



Nodular gastritis and *Helicobacter pylori* in paediatric patients

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Abstract

Introduction: Nodular Gastritis is a frequent diagnosis in upper digestive endoscopies in children and much more common in those infected with *Helicobacter pylori*. Recent research suggests that this diagnosis in childhood may increase the risk of cancer in adulthood. With this study we aim to provide an approach to the theme at the Institute of Gastroenterology.

Materials and methods: An observational, descriptive, cross-sectional study was conducted in patients under the age of 19 with endoscopic diagnosis of nodular gastritis at the Gastroenterology Institute in Cuba between 2013 and 2019 in which they were diagnosed 312 patients and 70 of them met the selection criteria needed for research.

Results: 51.4 % of patients were male. Diagnosis of nodular gastritis and HP infection increased with the increase in age, with the age group being 15 to 19 years the most affected with 40 % of patients of whom 68.7 % were infected with the bacteria and the highest positivity was in the 11-14 years with an increase a ratio of 1.6 positives per year. The antral location was more significant with 72.8 % of which 64.7 % were HP positive. An increase in chronic inflammatory infiltrate and the extent of the inflammation was appreciated with increased age and most hp patients had activity. 90% of patients with moderate activity had HP.

Conclusions: Nodular gastritis affects children of both sexes in equal measure, becoming more common as age increases. It affects the antral region to a greater extent and evidences an increase in lymphoplasmocytical infiltrate as age increases.

Helicobacter pylori infection was diagnosed in more than half of patients with nodular gastritis and increased their diagnosis as age increased. It was most commonly evident in patients over 10 years of age, with antral gastritis and in most of them degrees of activity were shown

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Introduction

Nodular Gastritis (GN) is one of the most common findings in Upper Digestive Endoscopies (EDS) in children, and constitutes an inflammatory injury of the gastric mucosa characterized by the endoscopic presence of multiple millimeter elevations most often located in the den but can spread to the entire organ. In children, many authors link it to *Helicobacter Pylori* (HP) infection [1,2].

It was initially considered a physiological change with little pathological significance and its term was coined in 1962 [3]; however in recent years this finding has been reported frequently in patients with diseases related to HP infection and often in young women with diffuse gastric cancer, suggesting possible clinical significance to GN [4].

In 1990 the endoscopic term was defined after multiple definitions it has received, micronodular gastritis, follicular gastritis, lymphoid gastritis, nodular antritis, antral nodular hyperplasia, including such definitions within the concept of Nodular gastritis [5].

It is present in 13.0–56.5 % of all children undergoing EDS, but increases to 28.0–81.3 % in children with chronic HP infection. The prevalence of HP infection in children under 19 years of age with GN is 65.7–98.5 %. GN gradually disappears into adulthood and in many cases chronic gastritis is converted to atrophic gastritis (GA) [6]. In the revised literature we find no prevalence data in Cuba.

Some studies suggest that nodular gastritis in childhood may increase the risk of developing cancer in adulthood [7,8].

Chronic gastritis is characterized by an infiltrate with lymphocytes, plasma cells or both, if they also have polymorphonuclears takes the name of active chronic gastritis [9].

During the performance of higher digestive endoscopies in children at the Institute of Gastroenterology (IGE), GN and HP infection are frequently diagnosed. We did a review of the subject and found no research in Cuba that dealt with the behavior of this problem so in search of an approach to the subject, it motivated us to carry out this research.

Materials and methods

An observational, descriptive, cross-sectional study was conducted in paediatric patients with endoscopic diagnosis of nodular gastritis in IGE between 2013 and 2019, with the aim of characterizing paediatric patients with gastritis and its relationship to HP infection.

The universe consisted of 312 patients under the age of 19 who were given EDS in the IGE during the study period and had as a diagnosis of nodular gastritis and sample by 70 patients with nodular gastritis in EDS performed in IGE in the period, which had results of urease test and histology, from which all the data necessary for the research could be obtained and the parent offered consent to authorize the use of the data in the study.

