



The Global Prevalence of Peptic Ulcer in the World: a Systematic Review and Meta-analysis

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Abstract

Peptic ulcer is one of the most common diseases of the gastrointestinal tract, which, if not addressed, can increase mortality in different communities. As regards the results of various studies around the world that have reported different prevalence, the aim of this study was to determine the overall prevalence of peptic ulcer in the world through systematic review and meta-analysis. In this systematic review and meta-analysis, articles focused on the prevalence of peptic ulcer were searched in the Scopus, Embase, Web of Science, PubMed and Science Direct, Google Scholar, Magiran, Irandoc, and Scientific Information Database databases, without time limit until April 2020. To analyze the eligible studies, the random effects model was used, and the heterogeneity of the studies was investigated using the I^2 index. The prevalence of peptic ulcer in the world in 21 studies with total sample size 788,525 in age range of 17–82 years was obtained as 8.4% (95% CI 5–13.7). According to the results from meta regression, the prevalence of peptic ulcer in the world decreased with an increase in sample size and increased with an increase in study years and age of participants in the study of the prevalence of peptic ulcer in the world. It was found that these differences were also statistically significant ($P < 0.05$). In conclusion, it is stated that due to the 8.4% prevalence of peptic ulcer, health system policy makers need to prevent and treat this disease through investigating the effective factors.

Keywords Peptic ulcer · Prevalence · Systematic review · Meta-analysis

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Background

Peptic ulcer disease (PUD) is known as one of the leading causes of death in the world. This disease is caused by an imbalance of invasive factors against gastric protective factors [1]. In fact, this disease occurs when the protective mechanisms of the gastrointestinal mucosa are affected by the destructive effects of stomach acid and pepsin [2].

In other words, stomach acid causes a gap in the mucosa and reaches the subcutaneous layer. These ulcers are usually found in the stomach and duodenum but can also occur in the esophagus [3]. On the other hand, ulcers may develop in unusual areas, such as the ileum due to Meckel's diverticulum, inlet patch in the proximal esophagus, or in the jejunum due to excessive acid secretion in Zollinger-Ellison syndrome [3].

One of the main symptoms of this disease is epigastric pain. Other symptoms include indigestion, bloating, premature satiety, nausea, heartburn, and bleeding. The most common symptom of PUD, which is more common in people over 60 years of age, and 50 to 170 out of every 100,000 people suffer from this complication. Taking NSAID drugs and *Helicobacter pylori* infections are the most common etiopathogenic symptoms of bleeding in the PUD [4, 5].

The prevalence of this disease in the world is reported to be 5–10% [3]. A meta-analysis study examined the prevalence of PUD in Iran and reported is prevalence as 34%. This study suggested that the statistics of PUD prevalence in Iran is several times higher than the global statistics and introduced smoking as the main cause of PUD in Iran [6]. Another study conducted in Saudi Arabia in 2010 reported the prevalence of PUD as 21.9% [7].

Another study conducted in China in 2007 found that the prevalence of gastric ulcer (GU) was 8.82% in men and 5.4% in women. On the other hand, this study showed that the prevalence of Duodenal ulcer (DU) is 11.4% in men and 3.7% in women [8, 9]. These statistics show that the prevalence of peptic ulcer in the world has different and heterogeneous reports.

Considering that PUD is one of the most common and dangerous diseases and since different factors play a role in the incidence rate of this disease in an area and cause differences in the prevalence of this disease in different regions and in order to homogenize different prevalence's, this study aims to determine the general prevalence of PUD in the world through a systematic review and meta-analysis.

