

SYSTEMATIC REVIEW

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The prevalence of Barrett's esophagus in Iranian patients with gastrointestinal symptoms: a systematic review and meta-analysis

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Abstract

Background Barrett's esophagus (BE) is a premalignant columnar metaplasia of the esophagus that predisposes victims to esophageal adenocarcinoma (EAC). Depending on differences in the study population and risk factors, the prevalence of BE may vary, from 0.4 to 20% globally. The current study aimed to systematically review and analyse the prevalence of BE in patients with gastrointestinal symptoms in Iran. Furthermore, gastrointestinal malignancies are among the most common tumours in Iran, making this study even more significant.

Methods A systematic search was carried out in PubMed, Web of Science, Scopus, and EMBASE as well as some domestic databases including SID, Magiran, IranDoc, IranMedex from inception to the end of 2023. We included all cross-sectional studies which reported the prevalence of BE and calculated pooled prevalence.

Results The results of the analysis, including 9 studies in a total of 4978 cases (213 Barrett diagnoses), revealed that by the results of these studies, the prevalence of Barrett's esophagus is 4.4% [I² = 94.9% [92.2%; 96.6%]/p-value < 0.0001]. Subgroup analysis, divided by region and year, revealed significant differences between groups.

Conclusions The epidemiology of BE in Iran is not completely identified. This is the first systematic review and meta-analysis evaluating the prevalence and of BE in Iran. Due to the importance of BE in progressing to esophageal adenocarcinoma, much importance should be given to its timely diagnosis. It is strongly recommended to conduct more comprehensive studies including more patients in this field.

Keywords Barrett's esophagus, Prevalence, Columnar metaplasia, Iran, Systematic review

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Background

Barrett esophagus (BE) is a premalignant condition in which normal esophageal squamous cell epithelium replaces with columnar metaplasia. It may develop to dysplasia and esophageal adenocarcinoma (EAC), if left untreated. Approximately 3–5% of patients with BE will be diagnosed with EAC [1].

Interest in BE has increased due to the unfavorable prognosis of EAC and a raise in prevalence in recent years. Preventing EAC requires identifying and treating BE [2, 3]. Since gastroesophageal reflux disease (GERD) has been linked to a higher risk of BE, most guidelines suggest considering screening of patients with persistent GERD, even though they discourage population-based screening. Nonetheless, 50% of EAC patients have never had GERD in their lifetime [4–6]. In the matter of diagnosis, controversy has surrounded BE. Its meaning and application have changed over time and in different parts of the world. The Prague categorization, which was introduced in 2006, has enhanced reporting reliability and BE diagnosis [7]. The American Gastroenterological Association defines BE as any extent of intestinal metaplasia, and the British Society defines it as any columnar metaplasia (CM) (fundic type, cardiac type, and intestinal type) lining in the distal esophagus with a minimum length of 1 cm. In contrast, the European, American Society for Gastrointestinal Endoscopy and American College of Gastroenterology define BE as intestinal metaplasia (IM) lining in the distal esophagus with a minimum length of 1 cm [3, 8, 9].

Depending on the population under study, risk factors for BE in the general population might range greatly, from 0.4 to 20% globally. In comparison to those of Hispanic or Asian heritage, White people over 50 had the highest frequency of Barrett's esophagus in the US, whereas Black people have the lowest prevalence. BE can develop as a result of a number of conditions, such as GERD, peptic stricture, and erosive esophagitis [10].

Because most cases go misdiagnosed, it is challenging to comprehend the epidemiology of BE. In fact, it is unknown how common BE is; some research suggests that it is 1–2% in the general population and 15% in people with chronic GERD. It's critical to establish and assess the BE prevalence (priori probability) while developing a screening approach [11].

Our goal was to determine the prevalence of BE in Iranian gastrointestinal patients, we also sought to evaluate the variation in BE prevalence by definition, geography, time period, and technique. Only patients with a diagnosis of Barrett's esophagus could be included in the endoscopy of gastrointestinal disorders due to the inadequate nature of the tests that were carried out. The prevalence of Barrett's esophagus in patients with gastrointestinal diseases in Iran has never been examined in

a systematic review and meta-analysis study before. Furthermore, gastrointestinal malignancies are among the most common tumours in Iran, making this study even more significant.

