



Prevalence of *helicobacter pylori* infection in children (Prospective study)

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ABSTRACT

The current guidelines for eliminating *Helicobacter pylori* (*H. pylori*) in adults vary from those for children. Infected with *H. pylori* should always seek treatment to eliminate the infection.

as a result of the possibility of contracting infections outside of the digestive system. Instead of focusing just on *H. pylori* infection, we should evaluate all potential reasons before treating affected infants. In fact, the test-and-treat approach is not recommended for kids according to worldwide pediatric standards. Therefore, in order to properly analyse all of the potential causes of the symptomatology and to enhance the eradication rate, gastroscopy with antimicrobial susceptibility testing by culture on stomach biopsies should be conducted before to beginning the eradication therapy in children. If antibiotic susceptibility testing is unavailable, gastroscopy is nevertheless advised in order to determine the true source of any symptoms rather than only looking for *H. pylori*. Because there aren't as many antibiotics available for kids as there are for adults, doctors sometimes resort to antimicrobial susceptibility testing to cut down on treatment failures. Amoxicillin, clarithromycin, and metronidazole, in various combinations, are the principal antibiotics prescribed for children. When treating an infection without first determining its antimicrobial susceptibility, it is common practice to use a 14-day course of triple therapy. In cases of double-resistance or as a secondary therapeutic option, triple therapy with a high dose of amoxicillin is an option worth considering. From there, we might choose quadruple treatment with or without bismuth salts, which is based on therapeutic regimens typically administered to adults. Unfortunately, many children are less compliant with treatment regimens because of the severe side effects they may experience. This analysis also takes a look at several alternatives to standard pediatric care that are gaining popularity.

Patients and method: Susceptibility testing, *Helicobacter pylori*, adjuvants, children, combined therapy, eradication. From March 2021 to March 2022, 51 children, people were included in prospective case-control research, with 29 of them serving as patients and 22 as controls.

Conclusion: Patients with *H. pylori* were more likely to be in the 6-plus age group and have a higher level of parental education if they were in the latter group.

Aim : *H. pylori*'s association with patient age, sex, parental education, smoking status, and blood group.

Keywords:

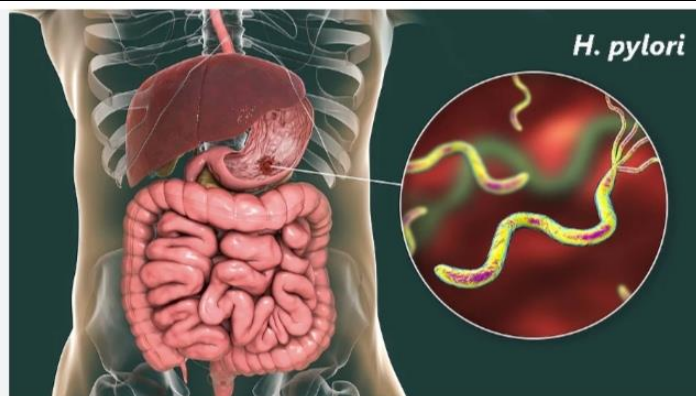
Helicobacter pylori, children, education, blood group.

Introduction

The bacterium known as *Helicobacter pylori* (*H. pylori*) has a helical structure and can cause stomach ulcers. A previously undiscovered gram-negative bacteria 1981's Warren and Marshall Discourse, infects the stomach and has the potential to cause local ammonia production depends on urease.¹ *H. pylori* Both stomach and duodenal gastritis can be brought on by infection. mucosal injuries, gastric atrophy, and ulcers associated malignancy of lymphatic tissue and stomach cancer

including, but not limited to, extra digestive adenocarcinoma iron deficiency anaemia and other problems immunological thrombocytopenia and anaemia purpura.²⁻⁵ Human immunodeficiency virus (*H. pylori* infection is in the vicinity of fifty percent, however infection rates rely on varying degrees of development, commonly falling between the range of 20% - 80%. The results of a recent epidemiological research authored by H. Zamani and co-authors. the *pylori* infection was more prevalent in prevalence in underdeveloped countries is higher countries that are developed (34.7%). On top of that, the illness is more common among adults than parents with children (48.6% vs. 32.6%)³. In light of the recent uptick in occurrences of Indicators for this illness throughout the past few years care for *H. pylori* an increase of *pylori* bacteria. Unfortunately, the percentage of resistant strains resistance to certain medications has risen, too, which This makes eradication more challenging, especially in children.^{2,7,8} Children's Gastroenterology and Nutrition Society of America, North American Society for Gastrointestinal, Organization for Pediatric Gastroenterology in the United States Nutrition and Hepatology (NASPGHAN), a Latin acronym U.S. Chapter of the American College of Gastroenterology, Nutrition (LASPGHAN) and Hepatology (LASPGHAN). The Gastroenterology Association of Pediatrics in Japan Food and Nutrition (JSPGHAN) recommendations for hepatology I would suggest looking for *H. pylori* only when the costs are outweighed by the advantages test and subsequent treatment expenses and hazards. treatments. In addition,

