Systematic Reviews

SYSTEMATIC REVIEW UPDATE

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Global prevalence of gastric intestinal metaplasia: a systematic review and meta-analysis

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Abstract

Background Gastric intestinal metaplasia (GIM) is a precancerous lesion that increases the risk of gastric cancer. Several preliminary studies have examined the prevalence of GIM. The present systematic review and meta-analysis were conducted aimed estimating the global prevalence of GIM.

Methods The present systematic review and meta-analysis was conducted based on the PRISMA reporting guidelines in the range of 1988–2022. Articles related to the purpose of the study were obtained from Embase, PubMed, Scopus, Web of Science (WOS), MagIran, SID databases, and Google Scholar search engine using relevant and validated keywords in MeSH/Emtree. Inclusion criteria were observational articles, access to the full text of the article, and articles that reported prevalence. Heterogeneity among studies was examined using the I^2 index. The random effects model was used in this review due to the high heterogeneity between the results of the studies. Data were statistically analyzed using the Comprehensive Meta-Analysis (CMA) software.

Results In the initial search, 4946 studies were found, of which 20 articles with a sample size of 57,263 met all the criteria for inclusion in the study. The global prevalence of GIM was 17.5% (95% confidence interval: 14.6–20.8%). The highest percentage of prevalence of GIM belonged to American continent with 18.6% (95% confidence interval: 13.8–24.6%) and patients with gastroesophageal reflux with 22.9% (95% confidence interval: 9.9–44.6%).

Conclusion The results of this study showed that the prevalence of GIM in the world is high and needs further investigation. Therefore, it is recommended to be given more attention by experts, officials, and health policymakers.

Keywords Intestines, Meta-analysis, Metaplasia, Prevalence, Stomach

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Background

Gastric intestinal metaplasia (GIM) is a mucosal phenotype change of a specialized set of cells (gastric) to another range of mucosal cells with intestinal characteristics and is generally considered to be a precursor of gastric cancer [1]. The most well-known risk factors for GIM are *Helicobacter pylori* (*H. pylori*) infection, rheumatic disorders, diet, excessive dietary salt (sodium chloride) intake, smoking, alcohol consumption, and chronic bile reflux [2]. It has been claimed that GIM rarely occurs in the gastric mucosa without any associated pathology, the most common cause of which is chronic gastritis mainly caused by *H. pylori* infection [3, 4]. GIM is also frequently seen in autoimmune chronic atrophic gastritis (ACAG) of the fundal mucosa (ACAG) [5].

Although there are several classifications of gastrointestinal metaplasia, currently, the most prominent of them is the classification of GIM as complete (type 1) and incomplete (types 2 and 3). The incomplete type, especially type 3, has a higher risk of stomach cancer than the complete type [6, 7]. Therefore, in the complete type and the absence of other risk factors for gastric cancer, patients do not need long-term endoscopic care. Previous studies have shown that type 3 is associated with gastric epithelial dysplasia and intestinal type of gastric carcinoma [6].

H. pylori colonization of the gastric mucosa in the complete type of GIM might be patchy. Patients with incomplete metaplasia should have a gastric endoscopy to determine the extent of metaplasia and rule out dysplasia or adenocarcinoma. The development of intestinal-type gastric adenocarcinoma is thought to progress sequentially through four stages: non-atrophic gastritis, multifocal atrophic gastritis, metaplasia, and dysplasia. Chronic *H. pylori* infection causes chronic inflammation in the gastric mucosa, which may turn into atrophy and metaplasia [8].

Globally, screening guidelines have been established in high-prevalence countries. The American Society for Gastrointestinal Endoscopy recommends a case-by-case evaluation of the patient based on epidemiology, genetics, and environmental risk factors. Studies have investigated the use of serologic biopsy to stratify risk based on factors such as *H. pylori* status and pathogenic factors. Surveillance guidelines for patients with gastric intestinal metaplasia have not been definitively established but include repeat endoscopy at intervals according to the histological risk for malignant transformation [9].

The incidence of gastric cancer varies in different parts of the world [10, 11]. Gastric cancer is the third cause of cancer-related deaths in the world. In 2018, approximately 800,000 people died due to gastric cancer, and more than 1 million new cases of gastric cancer were diagnosed [12]. Also, gastric intestinal metaplasia is a precancerous lesion that increases the risk of gastric cancer up to 6 times. The prevalence of GIM varies in different regions of the world, from 3.4% in Northern Europe to 23.9% in South America [2]. Certain ethnic groups, such as Hispanics and East Asians, have significantly higher prevalence than others [13].

Although several preliminary studies have investigated the prevalence of GIM, no systematic and comprehensive study has been conducted in this field. A systematic review is a comprehensive review of the literature that systematically and transparently identifies, selects, and critically evaluates all related studies as well as collects and analyzes the data from the conducted studies. Also, a systematic review with explicit and clear objectives summarizes the reported results and provides the most coherent form of evidence for unbiased judgment; therefore, the current systematic review was conducted to investigate the prevalence of GIM in the world.

