

Gastric cancer in the Arab World: a systematic review

Marc Aoude,¹ Marc Mousallem,¹ Majd Abdo,¹ Bryan Youssef,¹ Hampig Raphael Kourie⁴ and Humaid O. Al-Shamsi^{2,3,4,5}

¹Department of Hematology-Oncology, Hotel Dieu De France Hospital, Saint Joseph University of Beirut, Riad El Solh, Lebanon. ²Department of Oncology, Burjeel Cancer Institute, Burjeel Medical City, Abu Dhabi, United Arab Emirates. ³Innovation and Research Center, Burjeel Cancer Institute, Burjeel Medical City, Abu Dhabi, United Arab Emirates. ⁴College of Medicine, University of Sharjah, Sharjah, United Arab Emirates. ⁵Emirates Oncology Society, Dubai, United Arab Emirates. (Correspondence to: Marc Aoude: marc.aoude@net.usj.edu.lb).

Abstract

Background: Gastric cancer (GC) is the fourth most common cancer worldwide, characterized by multifactorial pathogenesis and a heterogeneous geographic distribution. The complexity of this malignancy has evolved, with environmental and genetic factors and treatment strategies being more studied.

Aims: We aimed to group and organize the clinicopathological and epidemiological features of GC in the Arab World and compare with data from Western countries.

Methods: To obtain the highest number of topic-related articles, an extensive electronic search was conducted in the PubMed MEDLINE and Cochrane databases up to March 2022 using Boolean operators with a combination of keywords and MeSH terms. A total of 42 articles were retained after screening in accordance with the objectives of the study. The estimated age-standardized incidence rates in the Arab World were collected from the GLOBOCAN 2020 database.

Results: A total of 46 articles were retrieved from 11 countries in the Arab World. Epidemiological elements were collected, especially tumour attributes, risk factors and population characteristics, in addition to some therapeutic strategies. Results were regrouped by theme and then organized in tables and charts, allowing a global and regional approach to the subject.

Conclusion: This review shows that the Arab World is considered a low-rate GC incidence region, presenting almost the same tumour characteristics as the Western countries. The lack of GC data in the Arab World should trigger a rise in research on this type of malignancy to better understand the subject.

Keywords: gastric cancer, review, Arab World, incidence, epidemiology

Citation: Aoude M; Mousallem M; Abdo M; Youssef B; Kourie HR; Al-Shamsi HO. Gastric cancer in the Arab World: a systematic review. *East Mediterr Health J.* 2022;28(7):521–531. <https://doi.org/10.26719/emhj.22.051>

Received: 03/01/22; accepted: 11/05/22

Copyright © World Health Organization (WHO) 2022. Open Access. Some rights reserved. This work is available under the CC BY-NC-SA 3.0 IGO license (<https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Introduction

Gastric cancer (GC) is the fourth most common cancer worldwide (1,2). The male to female ratio is 2:1. It ranks fourth in cancer-related mortality, with more than 768 000 deaths in 2020 (1). In most cases, this type of malignancy grows from epithelial cells, leading to adenocarcinomas, commonly divided into 2 types according to Lauren's classification: diffuse and intestinal (3,4). As with all types of cancer, GC presents at specific metastasis sites, with liver, peritoneal surface and distant lymph nodes being the most frequent (2,5).

The pathogenesis is multifactorial with a heterogeneous geographic distribution. The environmental factors are: high consumption of salted food, low socioeconomic status, smoking, low intake of fruits and vegetables, Epstein-Barr virus infection (6,7) and, especially, *Helicobacter pylori* infection (8,9). The genetic factors are less detailed, although some genetic profiles, such as the E-cadherin, *IL-1B*, mutation, are known to increase the risk of developing this malignancy (6,10,11).

The epidemiological features of GC have been widely studied in Western countries, making them well understood (12,13). However, there is a lack of unified data when considering the epidemiology of GC in the Middle East and Arab countries (14,15).

Arab countries are countries in North Africa and West Asia that have Arabic as their native language. Despite the large differences in the environment and lifestyle of these countries, they still share genetic and cultural similarities and have common scientific societies. Therefore, they can be looked on as a single epidemiological entity.

This review, the first of its kind in the Arab World, aims to regroup all the available information on GC in this region, discuss the clinicopathological and epidemiological factors and compare them with data from Western countries, and propose new public health strategies for GC control.

Methods

To obtain a maximum number of articles, an extensive electronic search of the literature was conducted in the PubMed MEDLINE and Cochrane Library databases, retrieving all the articles published from December 1971 to March 2022. Using Boolean operators, the MeSH terms “stomach neoplasm” and keywords “gastric” and “cancer” were used in combination with MeSH terms and keywords related to the Arab World: “Lebanon”, “Tunisia”, “Algeria”, “Egypt”, “Libya”, “Saudi Arabia”, “Bahrain”, “Kuwait”, “Syria”, “Somalia”, “Djibouti”, “Comoros”, “Oman”, “Emirates”, “Palestine”, “Jordan”, “Qatar”, “Morocco”, “Iraq,

“Mauritania”, “Sudan”, “Yemen”, “East Mediterranean”, “Middle East and North Africa”, “Arab”.

A total of 177 articles were extracted. Four of the investigators (Aoude, Moussallem, Abdo and Youssef) screened titles and abstracts of the retrieved articles, and then entire texts were analysed. This was to include studies in English or French from the Arab World that contain data on GC. Studies emphasizing *H. pylori*, or other topics not directly related to cancer, or cancer types other than GC, as well as studies from countries other than the Arab World were excluded. The 46 papers that correspond to the objectives were used for this review. The selection process is summarized in the PRISMA diagram (Figure 1).

This review features a collection of the estimated age-standardized incidence rates per 100 000 of GC in 2020, for both sexes and all ages in the Arab World from the GLOBOCAN 2020 database.

Results

Overview

A total of 46 articles contained information about the characteristics of GC in the Arab World. Most of the publications retrieved discussed molecular studies and risk factors, while the others presented descriptive epidemiology and treatment outcomes. Figure 2 shows the contribution of each country: Tunisia was the most

active with 12 publications, followed by Oman with 8 and Egypt with 7.

Incidence

We studied the GLOBOCAN 2020 database to extract the estimated age-standardized incidence rate per 100 000 for GC in the Arab World for both sexes and all ages (40). The rates were generally in the same range for the northern part of the Arab World (Table 1). The highest incidence rates were found in Oman (8.0) and Yemen (7.1), while the rates were lowest in Kuwait and Saudi Arabia (both 2.7), Sudan (2.5) and the Comoros (1.3).