before settling on learn more about *H. pylori* in young people who have in the event of stomach discomfort, a thorough evaluation questioning whether or not an esophago-gastric endoscopy is needs more research into potential causes and, rather than only concentrating on *H. pylori* bug in your stomach. In addition, the primary international 'Test and treat' is not recommended in accordance with guidelines for children. Once more, if *H. pylori* infection identified via a gastroscopy for a clinical suspicion unrelated to the initial. Treatment options other than eradication should not after weighing the potential downsides and upsides⁸⁻¹⁰ Years Old, in addition, Korean kids under the age of ten should be under the supervision of the revised ESPGHAN/ This is in accordance with the NASPGHAN's recommendations. Neither intrusive nor methodical, non-invasive approach of diagnosing and treating *H. pylori* in youngsters, *Helicobacter pylori* infections are not advised. children with special needs or those less than 10 weight less than 35 kg unless medically necessary peptic ulcer disease is hypothesized or endoscopically ulcers.¹¹ The Gold *H. pylori* Treatments for eradicating *pylori* might vary regionally and internationally because of changes in antibiotic treatment options ability of the bacteria to withstand. Indeed, due to the increasing number of failed treatments, the elimination of *H. pylori* is rising in prevalence, challenging. While there is the possibility that associated with modifications in the host's physiology, changes in the microbiota of the gut as a result of therapy, Proton pump inhibitors have a very fast metabolic rate. Using proton pump inhibitors (PPIs), antibiotics can be deactivated at apH or even more to low adherence,^{12,13} therefore it's a problem. On the other hand, it might be caused by an inadequate dosage or time needed for treatment to be effective or *H. pylori* virulence variables, such as natural selection, point mutations, and modulators of quorum sensing and signaling, pumps, and efflux, which can lead to it is resistant to several drugs. *pylori* phenotype.¹⁴ In a meta-analysis, Karbalaei et al.



Results from a meta-analysis of 19 separate trials showed namely, the frequency with which main MDR *H. pylori* In youngsters, the infection rate was around 6%.⁴ The researchers also found that main MDR *H. pylori* infection is a major health problem higher in Asian kids than white kids in the West (p 0.05), we can draw the following because it is contingent on a number of variables including antibiotic use, national and personal consumption complications, and genetic features of *H. pylori* varieties. Thus, *H. pylori* strategy for treating pylori should be modified according to individual drug susceptibility treatment risk assessment test failure.¹⁴ This is why the most recent studies on *H. pylori* Pediatric therapeutic protocols were data collected to determine how well these treatments, and assessing the alternatives mix-ups for the near future.

TRANSMISSION

A number of studies have shown that face-to-face person contagiousness in the family is common, and mother-to-child which is the largest and most significant Mouth-to-mouth transmission and gastrointestinal. Water contamination is a serious problem in 10 causes

of disease, where the bacteria maintain its viability for extended periods of time. Consensus suggests *H. pylori* infection with *Helicobacter pylori* and economic factors Regarding food choices, implying that dairy products, Vegetables and meat might have a significant role in transmission. Infectious microorganisms can also be found in saliva.

DIAGNOSIS

Diagnosis in children is often verified by means of techniques, and only applies to those people who can profit from them. are typical: when stomach/intestinal (G.D.) ulcers and/or erosive gastritis, intractable IDA for which no obvious triggers can be ITP was diagnosed after all other possible reasons were exhausted and is supported by the data shown below (figure 1):

1. Culture of positivity.
2. In the absence of culture or a negative result, two invasive Histology, RUT, or Other Molecular technique: PCR or FISH).
3. In the absence of culture or in the event of a negative culture, histology offers a non-invasive option that a viable option/method ...the SAT or UBT.

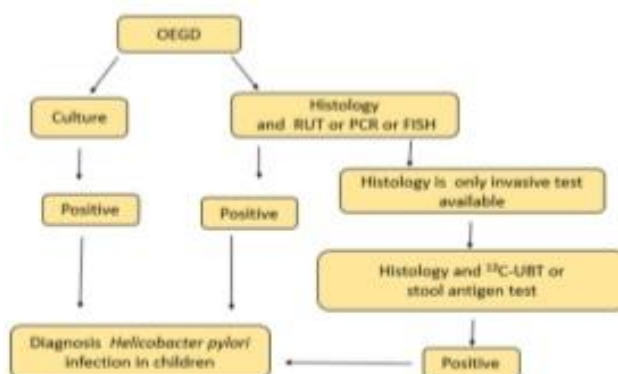


Figure 1 Legends ¹³C-UBT: urea breath test; OEGD: oesophago-gastro-duodenoscopy; FISH: fluorescence in situ hybridisation; RUT: rapid urea test.

Options for Treatment

Human immunodeficiency virus (H. Peptic ulcer disease relies on a cocktail of medications that inhibit secretion in addition to antibiotics. The initials are the most crucial because of the many benefits beyond just elevating stomach pH The letter H. antibiotic-resistant pylori, Direct antibacterial action of PPIs has been demonstrated against the microorganism² Triple treatment (TT) has been the gold standard for many years. include NSAIDs, AMO, and clarithromycin metronidazole (MET) or conjugated linoleic acid (CLA) represented the primary method of treatment for kids. Unfortunately, though, widespread use/abuse of antibacterial drugs, especially for sinus and bronchial infections, has led to a dramatic rise in

antibiotic resistances, however regional differences exist ...and international locations. To provide only one example, in northern Italy it a rise in resistance to CLA has been documented, even while the rate of MET resistance in kids is going down in recent years.¹⁵ However, AMO Confirmed susceptibility is quite uncommon,^{8,15}. Because of the antibacterial and antisecretory properties of this It's not always possible to completely get rid of narcotics. in any case, some academicians have employed substitute chemicals like plant-based pharmaceuticals Lactoferrin, Prebiotics, and Probiotics for Better Health. Despite the fact that the precise method of these elimination of result is yet being figured out.

