Relation between Helicobacter Pylori infection and Irritable Bowel Syndrome

Ali Taha Ali , Yasser Mohamed kamal, Romany mekhael kerollos,
Department of internal medicine , Sohag University

ABSTRACT

Background: Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder. The association of Helicobacter pylori(H. pylori) infection with IBS still remains controversial.

Objective: The objective of this study is to determine the rate of H. pylori infection among patients with IBS through the detection of H. pylori Stool Antigen Test titre (SAT)

Materials & Methods: This study will be performed on 80 patient attended GIT out patient clinic of sohag university hospital from 6/2017 to 3/2018 will be classified into:
1- controle group (20 patients) who do not fulfill criteria for diagnosis of irritable bowel syndrome
2- Affected group (60 patients) who fulfill criteria for diagnosis of irritable bowel syndrome
Those groups will be classified according to severity
Also the affected groups will be classified according to subtypes
All patients underlying the following:
(1) history will be taken including:
(2) Full clinical examination
(3) Laboratory investigations
   • Fasting blood glucose level, HBA1C
   • renal function, liver function, complete blood counting
   • Abdominal ultrasonography
   • H. pylori stool antigen test titr (SAT)

Results: Comparison was done among all types of IBS as regard H. Pylori SAT revealed constipation predominant cases have the highest number (33%) of H. Pylori SAT positive cases while lowest number of cases (4%) were unclassified. Comparison was done among all grades of IBS as regard H. Pylori SAT revealed grade 3 cases the highest number of H. Pylori SAT positive cases, lowest number of cases were grade 1

Conclusion: In this study revealed positive relationship between H. Pylori infection and irritable bowel syndrome as regard types of irritable bowel syndrome, the incidence of H. Pylori infection was more with constipation predominant patients and as regard severity of irritable bowel syndrome, H. Pylori infection more common in grade 3

Keywords: Irritable bowel syndrome, Helicobacter pylori infection

Introduction

(H. pylori) is a gram-negative, microaerophilic spiral bacterium found usually in the stomach; it causes chronic gastritis and gastric ulcers, and has been linked to the development of duodenal ulcers and stomach studies have linked H. pylori infection with a wide range of extra gastric diseases. Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder that is characterized by abdominal pain and changes in stool habits. Several studies have described the role of various risk factors in the pathogenesis of IBS, including different infections such as H. pylori infection. However, other studies have denied such association. The induction of typical abdominal discomfort associated with IBS occurs predominantly in H. pylori infected patients, indicating that H. pylori infection may be involved in triggering visceral hypersensitivity in patients.
with IBS. In contrast, several studies have reported that there is no association between H. pylori infection and IBS. Hence, it has been suggested that with the exception of unexplained iron deficiency anemia and idiopathic thrombocytopenic purpura, H. pylori infection has no proven role in other extra intestinal diseases.

**MATERIALS & METHODS:**
This study will be performed on 80 patients attended GI Tout patient clinic of Sha University Hospital from 6/2017 to 3/2018 will be classified into 1-control group (20 patients) who do not fulfill criteria for diagnosis of irritable bowel syndrome 2-affect group (60 patients) who fulfill criteria for diagnosis of irritable bowel syndrome. Those groups will be classified according to severity into: *Grade1 mild (awareness of the symptom but easily tolerated);* *Grade2 relevant (interference with normal activity);* *Grade3 severe (incapacitating)*

Also the affected groups will be classified according to subtypes:
1-constipation predominant
2-diarrhea predominant
3-mixed
4-unclassified

All patients underlying the following (1) history will be taken including:
Age, Sex, drug history
*History of abdominal pain: criteria, severity, aggravating factors, releasing factors* *History of diarrhea and or constipation associated with abdominal pain or not*
(2) Examination:
(3) Laboratory investigations
• Fasting blood glucose level, HBA1C
• Renal function, liver function, complete blood counting
• Abdominal ultrasonography

*Inclusion criteria:*
• All of the patients had been diagnosed and treated for IBS

* Exclusion Criteria.

1-who had recently undergone digestive surgery.
2-Intake of NSAIDs
3-Immunosuppressed drugs or antibiotics in the previous 3 months
4-Major psychiatric disease
5-Excessive alcohol consumption
6-Renal or Hepatic disease

**Stool antigen test (SAT)** is a noninvasive method with good sensitivity and specificity, 94% and 97% respectively in global meta-analysis, in the diagnosis of H. pylori infection. This method detects the presence of H. pylori antigen in stool samples. The accuracy of SAT is influenced by several factors, like antibiotic, PPI, N-acetyl cysteine, bowel movement and upper gastrointestinal bleeding. Preservation of the specimen, like temperature and transport time before testing, and cut-off valve also have impacts on diagnostic accuracy of SAT.

