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The Association between Helicobacter Pylori Infection and Recurrent Abdominal Pain in Children Aged 2-10 Years

Dariush Zohoori [1] ✉, Omid Sadeghi Ardakani [2]

[1]International Branch, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Student Research Committee, International Branch, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Background: Helicobacter pylori (H. Pylori) is a common infection in children, especially in the developing countries. The infection is usually asymptomatic but it may cause gastro-intestinal diseases. In children, the symptoms include abdominal pain, vomiting and anemia. Recurrent abdominal pain (RAP) is a common cause of children's referral. But, whether H. Pylori causes RAP in children has to be scrutinized to prevent further complications by proper diagnosis and treatment. However, there is still controversy in the literature regarding this issue. Therefore, we aimed to assess the association between H. Pylori and RAP in children. **Materials and Methods:** In this case-control study, the children with RAP aged 2-10 years who referred to a private pediatric clinic in Marvdasht, Iran, were compared to other children without RAP, during 2015. The sample size was calculated to be 70 for each case and the control group. The patients were visited by a gastro-enterologist who recorded the demographic data of all the patients and the findings of stool test for H. Pylori. To assess the association of RAP with H. Pylori, the odds ratio was calculated. The statistical analysis was performed using SPSS 20.0 software. The P-values less than 0.05 were considered as statistically significant. **Results:** The mean age of the participants was 7.35±3.11 (with a range of 2-10). In the case group, 41/70 and 69/70 of the control group were girls. H. Pylori was found positive in 37 cases (52.9%) of the case group and 11 (15.7%) in the control group (P<0.001, OR=6.01, 95% CI=2.71-13.34). Logistic regression with adjustment for age indicated that there was a positive association between positive H. Pylori and abdominal pain (OR=16.69, 95% CI=4.71-59.18). This model also showed that by adjusting the H. Pylori test result, age was also positively associated with abdominal pain (OR=0.27, 95% CI=0.18-0.45).A T-test also indicated that the mean titer of H. Pylori was significantly higher in case group (1.42±1.29) than the control group (0.86±1.52) (P=0.020). **Conclusion:** There was a statistically significant correlation between H. Pylori and RAP. **[GMJ. 2016;5(1):19-24]**

Keywords: Helicobacter Pylori; Abdominal Pain; Children

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Fax: +98 731 2227091
PO Box 7461686688
Email:info@gmj.ir

✉ **Correspondence to:**
Dariush Zohoori, International Branch, Shiraz University of Medical Sciences, Shiraz, Iran
Telephone Number: +989177124267
Email Address: dzohoori@gmail.com

Introduction

Helicobacter pylori (H. Pylori) is a gram negative bacterium that affects a large number of children worldwide [1, 2]. Its prevalence differs by age, sex, race, and many other factors. Its prevalence is reported to be significantly higher in the developing countries and lower socioeconomic communities [3] but the exact prevalence of each community should be determined for a more meticulous evaluation. In Shiraz, Southern Iran, its prevalence is reported to be 88-98% in children aged 2 to 15 years [4] and in other provinces as high as 40-50% [5, 6].Once a child acquires the infection, mainly through intra-familial spread [7], it remains in the body lifelong and may cause disorders in adulthood. Although it is usually asymptomatic and silent, it is the most common cause of chronic gastritis, peptic ulcer disease, gastric cancer and other diseases [8, 9]. As a result of gastrointestinal diseases, it may cause abdominal pain, vomiting, anemia, and other complications [10]. Recurrent abdominal pain (RAP) affects 7-20% of the school children and accounts for 2-4% of children's medical referrals [11, 12] and several treatments have been proposed for RAP but not all of them are found to be effective [13]. The cases that have not been cured may suffer from its comorbidities like headaches [12], psychiatric problems [14] for a long time and these complications may even extend into their adulthood [15]. Some studies have associated the factors to its prevalence and to the factors like age, sex, and organic disorders [12]. So, whether the gastro-enterologists should assess every child who refers with RAP for H. Pylori infection has been assessed by several studies. But, controversial results have been obtained. An Arabian study has found a significant association between school children's RAP and H. Pylori [16], while other studies have suggested no association [17, 18]. As far as a child referring with RAP may undergo several examinations to determine its etiology and eradicate it, H. Pylori can be easily determined by non-invasive inexpensive methods and it would be worth assessing H. Pylori infection in the patients with RAP if the association between them is confirmed.

Therefore, the association between RAP and H. Pylori has to be determined in the Iranian population of children to enable us diagnose and treat children properly to prevent further complications and diseases in adulthood. Thus, this study aimed to assess the relationship between H. Pylori and children's RAP.