Table 1 Clinical presentation	
Clinical manifestations	Comments
Asymptomatic	Majority of children. The infection should not be investigated.
Digestive manifestations	
Nausea	Meta-analysis showed significant association between nausea and and <i>Helicobacter pylori</i> infection. ¹² The infection should not be investigated.
Epigastric pain	Meta-analysis documented statistical significant association. ¹³ Other studies do not find predominance of this symptom in infected cases. It is a common indication of OEGD.
Chronic abdominal pain without any alarm signs or symptoms	The pain is probably independent of the presence of <i>H. pylori</i> . The infection should not be investigated or treated.
Vomiting	Meta-analysis showed no direct link between infection and vomiting. ¹³
Heartburn, halitosis, regurgitation	Non-specific symptom. It does not constitute indication of study or treatment.
Extradigestive manifestations	
Unexplained iron deficiency anaemia	After other causes have been ruled out, the infection should be investigated.
Chronic immune thrombocytopenic purpura	Unexplained thrombocytopenia should undergo <i>H. pylori</i> testing. Eradication and therapy have shown promising results with improved platelet counts and the normalisation of autoplatelet antibodies without relapse.
Henoch-Schonlein purpura	More research are needed to associate <i>H. pylori</i> infection with abdominal manifestations and also to define the need for eradication therapy.
Inflammatory bowel disease	Meta-analysis suggests strong inverse association with Crohn's disease in children. ^{16 17}
Bronchial asthma, other allergic diseases	Meta-analysis showed an inverse relationship. More research is needed. ¹⁸

Table 2 Diagnostic methods for *Helicobacter pylori* infection

Methods	Advantages	Disadvantages
Invasive		
Histology	Degree of chronic inflammation and activity, diagnosis of premalignant lesions such as grade of atrophy and gastric intestinal metaplasia, malignancy and coccoid forms.	Need special skills, and costly observer-dependency; time-consuming; dependence of accuracy on the receiver of antibiotics, proton pump inhibitors (PPI); size, site and number of biopsies.
Culture	Specificity (100%), provides pattern of antimicrobial resistance.	Important location of the biopsies, digestive haemorrhage, recent treatments with antibiotics, PPI, bismuth; is expensive and time-consuming test. Sensitivity on the staff skill and culture media.
Rapid urease test	Rapid, inexpensive, high sensitivity and specificity (almost 100%).	False-negative: bismuth, antibiotics, PPI, achlorhydria and the prevalence rate of infection, bacteria density digestive haemorrhage. False-positive: <i>Proteus mirabilis</i> , <i>Citrobacter freundii</i> , <i>Klebsiella pneumoniae</i> , <i>Enterobacter cloacae</i> , <i>Staphylococcus aureus</i> .
Non-invasive or invasive		
PCR	Antimicrobial susceptibility, fast, high sensitivity and specificity.	False-positive results due to detect DNA pieces of dead bacteria.
Non-invasive		
Urea breath test	Ideal for evaluating treatment response in children over 6 years of age.	High false-positive results in children aged <6 years; false-negative in recent treatments with bismuth, PPI antibiotics, not to use in children as an initial diagnosis.
Stool antigen test	No age dependency; fast, easy; useful after therapy.	False-negative results in recent treatments with bismuth, PPI, antibiotics; dependency of accuracy on the cut-off value and treatment status.
Serology	Widely available, cheapest.	Sensitivity in children is low, not used to confirm the eradication, inability to detect acute or chronic infection.

PPI, proton pump inhibitor.

Synthetic Drugs

Primarily, antimicrobial medicines and proton pump inhibitors drugs to treat H. removal of H. pylori, although the resistance to antibiotics is rising at an alarming rate. has resulted in a lower-than-expected success percentage. Moreover, Antibiotics change the flora of the microbiome, leading to unfavourable consequences. As a result, there is an absolute requirement for improving existing treatments; in this context Specifically, there is the existence of alternate treatment options.

...and did some research.

Probiotics

There is no doubt that H. A gastric pylori infection Since there is evidence of a varied intestinal microbiota, It has not been fully explained yet,16 although probiotics have been designated by the WHO as "active microorganisms that, when given to a patient, health benefits when consumed in sufficient quantities 'the host,'17 Probiotics and their impact on H. pylori-infected patients is complex and has variable outcomes. children. Probiotics have been hypothesized to have two main they go about competing with H. binding of pylori

receptors on the intestinal epithelial cells' surface

decreasing stomach mucosal adhesion leading in anti-inflammatory effects, in increased secretion chemicals used as antimicrobials, leading to a decrease in lots of microorganisms, and fortifying the intestines physical or obstruction. Decrease the and the Probiotics, polyangiitis treatment, and associated negative effects to improve patients' adherence to treatment.18,19. Additionally, probiotics' antibacterial properties allow them to preventing H. pylori from producing urease. the bacterium *Helicobacter pylori*, but also leading to a decrease in pH through the production of fatty acids decrease, leading to an ecosystem that cannot sustain human life. to the bacteria, twenty. Most of the strains only had one experiment conducted on them. simply, without any strain requirements, therefore it stays not clear which probiotic kind accomplishes best outcomes, given that a comparable study was not conducted. Additionally, several antibiotics are used in investigations. and PPIs, in a variety of dosing forms durations; hence, we do not have enough

