PREVALENCE OF GASTRIC PRECANCEROUS CONDITIONS : A SYSTEMATIC REVIEW

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ABSTRACT

Background: *Gastric carcinoma is a common malignant disease associated with an unfavorable prognosis in the case of late dia-gnosis. The most significant precancerous condition is chronic atrophic gastritis and intestinal metaplasia caused by Helicobacter pylori infection. These longlasting changes may lead to formation of dysplastic precancerous lesions.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 1.045 articles, whereas the results of our search on SagePub brought up 701 articles. The results of the search conducted for the last year of 2013 yielded a total 12 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 4 papers, 3 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.*

Conclusion: *Precancerous conditions including chronic atrophic gastritis gastritis, metaplasia, foveolar hyperplasia and gastric hyperplastic polyps derived from the gastric epithelium have been concluded, based on the overview of gastric epithelial histological organization and its renewal.*

Keyword: *Gastric Precancerous, Prevalence, Incidence*

INTRODUCTION

Gastric cancer (GC) is a major global problem, ranking fifth in incidence and third in cancer-related mortality worldwide, and it was responsible for over 1000000 new cases in 2018 and an estimated 783000 deaths. The incidence of GC varies by sex and region. The incidence is twice as high in men as in women. Incidence rates are markedly elevated in Eastern Asia, whereas the rates in Northern America and Northern Europe are generally low and are equivalent to those seen across African regions.[1]

Risk factors include *Helicobacter pylori* (*H. pylori*) infection, family history (hereditary diffuse GC due to germline mutations in CDH1), dietary intake of foods preserved by salting and low fruit intake, Epstein–Barr virus infection, alcohol consumption, active tobacco smoking, consumption of foods contaminated with aflatoxin, nitrates and fungi, and pernicious anemia.[2]

The GC incidence has decreased in a growing number of countries partly due to decreasing risk factors, improving standards of living and increasing use of screening programs in high-risk populations.[3,4]

In Asian guidelines, high-risk individuals, including male patients, Chinese patients, patients with first-degree relatives who have GC, patients with persistent *H. pylori* infection and patients with age 40–45 years or older, should be considered for targeted invasive screening in regions with moderate or low incidence of GC.[5]

In contrast with Asian guidelines, European guidelines recommend that patients with advanced stages of atrophic gastritis (including severe atrophic changes or intestinal metaplasia (IM) in both the antrum and corpus, OLGA/OLGIM III/IV) should be followed up with high-quality endoscopy every 3 years. Patients with advanced stages of atrophic gastritis and with a family history of GC may benefit from a more intensive follow-up (every 1–2 years after diagnosis; every 3–5 years for those with autoimmune gastritis).[6]

Patients with IM specifically at higher risk of GC (those with incomplete IM or extensive IM and a family history) and/or who are at overall increased risk for GC (racial/ethnic minorities, immigrants from regions with high GC incidence, or individuals with a first-degree relative with GC) may reasonably elect to undergo repeat endoscopy within 1 year for risk stratification.[7]

H. pylori gastritis accounts for more than 80% of gastritis, and persistent infection may eventually cause chronic atrophic gastritis (CAG) through the canonical process originating from acute-on-chronic inflammation. *H. pylori* eradication abolishes the inflammatory response.[8]

A noninvasive test-and-treat strategy is appropriate for uninvestigated dyspepsia.[9]

An endoscopy-based strategy combined with Sydney system biopsies is supposed to be considered in patients who have dyspeptic symptoms and/or alarm symptoms or older patients, particularly in low-prevalence *H. pylori* populations (< 10%). A screen-and-treat strategy is recommended in communities at high risk of GC.[10]

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we review published literature about the prevalence of gastric precancerous condition. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "gastric precancerous" and "prevalence" as keywords.The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: *(("gastrics"[All Fields] OR*

"stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND "precancerous"[All Fields] AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields])) AND ((clinicaltrial[Filter]) AND (2013:2023[pdat])) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.
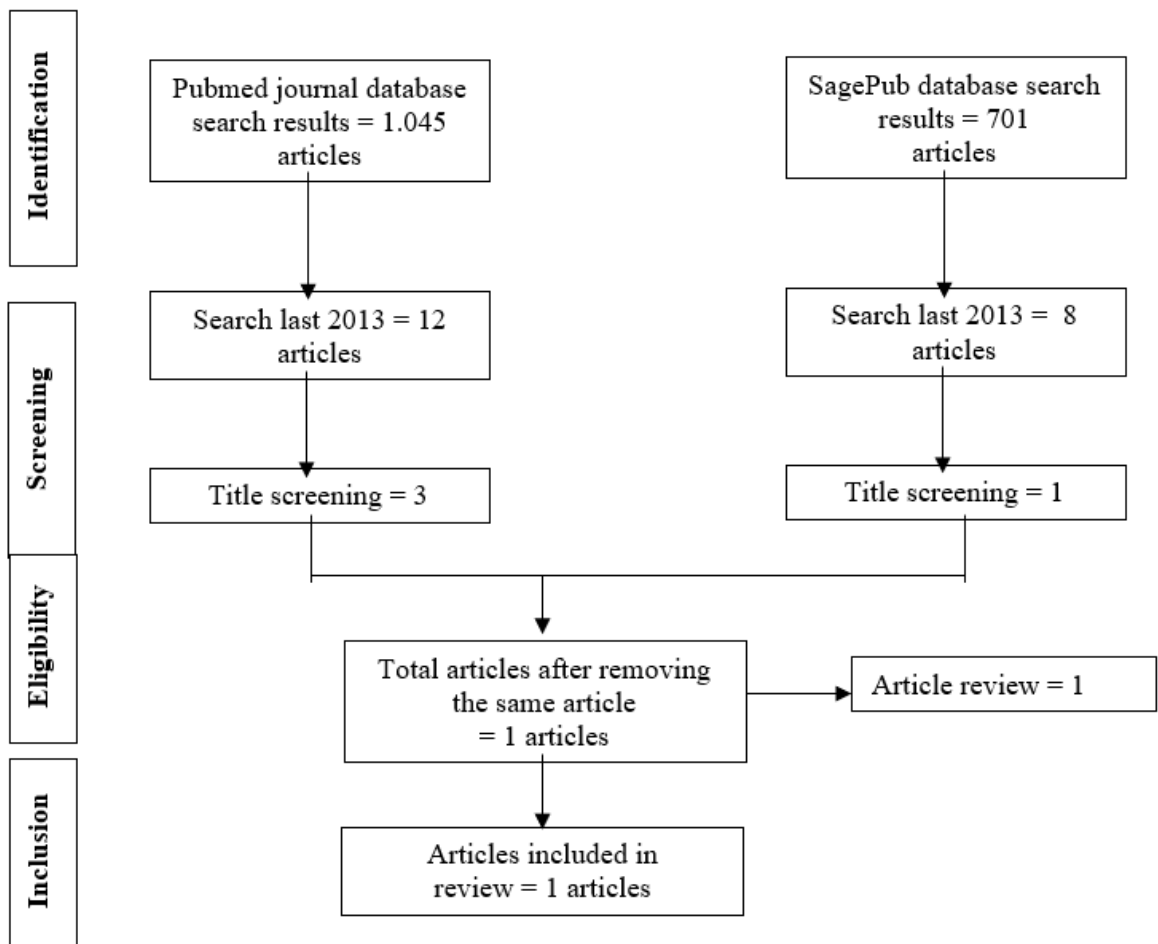

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 1.045 articles, whereas the results of our search on SagePub brought up 701 articles. The results of the search conducted for the last year of 2013 yielded a total 12 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 4 papers, 3 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.

Mera, et al[11] (2018) showed that long-term exposure to *H. pylori* infection was associated with progression of precancerous lesions. Individuals infected with *H. pylori* with these lesions may benefit from eradication, particularly those with atrophic gastritis without IM. Incomplete-type IM may be a useful marker for the identification of individuals at higher risk for cancer.

Xiao, et al[12] (2020) showed that age, sex, a family history of cancer, intake of meat-egg-milk frequently, superficial gastritis, and clinical symptoms of gastric cancer were associated with the presence of precancerous lesions. The detection rate was low using endoscopic screening in non-high-incidence area given the relatively low compliance rate. These findings provide a reference for designing effective community-based UGC screening strategies in non-high-incidence urban areas.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Mera et al, 2018[11]	USA	Retrospective study	795 patients	Individuals who were continuously infected with *H. pylori* for 16 years had a higher probability of progression to a more advanced diagnosis than those who cleared the infection and remained negative after baseline (p=0.001). Incomplete-type IM was associated with higher risk of progression to cancer than complete-type (OR, 11.3; 95% CI 1.4 to 91.4). The average histopathology score increased by 0.20 units/year (95% CI 0.12 to 0.28) among individuals continuously infected with *H. pylori*. The effect of cumulative time of infection on progression in the histopathology score was significantly higher for individuals with atrophy (without IM) than for individuals with IM (p<0.001)
Xiao et al, 2020[12]	China	Retrospective study	9.565 patients	The primary outcome was the UGC mortality, and secondary outcomes included the UGC

