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Helicobacter Pylori Infection among Children with Recurrent Abdominal Pain: A Single Center Study

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Abstract **Original Research Article**

Background: Recurrent abdominal pain (RAP) is a common problem in children. Mostly it is functional, but due to recent advanced diagnostic technologies more organic causes are identifying. Among the organic causes Helicobacter pylori (H. pylori) infection is common, especially in developing countries. Early detection and treatment of this infection may prevent some serious gastrointestinal problems in later age. ***Objective:*** To evaluate the frequency of H. pylori infection as a cause of recurrent abdominal pain in children. ***Methods:*** This cross sectional study was conducted among the children with recurrent abdominal pain (RAP) in the pediatric Gastroenterology, Hepatology & Nutrition Department of Bangladesh Shishu Hospital & Institute in Bangladesh from January 2019 to December 2020. A total of 70 patients were included in the study. Demographic data, clinical manifestations, laboratory parameters were recorded in a standard data sheet. All the participants underwent to upper GI endoscopy and gastric biopsy were taken in all the patients. Rapid urease test and histopathology of gastric biopsy samples were done to confirm H. pylori infection. Collected data were checked manually and analyzed by SPSS version 22.0. Association of parameters with infection were done by unpaired t-test, chi-square test and fisher's exact test. ***Results:*** Helicobacter pylori infection in children with RAP was 35.7%. Mean age of the infected children was 9.49±2.47 years with male (52%) predominance. There was significant association of infection with lower socioeconomic class (p=0.003). Patients with RAP for>6 months' duration were significantly associated with infection (p=0.003). Family size and source of drinking water had no effect on results. Most of the RAP patients with positive infection had poor growth (p=0.003). Pallor, abdominal tenderness or vomiting were not significantly associated clinical manifestations of H. pylori infection. ***Conclusions:*** Helicobacter pylori infection is common in children with recurrent abdominal pain. H. pylori infection is associated with lower socioeconomic condition, prolonged duration of recurrent abdominal pain. It affects the growth of the children.

Keywords: Helicobacter pylori infection, Recurrent abdominal pain (RAP), Upper GI endoscopy, Gastric biopsy.

INTRODUCTION

Abdominal pain is one of the most common symptom in children [1]. British Pediatrician J Apley, observed that, about 10% of school aged children get recurrent episodes of abdominal pain. He named this symptom as recurrent abdominal pain [2]. Recurrent abdominal pain (RAP) is defined as at least three episodes of abdominal pain, severe enough to affect their activities over a period of longer than three months [3]. It is often interfering with school attendance and performance, peer relationships, participation in sports and family activities [4]. About 4% to 25% of school aged children experience RAP [5]. In Bangladesh, it occurs in 11.5% of children [3]. Recurrent abdominal