Methods

Search and Selection Strategy of Studies

The present study was conducted to investigate the prevalence of gastric ulcer in the world through a

systematic review and meta-analysis. To collect data in this study, the international databases of Embase, Scopus, Web of Science (WoS), PubMed, Science Direct, Google Scholar, Scientific Information Database (SID), Magiran, and Irandoc were used without time limit until April 2020. The search process in the mentioned databases was performed using the search terms of “stomach ulcer,” “peptic ulcer,” “gastric ulcer,” “duodenal ulcer,” “prevalence,” “observational study,” and their possible combination in international databases. For example, the way to search in the PubMed database is described in the box below. To review the gray texts (Gray literature), the review of related sites was also on the agenda. In order to maximize the comprehensiveness of the search, the list of references used in all relevant articles found in the above search was manually reviewed. Initially, studies that were repeated in various searched databases were excluded from this study. Then, a list of titles of all the remaining articles was prepared by the researchers in this study in order to obtain eligible articles through evaluating the articles in this list. In the first stage, screening, the title, and abstract of the remaining articles were carefully studied and irrelevant articles were removed based on the inclusion and exclusion criteria. In the second stage, the evaluation of the eligibility of the studies, the full text of the possible relevant articles remaining from the screening stage was examined based on the inclusion and exclusion criteria, and the irrelevant studies were also eliminated in this stage. To avoid bias, all steps in reviewing resources and extracting data were performed by two researchers independently of each other. In the case where the articles were not entered, the reason for their deletion was mentioned. In cases where there was disagreement between two researchers, the article was reviewed by a third party. A total of 21 studies were entered the third stage, i.e., quality evaluation. PubMed search strategy: (((“stomach ulcer”) OR “peptic ulcer” OR “duodenal ulcer”) AND “prevalence”) OR “observational study”) AND (“stomach ulcer” and “prevalence”) AND (“stomach ulcer” or “peptic ulcer” or “gastric ulcer” or “gastrointestinal ulcer” and “prevalence” or “observational study”):

Inclusion and Exclusion Criteria

Inclusion criteria for entering articles included the following: (1) Cross-sectional studies of case control studies, (2) cohort studies, (3) studies that have examined the prevalence of gastric ulcers worldwide, (4) studies that were observational (i.e., non-interventional studies), (5) studies in Persian language, and (6) studies in

English language or abstracts in English. The exclusion criteria included the following: (1) case report, (2) interventional studies, (3) letter to editor, and (4) studies that their full text is not available; (5) studies not related to the study subject, (6) studies without sufficient data, and (7) duplicate studies; (8) systematic reviews and meta-analysis studies.

Quality Evaluation

To validate and examine the quality of articles (i.e., methodological validity and results), a checklist appropriate to the type of study was used. The STROBE checklist is commonly used to critique and evaluate the observational studies such as the present study. The STROBE checklist consists of six scales/general sections, including title, abstract, introduction, methods, results, and discussion. Some of these scales have subscales, and in total, this statement contains 32 items. In fact, these 32 items describe different methodological aspects of the study, including title, problem statement, study objectives, type of study, statistical population of the study, sampling method, determining the appropriate sample size, definition of variables and procedures, data collection tools, statistical analysis methods, and findings. Accordingly, the maximum score obtained from the quality evaluation in the STROBE checklist will be 32, and considering the score of 16 as the cut-off point, the articles with scores of 16 and above are considered as articles with good and average methodological quality, while the articles with score below 16 were considered as low methodological quality and were therefore excluded from the study.

Data Extraction

Data related to all final articles entered the static review and meta-analysis process was extracted from a pre-prepared checklist. This checklist includes the title of the article, the name of the first author, year of publication, type of ulcer, country, sample size, number of patients in the sample, mean age of the sample, and parentage of prevalence.

Statistical Analysis

The I^2 test was used to assess the heterogeneity of the selected studies. To investigate the publication bias, the Egger test at a significance level of 0.05 and its corresponding Funnel plot were used considering the high volume of samples included in the study. Data analysis was performed using Comprehensive Meta-Analysis software (Version 2).

