (*18,32–35*) (Tables 1,2). We considered the WHO report as a single study with coverage of 4 countries that met our inclusion criteria (*25*).

Patient delay

Patient delay was measured in 17/20 studies. Measures of patient delay depended on patient recall of first symptoms for PTB. The majority of studies measured delay as a dichotomous variable based on a cut-off point, usually the median. The shortest (12.5 days) and longest (73 days) mean duration of patient delay was reported in the Islamic Republic of Iran (26,33). However, the quality of these studies should be considered before drawing any conclusion from this observation.

Factors associated with patient delay

At least one factor attributing to patient delay was analysed in 10 studies (*16,18–25,35*). Studies mostly assessed predisposing factors such as patient sociodemographic characteristics, TB knowledge and perception about TB. Enabling factors were less often assessed, while none of the studies assessed at least one needs factor.

Predisposing factors that were significantly associated with patient delay were older age (OR = 1.24; 95% CI: 1.02 to 1.50), female sex (OR = 1.42; 95% CI: 1.19 to 1.69), unemployment (OR = 0.83; 95% CI: 0.72 to 0.95), low patient income (OR = 1.95; 95% CI: 1.07 to 3.55) and low crowding index (OR = 0.75; 95% CI: 0.57 to 0.99) (Figure 2).

Factors found to be significantly associated with patient delay were: inadequate TB knowledge (20,25*a*), although in 4 studies the summary OR was not significant for literacy (16,20,21,35); residing in rural areas (16); presence of chronic health problem (21,22); contact with a TB case (21) [yet protective against delay in another study (19)]; self-medication (25*a*) [although not significantly associated in another study (23)]; and high cost of medical services (20).

Factors found to be protective against patient delay were high TB perception (*16,35*); however, this predisposed to delay in 1 study (*22*); TB-related stigma was found to be protective from patient delay in 1 study (*16*) and predisposed to patient delay in another (*25a*). Marital status, smoking, a HIV positive status and travelling time were not associated with patient delay in any of the studies that interrogated these factors.

Health care provider (OR = 0.77; 95% CI: 0.70 to 0.85) (Figure 2) was the only enabling factor that had sufficient information to calculate summary OR. The type of provider at first consultation, i.e. consulting a non-health care provider, was associated with extended patient delay (19,20,21,23,25a). The high cost of medical services was significantly associated with patient delay in one study (20).

Health system delay

Duration of health system delay was measured in 15/20 studies. All 15 studies used the health facility's record of first consultation as entry point to health care and 13/15 used start of treatment as the endpoint of time spent in the health system. Two studies used TB diagnosis as the endpoint. The majority of the studies measured delay versus non-delay as a dichotomous variable based on a cut-off point, usually the median. In patients who had health system delay, the shortest mean duration of health system delay (5 days) was reported in Iraq (*25a*) whereas the longest mean duration (129.25 days) was reported in the Islamic Republic of Iran (*28*).

Factors associated with health system delay

At least one factor associated with health system delay was analysed in 6/15 studies (19,23–25,29,34). Enabling factors such as type of facility, type of providers at first visit, number of visits, number of providers consulted before reaching a TB diagnosis and expenses plus travel time were assessed. These factors were related to the aspect of health system delay in which patient return for diagnosis and treatment were required.

Predisposing factors that assessed health system delay were female sex, older age and patient income. Being female was significantly associated with health system delay (OR = 2.12; 95% CI: 1.24 to 3.60) (Figure 3) in 3 studies that contributed to the summary OR (19,23,24). Older age and patient income were not associated with health system delay in any of the studies that interrogated this factor. The enabling factors that were associated with health system delay were: high cost of medical services (25c); visiting a non-health care provider, i.e. a traditional healer and community or village healer at first visit (25c); more than 3 visits to a health care provider (24); and repeated visits to the same provider (23). Studies that reported lack of examination of sputum on the first visit (25b), obtaining a negative smear result for acidfast bacilli (25b) and underutilization of chest X-ray and smear microscopy (Turkey and Sudan) (19,23), and a low suspicion index in 3 studies from Turkey (17,19,34) were not combinable to calculate the OR.