pain is one of the most common and challenging diagnostic problem in pediatrics. It is a frustrating concern for the child, parents and physician. [6] It is most often considered functional (nonorganic) abdominal pain, but organic causes are found in 5% to 10% of cases [7]. Now a days advanced medical technologies and better understanding of the pathophysiology of abdominal pain, more and more organic causes have been identified [1]. Among organic causes parasitic infestation, urogenital disease, inflammatory bowel disease, peptic ulcer disease associated with Helicobacter pylori (H. Pylori) infection are common [8]. In several studies, it has been proposed that H. pylori infection may be a cause of RAP in one quarter to one third of children [9, 10]. H. pylori is one of the most common chronic bacterial infection worldwide, which infects at least 50% of world's population. This infection is more prevalent in developing countries than developed countries. The prevalence may vary between populations and between groups within the same population [12]. It is associated with poverty and risk factors include overcrowded households, poor sanitation and poor water supply [13]. It is acquired during early childhood and if left untreated, it may persist throughout the life [14]. Acute infection is often silent. It is one of the main cause of chronic gastritis in children. This infection is suspected to cause recurrent abdominal pain [15]. Infection is usually progresses to severe inflammation and infected gastric mucosa may lead to atrophy, metaplasia and cancer at an older age [16]. H. pylori is also classified as a Group I carcinogen by the World Health Organization and the International Agency for the Research on Cancer [17]. H. pylori infection in children differs from the adults, from the point of view of epidemiology, host response, clinical features, related diseases, diagnosis and also in treatment strategies [18]. Guidelines on screening for H. pylori in children are often contradictory. Recommendations vary from no need to routine screening of children with RAP [19]. Accurate diagnosis of H. pylori infection is a crucial part in the effective management of RAP. Several invasive and noninvasive diagnostic tests are available for the detection of H. pylori and each test has its usefulness and limitations [20]. Invasive tests require endoscopy and biopsy followed by histology, culture, rapid urease test and polymerase chain reaction. Non-invasive tests include the urea breath test, detection of antigen in stool and detection of antibodies in serum, urine and saliva [21]. For the diagnosis of infection, gastrointestinal endoscopy with histology is considered to be the gold standard. Both North American Society for Pediatric Gastroenterology, Hepatology & Nutrition and European Society for Pediatrics Gastroenterology Hepatology and Nutrition has recommended that early detection of H. pylori infection should be based on invasive methods such as rapid urease test, histopathology and cultures. In a study regarding the diagnostic tests for H. pylori infection in children by reviewing literature from 1999 to 2009 and showed that endoscopy with histopathology is the only method which can diagnose and confirm the infection [22]. Performing a noninvasive test to detect infection and treat accordingly may not be accurate. So, the 'test and treat' strategy based on noninvasive methods is not recommended [14]. Most studies focusing on H. pylori infection focused on adults. Only a few studies on children are available. There are some pediatric studies in both developed and developing countries focused on the relationship between H. pylori infection with recurrent abdominal pain, where most of the developing countries shows significant association in comparison to developed countries [4]. Recurrent abdominal pain may be the early and classical symptom of childhood H. pylori infection in developing countries where prevalence rate is significantly high. Early detection and treatment of such infection will improve the day to day activities of the child and might be helpful in the prevention of peptic ulcer and gastric cancer.

OBJECTIVES

General objective:

To evaluate the role of H. pylori infection in children with recurrent abdominal pain.

Specific objectives:

- To find out the upper gastrointestinal endoscopic features of suspected H. Pylori infection in children with RAP.
- To detect H. pylori from gastric tissue biopsy by rapid urease test in children with RAP.
- To detect the H. pylori by histologic staining of gastric tissue biopsy in children with RAP.
- To estimate the H. pylori infection in children with RAP.

METHODOLOGY

This study was Cross sectional study, by using Purposive sampling method on January 2019 to December 2020 Department of Pediatric Gastroenterology, Hepatology and Nutrition of Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh. The patient was 5 years to 15 years old children with RAP admitted in Bangladesh Shishu Hospital & Institute. A total of 70 patients were included in this study as study population.

Inclusion criteria:

Age: 5 years to 15 years. Gender: Both male and female. Clinically diagnosed as RAP.

Exclusion criteria:

- Children with active upper gastrointestinal bleeding.
- Children with already diagnosed as urinary tract infection, inflammatory bowel disease, malignancies or other organic causes of pain.
- Children with intake of any antimicrobial, proton-pump inhibitors, H2 receptor blockers,

NSAIDs 2 weeks prior to endoscopic examination.

Study procedure

Clinical and demographic data were recorded including age, gender, family member, socioeconomic condition, source of drinking water, duration of symptoms at presentation. Weight and height of all participants were measured by Turine ZT-120 machine. Pallor, abdominal tenderness was examined. Prior to upper gastrointestinal endoscopy and biopsy, other causes of recurrent abdominal pain were ruled out from investigation reports that were included complete blood count, urine routine microscopic examination and culture reports, stool routine microscopic examination, Serum glutamate pyruvate transaminase, serum creatinine, serum amylase, serum lipase, abdominal ultra-sonogram. All participants were under went into endoscopy of upper gastrointestinal tract. Patient were kept fasting for at least 4 hrs. before procedure. After that conscious sedation was administered to the patient with injection midazolam 0.15- 0.30 mg/kg IV slowly with dilution. Then long, flexible, lighted tube called endoscope was guided through the mouth and throat, through the esophagus, stomach and duodenum. Multiple images were recorded, among these four to six of the recorded images specifically of the antrum, lesser and greater curvature of the body and cardia of the stomach were used for analysis in each case. Studying the biopsy specimens for morphological changes under low and high power magnification, slides were screened under oil emulsion for the detection of H. pylori. Presence of the histological variables like mononuclear infiltrate, neutrophilic infiltrate, bacterial density and gastric atrophy was termed as gastritis.