Results

Study Selection and Data Extraction

This study examined the prevalence of peptic ulcers in the world through systematic review and meta-analysis. After searching in different databases, 4459 articles were included in the study. A total of 552 articles from EMBASE database, 577 articles from PubMed database, 160 articles from science direct database, 1339 articles from Scopus database, 443 articles from Web of Science database, 360 articles from Google Scholar database, 130 articles from database Iran-doc, 226 articles from Magiran database, and 152 articles from SID database were included in the study. Out of a total of 4459 identified studies, 520 were duplicate studies and were therefore excluded. In the screening stage, out of 3939 studies, the remaining 3280 articles were removed through reviewing the titles and abstracts based on inclusion and exclusion criteria. At eligibility evaluation stage, out of 659 studies, the remaining 621 articles were removed after examination of their full texts based on inclusion and exclusion criteria due to irrelevance. At the quality evaluation stage, out of the remaining 38 studies, 17 articles were removed due to low methodological quality after examination of their full texts based on the STROBE checklist.

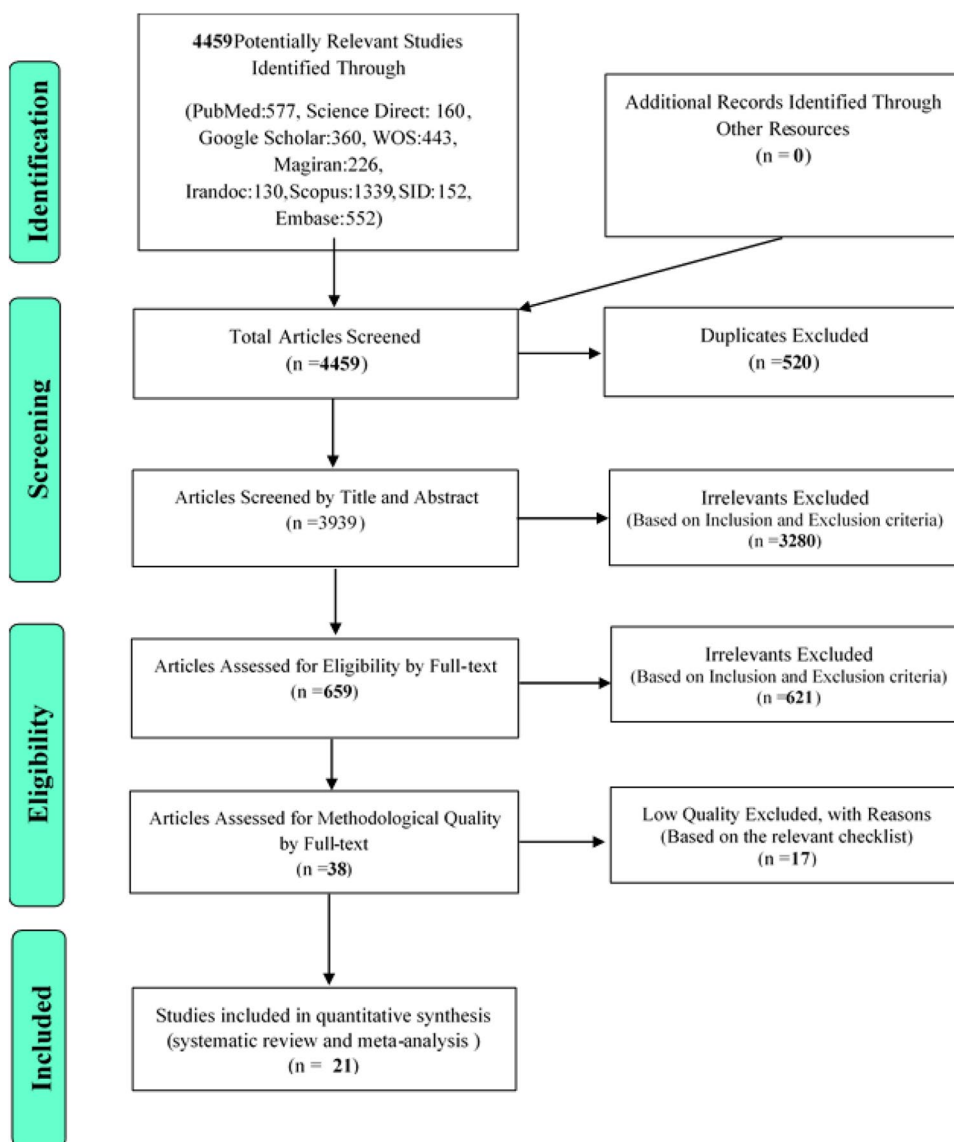
The studies were reviewed based on the four-step PRISMA 2009 process, including article identification, screening, reviewing of article acceptance criteria, and articles entered to the meta-analysis (Fig. 1). Finally, 21 studies were entered the final analysis, whose data was presented in the tables (Table 1). The probability of publication bias of the results of the peptic ulcer prevalence in the world by the funnel diagram and Egger test at a significance level of 0.05 showed no publication bias in the present study ($P=0.498$) (Fig. 2).