Risk factors

Helicobacter pylori infection

Helicobacter pylori infection was one of the main GC risk factors in both sexes (16). This bacteria was relatively prevalent in the Arab World in patients with GC; a Moroccan cohort study showed an *H. pylori* infection rate of 57.5% (9). However, it is important to note that some countries, such as Tunisia (15), witnessed a decrease in *H. pylori* infection in the last decade.

In contrast, a 2009 case-control study in Oman demonstrated an absence of significant interaction between *H. pylori* infection and the development of GC (17).

Epstein-Barr and other viral infections

It is controversial whether Epstein-Barr virus is an important etiological factor for GC. Its prevalence in GC

Figure 1 PRISMA flowchart for article selection process

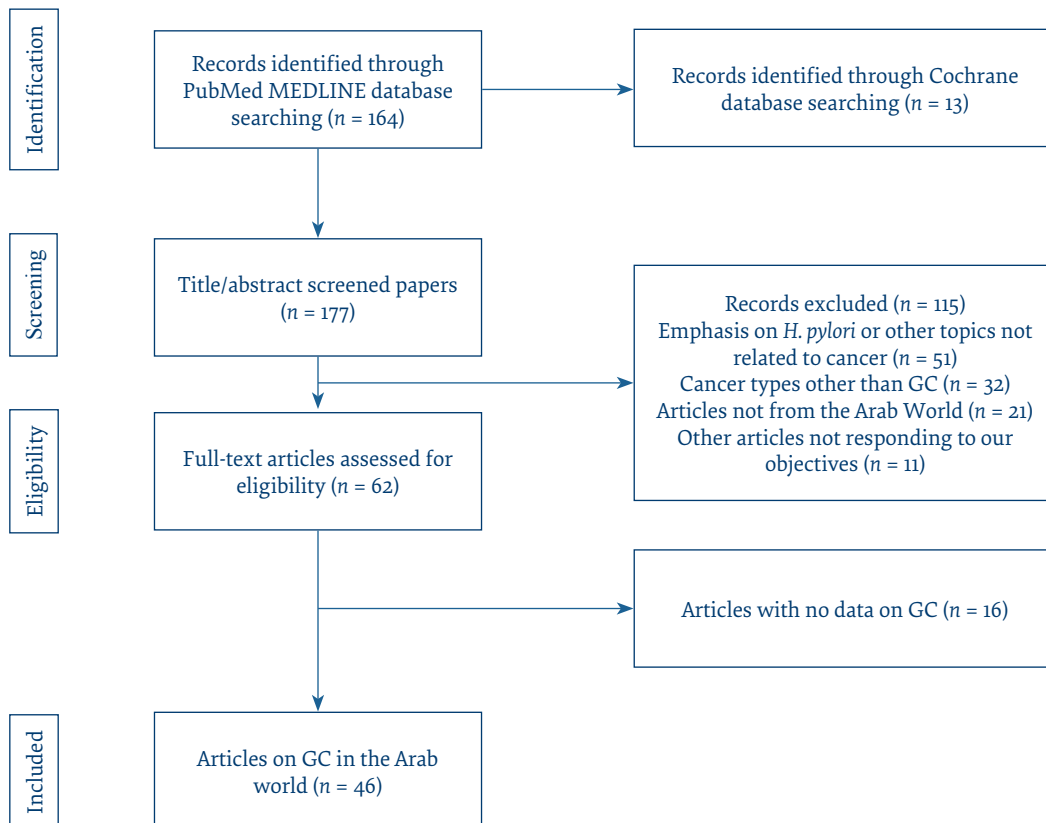
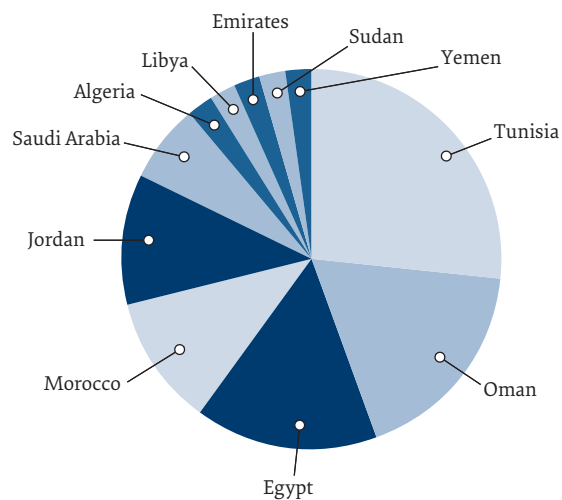


Figure 2 The contribution of different Arab countries in studies on gastric cancer (n = 46), 1971 to 2022



patients in the Arab population has been subject to many studies that demonstrated inconsistencies, noticeable even within the same country. This can be corroborated by 3 Tunisian studies showing a prevalence of 14.8% (18), 10.1% (19) and 4.1% (7) for Epstein-Barr virus infection in GC patients.

On another note, a potential emerging risk factor for GC, the John Cunningham (JC) virus, was detected in 26% of stomach cancer cases (20), with a significant predominance in the elderly and in a majority of the intestinal histological type.

Lifestyle

Lifestyle plays a major role in the development of all types of cancer, including GC. Several modifiable lifestyle risk factors have been studied in the carcinogenesis of stomach tumours. The most relevant risk factor in the Arab populations was tobacco (4), with a prevalence of 30.4% ($P = 0.02$). Alcohol, tea, high nutrient intake (21) and drinking untreated water (22) were associated with 3 times greater odds of developing GC.

On the other hand, one particular Omani study conducted in 2009 demonstrated the absence of significant interaction between smoking and GC development (17) and certain protective factors have been described in previous research, notably adherence to the Mediterranean diet along with a high level of education (21).

Genetics – biomarkers

Over the last few years, modern medicine has increasingly revealed relationships between genetics and carcinogenesis, focusing on its contribution to the diagnosis, prognosis and treatment outcome of tumours.

Several genetic biomarkers have been identified among GC patients in a number of studies conducted in the Arab region. Some genetic characteristics have been linked to an increased risk of developing gastric carcinoma when associated with *H. pylori* infection,

notably: polymorphism in IL-1 β -31C and IL-1RN alleles (23,24); serum soluble E-cadherin level above 5 μ g/mL (25); plasma miR-204, miR-182 and lncRNA H19 (26). Stomach cancer patients had significantly higher levels of Braf, K-ras, methylated MGMT and methylated *MLH1* (27) as well as *TP53* promoter hypomethylation (28). In a 2019 Saudi Arabian study, the prevalence of HER3 was 16% in GC patients (29).