Data processing and data analysis

All the data were entered into a personal computer and thoroughly checked for any possible errors and then processed and analyzed by SPSS version 22.0. Data were expressed as numbers and percentages for categorical variables and as mean and range (minimum and maximum) for quantitative variables. Associations between categorical variables were evaluated using the chi-square (χ^2) test and Fisher's exact test. Unpaired t- test was used for continuous variables. For all statistical test p value of less than 0.05 was considered as statistically significant.

Ethical Consideration

Ethical approved was taken from the Ethical Review Committee (ERC) of Bangladesh Shishu Hospital & Institute.

RESULTS

Table 1: Baseline characteristics of the Participants, (N=70)

Variables	Frequency (n)	Percentage (%)
Age groups (years)		
5-<10 yrs.	46	65.7
≥10-15 yrs.	24	34.3
Mean ± SD	8.58±2.80	
Range	(5.0-14.0) years	
Gender		
Male	37	52.9
Female	33	47.1
Male: Female ratio	1.1:1	
Socio-economic status		
Lower class	24	34.3
Middle class	32	45.7
Upper class	14	20
Water source		
Tube well	22	31.4
Tap water	48	68.6
Family members		
≤4	14	20
>4	56	80
BMI		
Normal weight	42	60.0
Under weight	19	27.1
Over weight	9	12.9

Table 1 showed, baseline characteristics of the studied population, majority of them were male and younger than 10 years. Most of the patientss came from middle class with large family size and were used tap water for drink. Majority of them had normal BMI.

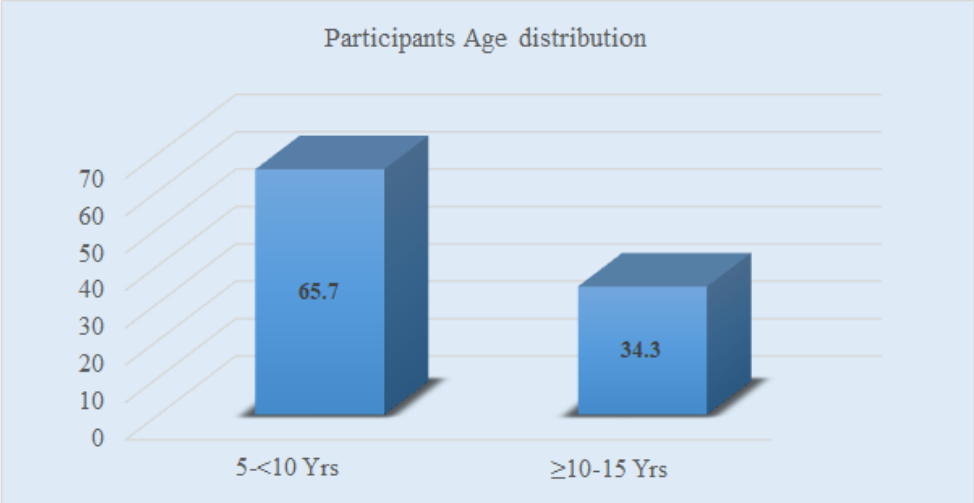

Figure I: Bar chart showed age distribution of the Participants, (N=70)

