

Frequency of Helicobacter Pylori Infection Among Children Presenting with Recurrent Abdominal Pain in Pediatrics Outpatient Department

Babar Ali, Zeeshan Ahmed, Zohaib Akhtar*, Abdullah Akram*, Rehan Mehmood*, Waseem Ahmed*

Department of Paediatrics, Pak-Emirates Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan,

*Department of Paediatrics, Combined Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the frequency of Helicobacter pylori infection in paediatric patients presenting with recurrent abdominal pain.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Paediatrics, Pak-Emirates Military Hospital Rawalpindi, Pakistan Jan to Aug 2022.

Methodology: The study sample was composed of 152 patients aged between 3 and 12 years, of either gender, reporting with recurrent abdominal pain. Patients with a past history of Helicobacter pylori infections, or those who had received antibiotics, H2 receptor antagonists or proton pump inhibitors within the past month were excluded. All patients underwent testing for infection using polymerase chain reaction assays using stool samples. Variables were compared to test positivity via PCR for H. pylori infection using the Chi square test and t-test, and a p -value of ≤ 0.05 was considered significant.

Results: The mean age of the study sample was 7.32 ± 2.62 years, of whom 86 (56.6%) were female. A total of 63 (41.4%) patients tested positive for H. pylori infection, while 32 (21.2%) were suffering from iron deficiency anaemia. Patients who tested positive for H. pylori infection had a higher chance of suffering from concurrent iron deficiency anaemia, ($p=0.002$). In addition, females generally presented at an older age with recurrent abdominal pain than males with the same condition, ($p=0.016$).

Conclusion: Pakistani children with recurrent abdominal pain have a high chance of being infected with H. pylori, which should be screened for when managing such patients.

Keywords: Abdomen, Helicobacter pylori Infection, Paediatric Population, Recurrent Abdominal Pain.

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INTRODUCTION

Helicobacter pylori is a spiraled, gram-negative bacillus, which is found as a colonizing organism in approximately one-half of the global population.¹ It is associated with a significantly increased risk for the development of peptic ulcer disease, chronic atrophic gastritis and the development of gastric malignancies such as mucosa-associated lymphoid tissue (MALT) lymphoma and gastric carcinoma.² H. pylori is microaerophilic and capable of surviving within the harsh microenvironment of the stomach for prolonged periods.³ Humans appear to acquire H. pylori infection during early childhood, and this is especially true of the developing world, and the contagion is usually acquired through contaminated food or water.^{4,5}

H. pylori is also linked to iron and vitamin B12 deficiency anaemia in children, the development of immune thrombocytopaenic purpura as well as

deficient growth and maturation.⁶ The majority of patients are asymptomatic while some present with complaints of nausea, vomiting, dyspepsia/heartburn and/or abdominal pain.⁷ Recurrent abdominal pain in children is a common malady, with patients receiving diagnoses such as irritable bowel syndrome, functional dyspepsia or constipation, attribution being given to altered diet, gastrointestinal infection and mental health disorders in the etio-pathogenesis of these complaints.⁸ H. pylori may represent a potentially significant cause of abdominal pain in these children, especially in the developing world, which may result in the misdiagnosis of these children as having functional disorders, which may limit the provision of timely, effective and appropriate management, as well as expose the patient to the long-term complications associated with the infection.^{9,10}

Pakistan is a developing country, and its children are at high risk for the development of infections with H. pylori. This study was conducted for estimating the prevalence of infection with this bacterium in cases of recurrent abdominal pain in the paediatric population.

Correspondence: Dr Babar Ali, Department of Paediatrics, Pak-Emirates Military Hospital, Rawalpindi Pakistan

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METHODOLOGY

We conducted this descriptive cross-sectional study between Jan 2022 and Aug 2022 in the Department of Paediatrics, Pak-Emirates Military Hospital, Rawalpindi after approval from the Institutional Ethical Review Committee (vide letter no.A/28/EC/449/1-22).

Inclusion Criteria: Patients of either gender aged between 3 and 12 years, of both genders, who suffered from recurrent abdominal pain, were included.

Exclusion Criteria: Patients who had a past history of suffering from H. pylori infections or had used antibiotics or proton pump inhibitors/H2 receptor antagonists within the past one month were excluded.

WHO calculator was used to calculate the sample size keeping the proportion of patients with recurrent abdominal pain who suffered from H. pylori infection at 0.739%.¹¹

The sample size came to 152 patients, who we recruited using non-probability consecutive sampling, after obtaining informed consent for participation from their parents/guardians.

Recurrent abdominal pain was defined as the development of a minimum of three episodes of abdominal pain occurring in the space of twelve weeks, each episode being severe enough to affect daily activities.