Based on the results of the present study, the prevalence of peptic ulcer in the world in reviewing 21 studies and the sample size of 788,525 in the age range of 17–82 years was 8.4% (95% CI 5–13.7). The midpoint of each segment shows the prevalence in each study and the diamond shape shows the prevalence in the population for the whole studies (Fig. 3).

Meta Regression Test

In order to investigate the effects of potential factors influencing the heterogeneity of the prevalence of peptic ulcer in the world, meta regression was used for three factors of sample size, year of study, and age of the study participants (Figs. 4, 5, 6). According to Fig. 4, with increasing sample size, the prevalence of peptic ulcer in the world decreases, which is statistically significant ($P<0.05$). Also, in Fig. 6,

Fig. 1 The flowchart on the stages of including the studies in the systematic review and meta-analysis (PRISMA 2009)



it was reported that with increasing the age of study participants, the prevalence of peptic ulcer in the world increases, which was also statistically significant ($P < 0.05$).

Discussion

Peptic ulcers usually occur in the stomach and proximal duodenum, but may also occur in the esophagus or Meckel diverticulum [30]. The prevalence of ulcers varies around the world, duodenal ulcers are predominant in Western populations, and gastric ulcers are more common in Asia, especially in Japan [17]. According to the results of a meta-analysis study conducted in Iran in 2016, more than 83% of patients with gastric ulcers had clinical symptoms such as epigastric pain, bloating, vomiting, and anorexia [6].

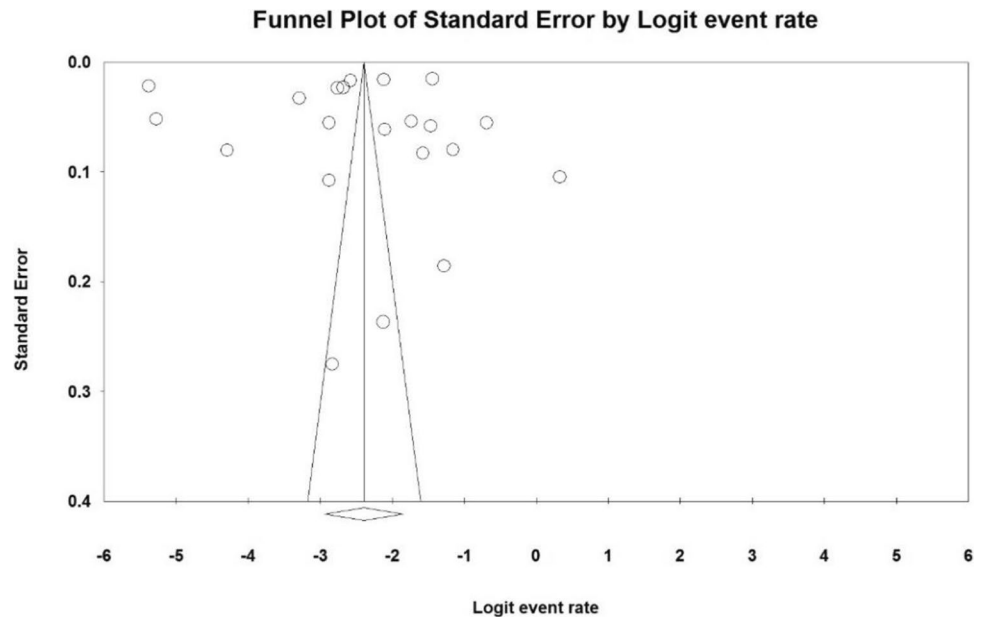
Based on this study, the prevalence of peptic ulcer in the world in 21 studies with total sample size 788,525 in age range of 17–82 years was obtained as 8.4%. According to a study in Taiwan in 2011, 9.4% of people with PUD were asymptomatic. This study also found that factors such as low education, high BMI, and smoking were among the factors contributing to the increase in asymptomatic patients with gastric ulcers [31].