Materials and methods

In this prospective case-control study, children aged 2-10 years who referred to a private pediatric clinic in Marvdasht, Iran, with RAP were compared to other children aged 2-10 years without RAP during March 2015 to October 2015. The participants were selected randomly from children referring with or without RAP.

The Sample size was calculated to be 70 for each group of experimental and control (P1=50% and P2=50%). The patients were recruited for the study by the convenience sampling method. Exclusion criteria comprised of urinary infection assessed by urine sample, any other diseases presenting with abdominal pain, any significant finding on abdominal ultrasonography causing abdominal pains like urolithiasis and gall stone, the patients having used proton pump inhibitors one week before stool examination or having received antibiotics during the last four weeks, patients with subacute and chronic diarrhea or constipation, patients with lactose deficiency, and any positive history of gastro-esophageal reflux.

The demographic data of all the patients and the findings of stool test for H. Pylori were recorded. All patients were visited by a pediatrician in a clinic and the details of history having been taken and the physical examination were also recorded.Urinary infection was considered positive if more than 5 white blood cells as well as positive nitrate could be found in the urine sample. Recurrent abdominal pain was considered to exist, based on Apley's definition [19], if there were three episodes over three or more months with sufficient severity to interrupt normal activities. Stool exam was performed by ELISA method for the evaluation of H. Pylori. The HP Ag ELISA kit used in this study was ACON (China) and the ELISA reader was Stat Fax 2300 (Awareness, USA).

Ethical considerations

The protocol of the study was approved by the Shiraz University of Medical Sciences. The design and objectives of the study were explained to all participants and the written informed consent form was obtained from the parents of the participants who were willing to participate in the study and they were informed that they would be free not to participate in the study. The costs of the examinations were provided by the research administrators and no cost was imposed on the participants.

Statistical analysis

To assess the association of RAP with H. Pylori, the odds ratios (OR) and 95% confidence intervals (95% C.I.) were calculated by a Chi-square test. An independent student's T-test was used to compare the mean levels of H. Pylori and the age of groups. A logistic regression model was used to compute adjusted Ors. The statistical analysis was performed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). The P-values less than 0.05 were considered statistically significant.

Results

The mean±SD age of the patients was 7.35±3.11 (with a range of 2-10). In the case group, 41 patients were females while in the control group 69 were females. H. Pylori was found positive in 37 (52.9%) children in the case group and 11 (15.7%) in the control group. Univariate analysis showed that children with positive HP results were 6.01 times more likely to develop abdominal pain when compared to those with negative HP results (P<0.001, OR=6.01, 95% CI=2.71-13.34) (Table 1). T-test also indicated that the mean titer of H. Pylori was significantly higher in case group (1.42±1.29) than the control group (0.86±1.52) (P=0.020).

The mean age of the children in the case group (5.21±1.84) was significantly less than that of the control group (8.57±0.86, P<0.001).

The Logistic regression with adjustment for age indicated that there was a positive association between positive HP and abdominal pain (OR=16.69, 95% CI=4.71-59.18). This model also showed that by adjusting the HP test result, age was also positively associated with abdominal pain (OR=0.27, 95% CI=0.18-0.45).

Discussion

As the results of this case-control study indicated, the positive cases of H. Pylori were significantly more and H. Pylori titer was higher in children with RAP, compared to the control group. In this case-control study, the socioeconomic status of the participants were matched, as an important factor affecting H. Pylori infection. Matching was also done for age.The association between H. Pylori and RAP has been assessed by previous studies, which have reported different results. The authors of the present study stick to the view that this diversity can be associated to the difference in variables such as age, race, and socio-economic status of the patients which

Table 1. The Frequency of Positive and Negative H. Pylori in the Case and Control Groups and Adjusted and Unadjusted Ors with Respect to Age

Variable		Group		P value	OR* (95% CI)	OR† (95% CI)
		Case	Control			
H.Pylori	Negative	59 (84.3%)	33 (47.1%)	<0.001	1	1
	Positive	11 (15.7%)	37 (52.9%)		6.01(2.71-13.34)	16.69(4.71-59.18)
Age		8.57±0.86	5.21±1.84	<0.001	0.36(0.25-0.51)	0.27(0.18-0.45)

* Univariate Odds Ratio (unadjusted OR)

† Adjusted Odds Ratio using a logistic regression model

strongly affect H. Pylori infection, and also can be related to the concurrent gastro-intestinal diseases in addition to different diagnostic tools used to diagnose H. Pylori with different sensitivity and specificity. We have therefore tried to limit the confounding factors by excluding the cases with effective variables and matching the patients through the case-control design of the study. Besides, we have tried to use a sensitive tool for diagnosis of H. Pylori infection to strengthen the results.

