



Systematic Review

Prevalence of Dyspepsia in Iran: A Systematic Review and Meta-analysis

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Abstract

Background: Dyspepsia is a highly prevalent gastrointestinal problem. The present study was carried out to assess the prevalence of dyspepsia in Iran.

Methods: The present study was registered at PROSPERO with the code CRD42019148610. It was carried out based on MOOSE and reporting was performed according to the PRISMA protocol. Systematic search of the literature was performed in July 2019 on international databases of PubMed/Medline, Web of Science (ISI), Cochrane Library, EBSCO, CINAHL, EMBASE, Scopus, Science Direct, and local databases as well as the Google Scholar search engine. Heterogeneity was evaluated using I^2 and Chi-square tests. All analyses were done using Comprehensive Meta-Analysis software.

Results: Overall, 14 studies with a sample size of 54,118 subjects entered in this meta-analysis. The prevalence of dyspepsia in Iran was 14.6% (95% CI: 9.6–21.7). Large heterogeneity was detected among studies ($I^2=99.62\%$, $P<0.001$). The prevalence of dysmotility-like, ulcer-like, and unspecified dyspepsia was estimated to be 9.7% (95% CI: 4.9–18.4), 12.1% (95% CI: 5.2–25.7) and 17.0% (95% CI: 7.8–33.4), respectively. The prevalence of dyspepsia in Iranian men and women was found at 11.1% (95% CI: 6.3–18.8) and 17.8% (95% CI: 10.0–29.7), respectively.

Conclusions: The prevalence of dyspepsia in Iran is relatively high. However, it is lower than global estimates.

Keywords: Dyspepsia, Iran, Meta-analysis, Prevalence

Cite this article as: Karimian M, Ranjbar R, Salamati M, Adibi A, Kazemi F, Azami M. Prevalence of dyspepsia in Iran: a systematic review and meta-analysis. Arch Iran Med. 2021;24(7):568-578. doi: 10.34172/aim.2021.80

Received: August 25, 2019, Accepted: January 12, 2021, ePublished: July 1, 2021

Introduction

Dyspepsia is a very prevalent gastrointestinal disease and its prevalence has been reported to be 40% in population-based studies.¹ The Rome II Criteria for the diagnosis of functional dyspepsia (FD) include: FD for more than twelve weeks, which does not need to be continuous, within the past twelve months with: (a) Constant or repeated symptoms (any kind of discomfort or pain focused in the upper part of the abdomen); (b) No sign of organic illness (on endoscopic examination) that is probable to describe the manifestation; and (c) No sign to demonstrate that FD is just improved by defecation or related to the beginning of a change in form or frequency of stool (i.e., not irritable bowel syndrome [IBS]). FD includes (1) ulcer-like FD: Discomfort or pain concentrated in the epigastric part of the abdomen is the main manifestation (the most annoying); (2) Dysmotility-like FD: A disagreeable or irritating painless sensation concentrated in the epigastric part of the abdomen is the main manifestation; this sensation is perhaps identified by or associated with early satiety, fullness of upper abdominal, nausea or bloating;

(3) Unspecified FD: patients whose manifestation do not meet the prerequisites for dysmotility or ulcer-like FD.² According to the Rome IV criteria, which were recently revised,³ FD is characterized by: (a) Constant or repeated dyspepsia for above three months within the past six months; (b) No sign of a probable organic reason of the endoscopic examination; and (c) No evidence that the dyspepsia is only ameliorated by defecation or any relation with stool abnormalities. This last criterion serves to omit IBS as a possible reason of the manifestation, although about 30% of patients with FD suffer from IBS.

Although clinical assessment is needed to specify if dyspepsia is FD or structural in a person, endoscopic examination shows that most are FD. FD is a complex issue with probable factors such as visceral hypersensitivity, immune activation, brain-gut axis dysfunction, and delayed gastric emptying and *Helicobacter pylori* infection.⁴⁻⁸

Although FD is a serious issue worldwide, most of the reports come from Western countries. Dyspepsia is usually of structural type in developing countries, while in

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developed countries, FD is more prevalent.^{9,10}

Although FD is not a life-threatening illness which usually does not require surgery and has not been shown to decrease survival,¹¹ it disrupts the quality of life significantly and is associated with high rates of absence from work, poor efficiency, fewer activities around the house, and higher medical expenses,^{12,13} demonstrating that dyspepsia in general causes many mental health complications for the population.¹⁴

Many researchers have investigated the prevalence of dyspepsia in the Iranian population, but the results are not consistent.¹⁵⁻²⁸ Thus, a coherent survey of all documents and combining them can provide a more comprehensive picture of the dimensions of this illness in Iranian community. The results of this meta-analysis can provide a more accurate estimate regarding the effect of therapies or risk factors for the illness or other results through combining different studies.²⁹⁻³¹ The present research was carried out to assess the prevalence of dyspepsia in Iran.

Materials and Methods

Study Protocol

This research was carried out according to Meta-analyses Of Observational Studies in Epidemiology (MOOSE) guideline³¹ and reporting was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) protocol.³² This meta-analysis was recorded in PROSPERO with code (CRD42019148610).

Two authors performed each step of the study independently. A third author resolved the inconsistencies in each step of the research and they were confirmed through discussion.