Visiting a public, compared with a private facility, at first consultation was the only enabling factor that we had sufficient information for to calculate summary OR. In 3 studies (21,24,25b), visiting a private facility was significantly associated with health system delay (OR = 1.41; 95% CI: 1.06 to 1.88) (Figure 3).

Heterogeneity

Patient delay factors

Heterogeneity was significant in terms of sex (P < 0.1; $I^2 = 45\%$), patient's income (P < 0.00001; $I^2 = 92\%$), and crowding (P = 0.15; $I^2 = 47\%$). Upon further investigation, we found one study as the source of heterogeneity in terms of sex (16). Participants in this study were TB suspects rather than the confirmed TB cases in the other studies.

Table 1 Assessing risk of bias in case-control studies included in the systematic review (13)										
Study		А			В			С		Quality
	Aı	A2	A3	A4	B 1	B2	Cı	C2	C3	score
Al-Absi 2006 Yemen (20)	1	1	0	0	1	1	0	1	1	6
Alavi et al. 2015 Iran (18)	1	1	0	0	0	0	0	1	1	4
Akrim et al .2014 Morocco (24)	1	1	1	1	1	1	0	1	1	8
Date & Okita 2005 Yemen (35)	1	1	0	0	0	0	0	1	1	4
Maamari 2008 Syria (21)	1	1	1	1	1	1	0	1	1	8
Güneylioglu et al. 2004 Turkey (19)	1	1	1	1	0	0	0	1	1	6
Mohamed et al. 2013 Sudan (22)	1	1	1	1	0	0	0	1	1	6
Rahim et al.2004 Sudan (23)	1	1	1	1	1	1	1	1	1	9
Rumman et al. 2008 Jordan (18)	1	1	1	1	1	1	0	1	1	8
WHO 2008 Iraq (25a)	1	1	0	0	1	1	0	1	1	6
WHO 2008 Iran (25b)	1	1	1	1	1	1	0	1	1	8
WHO 2008 Egypt (25c)	1	1	1	1	1	1	0	1	1	8
WHO 2008 Somalia (25d)	1	1	1	1	1	1	0	1	1	8

A = Selection of the study groups: A1 right case definition; A2 right controls definition; A3 the representativeness of the cases; A4 the representativeness of controls.

 $B=Comparability\ of\ the\ groups: B1\ control\ of\ main\ confounders; B2\ control\ of\ any\ additional\ factor.$

C = Ascertainment of exposure: C1 appropriate method of exposure ascertainment; C2 same method of exposure ascertainment for cases and controls; C3 same non-response rate of case and control groups.

1: study met the criteria; 0: the study did not meet the criteria.

Quality score: \leq 5 high risk of bias. > 5 low risk of bias

Table 2 Assessing risk of bias in cross-sectional studies using the quality assessment tool (14) modified by (15)											
Study	Aı	A2	A3	A4	B1	B2	B3	B4	B5	B6	Quality score
Bashour & Mamaree 2003 (31)	1	U	1	0	1	1	U	1	1	1	7
Ekinci et al. 2014 (17)	1	U	U	U	1	1	U	1	1	1	6
Masjidi et al. 2007 (26)	0	1	0	U	1	1	U	1	1	1	6
Mirsaeidi et al. 2007 (27)	1	0	0	U	1	1	0	1	1	1	6
Okur et al. 2006 (29)	0	0	1	1	0	1	0	1	1	1	6
Okutan et al. 2005 (30)	0	1	1	1	1	1	0	1	0	1	7
Shahriyar et al. 2012 (33)	0	1	0	0	1	1	0	1	0	1	5
Shamaei et al. 2009 (28)	1	1	1	0	0	1	0	1	1	1	7
Nasehi et al. 2012 (32)	1	1	1	0	0	0	0	0	0	1	4
Yilmaz et al. 2001(34)	U	U	U	U	1	1	U	1	1	1	5

External validity: A1 = representative of the target population; A2 = appropriate recruitment of the participants; A3 = appropriate sampling frame; A4 = minimal non-response bias. Internal validity: B1 = data collected directly from the subjects (as opposed to a proxy); B2 = acceptable case definition; B3 = valid and reliable study instrument; B4 = same mode of data collection used for all subjects; B5 = appropriate shortest prevalence period for the parameter of interest; B6 = appropriate numerator(s) and denominator(s) for the parameter of interest. 1: study met the criteria; 0: study did not meet the criteria; U: response was unclear.