normalization due to obvious heterogeneity.²⁰ A meta-analysis of networks and systematic reviews

by Feng et al., looking at the results of 29 studies with 17 conclusions reached on probiotic routines

boosted H by a great deal when added to TT. pylori rates of eradication with an RR of 1.19 (95 percent CI: 1.13, 1.25), and lessens adverse effects by 95% confidence interval [CI] RR = 0.49 (0.38–0.65). Association with *Lactobacillus casei* L. acidophilus and *L. casei*. rhamnosus was the most effective for rates of elimination, and for the adverse consequences, respectively.²¹

Another meta-analysis and systematic review by After looking at the results of 18 experiments, Zhou et al.

Supplementing with *Saccharomyces boulardii* greatly Enhanced eradication treatment with a relative risk 1.09 (95% confidence interval [CI]: 1.05–1.113) and a lower occurrence diarrhea) with an incidence rate (RR) 0.47 (95% CI, 0.36–0.61), while having moderate-to-high uncertainty.

respectively low-quality evidence²² In a randomized controlled trial meta-analysis, other authors

that *Lactobacillus*, particularly when taken in large quantities and extended supplementation, combined with TT

to rise in young children. Getting rid of pylori rates with a 95% confidence interval (CI) of 1.07 to 1.33 and lessen the occurrence of Concomitant Illnesses (most noticeably the frequency of diarrhea) with an RR of 0.30 (95% CI, 0.10–0.85).²³ Wen et al. conducted a second network meta-analysis, which

In 17 randomized controlled trials, researchers found that when *Bacillus mesentericus* + *C. butyricum* + *S. pneumonia faecalis*, when subjected to a 14-day TT, markedly H. rates of H. pylori eradication with a 95% CI of 1.16 Confidence Interval, 1.07–1.26) and fewer adverse effects with a

A 0.40 (95% CI 0.34–0.48) relative risk among Asians children. Taking everything into account, a recent study found that H. pylori is affected by probiotics. Peptic ulcer disease is convoluted, and they may not be able to completely if given without combination, they have the potential to

boost eradication rates by as much as 10% off when used with regular To lessen the side effects of TT or sequential treatment (ST), unintended consequences of elimination therapy.¹⁶ .The most up-to-date Maastricht VI/Florentine regulations reported that numerous types of probiotic bacteria, Species of *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces boulardii* has been shown to enhance the elimination rate, but it appears to be secondary in adults. effect, since fewer negative outcomes have been experienced concerning methods of complete elimination. A smaller angle of attack impacts, the greater the likelihood of elimination compliance treatment, rather than through influencing one's health in a H. pylori.²

Prebiotics/symbiotics

Nondigestible nutrients are one type of prebiotic. by humans, but are broken down by microorganisms in the gut. By increasing blood flow to the development or action of a particular group of gut microbes. Instead, symbiosis is the interplay between probiotics and prebiotics.

There is a dearth of research on the use of both prebiotics and sterilization treatment for H-infected kids. pylori.²⁰ Two Turkish studies published in 2017 found contradictory outcomes with respect to the inclusion of B. protein and inulin H. influenzae eradication efforts. pylori in young people.

Results from the studies conducted by Sirvan et al. rates of 16% in the symbiotic treatment group

when combined with established treatment against treatment as usual by itself. Similarly, these

authors improved side effects as well with high predictive power for abdominal discomfort, sickness, and loose stools, but not metal taste. But Ustundag et al. found no such discrepancies. not in terms of the rate of elimination (p = 0.16 and p = 0.19) per-protocol (PP) and intention-to treat (ITT) studies, and neither in reducing unwanted consequences relative risk in the cohort was 0.97 (95% CI: 0.14–6.71) affected by B. Additional 14 days of lactis and inulin TT in comparison to just 14 days of TT. Prebiotic supplementation has also been shown in other research to have symbiotic bacteria after taking

probiotics is a huge step improved the rate of elimination, and 95% fewer cases of adverse reactions in older patients 85.7% probiotic, 83.3% placebo, and 86.3% prebiotics group, in each case).

Bovine lactoferrin

The iron-binding glycoprotein bLf, which is found in bovine milk, milk, bodily fluids, pancreatic juice

as well as the granules of the seminal fluids and the

Leukocytes with a polymorphonuclear nucleus in people and bovines. The role of has been described in a few research including adults. bLf as a complementary treatment for obliterating H. infection, with contradictory findings; bLf instead appears to lessen the impact of the unfavourable

therapy eradication-related occurrences that occur. No pediatric usage of bLf has been reported to far. with H. pylori infection, up to this point. Therefore, even while probiotics can't completely

H. infection caused by H. pylori when used alone, several researchers agreed that H. elimination of H. pylori, Probiotics have the potential to aid with weight gain. the pace of elimination and lessen the associated adverse symptoms, most notably abdominal distention and diarrhea. In terms of how long you should take probiotics, choosing a treatment plan of at least 14 days of therapy, almost the same as the suggested using methods of sterilization. Nonetheless, probiotics' potential in H. children with pylori infection is still low, and fewer Research is required for a fuller comprehension. standardize which probiotic strains to use and at what dose in a helpful approach. Pediatrics' Primary Contrary to what is advised by international standards, regular single or multiple addition treatment with probiotics to prevent or eliminate unwanted effects or boost elimination rates. The study of symbiotic relationships, on the other hand, has lagged the connection between probiotics .and elimination is currently being studied. inconsistency is more noticeable in younger people.

