

Research status of risk factors of chronic atrophic gastritis

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Abstract. Gastritis, also known as inflammation of the gastric mucosa, is a prevalent disorder of the digestive system that can be attributed to a range of reasons. Based on the level of illness severity, gastritis can be categorized into two distinct types: acute gastritis and chronic gastritis. Based on the observed pathological alterations, acute gastritis can be categorized into several subtypes, namely simple gastritis, erosive and hemorrhagic gastritis, corrosive gastritis, and suppurative gastritis. Based on the observed pathological alterations, chronic gastritis can be categorized into three distinct types: non-atrophic gastritis, atrophic gastritis, and special type gastritis. The primary method for diagnosing and distinguishing between different kinds of gastritis is by the use of gastroscopy. Chronic atrophic gastritis (CAG) is a multifaceted illness characterized by atrophic lesions in the stomach mucosa resulting from several etiologies. This condition can be attributed to either *Helicobacter pylori* infection or autoimmune factors. Contemporary individuals are susceptible to encountering severe health consequences, including cancer and anemia, as a result of chronic atrophic gastritis (CAG). Conducting research on the etiological factors of CAG holds significant potential in terms of disease prevention and treatment strategies. This paper aims to conduct a literature review to examine the many risk factors associated with atrophic gastritis.

Keywords: Atrophic Gastritis, Risk Factors, *Helicobacter Pylori* Infection.

1. Introduction

Gastritis refers to the inflammatory condition of the stomach mucosa, which can be attributed to a range of causative factors. This particular ailment is widely recognized as one of the most prevalent disorders affecting the gastrointestinal tract. Based on the extent of pathological manifestations, the disease can be classified into two distinct categories: acute gastritis and chronic gastritis. Based on the observed pathological alterations, acute gastritis can be categorized into several distinct subtypes, namely simple gastritis, erosive and hemorrhagic gastritis, corrosive gastritis, and suppurative gastritis. Based on the observed pathological alterations, chronic gastritis can be categorized into three distinct subtypes: non-atrophic gastritis, atrophic gastritis, and special type gastritis. The primary method for diagnosing and distinguishing between different kinds of gastritis is by the use of gastroscopy. Chronic atrophic gastritis, characterized by atrophic lesions of the stomach mucosa resulting from various etiologies, represents a multifaceted illness that can arise from *Helicobacter pylori* infection or autoimmune mechanisms. Atrophic gastritis poses numerous adverse effects for contemporary individuals. Gastric bleeding, a very common occurrence, is characterized by vascular exposure, mucosal erosion, mucosal atrophy, and thinning. The primary presentation is melena, however in cases of significant bleeding, hematemesis,

acute dizziness, or even shock may occur. Furthermore, the occurrence of anemia can be attributed to atrophic gastritis, which is characterized by a significant loss of blood accompanied by symptoms commonly associated with anemia. Furthermore, if gastric ulcer and atrophic gastritis are not promptly treated, there is a risk of ongoing inflammatory bacterial assault on the gastric mucosa, resulting in its weakening. This can further lead to the development of erosive ulcers, as well as the occurrence of gastric ulcer and erosive gastritis. Chronic atrophic gastritis arises from a combination of causes, primarily associated with *Helicobacter pylori* infection or autoimmune dysregulation. Additionally, environmental factors, including dietary patterns, dining surroundings, and familial genetic predisposition, contribute to its development. In the present setting, it is imperative to enhance our comprehension of the risk factors associated with chronic atrophic gastritis in order to enhance the efficacy of preventive measures and treatment strategies.

This paper will employ a literature review method to examine the pertinent risk factors associated with chronic atrophic gastritis. Chronic atrophic gastritis has been found to be correlated with various causes, including *Helicobacter pylori* infection, autoimmune dysregulation, familial and social environmental influences, and other contributing factors. Hence, the examination of risk factors associated with gastritis holds valuable implications for the field of gastroenterology and the prevention of this condition. This research has substantial importance in terms of illness prevention and control.