Search Strategy and Selection of Studies

A systematic search was conducted in July 2019 using international databases, including PubMed/Medline, Science Direct, Web of Science (ISI), Cochrane Library, Scopus, EMBASE, EBSCO, CINAHL, and national databases such as Magiran, Iranian Research Institute for Information Science and Technology (IranDoc), Scientific Information Database (SID), Barakat Knowledge Network System, Regional Information Center for Science and Technology (RICST), and the Iranian National Library, as well as Google Scholar.

The key terms are introduced in Table 1. We selected the "All Fields" option as the field of search. We combined the terms "descriptive", "population sentences" and "outcome" using the Boolean operator "AND".

Table 1. Search terms

Search Term	Boolean Keywords
Descriptive term	frequency OR Incidence OR detection OR prevalence OR occurrence OR identification OR characterization OR isolation OR investigation OR survey OR rate
Population term	Iran
Outcome term	Dyspepsia OR Epigastric pain syndrome OR postprandial distress syndrome OR gastrointestinal diseases

To identify all potential studies, the reference lists of all found articles were manually reviewed.

Inclusion and Exclusion Criteria

The inclusion criteria were all cross-sectional articles on the prevalence of dyspepsia in Iran in both Persian and English. The exclusion criteria were: (1) non-adult samples (more than 10% below the age of 15); (2) non-random samples; (3) non-Iranian subjects; (4) non-related subject; (5) sample size below 100 participants; (6) participants not from the general population or community; (7) case reports, case series, congresses, letters to the editor without quantitative data, reviews, and dissertations.

Study Selection

A reviewer (M.A) reviewed the titles and abstract of all detected reports and the full text was then assessed. The same action was repeated by a second researcher (M.K) independently. Eventually, any disagreement was discussed and resolved in the presence of a third researcher (M.S).

Data Extraction

The following data were recorded on a spreadsheet from each study: first author's name, publication date, year of study, mean age and standard deviation, how the data were collected, the diagnostic technique for dyspepsia, duration of symptoms for dyspepsia and prevalence of dyspepsia. At the end, the obtained data were imported into Excel.

For overlapping articles, we emailed the corresponding authors to determine the original article, and in case we did not receive any answer, we chose the article with the highest number of subjects for cases that overlapped.

Quality Assessment

Since all articles included the cross-sectional studies, the quality of the each study was assessed using the modified form of Newcastle Ottawa Scale.³³ The study quality was categorized as follows: poor quality=0-5; medium quality=6-8; high quality=9-10. Articles with poor quality were excluded.

Statistical Synthesis

All analyses were performed using the Comprehensive Meta-Analysis software version 2. Heterogeneity was evaluated using I^2 and chi-square tests. Heterogeneity was classified as follows: I^2 values 0%-25%, 26%-50%, 50%-75% and greater than 75% showed low, medium, high and very high heterogeneity, respectively, with P value <0.10 considered statistically significant.^{34,35} In cases of

high levels of heterogeneity among studies, we used the random effects model. The male/female odds ratio (OR) was used to show the impact of gender on dyspepsia. For this goal, the prevalence of dyspepsia in males, females and the total sample size was evaluated. Subgroup analysis was performed according to areas, population groups, study period, and diagnostic technique. Mixed effects meta-regression was utilized to assess the relationship between study time and the prevalence of dyspepsia. Subgroup differences were also tested.³⁶ Sensitivity analysis also was done. Publication bias was evaluated by an in-depth analysis of the funnel plot, using the proposed correlation tests of Egger and Begg's.^{37,38} *P* value less than 0.05 was considered statistically significant.

Results

Search Results and Features

Overall, 1460 articles were retrieved. Of these, 1446 studies were excluded because of: duplicate publications (*n* = 730), unrelated literature (*n* = 651), non-epidemiological studies

(*n* = 17), non-random samples or studies on children (*n* = 28), participants not from general population or community (*n* = 18), as well as case reports, case series, congresses, letters to the editor without quantitative data, reviews, and dissertations (*n* = 2). Finally, fourteen studies remained for the meta-analysis (Figure 1). The mean age of samples was 37.41 years (95% CI: 33.70–41.11). Three, two, one, two, four, one, and one studies were conducted in Tehran, Fars, East Azarbaijan, Hamadan, Isfahan, Kurdistan, and Kerman provinces, respectively. Ten, two, one, and one studies were conducted on the general population, healthcare workers, outpatient clinics, and blood donors, respectively. Four and ten studies had low and medium quality, respectively. Table 2 demonstrates the characteristics and general information of each study.