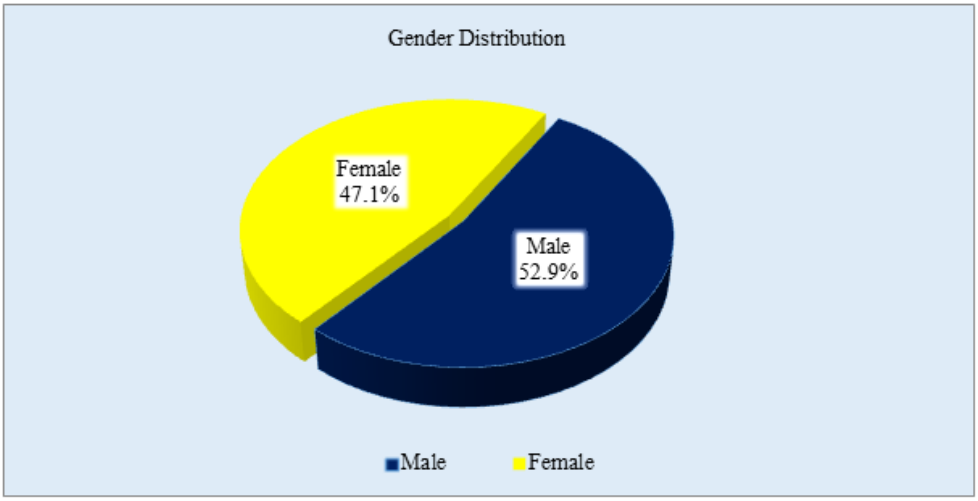

Figure II: Pie chart showed gender distribution of the Participants, (N=70)

Table 2: Investigation findings of the Participants, (N=70)

Diagnostic Tests	**Results**	**n (%)**
Endoscopy	Gastritis	2(45.7%)
	Normal	38(54.3%)
Rapid urease test	Positive	29(41 4%)
	Negative	41(58.6%)
Histopathology	H. pylori gastritis	25(35.7%)
	H. pylori absent	45(64.3%)

Table 2showed Endoscopic gastritis was present in 45.7% patientss, among them 41.4% were rapid urease test positive and finally 35.7% were H. pylori positive gastritis.

Table 3: Endoscopic findings of the Participants, (N=70)

Endoscopy findings	**H. pylori**			**p value**
	Positive	Negative	Total	
	n (%)	n (%)	n (%)	
Gastritis	24(96.0%)	8(17.8%)	32(45.7%)	<0.001**
Normal	1(4.0%)	37(82.2%)	38(54.3%)	

Table 3 showed, gastritis was significantly associated with recurrent abdominal pain among the participants. (N=70)

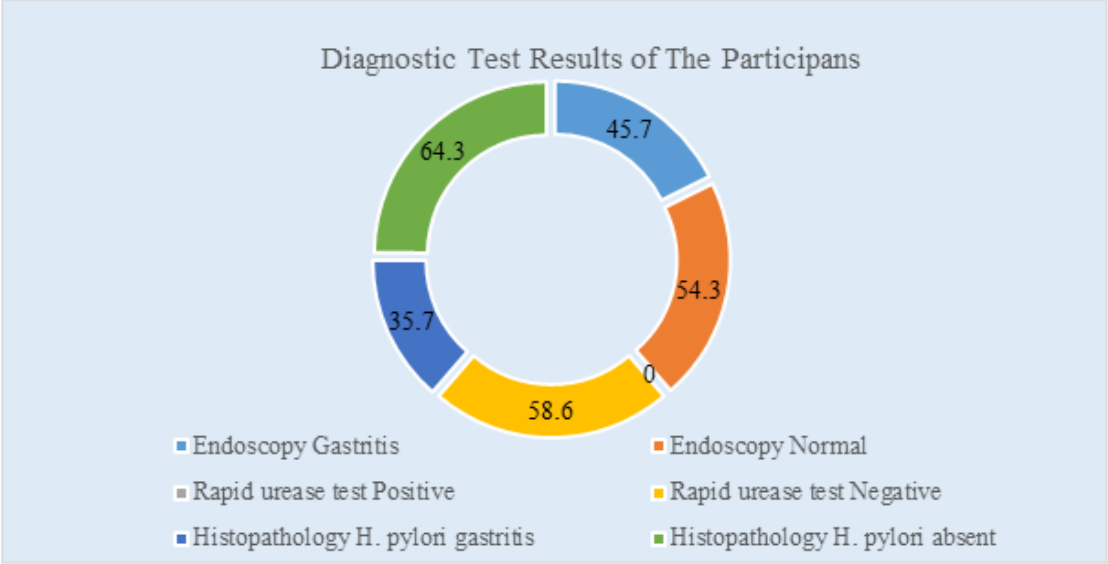

Figure III: Ring chart showed diagnostic test results of the Participants, (N=70)

Table 4: Rapid urease test results of the Participants. (N=70)

Rapid Urease test	H. pylori			p value
	Positive	Negative	Total	
	n(%)	n (%)	n (%)	<0.001**
Positive	25(100.0%)	4(8.9%)	29(41.4%)	
Negative	0(0.0%)	41(91.1%)	41(58.6%)	

Table 4 showed, rapid urease test was significantly positive in the participants with recurrent abdominal pain.