A 2009 case-control study in Oman suggested that vascular endothelial growth factor (VEGF) polymorphisms do not play any role in GC risk predisposition (30).

Prognostic factors

The prognostic aspect of genetic biomarkers has been considered in several studies. For instance, CD133 was found to be a predictive biomarker of tumour recurrence and metastasis (31). It has been demonstrated that methylation of the tumour-related gene p16INK4a (19), the genetic profile p53+/Ki-67+/Bcl2- (32), as well as COX-2 expression, could be potentially predictive of poor prognosis (33).

Epidemiological and histopathological features

Research studies from the Arab World having extensive data on tumour location, staging, grading, Lauren's classification and *H. pylori* infection are illustrated in Table 2. Findings from other studies with less extensive information are reported in the introduction section.

The most common histological type among GC patients in the retrieved articles was primary adenocarcinoma (34); the rest were mainly malignant stromal tumours, lymphomas and carcinoids (14) (Table 1). Among the adenocarcinoma groups, Lauren's intestinal type was the commonest (23,29), followed by diffuse type, mixed type and adenosquamous carcinoma (25,35). However, the findings vary from one region to another, with some studies showing a higher frequency of diffuse-type than intestinal-type (7).

Tumour localization was described in most of the studies included in our review, with third distal localization (antrum, pylorus) being the most frequent (14,25), followed by, body (middle part) and proximal (cardia, fundus) sites (Table 1).

Most GC patients were diagnosed at advanced stages (III and IV) (7,34) (Table 1). The 5-year overall survival rate of the patients was low in advanced cancer stages (36).

Treatment outcomes

Cancer treatment has been evolving throughout the years, with many improvements in surgical procedures, chemotherapy protocols and targeted therapies, along with a more personalized approach to cancer management (37). Surgery is the main treatment for GC, because it offers the only potential for cure, with total, subtotal and distal gastrectomy being the most common procedures (15,36).

Some clinical trials have been conducted in the Arab World to assess the efficacy of chemotherapy drugs in patients with GC. On the one hand, preoperative

Table 1 Estimated age-standardized incidence rates per 100 000 population of gastric cancer in countries of the Arab World, both sexes, all ages; source: GLOBOCAN 2020 database

Country	Rate per 100 000
Oman	8.0
Yemen	7.1
Jordan	6.0
Algeria	5.7
Morocco	5.7
Mauritania	5.6
Palestine	5.2
Qatar	5.2
Bahrain	4.8
Iraq	4.8
Somalia	4.7
Syrian Arab Republic	4.6
United Arab Emirates	4.4
Egypt	4.1
Libya	3.7
Tunisia	3.2
Lebanon	3.0
Djibouti	2.9
Kuwait	2.7
Saudi Arabia	2.7
Sudan	2.5
Comoros	1.3

administration of Imatinib was stated as being very effective, producing a great improvement in symptoms and an overall reduction in tumour size and density, which subsequently made the resection process a lot easier (38). On the other hand, neoadjuvant chemotherapy using 5FU-Cisplatin and Docetaxel has shown no benefit in advanced GC, with significant toxicity, such as neutropenia and weight loss (39).

Discussion

Gastric cancer data in the Arab World

Data on incidence of gastric cancer in the Arab World is scanty. Although an extensive search was conducted using several keywords and MeSH terms, including all types of studies, in French or English, for all years, only 46 articles were retrieved. An important observation was that only 11 out of the 22 Arab countries were indicated in the selected papers.

The cancer incidence and mortality data in GLOBOCAN (41) related to the Arab countries were not all extracted from national cancer registries due to a lack of data in some countries. For example, statistics from the Syrian Arab Republic and the Comoros were estimated from nearby regions because of the lack of national data.

These findings suggest that the Arab World needs major investment in cancer research by establishing national registries and publishing new studies.

Incidence

Looking at global statistics, the hotspots for GC incidence and mortality are in East Asia, Eastern Europe and South America (42). A recent review identified the low-risk regions as Southern Asia, North America, Africa, Australia and New Zealand (43). Some consistent numbers can be extracted from a 2014 American review; for example, the age-standardized incidence rate per 100 000 in men was 65.9 in Korea versus 3.3 in Egypt (44).

The totality of these findings is compatible with the GLOBOCAN 2020 database, and the study can conclude that the Arab World is categorized among the low GC risk regions.

Demographics

The mean age of the GC populations in the Egyptian articles was around 50 years, while the average for the rest of the Arab World countries was around 60 years; the median age at diagnosis was 70 years in Western studies (43,44). Further investigations are needed to determine if these findings are related to the younger age of the Arab populations in general.

According to the Western series, men are 2–3 times more susceptible than women to developing GC (42,43), which is similar to findings for the Arab population.

Risk factors

The association between tobacco and GC is relatively controversial. In most of the studies, smoking was a significant risk factor (4) and could increase the odds of GC development by a factor of 3 (22). In Lebanon, smoking was considered a major GC risk factor (16). A meta-analysis of cohort studies conducted in Portugal demonstrated that the GC risk increased by 60% in male smokers and 20% in female smokers (45). In contrast, a study in Oman determined an absence of association between smoking and GC (17). Other research efforts have failed to establish any positive association (46).

On the other hand, the relationship between the Mediterranean diet and GC was much clearer. Numerous studies in this review highlighted the fact that the Mediterranean diet was a protective factor against developing GC. The World Cancer Research Fund/American Institute for Cancer Research summed up that fruit and vegetables protect against GC. An Italian case-control study generated the same findings, alongside the fact that non-alcohol consumption played a defensive role against GC (47), which is also shown in our review. These findings could partially explain the low incidence rates of GC in the Arab population.