Prevalence of Dyspepsia

The prevalence of dyspepsia by combining fourteen studies with a sample size of 54 118 subjects was 14.6% (95% CI: 9.6–21.7) (Figure 2A). The minimum and maximum

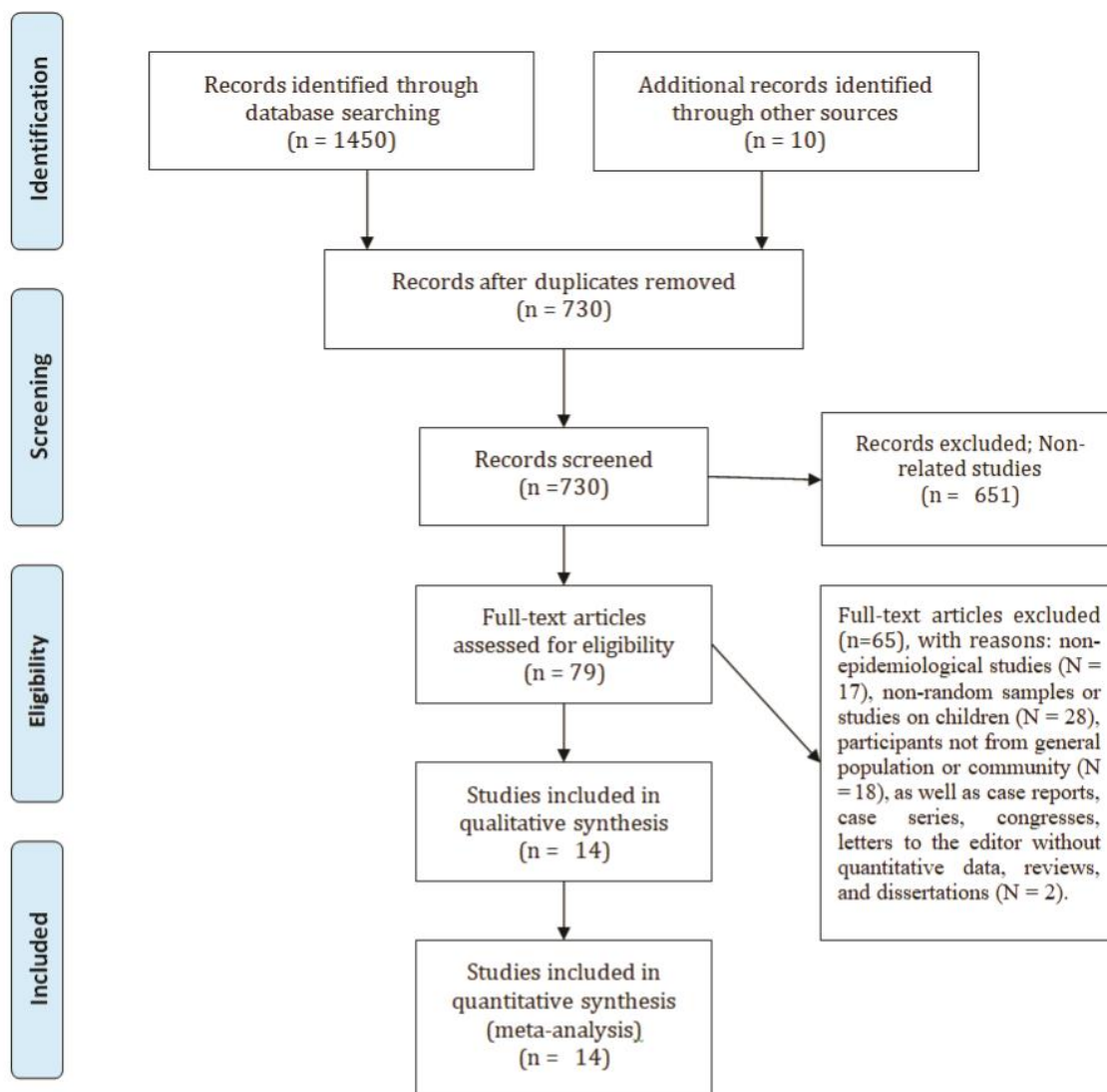


Figure 1. Flowchart of Study Selection.

Table 2. Summary of Systematic Review of Studies

Author, Year	Year of Study	Location	Population	Mean Age	Technique to Collection Data	Criteria for Dyspepsia	Time*	Sample Size			Quality	Ref.
								All	Male	Female		
Ganji A, 2009	2005	Tehran	Outpatient clinic	36.1±12.4	Interview	NR	NR	7985			Medium risk	15
Khademolhosseini F, 2010	2005	Shiraz	General population	37.2±0.2	Interview-administered questionnaire	Discomfort or pain focused in the upper part of the abdomen at least 3 M	3 M	1978	709	1269	Medium risk	16
Khoshbaten M, 2004	2001	Tabriz	General population	38.8±12.9	Interview-administered questionnaire	Symptoms in the last 2 W	2 W	3983	2080	1903	Medium risk	17
Moghimi-Dehkordi M, 2011	2004	Tehran	General population	NR	Interview-administered questionnaire	Rome III criteria	6 M	18180	8680	9500	Medium risk	18
Aghazadeh R, 2005	2001	Nahavand	General population	43.1±14.2	Interview-administered questionnaire	Pain focused in epigastric part, flatulence, nausea, vomiting, and fullness for at least once in past 6 M	6 M	1518	653	865	Medium risk	19
Majlesi A, 2004	2006	Hamadan/rural areas	General population	43.1±14.2	Interview-administered questionnaire	Pain focused in epigastric part, flatulence, nausea, vomiting, and fullness	12 M	2700	1300	1400	Low risk	20
Hatami K, 2008	2005	Tehran	Blood donors	22.5±1.9	Interview-administered questionnaire	Discomfort or pain focused in the upper part of the abdomen at least 3 Min the past one year	3 M	3517	3115	402	Medium risk	21
Adibi P, 2012	2002	Isfahan	General population	NR	Questionnaire	ROME III criteria	3 M	995	520	475	Low risk	22
Yazdanpanah K, 2012	2013	Sanandaj	General population	NR	Interview-administered questionnaire	Upper abdominal pain accompanied by (or without) other gastrointestinal symptom such as, vomiting, nausea, excessive belching, heartburn, abdominal fullness	1 M	590	187	403	Medium risk	23
Seyedmirzaei SM, 2014	2006-2007	Kerman	General population	NR	Interview-administered questionnaire	ROME III criteria	3 M	2210	1049	1161	Low risk	24
Esmailzadeh A, 2014	2000	Isfahan	General population	NR	Questionnaire	ROME III criteria	3 M	1933			Medium risk	25
Adibi P, 2016	2006	Isfahan	Healthcare workers	50.7±17.7	Questionnaire	ROME III criteria	3 M	4769	2016	2747	Low risk	26
Masoumi SJ, 2015	3002	Fars	General population	NR	Interview-administered questionnaire	ROME II criteria	3 M	397	142	255	Medium risk	27
Saneei P, 2017	2010	Isfahan	Healthcare workers	NR	Questionnaire	ROME II criteria	3 M	3363			Medium risk	28

