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Prevalence of Helicobacter Pylori Infection in Children and Adolescents

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Abstract:
Background: The prevalence of *Helicobacter pylori* has declined over recent decades due to improved sanitation, socioeconomic development, and better living conditions; however, its prevalence remains high in the developing world *H. pylori* has infected nearly 50% of the population worldwide, with rates of 35%–90% depending on population diversity and geographic area.
Objectives: The objectives of this study are to study the H. *pylori* infection to children by identifying seroprevalence of *H. pylori* in pediatric patients.
Material and Methods: The data was collected from the records of privet lab in Derna city where the sample collected from children who came to the in order to investigate for H.pylori infections.
Results: Total, 200 children—89 boys (44.5%) and 111 (55.5%) girls were enrolled in the study.
Of the 200 children studied, 167 (83.5%) were living in Derna (urban area) and 33 (16.5%) in Umarzam, Alqba and AinMarah (rural area), 12(6.0%) in Umarzam, 13(6.5%) in Alqba and 8(4%) in Ainmarah. The overall prevalence of H. pylori infection in children was 37.5%
Conclusion: This infection is largely acquired during early childhood and the infection increased with age. Traditional diagnostic tools such as endoscopy and serology can be too invasive for children noninvasive urea breath test Analyzed group included 111 girls and 89 boys between 3years and 15years (mean age 9).

Keywords: Helicobacter, Pylori Infection, Children, Adolescents.

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INTRODUCTION

The prevalence of *Helicobacter pylori* has declined over recent decades due to improved sanitation, socioeconomic development, and better living conditions; however, its prevalence remains high in the developing world *H. pylori* has infected nearly 50% of the population worldwide, with rates of 35%–90% depending on population diversity and geographic area. The H. pylori infection status in children versus adults is not fully known since most infected children remain asymptomatic and studies are limited (1).
The diagnostic diversity of H. pylori can contribute to variable infection rates in children. (8) It is important to investigate the current H. pylori infection rate in children because it can be helpful for predicting the future incidence of H. pylori-related gastric diseases. This review examines the trend of H. pylori infection and risk factors associated with its transmission in children and adolescents based on a literature review and our own research (2).

OBJECTIVES

The objectives of this study are to study the H. *pylori* infection to children by identifying seroprevalence of *H. pylori* in pediatric patients.

LITERATURE REVIEW

History

The first well-known report of gastric Helicobacter has been credited to an Italian anatomist Giulio Bizzozero, as early as in 1893. In hand drawn illustrations, Bizzozero documented the presence of "spirochetes" with approximately 10 wavelengths within the parietal cells and gastric glands in the stomachs of dogs. However, the first record on the presence of spiral organisms in the human mucosa, adjacent to carcinoma. In 1939, Doenges showed 43% of human stomach autopsies harbored spiral organisms and a year later, Freedberg and Baron (1940) presented findings of "spirochetes" in about 40% of the resected gastric specimens (3).

These findings were viewed with skepticism as most of the samples of spiral organisms were obtained post mortem and the possibility of contamination could not be disregarded. Moreover, the hypothesis of contamination gained superiority in the early 1950s when Palmer performed a study on more than 1,000 gastric biopsies taken with a blind suction biopsy instrument and found no evidence of spirochetes. This incorrect conclusion drawn during that period could be due to the rigid endoscopes available, which only allowed biopsies to be taken from the fundus and not from the antrum, where H. pylori is usually located. The possibility that the appropriate staining solutions were not used could not be ruled out (4).

Unfortunately, attempts to culture the organism yielded only growth of Pseudomonas aerginosa. This was later assumed the contaminants from the endoscope. A major breakthrough in locking the link between gastroduodenal diseases and the spiral bacteria was established after numerous unsuccessful attempts, managed to culture the Campylobacter-like organism (CLO) by chance (5).