Methods

We conducted current study according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Statement (PRISMA 2020) [12]. The protocol of our study was registered in the PROSPERO International Prospective Register of Systematic Reviews (Registration ID = CRD42024526411).

Search strategy

A comprehensive search strategy was developed and then applied to search in some international electronic databases, including PubMed, Embase, Scopus, and Web of Sciences, and some domestic databases including SID and Magiran, IranDoc, IranMedex, using standard keywords from inception to the end of 2023. We combined the following keywords using Boolean operators, 'AND' 'OR' for our comprehensive search: 'prevalence', 'epidemiology', 'incidence', 'risk', 'screen', 'Barrett', 'intestinal metaplasia', 'gastroesophageal reflux', 'esophagitis', and 'Iran'. No language restrictions were applied during the search process. The search strategy is presented in detail in Supplement 1. As all authors are Persian, they could handle Persian articles. The reference list of retrieved articles was searched manually for additional studies. To identify additional relevant reports, we also sent letters to relevant Iranian research centers that if they had completed research on Barrett's esophagus prevalence, they sent us their results that none of them had research on this matter.

Study selection

Inclusion criteria were original full-text articles published up to December 2023 pointing out BE in general and the GERD population, which assessed BE with accepted criteria. When the full text was not available, attempts to contact the corresponding authors were made. In the matter of exclusion criteria, interventional studies, case reports, case-controls, editorials, letters to editors, and reviews with BE cases were disqualified.

Data extraction and quality assessment

As all studies were imported and duplicated records were removed, the title and abstract of records ($n=479$) were screened by two independent investigators (KB and MR). Full-text eligibility was done by the same investigators. disagreements were resolved through consensus.

After developing a spreadsheet in Excel, two investigators extracted data independently and cross-checked it (HS and FB). First author's name, publication year,

region, sample size, male, mean age, quality of endoscopy, way of EGJ detection, protocol, esophagitis present during be diagnosis, and the prevalence of BE were investigated through articles to assess variability in prevalence across regions and diagnostic criteria. Two researchers investigated study quality independently, using the Newcastle-Ottawa Scale (NOS) for cross-sectional studies (MR and MM). This scale includes eight questions in about selection, comparability, and outcomes. Each question is scored as follow, A score of “0” was assigned if the item was not addressed, while “1” was given if it was addressed; the item “comparability” could be given a maximum score of “2” [13]. Any disagreements were resolved through discussion or by consulting a third reviewer.

Statistical analysis

Pooled prevalence Meta-analysis was performed using the R ‘meta’ package. Chi-square based on the Q test and I square statistics were used to assess the heterogeneity of reported prevalence among the studies. $P < 0.1$ was regarded as statistically significant. Due to severe heterogeneity among studies regarding reported prevalence, the pooled prevalence was estimated using a random-effect meta-analysis proposed by Der-Simonian and Laird. Subgroup analysis was conducted by dividing studies by Region and Year.

Results

Search results

The initial search yielded a total of 884 articles from the mentioned databases. After removing duplicates 479 articles remained of which the titles and abstracts were screened. 139 studies as well as three included Persian studies were chosen for full-text review. Following the full-text review, nine studies met the inclusion criteria and were included in the quantitative synthesis [14–20]. A flow diagram delivering the study selection process is presented in Fig. 1.

Study characteristics

Table 1 shows the general characteristics of the selected studies. The included studies were published between 2003 and 2014 from four different cities in Iran, including Tehran ($n = 5$), Tabriz ($n = 2$), Kashan ($n = 1$), and Yazd ($n = 1$). All studies were cross-sectional concerning study design. The sample sizes ranged from 100 to 1248 participants, and the reported prevalence ranged from 0.2 to 10.7%. The highest prevalence of BE was observed in Yazd province (10.7%). T. Khamechian (2013) investigated BE prevalence in patients with dyspepsia. Studies by S. Taghipour-Zahir (2012), M. Rezailashkajani (2007) and R. Aghazade (2005) evaluated the BE prevalence in

individuals undergoing endoscopy regardless of indication. Other studies included individuals with GERD symptoms.

