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Presence of Stool H. Pylori Antigen among Children with Abdominal Symptoms: A Sudanese Hospital Based Study

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Abstract: ***Background. pylori infection is one of the most common infections in the world. It is usually acquired during childhood and without antibiotic therapy, it generally persists for life. A causal relationship between H. pylori infection and abdominal symptoms of childhood is still not proven. In addition, there seems to be a relationship between ulcer disease and abdominal symptoms but it is still not confirmed. The aim of this study is to evaluate the association between abdominal symptoms and positivity of H pylori in their stool. Methodology: This is hospital based study done in pediatric gastroenterology clinic in Sudan, A total of 50 children were selected according to specific criteria, any child presented with abdominal symptoms were included according to certain inclusion and exclusion criteria, The age of the study group was between one month and 15 yrs. The stool antigen test for H. pylori was performed, data was analyzed using SPSS. Results: Out of Fifty selected patients, 20(40%) had only recurrent abdominal pain, 15(30%) presented with concomitant abdominal pain and diarrhea, and 3(6%) had both abdominal pain and vomiting, while 4(8%) had tripled symptoms of abdominal pain, diarrhea, and vomiting, just 6(12%) presented with isolated diarrhea, also 2(4%) presented with isolated vomiting. Positivity of H. pylori antigen was 29(58%) of the whole group, 20(70%) of those had positive H. pylori were under five years, furthermore 7(63.6%) of those had family history of similar condition were harboring the H. pylori antigen in their stool, in addition 27(93%) of those had positive stool test lived in very poor or poor socioeconomic conditions, indicating existence of strong and significant correlation between detection of antigen and their living condition. More analysis showed 25 out of 29 of those positive for the H. pylori stool test were presented with isolated recurrent abdominal pain, or in association with vomiting/diarrhea or both, while just 4 cases out of 29 who had the antigen were presented with isolated one symptom (diarrhea or vomiting) and this showed statistically significance correlation between abdominal pain+/- other symptoms and the presence of the stool H pylori. Conclusion: The authors concluded that the most common GI presentation associated with fecalantigen for H. pylori was abdominal pain whether alone or in association with other symptom, while isolated diarrhea or vomiting has no significant association, moreover concluded that presence of H. pylori fecal antigen in children less than five is more than those who areabove than five year old.***

Keyword: H. Pylori Stool Antigen, Pediatrics, Sudan, Abdominal Symptoms.

1. Introduction

H. pylori is a helix-shaped (classified as a curved rod) Gram-negative bacterium about 3 µm long with a diameter of about 0.5 µm. It is microaerophilic; that is, it requires oxygen, but at lower concentration than is found in the atmosphere. H. pylori can be demonstrated in tissue by Gram stain, Giemsa stain, haematoxylin-eosin stain, Warthin-Starry silver stain, acridine-orange stain, and phase-contrast microscopy(3).

Prevalence of *H. pylori* infection correlates best with socio-economic status rather than race. In the United States, probability of being infected is greater for older persons (>50 years = >50%), minorities (African Americans 40-50%) and immigrants from developing countries (Latino > 60%, Eastern Europeans > 50%). The infection is less common in more affluent Caucasians (< 40 years = 20%) (6, 10).

H. pylori infection is one of the most common infections in the world. It is usually acquired during childhood and without antibiotic therapy, it generally persists for life (7). It is currently estimated that approximately half of the world's human population is infected with this gastric bacterial pathogen. However, the prevalence of H. pylori is not evenly spread around the world. In western countries, for example, the prevalence of infection has been decreasing during the past decades (10). However a new study says there is global reduction in the prevalence including under developed countries in all age groups. The reasons for this are unclear but it is unlikely that treatment of infection or improvement in socioeconomic conditions fully explains thedecline (8, 17).

Any mechanism that transfers H. pylori organisms from the stomach of one infected individual to the stomach of an uninfected individual is a potential mode of transmission. H. pylori can be spread in various ways, Person-to-person, fecal-oral and oral-oral transmission can play a role in transmission of the infection, feces, saliva or vomit can potentially transmit the organism, mothers may play a key role in the transmission of H. pylori within the family (5, 10).

