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RESEARCH ARTICLE

Clinical characteristics and endoscopic findings in autoimmune gastritis – A retrospective study

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Objectives: Autoimmune gastritis (AG) is a rare condition that increases the risk of developing stomach adenocarcinomas or carcinoid tumours. The objectives of the present research were to summarise the clinical traits of AG patients, together with gastroscopic and histopathologic findings, demographic data, and hematologic characteristics. **Patients and methods**: A medical centre assessed 58 AG patients from January 2019 to December 2022. **Results**: The majority of the patients were female (73.7%), and the mean age of the participants at the time of the diagnosis was 57.7 ± 12.1 years. We identified pernicious anaemia (54.4%), iron deficiency anaemia (21.1%), as well as autoimmune disorders (96.5%). Though 78.9% of patients reported having gastrointestinal symptoms, 69% presented exclusively upper gastrointestinal symptoms, 17% only had lower, and 14% had concurrent upper and lower gastrointestinal symptoms. All 58 AG patients were examined for associated gastric lesions, although abnormal injuries were detected in only 22 of them. One patient (1.8%) had adenocarcinoma, while five patients (8.8%) had type 1 neuroendocrine tumours (NET). In addition, hyperplastic polyps were found in 16 (28.1%) individuals. **Conclusions**: Other autoimmune diseases were present with AG, which showed a female predominance. Clinicians should give AG more significant thought by allowing access to interdisciplinary teams.

Keywords: autoimmune gastritis, iron/vitamin B12 deficiency, antiparietal cell antibody, multidisciplinary team

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Introduction

Autoimmune gastritis (AG), a form of chronic gastritis, is caused by the generation of autoantibodies against the proton pump in parietal cells, which destroys the gastric parietal cells [1]. Atrophy and inflammation are limited to the gastric corpus and do not impact the antrum because parietal cells are located in the fundus and corpus glands. The complete destruction of the parietal cells that produce hydrochloric acid and an intrinsic factor results in pernicious anaemia and iron deficiency anaemia. This condition also induces enterochromaffin-like cell hyperplasia and hypergastrinemia, which result in side effects such as hyperplastic polyps, gastric cancer, or NETs [2-8].

Additionally, autoimmune diseases of extra-stomach epithelial tissues like the pancreas or thyroid gland and a high prevalence of malignant neoplasms in other organs have been linked to AG [9-13]. Therefore, AG is a gastric disorder but should be identified as a systemic disease [13]. In the early stages of the disease, AG is clinically "silent." Consequently, the diagnosis of this condition is based only on clinical suspicion [13].

Early detection is essential because AG can develop iron deficiency and/or pernicious anaemia, which are connected to a higher risk of developing gastric pre-malignant and malignant conditions [12,13]. Unawareness of this illness may lead to patients being misdiagnosed and, as a result, receiving poor treatment. Our study sought to identify the clinical symptoms, endoscopic, laboratory, and related variables in patients with AG for this reason.

Methods

Patients

Analysis was performed on 58 adult AG patients (>18 years) diagnosed from January 2019 to December 2022. The Sydney-Houston pathologic criteria [14] and the occurrence of antiparietal cell antibodies (APA) were used to confirm the diagnosis of AG. According to the evaluation of at least five biopsy fragments taken from the corpus (2), the incisura angularis (1), and the more significant and lesser curvature of the antrum (2), AG was defined by the occurence of moderate to severe atrophy of the fundus/body with antrum sparing (1). In addition, the demographic information of each patient was also recorded, including age, gender, family and medical history, associated diseases, age at diagnosis, the presence of concurrent autoimmune disorders, medication history, and symptoms or indications possibly requiring an upper gastrointestinal (UGI) endoscopy.

Through a structured interview, we also evaluated the incidence and frequency of gastrointestinal (GI) symptoms at the patient's initial visit, including heartburn, nausea, early satiety, vomiting, regurgitation, postprandial fullness, epigastric and abdominal pain, diarrhoea, constipation and bloating.

