

Assessment of Risk Factors and Prevalence Patterns of Gastric Metaplasia in Asian Populations: A Systematic Literature Review

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1. Abstract

1.1. Objective: This systematic literature review aims to comprehensively examine the specific risk factors contributing to the development of gastric metaplasia in Asian populations. Additionally, the review seeks to determine the prevalence of different types of gastric metaplasia among Asians while exploring variations across different Asian countries and ethnicities.

1.2. Background: Gastric metaplasia is a significant concern in Asian populations due to its potential progression to more serious conditions. Understanding the specific risk factors associated with its development, such as dietary patterns, smoking habits, and *Helicobacter pylori* infection, can provide insights into preventive strategies and tailored interventions.

1.3. Methods: A comprehensive search was performed in PubMed, Scopus, and Google Scholar, encompassing articles published from inception until August 2023. Furthermore, the reference lists of the selected studies were scrutinized to identify potential supplementary research. Data extraction and synthesis were performed to provide a comprehensive overview of the current knowledge landscape.

1.4. Results: The database search yielded 1552 articles but only 23 were included in this systematic review. The review reveals a consistent association between certain dietary habits, smoking, and *Helicobacter pylori* infection, and an increased risk of gastric metaplasia. The prevalence of different types of metaplasia exhibited intriguing variations across Asian countries and ethnicities, suggesting regional and ethnic influences.

1.5. Conclusion: The findings from this systematic review corroborate the significant roles of dietary habits, smoking, and *Helicobacter pylori* infection as risk factors for gastric metaplasia in Asian populations.

2. Background

Gastric-related conditions have garnered increasing attention due to their rising prevalence and significant impact on public health [1, 2]. Among these conditions, intestinal metaplasia, a precancerous lesion of the stomach, has emerged as a critical concern, particularly within Asian populations. Intestinal metaplasia is characterized by the transformation of the normal gastric epithelium into an intestinal-like epithelium and is considered a precursor to gastric cancer [3, 4, 5, 6]. Understanding the specific risk factors associated with the development of intestinal metaplasia in Asians is of paramount importance for devising effective preventive strategies and improving patient outcomes and enhancing preventive strategies and healthcare interventions. While gastric cancer's prominence is well-known, the pivotal role of intestinal metaplasia as a precursor has garnered recognition as a potential avenue for early intervention [7, 8]. This transformation marks a critical point in the progression toward malignancy, thereby necessitating a detailed exploration of the factors shaping its development. This is particularly pertinent within Asian populations, where variations in disease incidence and risk factors often deviate from global trends. The disproportionate prevalence of gastric-related conditions within Asian countries underscores the pressing need to comprehend the nuances of these diseases within

these populations [9, 10, 11]. Intestinal metaplasia, in particular, has shown remarkable variation in its occurrence across diverse Asian regions and ethnic groups.

Gastric adenocarcinoma is divided into two subtypes: intestinal and diffuse. The intestinal subtype is strongly linked with intestinal metaplasia, whereas the diffuse subtype is predominantly genetically determined and has a weaker connection to environmental factors and the inflammatory process [12]. The majority of gastric cancer cases are attributed to intestinal-type adenocarcinoma [13]. Intestinal metaplasia, referred to as GIM, is a precancerous lesion characterized by the replacement of surface, foveolar, and/or glandular epithelium in either the oxyntic or antral mucosa with intestinal epithelium [14]. Anatomically, GIM is categorized as limited when confined to a single stomach region or extensive if it involves two regions. Histologically, GIM comes in two forms: complete and incomplete [14]. Complete [type I] intestinal metaplasia displays small intestinal-like mucosa containing mature absorptive cells, goblet cells, and a brush border. Incomplete [type II] intestinal metaplasia secretes sialomucins and resembles colonic epithelium with columnar “intermediate” cells at varying differentiation stages, irregular mucin droplets, and the absence of a brush border [15,16]. The most elevated risk of gastric cancer is associated with incomplete and/or extensive GIM [17]. The development process from precancerous lesions to intestinal-type gastric adenocarcinoma has been suggested to involve a sequence starting from the normal gastric epithelium, moving through stages of inflammation, atrophy, intramucosal carcinoma, and ultimately invasive carcinoma [18]. The progression is influenced by a complex interplay of various factors, including *Helicobacter pylori* genomics, host genetic elements, the surrounding environment, dietary patterns, and the composition of the intestinal microbiota. This interplay makes the gastric mucosa prone to an inflammatory sequence that carries the potential for cancerous transformation [19]. Identifying the specific risk factors associated with the development of intestinal metaplasia forms the cornerstone of unraveling its etiology. These factors encompass a range of influences, including dietary habits, smoking behaviors, and *Helicobacter pylori* infection. Moreover, the genetic predisposition to intestinal metaplasia is a growing area of interest, particularly within the context of Asian populations. *Helicobacter pylori* stand out as the primary influential factor [20] for gastric cancer [21,22] and its preceding stages [23,24]. Other environmental factors, such as limited fruit and vegetable intake [25] and smoking [26,27], have established connections with gastric cancer. Several research efforts have delved into the correlation between distinct lifestyles and the emergence of precancerous gastric conditions, particularly intestinal metaplasia [IM]. Among these lifestyle factors, smoking has been the most extensively examined and notably elevates the risk of both IM and its progression [28-31]. In terms of the genetic makeup of individuals, variations in genes encoding pro-inflammatory cytokines, notably interleukin-1B and its receptor antagonist, contribute to heightened susceptibility to the development

of cancerous [32,33] and precancerous gastric conditions [34,35]. However, despite the continued decline in gastric cancer mortality on a global scale, it's important to note that this trend is not solely attributed to the aforementioned factors. While an increase in the consumption of fruits and vegetables, along with a reduction in exposure to salty foods [36] due to enhanced food refrigeration, has played a pivotal role, other elements also contribute. For instance, the second Expert Report issued collaboratively by the World Cancer Research Fund and the American Institute for Cancer Research [37] has categorized salt, salted foods, and sodium-rich items as potential risk factors for gastric cancer. This classification is grounded in robust mechanistic evidence and findings from diverse studies, encompassing ecological, case-control, and cohort investigations, despite the inherent heterogeneity present in the results of studies that utilize individuals as the observation unit. Although the prevalence of intestinal metaplasia is acknowledged, significant gaps persist in our understanding of the factors governing its development, particularly within Asian populations. These gaps extend to variations in risk factor profiles across diverse Asian countries and ethnicities, warranting a comprehensive review of existing literature. This systematic literature review addresses two core research questions. Firstly, it seeks to identify the specific risk factors—such as dietary patterns, smoking behaviors, and *Helicobacter pylori* infection—associated with the development of intestinal metaplasia in Asian populations. Secondly, the review delves into the prevalence of different types of intestinal metaplasia among Asians, analyzing variations across different Asian countries and ethnic groups.

2.1. Research Objectives

This study aims to comprehensively explore the risks associated with the development of intestinal metaplasia in Asian populations through a systematic literature review. The research objectives are twofold: firstly, to identify and thoroughly analyze the specific risk factors that contribute to the development of gastric metaplasia in Asians, with a particular focus on dietary habits, smoking behaviors, and *Helicobacter pylori* infection. Secondly, investigate and synthesize the prevalence of different types of gastric metaplasia, including complete vs. incomplete, fundic, and antral metaplasia, among Asians. Furthermore, the study will explore potential variations in the prevalence of these metaplasia types across different Asian countries and ethnicities.