1.1. Association of H pylori infections and abdominal symptoms

A causal relationship between H. pylori infection and abdominal pain of childhood is still not proven. In addition, there seems to be a relationship between ulcer disease and abdominal symptoms but it is still unclear whether chronic gastritis causes symptoms in children (18). A study from India found a possible association of H. pylori with recurrent abdominal pain in H. pylori positive children (age: 3–12 years)with recurrent abdominal pain. In this study, 83%of the children had complete symptomatic relief after eradication therapy(5, 11).

However other studies suggest that early acquisition of H. Pylori may play a role in the development of recurrent abdominal pain in children less than 5 years of age. In addition symptoms of nausea associated with vomiting are quite likely to be caused directly by a stomach condition and can be symptoms of H. pylori infection. If the vomit is initially clear and subsequently contains blood, it is likely to be caused by a tear in the lower part of the oesophagus caused by the initial vomiting. If blood is present in the vomiting, it can also be caused by a bleeding ulcer in the stomach (8, 16).Vomiting, diarrhea and nausea are very common in pediatric population as general. They are non-specific and can be a symptom of various organic diseases and, more often, of functional gastrointestinal disorders. Whether H. pylori infection without PUD can cause recurrent abdominal pain remains a matter of debate. Recently published studies indicate that further testing for H. pylori should only be performed when, based on alarm features, organic disease is suspected. (4, 12)

1.2. Diagnosis

The diagnosis of H. pylori-associated diseases in children can reliably be made through gastro-duodenal endoscopy with biopsies as gold standard test. Studies demonstrated the efficacy of the C-urea breath test and monoclonal stool antigen tests for the noninvasive diagnosis of pediatric *H. pylori* infection.(3, 5) The diagnostic accuracy of different tests was as follows: culture 98.1%,RUT (rapid urea test) 96.2%, pathology 98.1%, PCR 94.3%,serology 84.9%, UBT(urea breath test) 100% and HpSA (H. pylori stool antigen) 96.2%.According to this study, all the above-mentioned methods, except serology,are considered valuable diagnostic methods in the diagnosis of H. pylori in children.(1)

1.3. Stool Antigen Detection:

An enzymatic immunoassay which detects the presence of H pylori antigen in stool specimens has become available and has undergone testing in the initial diagnosis of H pylori infection and in the confirmation of eradication after treatment. A polyclonal anti-H pylori capture antibody absorbed to micro wells is the most widely used test but a monoclonal antibody test has recently been described and is under investigation. (2, 10)

1.4. Stool Versus Other Method

The performance of stool detection of HpSA (H. pylori stool antigen) is an alternative and reliable substitute for the UBT test as anon-invasive diagnostic method in children. Secondly, the test is not expensive and doesn't require a blood sample.

1.5. Objective

The purpose of this work was to evaluate the association between abdominal symptoms and positivity of H pylori in their stool, and to estimate the incidence of H pylori infection in the group. (1)

2. Methodology

2.1. Design

A hospital based cross-sectional study, done in the period of April to June, 2014, in pediatric gastroenterology clinic in Omdurman Military Hospital in Sudan.

2.2. Patient

A total of fifty children were recruited according to specific selection criteria, any child presented to the clinic with abdominal symptoms (recurrent abdominal pain, diarrhea, vomiting or more than one symptoms)were included, while those who had acute diarrhea with any degree of dehydrationor had taken antibiotic, acid suppressive drugs (proton pump inhibitors, H2 receptor antagonists, antacids, bismuth preparations) within the last four weeks were excluded. The age of the study group was between one month and 15 years they were divided into three group, group A: from one month up to five years, group B: from five up to ten years and group C: from ten to 15 years old

2.3. Data

A questionnaire was filled by the investigators with the cooperation of the parents of each child to obtain demographic information, and to gather data retrospectively on the presence and frequency of the child's abdominal symptoms during the previous three months. The symptoms were assessed by a physician, and unclear answers were clarified by interviewing parents again. Elicited symptoms included recurrent abdominal pain in isolation, or in association with diarrhea/vomiting, or isolated diarrhea/vomiting. The questionnaire scored abdominal symptoms as present if they occurred more than once per week during the previous three months. For vomiting and diarrhea, the criteria were an episode of 5–8 days of length once or more in the last three months, family history of similar condition, socioeconomic status also were collected, Informed consent was obtained from children's parents for participation in the study, and the study protocol was approved by the Ethics Committee of the hospital.