Furthermore, Barry Marshall himself had fulfilled the Koch's postulate, confirming an association of the bacteria and clinical disease by voluntarily ingesting a culture of H. pylori and was subsequently diagnosed with gastritis. The brief history on the discovery of H. pylori as illustrated in Table (2), shows that H. pylori has existed all this while, but investigators were not able to detect the bacteria in biopsies or merely considered their findings a result of contamination. The discovery of the gastric pathogen, H. pylori, has indeed led to a revolution in our understanding of gastroduodenal pathology, mainly gastritis and peptic ulcer (6).

Tabl1 1: The story of the discovery of *H.pylori*

The story of *H.pylori*		
Year	**References**	**Report**
1893	Bizzozero	Spiralorganismsin dogs
1896	Salomon	Spiralorganisms indogs and cats
1906	Krienitz	First description in a human with gastric cancer
1938	Doenges	Spirochetesinstomach(autopsies)
1940	Freedburg&Barron	Spirochetesinstomachwithulcersor carcinoma

1954	Palmer	Allbacteriainstomachsbelievedtobe contaminants
1975	Steer& Colin-Jones	Bacteria in gastric ulcer patients identifiedas*Pseudomonasaeruginosa*
1983	Warren&Marshall	Firstcultureof*H. pylori*

Morphology and physiology of H.pylori

H. pylori is a helical S shaped gram-negative bacterium. It is 2.5-5 µm in length, 0.5-1 µm in width and possesses a tuft of 4 to 6 polar-sheathed flagella. Each flagellum is 2.5 µm long and about 30 nm in thickness, with a membranous terminal bulb. The characteristic corkscrew motility enables the bacterium to burrow into the mucin lining the epithelial mucosa of the stomach. The flagella components consist of the hook protein (Flg E) and two flagellin proteins, FlaA and FlaB. H. pylori with disrupted flgE were non-motile and lacked the filaments, although both flagellin proteins were produced. Both flagellin subunits were found to be essential for motility and colonization of the stomach (7).

H. pylori prefer a microaerophilic environment with 5-10% carbon dioxide environment for in vitro culture. A variety of solid media containing 5-10% horse/sheep blood was used to culture the bacteriam. Under microaerophilic atmosphere, H. pylori colonies usually appeared after 3-5 days incubation at 37**C**.H. pylori presents 2 different morphologic manifestations: spiral and coccoid forms. The role of the spiral form has been shown to be strongly associated with gastroduodenal diseases (8).

However, the biological significance of the coccoid form, which is non-cultural in vitro, has yet to be determined. Some investigators postulated that the coccoid form may represent a persistent form in which H. pylori can exist in the environment as Viable but non-culturable **(**VBNC) and could possibly play a role in the transmission cycle and treatment failure (9).

***H. Pylori* infections and clinical consequences**

H. pylorus is the known major human bacterial pathogen responsible for gastroduodenal diseases. Once acquired and colonized, it can persist for life in the stomach. Many of those infected in the population experience no apparent adverse clinical consequences. However, a small population of carriers develop acute chronic gastritis, peptic ulcer disease, gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma (10).

Non-ulcerdyspepsia(NUD)

NUD or functional dyspepsia is defined as persistent upper abdominal pain or discomfort in patients without detectable abnormalities in structural or biological examinations. In subjects with dyspepsia, endoscopic studies have reported that 15-20% have peptic ulcer, 5-15% gastro- oesophageal reflux, <2% gastric cancer while majority (60%) have NUD.

It was observed that NUD occurs more frequently in younger patients (38% in patients younger than 25 years old) compared with older patients (3%-7% in patients older than 60 years old) (11).