				detection rate, incidence rate, survival rate, and clinical stage at the time of diagnosis. A total of 10,416 and 9,565 individuals were recruited into the screening and control arms, respectively. The participation rate was 74.3%. In the screening arm, 5,242 individuals (50.3%) were estimated to be high-risk. Among them, 2,388 (45.6%) underwent endoscopic screening. Age and household income were associated with undergoing endoscopy. Three early esophageal cancer (0.13%), one gastric cancer (0.04%), 29 precancerous esophageal lesions (1.21%), and 53 precancerous gastric lesions (2.22%) were detected
Esmaeilzadeh et al, 2021[13]	Iran	Cross sectional study	469 patients	*H. pylori* infection was identified in 469 patients (80.2%) with the highest prevalence (84.2%) in those aged 40–60 years. Opium addiction correlated with a higher a *H. pylori* infection rate, while alcohol consumption was associated with a lower rate by Odds Ratio 1.98 (95% CI 1.11–3.52) and 0.49 (95% CI 0.26–0.92), respectively. The prevalence of intestinal metaplasia, gastric atrophy and gastric dysplasia was 15.2, 12.6 and 7.9%, respectively. Increased age, positive *H. pylori* infection, endoscopic abnormal findings and opium addiction showed a statistically significant association with all precancerous conditions, while NSAID consumption was negatively associated with precancerous conditions. For 121 patients (20.7% of all), the EGD examination revealed normal gastric mucosa, however, for more than half (68/121, 56.2%) of these patients, the histological evaluation showed *H. pylori* infection, and also signs of atrophic mucosa, intestinal metaplasia and dysplasia in 1.7, 4.1 and 1.7%, respectively.
Song et al, 2015[14]	Sweden	Cohort study	1.599 patients	After excluding the first two years of follow-up, 1599 cases of gastric cancer were

				identified. The annual crude incidence of gastric cancer was 20×10^{-5} for those in the normal mucosa group (standardised incidence ratio 1.0), 42×10^{-5} for those with minor changes (1.5), 59×10^{-5} for the gastritis group (1.8), 100×10^{-5} for the atrophic gastritis group (2.8), 129×10^{-5} for the intestinal metaplasia group (3.4), and 263×10^{-5} for the dysplasia group (6.5). Cox regression modelling confirmed that excess risks increased monotonically with progressive severity of gastric lesions, with the highest hazard ratio of 10.9 (dysplasia versus normal mucosa, 95% confidence interval 7.7 to 15.4). The increased incidence was stable throughout the follow-up period, and the gaps between cumulative incidence curves grew continuously.

Esmaeilzadeh, et al[13] (2021) showed that EGD with gastric biopsy mapping should be performed even in the presence of normal-appearing mucosa, especially in dyspeptic patients older than 40 years with opium addiction in north-eastern Iran. Owing to the high prevalence of precancerous conditions and *H. pylori* infection among patients with dyspepsia in parts of Iran, large-scale national screening in this country should be beneficial.

Song, et al[14] (2015) showed that among patients who undergo gastroscopy with biopsy for clinical indications, approximately 1 in 256 with normal mucosa, 1 in 85 with gastritis, 1 in 50 with atrophic gastritis, 1 in 39 with intestinal metaplasia, and 1 in 19 with dysplasia will develop gastric cancer within 20 years. These numbers, along with cost-benefit analyses, should guide future surveillance policies for these particular patient groups.