Quality score: 0-5 high risk of bias; 6-8 moderate risk of bias; > 8 low risk of bias.

Figure2 Factors associated with patient delay

8		······································	
		Odds Ratio	Odds Ratio
Study or Subgroup	_	I-H, Random, 95% Cl	M-H, Random, 95% Cl
Akrim et al. 2014 Al-Absi 2006	7.5% 13.6%	1.59 [0.89, 2.86] 0.84 [0.59, 1.20]	
Alavi et al.2015	3.0%	2.91 [1.03, 8.23]	
Date & Okita 2005	3.7%	1.43 [0.57, 3.59]	
Guneylioglu et al. 2004 Maamari 2008	4 7.8% 15.7%	1.34 [0.76, 2.37] 0.94 [0.70, 1.27]	
Mohamed et al. 2013	8.9%	1.51 [0.90, 2.53]	+
Rahim 2004	8.2%	1.25 [0.72, 2.16]	- -
Rumman et al. 2008	19.9%	1.52 [1.24, 1.86]	
WHO 2006/ Iraq	11.7%	1.04 [0.69, 1.58]	Ī
Total (95% CI)	100.0%	1.24 [1.02, 1.50]	◆
Total events			
Test for overall effect: 2		.26, df = 9 (P = 0.06); I ^z = 45%	0.02 0.1 1 10 50
reation overall effect. 2	2 - 2.10 (1 - 0.	00)	Male Female
Study or Subgroup	Weight N	Odds Ratio I-H, Random, 95% Cl	Odds Ratio M-H, Random, 95% Cl
Akrim et al. 2014	9.1%	0.88 [0.53, 1.47]	
Al-Absi 2006 Alavietal.2015	14.0% 2.8%	1.50 [1.02, 2.19]	
Guneylioglu et al. 2004		0.89 [0.33, 2.43] 1.30 [0.72, 2.34]	_ - _
Maamari 2008	18.5%	1.58 [1.16, 2.14]	
Mohamed et al. 2013 Rumman et al. 2008	9.1% 26.6%	0.97 [0.58, 1.61] 1.72 [1.39, 2.11]	-
WHO 2006/ Iraq	12.6%	1.66 [1.10, 2.50]	
Total (95% CI)	100.0%	1.42 [1.19, 1.69]	◆
Total events			
Heterogeneity: Tau ² = 1 Test for overall effect: 2		.15, df = 7 (P = 0.18); I ² = 31% 0001)	0.05 0.2 1 5 20
	- 0.000 0 0.	,	Younger age Older age
		Odds Ratio	Odds Ratio
Study or Subgroup	Weight M	-H, Random, 95% Cl	M-H, Random, 95% Cl
Al-Absi 2006	15.6%	0.90 [0.63, 1.28]	
Guneylioglu et al. 2004		22.45 [9.80, 51.44]	
Maamari 2008	15.6%	0.86 [0.61, 1.20]	
Mohamed et al. 2013	14.5%	4.04 [2.37, 6.90]	
Rahim 2004	13.0%	1.09 [0.51, 2.32]	_ _
Rumman et al. 2008	16.1%	1.02 [0.82, 1.26]	+
WHO 2006/ Iraq	12.6%	2.23 [0.98, 5.05]	
Total (95% CI)	100.0%	1.95 [1.07, 3.55]	-
Total events			
		77, df = 6 (P < 0.00001); l² = 92%	0.01 0.1 1 10 100
Test for overall effect: Z	Z = 2.18 (P = 0.0	33)	Mod-high income Low income
		Odds Ratio	Odds Ratio
Study or Subgroup	Woight M L	I, Random, 95% Cl	M-H, Random, 95% Cl
	-		M-H, Kandolii, 95% Ci
Al-Absi 2006	32.1%	0.66 [0.46, 0.95]	
Maamari 2008	39.5%	0.95 [0.71, 1.27]	
WHO 2006/ Iraq	28.4%	0.63 [0.42, 0.93]	
Total (95% CI)	100.0%	0.75 [0.57, 0.99]	•
Total events			
	0.03: Chi ž = 3	80, df = 2 (P = 0.15); I ² = 47%	
			0.05 0.2 i 5 20
Test for overall effect:	z – 2.03 (F = l		High index Low index
		Risk Ratio	Risk Ratio
Study or Subgroup	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Al-Absi 2006	16.6%	0.84 [0.67, 1.04]	-
Guneylioglu et al. 200		0.83 [0.73, 0.93]	
Maamari 2008	23.1%	0.66 [0.56, 0.79]	
Rahim 2004	1.4%	0.76 [0.34, 1.71]	
WHO 2006/ Iraq	18.2%	0.73 [0.59, 0.89]	+
	10.2.10		
Total (95% CI)	100.0%	0.77 [0.70, 0.85]	♦
Total events			'
	0.00.058-4	.84, df = 4 (P = 0.30); I ² = 17%	
Test for overall effect:			0.01 0.1 1 10 100
restion overall effect.	∠ = 0.40 (F ≤	0.00001)	Other HC provider
		Oddo Datia	Odda Datir
04		Odds Ratio	Odds Ratio
Study or Subgroup	Weight I	A-H, Random, 95% Cl	M-H, Random, 95% Cl
Al-Absi 2006	13.4%	0.77 [0.53, 1.11]	+
Maamari 2008	22.4%	0.94 [0.70, 1.25]	
Mohamed et al. 2013		0.60 [0.36, 1.02]	
Rumman et al. 2008	45.2%	0.82 [0.67, 1.00]	
WHO 2006/ Iraq	12.2%	0.90 [0.61, 1.34]	_
. 11 10 2000/ nay	12.2.70	0.00 [0.07, 1.04]	
Total (95% CI)	100.0%	0.83 [0.72, 0.95]	
Total (95% CI) Total events	100.0%	0.83 [0.72, 0.95]	•