NR, Not reported; M, Month; *Time for duration of symptoms

prevalence of dyspepsia pertained to the studies by Moghimi-Dehkordi et al¹⁸ (2.2%) and Yazdanpanah et al²³ (54.6%), respectively. The prevalence of dyspepsia, after removing two high-prevalence studies (Yazdanpanah et al²³ and Masoumi et al²⁷), was 11.3% (95% CI: 7.4–16.7) (Figure 2B).

Prevalence of all Types of Dyspepsia

The prevalence rates of ulcer-like dyspepsia in five studies with a sample size of 8,000 subjects, dysmotility-like dyspepsia in five studies with a sample size of 8000, and unspecified dyspepsia in four studies with a sample size of 4,483 were estimated to be 12.1% (95% CI: 5.2–25.7), 9.7% (95% CI: 4.9–18.4) and 17.0% (95% CI: 7.8–33.4), respectively (Figure 3).

Gender-Specific Prevalence of Dyspepsia

The prevalence of dyspepsia in Iranian males (in eleven studies with a sample size of 20,541) and females (in

eleven studies with a sample size of 20380) was estimated at 11.1% (95% CI: 6.3–18.8) and 17.8% (95% CI: 10.0–29.7), respectively. The females/males OR for dyspepsia was estimated at 1.52 (95% CI: 1.32–1.75, $P < 0.001$), which was significant (Figure 4C).

Subgroup Analysis for Dyspepsia

The prevalence of dyspepsia according to geographic area in Center, South, North and West of Iran was found to be 9.1% (95% CI: 5.5–14.9), 29.6% (95% CI: 16.4–47.5), 2.9% (95% CI: 2.4–3.5) and 30.2% (95% CI: 15.1–51.3), respectively (Figure 5A). The prevalence of dyspepsia based on population groups in blood donors, general population, healthcare workers and outpatient clinics was estimated to be 8.9% (95% CI: 8.0–9.9), 15.7% (95% CI: 7.9–28.7), 15.1% (95% CI: 14.1–16.1), and 11.4% (95% CI: 10.7–12.1), respectively (Figure 5B). The prevalence of dyspepsia based on duration of symptoms in ≤ 1 , 3, 6 and 12 months was estimated to be 15.9% (95% CI: 0.5–87.6),

