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Nature and extent of gastric lesions in symptomatic Chilean children with *Helicobacter pylori*-associated gastritis

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Chile has one of the highest rates of gastric cancer in the world and most children and adolescents in the country are colonized by *Helicobacter pylori*. This study assessed the nature and extent of the gastric lesions in 73 consecutive patients aged 5–17 y, referred for upper gastrointestinal endoscopy. Their *H. pylori*-associated gastric pathology was characterized and these data were compared with their sociodemographic status. Endoscopic assessment was normal in 43 patients while in 30 there was a variety of mucosal lesions. Sixty patients (83%) had histological chronic gastritis of the antrum and in 45 (63%) the lesions also involved the gastric corpus; 90% of patients with chronic gastritis were colonized by *H. pylori*. Although most of these patients had epithelial erosions and dedifferentiation of the pit epithelium, atrophy and metaplasia were not found. Patients' socioeconomic status was inversely correlated with their rate of colonization by *H. pylori* ($p < 0.005$), the frequency of gastric lesions on endoscopy ($p < 0.01$) and the frequency of involvement of antral and corpus mucosa by chronic gastritis ($p < 0.002$). This latter feature was positively correlated with age ($p < 0.001$).

Conclusion: This study shows a high frequency of extensive lesions of *H. pylori*-associated chronic gastritis in young Chilean patients. This histological picture is consistent with the hypothesis of a *H. pylori*-associated progressive gastric pathology which may represent a major factor in the high local rate of gastric cancer.

Key words: *Children, Chilean, gastritis, gastric cancer,* Helicobacter pylori

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Helicobacter pylori, the most common aetiological agent of chronic active gastritis in both children and adults (1–4), is also associated with predisposition to peptic ulcer disease, gastric mucosa-associated lymphoid tissue lymphoma and gastric carcinoma (3–5). In populations living in underdeveloped areas *H. pylori* infection affects a majority of individuals, even in the paediatric and adolescent age group, in whom infection usually adopts a chronic and asymptomatic course (6–9). Chile is one such area, where a majority of the population is already infected with *H. pylori* by the age of 15 y (10, 11). Indeed, it has been proposed that this early and highly prevalent gastric infection by *H. pylori* may partially account for the fact that in Chile the risk of developing gastric carcinoma is one of the highest in the world (12).

While the precise pathogenic mechanisms by which *H. pylori* predisposes to gastric carcinogenesis are still unclear, infection by the bacterium has been associated with sequential pathological changes that may ultimately lead to the development of gastric cancer (13). It is likely that concurrent modulating factors, such as an excess intake of salt, nitrate, a lack of vitamin C and β-carotene (14–16), collaborate in the production of this ongoing gastric process, i.e. the evolution from normal gastric tissue through superficial gastritis, multifocal atrophic gastritis, intestinal metaplasia and dysplasia to carcinoma (17). If cancer evolves as a final stage of such a multistage process, then prolonged infection by *H. pylori* is one prerequisite for its development. It has been suggested that the risk for gastric carcinoma is largely established around 25 y of age (3). Since the prevalence of preneoplastic lesions is high in young adults from countries with high rates of *H. pylori* infection (18), it is possible that extensive and intense pathological changes in the gastric mucosa are already present in early life, in adolescents and even in schoolchildren.

This study investigated a group of Chilean paediatric patients referred for diagnostic endoscopy because of

upper gastrointestinal complaints, with the purpose of characterizing the nature and extent of the gastric mucosal lesions associated with *H. pylori*.

Patients and methods

Patients

Consecutive outpatients referred for diagnostic upper gastrointestinal endoscopy to three paediatric centres in Santiago, Chile, were entered into the protocol. Patients were included if they met at least one of the following criteria: (i) symptoms suggestive of peptic disease (recurrent epigastric pain, nocturnal or burning abdominal pain, recurrent abdominal pain and chronic vomiting, haematemesis); or (ii) a history of recurrent abdominal pain and a first-degree relative with an endoscopically proven diagnosis of peptic ulcer disease. Patients were recruited over an 18 mo period in two of the participating centres and over a 3 mo period in the third centre. A detailed clinical history was obtained that included the characteristics of the abdominal pain and other clinical manifestations, family history of peptic ulcer disease, and recent therapy with antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), bismuth compounds or acid suppressing drugs. The patients' socioeconomic status was classified according to a locally validated version (19) of the Graffar score (20).