Materials and methods

Decision analytic modeling

The present systematic review and meta-analysis were conducted in the range of 1988–2022. This study was conducted based on the PRISMA 2020 reporting guidelines (http://www.prisma-statement.org/), including the following steps: identification, screening, eligibility, and inclusion [14]. To reduce errors, all steps of searching, identifying, screening, selecting articles, and extracting data were done independently by two researchers (M.K and S.S). In the case of disagreement between the two researchers, a discussion and re-examination was done in pairs, and, finally, a consensus was reached with the opinion of the third researcher (Z.J).

Identification of articles

To find articles related to the research question (What is the prevalence of Gastric Intestinal Metaplasia?), a comprehensive search was done in Persian information sources including Scientific Information Database (SID; https://www.sid.ir) and MagIran (https://www.magiran.com) as well as the international databases including PubMed, Embase, Scopus, and Web of Science (WoS). To search, validated keywords in Medical Subject Headings (MeSH) were used for PubMed as well as Elsevier's authoritative life science thesaurus (Emtree) for Embase and combined using OR and AND operators. For example, the search strategy of PubMed was determined as follows:

((((((Epidemiology[MeSH Terms]) OR (Epidemiology[Title/Abstract])) OR (Prevalence[MeSH Terms])) OR (Prevalen*[Title/Abstract])) AND (((Stomach[MeSH Terms]) OR (Stomach[Title/

Abstract])) OR (Gastric*[Title/Abstract]))) AND (((Intestines[MeSH Terms]) OR (Intestinal*[Title/Abstract])) OR (Intestine*[Title/Abstract]))) AND ((Metaplasia[MeSH Terms]) OR (Metaplasia*[Title/Abstract])).

We did not apply any time or language restrictions in the search of studies to retrieve all potentially relevant articles until July 2022. Finally, in order to maximize the comprehensiveness of the search, the Google Scholar search engine and the references of all the articles included in the study were checked manually.

Inclusion criteria

The inclusion criteria were as follows: original research articles, observational articles (cross-sectional study, cohort study, etc.), full text articles, and studies that reported the percentage or frequency of GIM.

Exclusion criteria

These articles were excluded from the review: studies unrelated to the research question, interventional studies (Clinical trial study, Field trial study, and Social trial study), case series, case reports, qualitative studies, articles presented in conferences and proceeding papers, letters to the editor, theses and dissertations, secondary studies, animal studies, articles whose full text was not provided after three emails to the corresponding author, and repeated and overlapping studies in different databases.

Selection process of studies

All articles received from different databases were entered into the EndNote X8 software. First, all duplicate and overlapping studies in different databases were removed. Then, the names and affiliations of the authors and the titles of the journals were removed from all the articles. In the next step, the title and abstract of the studies were reviewed and the studies unrelated to the objective of the study were excluded. Then, the full texts of the remaining articles were carefully reviewed according to pre-determined inclusion and exclusion criteria, and at this stage also, irrelevant studies were excluded. Finally, the articles that met all the inclusion criteria entered the qualitative evaluation stage.

Qualitative evaluation of the studies

In the present study, the Joanna Briggs Institute (JBI) checklist was used to evaluate the quality of the studies [15]. This checklist includes 9 questions regarding sample frame, participants, sample size, study subjects and the setting described in detail, data analysis, valid methods for identifying conditions, measuring the situation, statistical analysis, and adequate response rate. For scoring, if indicated "Yes" was assigned, "No" if not indicated, and "NA" if not reported. The minimum and maximum scores were zero and 9, respectively. Scores of 1–3 were considered as low quality, scores of 4–6 as medium quality, and scores of 7–9 as high quality [16]. Table 1 shows the results of the qualitative evaluation of the studies included in the meta-analysis.

Data extraction

We used a prepared checklist to extract data including the following items: first author's name, year of publication, country and continent, sample size, age of samples, study type, diagnostic tool, prevalence percentage, study population, and qualitative score using JBI.

Statistical analysis

The index investigated in this study was the prevalence of Gastric Intestinal Metaplasia, and the percentage or relative frequency in each study was used to combine the results of the various studies. Heterogeneity among studies was assessed using I^2 and Tau index. The I^2 index less than 50% was considered as "low heterogeneity," and more than 50% was considered as "high heterogeneity." The random effects model was used in this review due to the high heterogeneity between the results of the studies ($I^2 > 50\%$). In this model, the parameter changes among the studies are also calculated, so the results of this model are more generalizable than the fixed effect model in high heterogeneity conditions [35]. To identify the source of heterogeneity, sensitivity analysis was used. Egger's regression intercept was used to check publication bias, because this test detects publication bias more than other tests in meta-analyses where the number of articles is between 10 and 75 [36]. Sensitivity analysis was used to see how the general results change by removing each article. Meta-regression was also used to examine the relationship between the global prevalence of GIM with sample size, publication year, and age. We also performed subgroup analysis according to different continents, study population, JBI scores, and type of study. Data were statistically analyzed using the Comprehensive Meta-Analysis (CMA) software, and a *P*-value less than 0.05 was considered statistically significant.

