Correlation between functional gastrointestinal disorders and gastric mucosa histopathology findings, including *Helicobacter pylori* infection, in Lima, Peru

Correlación entre síntomas gastrointestinales funcionales y la histopatología de la mucosa gástrica, incluyendo la infección por Helicobacter pylori, en Lima, Perú

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ABSTRACT

Objective: This study aims to investigate the relationship between functional gastrointestinal disorders and histopathology characteristics, including *H. pylori* infection, of gastric mucosa, at Cayetano Heredia National Hospital, Lima-Peru, in 2013. **Materials and methods:** 112 patients were interviewed prospectively between June and July 2013 in the gastroenterology service. Dyspepsia, irritable bowel syndrome, and postprandial distress syndrome were characterized using the Rome III Survey. **Results:** Pathology results were determined by gastric biopsies obtained by endoscopy. Of the patients interviewed, biopsy results were obtained for 101. 22.8% had atrophy, 24.8% had intestinal metaplasia, 57.4% presented with *H pylori*. **Conclusions:** Using chi-square analysis, no statistically significant relationship could be identified between clinical presentation and biopsy results.

Key words: *Functional GI disorders, dyspepsia, irritable bowel syndrome, postprandial distress syndrome, gastric biopsy, Helicobacter pylori.*

RESUMEN

Objetivo: El objetivo de este estudio fue investigar la correlación que existe entre la presencia de síntomas gastrointestinales y los hallazgos histopatológicos de la biopsia gástrica incluyendo la presencia de la infección por *Helicobacter pylori*. **Materiales y métodos**: Este estudio prospectivo comprendió a 112 pacientes que se incluyeron entre junio y julio de 2013 en el Servicio de Gastroenterología del Hospital Nacional Cayetano Heredia, Lima-Perú a los que se les hizo endoscopía y biopsia gástrica. Los síntomas de dispepsia, síndrome de intestino irritable y síndrome de distrés post prandial fueron obtenidos usando las encuestas de Roma III. **Resultados:** De los pacientes a los que se les hizo la encuesta sólo en 101 se les evaluó la biopsia. 22,8% tuvo atrofia, 24,8% presentó metaplasia intestinal, y en 57,4% se reportó la infección por *Helicobacter pylori*. **Conclusiones:** Usando el análisis con chi-cuadrado no se pudo establecer ninguna correlación estadísticamente significativa entre la presentación clínica y los resultados de las biopsias.

Palabras clave: *Trastornos digestivos funcionales, dispepsia, síndrome de intestino irritable, síndrome de distrés post prandial, biopsia gástrica, Helicobacter pylori.*

INTRODUCTION

Gastric cancer is the most common cause of cancer mortality in both men and women in Peru. In fact, 94% of gastric cancer cases in Peru are detected at an advanced stage [(1)]. Infection with *Helicobacter pylori* has been associated with an increased risk for development of gastric cancer [(2-4)]. This association has led the World Health Organization to classify *H. pylori* as a type I carcinogen [(5,6)]. *H. pylori* has also been implicated in the development of a progressive series of precancerous lesions and other gastric pathology, including atrophic gastritis, intestinal metaplasia and gastric and duodenal ulcers [(7-9)]. Lasting eradication of *H. pylori* infection from the gastric mucosa may be able to halt this progression to cancer and serve as a cancer prevention strategy [(3)].

As with all cancers, early detection is the key. If symptoms could be found to direct attention to the possible or likely presence of *H. pylori* and/or precancerous lesions, clinicians could better monitor patients at risk for developing gastric cancer. While numerous studies have failed to find a significant relationship between gastrointestinal symptoms of dyspepsia and the presence of *H. pylori* [(10-14)], others have found a direct association. Perri et al found an association between pain-prevalent dyspepsia and *H. pylori* infection [(15)]. Vaira et al found that originally asymptomatic *H. pylori*-positive subjects were more likely to develop symptoms of dyspepsia than non-infected controls; additionally, *H. pylori* eradication was shown to prevent future development of both dyspepsia and peptic ulcers [(16)]. The aim of our study is to correlate clinical presentations of dyspepsia, postprandial distress syndrome and irritable bowel syndrome with histological findings on biopsy, namely the presence of *H. pylori* and precancerous lesions.