Total events Heterogeneity: Tau² = 0.00; Chi² = 2.49, df = 4 (P = 0.65); i² = 0% Test for overall effect: Z = 2.69 (P = 0.007)



		Odds Ratio	Odds Ratio					
Study or Subgroup	Weig	ht M-H, Random, 95% Cl	M-H, Random, 95% Cl					
Akrim et al. 2014	37.2	% 2.04 [1.13, 3.68]						
Guneylioglu et al. 20	04 22.2	% 4.32 [1.71, 10.89]						
Rahim 2004	40.6	% 1.48 [0.87, 2.52]	+=-					
Total (95% CI)	100.0	% 2.12 [1.24, 3.60]	◆					
Total events								
Heterogeneity: Tau ² = 0.11; Chi ² = 3.92, df = 2 (P = 0.14); l ² = Test for overall effect: Z = 2.77 (P = 0.006)			49%					
		lds Ratio (Non-event)	Odds Ratio (Non-event)					
Study or Subgroup	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl					
Akrim et al. 2014	31.2%	1.75 [1.05, 2.92]						
Al-Absi 2006	0.0%	0.87 [0.60, 1.27]						
Maamari 2008	66.0%	1.26 [0.88, 1.79]						
WHO 2006/ Iraq	2.8%	2.04 [0.37, 11.34]						
Total (95% CI)	100.0%	1.41 [1.06, 1.88]	◆					
Total events								
Heterogeneity: Tau ² =	: 0.00; Chi ² =	1.27, df = 2 (P = 0.53); l ² = 0%						
Test for overall effect:			0.01 0.1 1 10 100					
		,	Private health facility Public health facility					

Figure 3 Gender and facility at 1st consultation vs. health system delay

Removal of this study from the meta-analysis for subgroup analysis rendered the heterogeneity nonsignificant (H, P = 0.47; $I^2 = 0\%$). Two studies were different from the rest in terms of patient income (19,22); removal of these studies from the meta-analysis rendered the heterogeneity nonsignificant (H, P = 0.30; $I^2 = 18\%$). Removal of the study having a higher cut-off point for the crowding index eliminated heterogeneity (H, P = 0.84; $I^2 = 0\%$) when considering this outcome (21).