Variable operationalization

Age: Quantitative variable continues, which will be measured according to the chronological age of the patient from birth to the time of inclusion in the study. Patients will be distributed on a closed frequency scale with intervals of unequal amplitude classes as shown below:

5 to 10 years, 11 to 14 years and 15 to 19 years

Sex: Nominal qualitative variable dichotomous to be measured according to biological sex, in: Male, Female.

Endoscopic diagnosis: polytomic qualitative variable will be explored through findings in upper digestive endoscopy.

Gastritis according to Sydney classification [11].

- Topographical terms: antrum, corpus and pangastritis.
- Degrees of intensity: mild, moderate or severe.

Histological variables: A nominal polytomic qualitative variable in which histological findings will be described according to the Sydney classification [11].

Findings	Definition	Degree of Intensity
Chronic inflammation	Increased lymphocytes and plasma cells in the lamina propria .	Mild, moderate, or severe increase in density
Activity	Neutrophilic infiltrates of the lamina propria, pits, or surface epithelium	Less than one third of pits and surface infiltrated = mild; one third to two thirds = moderate; more than two thirds = severe
Atrophy	Loss of specialized glands from either antrum or corpus	Mild, moderate, or severe loss
Intestinal metaplasia	Intestinal metaplasia of the epithelium	Less than one third of mucosa involved = mild; one third to two thirds = moderate; more than two thirds = severe
Intestinal metaplasia	Intestinal metaplasia of the epithelium	Less than one third of mucosa involved = mild; one third to two thirds = moderate; more than two thirds = severe. But we use negative or positive

In many biopsies density was not determined and only the presence of the bacteria was reflected so we decided to take the data only by the presence of the bacteria

Urease test: A rated dicotomic qualitative variable that was evaluated according to result: positive or negative.

Data collection

The necessary data were collected from the ProGastro Database of the Endoscopy Room through which we obtained the result of the EDS and the urease test and the pathological anatomy records through which the biopsy result was obtained.

All patients who were EDS in the period and took sample of the gastric mucosa, for urease test and histological study were selected, subsequently the results of these tests were requested and were called to request the informed consent to use your data for research purposes.

Research data from the PROGASTRO register and pathological anatomy were collected and organized by the researcher on the information collection forms.

The resulting data will be processed on a Pentium 4 PC computer, the variables will be recorded in a database created in EXCEL 2010, then processed in SPSS version 21.0 and exposed in absolute and relative frequency tables.

Ethical considerations

For ethical reasons all patients included in the study will be provided with information on the characteristics of the research and will be requested for their consent and consent to participate in the research

The data obtained will only be used for scientific purposes, complying with the ethical principles existing for this purpose, at all times the privacy of patients will be protected and the confidentiality of the results will be maintained, without disclosing to third parties or publishing data that may have any consequence for the participants. The protocol followed in this study will be reviewed in advance, and approved by the Ethics Committee and the Scientific Council of the institution where the study will be conducted.

Results

The study does not document a significant difference in sex, slightly predominating the male sex with 51.4%.

The distribution of paediatric patients with nodular gastritis according to age groups and HP infection was reflected in Table 2 and Figure 1, in which an increase in the percentage of patients with nodular gastritis was observed in the different groups of age increased by 25.7 %, 34.2 % and 40 %, in age groups 5 -10.11-14 and 15-19 respectively, and 55.5 % respectively, 62.5 % and

68.7 % were infected with HP. Therefore, the 15-19 age group was most affected with 28 patients (40 %), 60 % of whom had the infection. Infection in all age groups was found in more than half of patients, Positivity was higher in children aged 11 to 14 years, where positivity increased at a rate of 1.6 % per year.

Table 1: Distribution of patients diagnosed with nodular gastritis according to sex.

Sex	No.	%
Female	34	48,5
Male	36	51,4
Total	70	100

Table 2: Pediatric patients with nodular gastritis according to age group and HP infection.