2. Research status of chronic atrophic gastritis

2.1. Introduction to chronic atrophic gastritis

Helicobacter pylori and gastric cancer are both common in China [1]. To better endoscopic diagnosis and standardize treatment protocols, the second Chinese National Consensus Conference on chronic gastritis was organized in Shanghai from September 14 to 16, 2006. Using the Delphi method, participants at the conference cast their votes in secret. There was documentation of the dissemination of the Second Chinese National consensus on chronic gastritis [2]. Still, there is a lack of clarity about the current condition of diagnosis and treatment of chronic gastritis in China, despite the implementation of the national consensus. Screenings of people aged 18-65 with esophageal or gastric-related symptoms were performed at 33 endoscopy locations across the country between June and December of 2011. In addition to other related symptoms, they included upper abdomen pain, abdominal distension, postprandial satiety, early satiety, belching, reflux, heartburn, loss of appetite, and nausea. Patients having their first upper endoscopy for diagnostic purposes were the only ones included in the study. Participants were not allowed to be taking any medications within the last month that could affect the study's results, including proton pump inhibitors, NSAIDs, antiplatelet drugs, anticoagulants, or mucosal protective agents. Having had stomach cancer or surgery in the past. Significant changes in body mass index (BMI), vomiting, dysphagia, anemia, pregnancy, substance misuse, severe cardiovascular, renal, and pulmonary comorbidities, and mental disorders are cause for concern. Reflux esophagitis, peptic ulcers, polyps, and malignancy were all conditions that were ruled out during the endoscopic screening process.

2.2. Prevalence of chronic atrophic gastritis

A comprehensive screening was conducted between June and December 2011, involving a total of 8897 patients from 33 different locations [3]. Out of these patients, only 5 declined to participate in the study following the endoscopic procedure. Consequently, a final sample size of 8892 patients was included in the study. The distribution of cases supplied by each area can be found in Table 1. The research also displays the demographic information pertaining to the patient group. The average age of the participants in this study was 49.4 years, ranging from 18 to 65 years. The gender distribution of the patients was slightly skewed towards females, with 51.2% being female and 48.8% being male. The predominant primary symptom reported by the majority of participants was upper abdomen pain, with a prevalence rate of 52.9%. This was closely followed by abdominal distension, which was reported by 48.7% of participants. Other less frequently reported symptoms included postprandial satiety, reported by 14.3%

of participants, and early satiety, reported by 12.7% of participants. Among the cohort of 8892 individuals under study, a total of 1161 patients were found to be asymptomatic with regards to upper abdomen pain, bloating, postprandial satiety, and early satiety. The remaining 53.9% of patients exhibited only one of these symptoms, while the remaining 32.9% had multiple symptoms concurrently, as indicated in Table 2. Furthermore, a notable fraction of patients reported secondary symptoms in conjunction with the aforementioned core symptoms. In a similar vein, around 25% of these patients exhibited many secondary symptoms.

During the endoscopic examination, a total of 4389 patients were diagnosed with superficial gastritis, 3760 patients were diagnosed with chymous gastritis, and 1573 patients were diagnosed with atrophic gastritis. It is worth noting that the severity of these lesions was predominantly mild to moderate, as indicated in Table 2. The results of the pathological examination revealed a high prevalence of atrophic gastritis and intestinal metaplasia in the patient group, constituting 25.8% and 23.6% respectively. However, it is important to note that only a minority of these precancerous lesions were classified as serious. In the study, a total of 652 patients were identified as having dysplasia, accounting for 7.3% of the overall population. Among these patients, 642 individuals (98.5%) exhibited mild to moderate dysplasia, while the remaining 10 patients presented with severe dysplastic lesions.

Table 3 presents the diagnostic accuracy according to the endoscopic characteristics associated with pathological atrophy and chylous gastritis. It is worth mentioning that the endoscopic appearance exhibited low sensitivity but demonstrated a good level of specificity in the diagnosis of pathological atrophy. Furthermore, the point estimate for the positive likelihood ratio (PLR) of the endoscopic manifestation of pathological atrophy was 4.78 (95% confidence interval [CI]: 4.33-5.28), suggesting that individuals exhibiting endoscopic signs of atrophy were more prone to having pathological atrophy. Nevertheless, the endoscopic visual assessment did not demonstrate use in the prediction of neutrophil infiltration among individuals diagnosed with chylous gastritis (positive likelihood ratio [PLR] 1.18, 95% confidence interval [CI]: 1.12-1.25). Furthermore, the positive likelihood ratio (PLR) was determined to be 0.86 (95% confidence interval [CI]: 0.81-0.91), indicating that the endoscopic appearance did not possess sufficient accuracy in predicting the presence of mononuclear cell infiltration.

Based on the findings of the investigation, it was seen that a total of 1573 patients received a diagnosis of gastric atrophy through endoscopy, while 2291 patients had pathological atrophy. Our study revealed that the endoscopic characteristics, including the lack of rugae and the presence of visible blood vessels, demonstrated limited sensitivity in diagnosing pathological atrophy. However, these characteristics exhibited high specificity in predicting pathological atrophy, as evidenced by a positive likelihood ratio (PLR) of 4.78. This finding indicates that the presence of endoscopic atrophy appearance significantly enhances the probability of pathological atrophy. The results of this study align with a previous investigation conducted in Sweden, which demonstrated a sensitivity and specificity of 48% and 87%, respectively, for the detection of moderate to severe atrophy of the stomach mucosa using endoscopic examination. Similarly, the study found that the sensitivity and specificity for identifying moderate to severe gastric endoscopic atrophy were 14% and 91%, respectively.

