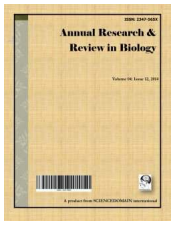

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Relation between Recurrent Abdominal Pain and *Helicobacter pylori* Stool Antigen in Children

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Authors' contributions

This work was carried out in collaboration between all authors. Author SA designed the study, wrote the protocol and interpreted the data. Author KA anchored the field study, gathered the initial data and performed preliminary data analysis. While authors AM and NS managed the literature searches and produced the initial draft. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Recurrent abdominal pain (RAP) is the most common gastrointestinal problem in children. The role of *Helicobacter pylori* (*H. pylori*) with recurrent abdominal pain is not known precisely. Since *H. pylori* infection may be one of the symptoms of abdominal pain. The aim of this study was to determine the prevalence of *H. pylori* Stool antigen in children with recurrent abdominal pain and compared with the control group.
Materials and Methods: In this cross-sectional study, 107 children with recurrent abdominal pain and 107 healthy children were enrolled. Children in both groups did not have history of the liver, the kidney and the digestive disease and at least 2 weeks before the sampling had no history of using antibiotics, pump inhibitors (PPI) and antacids. Both groups were compared for age, sex, location, type of feeding in infancy, history of gastro-intestinal problems in the family. Morning Stool antigen

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of *H. pylori* of both groups were measured with ELISA, The kits containing polyclonal antibody against *H. pylori* in the reference laboratory. After data collection Descriptive statistics were used to calculate ratios and frequency, SPSS software was used for data analysis. To compare the frequency of HpSA in two groups, Chi-square test was used.

Findings: The average age of children with RAP and control group was 6.1±3.1 and 6.04±2.7 year respectively, the difference was not statistically significant (P =0. 94). There was no difference between the two groups in terms of gender. 83 children with RAP and 78 children in the control group were in urban areas. Distribution of location in groups was not statistically significant (P =0.426). In 73 children with RAP (68.2%), HpSA was positive while only 12.1% in the control group were positive for it and this difference was statistically significant (P =0.001). positive family history of gastrointestinal problems in children with RAP and control group was 54.7% and 27.1% respectively which this difference was also statistically significant (P =0.001).

Conclusion: In this study, HpSA is significantly higher than in children with RAP especially who have a family history of gastritis. This study suggests that in children with RAP, HpSA measurement which is a noninvasive method can help

Keywords: Children; recurrent abdominal pain; stool antigen; Helicobacter pylori.

ABBREVIATIONS

H. pylori : Helicobacter pylori
HpSA : Helicobacter pylori Stool Antigen
RAP : Recurrent Abdominal Pain

1. INTRODUCTION

H. pylori is a spiral, microaerophilic, gram-negative bacterium with four to six unipolar sheathed flagella *with* a widely prevalent and important component of gastric microbiology. It is usually acquired in childhood. It is more common in poorer sections of society especially of developing countries. It can cause peptic ulcer disease and dyspepsia. It may be spread by unclean food and water, but researchers aren't sure. *H. pylori usually can be* found in gastric. Being infected by this pathogen plays a role in gastritis, peptic ulcer [1-5]. In addition, this bacterium is associated with MALT lymphoma and regression of lymphoma is verified by eradication of this factor [3,6,7]. Infection is more prevalent in developing countries, in some studies the prevalence in individuals is up to 66% [7-10]. Different invasive and non-invasive diagnosis ways are available to diagnose infection by this bacterium and among invasive methods endoscopy and biopsy could be mentioned, which are exact methods but they may not be desirable for families and children. Non- invasive methods are rapid urea breath test and Detecting bacterial antigens in stool. The *H. pylori* stool antigen (HpSA) test is a non-invasive immunoassay to diagnose active infection with *H. pylori*. Its performance in children and teenagers has been tested in some developed countries, showing a sensitivity and specificity above 90% [11].

Recurrent abdominal pain (RAP) is the most common digestive problem in children that results in recurrent visits to pediatric clinics. It is defined as three cycles of severe abdominal pain at least that affects the child's activity and its symptoms last more than 3 months. RAP could be the result of organic disorders such as being infected by parasites, urogenital diseases, inflammatory bowel disease, peptic ulcer and other factors. In some countries, *H. pylori* related to pediatric RAP [12,13]. However, some studies show that there is no relation between abdominal pain and *H. Pylori* infection [14]. Therefore, the aim of the current study is investigating the relation to RAPs and *H. Pylori* infection in children visiting to Pediatric Clinic of Khorram Abad city (the capital of Lorestan province, Iran) compared to healthy children.