Hp	Age group.						Total	%
	5-10	%	11-14	%	15-19	%		
Hp positive	10	55,5	16	66,6	17	68,7	43	61,4
Hp negative	8	44,4	8	33,3	11	39,2	27	38,5
Total	18		24		28		70	

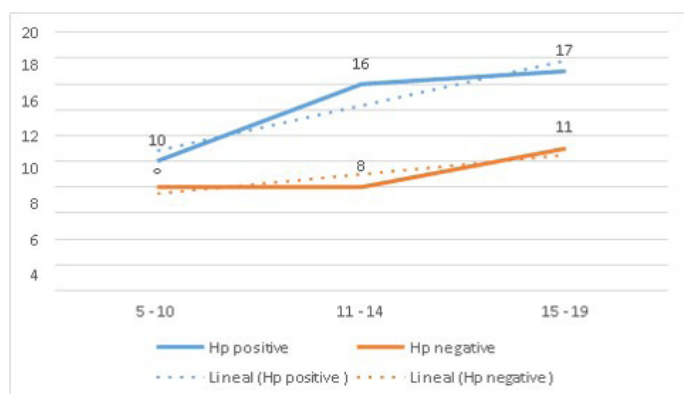


Figure 1: Paediatric patients with nodular gastritis according to age group and Helicobacter pylori infection. Source: Table 2

Table 3 shows paediatric patients with nodular gastritis according to the result in upper digestive endoscopy and the presence of HP. It can be seen that 51 patients (72.8 %) they had antral nodularity and of these 64.7 % were infected with HP. Pangastritis was evident in 18 patients (25.7 %) more than half of which had HP (55.5 %) and only one patient was diagnosed with localized gastritis in the body and was not infected by the bacteria.

Patients with nodular gastritis according to chronic gastritis extension and intensity of lymphplasmocytical infiltrate and age group were presented in Figure 2. In which 94.7 % of patients between the ages of 5 and 10 are shown to have antral location of chronic inflammatory infiltrate and 68.4 % had a light inflammatory infiltrate. In the 11-14 age group, an increase in intensity was observed as 53.8 % of patients were moderately intense and also increased the extent as 34.6 % had pangastritis. In the group of patients between 15 - 19 years, patients with moderate intensity increased a little more, making it the group most affected with 48.2 %. In all age groups, antral nodular gastritis predominates and there is a tendency to increase the intensity of chronic inflammatory infiltrate with age

Table 3: Paediatric patients with nodular gastritis based on upper digestive endoscopy and HP infection

HP	Antrum		Corpus		Pangastritis		Total	
	No.	%	No.	%	No.	%	No.	%
HP positive	33	64,7	-	-	10	55,5	43	61,4
HP negative	18	35,2	1	100	8	44,4	27	38,5
Total	51	72,8	1	1,4	18	25,7	70	100

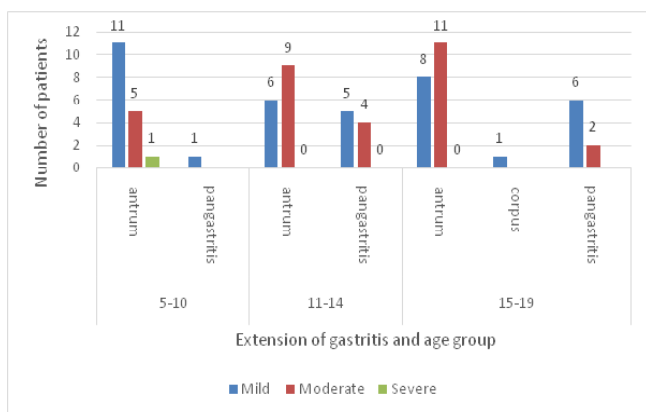


Figure 2: Paediatric patients with nodular gastritis according to extent of chronic gastritis and intensity of lymphoplasmocytal infiltrate. Source: Table 4

Patients with nodular gastritis according to the degree of activity of chronic gastritis and HP infection are exposed in Figure 3, which shows that 26 patients (37.1%) they did not have activity independently whether they were infected with HP; but 74% of them were HP negative. 30 patients (42.8 %) 60% of which were infected. 11 patients (15 %) they had moderate activity that accounted for 25.5 % of all positives, and 10 patients out of 11, with moderate activity and were infected with the bacteria representing 90.9 % of all those with moderate activity.