Ethical considerations

The study was approved by the local institutional review board. Written informed consent was obtained from patients' parents or guardians.

Endoscopy

Endoscopy was performed using the Olympus endoscope GIF P10. Topical anaesthesia was not used. The endoscopic findings in the oesophagus, stomach and duodenum were described in a standardized way by the participating endoscopists. The macroscopic appearance of the oesophagus, stomach and duodenum was recorded according to the presence of erythema, antral nodularity and erosion or ulceration.

Biopsy studies

Four gastric biopsy specimens were obtained: two were from the distal antrum, one from the incisura angularis and one from the corpus. One biopsy specimen from the antrum was subjected to direct urease test. The three remaining biopsy samples were fixed in 10% buffered formalin, embedded in paraffin, cut in serial sections of 5 μm each, and stained with haematoxylin–eosin, Warthin–Starry silver stain and May–Grünwald–Giemsa. All histological assessments were done on codified slides, and independently by two experienced pathologists. Specimens were graded according to the Sydney classification (21). Graded variables included the density of *H. pylori* organisms, inflammation, activity, atrophy and intestinal metaplasia. For each variable, 0 is none, 1 is mild, 2 is moderate and 3 is severe. In addition, an "extension and grading" histopathological score was applied. This score, which was validated in the laboratory, was obtained from the sum of qualified grades for each feature in all three samples (22). Classification of histological changes was as follows: normal mucosa was defined as one with absence of acute or chronic inflammatory infiltrate as well as epithelial or glandular lesions; active chronic gastritis as one with polymorphonuclear or lymphoplasmocytic infiltrate with epithelial lesions, with or without glandular involvement; and non-active chronic gastritis as one with lymphoplasmocytic infiltrate without polymorphonuclear infiltrate or epithelial lesions. The presence of lymphoid folliculi was also recorded. Inter-observer variation between pathologists was assessed by kappa statistics (23). Discrepancies between the two observers were resolved by consensus.

Presence of Helicobacter pylori

The patient was considered to be infected by the organism if urease or histological assessment was positive for *H. pylori*.

Analytical methods

The χ^2-test (or Fisher's exact test) was used to compare qualitative variables. The extended Mantel–Haenszel χ^2-test was used to test for trends. A p-value of less than 0.05 was considered statistically significant.

Results

Seventy-three patients were entered into the protocol (42F, 31M; ratio 1.4:1). The mean ± SD age on referral was 12.2 ± 2.6 y (range 5–17 y). The prior duration of symptoms on referral was 12.8 ± 6.0 mo. The reasons for endoscopic assessment of the patients and the results of the procedure are shown in Table 1. The endoscopic study was normal in 43 patients, while 30 patients had at least one discernible abnormality. Fifty-nine (81%) of the patients had evidence of gastric colonization by *H. pylori*. Positivity for *H. pylori* was found more often in patients with nodular antritis on endoscopy (23/25; 92%) than in those who did not have this appearance (36/48; 75%), but this difference did not attain statistical significance. In this regard, the positive predictive value of endoscopic nodular antritis was 0.92; however, its negative predictive value was only 0.25.

Duodenal ulcers were observed in five patients (all male), all of whom were positive for *H. pylori*. Erosive duodenitis was found in eight additional patients; five of these were positive for *H. pylori* and one was taking NSAIDs. Three *H. pylori*-positive female patients had

Table 1. Endoscopic assessment of 73 study patients.

Reason for endoscopy	No. of patients[a]
Recurrent abdominal pain with characteristics of peptic disease	39
Recurrent abdominal pain with family history of peptic ulcer	24
Upper gastrointestinal bleeding	11
Chronic vomiting	9
Endoscopic diagnosis	
Oesophagitis	11 (2/9)[b]
Nodular antritis	25 (13/12)
Gastric ulcer	3 (0/1)
Gastric erosions	3 (2/1)
Active duodenal ulcer	5 (5/0)
Healed duodenal ulcer	1 (0/1)
Erosive duodenitis	8 (3/5)
Normal endoscopic study	43 (19/24)

[a] In several patients there was more than one reason for endoscopic assessment and more than one abnormality found on endoscopy.
[b] Male/female.