Each participant gave informed consent, and the study received approval from the hospital ethics committee.

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Laboratory Tests

After being subjected to overnight fasting, all patients underwent a procedure for obtaining a venous blood sample in order to determine serum gastrin, iron, vitamin B_{12}, APA and anti-H. Pylori IgG levels. Routine laboratory procedures determined regular haematological and biochemical tests. The pattern of anaemia was assessed by measuring the haemoglobin, mean corpuscular volume (MCV), vitamin B12, and ferritin levels. A low haemoglobin concentration, an MCV > 100 fl, and vitamin B12 deficiencies were symptoms of pernicious anaemia that responded to intramuscular B12 vitamin therapy. Low haemoglobin concentration, MCV<80 fl, and ferritin<30 ng/mL were used to define iron deficiency anaemia [15,16]. Plasma gastrin level was determined using the radioimmunoassay with polyethylene glycol, and the presence of APA was determined in serum with an immunofluorescence technique. The threshold for an APA positive finding was 10≥U, and the threshold for a serum gastrin typical result was ≤120 pg/mL. Both serologic testing and histological examination of H. pylori infection were performed. Patients had not taken proton pump inhibitors (PPIs) for at least two months before the examination date. The investigation removed five patients having pathologic results consistent with AG but APA negative.

Gastroscopic Examinations

After temporary fasting, a certified endoscopist conducted endoscopic examinations at our hospital using a FUJIFILM endoscope, particularly on gastric macroscopic lesions. The endoscopist evaluated each patient registered in this study in order to detect the existence of specific endoscopic findings such as corpus-dominant atrophy, removal of the gastric folds, sticky adherent dense mucus and remnant oxyntic mucosa; moreover, the investigation was meant to highlight other comprehensive results like cancer, NET, adenoma, and hyperplastic polyps. Findings were concordant to the global impression of the particularity of any macroscopic lesion. Polypoid lesions were categorized macroscopically in accordance with Kudo's Classification [17]. When the corpus and fundus showed more evidence of gastric mucosal atrophy than the antral region, as was predicted based on visible submucosal vessels in endoscopic appearances, those cases were recorded as suspected AG.

Statistical Analysis

Descriptive statistics included computing means and standard deviations (SD) for numeric variables and absolute and relative frequencies (%) for categorical variables. Comparisons were performed between (a) patients with gastrointestinal symptoms vs anaemia, and (b) patients with vs without HPA. We used the Kolmogorov-Smirnov test to determine normality of data. Furthermore, to compare numerical data with normal and non-normal distribution the Student's t-test and Mann-Whitney test were used. In order to compare categorical data we used the Fischer exact test. Two-tailed p-values were calculated at a significance level of 0.05.

Results

In our investigation, we included a total of 58 patients diagnosed with AG, out of which 42 (73.7%) were women and 15 (26.3%) were men; the female-male ratio was 2.8:1. At the time of diagnosis, the patient's mean age was 57.7 ± 12.1 years (range 30–80). 4.9% (n=37) of patients reported moderate coffee intake (1-3 cups/day), while 14.0% (n=8) of patients reported regular smoking. In addition, 1.8% of our patients reported drinking on a daily basis (n=1). In contrast, 91.2% (n=52) of AG patients did not drink alcohol, while 7% (n=4) did so occasionally. Gastrointestinal symptoms (group 1, n=45, 78.9%) and anaemia (group 2, n=21, 36.8%) were the first triggers for a UGI endoscopy. Hypergastrinemia (4/58, 7%) and neurological symptoms (1/58, 1%) were additional clues. In 78.9% (n=45) of the AG patients, there were one or more gastrointestinal problems. Table I lists the gastrointestinal signs and symptoms that patients were referred to our clinic for. Notably, none of these complaints is regarded as indicators of AG.

In the group of symptomatic patients, the majority (n = 40) complained only of upper gastrointestinal symptoms. In contrast, a smaller number (n = 10) complained only of lower gastrointestinal symptoms, while eight patients had concurrent upper and lower gastrointestinal symptoms (Figure 1).

