JOURNAL OF
CONTEMPORARY MEDICINE

DOI: 10.16899/jcm.705046
J Contemp Med 2020;10(1):31-34

Orjinal Araştırma / Original Article

H. Pylori Infection and Antral Nodular Gastritis in Children

Çocuklarda *Helicobacter Pylori* Enfeksiyonu ve Antral Nodülerite

Nafiye Urgancı [1], Derya Kalyoncu [2,3], Banu Yılmaz Ozguven [4]

[1] SBU Sisli Hamidiye Etfal Training and Research Hospital, Division of PediatricGastroenterology, Istanbul, TURKEY.
[2] SBU Sisli Hamidiye Etfal Training and Research Hospital, Department of Pediatrics,Istanbul, TURKEY.
[3] İstinye State Hospital, Pediatrics, Istanbul, TURKEY.
[4] SBU Sisli Hamidiye Etfal Training and Research Hospital, Department of Pathology, Istanbul, TURKEY.

Abstract

Objectives: The aim of the study was to determine the prevalence of antral nodularity and establish its association with *Helicobacter Pylori* infection in children.

Material and Method: A total of 358 children (mean age: 10.35±3.15 years, M/F:0.95) who had upper gastrointestinal endoscopy were evaluated retrospectively in terms of clinical, endoscopic and histological findings. The association between antral nodularity and *H. pylori* infection was determined.

Results: Antral nodularity was observed in 158 (44.1%) patients. *H. pylori* was detected in 138 (83.4%) of those patients with antral nodularity. Infected children with *H. pylori* compared to non-infected group were older (p=0.0001). The antral nodularity was observed significantly higher in *H. pylori*-positive patients than in *H. pylori*-negative cases (p=0.0001). The sensitivity was 52%, specificity 78%, positive predictive value 87% and negative predictive value was 37%. Lymphoid follicle and aggregates formation was observed higher in patients with antral nodularity than patients without (p=0.0001 and p=0.017, respectively). Statistically significant difference was observed between antral nodularity and the grades of H.pylori density (p=0.0001).

Conclusions: Children with antral nodularity were more likely to have *H. pylori* gastritis compared to children without. The parameters associated significantly with antral nodularity were older age, *H. pylori* infection and *H. pylori* density.

Keywords: Children, endoscopy, *Helicobacter Pylori* , antral nodularity

Öz

Amaç: Çalışmanın amacı çocuklarda *Helicobacter Pylori* enfeksiyon sıklığını ve antral nodülerite ile ilişkisini saptamaktır.

Gereç ve yöntem: Üst gastrointestinal sistem endoskopisi yapılan 358 çocuk hasta (ort yaş:10,35±3,15, E/K:0,95) geriye dönük olarak klinik, endoskopik ve histopatalojik bulgular açısından değerlendirildi.

Bulgular: Antral nodülarite 158 (%44,1) çocukta saptandı. Antral nodüleritesi olan çocukların 138'inde (% 83,4) H.pylori tespit edildi. ***H. pylori*** ile enfekte çocuklar yaş olarak daha büyük (11,1±2,91 ve 9,7±3,19) saptandı (p=0,0001). Antral nodülarite ***H. pylori***-pozitif çocuklarda ***H. pylori***-negatif olanlara göre daha sık saptandı (p=0,0001, duyarlılık %52, özgüllük %78). Lenfoid foliküller ve agregat oluşumu antral nodülarite saptanan hastalarda daha sık gözlendi (p=0.0001 ve p=0.017, sırasıyla). ***H. pylori*** dansitesi ile antral nodülarite arasında istatistiksel olarak anlamlı fark saptandı (p=0.0001).

Sonuç: Antral nodülarite, ***H. pylori*** gastriti olan çocuklarda olmayanlara göre daha sık görülmektedir. Antral nodülarite ile istatistiksel olarak büyük yaş, ***H. pylori*** enfeksiyonu ve ***H. pylori*** dansitesi ilişkili bulunmuştur.