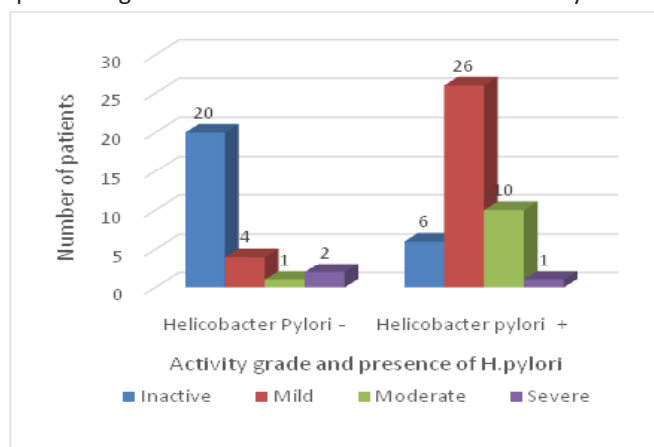


Figure 3: Patients with nodular gastritis according to degree of activity of chronic gastritis and helicobacter pylori infection. Source: Table 5

Discussion

GN is a common finding in children's EDS. Some authors classify it as pathognomonic for HP infection for research results, showing an important association between the two [12].

The study does not document a significant difference in sex, the male sex predominated very slightly, the same result was

obtained in the study conducted by Nayina [13]. Several studies document results other than this, such as Frago Arbelo in Cuba, which found that 53% was female[14], Prasad KK documented 53.7 % in females [15] and Trakal 63.55 % [16].

Several causes of GN have been reported including Crohn's disease, allergic disease, PPI abuse, celiac disease, eosinophilic disease, collagen diseases, pernicious anemia, autoimmune diseases, gastric lymphoma (lymphoma associated with lymphoid tissue of the mucosa), eosinophilic disease, cytomegalovirus infection and other infectious causes [17]. In this study, it was difficult to rule out other possible infectious and autoimmune etiologies by conducting a study based on data from previous years, but it was shown that HP infection was diagnosed in more than half of patients. An increase in percent of patients with nodular gastritis was shown as age increased. Probably in relation to the increase in HP infection, which is described to increase with age by about 1 % per year [18]. A study by Prasad KK in India concluded that GN prevalence gradually increased with age [15]. According to Rastgoo endoscopic findings increase as age increases, so does the prevalence of HP colonization [19]. Positivity was higher in children aged 11 to 14, where it increased at a rate of 1.6 % per year. Several studies document that the infection occurs around age 10. Frago Arbelo found in a study in Cuba that 59.7 % of patients diagnosed with HP infection were between 10 and 14 years [14], in a study conducted in Peru by Mecías the average age of infection was around 13 years [7]. Neyra found that the most common age range in her study was 13-14 years with 21.5 % [20].

Antral nodular gastritis predominated in 72.8 % of patients and 61.4 % of patients were Hp positive. It is important to note that the result had biases from the selection of cases, since because of the characteristics of the research it was not possible to indece ordean on the history of treatment with pump inhibitors and the consumption of antibiotics for four weeks prior to the EDS, which could constitute false negatives. The high prevalence of GN in HP-infected children is considered a benign manifestation of HP infection in children. appears to be the result of chronic inflammation and lymphoid hyperplasia caused by chronic bacterial infection, manifesting itself predominantly in the den. Age, duration of infection, pathogen species, pathogen density and degree of gastritis are related to the development of GN. The underlying development mechanisms in children have not been clarified [6]. Similar result obtained Mehmet which described 60.2% of patients with antral nodular gastritis in their study [21]. Andrade Ruiseco et al, [12] in their study found that more than half of the patients studied were infected with HP and predominated with nodular gastritis. Mejia concludes in her study that children with follicular gastritis are more likely to have Hp than those who do not have nodular gastritis given that 81.8 % of HP-infected patients had nodular gastritis [7]. Also CHEN Y, published 70.59 % of patients with HP-positive,