UGI endoscopy was performed on all 58 patients. The results showed varying degrees of mucosal thinness, planed or decreased rugal folds, and submucosal grid vessels in the corpus or fundus, whereas the antral mucosa was roughly normal. In 28 cases, a sticky, adhesive mucous that was firmly adhered to the mucosa of the fundus did not resemble the milky, clouded mucous formed by H. pylori infection.

Related gastric lesions were assessed in all 58 patients, and 22 presented abnormal lesions. One patient (1.8%) had adenocarcinoma, while five patients (8.8%) had type 1 NET. In 16/58 (28.1%) patients, hyperplastic polyps were found. The median diameter of type I NETs was 5 mm (range 1–25 mm). All NETs situated in the gastric fundus

Table I. Frequency and percentage of gastrointestinal symptoms in the 58 patients of AG

Symptoms	N	%
Epigastric pain	35	61,4
Abdominal pain	21	36,8
Bloating	18	31,6
Acid regurgitation	16	28,1
Heartburn	16	28,1
Vomiting	10	17,5
Nausea	8	14,0
Constipation	6	10,5
Diarrhea	5	8,8
Weight loss	5	8,8

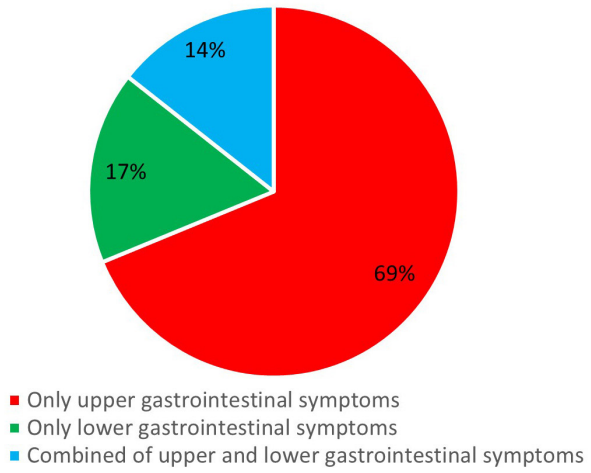

Fig. 1. Distribution of patients based on the type of reported gastrointestinal symptoms

and corpus, morphological characteristic shows principally protruding polypoid lesions (Figure 2). Central depression of the lesion appeared in 3 cases. The color tone was generally light yellow or red or was the same color as the surrounding mucosa. Type I NETs was treated via endoscopic resection in all five patients. The histopathological imaging of type I NET shows proliferation of neuroendocrine cells arranged in nests, cors or trabecules. The cells are bland, round to oval with typical salt amd pepper chromatin and amphophilic cytoplasm (Figure 3).

One patients had adenocarcinoma. The endoscopic picture shows an irregular depressed tumor in the posterior wall of the gastric corpus (Figure 4). Pronounced vascular visibility and the disappearance of folds are detected in the lesser curvature of the corpus. Biopsies from the lesion showed gastric adenocarcinoma (Figure 5). The patient underwent total gastrectomy.

Gastric hyperplastic polyps were found at endoscopy in 16 patients (six solitary, ten multiple) (Figure 6). Polyps were situated in the antrum alone in six patients, in the body and fundus in 10. Polyps of the body and fundus were mostly mutiple, while solitary polyps were more frequent in the antrum. Only five polyps were larger than 1cm in diameter, the greatest being 1.5 cm. Biopsies were taken from the surface of the polyps in 16 patients; and they proved to be hyperplastic on histology (Figure 7). Endoscopic polypectomy was performed.