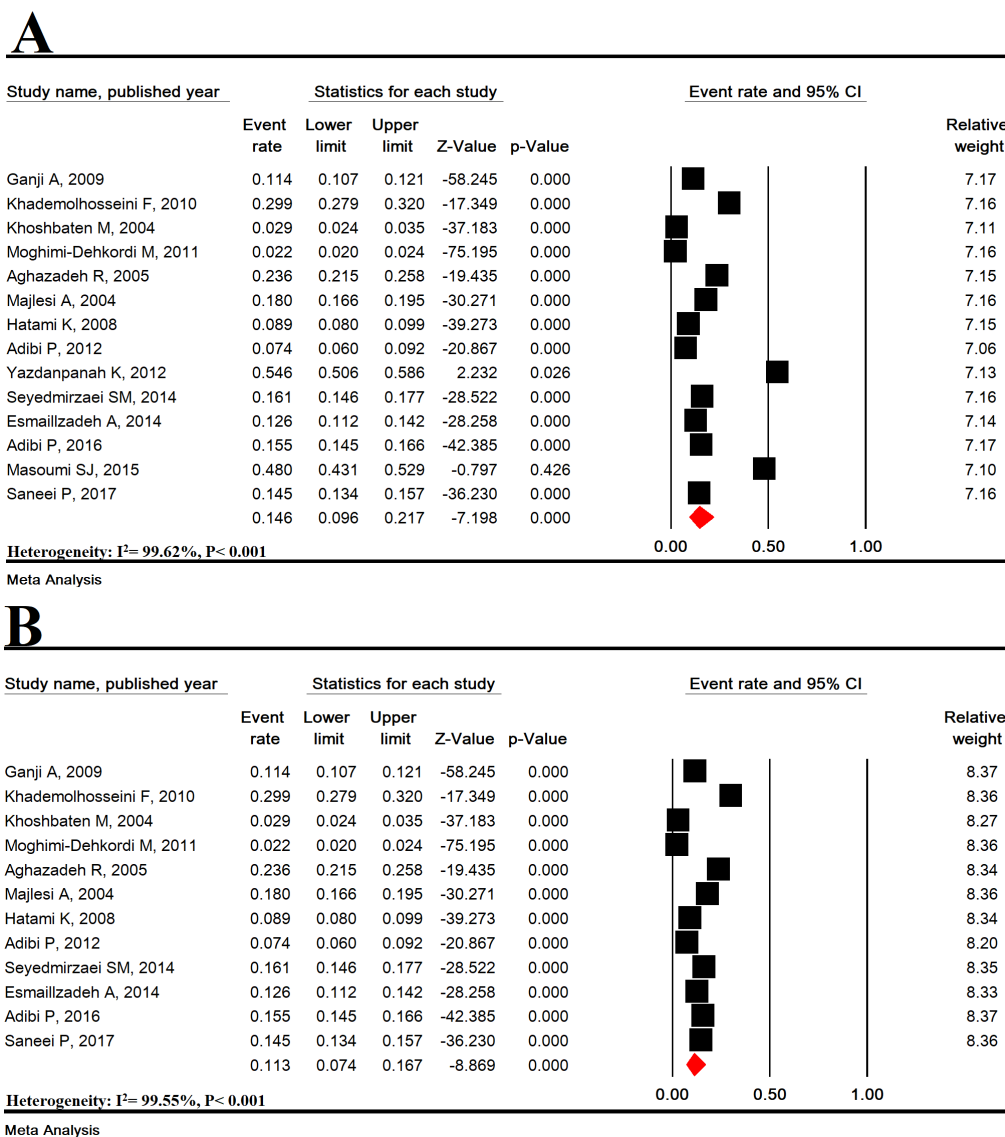


Figure 2. Prevalence of Dyspepsia in Iran.

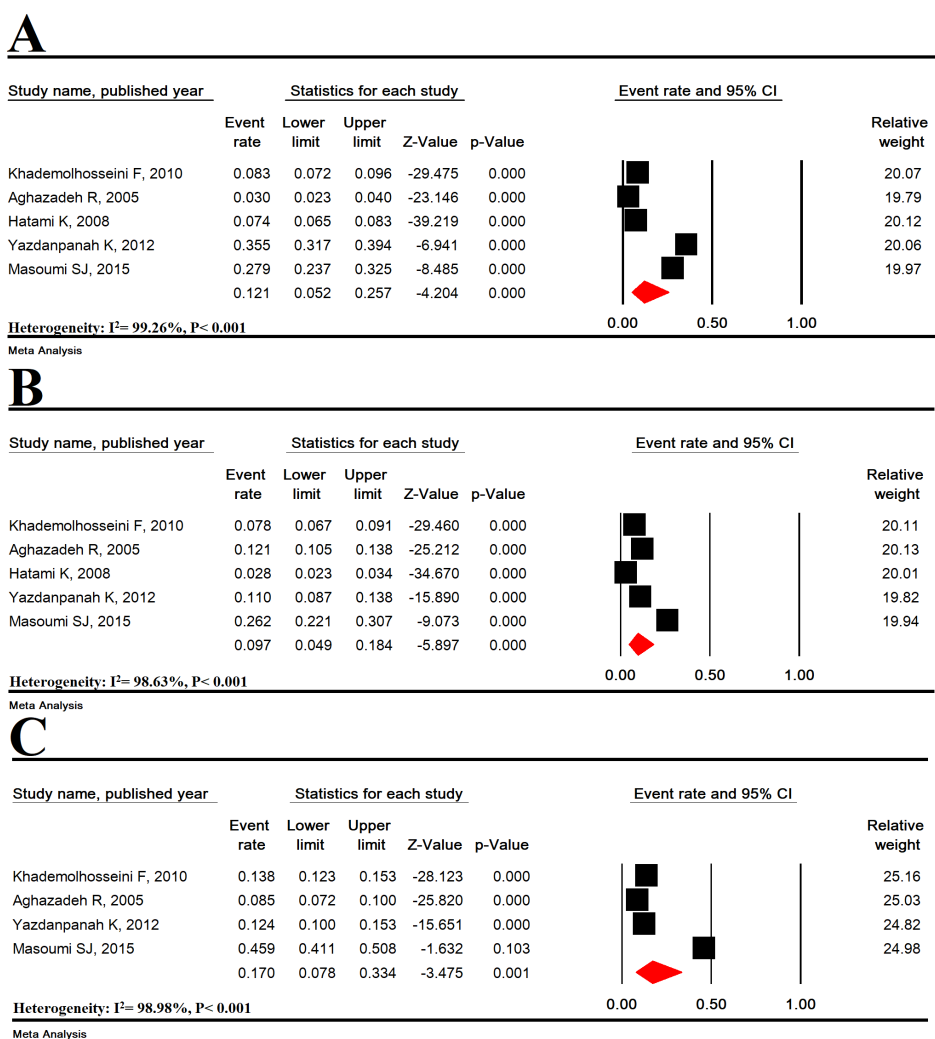


Figure 3. Prevalence of Ulcer-like (A), Dysmotility-Like (B) and Unspecified (C) Dyspepsia.