2.2. Research Questions

This review addresses two pivotal research questions:

1. What are the specific risk factors, such as dietary habits, smoking, and *Helicobacter pylori* infection, associated with the development of gastric metaplasia in Asian populations?
3. What is the prevalence of different types of gastric metaplasia [complete vs. incomplete, fundic, antral] among Asians, and how does it vary across different Asian countries or ethnicities?

3. Methods

This review was carried out by the 2020 guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis [PRISMA] [38]. The search encompassed two databases, PubMed and Scopus, targeting articles published in English. The inclusivity spanned articles released from inception through August 2023. The focal point was to extract information about risk factors contributing to the emergence of intestinal metaplasia and the diverse classifications of gastric metaplasia [namely complete, incomplete, fundic, and antral] within Asian populations. It's noteworthy that PubMed took

Table 1: Search strings

Database	Search field	Search String
PubMed	Title, Abstract	("intestinal metaplasia" OR "gastric metaplasia") AND (risk factors OR "specific risk factors" OR dietary habits OR smoking OR "Helicobacter pylori infection") AND (prevalence OR incidence OR frequency) AND ("complete metaplasia" OR "incomplete metaplasia" OR fundic OR antral)
Scopus	All fields	("intestinal metaplasia" OR "gastric metaplasia") AND (risk factors OR "specific risk factors" OR dietary habits OR smoking OR "Helicobacter pylori infection") AND (prevalence OR incidence OR frequency) AND ("complete metaplasia" OR "incomplete metaplasia" OR fundic OR antral)

No data range was used in any of the index databases.

3.2. Secondary Search

Apart from the exploration carried out on the two databases, an immediate inquiry was performed using the Google Scholar database. To ensure that the initial pages displayed the most pertinent results, the search incorporated keywords on prevalence, incidence, and risk factors. Furthermore, the reference lists of the studies that were incorporated were combed through to identify any supplementary relevant articles.

3.3. Eligibility Criteria

This systematic literature review encompasses research investigating the prevalence and factors influencing intestinal metaplasia within the Asian region. The selection process adheres to the modified PICOS criteria as outlined by Methley et al. [39].

The following were the adapted PICOS criteria for the inclusion of studies:

Population [P]: Asian populations afflicted with intestinal metaplasia.

Intervention [I]: The study focuses on assessing the prevalence of different types of gastric metaplasia and the contributing factors, rather than involving an intervention.

Comparison [C]: The study focuses on the prevalence of gastric metaplasia within the Asian region.

Outcomes [O]: The primary outcomes of interest involve the prevalence of Intestinal metaplasia and the identification of associated risk factors.

Study Design [S]: Randomized controlled trials, observational studies, and clinical studies are deemed crucial sources of evidence.

All studies had to meet the following pre-defined inclusion criteria:

precedence as the primary database, serving as a representation of internationally recognized articles hailing from that region.

3.1. Primary Search

The approach employed for searching PubMed involved a blend of unconstrained keyword queries and regulated MeSH terms. The keywords employed were subject to a comprehensive textual analysis, aimed at enhancing the search strategy's inclusivity. The methodology used for Scopus closely resembled PubMed's search strategy, albeit with minor adjustments. Refer to [Table 1] for a compilation of the core keywords utilized in the database searches.

- Peer-reviewed journal articles.
- Studies conducted on Asian populations.
- Studies investigating the association between risk factors [dietary habits, smoking, Helicobacter pylori infection] and the development of gastric metaplasia in Asians.
- Studies reporting the prevalence of different types of gastric metaplasia [complete vs incomplete, fundic, antral] among Asians.
- Studies conducted in various Asian countries or specific Asian ethnicities.
- Studies published in English.

Studies that satisfied the following criteria were excluded:

- Conference abstracts, letters, editorials, and reviews.
- Studies conducted outside Asian populations.
- Studies not examining the risk factors or prevalence of gastric metaplasia.
- Studies conducted outside of Asia.

3.4. Study Selection Process

The articles identified through the study's search underwent a selection procedure guided by the PRISMA guidelines. This procedure was executed utilizing the functionalities provided by the Zotero software application.

3.5. Study Quality Assessment

The Newcastle-Ottawa scale for cohort studies was employed to evaluate the methodological rigor of the studies that were incorporated. The scale's highest attainable score was 8.

3.6. Data Extraction

After the selection of articles for inclusion, data was extracted into

a predefined data descriptor table with the following fields: author, year of publication, study design, geographical location, sample size, gender, age [average], outcome measure, risk factors, and exposures and results.

4. Results

The initial literature search generated a total of 1552 articles. During the screening phase, reviews, meta-analyses, studies involving non-human subjects, and articles in languages other than English were excluded, leaving 39 duplicates to be removed. Subsequently, after title and abstract screening, 1436 articles were further excluded. The remaining 63 articles underwent a retrieval process, resulting in the inclusion of 23 studies that aligned with the eligibility criteria.

The outcomes are visually depicted in [Figure 1].

4.1. Quality Appraisal

Among the entire pool of articles evaluated using the Newcastle-Ottawa scale, 21 studies exhibited elevated quality levels, achieving scores spanning from 6 to 8. These articles fulfilled the stipulated criteria and furnished strong substantiation for the review. On the other hand, a pair of articles were deemed to possess lower quality, receiving a score of 5. The findings of the quality evaluation are depicted in the table provided below [Table 2].

4.2. Data Extraction Results

[Table 3]: study Descriptor Table

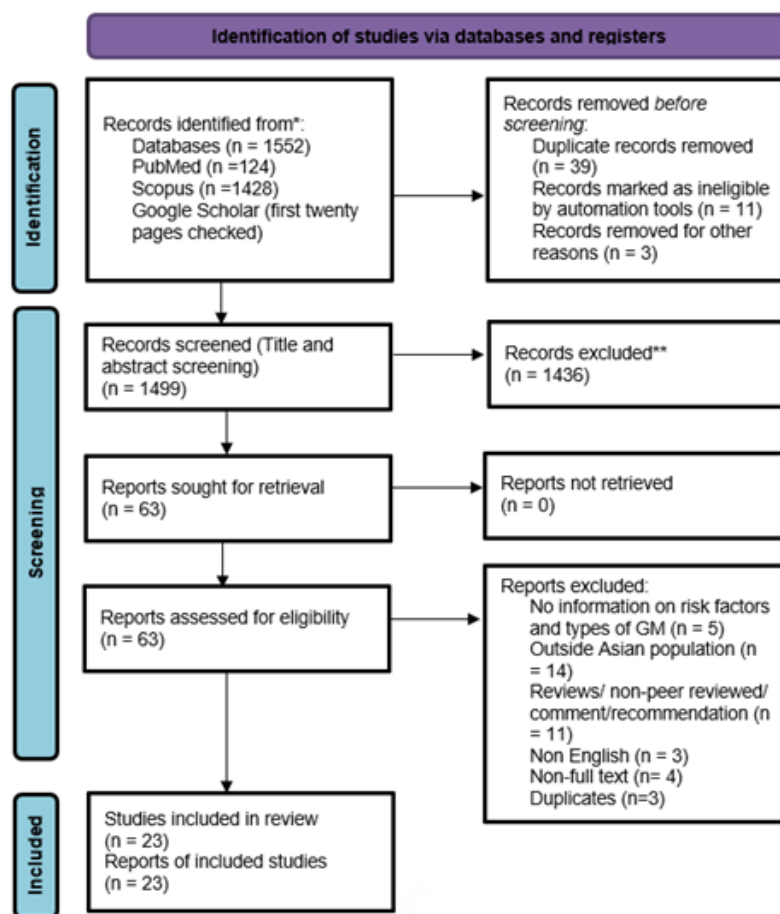


Figure 1: PRISMA chart

Table 2: Quality Appraisal

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Total
Alhomsy and Adeyemi, 40	1	1	1	1	0	1	1	0	6
Al-Knawy et al., 41	1	1	1	1	1	1	1	1	8
Chalise et al., 42	1	1	0	1	1	1	0	1	6
Choi et al., 43	1	1	1	0	0	1	1	1	6
Evrensel et al., 44	1	1	1	0	0	1	1	0	5
Joo et al., 45	1	1	1	1	1	1	1	1	8
Kang et al., 46	1	1	1	1	1	1	1	1	8