It has been found that the higher incidence of gastric ulcer disease is related to man gender, smoking, and chronic medical diseases [32]. It has also been observed that the prevalence of gastric ulcers increases with age [32]. Additionally, peptic ulcer is associated with gastrinoma, medications (bisphosphonates, corticosteroids, potassium chloride, and chemotherapeutic agents), stress, alcohol consumption, and family history [30].

Table 1 Data of articles entered to study

Sample number	Author	Year of publication	Type of ulcer	Country	Total number	Number of ulcers	Prevalence
1	Kim, J. I. [10]	2009	Gastrointestinal disease	Korean	28,893	5537	19.2
2	Kim, M [11]	1981	Peptic ulcer	US	1700	91	5.4
3	Landau, D. A. [12]	2008	Peptic ulcer	Israel	466,855	2147	0.46
4	Li, Z. [13]	2010	Gastric ulcer	China	1022	176	17.2
5	Loffeld, R. J. L. F. [14]	2001	Duodenal ulcer	Netherlands	375	218	58.8
6	Malaty, H. M. [15]	1997	Peptic ulcer	Korean	867	208	24
7	Manfredini, R. [16]	2010	Gastric ulcer	Italy	26,848	966	3.6
8	Marques, S. B. [17]	2011	Peptic ulcer	Brazil	1478	494	33.4
9	McJunkin, B. [18]	2011	Peptic ulcer	US	251	14	5.6
10	Pyo, J. H. [19]	2019	Peptic ulcer	Korean	32,472	1940	5.9
11	Ramirez-Ramos, A. [20]	2006	Peptic ulcer	Peru	31,446	510	1.62
12	Schabowski, J. [21]	2002	Peptic ulcer	Polish	6512	348	5.3
13	Segawa, K. [9]	1987	Peptic ulcer	Japan	11,657	158	1.35
14	Sonnenberg, Amnon [22]	1996	Peptic ulcer	US	41,457	4470	10.7
15	Sonnenberg, A. [23]	1986	Peptic ulcer	Germany	73,615	376	0.51
16	Türkdoğan, MK [24]	1999	Peptic ulcer	Van	2735	298	10.9
17	Wong, S. N. [25]	2005	Ulcer disease	Philippines	1952	367	18.8
18	Wroblewski, M. [26]	1990	Peptic ulcer	Sweden	170	37	22
19	Wu, H. C. [27]	2007	Peptic ulcer	China	55,336	3913	70.7
20	Xia, B. [28]	2005	Peptic ulcer	Hong Kong	2700	405	15
21	Yeomans, N. D. [29]	2005	Gastroduodenal	Sydney, Melbourne	187	20	11

Fig. 2 Funnel plot of results for the prevalence of peptic ulcer in the world



A study showed that *H. pylori* infection is still considered to be the main cause of PUD. According to the results of this study, only 1.6% of DU and 4.1% of GU observed in different individuals are not associated with *H. pylori* infection and NSAID drugs [33].