Results of metaanalysis

The results of the analysis, including 9 studies in a total of 4978 cases (213 Barrett diagnoses), revealed that by the results of these studies, the prevalence of Barrett’s esophagus is 4.4% [$I^2 = 94.9\%$ [92.2%; 96.6%]/ p -value < 0.0001]. (Fig. 2) The leave-one-out analysis was applied, showing that all the pooled estimates after one survey at a time are still within the 95% confidence interval of the overall estimate. Subgroup analysis, divided by region and year, revealed significant differences between groups. Yazd has a high prevalence of Barrett (10.7%). Tabriz, Kashan, and Tehran had similar results (Fig. 3). There was no meaningful relationship between the year of study and results (Fig. 4).

Quality assessment

The Newcastle-Ottawa Scale (NOS) is a validated, scale consisting of 8 items across three domains: selection, comparability, and outcome with a maximum score of 10. Score 0–4, 5–6, 7–8 and 9–10 were considered as unsatisfactory, satisfactory, good studies and very good studies, respectively. Our quality assessment for included articles revealed all of them with low risk of bias. The detailed result of quality assessment is illustrated in Table 2.

Discussion

Barrett’s esophagus (BE) is known as the metaplasia of the squamous lining of the esophagus to the specialized columnar tissue of the intestine and is highly related to the prognosis of esophagus adenocarcinoma. The epidemiology of BE in Iran is not completely identified. This is the first systematic review and meta-analysis evaluating the prevalence and of BE in Iran.

In the included studies, a prevalence of any length BE with histologic confirmation was estimated about 4.4%. Heterogeneity among the included studies were approximately 94.9% which can be due to differences in risk factors such as mean age, nationality (Afghans), BMI, smoking, alcohol, existence of GI disturbances as a cause for endoscopy mostly dysphagia, heartburn, abdominal pain, weight loss, gastrointestinal bleeding, and regurgitation, frequency, severity, and duration of symptoms, various habitual and nutritional history in provinces, use of anti-acid and acid-suppressing drugs, sensitivity and specificity of diagnosis, coexistence of esophagitis, GERD, peptic ulcers, helicobacter pylori infection, hiatal hernia, and the definition for each risk factor. Histological confirmation includes evaluating esophageal mucosal biopsy specimens, which were taken proximal to the Z-line (gastroesophageal junction) through endoscopy by expert pathologists. The specimens were also assessed for