Table 2. Frequency of histopathological features in patients with histological evidence of chronic gastritis.

Feature	No. (%) of patients with the given feature	Degree of the given character
Inflammation	60 (100)	
Polymorphonuclear infiltration of lamina propria	58 (97)	Degree 0: 14%
		Degree 1: 79%
		Degree 2: 7%
Intraepithelial polymorphonuclear infiltration	52 (87)	
Epithelial erosions	34 (57)	
Dedifferentiation of the pit epithelium	31 (52)	
Lymphoid follicles	25 (42)	
Atrophy	0 (0)	
Intestinal metaplasia	0 (0)	
Presence of *Helicobacter pylori*	54 (90)	Density:
		Degree 0: 14%
		Degree 1: 33%
		Degree 2: 39%
		Degree 3: 14%

gastric ulcers; one of them also had a recent history of NSAID intake.

Gastric biopsy specimens were deemed as appropriate for complete histological evaluation in 72 patients (they included the presence of muscularis mucosa), while in 1 patient all 3 biopsies were considered too superficial for analysis. Therefore, the ensuing histological results include data of 72 patients. Sixty patients (83%) had evidence of chronic gastritis in the antrum and in the incisura angularis, and 45 patients (63%) also had chronic gastritis of the gastric corpus, which was usually of a lower degree of severity than the corresponding antral lesion. Gastritis of the corpus was not observed in any patient who did not have antral gastritis as well. While 54 (90%) of patients with any degree of chronic gastritis had evidence of gastric *H. pylori* colonization, this organism was found only in five patients (42%) without gastritis ($p < 0.001$). Overall, in 32 patients (44%), at least one lymphoid follicle was observed. The presence of lymphoid folliculi had no correlation with a nodular appearance of the stomach on endoscopy, with the presence of chronic gastritis or with positivity for *H. pylori*.

The different histopathological characteristics of the gastric mucosa in the patients with evidence of chronic gastritis are presented in Table 2. Mild features of activity and polymorphonuclear infiltration of the lamina propria and polymorphonuclear infiltration of the epithelium were present in most patients. Less common, but still present in a majority of patients, were epithelial erosions and dedifferentiation of the pit epithelium. Most biopsy specimens showed a mild degree of inflammation and a mild degree of activity (degree 0, 14%; degree 1, 79%; degree 2, 7%). The distribution of *H. pylori* density was as follows: degree 0, 14%; degree 1, 33%; degree 2, 39%; degree 3, 14%. Atrophy and intestinal metaplasia were not found in this population.

Table 3 shows the relationship between endoscopic lesions, *H. pylori* colonization and the socioeconomic status of the patients. There was a significantly inverse relationship between socioeconomic status and rate of colonization by *H. pylori*, and the frequency of endoscopic gastric lesions followed the same gradient. In contrast, no clear pattern was found in this respect in the frequency of endoscopic duodenal lesions. Coexisting involvement of antrum and corpus by chronic gastritis was significantly more frequent with increasing age (Table 4) and with decreasing socioeconomic status (Table 4). The youngest patient with such a picture of "pangastritis" was only 8 y old.

Kappa values for interobserver variation in grading of different characters of gastric mucosa were as follows: inflammatory infiltrate, 0.86; activity, 0.81; neutrophils in lamina propria, 0.71; intraepithelial neutrophils, 0.75; mucosal erosions, 0.83; epithelial dedifferentiation, 0.81.

Discussion

This study confirms previous reports on the high prevalence of *H. pylori* colonization of Chilean children and adolescents, in general (10, 11), and in young patients referred for upper gastrointestinal endoscopy, in particular (24). As expected, in any population that includes a high proportion of individuals infected by *H. pylori*, chronic gastritis was the rule. Ninety percent of all patients with histological evidence of chronic

Table 3. Relationship between gastroduodenal lesions, colonization with *Helicobacter pylori* and socioeconomic condition of the patients (expressed as Graffar's score).