Two Tunisian studies found that the prevalence of Epstein-Barr virus-associated GC was 10% and 14.8% (18,19). This is generally compatible with an international meta-analysis of 70 studies with a total of 15 592 GC patients distributed in Europe, America and Asia where

Table 2 Distribution of the gastric cancer characteristics in 19 research articles from the Arab World, 1971–2022

Author, year, country (Reference No.)	Type	No.	Mean age (years)	M:F ratio	Tumour location		Tumour size				Nodes				Metastasis No. (%)	Overall stage No. (%)	Grade No. (%)	Lauren's classification No. (%)	H. Pylori+ No. (%)		
					Proximal (fundus, cardia)	Body (middle part)	Lower part (antrum, pylorus)	T1	T2	T3	T4	No	N1	N2						N3	M0
Ksiao et al. 2010 Tunisia (20)	R	61	62.0	1.3:1	-	25 (43)	33 (57)	11 (18)	50 (82)	33 (54)	28 (46)							24 (39)	37 (61)	36/61 (59)	
Ben Ayed-Guerfali et al. Tunisia 2011 (19)	R	79	59.6	1.5:1	8 (10)	22 (30)	46 (60)											45 (57)	34 (43)	26/73 (36)	
Ayed et al. 2014 Tunisia (32)	R	90	63.0	1.4:1	8 (10)	23 (27)	54 (63)	17 (19)	71 (81)	16 (20)	66 (80)		42 (69)	19 (31)				52 (59)	38 (41)	31/79 (39)	
Ayed-Guerfali et al. Tunisia 2014 (58)	R	80	59.6	1.3:1	8 (11)	20 (26)	48 (63)	16 (22)	44 (59)	15 (21)	58 (79)		37 (68)	17 (32)				48 (60)	32 (40)	29/71 (40)	
Elghali et al. 2018 Tunisia (15)	R	876	59.1	1.4:1	162 (21)	608 (79)	23 (6)	106 (28)	188 (50)	128 (36)	149 (42)	69 (81)	12 (19)	663 (81)	152 (19)			635 (72)	241 (28)	171/876 (19)	
El-Shahat et al. 2005 Egypt (59)	R	66	52.8	2.3:1	12 (18)	21 (32)	33 (50)	16 (24)	50 (76)	20 (30)	46 (70)										
Zeeneldin et al. 2014 Egypt (60)	R	168	54.0	1.3:1	32 (28)	37 (32)	45 (40)							14 (8)	36 (21)	58 (36)					
Mohamed et al. 2019 Egypt (26)	C	35	45.2	4:1				24 (25)	72 (75)	24 (25)	72 (75)		89 (93)	7 (7)				38 (39)	58 (61)		
Attia et al. 2019 Egypt (31)	R	77	54.4	1.4:1				3 (4)	14 (18)	2 (2)	20 (26)				10 (13)	27 (35)	30 (39)	60 (78)	17 (22)		
Joutei et al. 2018 Morocco (61)	R	55	57.0	1.8:1				5 (9)	10 (18)	14 (25)	13 (24)		51 (93)	4 (7)	17 (31)	38 (69)	17 (31)	33 (60)	22 (40)		
Joutei et al. 2020 Morocco (62)	R	98	58.0	2:1				13 (13)	21 (21)	27 (28)	26 (27)	19 (19)	94 (96)	4 (4)	27 (28)	71 (72)	24 (24)	30 (31)	71 (72)		
Nshizirungu JP et al. Morocco 2021 (63)	R	97	59.8	1.6:1	31 (32)	66 (68)												65 (67)	32 (33)		
El Zouki et al. 2012 Libya (51)	R	114	55.5	2.2:1	34 (30)	25 (22)	55 (48)						63 (65)	51 (45)	0 (15)	24 (23)	65 (62)	46 (45)	56 (55)	72/114 (63)	
Al-Moundhri et al. Oman 2005 (64)	R	121	60.2	2:1	14 (11)	47 (39)	60 (50)	27 (31)	59 (69)	21 (24)	65 (76)				34 (28)	87 (72)	30 (25)	56 (79)	15 (21)		
Al-Moundhri et al. Oman 2006 (6)	R	339	59.8	1.9:1	30 (9)	98 (30)	200 (61)	5 (2)	66 (28)	34 (14)	127 (54)	43 (18)	10 (4)	23 (7)	69 (20)	133 (39)	52 (16)	189 (82)	41 (18)		
Al-Moundhri et al. Oman 2010 (65)	C	192	1.4:1					32 (17)	160 (83)	26 (13)	166 (87)			33 (17)	159 (83)	11 (6)	80 (42)	93 (48)	99 (52)	67/116 (57)	
Al-Moundhri Oman et al. 2012 (66)	R	115	59.2	1.7:1	63 (55)	52 (45)		37 (31)	81 (69)	20 (17)	28 (25)	67 (58)			38 (33)	77 (67)		66 (56)	52 (44)		

protein expression was detected in 39% of the GC cases and none of the non-neoplastic tissues. A Tunisian study also found that this virus is a potential emerging risk factor with a prevalence of 26% of the cases (20).

Strengths and weaknesses

First, a wide combination of MeSH terms along with keywords was used, which helped in the extraction of a maximum number of articles on GC in the Arab World in 2 different databases. In addition to articles in English, we analysed papers published in French since it is also a commonly used language in the region. Most importantly, this review is the first of its kind in the Arab countries combining the few original articles on the subject. The current work summarizes GC tumour characteristics along with an overview of endemic risk factors and other particularities of the region.

Weaknesses are identified as missing data on prevention and screening strategies, as well as genomic

characteristics and hereditary syndromes such as hereditary diffuse GC and familial adenomatous polyposis.

Conclusion

In conclusion, this review shows that the Arab World is a low-rate GC incidence region, presenting tumour characteristics similar to those of Western countries, despite some differences like age of presentation. However, the number of studies and the overall data regarding this subject are scarce. A greater number of studies and an increase in national data are required to obtain a more representative overview and a better understanding of the disease in this region.

Funding: None

Competing interests: None declared.

Cancer de l'estomac dans le monde arabe : une analyse systématique

Résumé

Contexte : Le cancer de l'estomac est le quatrième cancer le plus fréquent dans le monde. Il se caractérise par une pathogenèse multifactorielle et une distribution géographique hétérogène. La complexité de cette tumeur maligne a évolué, les facteurs environnementaux et génétiques ainsi que les stratégies de traitement étant davantage étudiés.

Objectifs : Notre objectif consistait à regrouper et organiser les caractéristiques clinicopathologiques et épidémiologiques du cancer de l'estomac dans le monde arabe et les comparer aux données provenant des pays occidentaux.