2. MATERIALS AND METHODS

To conduct this cross sectional descriptive-analytic study, children with RAP visiting to Khorram Abad pediatric clinic from 23 July 2014 to 19 February 2015 were selected on a voluntary basis; children with the history of digestive, liver, kidney diseases and parasitic infections were excluded from the study. After selecting the group of pediatric patients, the control group was selected from those healthy children with no history of previous disease, who were visiting to evaluate their health status without any history of disease and had no history of using antibiotics, proton pump inhibitors (PPIs) and H2 blocker was considered in 2 recent weeks. Both groups hadn't the history of infection with pinworm parasite and were similar in age and gender. HpSA was measured in children's

morning stool sample. The samples were stored at –20℃ until analyzed. The presence of *H. pylori* organisms in stool was determined by an enzyme-linked immune sorbent assay using a commercially available polyclonal antibody kit. Stool samples were diluted, and incubated. *H. pylori* -specific polyclonal antibodies conjugated to horseradish peroxidase were added, incubated, and washed before peroxidase was added; a visible blue reaction indicated the presence of *H. pylori*.

2.1 Statistical Analysis

Statistical analysis of the data was performed with SPSS 11.0 computer program. The mean age of both groups were compared by student t test. Other comparisons were evaluated by chi-square test and Odd ratios with 95% confidence intervals. A p value ≤ 0.05 was considered significant.

3. RESULTS

In this study, 107 children with RAP and 107 healthy children were investigated in terms of the frequency of *H. pylori* Stool Antigen (*HpSA*). The average age of children with RAP and healthy children were 6.1±3.1 and 6.04±2.7 year respectively; this difference was not statistically significant (P =0.94). In groups under study, there were 51 males (47.7%) and 56 females (52.3%) and frequency distribution of gender was similar in both groups. 83 children with RAP and 78 children in the control group were in urban areas. Frequency distribution of habitat for both groups was not statistically significant (p = 0.426).

51.4% of children with RAP and 57.9% of control group children have been breastfed since birth and frequency distribution of type of feeding in childhood was not statistically significant according to chi-square test (p= 0.621) (Table 1). According to the results of Table 1, family history was positive in 54.7% of children with RAP and in 27.1% of control group, which was statistically significant (p=0.001). Family numbers in the majority of children with RAP was 5 members (36.4%) and in the majority of children of control group, it was 4 members (36.4%). However, according to chi-square test, difference between family numbers was not statistically significant in both groups (p=0.198).

Table 1. Distribution of location, type of feeding, family history, and family number in groups under study

Details	Patients' group number (percent)	Control group number (percent)	P-value
Location			
Urban	83 (77.6)	78 (72.9)	0.426
Rural	24 (22.4)	29 (27.1)	
Total	107 (100)	107 (100)	
Type of feeding			
Breast-fed	55 (51.4)	62 (57.9)	0.621
Formula-fed	9 (8.4)	8 (7.5)	
Both	43 (40.2)	37 (34.6)	
Total	107 (100)	107 (100)	
Family history			
Yes	58 (54.7)	29 (27.1)	
No	48 (45.3)	78 (72.9)	0.001
Total	106 (100)	107 (100)	
Family number			
3 members	8 (7.5)	16 (15)	
4 members	34 (31.8)	39 (36.4)	0.198
5 members	39 (36.4)	29 (27.1)	
6 members and more	26 (24.3)	23 (21.5)	
Total	107 (100)	107 (100)	

HpSA was positive in 73 children with RAP (68.2%); while it was positive only in 13 children of control group (12.1%) and this difference was statistically significant (p=0.001) (Table 2).

According to the results of independent T-test shown in Table 3, in children with RAP, the difference between average age of children with positive *HpSA* compared to children with negative *HpSA*, was not statistically significant (p =0.25). This difference was not significant in control group as well (p=0.134).