Health system factors

Heterogeneity was significant (P = 0.14; $I^2 = 49\%$) in terms of sex and was based on a single study (19). Removal of this study from the meta-analysis rendered the heterogeneity nonsignificant (H, P = 1.00; $I^2 = 0\%$).

Grade quality of evidence

The GRADE system produced a low quality grading for evidence in this review. This was a result of the shortcomings inherent in the observational study design of articles included in the review, plausibility of bias and small size estimates, which all have implications for the generalizability of estimates; for example, measurement of outcomes in these studies was dependent on patient self-reporting which created a possibility of recall bias. Nevertheless, the effects of exposure in these 12 studies were assessed as being similar and consistent thus, making them amenable to a meta-analysis.

Discussion

Overview

This review, which evaluated facilitators and barriers to TB diagnosis and health system delay, provides evidence for TB awareness and interventions targeting the elderly and those from lower-income settings, as a strategy for successful TB control in the MENA region. The predisposing factors that were significantly associated with patient delay were older age, being female, unemployment, low patient income, and crowding. Notably, being female was the only factor associated with both patient and health system delay.

Implications for practice

Tuberculosis control programme managers in the MENA region need to be cognizant of the range of factors which impact on patient and health systems delays. Such factors need to be considered when proposing policy interventions to reduce and contain transmission of TB disease, thus enhancing TB service delivery aimed at increased case detection rates in the MENA region.

This review provides evidence for the need to focus on health system enabling factors and to act on opportunities that will lead to a reduction in delays. Efforts to increase public awareness and to promote health education about TB, especially in outreach areas, should be prioritized. Maintaining a high suspicion index for TB among all health care providers is mandatory. This can be achieved through effective training, including monitoring and evaluation, of health care professionals.

Implications for research

This systematic review underlined a couple of research-related caveats. The majority of studies had a cross-sectional study design which, while useful when measuring prevalence and identifying associations, nevertheless lack sthe ability to determine causality as do cohort studies (7). Recently, the MENA region has seen the fastest growing HIV epidemic. HIV-related data from the region is lacking. Research related to diagnostic, patient and health system delays associated with TB among HIV patient is required to assist national TB programme managers in constructing policies and planning interventions.

The health system in general, and TB control in particular, in the region is expected to be severely impacted by the actual political instability and complex emergencies in the region, which will provide an environment where TB is very likely to occur. Hence, it is vital to establish structures to contain any potential flare-up of cases in these circumstances. These structures might be achieved through factors identified by this work, and research assessing the post-crises situation and illustrating the gaps and needs for TB control.

In summary, this review provides evidence for facilitators on barriers to TB diagnosis and health

system delays in the MENA region. For successful TB control in this region, TB awareness and interventions targeting the elderly and those in lower-income brackets, especially taking male-female differences into account, are essential.

Limitations

Most studies recruited patients from public health facilities and TB management units near the capital of the country. No recruitment from private health facilities or from the peripheries was done. The generalizability of this systematic review is limited as patients recruited from private health facilities and marginalized or remote areas were not included in the analysis.

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Facteurs associés aux retards en matière de diagnostic et de traitement de la tuberculose dans la Région du Moyen-Orient et de l'Afrique du Nord : analyse systématique

Résumé

Contexte : L'instabilité politique, les sanctions économiques et la qualité inférieure des soins de santé ont une incidence négative sur la lutte contre la tuberculose dans la Région du Moyen-Orient et de l'Afrique du Nord.