Jiang et al., 47	1	1	1	1	1	1	1	1	8
Ke et al., 48	1	1	1	1	1	1	1	1	8
Kneller et al., 49	1	1	1	1	0	1	0	1	6
Liu et al., 50	1	1	1	0	0	1	1	1	6
Malekzadeh et al., 51	1	1	1	0	0	1	1	1	6
Mansour-Ghanaei et al., 52	1	1	1	0	1	1	0	1	6
Aumpan et al., 53	1	1	1	1	1	1	1	1	8
Nomura et al., 54	1	1	1	1	0	1	1	0	6
Ozdil et al., 55	1	1	1	1	1	1	1	1	8
Pei et al., 56	1	1	1	1	1	0	1	1	7
Olmez et al., 57	1	1	1	1	1	1	1	1	8
Chen et al., 58	1	1	1	1	0	1	0	1	6
Stemmermann et al., 59	1	1	1	1	0	1	1	1	7
You et al., 60	1	1	1	0	0	1	1	1	6
Yang et al., 61	1	1	1	0	0	1	0	1	5
Leung et al., 62	1	1	1	0	1	1	1	1	7

Note: Item 1 = Representativeness of the Exposed Cohort, Item 2 = Selection of the Non-Exposed Cohort, Item 3= Ascertainment of Exposure, Item 4= Demonstration that Outcome of Interest Was Not Present at Start of Study, Item 5=Comparability of cohorts on the basis of the design or analysis, Item 6=Assessment of outcome, Item 7=Was follow-up long enough for outcomes to occur? Item 8=Adequacy of follow-up of cohorts

Table 3: study Descriptor Table

Author	Year of publication	Study design	Geographical location	Sample size	Gender	Age (average)	Outcome measure	Risk factors and exposures	Results
Alhoms and Adeyemi	1996	Comparative cohort study	United Arab Emirates	602	458 M, 144 F	5 to 70 yr (33 yr)	Prevalence of Hp gastritis and their utilization in the evaluation of treatment efficacy.	Helicobacter pylori infection	Intestinal metaplasia was found in 28.9% of the 602 patients and was seen more often in Hp-positive than Hp-negative patients (34.5 vs 14%, $P < 0.005$, for d.f. = 1; $\chi^2 = 10.35$).
Al-Knawy et al.	1999	Cohort study	Saudi Arabia	778	415 M, 363 F	10–100 yr (43 ± 17.6 yr)	Prevalence of intestinal metaplasia (IM) and Helicobacter pylori	Helicobacter pylori infection	The overall rate of infection with H. pylori was 75.4%. There was no difference in the frequency of IM in patients with or without H. pylori (15.5% versus 14.1%; $P = 0.65$). Of the 118 patients with IM, the 91 patients (77.1%) who also had H. pylori were older (55 ± 23 years) than those without H. pylori (47 ± 17 years, $P = 0.05$).
Chalise et al.	2020	Cross-sectional study	Nepal	57	N/A	26–72 yr (46.6 yr)	prevalence of intestinal metaplasia	Helicobacter pylori infection	The prevalence of intestinal metaplasia was found in 57 (12.2%) biopsies. Helicobacter pylori was positive in 28(49.1%) and it was negative in 29(50.9%) biopsies. No statistically significant correlation was seen in the subtypes of intestinal metaplasia with Helicobacter pylori status ($p > 0.05$).

Choi et al.	2006	Retrospective cohort study	Korea	15923	7787 M, 8136 F	47.83 yr	Risk factors for the development of metaplastic gastritis	Age, gender, Helicobacter pylori (H pylori) seropositivity, body mass index (BMI), family history of cancer, smoking, alcohol consumption, total daily calories, folate and salt intake, and dietary habit.	The prevalence of group II was 11% (13 578/113 449) increasing its prevalence with age (P = 0.000). But, there was no significant association between the 2 groups in BMI, family history of cancer, alcohol consumption, total daily calories, folate, and salt intake, and dietary habit (out-eating, overeating, irregular eating). Old age (P = 0.000), male gender (P = 0.000), H pylori seropositivity (P = 0.010), and current smoker (P = 0.000) were significantly more common in group II at the multiple logistic regression model.
Evrensel et al.	1996	Cohort study	Turkey	210	N/A	N/A	Relationship between HP and IM in endoscopic gastric biopsy specimens	Helicobacter pylori infection	HP was positive in 156 of the 210 patients examined (74.3%). The distribution of HP seropositivity did not differ between age groups (p > 0.05). IM was present in 101 patients in the entire study group (48%). Among the 156 HP-positive patients, the rate of IM was 44.8% (n = 70). The rate of IM among the 54 HP-negative patients was 57.4% (n = 31), which was not statistically significant (p > 0.05).
Joo et al.	2013	Prospective cohort study	Korea	4023	2358 M, 1665 F	15- 98 yr (48.7 ± 11.3 yrs)	Prevalence of endoscopic IM and risk factors	Age, male sex, positive H. pylori serology, IM, and education below the college level.	The prevalence of endoscopic IM was 12.5%. The risk factors for IM were age groups of 40 to 59 years and >60 years, male sex, positive H. pylori serology, AG, having relatives with gastric cancer, education below the college level, and consumption of dairy products (OR, 3.16, 3.25, 1.88, 2.17, 3.68, 1.48, 1.47, and 1.40, respectively).

Kang et al.	2009	Cohort study	Korea	861	506 M, 355 F	57.7 yrs	Relationship of intestinal metaplasia (IM) and Helicobacter pylori	Helicobacter pylori infection	In cases that were H. pylori-positive, the prevalence of IM subtype II in cancer and dysplasia groups was higher than in the control group in the body of the stomach ($P < 0.05$). The proportion of IM subtype III in the antrum increased in proportion with age ($P = 0.036$).
Jiang et al.	2016	Retrospective cohort study	China	28745	14625 M, 14120 F	40- 70 yrs (50.98 ± 13.33 yrs)	Gastric metaplasia was defined based on histological analysis of biopsy samples obtained during endoscopy.	Age, male gender, gastric ulcer, bile reflux, H. pylori infection, severe degree of chronic and acute inflammation	The incidence of intestinal metaplasia differed significantly in 17 municipal areas ranging from 16.79 to 38.56% and was positively correlated with the age range of 40-70 years, male gender, gastric ulcer, bile reflux, Helicobacter pylori infection, atrophic gastritis, dysplasia, gastric cancer, degree of chronic and acute inflammation, and gross domestic product per capita ($P < 0.01$).
Ke et al.	2016	Retrospective case-control	China	2157	1037 M, 1120 F	49.2 ± 11.7 yrs	Diagnosis of IM	Patients with age ≥ 60 yr, H. pylori infection, smoking, family history of gastric cancer, high salt diet, and spicy food.	The multivariate analysis showed that the risk factors of IM were age ≥ 60yr (OR, 2.27; 95% CI, 1.70 to 3.03; $P < 0.001$), H. pylori infection (OR, 2.67; 95% CI, 2.22 to 3.21; $P < 0.001$), smoking (OR, 2.20; 95% CI, 1.54 to 3.15; $P < 0.001$), family history of gastric cancer (OR, 2.22; 95% CI, 1.48 to 3.33; $P < 0.001$), high salt diet (OR, 1.58; 95% CI, 1.18 to 2.13; $P = 0.002$) and spicy food (OR, 1.46; 95% CI, 1.08 to 1.96; $P = 0.013$).
Kneller et al.	1992	Cross-sectional study	China	3104	1632 M, 1472 F	35-64 yrs	Risk factors for intestinal metaplasia	Tobacco and alcohol intake, diet, family medical history, and socioeconomic status	Cigarette smoking was found to nearly double the risk of transition to dysplasia and to be a mild risk factor for intestinal metaplasia. Smoking accounted almost entirely for the 55% higher prevalence of dysplasia among men than among women. The risk of transition to dysplasia had a weak association with several dietary factors and was increased among those participants with a family history of stomach cancer and with blood type A.