Table 2. Distribution of HpSA in groups under study

Groups under study	*H. pylori* stool antigen			P-value
	Positive number (percent)	Negative number (percent)	Total number (percent)	
Patients' group	73 (68.2)	34 (31.8)	107 (100)	0.001
Control group	13 (12.1)	94 (87.9)	107 (100)	

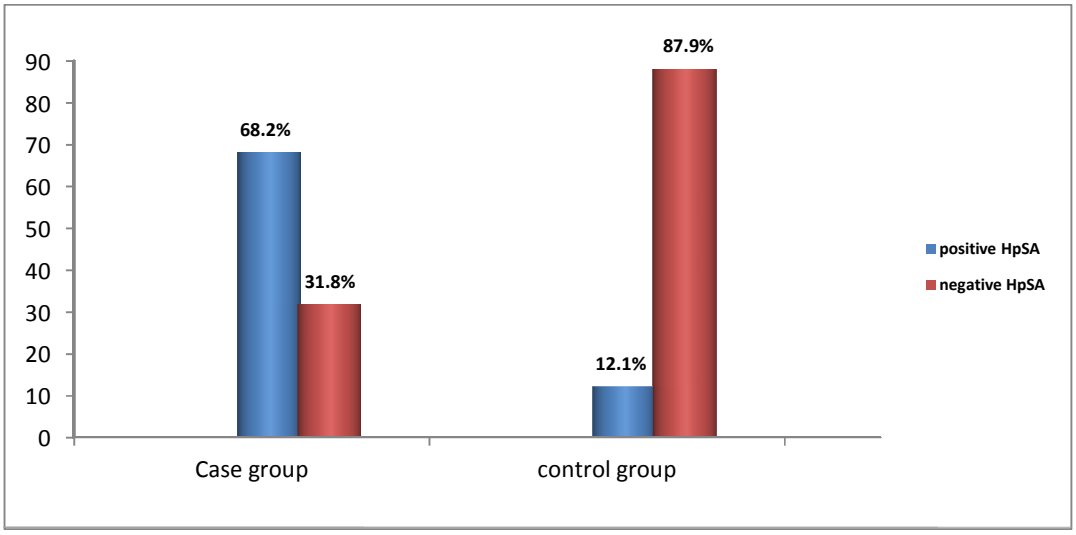
Frequency distribution of *HpSA* in children with RAP was not statistically significant in terms of gender (p=0.616). No difference in frequency distribution of *HpSA* was observed between male and female children (p=0.478).

In Table 4, frequency distribution of *HpSA* status in children in terms of location is mentioned.

According to the results of Table 5, difference in frequency distribution of HpSA in children with RAP was statistically significant in terms of their nutrition in childhood (p =0.004); such that in formula-fed children and children who are formula-fed combined with breast-feeding, the positivity of HpSA was significantly higher than children who were merely breast-fed.

In control group, in spite of higher positivity of HpSA in formula-fed children compared to other subjects, this difference was not statistically significant according to chi-square (p=0.054).

According to the results of Table 6, the difference in frequency distribution of HpSA in children with RAP and control group was not statistically significant in terms of the number of family members.



Graph 1. Distribution of HpSA in case and control groups under study

Table 3. Comparison of average age of antigen positive children with antigen negative ones in terms of *H. pylori* in groups under study

Groups under study	Antigen status	Age	t-statistic	P-value
		Average ± standard deviation		
Patients' group	Positive	6.24±3.35	-1.147	0.25
	Negative	5.52±2.23		
Control group	Positive	7.1±2	-1.5	0.134
	Negative	5.9±2.79		

** Type of statistical test: T-test*

Table 4. Distribution of *HpSA in* children in terms of location

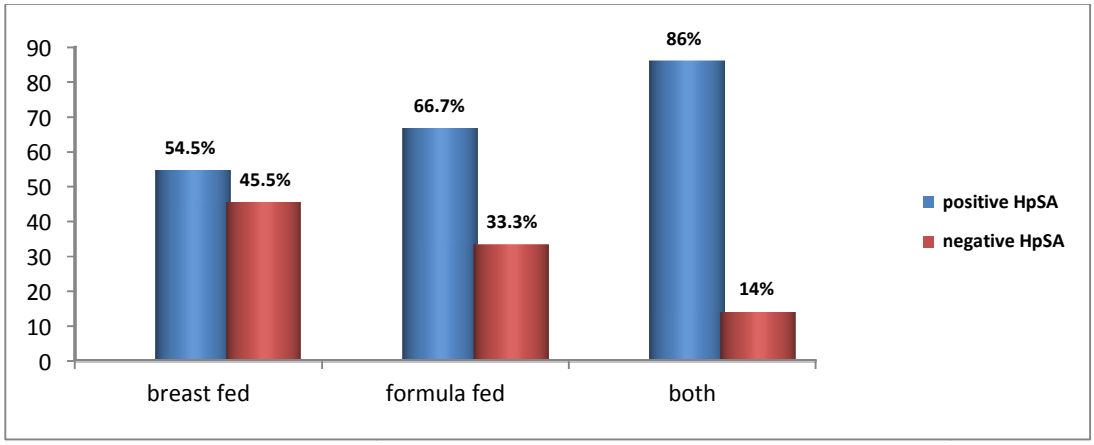
Groups	Habitat	*H. pylori* stool antigen			P-value
		Positive number (percent)	Negative number (percent)	Total number (percent)	
Case group	Urban	55 (66.3)	28 (33.7)	83 (100)	0.418
	Rural	18 (75)	6 (25)	24 (100)	
Control group	Urban	9 (11.5)	69 (88.5)	78 (100)	0.751
	Rural	4 (13.8)	25 (86.2)	29 (100)	