Results

Systematic review

Summary of how the articles were included in the meta-analysis

A total of 4938 studies were found through searching in determined databases and information sources, and 8 articles were added through manual search. Using EndNote, 1356 duplicate and overlapping studies in

Table 1 Characteristics and data of articles included in systematic review and meta-analysis

First author, year (reference)	Country (continent)	Sample size (*n*)			Age (year)	Type of study	Diagnostic tool	Prevalence (%)	Population	JBI score
		Total	Male	Female						
Nguyen, 2021 [17]	USA (America)	2179	2004	175	62.1	Cross-sectional study	Upper endoscopy with gastric mapping (7 biopsy sites)	19.0	General population	9, high
Eriksson, 2008 [18]	Finland (Europe)	505	-	-	54 ± 16	Cross-sectional study	Endoscopy and biopsy	19.0	General population	6, medium
Olmez, 2015 [7]	Turkey (Europe)	560	333	227	57 ± 15	Retrospective study	Esophagogastroduodenoscopy	13.8	General population	7, high
Fennerty, 1992 [19]	USA (America)	440	438	2	63	Cross-sectional study	Endoscopy of the upper gastrointestinal tract	19	General population	6, medium
Cruz-Cruz, 2021 [20]	USA (America)	4707	1833	2874	66.1 ± 12.3	Cross-sectional study	Endoscopy and biopsy	10.7	General population	8, high
Huang, 2020 [21]	USA (America)	36,799	-	-	36.7	Retrospective study	Endoscopy and biopsy	11.7	General population	7, high
Almouradi, 2013 [22]	USA (America)	677	314	363	69.5	Retrospective study	Endoscopy	43	General population	7, high
Kim, 2008 [23]	South Korea (Asia)	389	117	272	51.3	Prospective study	Gastroscopy	20.1	General population	5, medium
Csendes, 2003 [24]	Chile (America)	492	256	236	54.5	Descriptive study	Endoscopy	33	Patients with gastroesophageal reflux	6, medium
Nguyen, 2021 [17]	USA (America)	2179	-	-	62.1	Cross-sectional study	Upper endoscopy with gastric mapping (7 biopsy sites)	19	General population	7, high
Petersson, 2002 [25]	Sweden (Europe)	475	259	216	59.7	Cross-sectional study	Gastroduodenoscopy with biopsy	23	General population	8, high
Carrilho, 2009 [26]	Mozambique (Africa)	109	-	-	37	Descriptive study	Upper digestive endoscopy	8.3	General population	7, high
Joo, 2013 [27]	South Korea (Asia)	4023	2358	1665	48.7 ± 11.3	Prospective study	Endoscopy	12.5	General population	8, high
Wallner, 2000 [28]	Sweden (Europe)	312	-	-	54	Descriptive study	Gastroscopy	15	Patients with gastroesophageal reflux	6, medium
Voutilainen, 1999 [29]	Finland (Europe)	1058	-	-	57.3	Descriptive study	Endoscopy and biopsy	13	General population	6, medium
Aumpan, 2020 [30]	Thailand (Asia)	1370	617	753	60.7	Retrospective Cohort study	Upper gastrointestinal endoscopy	16.3	General population	4, medium
Recavarren-Arce, 1992 [31]	Peru (America)	204	85	119	36.5	Descriptive study	Endoscopy and biopsy	7.4	General population	7, high
Fitzgibbons, 1988 [32]	USA (America)	116	-	-	46	Prospective study	Upper gastrointestinal endoscopy	22	General population	4, medium
Craanen, 1991 [33]	Netherlands (Europe)	553	-	-	57.8 ± 16.8	Prospective study	Gastroscopy and endoscopy	25.3	General population	7, high
Eluri, 2021 [34]	USA (America)	116	-	-	67	Prospective study	Endoscopy and biopsy	15	Patients with Barrett's esophagus	8, high

different databases were removed; as a result, 3590 studies remained. After checking the titles and abstracts, 3535 studies were excluded due to lack of relevance to the topic of the study. Then, the full text of the remaining 55 studies were carefully examined, of which 35 studies were excluded due to not meeting all the inclusion criteria (No primary outcome = 5, Irrelevant studies = 8, Study design = 6, Overlapping data = 10, and Language = 6). Finally, 20 articles were included in the meta-analysis after qualitative evaluation. The steps of the PRISMA 2020 flow diagram are depicted in Fig. 1.