Table 1. Cases contributed by each region [3].

Centers	NO.	%
Shenyang	280	3.1
Dalian	500	5.6
Tianjin	964	10.8
Jinan	320	3.6
Beijing	991	11.1
Shanghai	898	10.1
Nanjing	472	5.3

Table 1. (continued).

Hefei	299	3.4
Hangzhou	716	8.1
Wuhan	1030	11.6
Changsha	109	1.2
Chengdu	465	5.2
Chongqing	198	2.2
Guangzhou	522	5.9
Shenzhen	295	3.3
Fuzhou	833	9.4
Total	8892	100
None	3393 (38.2%)	
1	3480 (39.1%)	
≥2	2019 (22.7%)	

Table 2. Major endoscopic findings of the study population [3].

	No. of patients (%)
Superficial gastritis (n = 4389)	49.4%
Mild	1845(20.7%)
1845(20.7%)	2095(23.6%)
Severe	449(5.0%)
Erosive gastritis (n = 3760)	42.3%
Mild	Mild
Moderate	1960(22.0%)
Severe	667 (7.5%)
Atrophic gastritis (n = 1573)	17.7%
Mild	920 (10.3%)
Moderate	576 (6.5%)
Severe	77 (0.9%)

Table 3. Diagnostic accuracy of endoscopic appearance for pathologic atrophic gastritis and erosive gastritis with pathologic results as gold standard [3].

Endoscopic AG(No.)	Pathologic AG (No.)	Sensitivity (95%CI)	Specificity (95% CI)	PPY (95% CI)	NPV (95% CI)	PLR (95% CI)	NLR (95%CI)
1573	2291	42%(40-44%)	91%(91-92%)	69%(67-71%)	77%(76-78%)	4.78 (4.33-5.28)	0.64 (0.62-0.66)

Table 3. (continued).

Endoscopic EG (No.)	Pathologic NI(No.)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95%CI)	NPV (95%CI)	PLR (95%CI)	NLR (95%CI)
3760	4672	45%(43-46%)	62%(60-64%)	64%(63-66%)	42%(41 – 44%)	1.18 (1.12-1.25)	0.89(0.86-0.92)
Endoscopic EG (No.)	Pathologic MI(No.)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95%CI)	NPV (95%CI)	PLR (95%CI)	NLR (95%CI)
3760	6007	41%(39-42%)	53%(50-55%)	75%(74-77%)	20%(19-21%)	0.86(0.81-0.91)	1.13 (1.08-1.19)
AG: atrophic gastritis; EG: erosive gastritis; NI: neutrophils infiltration; MI: monocytes infiltration.							

3. Effect of high serum testosterone and UBT positivity on chronic atrophic gastritis

3.1. The effect of UBT on chronic atrophic gastritis

In this particular study, a cohort of 1679 patients performed a 13 C Urea Breath Test (UBT) and *Helicobacter pylori* gastroscopic biopsy [4]. Out of this group, a total of 829 individuals successfully completed the Peptic Ulcerogenetic Gene (PG) test. A total of 591 individuals were diagnosed with *H. pylori* infection, comprising 561 patients (33.41%) who tested positive for the urea breath test (UBT) and 395 patients (23.53%) who tested positive through biopsy. The results indicate that the positive rate of *H. pylori* infection detected using the urea breath test (UBT) was significantly greater compared to that detected through biopsy ($P < 0.0001$). Out of the total of 591 individuals that tested positive, only 365 exhibited positive results for both the urea breath test (UBT) and biopsy for *H. pylori*, as depicted in Supplementary Figure 1c. The levels of PG I and PG II were found to be elevated, whereas the PGR was observed to be reduced in patients with a positive *Helicobacter pylori* infection, irrespective of whether the urea breath test (UBT) or biopsy was conducted (see Figure 2, $p < 0.0001$). The rates of CAG positivity, as determined by endoscopic CAG and pathological CAG, were shown to be greater in individuals who tested positive for *Helicobacter pylori* (HP), irrespective of whether the urea breath test (UBT) or biopsy was used (refer to Table 6). Simultaneously, the incidence of CAG detection was greater among individuals who yielded positive results for *H. pylori* using urea breath testing (UBT) compared to those who had biopsy.