Méthodes : Afin d'obtenir le plus grand nombre d'articles liés au sujet, une recherche en ligne approfondie a été menée dans les bases de données PubMed/MEDLINE et Cochrane jusqu'en mars 2022 en utilisant des opérateurs booléens avec une combinaison de mots-clés et de termes MeSH. Au total, 42 articles ont été retenus après une sélection conforme aux objectifs de l'étude. Les taux d'incidence standardisés selon l'âge dans le monde arabe ont été recueillis à partir de la base de données GLOBOCAN 2020.

Résultats : Au total, 46 articles provenant de 11 pays du monde arabe ont été extraits. Des données épidémiologiques ont été recueillies, notamment les caractéristiques des tumeurs, les facteurs de risque et les caractéristiques de la population, ainsi que certaines stratégies thérapeutiques. Les résultats ont été regroupés par thème, puis organisés sous forme de tableaux et de graphiques, de telle sorte qu'ils permettent de traiter le sujet à l'échelle mondiale et régionale.

Conclusion : Cette analyse montre que le monde arabe est considéré comme une région à faible incidence de cancer de l'estomac, où les caractéristiques des tumeurs sont sensiblement les mêmes que dans les pays occidentaux. Le manque de données sur le cancer de l'estomac dans le monde arabe devrait susciter une augmentation des recherches concernant ce type de tumeur maligne afin de mieux comprendre le sujet.

سرطان المعدة في العالم العربي: استعراض منهجي

مارك عودة، مارك مسلم، مجد عبده، براين يوسف، هامبيك رفايل كوريه، حميد عبيد الشامسي

الخلاصة

الخلفية: يُعدُّ سرطان المعدة رابع أكثر أنواع السرطانات شيوعاً في العالم، ويتميز بأنه ينشأ عن عوامل متعددة، وله توزيع جغرافي غير متجانس. وقد تطور تعقيد هذا الورم الخبيث، مع خضوع العوامل البيئية والجينية واستراتيجيات العلاج لمزيد من الدراسة.

الأهداف: هدفت هذه الدراسة إلى تجميع وتنظيم السمات السريرية الباثولوجية والوبائية لسرطان المعدة في العالم العربي ومقارنتها ببيانات من بلدان غربية.

طرق البحث: للحصول على أكبر عدد من المقالات المتعلقة بالموضوع، أُجريَ بحث إلكتروني موسع في قاعدتي بيانات PubMed MEDLINE و Cochrane حتى مارس 2022 باستخدام عوامل منطقية (Boolean) مع مزيج من الكلمات المفتاحية ومصطلحات العناوين الرئيسية للموضوعات

الطبية (MeSH). وجرى الاحتفاظ بها بمجموعه 42 مقالاً بعد الفرز وفقاً لأهداف الدراسة. وُجمعت معدلات الإصابة المقدّرة الموحّدة حسب السن في العالم العربي من قاعدة بيانات GLOBOCAN 2020.

النتائج: جرى الحصول على ما مجموعه 46 مقالاً من 11 بلداً في العالم العربي. وجرى جمع العناصر الوبائية، ولا سيما خصائص الأورام، وعوامل الخطر، وخصائص السكان، بالإضافة إلى بعض الاستراتيجيات العلاجية. وأعيد تجميع النتائج حسب الموضوع، ثم نُظمت في جداول ومخططات، الأمر الذي أتاح اتباع نهج عالمي وإقليمي إزاء الموضوع.

الاستنتاجات: يُبين هذا الاستعراض أن العالم العربي يُعدُّ منطقة ذات معدل منخفض للإصابة بسرطان المعدة، إذ تُظهر خصائص الأورام نفسها تقريباً التي تظهر في الدول الغربية. وينبغي أن يؤدي نقص بيانات سرطان المعدة في العالم العربي إلى زيادة الأبحاث المتعلقة بهذا النوع من الأورام الخبيثة، من أجل التوصل إلى فهم أفضل للموضوع.