16.7% (95% CI: 11.8–23.3), 7.7% (95% CI: 0.6–51.9), and 18.0% (95% CI: 16.6–19.5), respectively (Figure 5C). The prevalence of dyspepsia based on the diagnostic technique in dyspepsia symptoms, ROME II and ROME III was estimated to be 17.8% (95% CI: 9.0–32.1), 28.3% (95% CI: 7.0–67.5), and 9.0% (95% CI: 3.8–19.6), respectively (Figure 5D). The prevalence of dyspepsia based on data collection using interviews, interview-administered questionnaires and questionnaires was estimated to be 11.4% (95% CI: 10.7–12.1), 16.3% (95% CI: 7.9–30.8), and 12.4% (95% CI: 10.1–15.2), respectively (Figure 5E).

Differences in subgroup analysis based on geographic area ($P<0.001$), population groups ($P<0.001$) and duration of symptoms ($P<0.001$) were significant, but differences in subgroup analysis based on the method of data collection ($P=0.458$) and diagnostic technique ($P=0.276$) were not significant (Figure 5).

Meta-regression Model

No significant relationship was observed between year of study, the total prevalence of dyspepsia (Meta-regression: 0.086, 95% CI: -0.037 to 0.209, $P=0.172$), and the prevalence of dyspepsia in men (Meta-regression: 0.136,

95% CI: -0.036 to 0.308, $P=0.121$) and women (Meta-regression: 0.100, 95% CI: -0.096 to 0.088, $P=0.296$) (Figure S1, Supplementary file 1).

Sensitivity Analysis

Sensitivity analysis showed that the total estimates are robust for prevalence of dyspepsia and for males and females (Figure S2, Supplementary file 1).

Publication Bias

Publication bias was not significant according to Begg's ($P=0.912$) and Egger's ($P=0.669$) test (Figure S3, Supplementary file 1).

Discussion

This research is the first meta-analysis addressing the prevalence of dyspepsia in Iranian people. The prevalence of dyspepsia was estimated to be 14.6% based on 14 studies. In a review study, the global prevalence of dyspepsia was found to be 31%, while indicating different prevalence in various areas such as North America (30%), South America (29%), North Europe (29%), South Europe (37%), South Asia (49%), Southeast Asia (27%), and Australia