DISCUSSION

Gastric cancer accounts for about 6% of cancers worldwide, being the fifth most frequently diagnosed malignancy and the third leading cause of cancer related death, behind lung and colorectal cancer. According to the most recent GLOBOCAN cancer estimates, gastric cancer was responsible for over 1,000,000 new cancer cases and 783,000 deaths in 2018 [1]. Although there has been a steady decline in the incidence and mortality of gastric cancer over the last 15 years, as the result of the decrease of *Helicobacter pylori* prevalence and better dietary habits, the absolute incidence rate continues to rise, due to the advancing age of the world population.[1]

Gastric cancer incidence and mortality vary substantially across countries and within each country. Incidence rates are elevated (up to 32 cases per 100,000) in Eastern and Western Asia. Zones of low incidence (< 7 cases per 100,000) are Northern America, Northern Europe, and most regions of Africa. In Italy, gastric cancer ranks eighth among all cancers, with 12,803 new cases and 9,457 deaths in 2018. The poor clinical outcome of gastric cancer is mainly due to late diagnosis, poor response to therapeutic regimens and the highly heterogenous nature of the disease.[15]

Gastric carcinogenesis is a multistep and multifactorial process and is the result of the complex interplay between genetic susceptibility and environmental factors. Risk factors predisposing to gastric cancer include *Helicobacter pylori* infection, tobacco smoking, dietary habits (high intake of salt-preserved, smoked foods, red and processed meat, low intake of fresh fruit and vegetables), and Epstein-Barr virus (EBV) infection, as well as microbial community modifications by long-term use of proton-pomp inhibitors. A number of precancerous conditions have been recognized, such as chronic atrophic gastritis and intestinal metaplasia due to *Helicobacter pylori* infection or autoimmunity (pernicious anemia), peptic ulcer disease, gastric stump after partial gastrectomy and gastric polyps.[15]

Although most gastric cancers are sporadic, familial clustering is observed in up to 10% of patients. Among them, hereditary cases, related to known cancer susceptibility syndromes and/or genetic causes are thought to account for 1-3%

of all gastric cancers. The three major hereditable syndromes that primarily affect the stomach are hereditary diffuse gastric cancer (HDGC), gastric adenocarcinoma, proximal polyposis of the stomach (GAPPS), and familial intestinal gastric cancer (FIGC).[15]

Gastric carcinogenesis is a multistep process which involves, in most cases, a progression from normal mucosa through chronic gastritis (chronic inflammation of the gastric mucosa), mucosal atrophy (loss of gastric glands) and intestinal metaplasia (substitution of gastric epithelium by intestinal epithelium) to dysplasia (intraepithelial neoplasia) and carcinoma. This sequence of events may last several years and has been designated as the Correa's cascade of multistep gastric carcinogenesis [8]. According to this model, long standing inflammation is the primary pathogenic factor leading to gastric cancer development.[15]

Gastric dysplasia is defined as unequivocal neoplastic changes in the gastric epithelium, without evidence of lamina propria invasion. The diagnostic criteria are based on the presence of cellular atypia, abnormal differentiation, architectural disorganisation and increased mitotic activity. Endoscopically, gastric dysplasia may present as flat, depressed or polypoid lesions (the latter may be referred to as gastric – intestinal type and foveolar type – adenomas). It may arise de novo or may occur within pre-existing benign sporadic polyps, namely hyperplastic polyps and fundic gland polyps or hamartomatous polyps, such as juvenile polyps and Peutz-Jeghers polyps.[15]

A recent classification proposed by Hackeng WM et al, distinguishes gastric polyps according to the gastric mucosa compartment from which the gastric polyp arises. Gastric adenomas arising from the foveolar compartment include foveolar type adenomas (arising from foveolar epithelium without intestinal metaplasia). Gastric adenomas arising from the glandular compartment include pyloric gland adenoma (PGA) and oxyntic gland adenoma (OGA). Consistent with their glandular histogenesis, OGAs and PGAs show diffuse immunoreactivity for MUC6.[16]

Hyperplastic polyps (HPs) are benign gastric epithelial lesions consisting of hyperplastic and cystically dilated foveolar epithelium, in a background of prominent inflammatory changes. As HPs represent a hyperproliferative response to tissue injury, most of them arise in a background of longstanding gastric mucosal inflammation and are the prevalent polyp type in countries with a high prevalence of *Helicobacter pylori* infection. Foveolar or intestinal type dysplasia and adenocarcinoma (intestinal type or diffuse type) may arise in about 2% of larger HPs.[16]

CONCLUSION

Precancerous conditions including chronic atrophic gastritis gastritis, metaplasia, foveolar hyperplasia and gastric hyperplastic polyps derived from the gastric epithelium have been concluded, based on the overview of gastric epithelial histological organization and its renewal.

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