Liu et al.	2005	Cross-sectional study	Asian population*	1114	N/A	18- 75 yrs	Antral-Type: Intestinal epithelium resembling the antral region of the stomach. Anatomical localization of metaplastic changes was based on histological features and confirmed by immunohistochemical staining for specific markers.	Helicobacter pylori	The scores for intestinal metaplasia were low in general except for Xi-an, Japan, and Shanghai.
Malekzadeh et al.	2004	Cross-sectional study	Iran	1011	494 M, 517 F	53.32 yrs	Endoscopic screening and looking for associated Helicobacter pylori infection	Helicobacter pylori infection	Chronic gastritis with or without activity, reactive atypia of glandular epithelium, intestinal metaplasia, dysplasia, and cancer were found in 95.1%, 38.0%, 8.7%, 0.2%, and 0.3% of antral and 85.3%, 22.9%, 3.8%, 0.3%, and 0.1% of cardiac biopsies, respectively.
Mansour-Ghanaei et al.	2013	Case series study	Iran	71	40 M, 31 F	21-79 yrs (48.66 ±12 yrs)	Complete Metaplasia: Replacement of normal gastric epithelium by specialized intestinal epithelium.	Helicobacter pylori infection	Of the total of 71 patients with established IM who were enrolled, 50 had complete-type IM and 21 had incomplete-type IM. Secondary pathology findings of patients with IM were complete metaplasia (39.4%), incomplete metaplasia (32.4%), dysplasia (23.9%), and other precancerous lesions (4.2%).

Aumpan et al.	2021	Retrospective cohort study	Thailand	361	190 M, 171 F	65.4 ± 12.8 yrs	Risk factors associated with regression or progression of IM	Helicobacter pylori infection	<p>There were 1,551(76.6%) patients with chronic gastritis and 361(17.8%) with IM. Of 400 patients with chronic gastritis having follow-up endoscopy and repeated gastric biopsies, 104(26%) had persistent H. pylori infection and 27(26%) developed IM during a mean follow-up time of 24 months. Persistent H. pylori infection was significantly associated with the development of IM (OR 3.16, 95%CI 1.56–6.39, p = 0.001). Regression, persistence, and progression of IM were demonstrated in 57.3%, 39.2%, and 3.5% of patients, respectively. Age >65 years, persistent H. pylori infection, and diabetes mellitus were significantly associated with persistent IM or progression to dysplasia with OR 2.47(95%CI 1.33–4.61, p = 0.004), OR 2.64(95%CI 1.13–6.18, p = 0.025), and OR 2.54(95%CI 1.16–5.54, p = 0.019), respectively. Patients without H. pylori infection had more IM regression than patients with persistent infection (60.4% vs.39.4%, p = 0.035). Patients with persistent H. pylori infection significantly had higher IM progression to dysplasia (15.2%vs.2.1%; OR 11.15, 95%CI 1.18–105.24, p = 0.035) than non-infected.</p>
Nomura et al.	1982	Cross-sectional study	Japan	387	206 M, 181 F	22- 78 yrs	Risk factors for MI	Dietary	<p>More dried fish consumption and less vitamin A intake increased the extent of intestinal metaplasia in men. For women, there was a significant negative association of ume (pickled plum) intake with intestinal metaplasia.</p>

Ozdil et al.	2010	Cohort study	Turkey	3301	N/A	18- 60 yrs (45.97 yrs)	Prevalence of Helicobacter pylori (H. pylori) infection and intestinal metaplasia	Helicobacter pylori infection	H. pylori was established in 2353 patients (71.3%). Intestinal metaplasia was found in 586 patients (17.8%). Of these patients, 86% (n:504) had complete and 14% (n:82) had incomplete intestinal metaplasia. The frequency and severity of H. pylori infection decreased significantly in the older group ($p < 0.001$).
Pei et al.	2022	Retrospective cohort study	China	450	N/A	N/A	Diagnosis of IM	Helicobacter pylori infection	HP infection, pepsinogen I, gastrin-17, and the number of lesions are independent risk factors for intestinal metaplasia or dysplasia in patients with chronic atrophic gastritis (CAG).
Olmez et al.	2015	Retrospective cohort study	Turkey	560	227 M, 333 F	17- 98 yrs (57 ± 15 yrs)	Complete Metaplasia: Replacement of normal gastric epithelium by specialized intestinal epithelium. Incomplete Metaplasia: Presence of specialized intestinal epithelium alongside normal gastric epithelium. Prevalence of IM and its subtypes and the prevalence of H. pylori.	Helicobacter pylori infection	The prevalence of gastric IM was 13.8%. The prevalence of incomplete IM was statistically significantly higher than complete IM. Type III IM was the most frequent subtype.

Chen et al.	2004	Comparative cohort study	Taiwan	312	174 M, 138 F	16- 30 yrs	Development of Incomplete IM	Personal and familial history of stomach cancer, cigarette smoking, alcohol consumption, and intake frequency of various salted food items.	<p>A significant association between a history of stomach cancer among first-degree relatives and incomplete IM was found (odds ratio [OR] = 2.50; 95% confidence interval [CI] = 1.15-5.43).</p> <p>There was no association between H. pylori infection and incomplete IM. Alcohol drinkers for >20 years had an elevated risk compared to non-drinkers (OR = 3.34; 95% CI = 1.19-9.39). No associations between incomplete IM and plasma levels of selenium, retinol, alpha-tocopherol, alpha-carotene, and beta-carotene were found. Salted food including salted meat, dehydrated salted vegetables, and raw salted seafood consumed at ages of ≤ 15 and 16-30 years old was associated with an increased IM risk with OR ranging from 2-3. More striking associations between incomplete IM and salted food intake were observed among subjects with genotypes of GSTM1 null, GSTT1 non-null, and CYP2E1 c1/c1.</p>
Stemmermann et al.	1990	Cohort study	Hawaii Japanese men	350	350 M	N/A	Impact of diet and smoking on Risk of Developing Intestinal Metaplasia.	Dietary and smoking	<p>Nitrite-rich salty foods (e.g., cured meats) were directly related to metaplasia at both examinations. Vitamin C intake did not appear to have prevented the development of intestinal metaplasia. Smoking was directly related to the presence of metaplasia, but the association was weaker than was observed for cured meats.</p>

You et al.	1998	Cross-sectional study	China	214	107 M, 107 F	35-64 yrs	A dietary interview and measurement of serum Helicobacter pylori antibodies.	Dietary and Helicobacter pylori infection	OR of IM associated with H. pylori positivity was 31.5 (95% CI: 5.2-187). After adjusting for H. pylori infection, drinking alcohol was a risk factor for IM (OR = 7.8, 95% CI: 1.3-47.7). On the other hand, the consumption of garlic showed non-significant protective effects and an inverse association with H. pylori infection.
Yang et al.	1995	Retrospective cohort study	China	142	N/A	18-64 yrs	Risk factors for the development of metaplastic gastritis	Helicobacter pylori infection	Helicobacter pylori infection in the duodenal bulb was found more often in patients with moderate to severe gastric metaplasia (62.3%) than in patients with mild gastric metaplasia (20%).
Leung et al.	2005	Cohort study	China	270	127 M, 143 F	18-66 yrs	Risk factors associated with the presence of intestinal metaplasia	Age, male sex, H. pylori infection, birth order, alcohol use, siblings with stomach cancer, childhood living conditions, and water supply.	With multiple logistic regression, H. pylori infection [odds ratio (OR), 3.23], male gender (OR, 2.09), age (OR, 1.07), and a history of gastric cancer in siblings (OR, 1.91) were independent factors associated with the development of intestinal metaplasia in cancer relatives.