In AG patients under 40, no gastric endoscopic lesions were discovered; each patient who presented gastric lesions was older than 40. The incidence of gastric lesions was also unrelated to H. pylori ($p = 1.0$), iron deficiency ($p = 0.9086$), gender ($p = 0.3709$), accompanying autoimmune illnesses ($p = 0.7758$), and smoking ($p = 0.4657$). B12 levels were considerably lower in patients with gastric lesions than those without (140.8 pg/ml and 259.2 pg/ml, respectively; $p = 0.0318$). In patients with lesions, serum gastrin levels were substantially higher (611.7 pg/

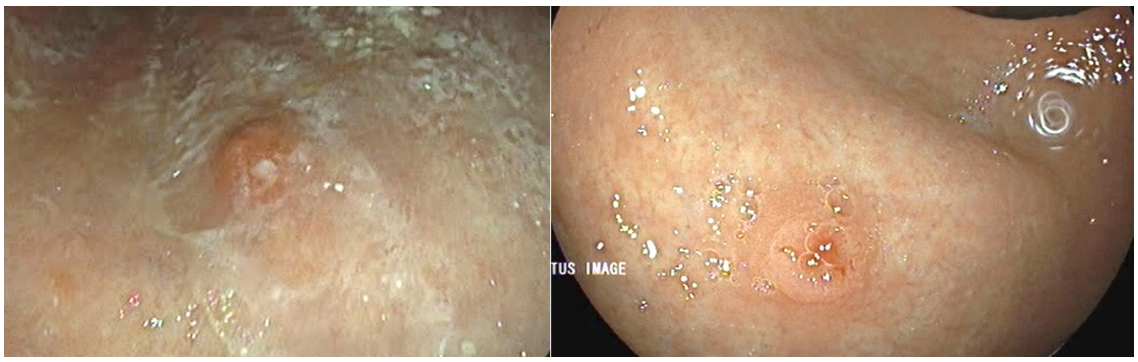

Fig. 2. Endoscopic images of type I gastric NETs with a background of atrophic gastritis. The endoscopic picture shows polypoid lesions in the greater curvature of the corpus with the disappearance of folds. The tumor is gently elevated.