General characteristics of the studies included in the meta-analysis

The oldest study was for 1988 and the latest study was for 2022. The USA had the highest number of studies with 8 articles. The total sample size of the 20 articles included in the meta-analysis was 57,263 people. The largest sample size belonged to the study by Huang et al., with 36,799 people [21]. All the articles included in the study had medium or high quality based on the JBI checklist. The characteristics and data of the articles included in the systematic review and meta-analysis are presented in Table 1.

Meta-analysis of global prevalence of gastric intestinal metaplasia

The I^2 index for the global prevalence of GIM showed great heterogeneity between studies ($I^2 = 97.98\%$), so the data were analyzed using a random effects model (Table 2). According to the results of Egger's regression intercept, there was no publication bias in the studies at the 0.01 level ($P = 0.013$) (Fig. 2). After combining the results of the preliminary studies included in the meta-analysis, the estimated global prevalence of GIM was 17.5% (95% confidence interval: 14.6–20.8%) based on the random effects model. In Fig. 3, the black square shows the prevalence rate and the length of the line segment on which shows the 95% confidence interval in each study, and the rhombus symbol shows the global prevalence of GIM. The results of the sensitivity analysis showed that the final result did not change significantly by removing any of the studies (Fig. 4).

Meta-regression

Meta-regression was used to investigate the association between sample size (Fig. 5), publication year (Fig. 6), and average age (Fig. 7) with the global prevalence of gastric intestinal metaplasia. Based on the results, the associations between the publication year and the sample size with the prevalence of gastric intestinal metaplasia were not significant ($P > 0.01$; Figs. 5 and 6). In contrast, increasing the average age resulted in the upward trend in the prevalence of gastric intestinal metaplasia ($P < 0.001$; Fig. 7).

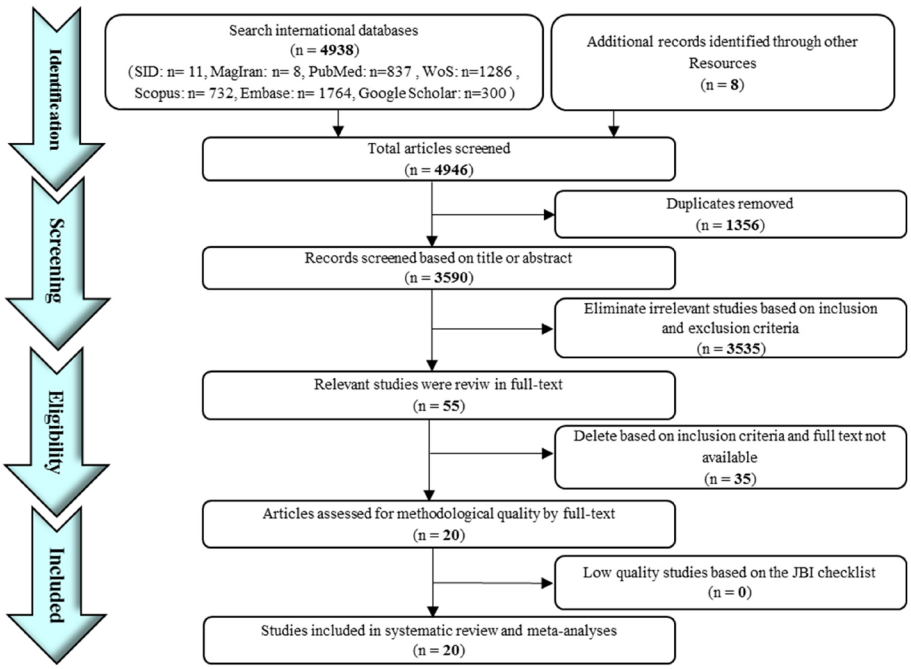


Fig. 1 PRISMA 2020 search flow diagram

Table 2 Report the results of the fixed and random effects model on meta-analysis

Tau	Variance	Standard error	Tau squared	I^2 (%)	*P*-value between	*P*-value	Upper limit	Lower limit	Point estimate	Number of studies	Model
0.468	0.021	0.144	0.219	97.98	0.000	0.000	0.141	0.135	0.138	20	Fixed
						0.000	0.208	0.146	0.175	20	Random