5. Results of Included Studies

5.1. Specific Risk Factors Associated with the Development of Gastric Metaplasia in Asian Populations

5.1.1. Dietary Habits and Gastric Metaplasia

The analysis of the included studies revealed a consistent association between certain dietary habits and the development of gastric metaplasia among Asian populations. Joo et al. [45] noted that certain factors were associated with an increased risk of IM. These factors included being in the age groups of 40 to 59 years and >60 years, being male, having a positive *H. pylori* serology, having AG [atrophic gastritis], having relatives with a history of gastric cancer, having education below the college level, and consuming dairy products. A cross-sectional study by Nomura et al. [54] indicated that in men, higher consumption of dried fish and a lower intake of vitamin A were linked to a greater prevalence of intestinal metaplasia. Conversely, among women, a noteworthy inverse connection was observed between the consumption of ume [pickled plum] and the occurrence of intestinal metaplasia. Chen et al. [58] discovered that the consumption of salted foods such as salted meat dehydrated salted vegetables, and raw salted seafood during early ages, specifically up to 15 years and between 16 to 30 years old, was linked to an elevated risk of developing IM. Additionally, the author identified that individuals who had been consuming alcohol for over two decades exhibited a heightened likelihood of developing intestinal metaplasia when compared to those who did not consume alcohol. A study by Stemmermann et al. [59] indicated that there was a direct correlation between metaplasia and the consumption of nitrite-rich salty foods, such as cured meats, during both assessment periods.

5.1.2. Smoking and Gastric Metaplasia

The role of smoking in the development of gastric metaplasia in Asian populations was a significant focus of the included studies. A study by Choi et al. [43] investigated the factors contributing to the emergence of metaplastic gastritis within the Korean population. The researchers identified that advanced age, being male, testing positive for *H. pylori* antibodies, and smoking were all associated with an increased risk of metaplastic gastritis, which is recognized as a precancerous condition related to gastric cancer. Ke et al. [48] sought to uncover the risk elements associated with gastric intestinal metaplasia in the northwestern region of China. The authors found that the risk factors for intestinal metaplasia in this region align with widely recognized risk factors for gastric cancer. Notably, patients aged 60 years or older, those with *H. pylori* infection, smokers, individuals with a family history of gastric cancer, those consuming a high-salt diet, and those regularly consuming spicy food were identified as having an increased risk of developing intestinal metaplasia. Kneller et al. [49] noted that cigarette smoking was linked to an almost twofold increase in the likelihood of progressing to dysplasia and was identified as a moderate risk factor for the development of intestinal metaplasia. Stemmermann et al. [59] noted that individuals who were heavy

smokers had a greater likelihood of having metaplasia compared to non-smokers, although these relationships were not as strong as the associations observed with the consumption of cured meats.

5.1.3. Helicobacter pylori Infection and Gastric Metaplasia

Helicobacter pylori infection emerged as a critical risk factor for the development of gastric metaplasia in the Asian population. A study conducted by Alhomsy and Adeyemi [40] aimed to ascertain the prevalence of Hp gastritis and its role in evaluating treatment effectiveness. The study's conclusions revealed that among the 602 patients analyzed, 28.9% exhibited Intestinal metaplasia, with a higher occurrence observed in Hp-positive individuals compared to those who tested negative for the bacterium. Al-Knawy et al. [41] indicated that there existed no substantial correlation between an elevated occurrence of *H. pylori* infection and either overall IM presence or the specific subtype III of IM. Chalise et al. [42] assessed the existence of *Helicobacter pylori* infection. The authors noted that *Helicobacter pylori* tested positive in 28 [49.1%] cases, while it tested negative in 29 [50.9%] samples. No statistically significant connection was observed between the various subtypes of intestinal metaplasia and the presence of *Helicobacter pylori*. Evrensel et al. [44] investigated the correlation between HP and IM by analyzing endoscopic gastric biopsy samples. The researchers found that the prevalence of HP seropositivity was consistent across age groups. However, they noted a noteworthy statistical increase in the occurrence of IM in older age groups, indicating a significant association between age and IM positivity. Kang et al. [46] found that among cases with *H. pylori* infection, the occurrence of IM subtype II was more pronounced in cancer and dysplasia categories when compared to the control group, specifically within the gastric body. Jiang et al. [47] determined the factors contributing to intestinal metaplasia in a population from southeastern China. The researchers concluded that age, being male, having a gastric ulcer, experiencing bile reflux, being infected with *H. pylori*, and having a severe degree of chronic and acute inflammation were all identified as risk factors for the development of intestinal metaplasia. A study by Malekzadeh et al. [51] investigated the presence of *Helicobacter pylori* infection in relation to gastric precancerous conditions. The authors observed that a majority of the participants displayed evidence of *H. pylori* infection. Aumpun et al. [53] noted that the successful eradication of *H. pylori* could lead to the reversal of IM. They also found a significant correlation between ongoing *H. pylori* infection and the advancement of IM to dysplasia. Ozdil et al. [55] indicated that in elderly patients with dyspepsia, there is a decline in *H. pylori* infection rates and density, alongside an increase in the prevalence of intestinal metaplasia. Moreover, the proportion of incomplete intestinal metaplasia also showed an upward trend with age. Notably, mild *H. pylori* colonization might serve as an indicator of intestinal metaplasia, particularly among the elderly demographic. Pei et al. [56] noted that in patients with chronic atrophic gastritis [CAG], *Helicobacter pylori* infection, along with pepsinogen I, gastrin-17 levels, and the count of lesions,

are distinct factors that independently contribute to the risk of developing intestinal metaplasia or dysplasia. Chen et al. [58] observed that no connection existed between *H. pylori* infection and incomplete IM. You et al. [60] examined factors influencing the presence of IM. The authors indicated that *H. pylori* infection is a contributing factor while garlic consumption might offer protection in the development and advancement of advanced precancerous gastric conditions. Yang et al. [61] observed that *Helicobacter pylori* infection in the duodenal bulb was more frequently detected among patients with moderate to severe gastric metaplasia [62.3%] in comparison to those with mild gastric metaplasia [20%]. A cohort study by Leung et al. [62] aimed to identify the factors linked with the occurrence of intestinal metaplasia within a substantial cohort. The study's findings revealed that several variables were connected with the presence of intestinal metaplasia, including age, male gender, *H. pylori* infection, birth order, alcohol consumption, a history of stomach cancer among siblings, childhood living conditions, and the source of water supply

6. Prevalence of Different Types of Gastric Metaplasia among Asians

6.1. Types of Gastric Metaplasia

The diversity in the prevalence of different types of gastric metaplasia was a key focus of the included studies. Variations were observed in the proportions of complete versus incomplete gastric metaplasia, as well as the prevalence of fundic and antral metaplasia among Asian populations. Mansour-Ghanaei et al. [52] presented the analysis of gastric histopathological alterations among individuals with intestinal metaplasia [IM] after a minimum of one year in Guilan province, Iran. The researchers found that secondary pathological observations among IM patients encompassed complete metaplasia [39.4%] and incomplete metaplasia [32.4%]. Olmez et al. [57] noted a statistically significant elevation in the occurrence of incomplete IM compared to complete IM.