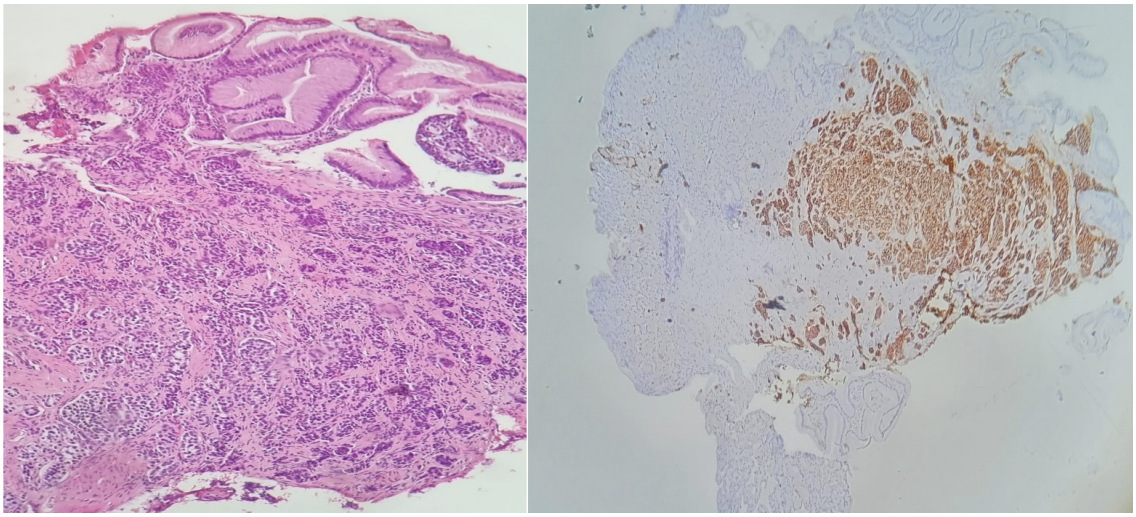

Fig. 3. Histopatological imaging of type I NET

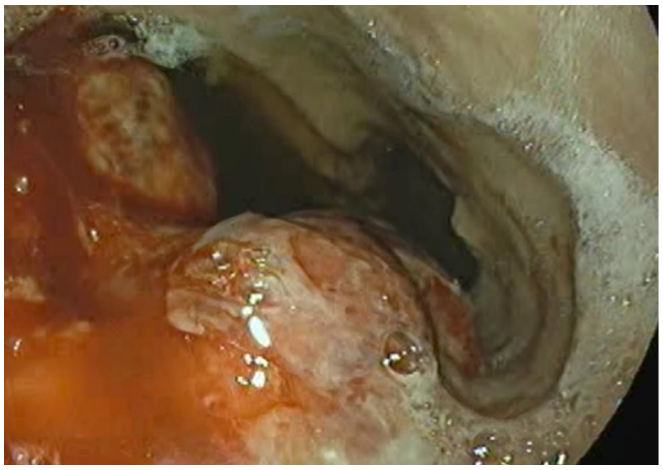

Fig. 4. Endoscopic images in gastric cancer patients with AG

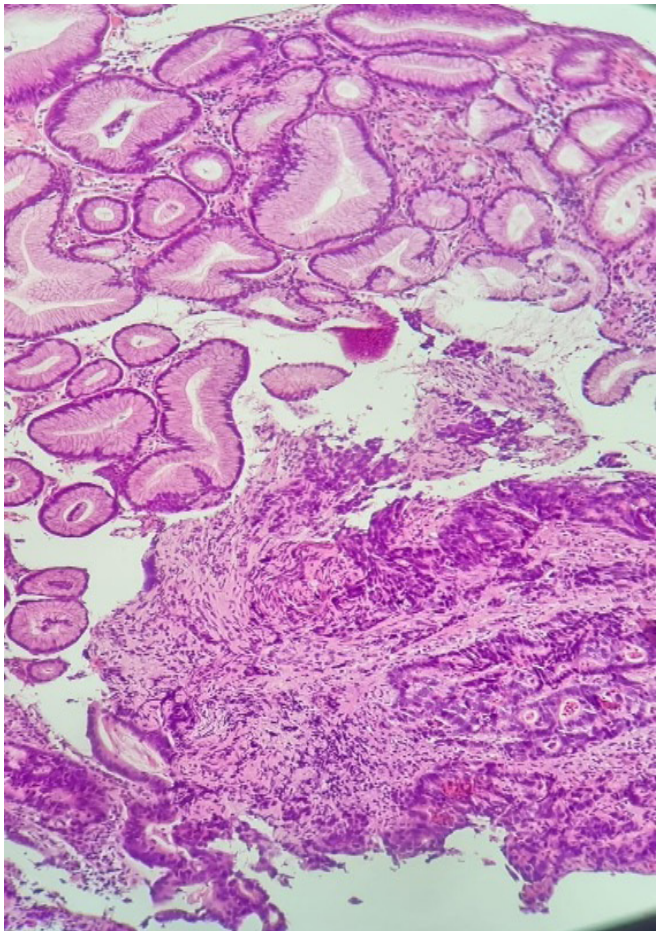

Fig. 5. Neoplastic tubules or intestinal glands resembling colonic adenocarcinoma, may contain apical mucin vacuoles