Phytotherapy

Bioactive plant compounds, concentrated plant extracts, and plant-based substances are widely known to be beneficial to health. and have made extensive use of for decades. Yes, indeed drug's active ingredients are well-known the bioactive ingredients used in the pharmaceutical compounds derived from the study of plants and other organisms. There has been a steady increase in the use of natural remedies for illness and wellness. Bioactive molecules can be found in botanical substances.

has the ability to alleviate symptoms via pharmaceutical means healing the sick, etc. Multiple researches were compared opposite of H. plant extracts with anti-H. pylori action. Some naturally occurring chemicals displayed incongruous ends up becoming H. the pylori bug in your stomach. Bergamot Orange resulting in bacterial and fungal resistance, blueberries extract from grape seeds, with TT did not reveal any noteworthy discrepancies in killing off rate in the adult population. Despite the fact that one in vitro research demonstrated activity H. mastic gum did not elevate pylori levels. human infection clearance rate, ginger and Treatment with curcumin increased the speed at which H. pylori-infected People who are adults are the focus here. Oil of cinnamon as agent used as an H. adult pylori eradication treatment increased the success rate of the elimination process ($p = 0.036$). significantly fewer adverse effects than the control group ($p 0.05$) group.

Flavonoids also have various anti-oxidant effects, anti-inflammatory, and protective to the liver.

cancer-fighting, virus-preventing, bacteria-killing properties, but Only in vitro research is done on them in H. pylori in the stomach, thus far.

Synergistic Treatment Protocols

Unlike adults, who may choose from a more extensive options are available for usage in H. pylori-infected Pediatric gastroenterologists have a dilemma: a scarcity of available antibiotics (2,8) A higher rate of effective eradication can be achieved by Three strategic evaluations would be required. points:

- 1) Regional rates of elimination
- 2) Relying on susceptibility tests routinely

3) A rate of treatment compliance of 90% or higher.³⁷

In pediatric clinical practice, the Detecting whether or not a strain of *H. pylori* infection is diagnosed with a biopsy of the stomach strategies used during a gastroscopy (ideally one antrum biopsy and a rectal biopsy corpus).⁸ There have been many permutations since its discovery. Antimicrobials and proton pump inhibitors have been employed. remedy *H. the pylori* bug in your stomach. A common cause of the The TT is the most common treatment regimen. ST, which contains bismuth, is another option. treatment, or BQT, and simultaneous quadruple therapy. treatment (CT, also known as non-BQT). However, In most cases, the eradication rate does not meet the the children's population, at a 90% objective. Reduced extinction rates in toddlers compared

to those seen in adults when regimen might probably be guessed at, such as varying responses to antibiotics or adherence to treatment in pediatric patients also, grown-ups. Both BQT and CT, a quadruple therapy, were used. also proposed as evidence-based primary care options for the young and the old alike. The use of tetracyclines (TETs) is generally discouraged. in youngsters under the age of 8 because of the consequences of which include irreversible tooth discoloration include bone growth retardation. Fluoroquinolones too are somewhat contraindicated in kids since to the drawbacks of expansion. So, given that the Children have restricted options when it comes to antibiotics, avoid using unapproved second-line first-line treatment, such as antibiotics, is critically significant⁸

Table 1. First-line treatment with known antimicrobial susceptibility.

Therapeutic choice	All susceptible antibiotics or MET-R	CLA-R	CLA-R and MET-R	AMO-R**
TT 14 days	PPIs 1-2 mg/kg/d	PPIs 1-2 mg/kg/d	PPIs 1-2 mg/kg/d	PPIs 1-2 mg/kg/d
	AMO 50-70 mg/kg/d	AMO 50-70 mg/kg/d	AMO 75 mg/kg/d	CLA 20-30 mg/kg/d
	CLA 20-30 mg/kg/d	MET 20-30 mg/kg/d	MET 30-40 mg/kg/d*	MET 20-30 mg/kg/d

All drugs are administered in two equal daily doses. ST for 10-14 days is a valid option in patients with fully antibiotic susceptibility: (a) PPIs 1-2 mg/kg/d + AMO 50-75 mg/kg/d for the first 5-7 days. (b) PPIs 1-2 mg/kg/d + CLA 20-30 mg/kg/d + MET 20-30 mg/kg/d for the second 5-7 days.
 *The *in vitro* MET resistance may be overcome *in vivo* by longer treatment (14 days) and/or higher doses (30-40 mg/kg/die).^{38A}
 **This regimen is also valid whether patients have allergy to penicillin (and both CLA and MET susceptibility).
 AMO, amoxicillin; CLA, clarithromycin; MET, metronidazole; PPIs, proton pump inhibitors; ST, sequential therapy; TT, triple therapy.

Table 2. Alternative first-line treatment when one antibiotic resistance is present.