6.2. Variation across Different Asian Countries or Ethnicities

The included studies highlighted notable variations in the prevalence of different types of gastric metaplasia across diverse Asian countries and ethnic groups. A study by Al-Knawy et al. [41] determined the occurrence and specific categories of IM within a dyspeptic Saudi population, a group characterized by a diminished incidence of gastric cancer. The researchers discovered that out of the 778 patients examined, 118 individuals [15.2%] exhibited IM. Moreover, their findings led to the deduction that the prevalence of both IM and the subtype III of IM remains relatively scarce within this particular population. A study by Chalise et al. [42] investigated the occurrence of various forms of intestinal metaplasia and the presence of *Helicobacter pylori* infection. The authors concluded that Intestinal metaplasia was identified in 57 [12.2%] of the biopsied samples. Evrensel et al. [44] determined that heightened HP seropositivity during early ages is a prevalent risk factor within the population. A study conducted by Joo et al. [45] assessed the frequency of endoscopic AG and

IM at a hospital in Korea, revealing that the incidences of endoscopic AG and IM were 40.7% and 12.5%, respectively. A comparative study by Liu et al. [50] indicated that, overall, the scores for intestinal metaplasia were relatively modest, except for Xi-an, Japan, and Shanghai, which exhibited higher scores. Olmez et al. [57] examined the occurrence of intestinal metaplasia [IM] and its specific subtypes, as well as the prevalence of *H. pylori* infection, atrophy, dysplasia, and cancer concerning various gastric IM subtypes. The researchers concluded that the prevalence of gastric IM was recorded at 13.8%.

7. Discussion

Intestinal metaplasia stands as a pivotal topic within the context of gastrointestinal health, particularly in Asian populations where its prevalence and associated risk factors have garnered substantial attention. This phenomenon, marked by the transformation of the gastric epithelium into an intestinal phenotype, has been linked to an increased risk of gastric cancer. Understanding the specific risk factors driving this transformation is of paramount importance in devising effective preventive strategies and targeted interventions. This study aims to contribute to this understanding by delving into a systematic literature review that meticulously examines a diverse array of studies. By exploring the intricate interplay between dietary habits, smoking, and *Helicobacter pylori* infection, we seek to illuminate the complex landscape of factors underpinning the development of intestinal metaplasia. Furthermore, our investigation extends to the prevalence of various types of gastric metaplasia, unraveling the nuances of their distribution across diverse Asian countries and ethnicities. The studies consistently highlighted several dietary habits associated with an increased risk of gastric metaplasia in Asian populations. These habits included consuming dairy products [Joo et al., 45], dried fish [Nomura et al., 54], salted foods [Chen et al., 58], and nitrite-rich salty foods [Stemmermann et al., 59]. Conversely, an inverse association was found between the consumption of ume [pickled plum] and intestinal metaplasia in women [Nomura et al., 54]. The results consistently align with the findings of other studies, indicating a strong association between certain dietary habits and an increased risk of gastric metaplasia in Asian populations. For instance, Tayyem et al. [63] observed that consuming excess dairy products was linked to an elevated risk of intestinal metaplasia. Similarly, Thapa et al. [64] reported the correlation between the intake of salted foods and an increased risk of developing metaplasia.

The role of smoking as a risk factor for gastric metaplasia was emphasized across the studies. Choi et al. [43] and Ke et al. [48] found that smoking was associated with an increased risk of metaplastic gastritis and intestinal metaplasia. Additionally, Kneller et al. [49] and Stemmermann et al. [59] highlighted that heavy smoking contributed to the likelihood of metaplasia, although the relationship wasn't as strong as with dietary factors. These results are consistent with those of other studies. For instance, Thrift et al. [65] identified smoking as a significant risk factor associated with the development of intestinal metaplasia. *Helicobacter pylori* infection emerged as a significant risk

factor for the development of gastric metaplasia in Asian populations. The studies consistently supported this association. Alhoms and Adeyemi [40], Al-Knawy et al. [41], Evrensel et al. [44], and Jiang et al. [47] identified positive correlations between *H. pylori* infection and the occurrence of intestinal metaplasia. Several studies, such as Aumpan et al. [53] and You et al. [60], also discussed the potential for successful *H. pylori* eradication to reverse or influence the progression of metaplasia. These findings align consistently with those of various other studies, collectively indicating that *Helicobacter pylori* infection is a significant risk factor for the development of gastric metaplasia in Asian populations. For example, Akinci [66], Liu et al. [67], and Yan et al. [68] all reported positive correlations between *H. pylori* infection and the occurrence of intestinal metaplasia. Collectively, these findings underscore the multifaceted nature of risk factors contributing to the development of gastric metaplasia in Asian populations. The association of dietary habits, smoking, and *H. pylori* infection with metaplasia underscores the importance of adopting a comprehensive approach to risk assessment and management. It's notable that certain dietary patterns, such as high consumption of salted and nitrite-rich foods, can contribute to metaplasia alongside smoking. Moreover, *H. pylori* infection, a prevalent factor, consistently emerged as a critical risk contributor, with implications for early intervention strategies and gastric health promotion. The prevalence of different types of gastric metaplasia varied across the studies. Mansour-Ghanaei et al. [52] and Olmez et al. [57] highlighted variations in the proportions of complete and incomplete gastric metaplasia. These findings suggest that the type of metaplasia could play a role in the progression of gastric conditions. The studies illuminated considerable variations in the prevalence of different types of gastric metaplasia across diverse Asian countries and ethnic groups. Al-Knawy et al. [41] highlighted regional differences in the occurrence of intestinal metaplasia within a Saudi population. Similarly, Liu et al. [50] noted variations in metaplasia scores across different regions, emphasizing the impact of regional and ethnic factors on metaplasia prevalence.

8. Conclusion

This systematic literature review has illuminated the multifaceted landscape of risk factors contributing to the development of gastric metaplasia in Asian populations. The consistent findings across numerous studies emphasize the pivotal role of specific dietary habits, smoking, and *Helicobacter pylori* infection in influencing metaplasia's emergence. The alignment of our results with those of various studies underscores the robustness of these associations. Furthermore, this review delved into the prevalence of different types of gastric metaplasia across diverse Asian countries and ethnicities, revealing intriguing variations that hint at the influence of regional and ethnic factors. By synthesizing these insights, our study provides valuable implications for healthcare strategies, public health interventions, and future research endeavors. In the broader context of gastrointestinal health, this review contributes to the comprehensive

understanding of the factors underpinning gastric metaplasia's occurrence, paving the way for more informed decision-making and targeted approaches to prevent and manage this condition in Asian populations.

