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Alimentary Tract

Changing prevalence patterns in endoscopic and histological diagnosis of gastritis? Data from a cross-sectional Central European multicentre study

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ABSTRACT

Background and aims: Traditionally, *Helicobacter* infection is considered to be the most common cause of gastritis. In the cross-sectional Central European *histo*GERD trial, we assessed the prevalence of different types of gastritis, correlating histological and endoscopic diagnoses.
Methods: A total of 1123 individuals participated in an observational multicentre study. Endoscopists classified individuals as positive or negative for gastritis and rendered the putative cause. Pathologists evaluated biopsy specimens based upon the Updated Sydney System.
Results: Histological diagnosis of gastritis was made in 639 (56.9%) participants. In all, 210 (18.7%) individuals were diagnosed with *Helicobacter* gastritis, 215 (19.1%) with post *Helicobacter* gastritis, 234 (20.8%) with reactive gastropathy, 26 (2.3%) with autoimmune gastritis, and 6 (0.5%) with focally enhanced gastritis related to Crohn's disease. In 46 out of 639 (7.2%) individuals diagnosed with gastritis, combinations of different histological subtypes were noted the most common being reactive gastropathy and post *Helicobacter* gastritis. Endoscopic diagnosis of gastritis was made in 534 (47.6%) individuals.
Conclusions: Reactive gastropathy was more common than active *Helicobacter* gastritis, and the majority of cases attributable to *Helicobacter* infection were no longer ongoing, i.e. post *Helicobacter* gastritis. Agreement between histological and endoscopic diagnoses was better in reactive gastropathy than in *Helicobacter* gastritis.

1. Introduction

Traditionally, *Helicobacter* infection is regarded as the most common cause of chronic gastritis. Its prevalence, however, is known to show considerable geographic variability mainly depending on the socio-economic status of the population. Thus, the prevalence of *Helicobacter* infection in Europe and the United States ranges up to 40% [1–4], while from South America and from Asia prevalence rates as high as 48–82% have been reported [3–5]. Reactive gastropathy represents another distinct type of gastritis that is caused by bile reflux through the pylorus and intake of nonsteroidal anti-inflammatory drugs [6,7].

The correlation between endoscopic appearance of the gastric mucosa and histological diagnosis of gastritis is considered to be weak [8–10]. Almost three decades after the discovery of *Helicobacter* infection as major cause of gastritis [11], ultimately leading to widespread eradication therapy, we posed the question if there is a shift in the prevalence of the different types of gastritis in Central Europe and if the routine use of high resolution endoscopy in routine diagnosis may have improved the correlation between

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endoscopic and histological findings. Therefore, our cross-sectional multicentre study aimed at assessing the actual prevalence of different types of gastritis, collecting epidemiologic data and correlating histological findings with endoscopic data.

2. Methods

2.1. Study design

Participants were recruited in the cross-sectional multicentre Central European *histo*Gerd trial that aimed at investigating clinical, particularly endoscopic data and histological findings in individuals, with and without symptoms of reflux disease who underwent endoscopic evaluation of their upper gastrointestinal tract.

In Austria three clinical departments (Department of Internal Medicine, Krankenhaus der Barmherzigen Brüder, St. Veit/Glan, Department of Surgery, Division of General Surgery, and Department of Internal Medicine, Division of Gastroenterology and Hepatology, Medical University of Graz, Graz, Austria) and in Germany two private practices (Dr. M. Geppert and Dr. B. Schmack, Bayreuth, and Dr. H. Bordel, Dr. R. Müller and Dr. B. Wigginghaus, Osnabrück) participated in the investigation.

During the study period, individuals (females and males) scheduled for elective endoscopic examination for various, unselected reasons were offered participation. We excluded those with previous surgery leading to abnormal anatomy in the upper gastrointestinal tract, particularly at the gastroesophageal junction. In Austria, participants were recruited between November 2011 and April 2012, in Germany between December 2011 and May 2012, respectively.

Data will be presented following the STROBE Statement aimed at strengthening the reporting of observational studies [12].

2.2. Endoscopy

The upper gastrointestinal tract was examined according to a standardised protocol devised for the study. Biopsies were systematically taken with a minimum of two antrum and two corpus biopsies, based upon the Updated Sydney System [13]. Routine biopsies of the incisura angularis were not taken, as their impact is controversial [14]. We used a standardised reporting system, including both clinical (basic demographic data, patients' symptoms and indication for the procedure, with multiple answers possible) and endoscopic data.