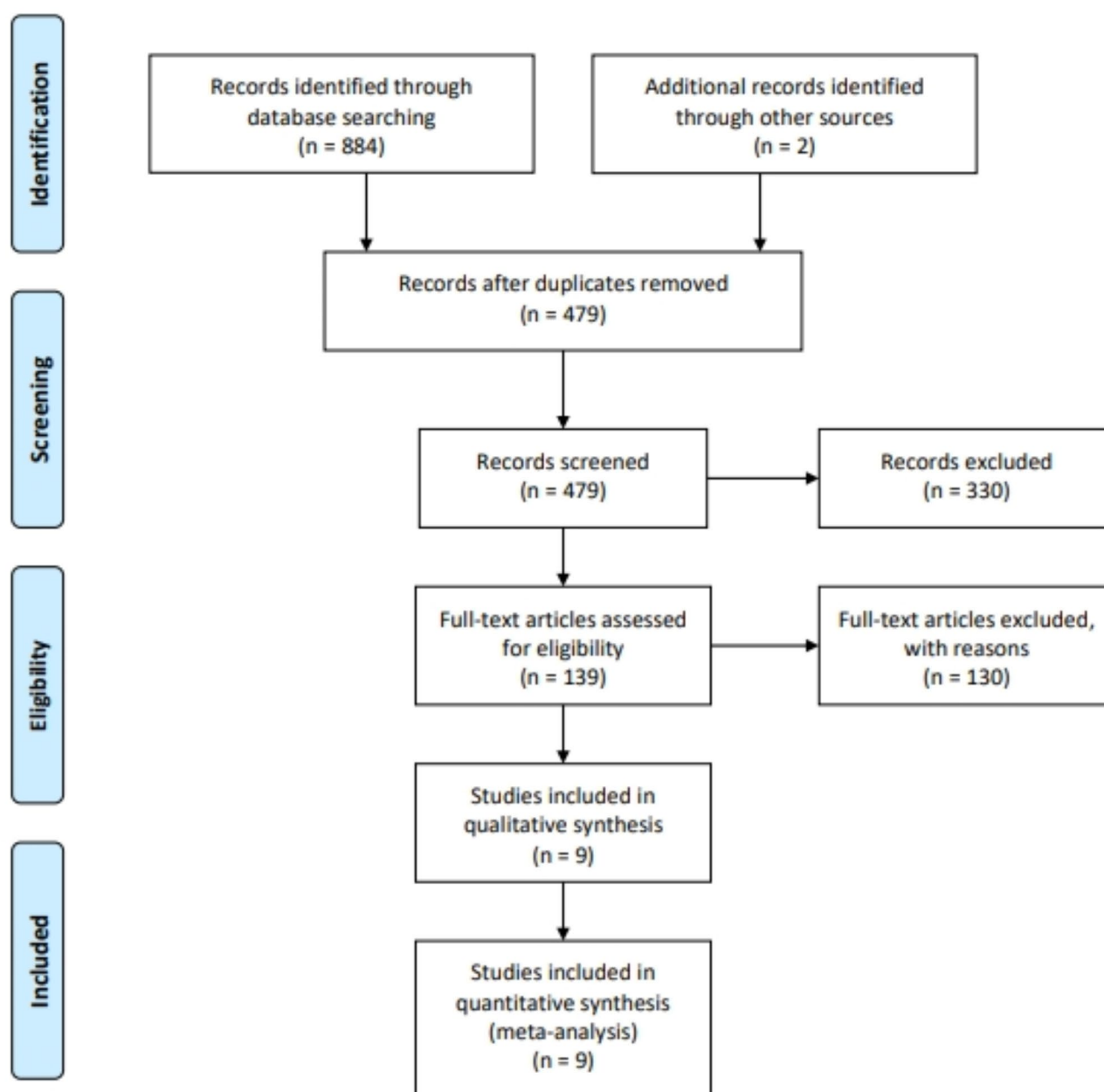


Fig. 1 PRISMA of Prisma flow diagram. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6 [6]: e1000097. doi:<https://doi.org/10.1371/journal.pmed1000097> For more information, visit www.prisma-statement.org

Helicobacter pylori infection. Most of the included studies define the BE as the presence of intestinal metaplasia in distal esophagus or columnar lined esophagus. The studies were from different provinces of Iran but most of them were conducted in Tehran. Length of segment is the strongest indicator of BE in endoscopy and it is also affected by the length of acid rise [23, 24]. Only one study exclusively assessed the short segment BE (intestinal metaplasia at a distance of less than 2 cm from the gastroesophageal junction) [19]. In one study, BE with short

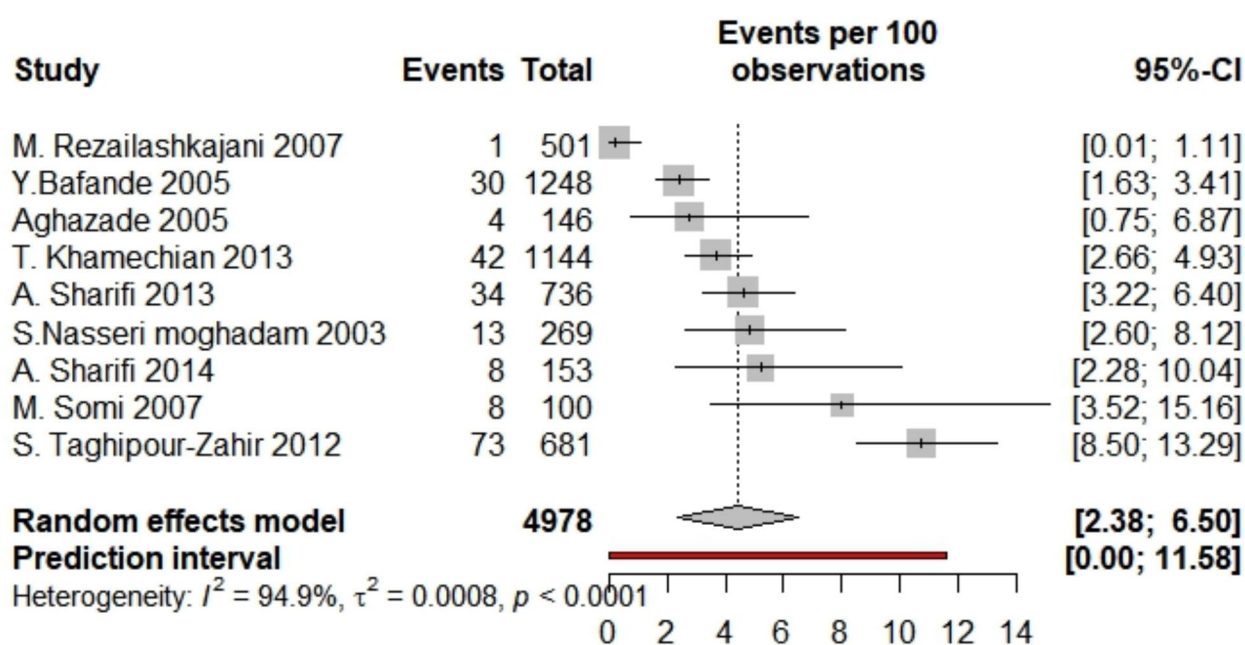
segment had a higher prevalence than BE with long segment (13% vs. 4.8%) [14]. A significant percentage of BE cases do not show endoscopic evidence or clinical signs of gastroesophageal reflux. Also, there are a small percentage of suspected cases of BE during endoscopy are confirmed by pathology examination.