Peptic ulcer disease

Epidemiological studies of *H. pylori* infection have provided evidence demonstrating the implication of *H. pylori* in the development of peptic ulcer. The prevalence of *H. pylori* infection in duodenal ulcer patients is about 70-98.9%. The causative relationship between *H. pylori* and peptic ulcer is reinforced when the organism was successfully eradicated in patients suffering from duodenal ulcer and the follow-up study over the next 4 years showed no duodenal ulcer recurred in *H. pylori*-negative patients. With the overwhelming research on the

causal link between *H. pylori* infection and peptic ulcer disease, the Maastricht 2-2000 Consensus Report strongly recommended *H. pylori* eradication therapy for patients with gastric and duodenal ulcers (12).

In a study which evaluated the risk factors (*H. pylori*, NSAIDs and smoking) for peptic ulcer and related serious upper gastrointestinal (GI) events, the population-attributed risk associated with peptic ulcer is 48% for *H. pylori* and 24% for NSAIDs usage. In addition, studies have also shown that occurrence of peptic ulcer have increased in *H. pylori* infected NSAIDs users (13).

However, the link between the use of NSAIDs and *H. pylori* infection is still a subject of clinical investigations, since conflicting results as to whether eradication of *H. pylori* would reduce the risk of peptic ulcer disease have been controversial. With regard to bleeding peptic ulcers, the report by showed a significant inverse relationship between *H. pylori* infection and NSAIDs usage. In their study population, the frequency of NSAIDs use in bleeding ulcers was shown to be high (79.2%). In contrast, the prevalence of *H. pylori* infection was lower in patients with bleeding. This negative interaction suggests a protective effect of *H. pylori* infection, lowering the risk of gastrointestinal bleeding in ulcer patients taking NSAIDs (14).

Gastric cancer

The World Health Organization International Agency for Research on Cancer (IARC) designated *H*. pylori as a Class I (definite) carcinogen. The association between *H. pylori* and cancer may be explained by 2 possible mechanisms: one is based on a carcinogenesis-promoting effect of the bacterium itself and the other is based on the establishment of a carcinogenic environment due to long-term infection. This long lasting infection may induce atrophic gastritis, which is considered the initial step in the gastritis-metaplasia-carcinoma squeals in the stomach.

Phospholipase A2 of H. pylori was shown to cause epithelial cell membrane damage. In addition, the vacuolating cytotoxin (VacA+) of *H. pylori* constitutes increased risk for the development of peptic ulcer and gastric cancer. The reactive oxygen species (ROS) generated from the inflammation response by the host during an infection can also induce DNA damage with the accumulation of DNA mutations, thus leading to pathogenesis of gastric cancer (15).

EPIDEMIOLOGY AND TRANSMISSION

Source of Infection

So far, human is the principle source of H. pylori, although several animals which were considered as potential reservoirs such as domestic cats and rhesus monkeys have been exonerated. In addition to isolation of H. pylori from the animals, the bacterium has also successfully infected many laboratory animals. Increased risk of infection with exposure to sheep was reported. Water has also been implicated as a source of *H. pylori* infection which reported that children from homes using a municipal water supply were three times more likely to be infected than those whose homes had internal water sources (16).

Transmission

The mode of *H. pylori* transmission is still subject of debate. However, the geographic and social patterns of *H. pylori* infection are consistent with human-to-human transmission via the faecal-oral or oral-oral route (17).

Interfamilial Transmission

Interfamilial spread is implicated as a major route for acquisition of *H. pylori* infection. Familial aggregation of the infection has been shown in many studies. The study assessed the role of parental infection status in the transmission of *H. pylori* infection in pre-school aged children. The results provided strong evidence for a transmission pathway via parents to children. Most of the epidemiological studies relied on the use of serology and urea breath test to define interfamilial clustering (18).

PATHOGENESIS OF *H. pylori* INFECTION

Adherence and Colonization

Being a bacterial pathogen, *H. pylori* have to establish itself in the stomach following transmission. Adherence to the gastric epithelium is a crucial step in colonization, a precursor of pathogenesis of *H. pylori*. All isolates expressed several putative colonization factors, including various adhesins, flagellar motility and urease (19).