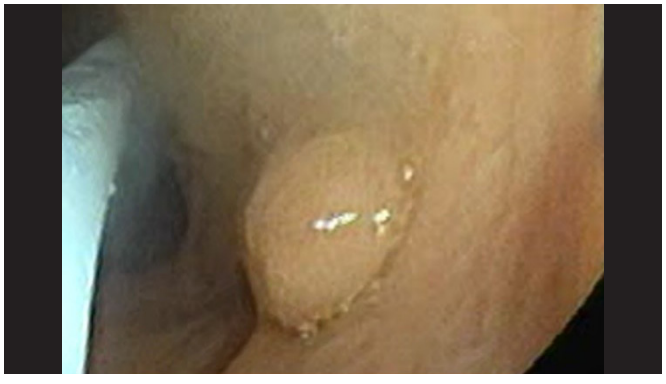

Fig. 6. Enoscopic image of hyperplastic polip

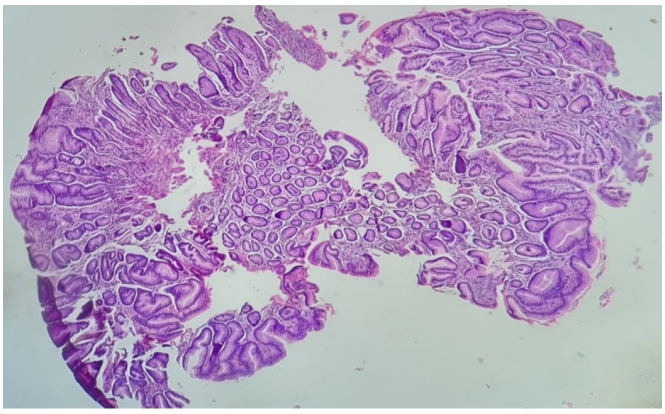

Fig. 7. Elongated, branching, and dilated hyperplastic foveolae lying in an edematous, hypervascular, inflammatory stroma

ml vs. 369.5 pg/ml; p = 0.0103). Patients in group 1 had more gastric endoscopic lesions than patients in group 2, according to research (p=0.4682). All of the patients had hypergastrinemia (mean, 462.9352.9 pg/mL; range, 122-2133 pg/mL), 100% of the serum APA tests were positive (58/58), and the average levels of blood B12 and iron were 66.639.2 ug/dl and 214.6185.5 pg/mL, respectively. Based on MCV, patients were distributed as follows: 24 patients presented an MCV > 100 fl, 4 had an MVC < 80 fl, while 26 had normocytic (MCV 82.9–98 fl) indices. Twenty-one cases (36.8%) were found to have anaemia, of which 12 (21.1%) had iron deficiency anaemia, and 30 (54.4%) had megaloblastic anaemia. Average folic acid levels were present in each subject. The histological examination revealed no evidence of H. pylori infection in any of the patients. However, a serologic test showed that 16 patients (28.1%) were positive for H. pylori. Fewer patients in group 2 tested positive for H. pylori by serology than in group 1 (3 vs 9). Nevertheless, the difference did not meet statistical significance (p=1). 56 of the 58 patients had other autoimmune illnesses at the same time. The most prevalent condition was chronic autoimmune thyroiditis (23 of 58; 41.1%), which was followed by alopecia (1 of 58; 19.3%), rheumatoid arthritis (8 of 58; 14%), vitiligo (6 of 58; 10.5%), psoriasis (5 of 58; 8.8%), and type I diabetes mellitus (3 of 58; 5.3%).

In 40% of patients with joint disorders such as diabetes, osteoporosis, cardiovascular diseases, and dyslipidemia, polypharmacy (the use of more than two medicines) was prevalent. Approximately 20% of patients took prokinetics. Serum gastrin levels significantly differed between group 1 — patients with abdominal symptoms — and group 2 — patients with iron/B12 deficiencies (Table II).

Sixteen (28.1%) patients tested positive for anti-H. Py lori IgG. Patients with and without H. pylori did not differ in terms of gender, age, smoking habits, serum gastrin, or vitamin B12. (Table III)

Discussion

The development of chronic, ongoing inflammation and gastric mucosal atrophy in the body and fundus of the

Table II. Demographic, laboratory and clinical features and comparison of these parameters according to the symptom groups.

	Group 1- abdominal symptoms	Group 2 - iron/B12 deficiency	p
Age (years); mean (SD)	58.2 (11.9)	63.2 (12.3)	0.2065 [a]
Sex; n (%)			
Female	29 (82.9)	6 (17.1)	0.1399 [b]
Male	8 (61.5)	5 (38.5)	
Smoking; n (%)			
Non-smoker	30 (73.2)	11 (26.8)	0.1791 [b]
Smoker	7 (100.0)	0 (0.0)	
Anti-H. pylori IgG; n (%)			
Yes	9 (75%)	3 (25.0)	1.0 [b]
No	28 (77.8)	8 (22.2)	
APA (U/ml); medie (SD)	57.7 (33.5)	65.7 (24.3)	0.4654 [c]
Gastrin (pg/ml); mean (SD)	388.9 (280.2)	711.8 (538.1)	0.0133 [a]
B12 (pg/ml); mean (SD)	257.7 (201.5)	141.2 (119.1)	0.1162 [a]