		No. (%) of patients with		
Graffar's category[a]	No. of patients	*H. pylori* colonization of gastric mucosa[b]	Gastric lesions on endoscopy[c]	Active duodenal ulcer
1 and 2	7	1 (14)	0 (0)	1 (14)
3	19	11 (58)	4 (21)	1 (5)
4 and 5	46	39 (85)	19 (41)	3 (7)

[a] In the Graffar classification, the higher the score, the lower the socioeconomic status of the patient.
[b] Correlation between the Graffar category and proportion of patients with *H. pylori* colonization of gastric mucosa: $p < 0.005$ by the extended Mantel–Haenszel χ^2-test (test for linear trend).
[c] Correlation between the Graffar category and proportion of patients with gastric lesions on endoscopy: $p < 0.01$ by the extended Mantel–Haenszel χ^2-test.

gastritis were colonized by *H. pylori*. In almost two-thirds of the overall study population, features of gastritis had spread out beyond the antrum and involved the gastric corpus. This is probably related to a massive exposure to *H. pylori* earlier in the life of these young patients and to a prolonged duration of the infection. Not surprisingly, given that infection by *H. pylori* is associated with poor hygiene and sanitary conditions and is more prevalent with increasing age, the frequency of involvement of antral and corpus mucosa by *H. pylori*-associated chronic gastritis in the patients was inversely correlated with their socioeconomic status and directly correlated with age. It is noteworthy that this extensive pattern of involvement of the gastric mucosa in this series was already present in almost 40% of patients younger than 11 y of age. Gastric endoscopic lesions, representative of the *H. pylori* colonization of the gastric mucosa, were also directly correlated with age and inversely correlated with the socioeconomic status of the patients (the latter being a proxy for an unfavourable sanitary environment).

Table 4. Frequency of involvement of antral and corpus mucosa in patients with chronic gastritis by age group and by socioeconomic status (expressed as Graffar's score).

Age group	No. of patients (total no. of patients in this age group)[a]	%
< 11 y	7 (18)	39
11–13 y	18 (29)	62
> 13 y	20 (25)	80
Total	45 (72)	63
Graffar category	**No. of patients (total no. of patients in this category)[b]**	**%**
1 and 2	2 (7)	29
3	8 (19)	42
4 and 5	35 (46)	76
Total	45 (72)	63

[a] Correlation between involvement of antral and corpus mucosa and age group: $p < 0.001$ by the extended Mantel–Haenszel χ^2-test.
[b] Correlation between involvement of antral and corpus mucosa and Graffar category: $p < 0.002$ by the extended Mantel–Haenszel χ^2-test.

A few patients with features of chronic gastritis did not harbour *H. pylori* at the time of endoscopy. A different cause of gastritis, either infectious or non-infectious, cannot be ruled out. Alternatively, a sampling error may have overlooked the presence of *H. pylori* or the organism may have been temporarily eradicated by previous therapy with antibiotics or acid-suppressant drugs. A nodular appearance of the antrum on endoscopy was usually correlated with *H. pylori* colonization but it was far from being a specific feature of *H. pylori* infection. Other authors had ascribed to endoscopic nodular antritis a high predictive value for the presence of the microorganism (25, 26). However, this was not the case in the present study. The significance of this difference, besides the obvious consideration of some methodological reasons, is not clear. Exogenous elements as well as intrinsic characteristics of the host and the microorganism could all play a role in the endoscopic picture.