2.4 Detection of H pylori Antigen in the stool

The stool antigen test was performed according to the manufacturer's recommendations; those performing and

reading the test were unaware of the *H pylori* status of the tested children. ICT kit from Chinese ***(zjdfjy.en.alibaba)*** company was used. This is a sandwich solid phase immunechromatogrophy assay. To perform the test an aliquot of diluted stool sample is added to the sample well of the test cassette. The sample flows through a labeled pad containing H pylori antibody coupled to red colored colloidal gold. If the sample contains H pylori antigen, the antigen will bind to the antibody coated on the colloidal gold particles to form antigen-antibodies-gold complexes, these complexes move on the nitrocellulose membrane by capillary action towards the test line region on which the H. pylori antibodies are immobilized. As the complexes reach the test line, they will bind to the antibodies on the membrane in the form of line. A second red control line will always appear in the result window to indicate that the test has been correctly performed and the test device function properly. If H. pylori antigen is not present or lower than the detection limit of the test, only the control line will be visible. If the control line doesn't develop, the test is considered invalid. For quality control a positive and a negative control sample were used in the study

2.4 Statistics

Analysis was performed using computer IBM SPSS program (version 20). Frequencies and demographic data along with the correlation between abdominal symptoms and the results of stool H. pylori antigen were calculated.

3. Results

Fifty children were included in this study, demographic data showed nearly equal male to female distribution, male were 27(54%) of the group, their age was distributed between one month and 15 years divided into three group, group A: under five years were 25(50%), group B: between 5-10 years were 19(38%) and group C: above ten years were 6(12%), their mean age was 7.5 years. 44(88%) of the studied group lived in poor or very poor socioeconomic status, Distribution of the abdominal symptoms showed 20(40%) of the studied group had only recurrent abdominal pain, 15(30%) presented with concomitant abdominal pain and diarrhea, and 3(6%) had both abdominal pain and vomiting, while 4(8%) had tripled symptoms of abdominal pain, diarrhea, and vomiting, just 6(12%) presented with isolated diarrhea, also 2(4%) presented with isolated vomiting **(Figure 3).** On the other hand 11(22%) of the whole group had family history of quite similar symptoms.

Positivity of H. pylori in the stool and its correlations: Positive helicobacter pylori antigen in the stool was 29(58%) of the whole group **(Figure1),** male were dominating 17(58.5%), in addition 20(70%) of those had positive H. pylori were under five year **(Figure 2).**

Furthermore 7(63.6%) of those had family history of similar condition were harboring the H. pylori antigen in their stool, also 27(93%) of those had positive stool test lived in very poor or poor socioeconomic conditions, indicating existence of strong and significant correlation between presence of the antigen and their living condition.

25 out of 29 of those positive for the H. pylori antigen presented with recurrent abdominal pain in isolation or association with vomiting/diarrhea or both, while just 4 cases out of 29 who had the antigen were presented with isolated one symptom (diarrhea or vomiting) and this showed statistically significance correlation between abdominal pain+/- other symptoms and the presence of the stool H pylori antigen (P<0.05) **(Table 1)**.