References

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021 May;71(3):209–49. doi:10.3322/caac.21660
- Aqel A, Khader Y, Arqoub K, Nimri O. Survival rate of gastric cancer patients in Jordan: secondary data analysis. *JMIR Public Health Surveill.* 2020 May 4;6(2):e14359. doi:10.2196/14359
- Bodoor K, Jalboush SA, Matalka I, Abu-Sheikha A, Waq RA, Ebwaini H, et al. Heat shock protein association with clinico-pathological characteristics of gastric cancer in Jordan : HSP70 is predictive of poor prognosis. *Asian Pac J Cancer Prev APJCP.* 2016;17(8):3929–37. PMID: 27644641
- Mellouki I, Laazar N, Benyachou B, Aqodad N, Ibrahim A. Epidémiologie du cancer gastrique: expérience d'un centre hospitalier marocain [Epidemiology of gastric cancer: experience of a Moroccan hospital]. *Pan Afr Med J.* 2014;17:42. doi:10.11604/pamj.2014.17.42.3342
- Oh SY, Cunningham J, Saif MW. Colonic metastasis from gastric cancer. *Clin Colorectal Cancer.* 2014 Dec;13(4):255–6. doi:10.1016/j.clcc.2014.09.009
- Al-Moundhri MS, Al-Bahrani B, Burney IA, Nirmala V, Al-Madhani A, Al-Mawaly K, et al. The prognostic determinants of gastric cancer treatment outcome in Omani Arab patients. *Oncology.* 2006;70(2):90–6. doi:10.1159/000092584
- Trimeche M, Ksiâa F, Ziadi S, Mestiri S, Hachana M, Gacem RB, et al. Prevalence and characteristics of Epstein-Barr virus-associated gastric carcinomas in Tunisia. *Eur J Gastroenterol Hepatol.* 2009 Sep;21(9):1001–7. doi:10.1097/MEG.0b013e32831f1f53
- Watari J, Chen N, Amenta PS, Fukui H, Oshima T, Tomita T, et al. Helicobacter pylori associated chronic gastritis, clinical syndromes, precancerous lesions, and pathogenesis of gastric cancer development. *World J Gastroenterol.* 2014 May 14;20(18):5461–73. doi:10.3748/wjg.v20.i18.5461
- Alaoui Boukhris S, Amarti A, El Rhazi K, El Khadir M, Benajah D-A, Ibrahim SA, et al. Helicobacter pylori genotypes associated with gastric histo-pathological damages in a Moroccan population. *PloS One.* 2013;8(12):e82646. doi:10.1371/journal.pone.0082646
- Gamboa-Dominguez A, Dominguez-Fonseca C, Chavarri-Guerra Y, Vargas R, Reyes-Gutierrez E, Green D, et al. E-cadherin expression in sporadic gastric cancer from Mexico: exon 8 and 9 deletions are infrequent events associated with poor survival. *Hum Pathol.* 2005 Jan;36(1):29–35. doi:10.1016/j.humpath.2004.09.020
- Troost E, Hold GL, Smith MG, Chow W-H, Rabkin CS, McColl KEL, et al. The role of interleukin-1beta and other potential genetic markers as indicators of gastric cancer risk. *Can J Gastroenterol.* 2003 Jun;17 (Suppl. B):8B–12B. doi:10.1155/2003/397060
- Johnson O, Ersumo T, Ali A. Gastric carcinoma at Tikur Anbessa Hospital, Addis Ababa. *East Afr Med J.* 2000 Jan;77(1):27–30. PMID: 10944835
- Wu CW, Tsay SH, Hsieh MC, Lo SS, Lui WY, P'eng FK. Clinicopathological significance of intestinal and diffuse types of gastric carcinoma in Taiwan Chinese. *J Gastroenterol Hepatol.* 1996 Nov;11(11):1083–8. doi:10.1111/j.1440-1746.1996.tb00041.x
- Bani-Hani K-E, Yaghan R-J, Heis H-A, Shatnawi N-J, Matalka I-I, Bani-Hani A-M, et al. Gastric malignancies in Northern Jordan with special emphasis on descriptive epidemiology. *World J Gastroenterol.* 2004 Aug 1;10(15):2174–8. doi:10.3748/wjg.v10.i15.2174
- Elghali MA, Gouader A, Bouriga R, Mahjoub M, Jarrar MS, Ziadi S, et al. Gastric adenocarcinomas in central Tunisia: evolution specificities through two decades and relation with Helicobacter pylori. *Oncology.* 2018;95(2):121–8. doi:10.1159/000488488
- Charafeddine MA, Olson SH, Mukherji D, Temraz SN, Abou-Alfa GK, Shamseddine AI. Proportion of cancer in a Middle eastern country attributable to established risk factors. *BMC Cancer.* 2017 May 18;17(1):337. doi:10.1186/s12885-017-3304-7
- Al-Moundhri MS, Alkindy M, Al-Nabhani M, Al-Bahrani B, Burney IA, Al-Habsi H, et al. Combined polymorphism analysis of glutathione S-transferase M1/G1 and interleukin-1B (IL-1B)/interleukin 1-receptor antagonist (IL-1RN) and gastric cancer risk in an Omani Arab population. *J Clin Gastroenterol.* 2009 Feb;43(2):152–6. doi:10.1097/MCG.0b013e31815853fa
- BenAyed-Guerfali D, Ayadi W, Miladi-Abdennadher I, Khabir A, Sellami-Boudawara T, Gargouri A, et al. Characteristics of epstein barr virus variants associated with gastric carcinoma in Southern Tunisia. *Virology.* 2011 Nov 3;85:500. doi:10.1186/1743-422X-8-500