Table 5: Histopathological findings of the Participants, (N=70)

Histopathology	H. pylori			p value
	Positive	Negative	Total	
	n (%)	n (%)	n (%)	
H. pylori gastritis	25(100.0%)	0(0.0%)	25(35.7%)	<0.001**
H. pylori absent	0(0.0%)	45(100.0%)	45(64.3%)	

Table 5 showed, H. pylori gastritis was significant in participants with recurrent patients. (N=70)

Table 6: Distribution of the Patients by frequency of H. pylori positive, (N=70)

H. pylori	Frequency (n)	Percentage (%)
Positive	25	35.7
Negative	45	64.3

Table 6 showed, frequency of H. pylori that 35.7% of RAP patients Were H. pylori positive.

Table 7: Association of H. pylori positive Patients with age group, (N=70)

Age group (years)	H. pylori			p value
	Positive	Negative	Total	
	n (%)	n (%)	n(%)	
5-<10 yrs.	12(48.0%)	34(75.6%)	46(65.7%)	0.042*
≥10-15 yrs.	13(52.0%)	11(24.4%)	24(34.3%)	
Mean ±SD	9.49±2.47	8.07±2.86	8.58±2.80	

Table 7 showed mean age (9.49±2.47 years) was more in H. pylori positive group in comparison to mean age (8.07±2.86 years) of negative that were statistically significant. It was more common in ≥10-15 years' group than 5- <10 years' group.

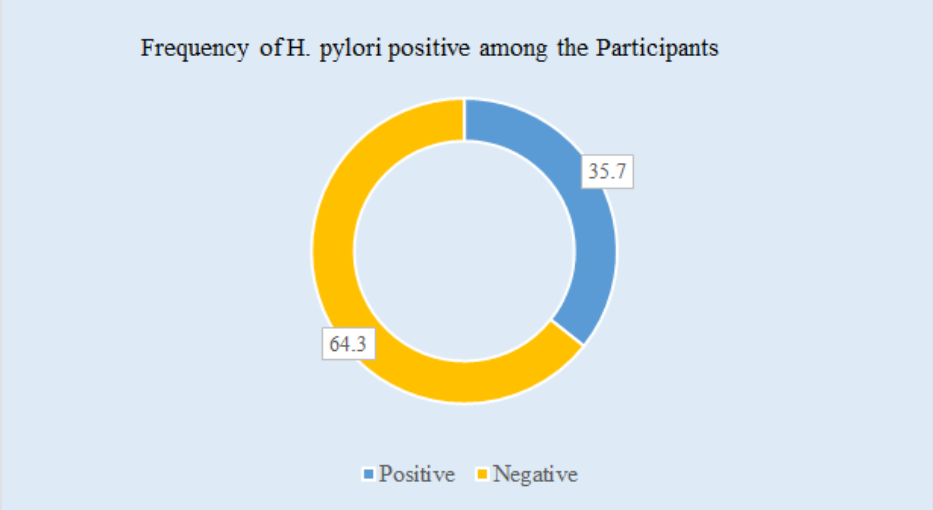

Figure IV: Ring chart showed H. pylori wise distribution of the Participants, (N=70)

Table 8: Association of H. pylori positive Patients with gender, (N=70)

Gender	H. pylori			p value
	Positive	Negative	Total	
	n (%)	n (%)	n (%)	
Male	13(52.0%)	24(53.3%)	37(52.9%)	0.915
Female	12(48.0%)	21(46.7%)	33(47.1%)	

Table 8 showed male were marginally more affected than female.

Table 9: Association of socioeconomic status of H. pylori positive Patients, (N=70)

Socioeconomic status	H. pylori			p value
	Positive	Negative	Total	
	n(%)	n (%)	n (%)	
Lower class	15(60.0%)	9(20.0%)	24(34.3%)	0.003**
Middle class	8(32.0%)	24(53.3%)	32(45.7%)	
Upper class	2(8.0%)	12(26.7%)	14(20.0%)	

Table 9 showed, majority of participants 32(45.7%) are in middle class of H. pylori negative but 15(60%) of lower class were H. pylori positive, which was statistically significant.