In this series, signs of histological activity were found in 97% of the patients with chronic gastritis but, in general, the activity was mild; only in 7% of biopsy samples were the features of activity beyond grade 1. Epithelial erosions and dedifferentiation of the pit epithelium were other prominent features of chronic gastritis in this series. It could be said that all of the mentioned histopathological features are consistent with a marked and broad degree of degenerative changes of the epithelium, secondary to a presumably long-standing effect of the *H. pylori* infection in most patients. However, neither atrophy nor the more advanced metaplastic changes of the gastric mucosa were seen in this young population. A series comprising 30 Peruvian children and adolescents with an age range similar to that in the present study also showed a high prevalence and severity of *H pylori*-associated chronic gastritis, which were age related (18). In Peru, the prevalence rate of peptic ulcer is significantly lower and the prevalence rate of gastric cancer significantly higher than those reported from most industrialized countries (27). A similar situation has been reported for Chile (28). The path leading to carcinogenic transformation of

the gastric mucosa seems to be basically the same in both countries. The early infection of the population with *H. pylori* and probably other environmental cofactors may be proposed to explain the relatively high rates of gastric cancer reported for these countries, as well as others sharing similar epidemiological conditions.

Kappa statistics (23) applied to several histopathological variables in this study yielded a good rate of agreement (0.71–0.86) between the two participant pathologists. This satisfactory inter-observer agreement confers a good degree of validity to the histopathological evaluation of the patients. It is essential to know the reliability of any histological diagnosis, both in clinical situations and in scientific studies, to realize the limitations of the method and judge their consequences (23).

Several of the patients had peptic ulcers and other discernible gastroduodenal lesions which are legitimate causes for their presenting symptoms (e.g. chronic abdominal pain, upper gastrointestinal haemorrhage, chronic vomiting). However, a sizeable proportion of the study population had a normal endoscopy with an underlying histological picture of chronic gastritis. To date, no convincing evidence has been presented that chronic gastritis, a condition which evolves silently in most individuals, should be an important cause of recurrent abdominal pain in children (29); this study was not designed to answer such a question.

In conclusion, this study has demonstrated a high frequency of extensive and marked lesions of *H. pylori*-associated chronic gastritis presenting early in life, in a group of Chilean children and adolescents. The prevalence and extension of these pathological changes were inversely correlated with socioeconomic status and positively correlated with age. The histological picture described here may further endorse the postulate of a *H. pylori*-associated progressive gastric pathology which is supposed to represent a major factor in the high local rate of gastric cancer.