H. pylori infection is a chronic infection and is considered unlikely that such infection remains with the absence of adhesin-host cell interactions. Adhesins are bacterial proteins, glycoconjugates or lipids that are involved in the initial steps of *H. pylori* infection and are important virulence factors. Presently, there is no consensus as to which *H. pylori* adhesins are most important *in vivo*. However, the best-characterized adhesin is the blood group antigen-binding adhesion (BabA) which binds to difucosylated Lewis^{b} (Le^{b}) blood group antigens found on the gastric epithelial cells (20).

H. pylori possess 4-6 sheathed flagella and their presence appears to be essential in *H. pylori* infection. An isogenic non-motile mutant in the flagellar secretion apparatus component filQ resulted in a 30% reduction in adherence to human gastric cancer AGS cells (American Type Culture Collection no.CRL-1739). In the *in vivo* study by, the non-motile *H. pylori* survived for only 6 days in infected piglets while the motile variant survived for a longer period of time (21 days). The study inferred that motility is necessary for full colonization of gnotobiotic piglets by *H. pylori* (21).

DIAGNOSISOF*H.pylori*INFECTION

The detection of *H. pylori* infection is a primary requisite for diagnosis of gastroduodenal diseases related to this bacterium. In the pediatric population, duodenal ulcer is strongly associated with *H. pylori* infection and the risk of development of gastric can cerise relatively high if the infection is acquired tayoungage (22).

In view of these critical issues, accurate diagnosis of *H. pylori* infection is a key step towards proper patient management. Two categories of diagnostic methods for *H. pylori* infection are defined: invasive and non-invasive.

Several factors suchasthe needtoevaluate the sensitivity, specificity, positive and negative predictive value of a given test must be taken into account when selecting for a test. In addition, the age of patients being tested also has to be considered.

At present, no singletestcanbeabsolutelyreliedupontodetect*H.pylori*colonizationbutiffeasible, a combination of two tests is recommended. The European *Helicobacter pylori* Study Group (EHPSG) also recommend that two or more tests be performed as the gold standard in comparative studies (23).

Invasive tests

The invasive methods require gastric biopsy specimens obtained during gastroduodenal endoscopy.Presently, invasive biopsy tests include staining of histological samples, biopsy urease test, culturing of biopsy specimens and polymerase chain reaction.

Non-Invasive tests

Clinical tests like the Urea breath test and serology test are well-established screening procedures which help to reduce the cost and workload of invasive endoscopy given the special niche of H. pylori, attempts are continuously made to improve the non-invasive diagnostic tests (25).

Othernon-invasivetests

Molecular biology techniques

Polymerase chain reaction (PCR) is particularly useful for molecular epidemiology and for finger printing H. pylori isolates. This technique has been used to genotype. Recently, molecular techniques such as real time PCR and fluorescent hybridization were evaluated for use in detection of H. pylori in gastric biopsy samples. The cagA and vacA genotypes were tested by melting curve using the real-time PCR and compared to the gastritis status and cell proliferation status. The study demonstrated that this bacterial pathogen was detected in 63 biopsy specimens as compared to 67 cultured positive specimens by fluorescent hybridization with rRNA-targeted fluorescence-labeled oligonucleotide probes specific for *H. Pylori* (26).

Serological tests

Serologic testing is based on the detection of anti-*H. pylori* IgG antibody in the patient's serum. The commonly employed serodiagnostic technique is the enzyme- linked immunosorbent assay (ELISA). The sensitivity and specificity of ELISA is dependent on the nature of the bacterial antigen preparation.

Stool Antigen test (HpSA)

The performance of HpSA was evaluated and compared with other diagnostic tests (Culture, biopsy urease test, histology, PCR, and serology).

The diagnostic accuracy of HpSA (sensitivity 92.6%, specificity 100%) was observed to be comparable to the other tests.This non-invasive test was also found to be a useful method for post-treatment eradication testing of infection in children. In addition, the European Helicobacter pylori Study Group has recommended the stool antigen test for diagnosis of the infection and eradication assessment in older children (27).