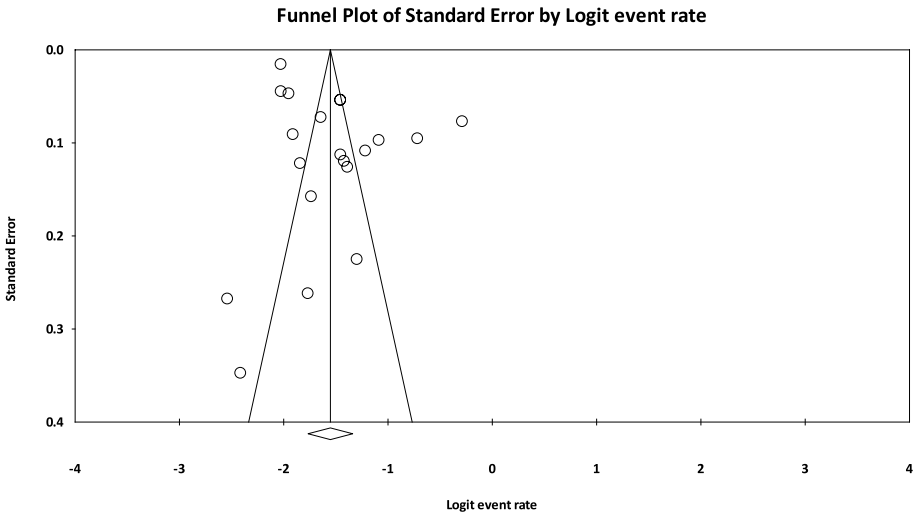
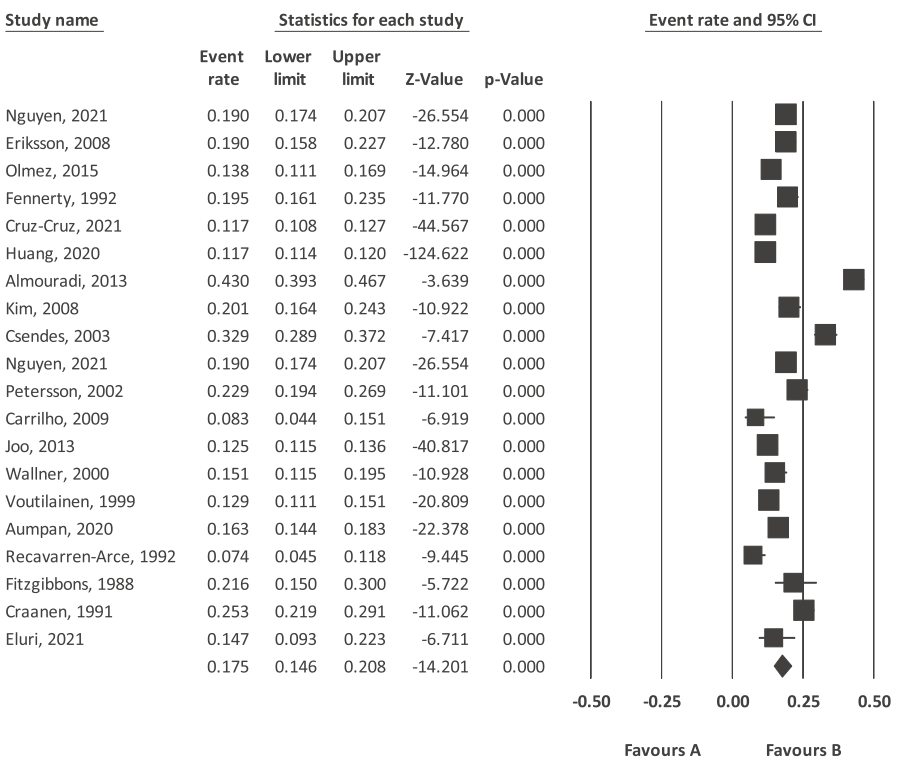


Fig. 2 Funnel plot for estimating the global prevalence of gastric intestinal metaplasia based on a random effects model



Meta Analysis

Fig. 3 Forest plot for estimating the global prevalence of gastric intestinal metaplasia based on a random effects model