Anahtar Kelimeler: Çocuk, endoskopi, *Helicobacter Pylori* , nodüler gastritis

Corresponding *(İletişim)*: Nafiye Urgancı , SBU Sisli Hamidiye Etfal Training and Research Hospital, Division of Pediatric Gastroenterology, Istanbul, TURKEY
E-mail *(E-posta)*: nafiyeurganci@yahoo.com
Received *(Geliş Tarihi)*: 30.11.2018 **Accepted *(Kabul Tarihi)*:** 12.02.2020

INTRODUCTION

Helicobacter Pylori (*H. pylori*) infection is a common bacterial infection, predominantly acquired in childhood and may persist throughout life. It causes chronic gastritis, gastric and duodenal ulcers, intestinal metaplasia and even gastric adenocarcinoma. Low socio-economic conditions, household crowding, poor hygiene, insufficient sanitation, and the absence of running water in the houses are associated risk factors for the high prevalence of *H. pylori* infection in developing countries.

In 1984 Warren and Marshall reported etiological role of *H. pylori* in chronic idiopathic gastritis due to toxins released by the organisms directly affecting the gastric epithelium and local microcirculation.[1] Although the stomach normally is devoid of lymphoid tissue, the development of gastric lymphoid hyperplasia is almost always thought to be mediated by a specific immune response to *H. pylori*.[2-4] *H. pylori* colonizes the stomach, induces inflammatory cytokines, and causes gastric inflammation.

Several endoscopic signs of *H. pylori* infection such as vascular pattern, edema, rugal hypertrophy, nodularity, rugal atrophy, erythema, flat erosions, and exudate has been described previously[5,6] with poor sensitivity and specificity. It has been reported that a strong association exists only between nodular gastritis and *H. pylori* infection in children.[7-17]

In present study, we aimed to determine the prevalence of antral nodularity and its relationship with *H. pylori* infection in children.

MATERIAL AND METHOD

A total of 358 children with chronic, recurrent abdominal pain in whom upper gastrointestinal endoscopy was performed between 2004 and 2008 at division of pediatric gastroenterology were evaluated retrospectively. The patients (n=120) were excluded if they had *H. pylori* eradication therapy or treatment with antibiotics and acid suppressors within 8 weeks prior to enrollment, as this could cause falsely negative test for *H. pylori*.

Endoscopic evaluation

Endoscopy was performed by the same pediatric gastroenterologist with an Olympus GİF-180 N (Olympus, Tokyo, Japan) in all of the patients during fasting under sedation with intravenous midazolam (0.1 mg/kg) or rectal midazolam 0.5 mg/kg was given as premedication 30 minutes before endoscopy. In each patient, biopsy specimens were taken from the body (2), antrum (2), oesophagus (1), and the duodenal bulb. Biopsy specimens were fixed in 10% formalin, embedded in paraffin and stained with hematoxylin and eosin.

All of the biopsy specimens were evaluated by two blinded pathologists. Informed consents were taken from all of the parents before endoscopy.

Nodular gastritis is defined as antral gastritis usually characterized endoscopically by a miliary pattern resembling gooseflesh and pathologically by prominent lymphoid follicles and infiltration of mononuclear cells[17,18]

Patients were considered positive for *H. pylori* when *H. pylori* was detected by at least two of the three methods; histological examination, culture and rapid urease test. *H. pylori* density was scored by using visual analogue scales described in the updated Sydney scoring system on a four-point scale (0, normal/absent; 1,mild; 2, moderate; and 3, marked).[19]

Statistical analysis

Statistical analysis were performed using the NCSS (Number Cruncher Statistical System) 2007&PASS 2008 Statistical Software (Utah, U.S.A). All results are expressed as the mean ±SD. Statistical comparisons were made using the unpaired Student's t tests. The analysis was conducted using Fisher's exact test and chi-square test to analyze qualitative variables. A value of $P<0.05$ was considered statistically significant.

RESULTS

The mean age of the patients was 10.35±3.15 years (range 2-18 years) and male:female ratio was 0.95. Antral nodularity was observed in 158 (44.1%) patients. *H. pylori* was detected in 138 (83.4%) patients with antral nodularity, in 108 (54%) patients without antral nodularity in histopathological examinations. The clinical characteristics, endoscopic and histopathological findings of the cases are given in **Table 1**.

The antral nodularity was observed significantly higher in *H. pylori*-positive patients than in *H. pylori*-negative cases (odds ratio (OR), 3.94; 95% confidence interval (CI), 2.45-6.32; P=0.0001). The sensitivity was 52%, specificity 78%, positive predictive value 87% and negative predictive value was 37%. Statistically significant difference was observed between antral nodularity and the grades of H.pylori density (**Table 1**). 55% of patients with antral nodularity, but without antral H.pylori (n=20) had H.pylori in their corpus, whereas among patients without antral nodularity and antral H.pylori (n=75), 34.6% of the cases had H.pylori in the corpus (P=0.0001). Lymphoid follicle and aggregate formation was found higher in patients with antral nodularity than patients without (p=0.0001 and p=0.017, respectively).