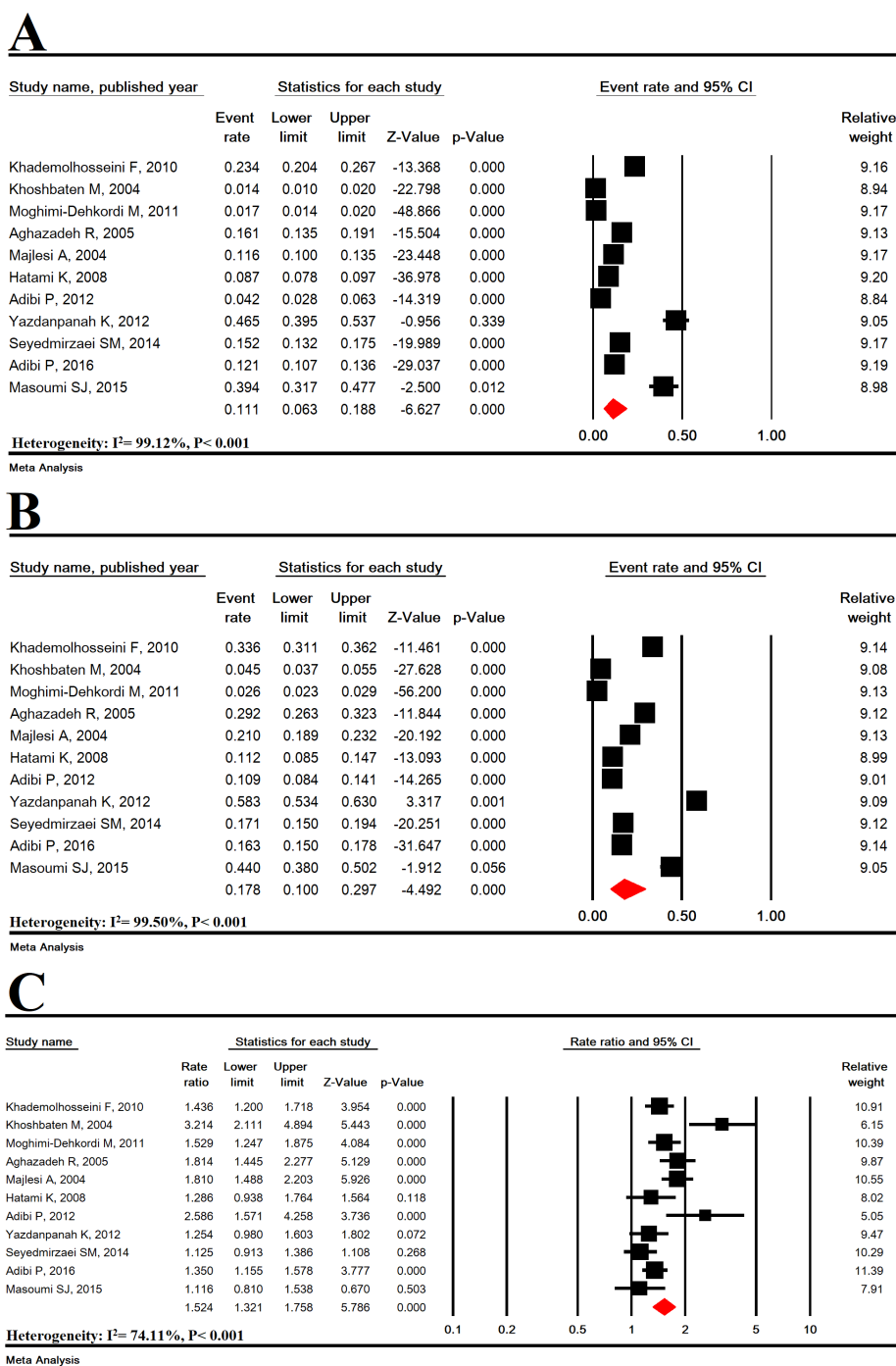


Figure 4. Prevalence of Dyspepsia in Iranian Males (A) and Females (B) and the Male to Female Odds Ratio for Dyspepsia (C).

(25%).³⁹ Various meta-analyses have been conducted on the prevalence of dyspepsia in special disorders, and the prevalence of dyspepsia was 43.9% in GERD patients,⁴⁰ 65.7% in patients with cholecystolithiasis⁴¹ and 9.55% after acute gastroenteritis.⁴² In another review, the global unexamined dyspepsia prevalence was 29%. However, in studies in the Middle East (including Iran), it was reported to be 15%.⁴³ A systematic review and meta-analysis study in Iranian population the daily, weekly, monthly, and overall prevalence of GERD symptoms was 5.64%, 12.50%, 18.62% and 43.07%, respectively.⁴⁴

The present meta-analysis has many strengths. We

utilized a universal and repeated search to increase the ability to detect all related papers. All phases of the study were independently carried out by two authors, and the disputes were resolved by a third author. We made contact with the first or corresponding authors to make sure we omit duplicate publications, and to gain additional data in certain cases. A random effects model was used to merge the data to prepare dependable estimates of dyspepsia prevalence. We also performed subgroup analysis to identify the reason for heterogeneity and to assess publication bias. Finally, the limitations of the present study are associated with the search in local databases,

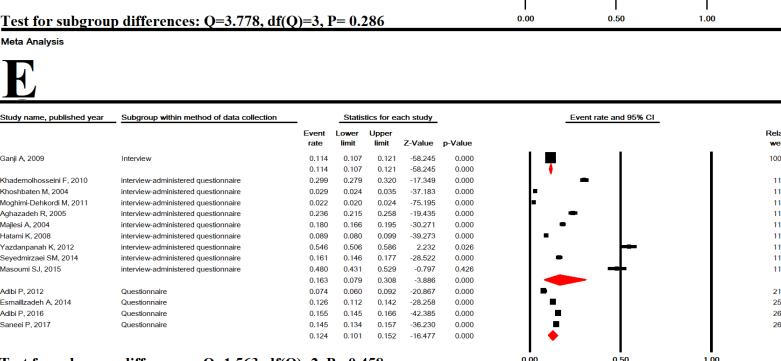
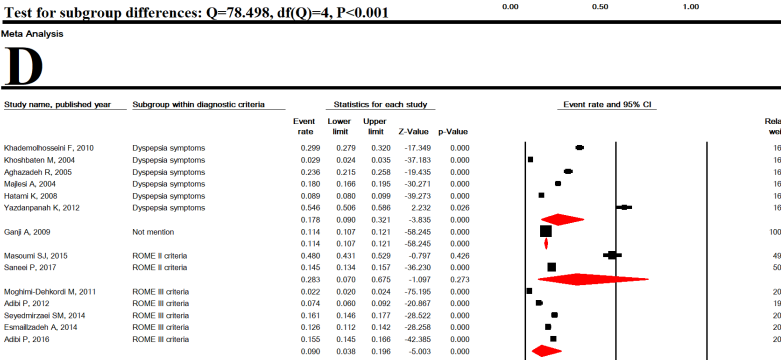
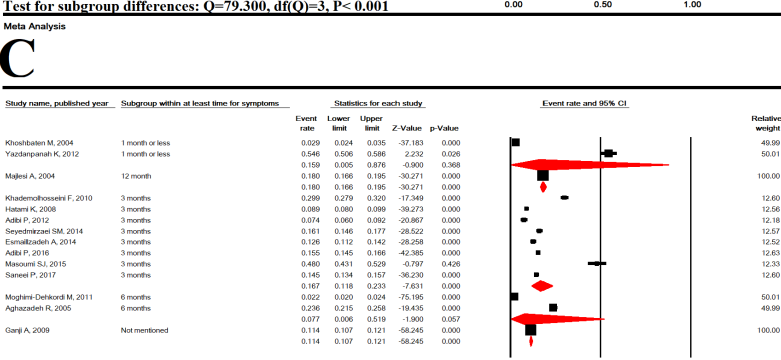
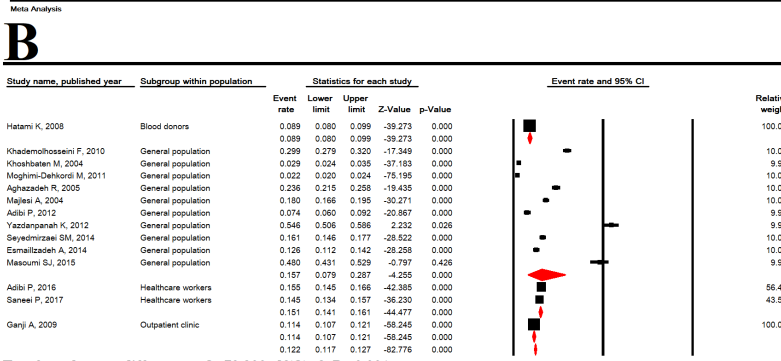
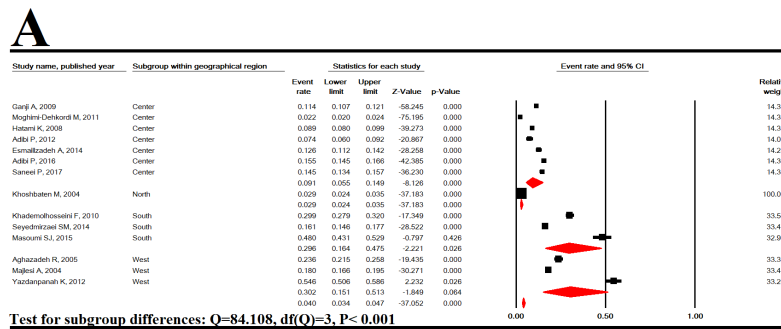