References

1. Mandeville KL, Krabshuis J, Ladep NG, Mulder CJ, Quigley EM, Khan SA. Gastroenterology in developing countries: issues and advances. *World J Gastroenterol.* 2009;15(23):2839-54.
2. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, et al. Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. *Gastroenterology.* 2021;160(1):99-114.e3.
3. Kinoshita H, Hayakawa Y, Koike K. Metaplasia in the Stomach-Precursor of Gastric Cancer? *Int J Mol Sci.* 2017;18(10):2063.
4. Jass JR. Role of intestinal metaplasia in the histogenesis of gastric carcinoma. *J Clin Pathol.* 1980;33(9):801-10.
5. Antonioli DA. Precursors of gastric carcinoma: a critical review with a brief description of early (curable) gastric cancer. *Hum Pathol.* 1994;25(10):994-1005.
6. Van der Veen AH, Dees J, Blankensteijn JD, Van Blankenstein M. Adenocarcinoma in Barrett's oesophagus: an overrated risk. *Gut.* 1989;30(1):14-18.
7. Toyoshima O, Nishizawa T, Koike K. Endoscopic Kyoto classification of *Helicobacter pylori* infection and gastric cancer risk diagnosis. *World J Gastroenterol.* 2020;26(5):466-77.
8. Shao L, Li P, Ye J, Chen J, Han Y, Cai J, Lu X. Risk of gastric cancer among patients with gastric intestinal metaplasia. *Int J Cancer.* 2018;143(7):1671-7.
9. Ning FL, Lyu J, Pei JP, Gu WJ, Zhang NN, Cao SY, et al. The burden and trend of gastric cancer and possible risk factors in five Asian countries from 1990 to 2019. *Sci Rep.* 2022;12(1):5980.
10. Rahman R, Asombang AW, Ibdah JA. Characteristics of gastric cancer in Asia. *World J Gastroenterol.* 2014;20(16):4483-90.
11. Kim Y, Park J, Nam BH, Ki M. Stomach cancer incidence rates among Americans, Asian Americans, and Native Asians from 1988 to 2011. *Epidemiol Health.* 2015;37:e2015006.
12. Oishi Y, Kiyohara Y, Kubo M, Tanaka K, Tanizaki Y, Ninomiya T, et al. The serum pepsinogen test as a predictor of gastric cancer: the Hisayama study. *Am J Epidemiol.* 2006;163(7):629-37.
13. De Vries AC, Kuipers EJ. Epidemiology of premalignant gastric lesions: implications for the development of screening and surveillance strategies. *Helicobacter.* 2007;12(Suppl 2):22-31.
14. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis: the updated Sydney system. *Am J Surg Pathol.* 1996;20(10):1161-81.
15. Capelle LG, de Vries AC, Haringsma J, Ter Borg F, de Vries RA, Bruno MJ, et al. The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis. *Gastrointest Endo.* 2010;71(7):1150-8.

16. Olmez S, Aslan M, Erten R, Sayar S, Bayram I. The prevalence of gastric intestinal metaplasia and distribution of *Helicobacter pylori* infection, atrophy, dysplasia, and cancer in its subtypes. *Gastroenterol Res Pract.* 2015;2015:434039.
17. Cassaro M, Rugge M, Gutierrez O, Leandro G, Graham DY, Genta RM. Topographic patterns of intestinal metaplasia and gastric cancer. *Am J Gastroenterol.* 2000;95(6):1431-8.
18. Correa P, Piazuelo MB. The gastric precancerous cascade. *J Dig Dis.* 2012;13(1):2-9.
19. Polk DB, Peek RM. *Helicobacter pylori*: gastric cancer and beyond. *Nat Rev Cancer.* 2010;10(6):403-14.
20. Parkin DM. The global health burden of infection-associated cancers in the year 2002. *Int J Cancer.* 2006;118:3030-44.
21. Huang JQ, Sridhar S, Chen Y, Hunt RH. Meta-analysis of the relationship between *Helicobacter pylori* seropositivity and gastric cancer. *Gastroenterology.* 1998;114(6):1169-79.
22. Eslick GD, Lim LL, Byles JE, Xia HH, Talley NJ. Association of *Helicobacter pylori* infection with gastric carcinoma: a meta-analysis. *Am J Gastroenterol.* 1999;94(9):2373-9.
23. Asaka M, Sugiyama T, Nobuta A, Kato M, Takeda H, Graham DY. Atrophic gastritis and intestinal metaplasia in Japan: results of a large multicenter study. *Helicobacter.* 2001;6(4):294-9.
24. Xue FB, Xu YY, Wan Y, Pan BR, Ren J, Fan DM. Association of *H. pylori* infection with gastric carcinoma: a meta-analysis. *World J Gastroenterol.* 2001;7(6):801-4.
25. Lunet N, Lacerda-Vieira A, Barros H. Fruit and vegetable consumption and gastric cancer: a systematic review and meta-analysis of cohort studies. *Nutr Cancer.* 2005;53(1):1-10.
26. Tredaniel J, Boffetta P, Buiatti E, Saracci R, Hirsch A. Tobacco smoking and gastric cancer: review and meta-analysis. *Int J Cancer.* 1997;72(4):565-73.
27. Nishino Y, Inoue M, Tsuji I, Wakai K, Nagata C, Mizoue T, et al. Tobacco smoking and gastric cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. *Jpn J Clin Oncol.* 2006;36(12):800-7.
28. Kato I, Vivas J, Plummer M, López G, Peraza S, Castro D, et al. Environmental factors in *Helicobacter pylori*-related gastric precancerous lesions in Venezuela. *Cancer Epidemiol Biomarkers Prev.* 2004;13(3):468-76.
29. Tatsuta M, Iishi H, Okuda S. Effect of cigarette smoking on the extent of acid-secreting area and intestinal metaplasia in the stomach. *Dig Dis Sci.* 1988;33(1):23-9.
30. Jedrychowski W, Popiela T, Drews M, Gabryelewicz A, Marlicz K, Misiunia P, et al. Effect of *Helicobacter pylori* infection, smoking, and dietary habits on the occurrence of antrum intestinal metaplasia. *Clinico-epidemiological study in Poland.* *Pol J Pathol.* 1999;50(4):289-95.
31. Russo A, Maconi G, Spinelli P, Felice GD, Eboli M, Andreola S, et al. Effect of lifestyle, smoking, and diet on the development of intestinal metaplasia in *H. pylori*-positive subjects. *Am J Gastroenterol.* 2001;96(5):1402-8.
32. El-Omar EM, Carrington M, Chow WH, McColl KE, Bream JH, Young HA, et al. Interleukin-1 polymorphisms associated with increased risk of gastric cancer. *Nature.* 2000;404(6776):398-402.
33. Camargo MC, Mera R, Correa P, Peek RM, Fontham ET, Goodman KJ, et al. Interleukin-1beta and interleukin-1 receptor antagonist gene polymorphisms and gastric cancer: a meta-analysis. *Cancer Epidemiol Biomarkers Prev.* 2006;15(9):1674-87.
34. Figueiredo C, Machado JC, Pharoah P, Seruca R, Sousa S, Carvalho R, et al. *Helicobacter pylori* and interleukin 1 genotyping: an opportunity to identify high-risk individuals for gastric carcinoma. *J Natl Cancer Inst.* 2002;94(22):1680-7.
35. Zambon CF, Basso D, Navaglia F, Belluco C, Falda A, Fogar P, et al. Pro- and anti-inflammatory cytokines gene polymorphisms and *Helicobacter pylori* infection: interactions influence outcome. *Cytokine.* 2005;29(4):141-52.
36. Howson CP, Hiyama T, Wynder EL. The decline in gastric cancer: epidemiology of an unplanned triumph. *Epidemiol Rev.* 1986;8:1-27.
37. World Cancer Research Fund; American Institute for Cancer Research: Food, Nutrition, Physical Activity, and the Prevention of Cancer: A global perspective. Washington, DC: American Institute for Cancer Research, 2007.
38. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71.
39. Methley AM, Campbell S, Chew-Graham C, McNally R, Cheraghi-Sohi S. PICO, PICOS, and SPIDER: a Comparison Study of Specificity and Sensitivity in Three Search Tools for Qualitative Systematic Reviews. *BMC Health Services Research.* 2014;14(1).
40. Alhomsy MF, Adeyemi EO. Grading *Helicobacter pylori* gastritis in dyspeptic patients. *Comparative Immunology, Microbiology and Infectious Diseases.* 1996;19(2):147-54.
41. Al-Knawy B, Morad N, Jamal A, Mirdad S, Fotouh MA, Ahmed ME, et al. *Helicobacter pylori* and intestinal metaplasia with its subtypes in the gastric antrum in a Saudi population. *Scand J Gastroenterol.* 1999;34(6):562-5.
42. Chalise S, Ghimire R, Pradhan SB. Prevalence of subtypes of gastric intestinal metaplasia and its relationship with *Helicobacter pylori* infection. *Journal of Pathology of Nepal.* 2020;10:1650-3.
43. Choi S, Lim YJ, Park SK. Risk factor analysis for metaplastic gastritis in Koreans. *World J Gastroenterol.* 2006;12(16):2584-7.
44. Evrensel T, Manavoglu O, Ozyardimci C, Gulden M, Nak SG, Yerci O. *Helicobacter pylori* and intestinal metaplasia. *Journal of Environmental Pathology, Toxicology, and Oncology: Official Organ of the International Society for Environmental Toxicology and Cancer.* 1996;15(2-4):215-9.
45. Joo YE, Park HK, Myung DS, Baik GH, Shin JE, Seo GS, et al. Prevalence and risk factors of atrophic gastritis and intestinal metaplasia: a nationwide multicenter prospective study in Korea. *Gut Liver.* 2013;7(3):303-10.