Material and Methods

The data was collected from the records of privet lab in Derna city where the sample collected from children who came to the in order to investigate for H.pylori infections. The data was gathered in wrote in a questioner design as the following:

Study population and study design (cross-sectional stud)				
1	***NAMES***			
2	***GENDAR***			
3	***AGE***			
4	***nationality and place of residence***			
5	***residing within the city***	***YES***	***NO***	**NAME OF CITY**
6	***Infection status was determined by***	**name of the system**		
		name of the test		
		Normal range		**from …….. to…….**

		positive result	
		negative result	
7	***Unit of measurement***		
8	***Type of samples***		
	stool , serium, plasma and breath test		
9	***notes or protocol about collection of samples***		
10	***Name the place that collection data from***		
11	***Date of test***		
12	***Date of collection data***		

Results

Total, 200 children—89 boys (44.5%) and 111 (55.5%) girls were enrolled in the study (Figure 1).

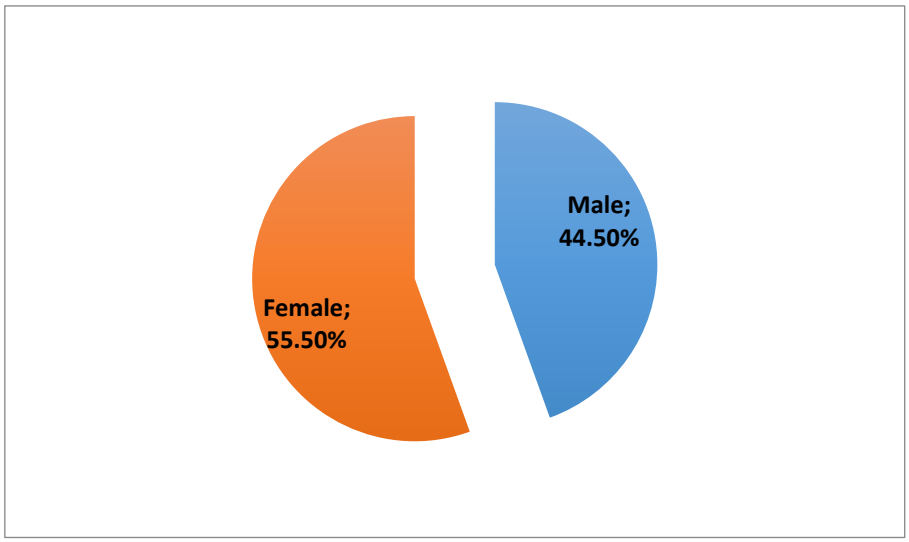

Figure 1: Gender of children

The overall prevalence of H. pylori infection in children was 37.5% (Figure 2).