Another study found that 62.3% of patients had PUD due to *Helicobacter pylori*. This study also found that 22% of people suffered from PUD due to NSAID consumption and 11% due to aspirin consumption, and the disease cause of 4% of people was unknown [34]. Additionally, a study showed that 66% of PUD are caused by *H. pylori* infection [35].

Fig. 3 Prevalence of peptic ulcer in the world and 95% confidence interval

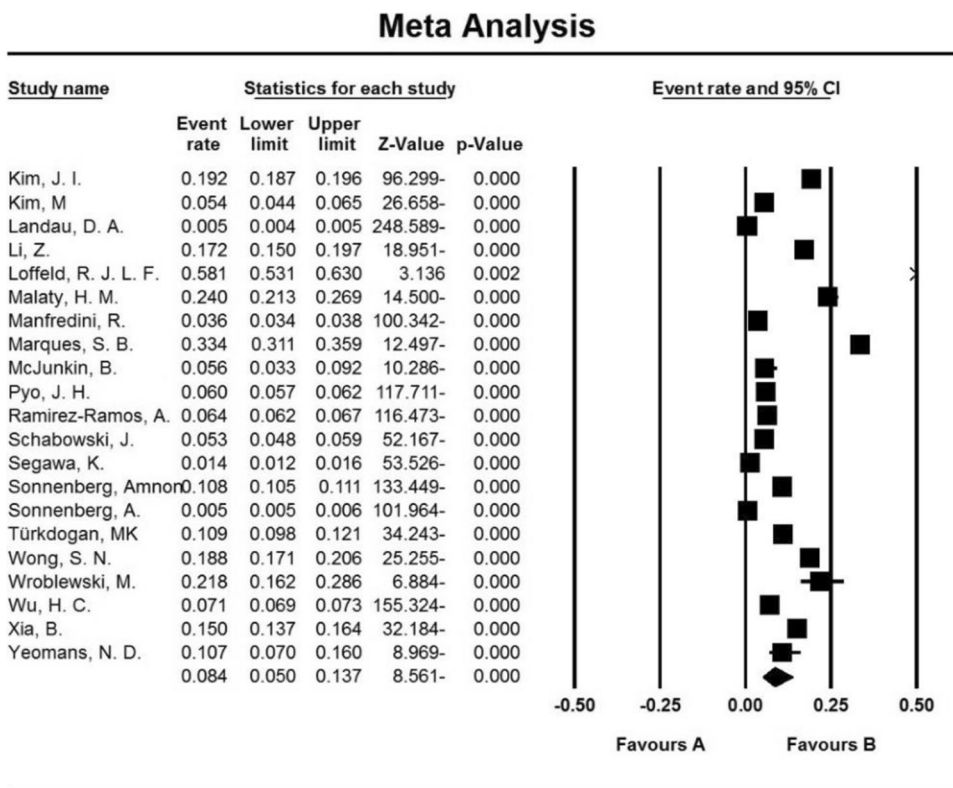
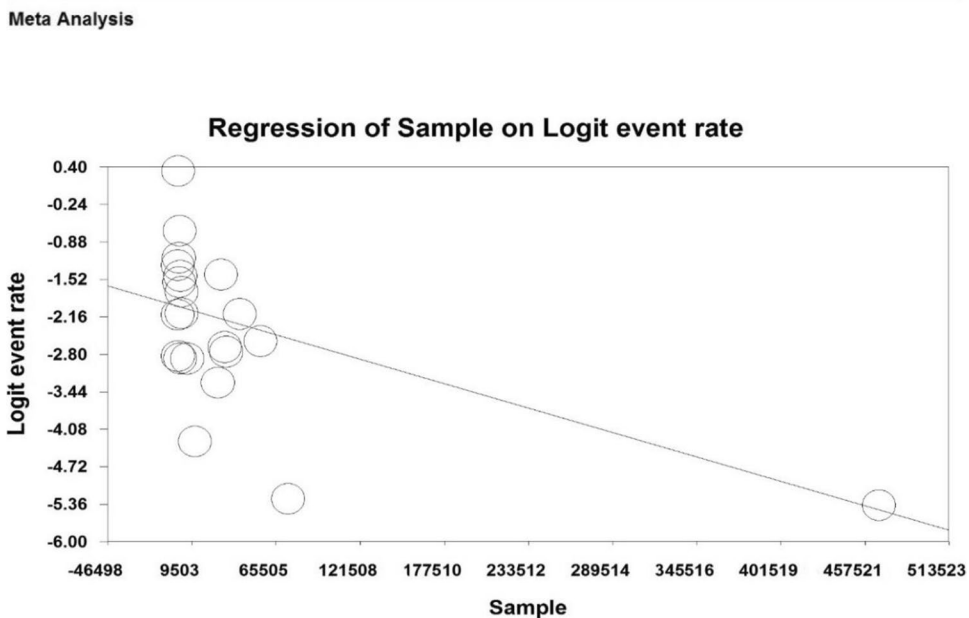