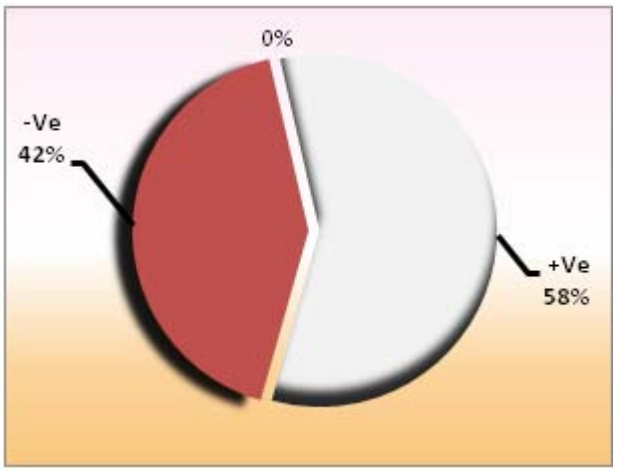

Figure1: Distribution of the studied population according to the result of stool H. pylori antigen

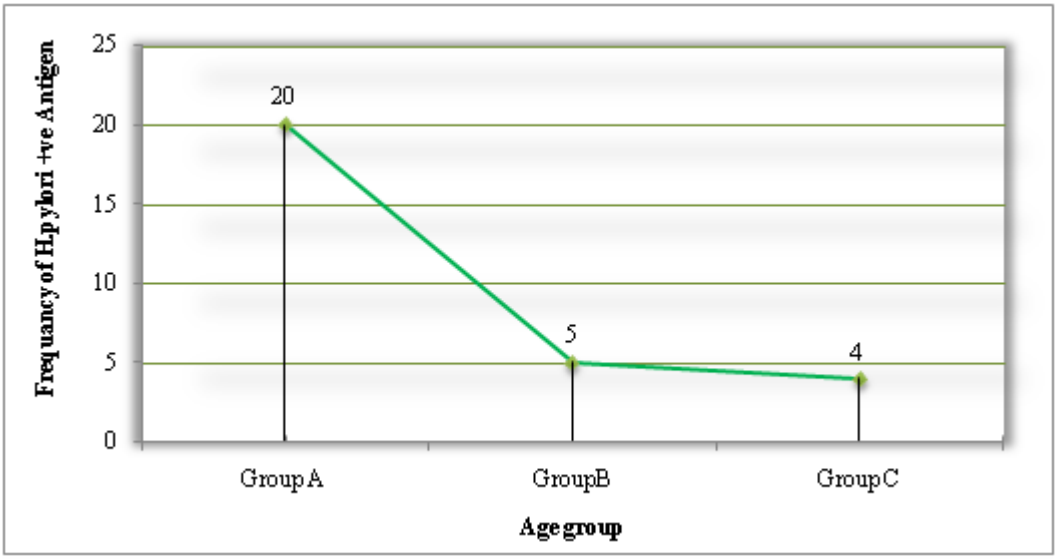

Figure 2: Age distribution in the positive H. pylori antigen group

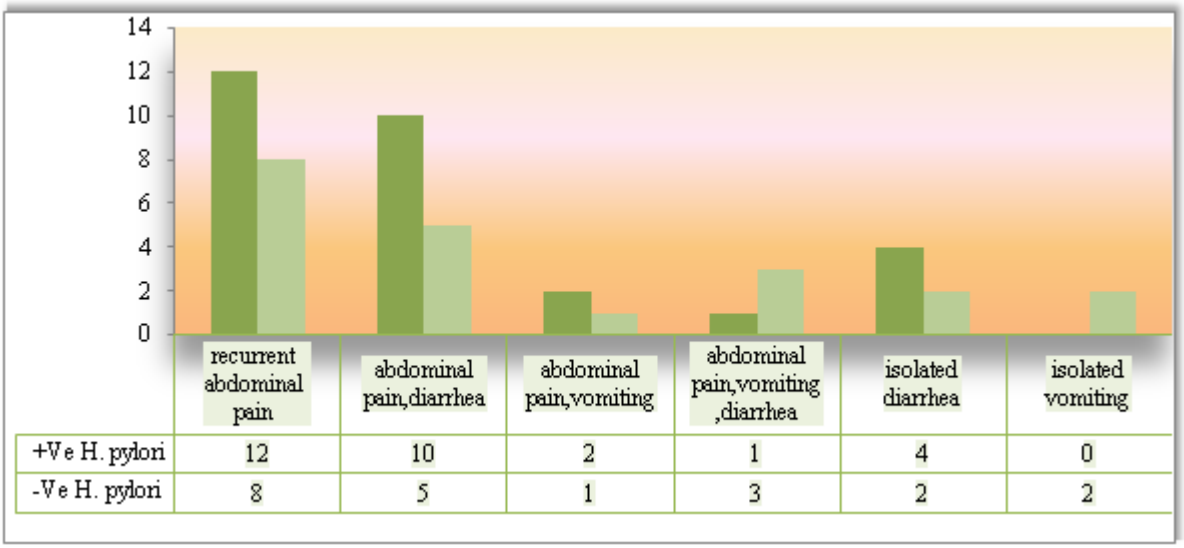

Figure 3: Association of H.pylori stool antigen andabdominal symptoms

Table 1: correlation between abdominal pain and the result of the stool

Abdominal symptoms	+Ve H. pylori stool antigen	-Ve H. pylori stool antigen	Total
Abdominal pain +/- vomiting +/- diarrhea	25	17	42
Isolated symptom (vomiting or diarrhea)	4	4	8
Total	**29**	**21**	**50**

P> 0.05

4. Discussion

The strength of this study is that it was conducted in one of under developed area in Africa where a higher incidence of H. pylori is expected in general population and particularly children, due to low socioeconomic status and poor sanitation, while the main limitation in our study is its sample size, which is a rather smaller one, but still consistent with various data from around the globe. H. pylori antigen is detected in the stools of more than half of the studied group 29(58%), which agreed with data from Africa, however other studies showed lower figure reaching (23%) and others reported higher figure near to 80% as in Alexander et al in Russia (14), the controversy in results is most probably due to geographical and ethnic variation of the studied groups. Interestingly most of H. pylori stool positivity was detected in children whose age less than five years old, in consistent with both *Gabor et al* and Okuda et al studies (8, 9, 19, and 20).

Low socioeconomic status had strong association with the existence of the H. pylori antigen in the stool which goes with most if not all the other studies from different countries for example two studies carried by Ndip et al (21) and Rodrigues et al(22,23), probably this association is due to poor hygiene and contaminated sources of water in this group of people. On the other hand the most remarkable symptoms which had statistical correlation with H. Pylori positivity was abdominal pain whether a recurrent pain alone or in concomitant with diarrhea or vomiting or both of them, representing 25 out of the 29 positive cases, and this is consistent with data from Tunisia done by Siai K et al (26), and Oderda et al study (24), (14), but surprisingly this is completely against two studies one was a meta-analysis