19. Ben Ayed-Guerfali D, Benhaj K, Khabir A, Abid M, Bayrouiti MI, Sellami-Boudawara T, et al. Hypermethylation of tumor-related genes in Tunisian patients with gastric carcinoma: clinical and biological significance. *J Surg Oncol*. 2011 Jun 1;103(7):687–94. doi:10.1002/jso.21875
20. Ksaa F, Ziadi S, Mokni M, Korbi S, Trimeche M. The presence of JC virus in gastric carcinomas correlates with patient's age, intestinal histological type and aberrant methylation of tumor suppressor genes. *Mod Pathol*. 2010 Apr;23(4):522–30. doi:10.1038/modpathol.2009.184
21. Baroudi O, Chaaben AB, Mezlini A, Moussa A, Omrane I, Jilson I, et al. Impact of lifestyle factors and nutrients intake on occurrence of gastrointestinal cancer in Tunisian population. *Tumour Biol*. 2014 Jun;35(6):5815–22. doi:10.1007/s13277-014-1771-x
22. Al-Qadasi FA, Shah SA, Ghazi HF. Tobacco chewing and risk of gastric cancer: a case-control study in Yemen. *East Mediterr Health J Rev Sante Mediterr Orient Al-Majallah Al-Sihhiyah Li-Sharq Al-Mutawassit*. 2017 Jan 23;22(10):719–26. doi:10.26719/2016.22.10.719
23. Al-Moundhri MS, Al-Nabhani M, Al-Bahrani B, Burney IA, Al-Madhani A, Ganguly SS, et al. Interleukin-1beta gene (IL-1B) and interleukin 1 receptor antagonist gene (IL-1RN) polymorphisms and gastric cancer risk in an Omani Arab population. *Gastric Cancer Off J Int Gastric Cancer Assoc Jpn Gastric Cancer Assoc*. 2006;9(4):284–90. doi:10.1007/s10120-006-0392-5
24. Drici AE-M, Moulessehoul S, Tifrit A, Diaf M, Turki DK, Bachir M, et al. Effect of IL-1 β and IL-1RN polymorphisms in carcinogenesis of the gastric mucosa in patients infected with *Helicobacter pylori* in Algeria. *Libyan J Med*. 2016;11:31576. doi:10.3402/ljm.v11.31576
25. Anwar MM, Youssef AI, Sheta MI, Zaki A, Bernaba NR, El-Toukhi MA. Evaluation of specific biochemical indicators of *Helicobacter pylori*-associated gastric cancer in Egypt. *East Mediterr Health J*. 2012 May;18(5):501–7. doi:10.26719/2012.18.5.501
26. Mohamed WA, Schaalan MF, Ramadan B. The expression profiling of circulating miR-204, miR-182, and lncRNA H19 as novel potential biomarkers for the progression of peptic ulcer to gastric cancer. *J Cell Biochem*. 2019 Aug;120(8):13464–77. doi:10.1002/jcb.28620
27. Sabry D, Ahmed R, Abdalla S, Fathy W, Eldemery A, Elamir A. Braf, Kras and *Helicobacter pylori* epigenetic changes-associated chronic gastritis in Egyptian patients with and without gastric cancer. *World J Microbiol Biotechnol*. 2016 Jun;32(6):92.
28. Rusiecki JA, Al-Nabhani M, Tarantini L, Chen L, Baccarelli A, Al-Moundhri MS. Global DNA methylation and tumor suppressor gene promoter methylation and gastric cancer risk in an Omani Arab population. *Epigenomics*. 2011 Aug;3(4):417–29. doi:10.2217/epi.11.65
29. Ahmed A. Prevalence of Her3 in gastric cancer and its association with molecular prognostic markers: a Saudi cohort based study. *Libyan J Med*. 2019 Dec;14(1):1574532. doi:10.1080/19932820.2019.1574532
30. Al-Moundhri MS, Al-Nabhani M, Burney IA, Al-Farsi A-A, Al-Bahrani B. Gastric cancer risk predisposition and prognostic significance of vascular endothelial growth factor (VEGF) gene polymorphisms—a case-control study in an Omani population. *Mol Carcinog*. 2009 Dec;48(12):1170–6. doi:10.1002/mc.20572
31. Attia S, Atwan N, Arafa M, Shahin RA. Expression of CD133 as a cancer stem cell marker in invasive gastric carcinoma. *Pathologica*. 2019 Mar;111(1):18–23. doi:10.32074/1591-951X-51-18
32. Ayed DB, Khabir A, Abid M, Bayrouiti MI, Gargouri A, Sellami-Boudawara T, et al. Clinicopathological and prognostic significance of p53, Ki-67, and Bcl-2 expression in Tunisian gastric adenocarcinomas. *Acta Histochem*. 2014 Oct;116(8):1244–50. doi:10.1016/j.acthis.2014.07.008
33. Ben Ayed-Guerfali D, Charfi S, Khabir A, Sellami-Boudawara T, Gargouri A, Mokdad-Gargouri R. Clinical and prognosis relevance of COX-2 expression in Tunisian patients with primary gastric adenocarcinoma. *Cancer Biomark Sect Dis Markers*. 2016 Jun 7;17(1):67–73. doi:10.3233/CBM-160618
34. Awad HA, Hajeer MH, Abulihya MW, Al-Chalabi MA, Al Khader AA. Epidemiologic characteristics of gastric malignancies among Jordan University Hospital patients. *Saudi Med J*. 2017 Sep;38(9):965–7. doi:10.15537/smj.2017.9.19371
35. El Hassan A, El Hassan L, Mudawi H, Gasim B, Own A, Elamin E, et al. Malignant gastric tumors in Sudan: a report from a single pathology center. *Hematol Oncol Stem Cell Ther*. 2008 Jun;1(2):130–2. doi:10.1016/s1658-3876(08)50044-6
36. Rebai W, Fterich F, Makni A, Ksantini R, Bedioui H, Daghfous A, et al. Adénocarcinome superficiel de l'estomac [Early gastric adenocarcinoma]. *Tunis Med*. 2010 Jan;88(1):1–4. PMID: 20415204
37. Baroudi O, Baroudi T, Omrane I, Moussa A, Mezlini A, Ayari H, et al. Thymidylate synthase polymorphism in sporadic colorectal and gastric cancer in Tunisian population: a predictive role in 5-fluorouracil based chemotherapy treatment. *Med Oncol*. 2014 Feb;31(2):825. doi:10.1007/s12032-013-0825-z
38. Saied GM, Kensarah AM. Six months neoadjuvant imatinib improves resectability potential of gastric stromal tumors in Egyptian patients. *Int J Surg Lond Engl*. 2010;8(2):105–8. doi:10.1016/j.ijso.2009.09.016
39. Ben Nasr S, Ayadi M, Bahloul R, Guesmi S, Allani B, Chraït N, et al. Perioperative chemotherapy in locally advanced gastric cancer. A retrospective study about 25 cases. *Tunis Med*. 2015 Apr;93(4):228–30. PMID: 26375739
40. Estimated age-standardized incidence rates (World) in 2020, stomach, both sexes, all ages. Geneva: World Health Organization, Cancer Today; 2020 (https://gco.iarc.fr/today/online-analysis-map?v=2020&mode=population&mode_population=continents&population=900&populations=900&key=asr&sex=0&cancer=7&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=10&group_cancer=0&include_nmssc=1&include_nmssc_