Similar to the results of the current study, Telmesani assessed 316 Arabian students and he reported 63.3% positive H. Pylori infection in the children with RAP, which was close to the present study (53%) and concluded a significant association between H. Pylori and RAP [16]. Although he concluded the same results, he assessed the children's H. Pylori infection by urea breath test (UBT), while stool antigen assay used in the present study has a higher sensitivity and specificity (91.5% and 89.6%, respectively) than UBT [20]. He also found a significant association between H. Pylori infection and RAP and suggested the eradication of H. Pylori in children with RAP, which confirms the results of the present study.Other studies have also suggested the same conclusion. Similarly, Malaty and colleagues compared H. Pylori infection in 223 children with RAP with 330 asymptomatic children and concluded an association in children younger than 5 years old [21]. Nakayama et al also assessed 182 children with RAP and found an association between RAP and H. Pylori infection, especially in children who met Rome criteria II compared to the Apley's definition, used by the current study, and suggested the evaluation of psychiatric disorders in the patients with RAP [22]. Mukherjee et al evaluated the positive cases of RAP by upper gastrointestinal endoscopy and tested the biopsy results by rapid urease test, gram's staining, and culture and histology and concluded a significant association, while suggesting more studies to be conducted in this regard [23]. Yang and colleagues also compared RAP with short-term RAP (SRAP) (defined as pain duration from 2 weeks to 3 months) and found higher seropositive H. Pylori in children with SRAP, who were symptom-free after one year [24].Contrary to the results of the present study, some other studies have found no association between H. Pylori and RAP [25]. Macarthur and colleagues performed a case-control study on 200 children aged 5-15 and concluded no association between H. Pylori and RAP [17]. The difference in the obtained results may be due to the fact that they established H. Pylori infection by serum IgG antibody and UBT, while the present study used stool examination. Besides, the percentage of positive cases in their study (4-5%) was much lower than the present study, which reflects higher prevalence of H. Pylori infection in the Iranian society, compared to Canadian one. Mansour and colleagues compared 244 children with RAP with 122 controls in the same country as Telmesani's study and concluded no association between H. Pylori and RAP [18]. They also established a higher prevalence for H. Pylori (42.6%) than Telmesani's study. This difference may also be due to the fact that H. Pylori may differ among nations. On the other hand, the results reported by different studies may reflect the different age range of the participants of the studies, as the rate of H. Pylori infection has been reported to be different in children with different ages [21,26]. Malaty et al [21] and Nakayama et al [22] also established a difference in the association of H. Pylori with RAP in children older than 10 years old. Also, false positive rates were been identified to be different by the cut-off of 6 years old [27, 28]. For instance, the age range in Telmesani's study was 7-18 years, while Mansour and colleagues assessed the children aged 2-16 years, the current study included the children aged 2-10 years. Masoodpoor et al also compared 40 children with RAP with 60 healthy controls in an Iranian population, and found no association between H. Pylori and RAP [29], but they assessed the children with an age range of 12-15 years. Besides, as Yang et al [24] maintained, the association of H. Pylori with RAP is affected by the duration of the abdominal pain and different studies might have used different definitions for RAP. Thus, the results of the studies conducted on this issue may not be easily comparable.

The strengths of the present study include controlling the confounding factors by matching the socio-economic status and the age of the

patients in case-control design of the study, in addition to excluding any factor that may affect H. Pylori infection to be able to obtain pure unbiased results. In addition, although the results of this case-control study is not applicable to all the Iranian children, it gives pediatricians a general perspective, as the prevalence of H. Pylori infection is not defined in epidemiologic Iranian studies, although some Iranian studies have reported its prevalence in some provinces [4-6]. In spite of the strengths of the current study, it also suffers from a few limitations like studying the patients referring to one center only that would cause the study population not to be representative of the entire society. Another limitation was due to the difference in the sex of the case and control groups although the control group were selected from girls, based on the former hypothesis of more RAP in female children [12].

Conclusion

Based on the results of the current study, H. Pylori may be a significant etiology of RAP and as far as H. Pylori infection can be easily determined by a simple stool exam, it will be an effective way to include H. Pylori examination for children who refer to clinic with RAP for H. Pylori infection. Yet, as far as the demographic characteristics of participants in different studies were not similar, meta-analysis studies or further studies, considering a larger sample size, can determine the real association.

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Conflict of Interests

The authors report that there is no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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