Figure 5. Subgroup Analysis Differences Based on Geographic Area (A), Population Groups (B) and at Least for Duration of Symptoms (C), Method of Data Collection (D) and Diagnostic Technique (E).

which lack the potential for combined search. We also excluded studies that were performed on special patients or had non-random sample size, so that the estimate would be attributable to the general population. Moreover, the limitations of the initial studies were about data collection, as some of them used questionnaires and some used interviews or both. Of course, more personal methods, such as interviews, which are the dominant methods in studies included in the meta-analysis, may overestimate the prevalence, but more impersonal techniques, like completing a questionnaire form on a website, might be more accurate. The absence of articles that show the prevalence of dyspepsia for some geographical regions such as eastern and northern Iran may be considered as other limitations. Moreover, there was significant heterogeneity across all studies in our analysis, and considering the accessible data, we could attribute this difference to the geographic area ($P < 0.001$), population groups ($P < 0.001$), and duration of symptoms ($P < 0.001$) by subgroup analysis. Nevertheless, it seems that due to other cultural differences between the population groups, such as diversities in lifestyle and ethnicity (given that Iranian people have comprise several ethnicities with different cultures),⁴³ the accuracy and robustness of data collection could not be evaluated based on the available data.

The combination of epidemiological studies in Iran in this research showed that the prevalence of dyspepsia was significantly higher in women compared to men (OR = 1.52). In a meta-analysis at the global level, the unexamined dyspepsia prevalence was significantly higher in women compared to men in the Middle East (OR = 1.91). However, it was not significant in African countries, Southeast Asia, South America, Central America and Australia.⁴⁵

In the present study, the lowest incidence of dyspepsia based on the diagnostic technique was observed for the ROME III criteria (9%). These criteria were published 12 years ago for defining dyspepsia⁴⁶; few studies have evaluated these criteria and no significant difference was observed between ROME III and previous criteria for dyspepsia in one study.⁴⁷

The prevalence of dyspepsia according to the study year showed an increasing trend in the meta-regression model, although it was not significant. This increase might be due to the fact that dyspepsia has no impact on mortality.^{11,48}

Evaluating publication bias in the results of this study showed that bias had no impact on these studies. The bias is often created in these articles, since such articles are more probable to be printed because of their positive results. However, no such bias was found about dyspepsia in this study.⁴⁹

In conclusion, the prevalence of dyspepsia in Iran is relatively high (14.6%) but is lower than worldwide estimates.

Authors' Contribution

MA, MK, AA, and ZJ MS performed data extraction. MA performed statistical analysis. MA and RR wrote the manuscript. MA, MK, AA, and ZJ, RR and MS performed the literature search and quality evaluation. MA, MK, AA, and ZJ, RR and MS revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interest Disclosures

The authors declare no conflict of interests.

Funding

Ilam University of Medical Sciences.

Ethical Statement

Not applicable.

Acknowledgment

The authors would like to thank the Clinical Research Development Unit of Baqiyatallah Hospital, Tehran, Iran, for guidance and advice.

Supplementary Materials

Supplementary file 1 contains Figures S1-S3.

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