- other=1&projection=natural-earth&color_palette=default&map_scale=quantile&map_nb_colors=5&continent=0&show_ranking=0&rotate=%25B10%25C0%25D, accessed 4 Aug 2021).
41. Data & methods. Geneva: World Health Organization, Cancer Today; 2021 (<https://gco.iarc.fr/today/data-sources-methods>, accessed 4 Aug 2021).
 42. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. *Lancet*. 2020 Aug 29;396(10251):635–48. doi:10.1016/S0140-6736(20)31288-5
 43. Machlowska J, Baj J, Sitarz M, Maciejewski R, Sitarz R. Gastric cancer: epidemiology, risk factors, classification, genomic characteristics and treatment strategies. *Int J Mol Sci*. 2020 Jun 4;21(11):E4012. doi:10.3390/ijms21114012
 44. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. *Cancer Epidemiol Biomark Prev*. 2014 May;23(5):700–13. doi:10.1158/1055-9965.EPI-13-1057
 45. Ladeiras-Lopes R, Pereira AK, Nogueira A, Pinheiro-Torres T, Pinto I, Santos-Pereira R, et al. Smoking and gastric cancer: systematic review and meta-analysis of cohort studies. *Cancer Causes Control*. 2008 Sep;19(7):689–701. doi:10.1007/s10552-008-9132-y
 46. Shakeri R, Malekzadeh R, Etemadi A, Nasrollahzadeh D, Abedi-Ardekani B, Khoshnia M, et al. Association of tooth loss and oral hygiene with risk of gastric adenocarcinoma. *Cancer Prev Res (Phila)*. 2013 May;6(5):477–82. doi:10.1158/1940-6207.CAPR-12-0491
 47. Stojanovic J, Giraldo L, Arzani D, Pastorino R, Biondi A, Persiani R, et al. Adherence to Mediterranean diet and risk of gastric cancer: results of a case-control study in Italy. *Eur J Cancer Prev*. 2017 Nov;26(6):491–6. doi:10.1097/CEJ.0000000000000371
 48. Murphy G, Pfeiffer R, Camargo MC, Rabkin CS. Meta-analysis shows that prevalence of Epstein-Barr virus-positive gastric cancer differs based on sex and anatomic location. *Gastroenterology*. 2009 Sep;137(3):824–33. doi:10.1053/j.gastro.2009.05.001
 49. Ishaq S, Nunn L. Helicobacter pylori and gastric cancer: a state of the art review. *Gastroenterol Hepatol Bed Bench*. 2015;8(Suppl. 1):S6–14. PMID: 26171139
 50. Helicobacter and Cancer Collaborative Group. Gastric cancer and Helicobacter pylori: a combined analysis of 12 case control studies nested within prospective cohorts. *Gut*. 2001 Sep;49(3):347–53. doi:10.1136/gut.49.3.347
 51. Elzouki A-NY, Buhjab SI, Alkialani A, Habel S, Sasco AJ. Gastric cancer and Helicobacter pylori infection in the eastern Libya: a descriptive epidemiological study. *Arab J Gastroenterol*. 2012 Jun;13(2):85–8. doi:10.1016/j.ajg.2012.06.002
 52. Malek A, Abdelbagi M, Odeh L, Alotaibi A, Alfardan M, Barqawi H. Knowledge, attitudes and practices of adults in the United Arab Emirates regarding Helicobacter pylori induced gastric ulcers and cancers. *Asian Pac J Cancer Prev*. 2021 May 1;22:1645–52. doi:10.31557/APJCP.2021.22.5.1645
 53. Lauren P. The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma. An attempt at a histo-clinical classification. *Acta Pathol Microbiol Scand*. 1965;64:31–49. doi:10.1111/apm.1965.64.1.31
 54. Marqués-Lespier JM, González-Pons M, Cruz-Correa M. Current perspectives on gastric cancer. *Gastroenterol Clin North Am*. 2016 Sep;45(3):413–28. doi:10.1016/j.gtc.2016.04.002
 55. Matsuda T, Saika K. The 5-year relative survival rate of stomach cancer in the USA, Europe and Japan. *Jpn J Clin Oncol*. 2013 Nov;43(11):1157–8. doi:10.1093/jjco/hyt166
 56. Isobe Y, Nashimoto A, Akazawa K, Oda I, Hayashi K, Miyashiro I, et al. Gastric cancer treatment in Japan: 2008 annual report of the JGCA nationwide registry. *Gastric Cancer*. 2011 Oct;14(4):301–16. doi:10.1007/s10120-011-0085-6
 57. Shin SK, Li M-S, Fuerst F, Hotchkiss E, Meyer R, Kim IT, et al. Oncogenic T-antigen of JC virus is present frequently in human gastric cancers. *Cancer*. 2006 Aug 1;107(3):481–8. doi:10.1002/cncr.22028
 58. Ayed-Guerfali DB, Hassairi B, Khabir A, Sellami-Boudawara T, Gargouri A, Mokdad-Gargouri R. Expression of APC, β -catenin and E-cadherin in Tunisian patients with gastric adenocarcinoma: clinical significance. *Tumour Biol*. 2014 Mar;35(3):1775–83. doi:10.1007/s13277-013-1236-7
 59. El-Shahat M, El-Masry S, Lotfy M, El-Kenawy AE-M, Nasif WA. Relationship of Helicobacter pylori to Bcl-2 family expression, DNA content, and pathological characteristics of gastric cancer. *Int J Gastrointest Cancer*. 2005;36(2):61–8. doi:10.1385/ijgc:36:2:61
 60. Zeeneldin AA, Ramadan H, El Gammal MM, Saber MM, Elgamel D, Sherisher MA. Gastric carcinoma at Tanta Cancer Center: a comparative retrospective clinico-pathological study of the elderly versus the non-elderly. *J Egypt Natl Canc Inst*. 2014 Sep;26(3):127–37. doi:10.1016/j.jnci.2014.04.002
 61. Joutei HAH, Marchoudi N, Mahfoud W, Sadaoui I, Fechtali T, Benomar H. Characterization of PI3KCA and BRAF mutations in gastric adenocarcinoma: An approach to a personalized targeted therapy for Moroccan HER2 overexpressed patients. *Arab J Gastroenterol*. 2018 Dec;19(4):155–8. doi:10.1016/j.ajg.2018.08.001
 62. Amrani Hassani Joutei H, Mahfoud W, Sadaoui I, Fechtali T, Benomar H. [Study of epidemiological clinical and pathological characteristics of gastric adenocarcinoma in a Moroccan population]. *Ann Pathol*. 2020 Nov;40(6):442–6. doi:10.1016/j.annpat.2020.04.014
 63. Nshizirungu JP, Bennis S, Mellouki I, Sekal M, Benajah D-A, Lahmidani N, et al. Reproduction of the Cancer Genome Atlas (TCGA) and Asian Cancer Research Group (ACRG) gastric cancer molecular classifications and their association with clinico-pathological characteristics and overall survival in Moroccan patients. *Dis Markers*. 2021;2021:9980410. doi:10.1155/2021/99804
 64. Al-Moundhri MS, Nirmala V, Al-Hadabi I, Al-Mawaly K, Burney I, Al-Nabhani M, et al. The prognostic significance of p53, p27 kip1, p21 waf1, HER-2/neu, and Ki67 proteins expression in gastric cancer: a clinicopathological and immunohistochemical study of 121 Arab patients. *J Surg Oncol*. 2005 Sep 15;91(4):243–52. doi:10.1002/jso.20324

65. Al-Moundhri MS, Al-Khanbashi M, Al-Kindi M, Al-Nabhani M, Burney IA, Al-Farsi A, et al. Association of E-cadherin (CDH1) gene polymorphisms and gastric cancer risk. *World J Gastroenterol.* 2010 Jul 21;16(27):3432–6. doi:10.3748/wjg.v16.i27.3432
66. Al-Moundhri MS, Al-Hadabi I, Al-Mawaly K, Kumar S, Al-Lawati F a. R, Bhatnager G, et al. Prognostic significance of cyclooxygenase-2, epidermal growth factor receptor 1, and microvascular density in gastric cancer. *Med Oncol.* 2012 Sep;29(3):1739–47. doi:10.1007/s12032-011-0098-
67. Bani-Hani KE. Clinicopathological comparison between young and old age patients with gastric adenocarcinoma. *Int J Gastrointest Cancer.* 2005;35(1):43–52. doi:10.1385/IJGC:35:1:043
68. Albasri AM, Elsawaf ZM, Hussainy AS, Alhujaily AS. Clinicopathological profile of gastric cancers in Al-Madinah, Saudi Arabia. *J Pak Med Assoc.* 2017 Jun;67(6):834–8.
69. Bibi F, Ali I, Naseer MI, Ali Mohamoud HS, Yasir M, Alvi SA, et al. Detection of genetic alterations in gastric cancer patients from Saudi Arabia using comparative genomic hybridization (CGH). *PLoS One.* 2018;13(9):e0202576.