Patients were documented for demographic data such as age, gender and weight, duration of complaints, as well as associated complaints with abdominal pain, if any, at the time of enrollment in the study. Stool samples were taken from each patient. Deoxyribonucleic acid (DNA) was purified from the stool sample using a standard kit (QIAamp® DNA Stool Mini kit; Hilden, Germany). DNA was detected using a polymerase chain reaction assay (Ready To-Go PCR beads kit; Buckinghamshire, UK) with primers targeting the 16S ribosomal RNA gene specific to H. pylori, specifically its 399 bp fragment, followed by amplification and subsequent detection of target sequence using the appropriate probe. This test was chosen over the simpler and cheaper H. pylori stool antigen test and the urea breath test due to its better diagnostic accuracy. All patients were also tested for iron deficiency anaemia which was defined as a haemoglobin level of <11.5g/dL, and a serum ferritin level of <10.0µg/L.¹²

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. Mean and

standard deviation were calculated for quantitative variables specifically patient age, weight, duration of complaints, serum haemoglobin level and serum ferritin level. Qualitative variables like gender, associated complaints such as nausea, vomiting, anorexia or diarrhoea, whether patient tested positive for H. pylori infection via PCR and whether patient had iron deficiency anaemia, were recorded in terms of frequency and percentage. Variables were stratified and compared to test positivity via PCR for H. pylori infection using the Chi square test and independent samples t-test. A *p*-value of ≤ 0.05 was considered significant.

RESULTS

Our study consisted of a total of 152 patients, with a mean age of 7.32±2.62 years. There were more females in the sample (n=86, 56.6%). The mean weight of the sample at the time of presentation was 28.98±13.63 kg. The mean duration for which the patient sample complained of recurrent abdominal pain was 8.80±3.92 months. A total of 39(25.7%) patients experienced nausea, 35(23.0%) complained of vomiting, while 19(12.5%) and 16(10.5%) complained of anorexia and diarrhoea, respectively. Table-I shows the patient characteristics distributed according to gender.

Table-I: Patient Characteristics according to Gender (n=152)

Variable	Males (n=66) Mean±SD	Females (n=86) Mean±SD	<i>p</i> -value
Age (years)	6.7 ± 2.4	7.7 ± 2.6	0.016
Weight (kg)	26.2 ± 12.9	31.0 ± 13.8	0.031
Duration of Recurrent Abdominal Pain (months)	8.4 ± 3.8	9.0 ± 3.9	0.393
Associated Complaints, n (%)			
Nausea	18 (27.3%)	21 (24.4%)	0.690
Vomiting	19 (28.7%)	16 (18.6%)	0.139
Anorexia	8 (12.1%)	11 (12.8%)	0.902
Diarrhoea	7 (10.6%)	9 (10.5%)	0.978

Table-II shows the results of the study according to gender. The mean haemoglobin level was 12.40±1.66 g/dL, while the mean serum ferritin level was 32.41±31.61 ng/mL. A total of 63(41.4%) patients tested positive for H. pylori infection, while 32(21.2%) were suffering from iron deficiency anaemia.

Table-II: Frequency of H. pylori infection in Children presenting with Recurrent Abdominal Pain and their Iron Status (n=152)

Variable	Males (n=66) n (%)	Females (n=86) n (%)	<i>p</i> -value
H. pylori Infection Present	29(43.9%)	34 (39.5%)	0.585
Haemoglobin Level (g/dL), Mean±SD	12.2±1.5	12.5±1.7	0.185
Ferritin Level (ng/mL), Mean±SD	37.1±33.2	28.7±29.9	0.107
Iron Deficiency Anaemia Present	12(18.1%)	20(23.3%)	0.477

A comparison between patients who tested positive for *H. pylori* and those who didn't was conducted, as shown in Table-III. Our analysis demonstrated that patients who were afflicted by *H. pylori* infection had a higher propensity to suffer from iron deficiency anaemia, ($p=0.002$). In addition, patients who were infected with *H. pylori* tended to have lower weights, ($p=0.017$).