Table 1. Clinical characteristics, endoscopic and histopathologic findings of the patients.

	Antral nodularity (+) (n=158)	Antral nodularity (-) (n= 200)	P-value	CI 95%
Age (years)	12	10	0.0001	
	11.1±2.91	9.7±3.19		
Gender (male/female)	0.92 (76/82)	0.98 (99/101)	0.83	
Serum Anti-Hp positivity	125(79.1%)	98 (49%)	0.0001	0.53-0.66
Other endoscopic findings				
Oesophagitis	15 (9.4%)	24 (12%)	0.49	0.09-0.16
Gastric mucosal erosions	10 (6.3%)	46 (23%)	0.001	0.14-0.23
Gastric ulcer	9 (5.6%)	2 (1%)	0.013	0.017-0.056
Duodenitis	52 (32.9%)	25 (12.5%)	0.0001	0.22-0.32
Duodenal ulcer	3 (1.8%)	4 (2%)	1.00	0.008-0.041
Type of gastritis Corpus				
Superficial	43 (27.2%)	71 (35.5%)	0.003	0.40-0.52
Panmucosal	93 (58.8%)	63 (31.5%)	0.001	0.70-0.82
Antrum				
Superficial	28 (17.7%)	38 (19%)	0.21	0.18-0.27
Panmucosal	114 (72.1%)	102 (51%)	0.18	0.55-0.65
Antral H.pylori density				
0	20 (12.6%)	75 (37.5%)	0.0001	0.30-0.42
1	46 (29.1%)	70 (35%)	0.25	0.41-0.54
2	56 (35.4%)	38 (19%)	0.0007	0.30-0.41
3	36 (22.7%)	17 (8.5%)	0.0003	0.13-0.22
Corpus H.pylori density				
0	36 (22.7%)	91 (45.5%)	0.0001	0.48-0.61
1	77 (48.7%)	87 (43.5%)	0.33	0.78-0.88
2	36 (22.7%)	16 (8%)	0.0001	0.13-0.21
3	9 (5.6%)	6 (3%)	0.28	0.02-0.08
Lymphoid aggregate				
Positive	25 (15.8%)	15 (7.5%)	0.017	0.04-0.16
Negative	133(84.1%)	185(92.5%)		
Lymphoid follicle				
Positive	42 (26.5%)	18 (9%)	0.0001	0.13-0.20
Negative	116 (73.4%)	182 (91%)		

P<0.05 is statistically significant

DISCUSSION

The prevalence of *H. pylori* infection increases with age.[9] The mean age was higher in our *H. pylori*-positive patients than in *H. pylori*-negative ones and also was higher in the group with antral nodularity than in the group without.

Antral nodularity is characterized by miliary pattern on endoscopy with cobblestone appearance. It has been reported to be 32.1-100% in previously published studies.[7,12,13,20-27]

The sensitivity has been reported to be 40-63.4%, specificity 85.2-100%, positive predictive value 42.4-100% and negative predictive value 36.4-82.5 %.[8-10,20,23,28] In our study, 44.1% of the patients had antral nodularity and the sensitivity was 52%, specificity 78%, positive predictive value 87% and negative predictive value 37%.

The host factors, strains of *H. pylori* expressing CagA, cytokine gene polymorphisms influence mucosal cytokine expression leading to an exaggerated immune response may induce antral nodularity.[29]

Commercially available serum-based immunoassays detecting anti-*H. pylori* Ig G have a sensitivity of 63-78% (30). Chen et al.[13] reported in their study that 71% of *H. pylori*positive patients had elevated anti-*H. pylori* Ig G titer and 15% in *H. pylori*-negative patients, sensitivity of 71% and specificity of 85%. In our study, 79.1% of *H. pylori*-positive patients had elevated anti-*H. pylori* Ig G titer, 49% in *H. pylori*-negative patients (P=0.0001).

Besides several previous studies reporting significant correlations between lymphoid follicles, lymphoid aggregates and antral nodularity, the degree of antral gastritis and density of *H. pylori* colonisation[8,9,31,32], also there are some reports opposing this relationship[33] Koh et al.[34] reported that a significant increase in the incidence of nodular gastritis with gastritis score, but not an association with sex, age, or *H. pylori* density. Similar with the former, we observed a significant increase in antral nodularity with increased *H. pylori* density.