Objectifs : La présente étude avait pour objectif de mettre en évidence les facteurs qui contribuent aux retards dans le diagnostic et le traitement de la tuberculose dans les pays de cette Région.

Méthodes: Deux examinateurs ont passé en revue indépendamment les articles éligibles aux critères de l'étude qu'ils ont identifiés au moyen de recherches exhaustives. Ensuite, ils ont extrait des données qui ont été soumises à une méta-analyse.

Résultats : Les retards dans le diagnostic de la tuberculose étaient associés à un âge plus élevé et à un revenu faible (odds ratio [OR] = 1,49 ; intervalle de confiance [IC] à 95 %: 1,31-1,70) et (OR = 1,26 ; IC à 95 %: 1,09-1,45) respectivement (n = 17 études). L'appartenance au sexe féminin était associée à un retard dans la prise en charge tant au niveau des patients que des systèmes de santé [(OR = 1,24 ; IC à 95 %: 1,02-1,50) et (OR = 1,68 ; IC à 95 %: 1,18-2,38) respectivement. La connaissance et la perception de la tuberculose, le fait d'avoir un emploi et un faible niveau de promiscuité jouaient un rôle déterminant pour limiter les retards dans la prise en charge des patients. Le système GRADE (grade donné aux recommandations, examen, élaboration et évaluation) a évalué les données comme étant de faible qualité.

Conclusion : La présente analyse fournit aux facilitateurs des bases factuelles sur les obstacles en matière de diagnostic de la tuberculose ainsi que sur les retards liés aux systèmes de santé. Pour réussir à lutter contre la tuberculose dans la Région du Moyen-Orient et de l'Afrique du Nord, la sensibilisation à la maladie et les interventions ciblant les personnes âgées et celles issues des milieux à revenu faible sont essentielles, en accordant une attention particulière aux différences entre les sexes.

العوامل المرتبطة بالتأخر في تشخيص السل وعلاجه في الشرق الأوسط وشهال أفريقيا: استعراض منهجي

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الخلفية: يؤثر انعدام الاستقرار السياسي، والعقوبات الاقتصادية، وتدني نوعية الرعاية الصحية سلبا على جهود مكافحة السل في منطقة الشرق الأوسط وشمال أفريقيا.

الأهداف: استهدفنا توضيح العوامل المسهمة في تأخير تشخيص السل وعلاجه في بُلدان منطقة الشرق الأوسط وشمال أفريقيا.

طرق البحث: قام مراجعان مستقلان بتقييم المقالات المؤهلة التي حُدِّدت من خلال البحث الشامل واستخلاص البيانات وخضعت للتحليل التلوي. **النتائج**: اقترن تأخير تشخيص السل بتقدم العمر وانخفاض الدخل (OR = 1.30 CI: 1.37 OK = 1.49) و (OR = 1.09) و (OR = 1.09) و (OR = 1.26; 95% CI: 1.09) و على التوالي (17 دراسة). وارتبط النوع الاجتهاعي للإناث بتأخر تشخيص المرضى وتأخر النظام الصحي [(OR = 1.24; 95% CI = 1.09) و (OR = 1.24; 95% CI: 1.00 - 1.50)] على التوالي. ووجد الباحثون أن المعرفة بالسل وفهمه، ووجود وظيفة، وانخفاض مستويات الازدحام، كان كل منها كفيلا بالحماية من تأخر تشخيص المرضى وعلاجهم. وصنف نظام تصنيف التوصيات وتقديرها ووضعها وتقييمها البيّنات المتاحة بأنها منخفضة الجودة.

الاستنتاج: يقدم هذا الاستعراض بيّنات للميسّرين بشأن العقبات التي تؤدي إلى تأخر تشخيص السل وعلاجه. ولكي تتكلل جهود مكافحة السل في منطقة الشرق الأوسط وشيال أفريقيا بالنجاح، فإن الحاجة تمس إلى إذكاء الوعي بالسل وتوجيه التدخلات إلى كبار السن والأفراد في السياقات ذات الدخل المنخفض، مع توجيهها بشكل خاص نحو مراعاة الفروق بين الجنسين.

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