In one study, no specific association was found between *Helicobacter pylori* infection and the incidence of BE [19]. In general, there is no consensus on the relationship between *Helicobacter pylori* infection and the

Table 1 The baseline characteristics of the included studies symptoms

Study	Region	Sampling	Sample size	Male N (%)	Mean Age \pm SE	Unknown quality reported	How EGJ was defined	Seattle protocol Used	Esophagitis during BE diagnosis	Prevalence N (%)
T. Khamechian (2013) [15]	Kashan	Patients with dyspepsia	1144	497 (43.4%)	53.2	Yes	Unknown	No	Yes	42 (3.7%)
S. Taghipour-Zahir (2012) [20]	Yazd	Patients underwent EGD	681	(62.7%)	62.04 \pm 6.43	No	Unknown	Unknown	Unknown	73 (10.7%)
M. Rezailashkajani, (2007) [16]	Tehran	Patients underwent EGD	501	195 (38.9%)	44.7 \pm 15	No	Unknown	Unknown	Yes	1 (0.2%)
A. Sharifi (2013) [18]	Tehran	Patients with GERD	736	411 (55.8%)	48.9	Yes	Unknown	Yes	Yes	34 (4.6%)
A. Sharifi (2014) [17]	Tehran	Patients with refractory GERD	153	78 (50.9%)	47.92 \pm 17.57	Yes	Gastric fold	Unknown	Yes	8 (6.5%)
M. Somi (2007) [19]	Tabriz	Patients with GERD	100	39 (39%)	42.3 \pm 15.12	Yes	Gastric fold	Unknown	Yes	8 (8%)
R. Aghazade (2005) [14]	Tehran	Patients underwent EGD	146	68 (46.6%)	40.1	Yes	Gastric fold	Unknown	Yes	4 (2.7%)
Y. Bafande (2005) [21]	Tabriz	Patients with GERD	1248	750	45 \pm 15.5	Unknown	Gastric fold	Unknown	Unknown	30 (2.4%)
S. Nasser Moghadam (2005) [22]	Tehran	Patients with GERD	269	134	41.6 \pm 13.9	No	Gastric fold	Yes	Yes	13 (0.04%)

EGJ - esophagogastric junction, BE - Barrett's esophagus, EGD - Esophagogastroduodenoscopy

**Fig. 2** Forest plot of BE prevalence among Iranian patients with gastrointestinal symptoms, using random effect model. CI indicates confidence interval

occurrence of Barrett's esophagus, and some researchers believe that this infection has a protective role in the occurrence of Barrett's esophagus, while others believe that not all strains of this bacteria but only Cag A positive strain are included. This relationship is attributed to the decrease in gastric acid secretion due to *Helicobacter pylori* infection [25, 26]. Multi-layered epithelium in the

gastroesophageal junction can be considered as an early histological manifestation of BE in the GERD patients [27]. In a study conducted by Khamechian et al., dyspepsia longer than 5 years was a risk factor for BE [15]. Older age is considered as a risk factor for BE among GERD patients whereas there was no significant difference between male and female gender [18].