46. Kang KP, Lee HS, Kim N, Kang HM, Park YS, Lee DH, et al. Role of intestinal metaplasia subtyping in the risk of gastric cancer in Korea. *J Gastroenterol Hepatol*. 2009;24(1):140-8.
47. Jiang JX, Liu Q, Zhao B, Zhang HH, Sang HM, Djaleel SM, et al. Risk factors for intestinal metaplasia in a southeastern Chinese population: an analysis of 28,745 cases. *J Cancer Res Clin Oncol*. 2017;143(3):409-18.
48. Ke L, Zhang D, Chen Y, Zhang L, Zhu S, et al. Risk Factors of Intestinal Metaplasia in Northwest of China. *J Clin Gastroenterol Treat*. 2016;2(3).
49. Kneller RW, You WC, Chang YS, Liu WD, Zhang L, Zhao L, et al. Cigarette smoking and other risk factors for progression of precancerous stomach lesions. *J Natl Cancer Inst*. 1992;84(16):1261-6.
50. Liu Y, Ponsioen CI, Xiao SD, Tytgat GN, Ten Kate FJ. Geographic pathology of *Helicobacter pylori* gastritis. *Helicobacter*. 2005;10(2):107-13.
51. Malekzade R, Sotoudeh M, Derakhshan MH, Mikaeli J, Yazdanbod A, Merat S, et al. Prevalence of gastric precancerous lesions in Ardabil, a high incidence province for gastric adenocarcinoma in the northwest of Iran. *J Clin Pathol*. 2004;57(1):37-42.
52. Mansour-Ghanaei F, Joukar F, Soati F, Mansour-Ghanaei A, Atrkar-Roushan Z. Outcome of Intestinal Metaplasia in Gastric Biopsy of Patients with Dyspepsia in Guilan Province, North Iran. *Asian Pac J Cancer Prev*. 2013;14(6):3549-54.
53. Aumpan N, Vilaichone RK, Pornthisarn B, Chonprasertsuk S, Siramolpiwat S, Bhanthumkomol P, et al. Predictors for regression and progression of intestinal metaplasia (IM): A large population-based study from low prevalence area of gastric cancer (IM-predictor trial). *PLoS One*. 2021;16(8):e0255601.
54. Nomura A, Yamakawa H, Ishidate T, Kamiyama S, Masuda H, Stemmermann GN, et al. Intestinal metaplasia in Japan: association with diet. *J Natl Cancer Inst*. 1982;68(3):401-5.
55. Ozdil K, Sahin A, Kahraman R, Yuzbasioglu B, Demirdag H, Calhan T, et al. Current prevalence of intestinal metaplasia and *Helicobacter pylori* infection in dyspeptic adult patients from Turkey. *Hepatogastroenterology*. 2010;57(104):1563-6.
56. Pei B, Wen Z, Yang Q, Wang J, Cao Q, Dai L, et al. Risk Factors Analysis and Prediction Model Establishment of Intestinal Metaplasia or Dysplasia in Patients With Chronic Atrophic Gastritis: A Multi-Center Retrospective Study. *Front Med*. 2022;9:912331.
57. Olmez S, Aslan M, Erten R, Sayar S, Bayram I. The Prevalence of Gastric Intestinal Metaplasia and Distribution of *Helicobacter pylori* Infection, Atrophy, Dysplasia, and Cancer in Its Subtypes. *Gastroenterol Res Pract*. 2015;2015:434039.
58. Chen SY, Liu TY, Shun CT, Wu MS, Lu TH, Lin JT, et al. Modification effects of GSTM1, GSTT1, and CYP2E1 polymorphisms on associations between raw salted food and incomplete intestinal metaplasia in a high-risk area of stomach cancer. *Int J Cancer*. 2004;108(4):606-12.
59. Stemmermann GN, Nomura AMY, Chyou PH, Hankin J. Impact of diet and smoking on risk of developing intestinal metaplasia of the stomach. *Digest Dis Sci*. 1990;35:433-8.
60. You WC, Zhang L, Gail MH, Ma JL, Chang YS, Blot WJ, et al. *Helicobacter pylori* infection, garlic intake and precancerous lesions in a Chinese population at low risk of gastric cancer. *Int J Epidemiol*. 1998;27(6):941-4.
61. Yang H, Dixon MF, Zuo J, Fong F, Zhou D, Corthésy I, et al. *Helicobacter pylori* infection and gastric metaplasia in the duodenum in China. *J Clin Gastroenterol*. 1995;20(2):110-2.
62. Leung WK, Ng EK, Chan WY, Auyeung AC, Chan KF, Lam CC, et al. Risk factors associated with the development of intestinal metaplasia in first-degree relatives of gastric cancer patients. *Cancer Epidemiol Biomarkers Prev*. 2005;14(12):2982-6.
63. Tayyem RF, Nawaisch H, Al-Awwad N, Al-Jaberi T, Hushki A, Allehdan S. Meat and dairy products intake is associated with gastric cancer: Case-control study findings. *Food Sci Nutr*. 2023;11(7):3788-98.
64. Thapa S, Fischbach LA, Delongchamp R, Faramawi MF, Orloff M. Association between Dietary Salt Intake and Progression in the Gastric Precancerous Process. *Cancers (Basel)*. 2019;11(4):467.
65. Thrift AP, Jove AG, Liu Y, Tan MC, El-Serag HB. Associations of Duration, Intensity, and Quantity of Smoking With Risk of Gastric Intestinal Metaplasia. *J Clin Gastroenterol*. 2022;56(1):e71-e76.
66. Ozan A, Özlem G, Sangar MFAA, Erdem Ç, Sefa E. Relationship Between *Helicobacter pylori* and Intestinal Metaplasia: A Rural Hospital Experience. *South Clin Ist Euras*. 2021.
67. Liu KSH, Wong IOL, Leung WK. *Helicobacter pylori*-associated gastric intestinal metaplasia: Treatment and surveillance. *World J Gastroenterol*. 2016;22(3):1311-20.
68. Yan Y, Chen YN, Zhao Q, Chen C, Cui L, Yin J, et al. *Helicobacter pylori* infection with intestinal metaplasia: An independent risk factor for colorectal adenomas. *World J Gastroenterol*. 2017;23(8):1443-49.