[22] and Broide found that nodular gastritis was less common in HP-negative gastritis (6.8 %) [23]. Yang J proposes that nodular gastritis in upper gastrointestinal tract endoscopy indicates that *H. pylori* will be identified in approximately 90 % of the gastric mucosa in children [5]. A different result was published by Prasad KK in which it demonstrated poor prediction of infection in children, HP was only shown in 14.5 % of children with nodular gastritis [15]. Mehmet established a relationship between HP's presence and endoscopic appearance; It found that 90% of HP-positive cases had antral nodular [21]. Also Chayakamon in his study in Thailand found a sensitivity and specificity of nodular gastritis and HP infection of 66.7 % and 100 %, respectively [24]. A different result published Broide who revealed that Pangastritis was most often associated with HP [23].

27.1 % of patients had reactive lymphoid follicles and most of them 78.9 % had HP infection, only two patients were diagnosed with glandular atrophy, and were related to HP infection. No intestinal metaplasia was diagnosed. Complications as well as cancer are rare in childhood and are likely to be related to exposure time [7,8,25]. Frago observed the presence of lymphoid nodules at 41.8 %. [14], In The study by Mejia, 37.6 % had reactive lymphoid follicles [7]. Broide and Prasad KK found that lymphoid follicles were most often associated with the presence of HP [15,23]. CHEN Y documented 64.71 % of patients with reactive lymphoid follicles [22]. 12.0 % of patients with reactive lymphoid follicles had nodular gastritis in study by YJ Kim [26].

There was also an increase in the intensity of chronic inflammatory infiltrate and degree of activity with increased age in HP-infected patients, which coincides with many studies [17].

Broide and CHEN documented that the degree of mononuclear infiltrate was more severe in the HP- positive group [22,23]. Prasad KK documented a significant increase in the degree of inflammation in histological evaluation in HP-positive patients with GN [15,22]. According to Rastgoo, it argues that as age increases, so does the prevalence of HP colonization and active inflammation [19]. Andrade Ruiseco et al, [12] demonstrated that in their study that most patients had moderate activity this result coincides with the outcome of this work; however Frago Arbelo achieved a different result by documenting moderate activity in 37.2 % of patients [14]. According to Rastgoo's findings, as age increases, so does the prevalence of HP colonization and active inflammation [19].

As far as we have reviewed in the literature we find no studies in Cuba that address this topic in children. This research is an approach to the subject and we believe it can be motivation for further research in the future.

Conclusions

Nodular gastritis affects children of both sexes in equal measure, becoming more common as age increases. It affects the antral region to a greater extent and evidences an increase in lymphoplasmocytical infiltrate as age increases.

Helicobacter pylori infection was diagnosed in more than half of patients with nodular gastritis and increased their diagnosis as age increased. It was most commonly evident in patients over 10 years of age, with antral gastritis and in most of them degrees of activity were shown.

Annexes

Table 4: Paediatric patients with nodular gastritis according to extent of chronic gastritis and intensity of lymphoplasmocytical infiltrate

Grupo de edad	Extension	Mild		Moderate		Severe		Total	
		No.	%	No.	%	No.	%	No.	%
5-10	gastritis antrum	11	61,6	5	27,7	1	5,5	17	94,4
	gastritis corpus			-		-			
	pangastritis	1	5,5					1	5,5
	subtotal	12	67,1	5	27,7	1	5,5	18	100
11-14	gastritis antrum	6	25	9	37,5	-		15	62,5
	gastritis corpus								
	pangastritis	5	20,8	4	16,6	-		9	37,5
	subtotal	11		13				24	100
15-19	gastritis antrum	8	28,5	11	39,2	-		19	67,8
	gastritis corpus	1	3,57					1	3,57
	pangastritis	6	21,4	2	7,14			8	28,5
	subtotal	15	53,5	13	46,4			28	99,87
Total	Total	38	54,2	31	44,2	1	1,42	70	100

Table 5: Patients with nodular gastritis according to degree of activity of chronic gastritis and helicobacter pylori infection.

	Helicobacter Pylori -	Helicobacter pylori +	Total
inactive	20	6	26
Mild	4	26	30
moderate	1	10	11
severe	2	1	3
Total	27	43	70

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