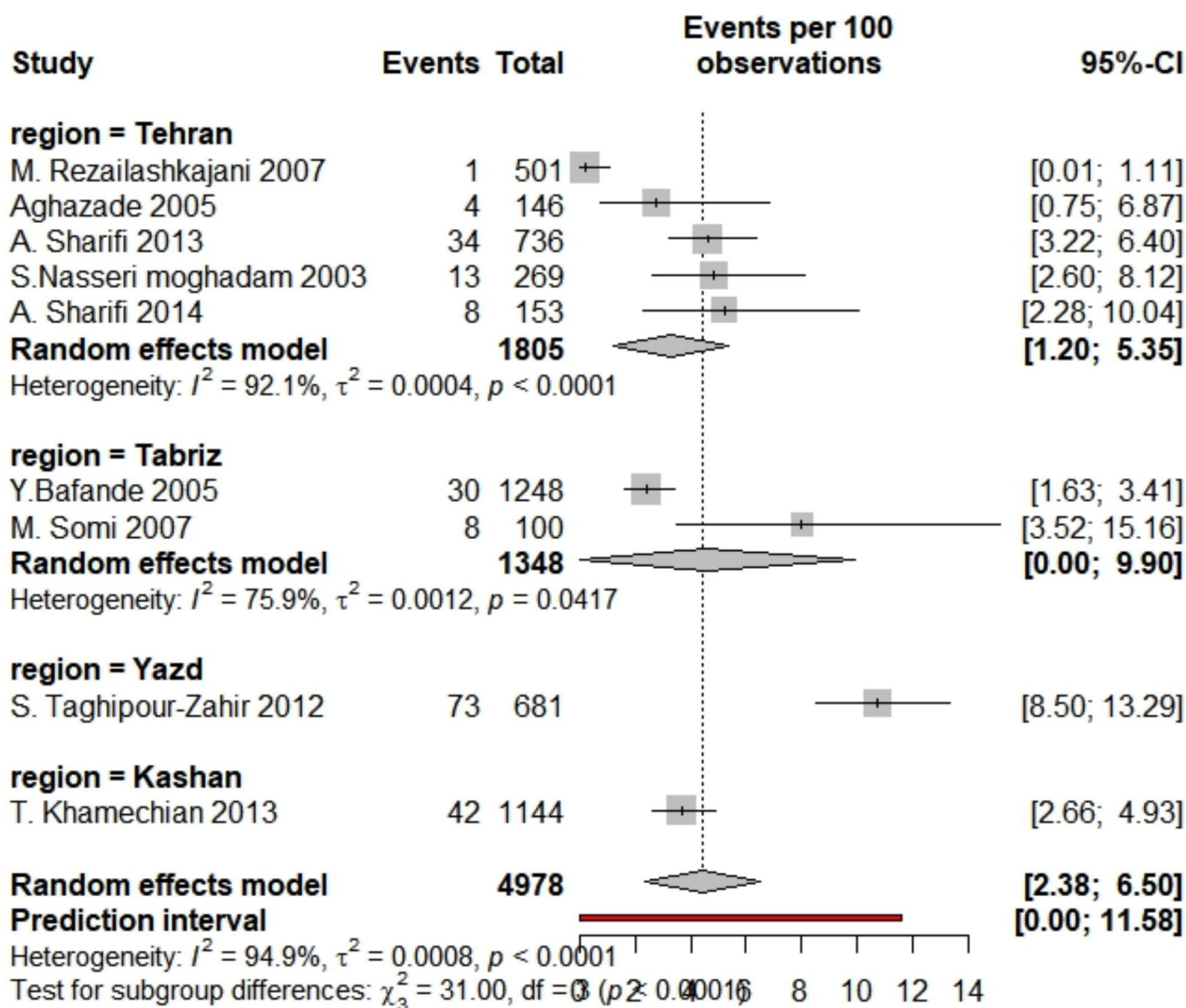


Fig. 3 Subgroup analysis forest plot of BE prevalence, sub grouped by region

In a systematic review, the global prevalence of BE with any length was 0.96% in the general population with histological confirmation and after excluding high-risk of bias studies was 0.70% [9]. There was significant heterogeneity among included studies due to their various biases, and also the data assessing several countries were minimal or absent. The BE prevalence among Asian countries was 7.8% and 1.3% was the prevalence of BE with histological confirmation in another systematic review and meta-analysis [28]. This study also revealed an increase in prevalence of the BE in this region. 82.1% of histologically confirmed BE were short segment (< 3 cm). The heterogeneity in this study was high because of publication, time period, geographical, and BE definition biases, and some of the included studies were conducted in high-risk patients, diagnosed BE without IM confirmation, and excluded patients with known BE.