** Type of statistical test: chi-square*

Table 5. Distribution of HpSA in children in terms of feeding in childhood

Groups under study	Type of feeding in infancy	*H. pylori* stool antigen			P- value
		Positive number (percent)	Negative number (percent)	Total number (percent)	
Patients' group	Breast-fed	30 (54.5)	25 (45.5)	55 (100)	0.004
	Formula-fed	6 (66.7)	3 (33.3)	9 (100)	
	Both	37 (86)	6 (14)	43 (100)	
Control group	Breast-fed	5 (8.1)	57 (91.9)	62 (100)	0.054
	Formula-fed	3 (37.5)	5 (62.5)	8 (100)	
	Both	5 (13.5)	32 (86.5)	37 (100)	

*Type of statistical test: chi-square



Graph 2. Frequency distribution of HpSA in children with RAP in terms of type of feeding

Table 6. Frequency distribution of HpSA status in children under study in terms of the number of family members

Groups under study	Family numbers	*H. pylori* stool antigen			P-value
		Positive Number (percent)	Negative Number (percent)	Total Number (percent)	
Patients' group	3 numbers	6 (75)	2 (25)	8 (100)	0.426
	4 numbers	26 (76.5)	8 (23.5)	34 (100)	
	5 numbers	23 (59)	16 (41)	39 (100)	
	≥6 numbers	18 (69.2)	8 (30.8)	26 (100)	
Control group	3 members	1 (6.3)	15 (93.8)	16 (100)	0.086
	4 members	2 (5.1)	37 (94.9)	39 (100)	
	5 members	4 (13.8)	25 (86.2)	29 (100)	
	≥ 6 members	6 (26.1)	17 (73.9)	23 (100)	

*Type of statistical test: chi-square

4. DISCUSSION

Among the organic causes of RAP, *H. pylori* and giardia are most commonly mentioned [15,16]. However, different studies conducted on the relation between RAP and *H. pylori* infection have presented different results. Evidence of some papers supports this hypothesis [17-21] while other studies reject this relation [22-24].

For instance, in a study within three years, gastritis resulted from *H. pylori* infection is mentioned as a Risk factor for RAP [16]. Another study on 141 children in Turkey, showing the relation between *H. pylori* infection and RAPs, provided evidence for treatment of children after eradication of the infection [19].

On the other hand, in a study no relation was observed between RAPs and *H. pylori* infection

[24]. In a different study, has shown positive relation with epigastria pain, nausea and a positive family history in spite of the lack of relation between *H. pylori* infection and RAPs [25].

5. CONCLUSION

In this study, the prevalence of HpSA in children with RAPs was 68.2% and in children without symptoms, it was 12.1%, which was statistically significant. There was a significant association between RAP and H Pylori infection. This relation was not dependent on sex or the number of family members, however; in children with family history of gastritis and those who were not exclusively breast-fed, it is observed more. RAP is an indication for a stool test for *H. pylori* infection in children. It seems that exclusive breast feeding have an important role in reducing pollution with *H. pylori* and RAP in childhood.

Unfortunately, there are not sufficient studies to support the effectiveness of the treatment of individuals infected by *H. pylori* to treat digestive symptoms. Therefore, it is better to conduct studies in this regard as well.

6. SUGGESTION

The presented data suggest that recurrent abdominal pain in children may be associated with *H. pylori* infection. It is recommended to conduct more studies with a higher population of patients to reduce the possibility of errors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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