3.2. Effect of high serum testosterone on chronic atrophic gastritis

Serum testosterone tests, UBT, *H. pylori* biopsy, and gastroscopy were performed concurrently on 321 women [4]. The study's conclusive examination encompassed a cohort of 169 women aged 40 years and above who tested negative for *H. pylori* infection using urea breath test (UBT) and biopsy. The analysis considered the potential influence of age and *H. pylori* infection on the observed outcomes. The endoscopic and pathological CAG groups had higher blood testosterone levels than the negative group ($P = 0.0030, 0.0333$, and 0.0076 , respectively;). Age differences between groups were not significant ($P = 0.3487, 0.2738$, and 0.5075). Serum testosterone levels identified CAG in women over 40 ($P = 0.0075$;). Congenital Adrenal Hyperplasia (CAG) was diagnosed with high specificity (55.56%) and sensitivity (69.81%) when testosterone levels exceeded 28.84 ng/dl. At 28.84 ng/dl, CAG prevalence was significantly higher in the high testosterone group than in the low testosterone group ($P = 0.0019$;). The expression of testosterone transport and metabolism genes was investigated in six CAG and 12 normal gastric mucosa samples (GSE27411). CAG mucosa displayed higher SHBG, HSD17B2, and decreased GNRH1. Statistics showed significant differences ($P = 0.0071, 0.0010, 0.0180$;).

3.3. *Application of multivariate analysis and its limitations*

Chronic atrophic gastritis is a pathological condition that arises due to the influence of several contributing causes. The evaluation of chronic atrophic gastritis cannot be adequately performed by relying solely on a single component. Doing so may either exaggerate or mask the influence of that particular element, so failing to capture the entire environmental context and thereby compromising the accuracy of the evaluation. The utilization of the multiple logistic regression model enables the simultaneous examination of multiple influencing factors of the disease, thereby fulfilling the criteria for conducting a comprehensive analysis of pathogenic factors. This approach allows for the concurrent assessment of the impact of UBT and high serum testosterone on the disease, thereby establishing a foundation for the development of preventive and therapeutic strategies.

Dialectical materialism posits a universal interconnectedness of entities, wherein mutual influence, interaction, and constraint occur between entities, as well as among diverse constituent elements within entities, and across different stages of their developmental progression [5]. In the context of a certain entity, its internal components and all other entities will exhibit a relationship with it. The term "influence" can be used to describe this link, while the various parts and aspects associated with it can be referred to as factors. Hence, a technique for problem analysis, known as factor analysis, might be proposed. Factor analysis is a systematic approach used to analyze and address problems by examining the elements that impact a specific phenomenon. This method involves investigating the direction and magnitude of influence exerted by these factors, as well as exploring the interplay between them. Additionally, factor analysis aims to identify strategies for modifying these influential components in order to effect change in the phenomenon under study. The fundamental purpose of this concept is to examine the overarching interrelation of various entities. Due to the ubiquitous nature of links, numerous elements exert influence on a given phenomenon. In order to enhance our understanding of the numerous aspects at play, it is imperative to categorise them initially. Various classification standards can be employed to categorize elements into distinct kinds. Based on the source of variables, it is possible to categorize them into two distinct groups: internal factors and external factors. Based on the direction of influence, hindering factors and promoting factors can be distinguished. Based on the level of impact, the factors can be categorized into significant, relatively significant, and secondary factors. In accordance with the categorization of influence, it is possible to distinguish between direct factors and indirect factors. Based on the extent to which elements can be modified, they can be categorized as factors that are changeable, factors that are somewhat changeable, and factors that are unchangeable. The multi-factor analysis method aims to comprehensively identify and analyze the pertinent elements in order to address the problem effectively [6].

The factor analysis approach is unable to quantify the magnitude of the influence of single variables on overall market changes, as well as the relative contribution of different forces to the overall comprehensive effect. The factor analysis method is limited in its ability to precisely capture the quantitative relationship among market variables. The factor analysis approach is reliant on subjective judgment, mostly influenced by the forecaster's level of experience and theoretical knowledge [7].

4. Conclusion

The prevalence of chronic atrophic gastritis is influenced by various factors, including environmental conditions and microbial agents. Nevertheless, other variables remain contentious and warrant additional investigation. By considering these aspects, it is possible to formulate distinct preventative and treatment strategies tailored to various groups, hence facilitating timely intervention, prompt identification, and immediate therapeutic measures. Simultaneously, we can delve further into the interconnected elements by considering these factors, so establishing a groundwork for subsequent factor determination.

One limitation of this paper is the lack of rigor in the selection of relevant literature, which results in a poor association. Simultaneously, the numerical value is quite low and the level of persuasion is lacking in strength. The examination of the data is preliminary, and its value as a subject of study remains inconclusive. The current study lacks rigorous inquiry and analysis, relying mostly on a literature review

methodology. Consequently, the article's content is quite limited, exhibiting weak correlations and a lack of persuasive evidence. In future research endeavors, it is recommended to employ more methodologically sound survey methodologies, employ more sophisticated statistical models with enhanced mathematical rigor, employ a diverse range of analytical approaches, and undertake comprehensive field analysis and study.

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