Male sex, smoking, reflux symptoms, and hiatus hernia were risk factors for histologically confirmed BE but *H. pylori* infection and obesity. Another systematic review reveals a prevalence of about 8% in the low-risk populations, about 1.1% in western populations, about 3% in patients with GERD, about 12.2% in patients with other risk factors and GERD, about 23.4% in patients with positive family history, about 6.1% in patients age more than 50, about 1.9% in obese patients, and about 6.8% in male sex.

This study had limitations that need to be considered in the analysis of future studies to achieve more accurate results. Eligible studies for inclusion were few and more studies are needed to achieve more comprehensive results. Incorporated studies in this analysis, were not categorize the included population based on the related risk factors, so that we also examine the prevalence

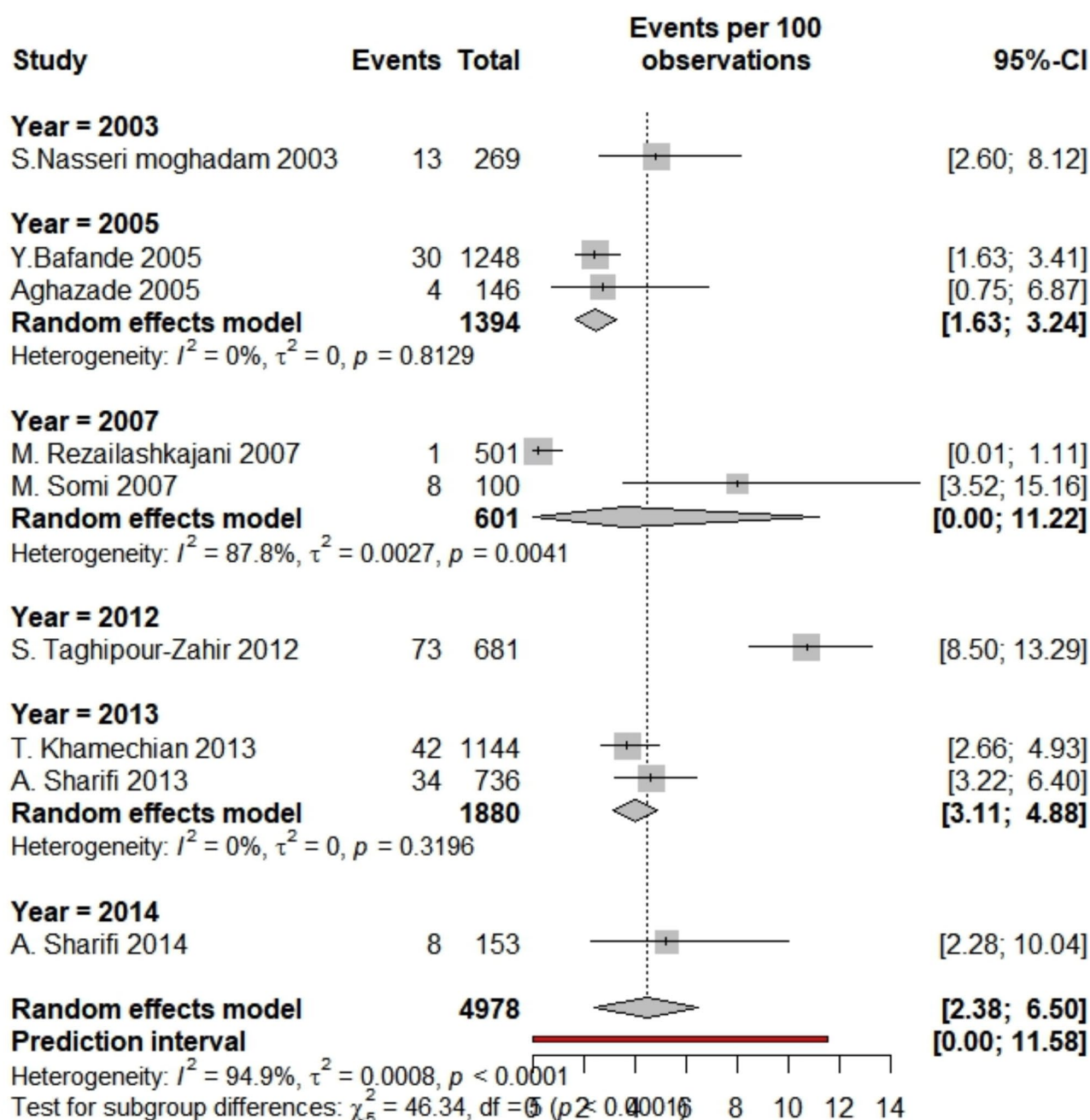


Fig. 4 Subgroup analysis forest plot of BE prevalence, sub grouped by year

among the total evaluated population. Prevalence is also affected by different definitions of BE and the distance from gastroesophageal junction, so that it is necessary to consider this difference in future studies. The diagnosis also depends on the ability and experience of the involved endoscopist and pathologist.

Considering the high prevalence of GERD in Iran and its impact on the subsequent development of BE and esophageal adenocarcinoma, it is essential to obtain

tissue specimens from the gastroesophageal junction even if the macroscopic evidence during endoscopy is normal. BE often remains undiagnosed, and a specimen is rarely taken from the macroscopic normal gastroesophageal junction. Due to the importance of BE in progressing to esophageal adenocarcinoma, much importance should be given to its timely diagnosis. It is strongly recommended to conduct more comprehensive studies including more patients in this field.

Table 2 Quality assessment of studies into the meta-analysis

Study	Selection				Comparability	Outcome		Total score
	Representativeness	Sample size	Non-respondents:	risk factor		Assessment**	Statistical test	
T. Khamechian (2013)	1	1	-	2	2	2	1	9
S. Taghipour-Zahir (2013)	1	1	1	2	2	2	1	10
M. Rezailashkajani, (2013)	1	1	-	2	2	2	1	9
A. Sharifi (2013)	1	1	-	2	2	1	-	7