Fig. 4 Meta regression diagram of the prevalence of peptic ulcer in the world by sample size



Although it is accepted that the etiology of peptic ulcer disease (PUD) is multifactorial, data on the relative impact of single risk factors are scarce. A number of population-based studies have been published, but so far, no study has assessed the effect of *Helicobacter pylori* infection together with other PUD determinants, but there are many risk factors for this disease.

Tobacco smoking seems to be a more important risk factor for PUD than *H. pylori* infection; recent studies have

suggested that tobacco smoking causes PU only if *H. pylori* infection is present; recent studies have shown a significant reduction in duodenal ulcer risk in American men who exercise regularly [31–35]. Older studies suggest that physical inactivity increases the likelihood of ulcer disease. Moderate energy expenditure was shown to reduce the overall likelihood of ulcer disease in this study [34, 35]. According to the study of Marques et al., in comparing the group with PUD and the group with normal endoscopy, it was found that *H.*

Fig. 5 Meta regression diagram of the prevalence of peptic ulcer in the world by year

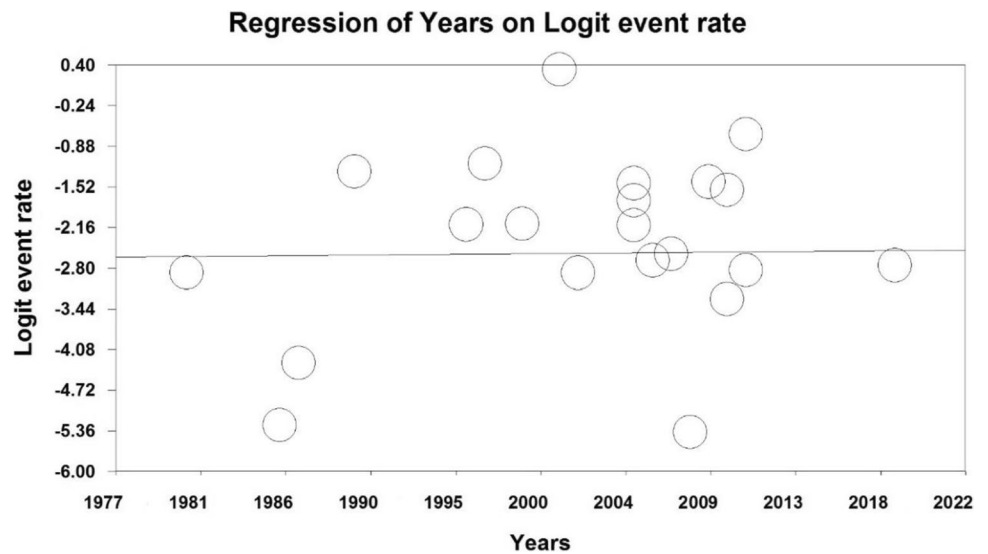
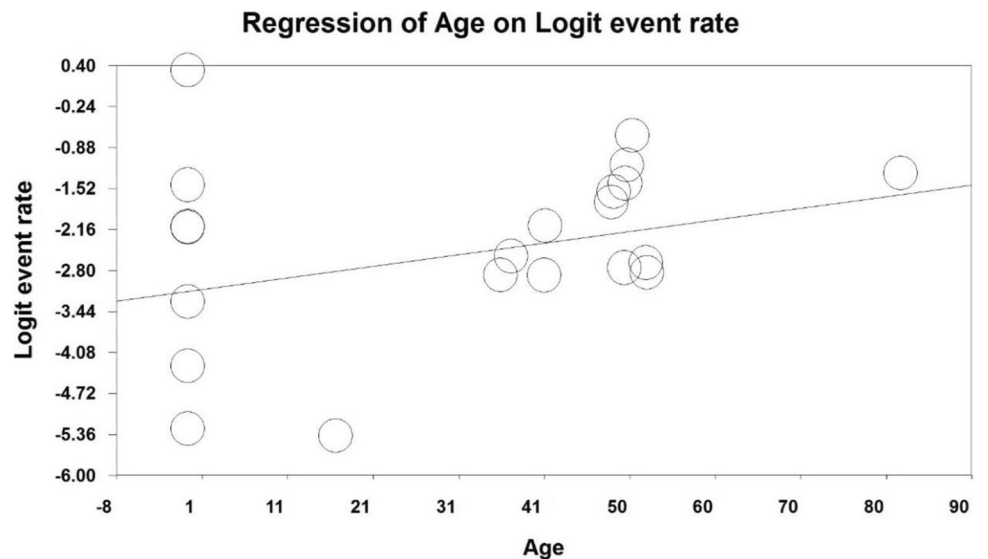