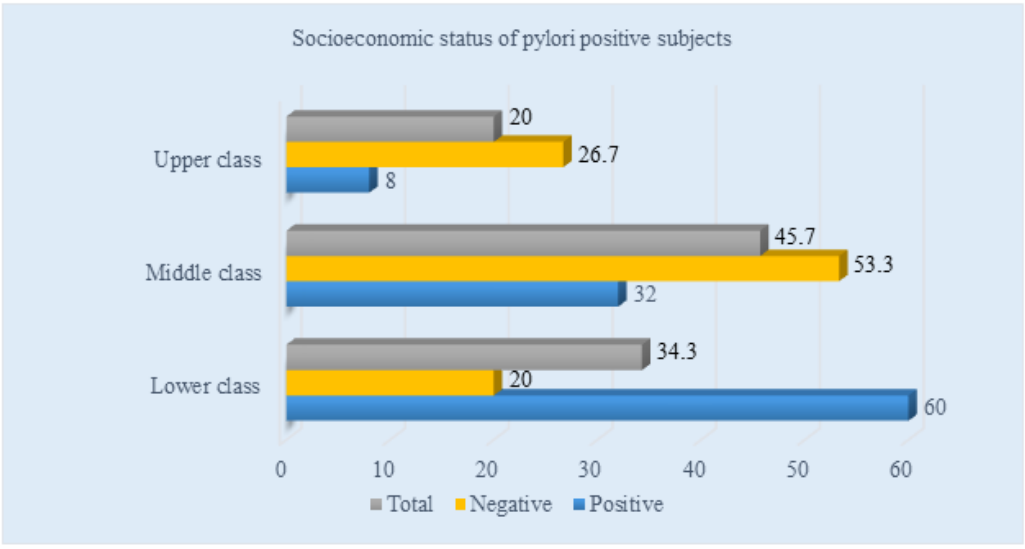

Figure V: Bar chart showed socioeconomic status H. pylori patients. (N=70)

Table 10: Association of H. pylori positive patients with source of drinking water, (N=70)

Source of drinking water	H. pylori			p value
	Positive	Negative	Total	
	n (%)	n(%)	n (%)	
Tube well	5(20.0%)	17(37.8%)	22(31.4%)	0.125
Tap water	20(80.0%)	28(62.2%)	48(68.6%)	

Table 10 showed tap water was the source of drinking water in maximum participants 48 (68.6%).

Table 11: Association of H. pylori positive patientss with duration of illness, (N=70)

Duration of illness	H. pylori			P value
	Positive	Negative	Total	
	n (%)	n (%)	n (%)	
>6 months	15(60.0%)	11(24.4%)	26(37.1%)	0.003**
≤6 months	10(40.0%)	34(75.6%)	44(62.9%)	

Table 11 showed, the duration of illness of RAP. Patients with long duration (>6 months) of RAP had significant association with H. pylori infection.

Table 9: Association participant family members of H. pylori, (N=70)

Family members	H. pylori			P value
	Positive	Negative	Total	
	n (%)	n (%)	n (%)	
≤4	2(8.0%)	12(26.7%)	14(20.0%)	0.061
>4	23(92.0%)	33(73.3%)	56(80.0%)	

Table 9 showed majority of RAP 56(80%) participants were in large family in H. Pylori negative and were 23(92%) in large family.

Table 10: Association of H. pylori positive Patients with BMI, (N=70)

BMI	H. pylori			P value
	Positive	**Negative**	**Total**	
	n (%)	**n (%)**	**n(%)**	
Normal weight	13(52.0%)	29(64.4%)	42(60.0%)	0.003**
Under weight	12(48.0%)	7(15.6%)	19(27.1%)	
Over weight	0(0.0%)	9(20.0%)	9(12.9%)	

Table 10 showed, majority patients 42(60%) had normal weight, but most of the underweight patients with RAP were H. pylori positive, which was statistically significant.