In conclusion, the parameters associated significantly with antral nodularity were older age, *H. pylori* infection and *H. pylori* density. Children with antral nodularity were more likely to have *H. pylori*-positive gastritis compared to children without. Antrum nodularity seems to be specific finding, although its sensitivity is low.

ETHICAL DECLARATIONS

Ethics Comittee Approval: In this research, the data before 2020 was used and the research was concluded before 2020. According to the Regulation on Clinical Researches published in the Official Gazette of the Republic of Turkey with the number 28617 dated 3 November 2015, the ethics committee approval was not obtained in accordance with the article "Retrospective studies are outside the scope of the regulation (article 2- (2))". This study was prepared in accordance with the Law on Protection of Personal Data, by anonymizing patient data and in accordance with the 2013 Brazil revision of the Helsinki Declaration and guidelines for Good Clinical Practice.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Status of Peer-review: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patient with gastritis and peptic ulceration. Lancet 1984;1:1311-5.
2. Wyatt JI, Rathbone BJ. Immune response of the gastric mucosa to Campylobacter pylori. Scand J Gastroenterol Suppl 1988;142:44–49.
3. Amieva MR, El-Omar EM. Host-bacterial interactions in Helicobacter Pylori infection. Gastroenterology 2008;134(1):30623.
4. Algood HM, Cover TL. Helicobacter Pylori persistence: an overview of interactions between H. pylori and host immune defenses. Clin Microbiol Rev 2006;19(4):597-613.
5. Ohkusa T, Fujiki K, Takashimizu I, Kumagai J, Tanizawa T, Eishi Y. Endoscopic and histological comparison of nonulcer dyspepsia with and without Helicobacter Pylori infection evaluated by the modified Sydney system. Am J Gastroenterol 2000;95(9):2195-9.
6. Cho JH, Chang YW, Jang JY, et al. Close observation of gastric mucosal pattern by standard endoscopy can predict Helicobacter Pylori infection status. J Gastroenterol Hepatol 2013;28(2):279-84.
7. Luzza F, Pensabene L, Imeneo M, et al. Antral nodularity and positive CagA serology are distinct and relevant markers of severe gastric inflammation in children with Helicobacter Pylori infection. Helicobacter 2002;7(1):46-52.
8. Luzza F, Pensabene L, Imeneo M, et al. Antral nodularity identifies children infected with Helicobacter Pylori with higher grades of gastric inflammation. Gastrointest Endosc 2001;53(1):60-4.
9. Bahú Mda G, da Silveira TR, Maguilnick I, Ulbrich-Kulczynski J. Endoscopic nodular gastritis: an endoscopic indicator of highgrade bacterial colonization and severe gastritis in children with Helicobacter Pylori . J Pediatr Gastroenterol Nutr 2003;36(2):21722.
10. Ukarapol N, Lertprasertsuk N, Wongsawasdi L. Recurrent abdominal pain in children: the utility of upper endoscopy and histopathology. Singapore Med J 2004;45(3):121-4.
11. Uhlig HH, Tannapfel A, Mössner J, et al. Histopathological parameters of Helicobacter Pylori -associated gastritis in children and adolescents: comparison with findings in adults. Scand J Gastroenterol 2003;38(7):701-6.
12. Uc A, Chong SK. Treatment of Helicobacter Pylori gastritis improves dyspeptic symptoms in children. J Pediatr Gastroenterol Nutr 2002;34(3):281-5.
13. Chen MH, Lien CH, Yang W, Wu CL. Helicobacter Pylori infection in recurrent abdominal pain in children--a prospective study. Acta Paediatr Taiwan 2001;42(5):278-81.
14. Serban R, Grigorescu-Sido P, Gheban D, Kiss E. Helicobacter Pylori gastritis in children: endoscopical and histological aspects. Rom J Gastroenterol 2002;11(4):297-301.