study done by Poddar U et al (25), in India, and the other was Italian study done by Maria et al, in which they claimed only correlation between H. pylori infection and vomiting/diarrhea while no association with abdominal pain (13), this strange results were against the postulation that H. pylori is a protective mechanism against diarrhea, the above contrast can be explained by the lack of a biological marker or valid measurement for pain, and the variation in tolerance of pain in the human beings, However there is a good study in Turkey, concluded that children with abdominal pain and *H.* pylori appear to benefit from eradication therapy of H. pylori(15).

Finally, majority of the negative correlation results and the conflict of data may be because were derived from studies conducted in developed countries and by means of detection of antibodies against *H. pylori* in the serum not antigen detection method. In addition, these children were those whom referred to tertiary hospital clinics, but the majority of the children with abdominal pain are managed in the primary care setting.

5. Conclusion

The authors concluded that the most common GI symptom associated with the presence of fecal antigen for *H. pylori* was abdominal pain whether alone or in association with other symptom, while isolated diarrhea or vomiting has no significance association, moreover concluded that existence of H. pylori fecal antigen in children less than five is more than those upper than five years old, and there is strong association between the presence of stool antigen and the socioeconomic status of the family.

6. Further Scope

Randomized trial with larger sample size studies will be helpful for more elaboration of the associated clinical symptoms for H pylori infection in children. Also setting of criteria for diagnosis of H. pylori infection in pediatric is recommended to determine when to treat this organism, particularly in under developed countries.

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