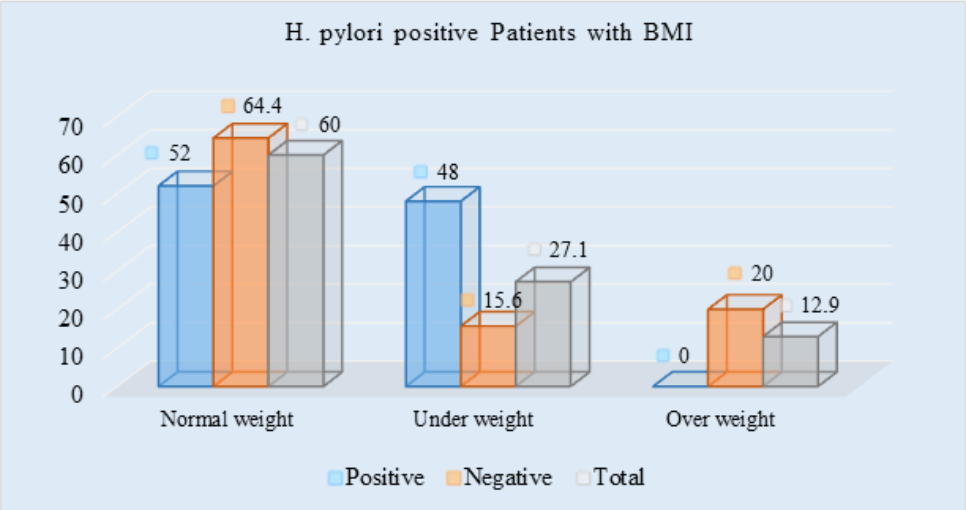

Figure VI: Bar chart showed BMI wise H. pylori positive Patients, (N=70)

Table 11: Associated clinical manifestations of the Participants, (N=70)

Clinical manifestations	H. pylori			P value
	Positive	Negative	Total	
	n (%)	n (%)	n (%)	
Abdominal pain	25(100.0%)	45(100.0%)	70(100.0%)	
Vomiting	3(12.0%)	3(6.7%)	6(8.6%)	0.75
Pallor	5(20.0%)	4(8.9%)	9(12.9%)	0.337
Abdominal tenderness	14(56.0%)	18(40.0%)	32(45.7%)	0.198

Table 11 showed, clinical manifestations of the patients. Vomiting, abdominal tenderness and pallor were not significantly associated with H. pylori infection.

DISCUSSION

In this study, H. pylori infection was positive in 35.7% patients with recurrent abdominal pain (RAP) (H. pylori was detected by rapid urease test and histopathology of gastric biopsy). Memon *et al*., (2009) [23], showed prevalence rate of H. pylori infection in children was 31%, Yu *et al*., (2014) [14], showed 32.1%. Mahmud, Shah and Ali (2015) [24]; Nazimuddin, Chohan and Memon (2017) [25] found 38%, 32.5% and 36.7% respectively. The results were similar to this study. A study conducted by Zangana and Abdullah (2020) [4], showed prevalence rate was 24% in patients with RAP. Some other studies done by Motamed *et al*., (2014) [26], and Khurshid, Ishaq, and Ahmad (2020) [27] found 55.7% and 62.5% respectively, that results were much higher than this study. The difference in the obtained results may be due to use of different diagnostic method, different age range of the studied patients. Controversial results can be justified by regional variation, different sample sizes and method of screening tests used [4]. In this study, the mean age of H. pylori positive patients was 9.49±2.47 years that was significant in comparison with H. pylori negative patients (mean age 8.07±2.86 years). Punhal, Malik and Iqbal (2016) [11] found the mean age of H. pylori positive patients was 9.40±3.54 years while negative patients were 7.12±3.12 years this results were similar to this study. In this study, majority of the patients of RAP associated with H. pylori infection were aged ≥10 years. Nadeem *et al*., (2006) [28], found similar result in their study. In contrary Mohsen *et al*., (2018) [29], showed no significant difference in age group. Khurshid, Ishaq and Ahmad (2020) [27] found significant association in ≤8 years of age. This difference may be due to different age range of their studied patients being 2 to 12 years. In this study, male (52%) were marginally more affected than female (48%) and there was no significant association between the gender and H. pylori infection. Study conducted by Nadeem *et al.*, (2006), [28] Nazimuddin, Mohsen *et al.*, (2018) [29], also identified gender has not been a relevant influencing characteristic for H. pylori infection. Some other studies conducted by Hestvik *et al*., (2010) [30], demonstrated that male were 1.3 times more affected than female. The present study showed 60% of the children with RAP were H. pylori positive belonged to low socioeconomic status and that was statistically significant. Nadeem *et al*., (2006) [28] found 92%, Senbanjo, Oshikoya and Njokanma (2014) [31] found 68.4%, Mahmud, Shah and Ali (2015) [24] showed 78.9%, Alimohammadi *et al*., (2016) [10], showed 72.1%; Khurshid, Ishaq and Ahmad (2020) [27] also showed 90.3% of low socioeconomic class group were more affected than other group, which was similar to this study. This was may be due to inadequate maintenance of proper hygiene, living conditions, sharing foods from same plates and poor sanitary habits [31]. In this study, majority of patients had recurrent abdominal pain with duration of ≤6 months. But, patients with recurrent abdominal pain for >6 months' duration (60%) were significantly associated with H. pylori infection. A study done by Alimohammadi *et al*., (2016), [10] also found progressed infection with increased age of the children. In contrary, Khurshid, Ishaq and Ahmad (2020) [27] found 82.5% of patients with recurrent abdominal pain duration <6 months were H. pylori positive. In this study, majority of RAP patients (80%) were in large family (>4) and H. pylori positive patients were also proportionately higher (92%) in large family. Therefore, family size had no effect on the association of RAP with H. pylori infection. Senbanjo, Oshikoya and Njokanma (2014) [31] also found 52.9% and 56.6% patients respectively came from large family and were not significantly associated with the H. pylori infection, which were similar to this study. Mansour, Al Hadidi and Omar (2012) [19] showed infection was significantly higher in large family. They stated crowding had a major role in spreading infection. Present study showed that, there was no significant relation between H. pylori infection with source of drinking water, 68.6% patients had drinking water from tap. Similar result was found in some previous studies done by Senbanjo, Oshikoya and Njokanma (2014) [31] where 65.5% of safe water drinker and 52.9% of unsafe water drinker were H. pylori infected. Alimohammadi *et al*., (2016) [10], showed 58.3% of tap water drinker and 52% of boiled water drinker had H. pylori. In contrary Mahmud, Shah and Ali (2015) [24] stated that there was an increased risk of H. pylori infection with the use of filtered water (81.6%) and hand pump water (82.5%) respectively. They revealed H. pylori can harbor and survive in water. In this study, showed significant difference in relation to body weight with H. pylori infection (p=0.003), majority of RAP patients (60%) were in normal weight, but among the 19 underweight patients with RAP 12 were H. pylori positive. Richter *et al*.,