15. Sýkora J, Varvarovská J, Kuntscherová J,et al. Symptomatology and specific characteristics of chronic gastritis caused by Helicobacter Pylori infection in children in the Czech population-epidemiologic, clinical, endoscopic and histomorphologic study] Cas Lek Cesk 2002;141(19):615-21.
16. Akcam M, Artan R, Gelen T, Yilmaz A, Eren E, Uygun V, Cig H. Long-term aspects of nodular gastritis in children. Pediatr Int 2007;49(2):220-5.
17. Prasad KK. Pathology and Pathogenesis of Helicobacter Pylori infection. In: Vaishnavi C, eds. Infections in gastrointestinal system. 1st ed. India: Jaypee Brothers Medical Publishers Ltd.;2013. p. 165-186.
18. Kamada T, Hata J, Tanaka A, et al. Nodular gastritis and gastric cancer. Digestive Endoscopy 2006;18(2);79-83.
19. Dixon MF, Genta RM, Yardley H, Correa P. Classification and grading of gastritis:the updated Sydney system. Am J. Surg. Pathol 1996;20:1161-81.
20. Prasad KK, Thapa BR, Sharma AK, Nain CK, Singh K. Reassessment of diagnostic value of antral nodularity for Helicobacter Pylori infection in children. Minerva Gastroenterol Dietol2008;54(1):1-6.
21. Carvalho MA, Machado NC, Ortolan EV, Rodrigues MA. Upper gastrointestinal histopathological findings in children and adolescents with nonulcer dyspepsia with Helicobacter Pylori infection. J Pediatr Gastroenterol Nutr 2012;55(5): 523-9.
22. Ozcay F, Kocak N, Temizel IN, Demir H, Ozen H, Yüce A, Gürakan F. Helicobacter Pylori infection in Turkish children: comparison of diagnostic tests, evaluation of eradication rate, and changes in symptoms after eradication. Helicobacter 2004;9(3):242-8.
23. Mazigh Mrad S, Abidi K, Brini I, Boukthir S, Sammoud A. Nodular gastritis: an endoscopic indicator of Helicobacter Pylori infection in children. Tunis Med 2012;90(11):789-92.
24. Crone J, Granditsch G, Huber WD, et al. Helicobacter Pylori in children and adolescents: increase of primary clarithromycin resistance, 1997-2000. J Pediatr Gastroenterol Nutr 2003;36(3):368-71.
25. Kostaki M, Fessatou S, Karpathios T. Nodular gastritis and Helicobacter Pylori infection in children. Ann Gastro 2000;13(2):138-141.
26. Szczepanowska A, Kozioł-Montewka M, Ligieza J, Papierkowski A, Mroczkowska-Juchkiewicz. Evaluation of invasive tests in diagnosis of Helicobacter Pylori infection and their correlation with endoscopic features in children with chronic gastritis. Wiad Lek 2005;58(7-8):403-6.
27. Hidaka N, Nakayama Y, Horiuchi A, Kato S, Sano K. Endoscopic identification of Helicobacter Pylori gastritis in children. Dig Endosc 2010;22(2):90-4.
28. Machado RS, Viriato A, Kawakami E, Patrício FR. The regular arrangement of collecting venules pattern evaluated by standard endoscope and the absence of antrum nodularity are highly indicative of Helicobacter Pylori uninfected gastric mucosa. Dig Liver Dis 2008;40(1):68-72.
29. Ladas SD, Rokkas T, Georgopoulos S, et al. Predictive factors and prevalence of follicular gastritis in adults with peptic ulcer and nonulcer dyspepsia. Dig Dis Sci 1999; 44: 1156–1160.
30. Czinn SJ. Serodiagnosis of Helicobacter Pylori in pediatric patients. J Pediatr Gastroenterol Nutr 1999;28(2):132-4.
31. Eidt S, Stolte M. Prevalence of lymphoid follicles and aggregates in Helicobacter Pylori gastritis in antral. J Clin Pathol 1993;46:832–835.
32. Chen XY, Liu WZ, Shi Y, Zhang DZ, Xiao SD, Tytgat GN. Helicobacter Pylori associated gastric diseases and lymphoid tissue hyperplasia in gastric antral mucosa. J Clin Pathol 2002;55(2):133-7.
33. Langner M, Machado RS, Patrício FR, Kawakami E. Evaluation of gastric histology in children and adolescents with Helicobacter Pylori gastritis using the Update Sydney System. Arq Gastroenterol 2009;46(4):328-32.
34. Koh H, Noh TW, Baek SY, Chung KS. Nodular gastritis and pathologic findings in children and young adults with Helicobacter Pylori infection. Yonsei Med J 2007;48(2):240-6.