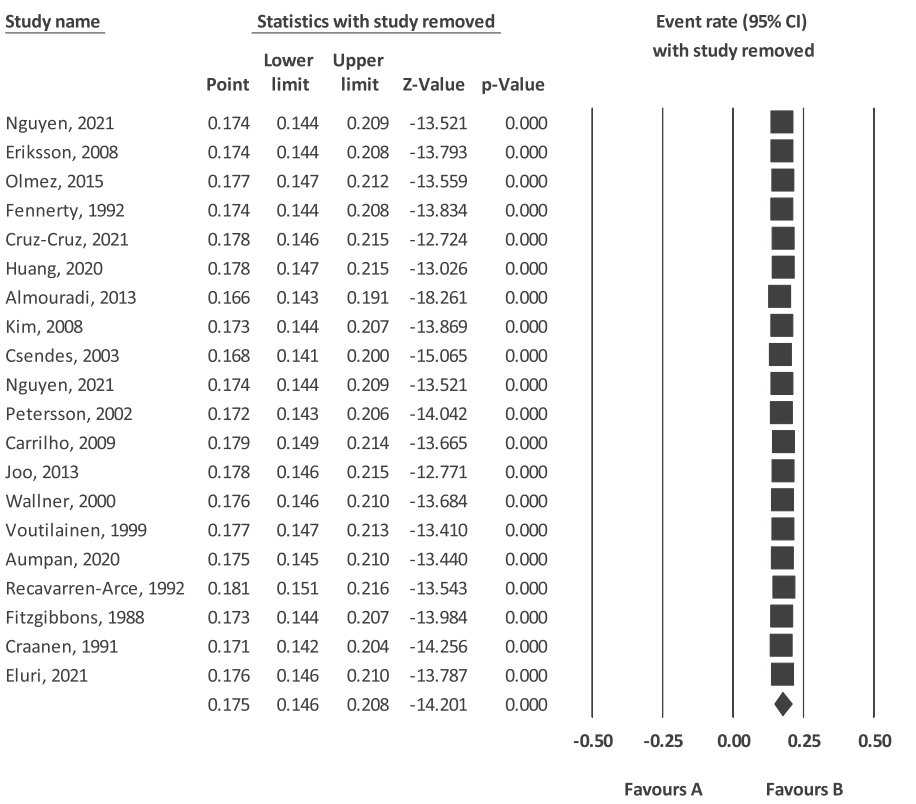


Fig. 4 Sensitivity analysis chart for estimating the global prevalence gastric intestinal metaplasia

Subgroup analysis

Due to the high heterogeneity among studies, subgroup analysis was done according to different continents, study population, JBI scores, and type of study. The highest percentage of prevalence of GIM belonged to American continent with 18.6% (95% confidence interval: 13.8–24.6%), patients with gastro-esophageal reflux with 22.9% (95% confidence interval: 9.9–44.6%), medium quality studies with 19.1% (95% confidence interval: 15.1–23.9%), and retrospective study with 20.1% (95% confidence interval: 7.2–45.0%). Although subgroup analysis was not significant in any of the subgroups, it reduced the degree of heterogeneity (Table 3).

Discussion

The current systematic review and meta-analysis study sought to estimate the global prevalence of gastric intestinal metaplasia in various populations. The global prevalence of GIM was estimated to be 17.5% after combining data from 20 articles. The study by Csendes et al. [24] found the greatest prevalence rate of GIM (33%), while the study by Recavarren-Arce et al. [31] reported the lowest percentage (7.4%). The study by Nguyen et al. [17] received the highest quality assessment score according to JBI checklist standards and reported the prevalence rate of GIM to be 19%.

The subgroup analysis of the present review revealed that the prevalence of GIM on different continents was significantly different, which shows that GIM prevalence is related to geographic variability. These findings are consistent with the study by Choi and Sonnenberg that reported GIM prevalence from 7.6 to 39.9 in the different ethnic groups of the USA [13].

In the review study of Altayar et al., GIM pooled prevalence among patients who had biopsies, based on 9 studies ($n=3558$) was 30.3% (95% CI: 28.8 to 31.8%) [2], which is inconsistent with the findings of the present review and can be explained by the large number of articles included in the present study (20 articles versus 9 articles in the study of Altayar et al.).

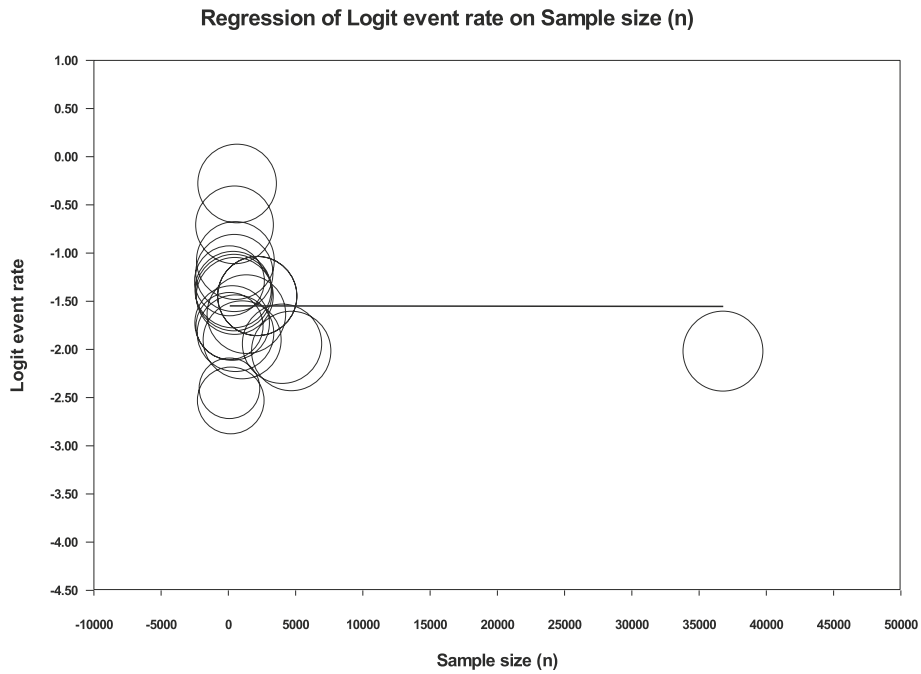


Fig. 5 Meta-regression of the relationship between sample size and global prevalence of gastric intestinal metaplasia