BQT 14 days, aged <8 years	PPIs 1-2 mg/kg/d
	AMO 50-70 mg/kg/d
	MET 20-30 mg/kg/d
	Bismuth 8 mg/kg/d
BQT 14 days, aged >8 years	PPIs 1-2 mg/kg/d
	MET 20-30 mg/kg/d
	TET 50 mg/kg/d
	Bismuth 8 mg/kg/d

PPIs, AMO, and MET are administered in two equal daily doses, TET and bismuth in four equal daily doses. AMO, amoxicillin; BQT, bismuth-containing quadruple therapy; MET, metronidazole; PPIs, proton pump inhibitors; TET, tetracycline.

Table 4. Eradication therapies in not-known antimicrobial susceptibility.

Therapeutic choices in children with not-known antimicrobial susceptibility
TT for 14 days
BQT for 14 days
CT for 14 days
ST for 10-14 days
HDDT for 14 days*
Vonoprazan-AMO 7 days

The treatment should be rely on clinical experience, regional antimicrobial susceptibility profiles, and recent antibiotic courses of the patient.
 *HDDT has never been used so far in children.
 BQT, bismuth-containing quadruple therapy; HDDT, high-dose dual therapy; CT, concomitant therapy; ST, sequential therapy; TT, triple therapy

Table 3. Second-line treatment.

Therapeutic choices	Fully antibiotic susceptibility	CLA-R, MET-S	MET-R, CLA-S	MET-R, CLA-R	AMO-R
TT 14 days as reported in Table 1, not used before	✓	✓	✓	✓	
BQT 14 days as reported in Table 2	✓	✓	✓	✓	✓
					Second part of Table 2
CT 14 days	PPIs 1–2 mg/kg/d	PPIs 1–2 mg/kg/d	PPIs 1–2 mg/kg/d	PPIs 1–2 mg/kg/d	PPIs 1–2 mg/kg/d
	AMO 50–70 mg/kg/d	AMO 50–70 mg/kg/d	AMO 50–70 mg/kg/d	AMO 50–70 mg/kg/d	AMO 50–70 mg/kg/d
	MET 20–30 mg/kg/d	MET 20–30 mg/kg/d	MET 20–30 mg/kg/d	MET 20–30 mg/kg/d	MET 20–30 mg/kg/d
	CLA 20–30 mg/kg/d	CLA 20–30 mg/kg/d	CLA 20–30 mg/kg/d	CLA 20–30 mg/kg/d	CLA 20–30 mg/kg/d
TT 14 days		PPIs 1–2 mg/kg/d	PPIs 1–2 mg/kg/d	PPIs 1–2 mg/kg/d	
		AMO 75 mg/kg/d	AMO 75 mg/kg/d	AMO 75 mg/kg/d	
		MET 20–30 mg/kg/d	CLA 20–30 mg/kg/d	MET 30–40 mg/kg/d*	

PPIs, AMO, MET, and CLA are administered in two equal daily doses.
 *The *in vitro* MET resistance may be overcome *in vivo* by longer treatment (14 days) and/or higher doses (30–40 mg/kg/die).^{5,64}
 AMO, amoxicillin; BQT, bismuth-containing quadruple therapy; CLA, clarithromycin; CT, concomitant therapy; MET, metronidazole; PPIs, proton pump inhibitors; TT, triple therapy.

Subjects and Method

Patient Group And Control Group:

A prospective comparative case-control study was carried from March 2021 to March 2022 ,total number of child is **51 divided to 29 patients** included (20 male and 9 female) **and control** 22 children (12 male and 10 female) the study admitted to pediatric unit for treatment at Hospital and their age ranged between 6 years to 12years, and regarded as patient group.

Method , data collection:

A special questionnaire was designed for the purpose of the study (Appendix I). The following informations were taken:

- -name, age (in month), and sex.
- -date of admission.
- -Residence of patients.
- -clinical features including symptoms and signs: epigastric pain ,dyspepsia, abdominal pain and Vomiting.
- -family history of peptic ulcer or endoscopy or recurrent abdominal pain. -consanguinity .
- -social history including father and mother smoking .

- -father and mother education.

laboratory data :Investigations were done in form of gastric aspirate culture for *H.pylori* and one step diagnostic test (which detect the antigen for H.pylori)

H.pylori gastric aspirate culture :Gastric aspirate culture was taken from the patients who are included in the study (by using nasogastric tube) and special culture media which is called (Columbia agar) with three antibiotics had been used to inhibit all gram positive and negative bacteria, the cultivation were done for five days and then examined to detect H.pylori.

Statistical analysis:

Statistical analysis was done using spss program, data where expressed and comparison of proportions was performed using chi-square value of less than 0.05 was considered as statistically significant , p value of less than 0.01 as highly significant and p value of less than 0.001 as extremely significant .

Results

Table 1: Distribution of patients and control according to age and sex:

		Patient group		Control group		P value
		No.	%			
Age	>6years	15	51.7%	12	54.5%	>0.05
	<12years	14	48.3%	10	45.5%	
Total		29	100%	22	100%	
Sex	Male	20	69%	12	54.5%	>0.05
	Female	9	31%	10	45.5%	
Total		29	100%	22	100%	

Regarding age group :51.7% of patient were >6 years in comparison to 54.5%of control were >12 years so there was no significant difference regarding age group between patient and control.