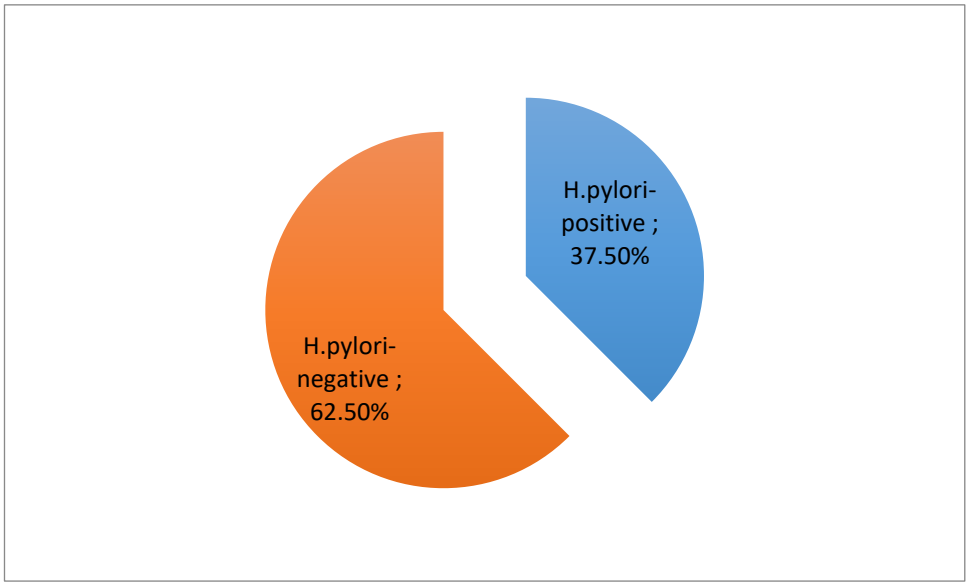

Figure 2: Prevalence of H. pylori infection in children

Table 1. The prevalence rates of H. pylori infection based on sex

	No (%)	Helicobacter pylori test		P-value
		-ve	+ve	
Male	89 (44.5%)	53(59.6)	36(40.4)	0.440
Female	111(55.5)	72(64.8)	39(35.2)	

The prevalence rates of H. pylori infection based on sex are shown in Table 1.

Females were 39(35.2%) and males were 36(40.4%) of H. pylori-positive group.However, there were no statistical significant different between gender and infected by Helicobacter pylori (Chi-square statistic is 0.595, P=0.440).

Table 2. The prevalence rates of H. pylori infection based on city

City	No (%)	Helicobacter pylori test	
		-ve No (%)	+ve No (%)
Derna	167(83.5)	102(61.1)	65(38.9)
Umarzam	12(6.0)	7(58.3)	5(41.7)
Alqba	13(6.5)	10(76.9)	3(23.1)
AinMarah	8(4.0)	8(100)	0(0.0)

Of the 200 children studied, 167 (83.5%) were living in Derna (urban area) and 33 (16.5%) in Umarzam, Alqba and Ain Marah (rural area), 12(6.0%) in Umarzam, 13(6.5%) in Alqba and 8(4%) in AinMarah (Figure 3).

According to H.pylori-positive results, 65/200(32.5%) children were living in Derna, 5/200(2.5%) in Umarzam and3/200(1.5%) in Alqba (Table 2).