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References

1. Morris, A, Nicholson, G. Ingestion of *Campylobacter pyloridis* causes gastritis and raised fasting gastric pH. Am J Gastroenterol 1987; 87: 192–8
2. Drumm B. *Helicobacter pylori* in the pediatric patient. Gastroenterol Clin North Am 1993; 22: 169–82
3. Blaser MJ, Parsonnet J. Parasitism by the "slow" bacterium *Helicobacter pylori* leads to altered gastric homeostasis and neoplasia. J Clin Invest 1994; 94: 4–8
4. Correa P, Fox J, Fontham E, Ruiz B, Lin Y, Zavala D, et al. *Helicobacter pylori* and gastric carcinoma. Serum antibody prevalence in populations with contrasting cancer risks. Cancer 1990; 66: 2569–74
5. Parsonnet J. *Helicobacter pylori* in the stomach—a paradox unmasked. N Engl J Med 1996; 335: 278–80
6. Megraud F, Brassens-Rabbe MP, Denis F, Belbouri A, Hoa DQ. Seroepidemiology of *Campylobacter pylori* infection in various populations. J Clin Microbiol 1989, 29: 1870–3
7. Graham DY, Malaty HM, Evans DG, Evans DE Jr, Klein PD, Adam E. Epidemiology of *Helicobacter pylori* in an asymptomatic population in the United States. Effect of age, race and socioeconomic status. Gastroenterology 1991; 100: 1495–501
8. Dooley CP, Cohen H, Fitzgibbons PL, Bauer M, Appleman MD, Perez-Perez G, et al. Prevalence of *Helicobacter pylori* infection in histologic gastritis in asymptomatic persons. N Engl J Med 1989; 321: 1562–6
9. Blecker U, Vandenplas Y. *Helicobacter pylori* seropositivity in symptom-free children. Lancet 1992; 339: 1537
10. Hopkins RJ, Vial PA, Ferreccio C, Ovalle J, Prado P, Sotomayor V, et al. Seroprevalence of *Helicobacter pylori* in Chile: vegetables may serve as one route of transmission. J Infect Dis 1993; 168: 222–6
11. Russell RG, Wasserman SS, O'Donnoghue JM, Taylor DN, Boslego J, Moreno JG, et al. Serologic response to *Helicobacter pylori* among children and teenagers in northern Chile. Am J Trop Med Hyg 1993; 49: 189–91
12. Harris P, Guiraldes E. Algunos aspectos epidemiológicos del cáncer gástrico y su relación con *Helicobacter pylori* en Chile. Rev Chile Pediatr 1996; 67: 89–91
13. Correa P. Human gastric carcinogenesis: a multistep and multifactorial process—First American Cancer Society Award Lecture on cancer epidemiology and prevention. Cancer Res 1992; 52: 6735–40
14. Armijo R, Detels R, Coulson AH, Medina E, Orellana M, González A. Epidemiología del cáncer gástrico en Chile. Rev Med Chile 1981; 109: 551–6
15. Bull P, Yáñez L, Nervi F. Mutagenic substances in red and white wine in Chile, a high risk area for gastric cancer. Mutat Res 1987; 187: 113–7
16. Correa P, Haenszel W, Tannenbaum S. Epidemiology of gastric carcinoma: review and future prospects. Natl Cancer Inst Monogr 1982; 62: 129–34
17. De Koster E, Buset M, Fernandes E, Deltenre M. *Helicobacter pylori*: the link with gastric cancer. Eur J Cancer Prev 1994; 3: 247–57
18. Recavarren-Arce S, León-Barúa R, Rodríguez C, Cok J, Berendson R, Gilman RH. *Helicobacter pylori*-associated chronic gastritis in Peruvian adolescents is very common and severe. J Clin Gastroenterol. 1995 20: 335–7
19. Valenzuela J, Díaz E, Klagges B. Empleo de un nuevo método de clasificación social. Cuad Méd Sociales (Santiago) 1976; 17: 14–22
20. Graffar M. Études d'agglomerations: cinq cents familles d'une commune de l'agglomeration bruxelloise. Monograph. Bruxelles: Laboratoire de Médecine Sociale de l'Université Libre de Bruxelles, 1957
21. Price AB. The Sydney System: histological division. J Gastroenterol Hepatol 1991; 6: 209–22
22. Duarte I, Schultz M, Chianale J, Bravo R, Vergara MT, Llanos J, et al. Análisis histopatológico semicuantitativo de la gastritis crónica: índice de extensión y grado. Rev Med Chile 1996; 124: 1200–6
23. Christensen AH, Gjorup T, Hilden J, Fenger C, Henriksen B, Vyberg M, et al. Observer homogeneity in the histological diagnosis of *Helicobacter pylori*: latent class analysis, kappa coefficient and repeat frequency. Scand J Gastroenterol 1992; 27: 933–9
24. Hodgson MI, Pantoja H, Latorre JJ, Vial P, Henriquez A, Wenger J, et al. *Helicobacter pylori*-associated gastroduodenal disease in symptomatic Chilean children: diagnostic value of a serological assay. J Pediatr Gastroenterol Nutr 1995; 21: 263–8
25. Hassall E, Dimmick JE. Unique features of *Helicobacter pylori* disease in children. Dig Dis Sci 1991; 36: 417–23
26. Prieto G, Polanco I, Larrauri J, Rota L, Lama R, Carrasco S. *Helicobacter pylori* infection in children: clinical, endoscopic

and histologic correlations. J Pediatr Gastroenterol Nutr 1992; 14: 420–5
27. Burstein M, Monge E, Leon-Barúa R, Lozano R, Berendson R, Gilman RH, et al. Low peptic ulcer and high gastric cancer prevalence in a developing country with a high prevalence of infection by *Helicobacter pylori*. J Clin Gastroenterol 1991; 13: 154–6
28. Correa P, Schmidt BA. The relationship between gastric cancer frequency and the ratio of gastric to duodenal ulcer. Aliment Pharmacol Ther 1995; 9 Suppl 2: 13–9
29. MacArthur C. *Helicobacter pylori*, non-ulcer dyspepsia, and childhood recurrent abdominal pain. Pediatr Res 2001; 49: 140

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