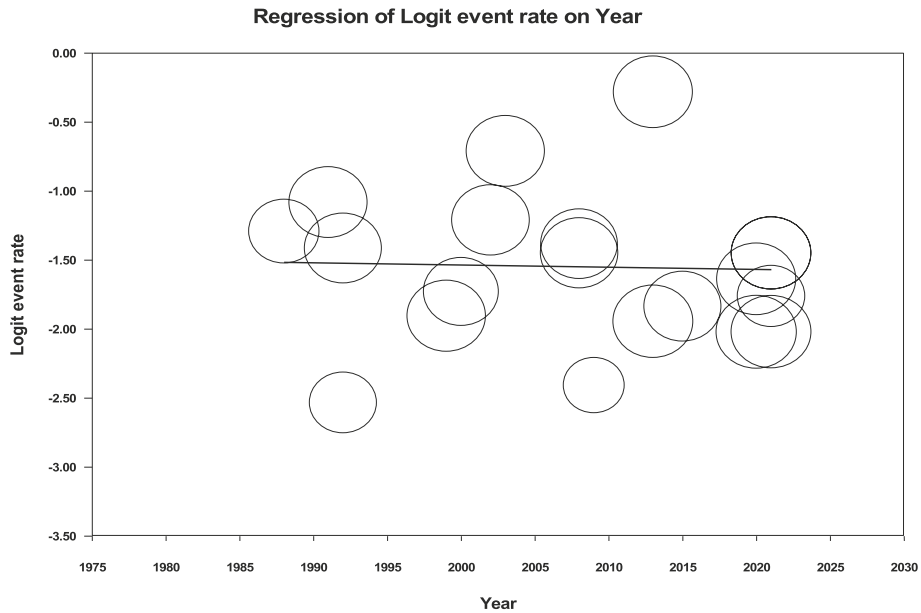


Fig. 6 Meta-regression of the relationship between the year of the study and the global prevalence of gastric intestinal metaplasia

The present study was carried out as a systematic review and meta-analysis, whereas the study of Altayar et al. was only conducted as a systematic review with no statistical analysis. In the present study, 56,343 out of 57,263 people included in the meta-analysis were from the general population. The remaining 920 were mostly patients with gastroesophageal reflux (2 articles, $n=804$) and Barrett's esophagus (1 article, $n=116$), and in the subgroup analysis, they had higher prevalence of GIM (22.6%), compared with the general population (17.1%). This suggests that GIM is more common in GI patients than in the general population. Studies that reported a higher prevalence of GIM may have focused on elderly or GI patients, or they may have been conducted in various

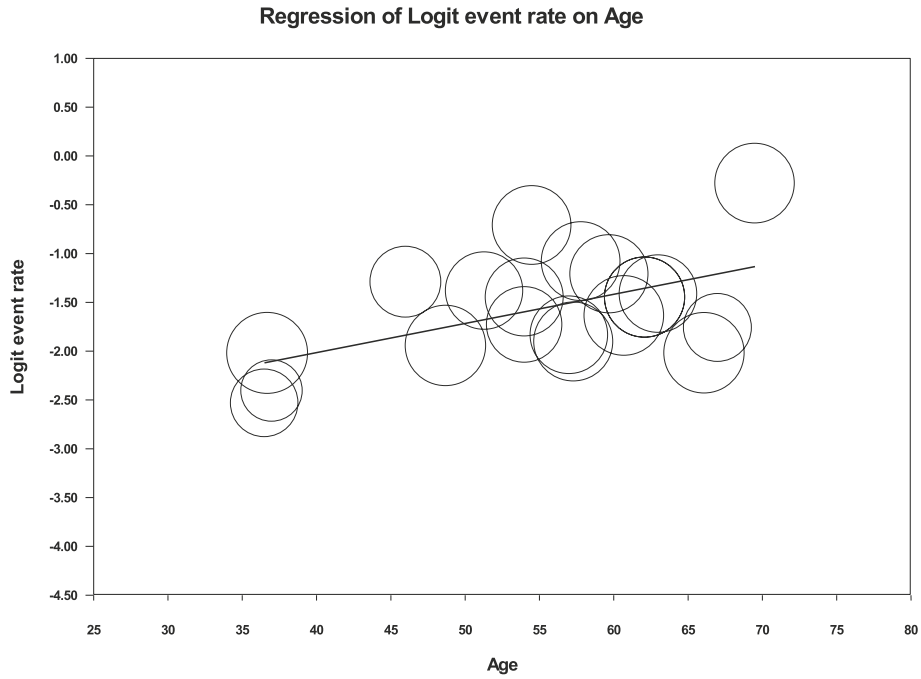


Fig. 7 Meta-regression of the relationship between the average age and the global prevalence of gastric intestinal metaplasia