Regarding sex groups,29 children were patient group the majority of them were male with male:female ratio equal to 2.2 ,while 22 children were control group with male:female ratio equal to 1.2 ,with a p value >0.05,so there was no significant difference between the two groups regarding sex.

Table 2 : Results of *H.pylori* antibody testing among patient and control :

One step diagnostic test	patient	control	Total	P value
H.pylori + ve	23 79.3%	12 54.5%	35 68.6%	< 0.05
H.pylori - ve	6 20.7%	12 54.5%	16 31.4%	
Total	29 100%	22 100%	51 100%	

Among 51 children included in the study ,29 children were patients (of them 79.3% having positive one step diagnostic test), while 22 children were control (of them 54.5 having positive one step diagnostic test).

There is statistically significant higher percentage of patient group having *H.pylori* comparing to control group with a p value < 0.05.

Table 3: Results of *H.pylori* culture (in the gastric aspirate) among patient and control :

Gastric asprate culture	patient	control	Total	OR	P value
H.pylori + ve	13 44.8%	4 18.2%	17 33.3%	0.274	< 0.05
H.pylori - ve	16 55.2%	18 81.8%	34 66.7%		
Total	29 100%	22 100%	51 100%		

Out of 29 patients; 44.8% having positive culture for *H.pylori* ,while only 18.2% of control having positive culture for *H.pylori*.

There is statistically significant higher percentage of patient group having *H.pylori* comparing to control group with a p value < 0.05.

Table 4 : Distribution of patient of both age and sex groups according to *H.pylori* gastric aspirate culture:

		age		total	P value	sex		total	P value
		<12years	>6years			male	female		
Patient	Gastric aspirate +ve	3 23.1%	10 76.9%	13 100%	<0.05	8 61.5%	5 38.5%	13 100%	>0.05
	Gastric aspirate -ve	12 75%	4 25%	16 100%		12 75%	4 25%	16 100%	
control	Gastric aspirate +ve	0 0%	4 100%	4 100%	<0.05	3 75%	1 25%	4 100%	>0.05
	Gastric aspirate -ve	10 55.6%	8 44.4%	18 100%		9 100%	9 100%	18 100%	

This table showed that there is a significant association between *H.pylori* and age more than 6 years with a p value more than 0.05 which is statistically significant among patient group.

This table also showed that there is no significant association between *H.pylori* and sex among both patient and control groups with a p value less than 0.05 which is statistically not significant.

Table 5 : Relation of H.pylori positive gastric aspirate culture among patient and control group to father education:

	Father education	Gastric aspirate + ve	Gastric aspirate - ve	Total	P value
Patient	Low education	8 61.5%	4 25%	12 41.3%	<0.05
	High education	5 38.5%	12 75%	17 58.7%	
	Total	13 100%	16 100%	29 100%	
control	Low education	4 100%	11 61.1%	15 68.2%	<0.05
	High education	0 0%	7 38.9%	7 31.8%	
	Total	4 100%	18 100%	22 100%	

There was statistically significant association between H.pylori among patient and control group and father education with a p value < 0.05 .

Table 6 : Relation of H.pylori positive gastric aspirate culture among patient and control group to mother education:

	mother education	Gastric aspirate + ve	Gastric aspirate - ve	Total	P value
Patient	Low education	11 84.7%	7 43.8%	18 62.1%	<0.05
	High education	2 15.3%	9 56.2%	11 37.9%	
	Total	13 100%	16 100%	29 100%	
control	Low education	4 100%	8 44.4%	12 54.5%	<0.05
	High education	0 0%	10 55.6%	10 45.5%	
	Total	4 100%	18 100%	22 100%	

There was statistically significant association between H.pylori among patient and control group and mother education with P value < 0.05 .

Table 7 : Relation of H.pylori gastric aspirate culture to father smoking:

	father smoking	H.pylori +ve	H.pylori -ve	total	P value
Patient	smoker	11 84.6%	13 81.3%	24 82.8%	>0.05
	Non smoker	2 15.4%	3 18.8%	5 17.2%	
	total	13 100%	16 100%	29 100%	
Control	smoker	4 100%	10 55.6%	14 63.6%	>0.05
	Non smoker	0 0%	8 44.4%	5 36.4%	
	total	4 100%	18 100%	29 100%	

Among father smoking variable, there was no statistically significant association between H.pylori among control group and father smoking with a p value > 0.05 .

Table 8 : Relation of H.pylori according to blood group of patient and control groups :

	Patient	Blood group				Total	P value
		A	B	AB	O		
patient	Gastric aspirate +ve	2 15.4%	4 30.8%	2 15.4%	5 38.5%	13 100%	>0.05
	Gastric aspirate - ve	2 12.5%	3 15.8%	2 12.5%	9 56.3%	16 100%	
control	Gastric aspirate +ve	2 50%	0 0%	1 25%	1 25%	13 100%	>0.05
	Gastric aspirate -ve	3 16.7%	5 27,8%	2 11.1%	8 44.4%	16 100%	

Table 11 shows that there is no significant association between H.pylori and blood group of the patient and control groups with a p value > 0.05.