(2001) [32], also showed infected patients had poor growth (p= 0.02) that was similar to this study. Senbanjo, Oshikoya and Njokanma (2014) [31] did not showed significant relationship with stunting (p=0.629) and thinness (p=0.789) in H. pylori infected patients. Mansour, Al Hadidi and Omar (2012) [19] found 17.3% patients with H. pylori had poor growth, that was not significant. Recurrent abdominal pain due to H. pylori infection and its effect on growth in children was controversial. Most of the positive patients had poor socioeconomic status which may independently suppress growth. But, infection may cause growth suppression in this vulnerable groups of children [31]. In the present study, 8.6% patients with recurrent abdominal pain had associated vomiting, 12.9% had pallor and abdominal tenderness was found in 45.7% of total patients, these were not significant in H. pylori infection. In a study done by Motamed *et al*., (2014) [26], found associated vomiting in 10%, abdominal tenderness had 62.5% patients and 23.8% had anaemia and these findings were also not significant, which was similar to this study. Mansour *et al*., (2012) [19] showed associated vomiting was present in 24.04% patients, had abdominal tenderness in 28.85% and anaemia in 19.23% patients and these were statistically significant in recurrent abdominal pain patients with H. pylori positive infection. It was stated that, iron deficiency anaemia occurred because of poor absorption of iron due to low gastric acid secretion, poor dietary intake and utilization of iron by the bacteria itself [19].

LIMITATIONS & RECOMMENDATION

Single center study. Small sample size. Recurrent abdominal pain is one of the most common health problem in children. We have to evaluate the organic causes of it. From this study it can recommend that, Helicobacter pylori infection should be evaluated as a cause of recurrent abdominal pain in children. But a multicenter study with larger sample size is needed to obtain more reliable results.

CONCLUSION

This study showed that Helicobacter pylori infection is common in children as a cause of recurrent abdominal pain. Helicobacter pylori infection is associated with lower socioeconomic condition, prolonged duration of recurrent abdominal pain. It affects the growth of the children.

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