MATERIALS AND METHODS

Subjects:

112 patients between the ages of 18-70 participated in this study. Eligible participants presented to the gastroenterology

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department at Cayetano Heredia National Hospital (HNCH) with indications for an endoscopy. Exclusion criteria included: TB infections, HIV/AIDS, and gastrointestinal bleeding. Patients who presented for screening purposes only were excluded.

Data collection:

Patients were interviewed face-to-face using two questionnaires: 1) risk factors for *H. pylori* infections and 2) Rome III of general GI symptomatology. Surveys were translated to Spanish prior to administration. The following variables were collected: age, gender, endoscopic diagnosis, and histologic findings of the biopsy. Patients were interviewed by non-native Spanish speakers with supervision by HNCH staff.

Endoscopy:

After obtaining signed informed consents, endoscopies were performed by residents and attending physicians in the gastroenterology department at HNCH. At endoscopy, an antral biopsy specimen was obtained using an Olympus GIF XP10, Olympus CF-VL, or Fujinon EPX-201 instrument with video and photo capture. Patients were sedated intravenously with midazolam and/or meperidine. Equipment was sterilized before each endoscopy. Diagnosis was made after visualizing the esophagus, antrum, stomach corpus, and duodenum.

Processing of biopsies:

Specimens obtained by endoscopy were analyzed for histological changes and the presence of *H. pylori* in the Department of Clinical and Anatomic Pathology at HNCH. Pathologists at HNCH used H&E staining to characterize intestinal metaplasia, dysplasia, atrophy, neutrophil activity, gastritis, and to identify the presence of *H. pylori* and lymphoid follicles. Chronic gastritis was considered as present if found in either the antrum or body of the stomach. This chronic gastritis was differentiated between superficial and profound based on presence of lymphoplasmocitary infiltrate above or below the glandular necks on the lamina propia. Intestinal metaplasia was considered absent-present on an incomplete or complete manner based on the presence of cells characteristic of the large intestine (incomplete) or small intestine (complete). Atrophy was classified as metaplastic, non metaplastic and mixed. Metaplastic when metaplasia is observed; non metaplastic when gland disappeared and there is not metaplasia. Neutrophil activity was characterized as present if the sample showed extravascular neutrophils.

Analysis:

Microsoft Excel was used to design the database collect information from risk surveys, Rome III surveys, endoscopy reports, and biopsy results. Rome III criteria were used to diagnose functional dyspepsia, irritable bowel syndrome, and postprandial distress syndrome [19,20]. Data was transferred to SPSS for chi-square analysis by the University of Michigan Center for Statistical Consultation & Research.

RESULTS

A total of 112 patients were surveyed at the hospital. A total of 11 patients were excluded from our final analysis. One patient had a polyp biopsied in place of other stomach tissue, and the biopsy report did not include the parameters being analyzed. The other ten patients were excluded due to lack of a biopsy report. Demographic information for the excluded patients was available for ten of the eleven. Seven of the excluded patients were women, and the average age of the excluded patients was 46.2 years.

Our final analysis was done on the 101 patients who completed the survey and for whom biopsy reports were obtained. Of this group, 75 (74.3%) were female. The average age was 48.6 years old with a standard deviation of 12.7 years.

Three different clinical conditions could be diagnosed from the Rome III survey results obtained. These were irritable bowel syndrome (IBS), dyspepsia, and postprandial distress syndrome (PDS). Of 101 patients, 58 had dyspepsia (57.4%), 37 had IBS (36.6%), and 12 had PDS (11.9%). It was possible for patients to have more than one diagnosis, and 31 patients (30.7%) did not meet criteria for any of the syndromes studied.

The reported parameters selected to study were intestinal metaplasia, atrophy, and the presence of *H. pylori*. Of 101 patients, 7 (6.9%) had incomplete intestinal metaplasia, 10 (9.9%) had complete intestinal metaplasia, and 8 (7.9%) had both types, for a total of 25 (24.8%) with any type of intestinal metaplasia. Atrophy was present in 23 (22.8%), and *H. pylori* was present in 58 (57.4%) of patients.