Fig. 6 Meta regression diagram of the prevalence of peptic ulcer in the world by the age of participants in the study



pylori infection, man gender, and older age increase the risk of developing PUD [17].

A study stated that PUD, especially GU, had a higher cumulative incidence in obese individuals compared to non-obese individuals [19]. Unlike DU, there was a significant relationship between the risk of GU and obesity. This significant relationship disappeared after adjusting the HR (hazard ratio) [19]. As a result, PID was not associated with obesity or metabolically healthy obesity [19]. Obesity is one of the risk factors for GUI in people with *H. pylori* infection [19].

According to the results, the prevalence of hospitalization due to PUD was higher in three peaks (i.e., autumn, winter, and spring). By analyzing the data by month, the late summer, autumn, and winter were the periods with the highest prevalence of PUD. In people who are at higher

risk, certain periods of the year can provide adequate drug support to reduce the risk of hospitalization due to PUD [16]. In conclusion, the etiology of PUD is multifactorial. Tobacco smoking, *H. pylori* infection, and the use of minor tranquilizers but not NSAID are the main determinants of PUD [36–38].

Conclusion

In conclusion, it is suggested that considering the 8.4% prevalence of peptic ulcers, health system policy makers need to take measures in order to prevent and treat this disease through investigating the factors affecting peptic ulcer.

Abbreviations WoS: Web of Science; SID: Scientific Information Database; PUD: Peptic ulcer disease; GU: Gastric ulcer; SID: Scientific Information Database; STROBE: The Strengthening the Reporting of Observational studies in Epidemiology; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis

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Author Contribution NS and ND and MA and MM contributed to the design, MM statistical analysis, and participated in most of the study steps. MM and SHSH prepared the manuscript. NS and MM and YB assisted in designing the study, and helped in the interpretation of the study. All authors have read and approved the content of the manuscript.

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Data Availability Datasets are available through the corresponding author upon reasonable request.

Declarations

Ethics Approval and Consent to Participate Ethics approval was received from the ethics committee of deputy of research and technology, Kermanshah University of Medical Sciences (IR.KUMS.REC.1400.005).

Consent for Publication Not applicable.

Competing Interests The authors declare no competing interests.

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