Table-III: Comparison of Symptomatology and Characteristics Among Patients with and without *H. pylori* Infection (n=152)

Variable	H. pylori Positive (n=63) n (%)	H. pylori Negative (n=89) n (%)	p-value
Iron Deficiency Present	21(33.3%)	11 (12.4%)	0.002
Iron Deficiency Absent	42(66.7%)	78 (87.6%)	
Age			
≤7 years	36(57.1%)	39 (46.0%)	0.106
>7 years	27(42.9%)	50 (46.0%)	
Gender			
Male	29(46.0%)	37 (43.8%)	0.585
Female	34(54.0%)	54 (56.2%)	
Weight			
≤30 kg	44(69.8%)	45 (50.6%)	0.017
>30 kg	19(30.2%)	44 (49.4%)	
Associated Complaints			
Vomiting	16 (25.4%)	19 (21.3%)	0.559
Anorexia	8 (12.7%)	11 (12.4%)	0.950
Diarrhoea	11 (17.5%)	5 (5.6%)	0.019
Nausea	18 (28.6%)	21 (23.6%)	0.489

DISCUSSION

H. pylori infection is a common malady afflicting the adult population in Pakistan and, since the most common source of infection is a contaminated water-supply.¹³ Our study sample primarily consisted of females, accounting for 86(56.6%) of cases. This is in keeping with existing literature where a preponderance of females is noted in paediatric patients reporting with recurrent abdominal pain.^{9,14} In fact, Piriyaikitphaiboon *et al.* reported a similar female preponderance: 61.7% for their paediatric patients with recurrent abdominal pain were female.⁸ While the exact reason from this is unclear, studies have proposed that poor diet and mental health have a some role to play in the increased attendance of paediatric females to the out-patient departments with recurrent abdominal pain.¹⁵

The mean age of children presenting with recurrent abdominal pain in our study was 7.32 ± 2.62 years. This is in keeping with other studies, showing that patients with this condition presented with a

mean age of 7.37 ± 3.0 years.¹⁶ However, we noted that females had a tendency to present at a slightly later age with recurrent abdominal pain than males, which may have a two-fold explanation: firstly, advancing age is seen to be associated with an increased frequency of infection with *H. pylori*, as demonstrated by studies including Nasri *et al.* and Polinonva *et al.*, and secondly, females that attain menarche can also report with recurrent abdominal pain which is usually associated with menstruation, but may also be acyclical.¹⁶⁻¹⁹ The advanced age at presentation also accounts for the statistically significant difference in weight that was seen in our study between males and females, moreover, *H. pylori* infection is associated with an increase in leptin levels, with a concurrent decrease in ghrelin levels, causing infected individuals to have longer periods of satiety, and lower weights than patients who are not infected, which was also clearly demonstrated in our study, and also accounts for the difference in weights between males and females, where the males in our study had slightly higher, albeit statistically insignificant, rates of infection.²⁰

Our study showed that 41.4% of patients with recurrent abdominal pain tested positive for *H. pylori* infection. Prasetyo *et al.*, in their study in Indonesia, reported that 30.9% of all paediatric patients with recurrent abdominal pain suffered from *H. pylori* infections, which was lower than our result.²¹ Hassan *et al.* reported that *H. pylori* infections occurred in 52.7% of their study sample of paediatric patients suffering from recurrent abdominal pain which was much higher than our figure, even though the study was conducted in the same country.²² Jang *et al.* reported a much lower 6.7% in their study on a similar population in South Korea.²³ These differences in frequency can be attributable to the variability in the socioeconomic conditions, availability of clean drinking water and sanitation, with populations from developed countries having a lower incidence compared to those from developing countries.²¹⁻²³ Moreover, this figure could also indicate that causes for recurrent abdominal pain in children varies across populations and the detection of infection may also be incidental.

Lastly, of the patients who were suffering from *H. pylori* infection, 33.3% suffered from iron deficiency anaemia, which was significantly higher than patients who did not have the infection. This finding is in keeping with existing studies on the

subject such as Boyanova *et al.* and Darvishi *et al.* who reported that *H. pylori* infection was present in 82.2% and 81.3% of children suffering from iron deficiency anaemia, likely as a result of alteration in the metabolism of iron.^{24,25}

LIMITATIONS OF STUDY

Our study did not have a control arm of paediatric patients without abdominal pain and, therefore, could not establish whether infection rate with *H. pylori* was generally higher in the entire population, or whether it was only high in patients with recurrent abdominal pain. In addition, we did not screen for other infections, especially parasitic ones, which are also sourced from contaminated water sources, and may result in abdominal pain and other gastrointestinal symptoms as well as iron deficiency anaemia. In addition, causality between the presence of infection and abdominal pain could not be clearly established. Lastly, menstruation was a potential confounding factor in our study, which may account for a female preponderance of recurrent abdominal pain seen in it, especially in the slightly older paediatric age group, a fact that requires further study.

CONCLUSION

H. pylori is a common infection afflicting the paediatric population in Pakistan and is associated with significant long-term risks. Children who present with recurrent abdominal pain have a high-rate of carriage in this country, and should be screened for it, and the appropriate treatment instituted, where necessary.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

BA & ZA: Conception, study design, drafting the manuscript, approval of the final version to be published.

ZA & AA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

RM & WA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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