Chi-square analysis was conducted to compare the diagnostic results of the Rome III survey with three parameters reported from the biopsy samples. For each possible diagnosis of IBS, dyspepsia, and PDS, a chi square test was done for the presence of *H. pylori*, the presence and type of intestinal metaplasia, and the presence of atrophy in the biopsy sample. The p-values for these comparisons are compiled in Table 1.

Table 1. Diagnostic Results of the Rome III survey of dyspepsia, IBS and PDS and H. pylori, intestinal metaplasia and atrophy. Chi-square analysis.

Comparison	*p* value
Dyspepsia and *H. pylori*	0.595
Dyspepsia and intestinal metaplasia	0.094
Dyspepsia and atrophy	0.921
IBS and *H. pylori*	0.602
IBS and intestinal metaplasia	0.441
IBS and atrophy	0.777
PDS and *H. pylori*	0.240
PDS and intestinal metaplasia	0.627
PDS and atrophy	0.591

Most of the p values obtained in chi-square analysis are well above the $p < 0.05$ threshold for statistical significance. The comparison that came closest to yielding a significant result, dyspepsia and intestinal metaplasia, was complicated by the fact that some of the cross-tabulation boxes contained very low values. Attempts to correct this chi-square analysis with a Fisher's Exact Test in SPSS were unsuccessful.

DISCUSSION

In this study, symptoms from clinical presentation according to the Rome III survey were compared to biopsy results. Previous studies demonstrated that *H. pylori* infection led to inflammation involved in atrophic gastritis, intestinal metaplasia, gastric and peptic ulcers [7-10]. Given this

mechanism, we expected clinical presentation to reflect these underlying processes. However, results from the chi-square cross tabulations were all statistically insignificant (Table 1) and did not yield any relationship between dyspepsia and intestinal metaplasia.

Of the clinical syndromes studied, two involve the upper gastrointestinal tract: dyspepsia and PDS. We expected these conditions would be more likely to correlate with *H. pylori* infection, which can occur only in the stomach. Though a neural connection between the stomach and colon is evidenced by the gastrocolic reflex, the upper and lower portions of the gastrointestinal tract are often distinguished in clinical practice. It was not surprising that a correlation between *H. pylori* or subsequent histological changes and IBS, thought to predominantly be an effect of colonic hypersensitivity, was not found.

Confounding factors contributing to our lack of significant results may have included verbal administration of the survey instrument, which was intended to be filled out in writing by the patients themselves. Verbal questionnaires may have led to more restricted disclosure about sensitive symptoms.

Another confounding factor could have been the length of *H. pylori* infection. Previous studies indicate that several decades are required to complete the pathogenetic sequence from *H. pylori* infection and chronic superficial gastritis to chronic atrophic gastritis and then to gastric cancer [21]. Since it is expected that many years should elapse between initial infection and symptoms or histopathological findings of metaplasia or atrophy are manifest, our data may have been insignificant due to the inclusion of patients of all ages between 18 and 70. The younger patients in our cohort may not have been infected for a long enough period of time to develop the findings studied here. The length of *H. pylori* infection could not have been determined through our method of selecting study participants, who may have been infected since childhood or acquired their infections more recently. Choosing to include only an older subset of participants may have increased the chances that study subjects had longstanding infection for many years and might have yielded more significant findings.

Statistically, examining many categories of intestinal metaplasia decreases the number of subjects in any category and increases the threshold for significance. Using simple yes/no categories for metaplasia may have made the correlation more significant as well.

Numerous studies by other investigators also failed to find a correlation between any presenting symptoms and presence of *H. pylori* infection [12-18]. Gastric cancer is difficult to diagnose in its early stages because it is often asymptomatic [19,20], and it is not surprising that the histological changes theorized to precede cancer similarly lack specific symptoms. Furthermore, our study was gender-biased with 74.3% women. Previous reports of gastric cancer in Lima have shown a greater prevalence of gastric cancer in men [1].

Attempts to find clinical markers for *H. pylori* infection and gastric cancer have consistently proved unfruitful. More recent attempts to find serum biomarkers for early gastric cancer suggest a more promising route. Assays of microRNA indicate that there may be consistent differences between early gastric cancer and normal controls [21], providing the basis for a future screening test. The benefits of a serological test include that fact that patients would not have to undergo endoscopy, which is time-consuming and requires anesthesia, for surveillance. A simple blood draw may improve surveillance because people would be more willing to undergo this procedure.

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