Table 3 Subgroup analysis of gastric intestinal metaplasia prevalence estimate

Subgroups		Number of studies	Point estimate	Lower limit	Upper limit	*P*-value	*P*-value between	I^2 (%)	Tau
Continents	Africa	1	0.083	0.044	0.151	0.000	0.102	0.000	0.000
	Europe	6	0.178	0.138	0.225	0.000		90.84	0.351
	America	10	0.186	0.138	0.246	0.000		98.88	0.559
	Asia	3	0.158	0.122	0.203	0.000		92.00	0.256
Population	General population	17	0.171	0.142	0.204	0.000	0.612	98.00	0.444
	Patients with gastroesophageal reflux	2	0.229	0.099	0.446	0.000		96.69	0.708
JBI score	High	12	0.164	0.129	0.206	0.000	0.363	98.53	0.475
	Medium	8	0.191	0.151	0.239	0.000		92.58	0.392
Type of study	Cross-sectional study	6	0.182	0.145	0.225	0.000	0.825	95.70	0.327
	Descriptive study	5	0.139	0.076	0.241	0.000		96.39	0.742
	Prospective study	5	0.184	0.126	0.259	0.000		96.71	0.477
	Retrospective cohort study	1	0.163	0.144	0.183	0.000		0.00	0.000
	Retrospective study	3	0.201	0.072	0.450	0.022		99.58	1.040

geographic regions. In the present study, according to subgroup analyses of GIM prevalence in different continents, America had the highest prevalence of gastric intestinal metaplasia (18.6%). Despite the high prevalence of GIM (30.3%) found in Altayar's review, none of the studies included in this review were conducted in the United States [2]. In Altayar's review, six out of nine studies were from years before 2006. In the current review, six studies were from years earlier than 2006 as well, but with the increase in the number of recent studies in our review, the GIM prevalence has decreased. However, meta-regression did not find a significant correlation between the publication year and the prevalence of GIM.

It was required to carefully study the prevalence of GIM across continents in order for health policymakers to pay more attention to its consequences, due to

the variation in population structures across different nations of the world. According to the subgroup analyses based on GIM on the different continents, America had the highest prevalence of GIM (18.6%), and Africa had the lowest (8.3%).

Taking these conditions and complications into account can help with GIM follow-up and enhance the quality of life for GIM patients. According to Fig. 7, the prevalence of gastric intestinal metaplasia is significantly related to mean age, as the elderly population has a higher prevalence of GIM. The current systematic review and meta-analysis study revealed that elderly people and patients with gastroesophageal reflux and Barrett's esophagus are more vulnerable to GIM, and they need precious follow-up and investigation. As a result of GIM complications and a significant relationship with of gastric cancers, we should be aware of its prevalence. Because GIM affects so many aspects of life, health care providers and planners should pay close attention to its prevalence.

One of the study's strengths was estimating the global prevalence of GIM in different populations for the first time with a sample size greater than 57,000 people and estimating the prevalence of GIM in continents using different diagnostic tools (endoscopy and biopsy). Furthermore, because of the high heterogeneity among studies (more than 95%), we performed a subgroup analysis, which reduced a small amount of heterogeneity. However, there is still significant heterogeneity across all subgroups, which could be attributed to sample size, demographic characteristics, and method.

Although the present results of the publication bias for Egger were not significant at the 0.01 level, they are significant at the 0.05 level. Therefore, it is necessary to be more cautious in interpreting the results. Of course, among the reasons may be the lack of access to gray sources, unpublished studies, search limitations in databases, etc.

The current study has some limitations, including a lack of uniform article reporting, nonrandom sample selection, a non-uniform study design, lack of publicly available protocol for this review, and a lack of access to the full text of conference papers. Additionally, there were not many studies done on the specific populations. As a result, additional research on some patients, such as those with gastroesophageal reflux disease and Barrett's esophagus, is suggested.

Conclusions

According to the findings of this study, the prevalence of gastric intestinal metaplasia is high in various populations and has been increasing in recent years. As a result, appropriate strategies for GIM follow-up should be used.

Abbreviations

GP Global prevalence
GIM Gastric intestinal metaplasia
SRMA Systematic review and meta-analysis

Acknowledgements

This study is the result of research project No. 50002301 approved by the Student Research Committee of Kermanshah University of Medical Sciences. We would like to thank the esteemed officials of that center for accepting the financial expenses of this study.

Authors' contributions

M.K., T.H., and S.S. contributed to the design; M.K., A.Z., S.S., and Z.J. participated in most of the study steps. M.K., S.S., K.Q., and Z.J prepared the manuscript. S.S., Z.J., and A.Z. assisted in designing the study and helped in the interpretation of the study. All authors have read and approved the content of the manuscript.

Funding

This study did not receive any funding from funding agencies.

Availability of data and materials

The datasets used in the study are available from the corresponding author on 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.1401.518).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 16 August 2023 Accepted: 5 August 2024
Published online: 28 September 2024

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