A. Sharifi (2014)	1	1	-	2	2	2	1	9
M. Somi (2007)	1	1	-	2	2	2	1	9
R. Aghazade (2005)	1	1	-	2	2	1	-	7
Y.Bafande (2005)	1	1	-	2	2	2	1	9
S.Nasseri Moghadam (2005)	1	1	1	2	2	2	1	10

Conclusions

The epidemiology of BE in Iran is not completely identified. This is the first systematic review and meta-analysis evaluating the prevalence BE in patients with gastrointestinal symptoms in Iran. The current study estimates BE prevalence higher than global frequency. There is a heterogeneity in BE prevalence between studies probably due to region, year of study, inpatient or outpatient-based research, genetic or cultural risk factors, inclusion criteria differences, etc. Due to the importance of BE in progressing to esophageal adenocarcinoma, much importance should be given to its timely diagnosis. It is strongly recommended to conduct more comprehensive studies including more patients in this field.

Abbreviations

BE	Barrett esophagus
EAC	Esophageal adenocarcinoma
GERD	Gastroesophageal reflux disease
CM	Columnar metaplasia
IM	Intestinal metaplasia
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12876-025-03822-1>.

Supplementary Material 1

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Author contributions

Maryam Rashidian, Fatemeh Bastan and Hedieh Soltani participated in data extraction and writing the first draft of the manuscript. Yasin Tabatabaei

Mehr and Kiyarash Bakhshande wrote search strategy. Kiyarash Bakhshande and Reza Ghosheni carried out screening. Mahdi Mohammaditabar, Khaled Rahmani and Mahmood Bakhtiyari participated in methodology and data analysis. Mahdi Mohammaditabar and Maryam Rashidian performed and quality assessment of studies and prepared figures. Mojgan Forootan, Mahsa Mohammadi and Mostafa Qorbani commented on previous versions of the manuscript. Mohsen Rajabnia contributed to the study conception and design. All authors read and approved the final manuscript.

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Data availability

The data that support the findings of this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate

This study was approved by the medical ethics committee of Alborz University of Medical Sciences on November 13, 2024. (IR.ABZUMS.REC.1403.213).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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