Discussion

Regional studies have found conflicting findings on the prevalence and related variables of Helicobacter pylori infection in children, which may have significant clinical significance. Our findings indicate that Helicobacter pylori infection occurs in 7.8% of cases, and is more prevalent in males than in girls, as well as older children. However, there was no correlation between the prevalence of Helicobacter pylori infection and the kind of gastrointestinal complaint, with abdominal discomfort being the most prevalent. Pediatricians in gastroenterology and general pediatrics clinics may find this information useful. There have been previous studies assessing the frequency and significance of this illness in kids. Helicobacter pylori has been the subject of several research looking at its prevalence in the general pediatric population and some assessing the symptomatic youngsters. In 2011, Oleastro and coworkers in Portugal studied 844 children with no symptoms. Helicobacter pylori infection was found to be 31.6% worldwide in this study's evaluation of the overall infection rate, with an increase with age but no difference between the sexes [16]. This increased incidence rate was attributed to factors not present in other places, it was said. In 2019, Miak and coworkers assessed the impact of Helicobacter pylori on children and found that it remains a major global health problem. Helicobacter pylori infection has been found in 6-15% of patients with a history of gastrointestinal distress. This study highlights the need of doing susceptibility testing prior to treatment [17], as high H pylori resistance and thus low eradication rates continue to be a serious problem. These findings highlight the prevalence and significance of asymptomatic Helicobacter pylori infection in children. Helicobacter pylori infection has been shown to be a major problem that needs to be recognized and treated as soon as feasible, according to studies evaluating symptomatic individuals and instances with gastrointestinal difficulties. The

frequency of Helicobacter pylori infection in children with celiac disease in Poland in 2015 was assessed by Jozefczuk and colleagues. The prevalence rate, gender distribution, and age categories of Helicobacter pylori infection were similar between pediatricians with celiac disease and healthy patients [18]. They found that 5.4% of pediatricians with celiac disease had Helicobacter pylori infection. De Martel and Parsonnet conducted a meta-analysis of large population-based studies [19] to assess the role of gender as a risk factor for H pylori infection. These researchers discovered a male preponderance of H pylori infection (OR: 1.16, 95% CI: 1.11-1.22) and that male gender was substantially linked with H pylori infection. In 2017, Zabala Torres and coworkers reviewed the literature on the prevalence and trends of Helicobacter pylori infection in children. They demonstrated that estimations of infection prevalence using noninvasive direct detection techniques ranged from 20% to 50% in children 5 and 38% to 79% in children >5 years. However, they demonstrated that model estimates of cross-sectional direct detection investigations in children with symptoms of infection with Helicobacter pylori indicated a very broad range of prevalence, anything from 7 to 54%. They also found that the incidence was 7-76% among children experiencing GI distress [21]. Our research confirms these conclusions. Possible explanations for our study's lower H pylori infection prevalence than earlier findings include variations in population size and regional prevalence rates. The frequency of Helicobacter pylori has been overestimated in earlier studies because researchers relied on stool exams and serology tests to determine its presence. In contrast, we relied on information from direct biopsies of symptomatic youngsters for our current investigation. These findings may also call into question the widely held beliefs about the significance of Helicobacter pylori infection in young people. Helicobacter pylori infection in symptomatic children in Belgium was evaluated over time in

a longitudinal study. The frequency of *H. pylori* was found to be 18.2% in children under the age of 6, and 49.3% in those between the ages of 12 and 17 [22]. According to a 2014 study [23] by Cai and colleagues, *Helicobacter pylori* infection affects 20% of children with chronic gastritis. These studies highlight the need of invasive diagnostic methods and the high prevalence of *Helicobacter pylori* infection in children with symptoms. Our findings contradicted these previous accounts. Our findings, which are in line with prior research, show that *Helicobacter pylori* infection is more common among males and those of older ages.

In 2017, Ibrahim and coworkers conducted review research to examine the correlation between sex and *Helicobacter pylori* infection in both young and old people. After reviewing 244 research, they concluded that males, regardless of age, had a higher risk of contracting *H. pylori* than females. It was also mentioned that the prevalence of this illness among children who are experiencing gastrointestinal distress might range from 5-15% [24]. These results corroborated our own study's low prevalence rate based on the biopsy procedure. In our opinion, further research is needed to determine the true prevalence rate of *Helicobacter pylori* infection in asymptomatic children before they are treated immediately with antibiotics if a stool exam or serology test comes back positive.

Concerning the low prevalence rate of infection among children with symptoms, it's possible that this percentage is much lower in the asymptomatic group. As a result, *H. pylori* infection in children may not be a major concern. Expert evaluation for the presence of other illnesses and functional abnormalities is also something we advise for kids who are complaining of stomach pain.

When compared to other locations, the prevalence rate of *Helicobacter pylori* infection in children was lower in our study. Our findings indicate that *Helicobacter pylori* infection is more prevalent in older individuals and male gender. Our research was hindered by a small sample size and a single location. We recommend conducting further research in our

area, but with larger samples and at other locations.

Conclusion and recommendation

In this research, we found, One, *H. pylori*-positive patients were more likely to be in the older age group (>6 years), but there was no correlation between *H. pylori* positivity and sex. Two, *H. pylori*-positive patients were more likely to have college-educated parents than those who smoked during pregnancy. Third, no correlation could be seen between *H. pylori* and the patient's blood type.

Children between the ages of 6 and 12 have an alarmingly high rate of *H. pylori* infection. Additionally, it may be one of the reasons why school-aged children experience gastrointestinal issues, such as chronic belly discomfort and dyspepsia. suggestion for more research.

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