a: Mann-Whitney test; b: Fischer exact test; c: student t test

stomach is caused by AG, which is created by cellular and humoral immune reactions against gastric parietal cells [1,18,19]. Anacidity, iron deficiency anaemia and pernicious anaemia are apparent in affected patients as the condition progresses [20,21]. The prevalence of AG varies depending on the criteria utilized, and no definitive criteria for diagnosis have been recognized [22]. The prevalence has also been noted to differ amongst various populations and groups [18,19]. The primary diagnostic criteria for this condition are mucosal atrophy and inflammation brought on by the immune system's response to parietal cells.

Our group exhibited a much larger percentage of female patients with AG, in line with studies on Western and Asian [23,24] populations demonstrating a higher frequency of AG in females and the elderly (73.3%).

The most frequent reasons for people to seek medical care are gastrointestinal symptoms and an iron/vitamin B12 deficiency. Purdy et al.[25] investigated 56 patients highlighting similar results with our findings. Thus, 74% of their patients were female, with a median age of 62 and most of their symptoms (29%) were pain related. In our study, pain was related to abdominal bloating. Most symptomatic AG patients (about 70%) reported upper gastrointestinal problems. One-fourth of the reported upper gastrointestinal symptoms were GERD-related, whether the condition was remote or in conjunction with dyspepsia.

The incidence of pernicious anaemia in our sample (43.1%, 25/58) is consistent with earlier publications [26], while the prevalence of iron deficiency anaemia in our group (13.7%, 8/58) is consistent with the most recent report [27].

Other autoimmune diseases, such as thyroid conditions or alopecia, were usually present in 56 out of 58 (98.5%) patients, a result highlighted in earlier publications [28, 29]. Therefore, even though gastric NETs and stomach cancer are frequently believed to be the side effects of AG, it is imperative to thoroughly take into account the consequences of other autoimmune diseases at the time of diagnosis and during follow-up [30].

Our data evidenced no ongoing H. pylori infection in patients included in the present study; still, anti-H. Pylori IgG was positive in 16 (28.1%) of them. Gender, age, smoking habits, vitamin B12 and serum gastrin levels did not differ between H. pylori-positive and H. pylori-negative individuals. When examined with serology and histology, two-thirds of patients who presented atrophic corpus gastritis confirmed H. pylori infection, according to Annibale et al. [31] In a similar study, the same researchers identified that H. pylori serology was positive in 62% of patients who presented atrophic corpus gastritis and pernicious anaemia [32]. Nevertheless, according to Mini et al. [33] among the 111 patients with atrophic corpus gastritis with negative H. pylori serology 95.5% presented positive immunoblotting. Unfortunately, we lacked the necessary conditions to use this method to research our patients. Subsequently, bacterial contamina-

Table III. Association between clinical and laboratory parameters and H.pylori status

	Serologic H.pylori positive AG patients	Serologic H.pylori negative AG patients	p
Age (years); mean (SD)	58.0 (12.7)	60.6 (11.6)	0.4674 a
Sex; n (%)			
Female	14 (33.3)	28 (66.7)	0.1896 b
Male	2 (13.3)	13 (86.7)	
Smoking; n (%)			
Non-smoker	14 (28.6)	35 (71.4)	1.0 b
Smoker	2 (25.0)	6 (75.0)	
Gastrin (pg/ml); mean (SD)	340.4 (206.3)	507.2 (391.3)	0.1081 c
B12 (pg/ml); mean (SD)	160.9 (159.6)	232.7 (192.3)	0.0639 c

a: Student t test; b: Fischer exact test; c: Mann-Whitney test

tion may be an essential autoimmune process in the advancement of AG.