Based upon standard criteria, such as mucosal redness and/or friability, the endoscopists had to classify participants as positive or negative for the diagnosis of gastritis. If participants were considered positive, the endoscopists were additionally asked to render the most probable aetiology, i.e. *Helicobacter* gastritis, reactive gastropathy, or autoimmune gastritis. Specifically, the endoscopists rendered a diagnosis of putative *Helicobacter* gastritis when they observed patchy or diffuse erythema, accompanied, in varying extent, by enlargement of mucosal folds, haemorrhage as well as signs of mucosal atrophy, such as discoloration, thinning, and transparency of vessels [15]. Reactive gastropathy was considered when the inflammatory changes were accentuated in the prepyloric antrum showing oedema and redness, typically as reddish streaks within intact mucosa, sometimes also superficial flat or elevated erosive changes [16]. Endoscopy was considered suggestive of autoimmune gastritis when inflammatory and, particularly, atrophic changes prevailed in the corpus. If classification did not appear feasible, individuals were recorded as "unclassifiable gastritis".

All endoscopists were very experienced in the field, the majority of them working in endoscopy units for at least one decade with more than 500 gastroscopies per year. Before the investigation, all endoscopists were trained in order to familiarise them with the biopsy protocol and the reporting system. For endoscopy, four institutions used the OLYMPUS EVIS EXERA II series (Olympus Europe Holding GmbH, Hamburg, Germany) with video gastroscopes GIF-H180 and Q180, respectively. One institution (Osnabrück) used the FUJI EPX-4450HD Electronic Video Endoscopy System with EG-590WR video gastroscopes (Fujifilm Corporation, Tokyo, Japan). Computed virtual chromoendoscopy (e.g. narrow-band imaging) was not applied routinely to detect gastritis.

2.3. Histology

Biopsy specimens were fixed in 10% neutral buffered formalin and embedded in paraffin, sectioned at 4–5 levels and stained with haematoxylin and eosin. In equivocal cases, *Helicobacter* infection was assessed using Warthin-Starry Silver stain. All biopsies were examined by two experienced gastrointestinal pathologists (M.V. and C.L.) who were blinded to clinical data including endoscopic findings.

The inflammatory infiltrate of *Helicobacter* gastritis, variations in *Helicobacter* density, and the extent of intestinal metaplasia were assessed according to the visual analogue scales presented in the Updated Sydney System [13]. Post *Helicobacter* gastritis (syn. ex-*Helicobacter* gastritis) was diagnosed in cases with mild, non-active, chronic inflammation, with or without lymphoid aggregates (and intestinal metaplasia), and normal surface epithelium [8,17]. Diagnosis of reactive gastropathy was made following Dixon's criteria [6]: foveolar hyperplasia, oedema and proliferation of ascending smooth muscle fibres in the lamina propria, vasodilatation and congestion of superficial mucosal capillaries, as well as paucity of acute and chronic inflammatory cells. Diagnosis of autoimmune gastritis was made in cases presenting with oxyntic cell injury and advanced glandular atrophy and intestinal metaplasia affecting the corpus mucosa. In end stage disease "pseudopyloric" mucus gland metaplasia and pancreatic acinar cell metaplasia are a common finding. In contrast to the gastric corpus, the mucosa of the antrum may appear normal or may show minor inflammatory changes [8,18]. In cases with established diagnosis of Crohn's disease, involvement of the stomach was diagnosed in the presence of focally enhanced gastritis, with or without non-caseating granulomas, aphthous erosions and/or fissures [18].

2.4. Ethics

The investigation was carried out in accordance with the Declaration of Helsinki. Each participant provided written informed consent. The study was approved by the Institutional Review Boards of the Medical University of Graz (EK 24-052 ex 11/12) and the University of Erlangen (EK 4571 ex 11/12), respectively, and was registered at ClinicalTrials.gov (NCT01576289).

2.5. Statistical analysis

All data were included within a joint database. The quality of this database was tested by random sample taking in 5% of the recruited participants which revealed mis-reporting in 0.14%. Categorical variables are presented as absolute and relative frequencies, numerical variables as medians and ranges, as well as means. Differences in categorical variables were examined using the chi-square test or Fisher's exact test, as appropriate. Differences in continuous variables between groups were analysed using the Mann–Whitney *U*-test or one-way ANOVA on ranks (Kruskal–Wallis test). All statistical calculations were performed using NCSS: Hintze, J. (2007).