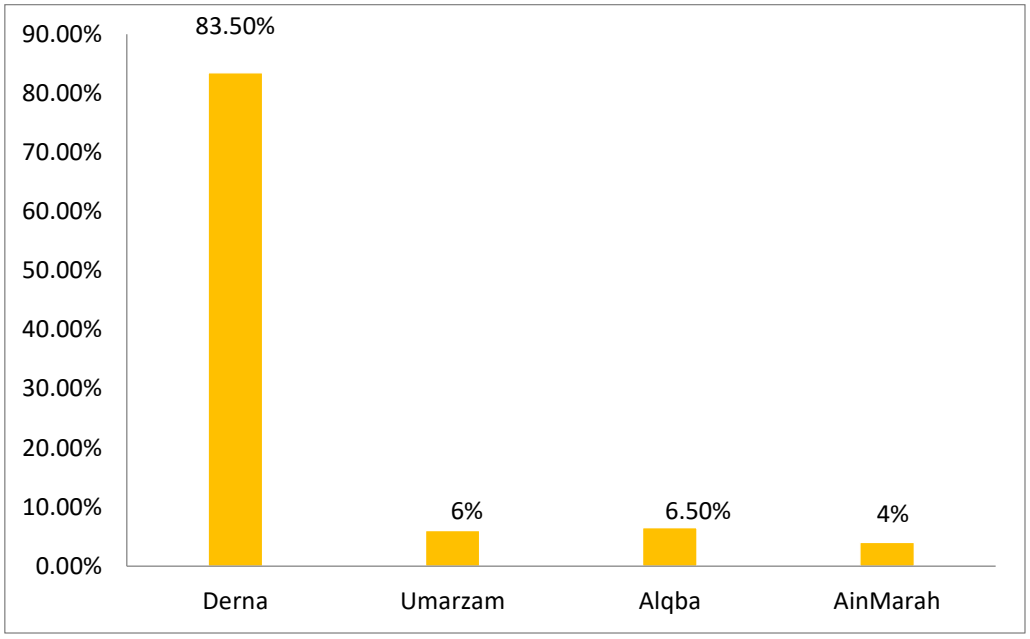

Figure 3: Residence of children

Table 3: The prevalence rates of H. pylori infection based on gender and age group

	No (%)	**Helicobacter pylori test**		P-value
		+ve No (%)	-ve No (%)	
Female				
0-10 years	27(24.3)	14(12.6)	13(11.7)	0.029
11-15 years	84(75.7)	25(22.5)	59(53.2)	
Male				
0-10 years	36(40.4)	12(13.6)	24(26.9)	0.2596
11-15 years	53(59.6)	24(26.9)	29(32.6)	

The prevalence of Helicobacter pylori was higher among female age 11-15 years old than 0-10 years. There were statistical significant different between age group among female (x2=4.7398,P=0.029).

The prevalence of Helicobacter pylori was higher among male age 11-15 years old than 0-10 years. However, there were statistical not significant different between age group among female (x2=1.271, P=0.2596) (Table 3).

Table 4: The prevalence rates of H. pylori infection based on gender and city

City	Gender	Helicobacter pylori test	
		-ve No(%)	+ve No(%)
Derna	Male	48(24)	32(16)
	Female	54(27)	33(16.5)
Umarzam	Male	0(0.0)	5(2.5)
	Female	5(2.5)	2(1.0)
Alqba	Male	3(1.5)	2(1.0)
	Female	7(3.5)	1(0.5)
AinMarah	Male	6(3.0)	0(0.0)
	Female	2(1.0)	0(0.0)

Helicobacter pylori were more prevalent in Derna than other city (Table 4).

Conclusion

The prevalence of H. pylori varies from country to country and by age-groups. H. pylori infection affects more than half of the world's population including children in developing countries acquire it early in life. Because of the fecal-oral rout and intrafamily are mode of transmission it is more prevalent in poor socioeconomic environments. This infection is largely acquired during early childhood and the infection increased with age. Traditional diagnostic tools such as endoscopy and serology can be too invasive for children noninvasive urea breath test Analyzed group included 111 girls and 89 boys between 3years and 15years (mean age 9).
Helicobacter pylori infection was observed in 73 patients (36.5%) of 200 analyzed cases.

The prevalence of Helicobacter pylori in Derna (65/200) was 32.5%. And Umm Al-Razm (5/200) 2.5% and Al-Qubba (3/200) 1.5%. Prevalence of H.pylori in a girl 52% (104/200) Prevalence of H .pylori in boy 19% (39/200) male positive in Derna for H. pylori is 32 children (16٪) female positive in Derna for H. pylori33 girls (16.5) male negative in Derna for H. pylori detection are 48boys (24%) female negative in Derna for H. pylori are 54(27%) Male positive in Umarzam for H .pylori (5/200)2.5% Female positive in Umarzam for H .pylori (2/200)1.0% male negative in Ainmarah for H. pylori are 6 boys (3%) female negative in Ainmarah for H. pylori are 2grill (1%) male positive in Alqba for H.pylori positive are2boys (1 %) female negative in Alqba are 7 (3.5%) male negative in Alqba for H. pylori are3(1.5%) female positive in Alqba for H. pylori are 1(0.5%) In addition, this result wasout of our expectations, the spread of H. pylori in my country much more than we expected The girl's result was 52% more than the boy's result was 19%.

Recommendation

We hope next year they will study the transmission of bacteria within a family that has a great impact on the spread of this bacterial infection And also to work on biopsy samples from the stomach with correct results.

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