Helicobacter-negative Chronic Active Gastritis is an Independent Nosologic Entity, Not Merely Missed *Helicobacter* Infection: A Nationwide Study of 600,000 Patients

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Background

Helicobacter-negative chronic active gastritis is a histopathologic entity characterized by diffuse chronic active inflammation in a pattern typically encountered in *H. pylori* gastritis, but with no organisms detectable by conventional histology or immunohistochemical staining.

The most commonly offered hypotheses to explain this finding include: 1) sampling error, presuming that organisms would be found if searched for in other areas of the stomach; 2) recent use of antibiotics, which may have resulted in incidental eradication or suppression; and 3) effects of proton pump inhibitors, which both decrease and shift proximally the bacterial load.

A recent study explored these hypotheses and could not find support for any of them (Nordenstedt et al., *Am. J. Gastro* 2012).

Aims

We hypothesized that if *H. pylori*-negative gastritis was nothing but a subset of cases of *H. pylori* gastritis in which no organisms could be found, its epidemiologic patterns should be essentially identical to those of *H. pylori* gastritis.

On the other hand, if the epidemiologic patterns of *H. pylori*-negative gastritis were substantially different from those of *H. pylori* gastritis, this evidence would provide support for the notion that these conditions represent two independent nosologic entities.

The aims of the present study were to compare the epidemiologic patterns of *H. pylori* positive and negative gastritis.

Methods

Using the Miraca Life Sciences database, we extracted histopathologic and demographic information from all patients who had an esophagogastroduodenoscopy (EGD) with gastric biopsies between January 2008 and June 2012.

We then selected two groups: patients from ZIP codes where the mean tissue prevalence of *H. pylori* infection was ≤ 6% ("low-prevalence zone") and those from ZIP codes with a mean prevalence ≥ 12% ("high-prevalence zone").

Each group was then stratified in 8 age strata, and the relative prevalence of *H. pylori* gastritis and *H. pylori*-negative gastritis in the two zones were compared for each age group.

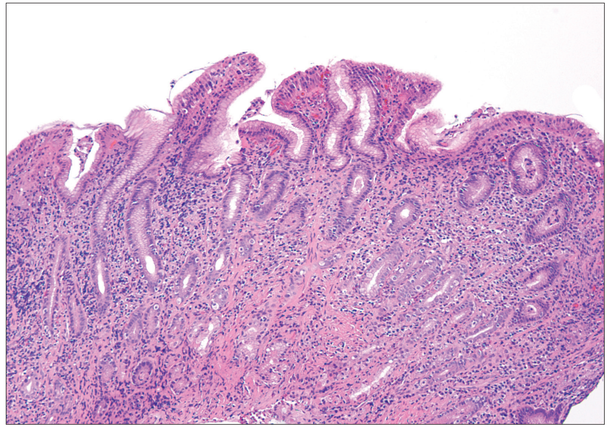

Figure 1 – This biopsy specimen shows the characteristic features of *H. pylori* chronic active gastritis; however, no organisms could be visualized in either this or other specimens from the same patient.

Results

There were 596,480 unique patients with gastric biopsies (median age 57 years; 62% female).

Low-prevalence zones included 79,874 subjects (median age 57 years; 60.8% female), while high-prevalence zones included 156,445 subjects (median age 61.9; 61.9% female).

The results are depicted in Figure 2.

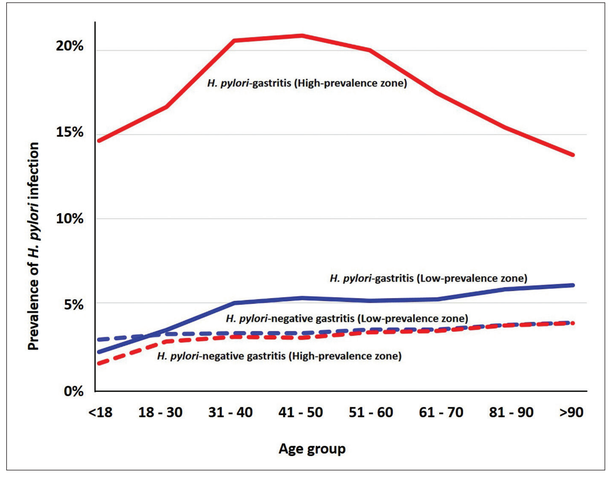

Figure 2 – In high-prevalence zones, *H. pylori* infection peaked in the 5th decade and declined after age 80 (solid red line); in low-prevalence areas it increased steadily at much lower levels in each decade (solid blue line).

In contrast, the prevalence of *Helicobacter*-negative-gastritis was very low in both zones (dotted red and blue lines), both showing only a small increase with age.

Study Highlights

- Although *H. pylori* DNA has been demonstrated in a small proportion of biopsy specimens with apparent *H. pylori*-negative gastritis, the vast majority of cases remain unexplained.
- Sampling error, recent use of antibiotics, and suppression of the infection caused by the use of proton-pump inhibitors have been shown to have no significant association with *H. pylori*-negative gastritis.
- **Our epidemiologic data confute the concept that *H. pylori*-negative gastritis merely represents a subset of *H. pylori*-positive gastritis in which organism are not seen ("missed infections").**
- Other yet undetected bacteria or viruses could be responsible for this entity, found in 1% to 4% of all patients who have gastric biopsies.

References

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