AG is characterised by progressive corpus dominant mucosal atrophy, pale mucosa with clear submucosal vascular visibility and non-atrophic mucosa in the antrum. Additional endoscopic features comprise remnant oxyntic mucosa and viscous adherent thick mucus [34]. AG can lead to neoplastic transformations as a chronic inflammatory illness, such as gastric adenoma or adenocarcinoma [6,35]. One of the typical concomitant gastric lesions of AG is type 1 NET. Type 1 NET is defined as having a variable prevalence in AG. According to a study, NET prevalence in AG ranged from 5.2% to 11% [36]. A histological review conducted in the USA [36] revealed a prevalence of NET of 9.97%, whereas a Chinese study [37] revealed a prevalence of 4.37%. Our analysis discovered a prevalence of 8.6% (5/58) consistent with other results.

Endoscopic lesions in 461 individuals with AG were evaluated by Park et al. [5]. They came to the conclusion that individuals with AG are much more likely to acquire polyps and neoplasms since 143 of these patients had 240 gastric endoscopic lesions (179 polyps, 46 gastric carcinoids, 11 adenocarcinomas, 3 lymphomas, and 1 gastrointestinal stromal tumour (GIST). We identified gastric lesions in 22 (37.9%) of our patients (type I NET in 5, adenocarcinoma in 1, and hyperplastic polyps in 16 patients). In this research, all the patients diagnosed with gastric lesions were older than 40 and had significantly lower B12 levels and higher serum gastrin levels ($p = 0.0103$) than those without lesions ($p = 0.0318$).

Consistent endoscopic surveillance of AG patients is essential to detect concurrent gastric neoplasms early. Unfortunately, especially in the early stages, diagnostic delays happen frequently, given the indolent progress and usually quiet clinical appearance of the disease. Therefore, clinicians should be knowledgeable about the best diagnosis and treatment techniques to lower the risk of unfavourable outcomes. Our research, we think, will make possible AG diagnosis simpler. According to our data, most AG patients were female, and comorbidity with other autoimmune diseases was relatively common. Although this group's clinical manifestations varied, most patients sought medical attention for symptoms associated with abdominal bloating and iron and/or vitamin B12 deficiencies. The heterogenity of this condition's clinical signs should be known to doctors. As a result, female patients who exhibit signs of stomach bloating or iron/B12 deficiency should be evaluated. Since patients with AG may develop many gastric lesions, it is critical to recognize AG in daily practice. Serum gastrin levels tended to be higher in patients with cancer than in those without cancer. Moreover to H. pylori infection, hypergastrinemia with severe corporal atrophy, the duration of the disease and age over 40 years may be considered a risk factor for gastric cancer complicated by AG. Due to its complexity and an elevated risk for malignancy, clinicians should give AG more serious consideration; it is crucial to establish a specialised multidisciplinary team (pathologists, gastroenterologists, endocrinologists, immunologists, haematologists, and surgeons) to thoroughly assess patients with AG.

The current study contains several drawbacks. Firstly, it was a retrospective study that took place in a single centre. Secondly, the levels of anti-intrinsic factor antibodies were not determined; the diagnosis of AG was restricted to endoscopically reported atrophy and serological APA levels. To better comprehend the aspects of this condition, a more thorough, comprehensive investigation is required.

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Authors' contribution

GG – significant contributions to conception and design, systematic literature research, choosing studies to include, data analysis and interpretation, writing the article and critically reviewing it for significant intellectual content, and final consent of the version that will be published.
VN - analysis and interpretation of the data, writing and critically editing the research for main intellectual content, and final publishing consent.
IN- analyzing and interpreting data, writing, and critically editing the research paper for important intellectual content, and final publishing consent
MP - data interpretation, critical revision for meaningful intellectual content, and final publishing consent
IB - data interpretation, critical revision for significant intellectual content, and final consent of the version that will be published
MB - data interpretation, critical revision for substantial intellectual content, and final consent of the version that will be published
CN- data interpretation, critical revision for important intellectual content, and final consent of the version that will be published

Conflict of interest

None to declare.

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