**Enzyme Immunoassay Test kit**
Enzyme Immunoassay Test kit used in this study used in Acon laboratories in USA. The H. pylori antigen EIA test is an enzyme immunoassay for the qualitative and quantitative detection in human stool. It is intended as an aid in the diagnosis of possible H. pylori infection and in the follow up of patients undergoing antimicrobial therapy.

**Principle:** The H. pylori antigen EIA test kit is a solid enzyme immunoassay based on sandwich principle for the qualitative and quantitative detection of H. pylori antigen in human stool. The microwell plate is coated with anti H. pylori anti bodies. During testing the antigens are extracted out with extraction solution and added to the antibodies to H. pylori and then incubated if the specimens contain H. pylori antigens.

It will bind to anti body coated on the microwell plate and simultaneously bind to the conjugate to form immobilized antibody – H. pylori.
antigen conjugate complexes if the specimen donot contain H.pylori stool antigens ,the complexes will not be formed. After initial incubation ,the micro well plate is washed to remove un bound materials. substrate A and are added and then incubated to produce blue color indicating the amount of H.pylori antigen present in the specimens .sulfuric acid solution is added to the microwell plate to stop the reaction producing color change from blue to yellow.the color intensity which correspond to the amount of H. pylori antigens present in the specimens, it is measured with microplate reader at 450/630-700nmor 450nm

**Interpretation of results:**

* **Qualitative Index value:**
  - Positive >1.1
  - Negative <0.9
  - Equivocal (0.9--1.1)

* **Quantitative index value:**
  - Positive >0.055
  - Negative <0.045
  - Equivocal (0.055--0.045)

**Performance characteristics**

1-sensitivity and specificity :
The H.pylori antigen EIA test kit habeen compared to a leadingcommercialH.pylori EIA test using clinical specimen ,the results showthat the clinical sensitivity ofH.pylori is 98.6%and specificity is 95.4%

**Results**

Our study on 80 patients including 27 female 53 male ranging from 20-60 years old,after complete history taking and full clinical examination of the cases in our study we found that 17.5% of those patients donot suffer from irritable bowel syndrome 82.5% were complaining from irritable bowel syndrome,IBS patients were classified according to type of IBS And about 33patients was constipation predominant(41%) , about 24 patients were diarrhea predominant( 30%) ,about 5patients were mixed (6.25%) ,and 4 patient were un classified (5%) Those patients were classified also according to severity of IBS About 32patient(40%) were suffering from mild degree(awareness of the symptom but easily tolerated) about 21patient (26.25%)moderate degree; relevant (interference with normal activity); and about 13patients (16.25%)severe (incapacitating) Stool antigen test titre(SAT) was done for all studied cases and about  43 patients (53.75%) were SAT positive and about 37 patients (46.25%) were SAT negativeDistribution of studied population according to H.Pylori SAT 46% SAT negative,53.7%sat positiveComparison was done among all types of IBS as regard H.Pylori SAT revealed constipation predominant cases have the highest number(33%) of H.Pylori SAT positive cases while lowest number of cases(4%) were unclassifiedComparison was done among all grades of IBS as regard H.Pylori SAT revealed grade 3 cases thethe highest number of H.Pylori SAT positive cases,lowest number of cases were grade1
Table 4: Comparison among types of IBS as regard H. pylori SAT

<table>
<thead>
<tr>
<th>Types of IBS</th>
<th>Mean ± SD Median (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No IBS</td>
<td>0.11±0.15 0.1 (0-0.36)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Type C</td>
<td>0.20±0.22 0.13 (0-0.9)</td>
<td></td>
</tr>
<tr>
<td>Type D</td>
<td>0.12±0.15 0.03 (0-0.5)</td>
<td></td>
</tr>
<tr>
<td>Type M</td>
<td>0.11±0.15 0.1 (0-0.36)</td>
<td></td>
</tr>
<tr>
<td>Type U</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

(p1compared no IBS with type C, p2compared no IBS with type D, p3compared no IBS with type M, p4compared no IBS with type U, p5 compared with type C &D, p6compared with type C &M, p7compared with type C &U, p8 compared with type D&M, p9 compared with type D&U, p10 compared with type M)

Comparison among types of IBS as regard H. pylori SAT

<table>
<thead>
<tr>
<th>Number (%)</th>
<th>H. pylori SAT Negative</th>
<th>H. pylori SAT Positive</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No IBS</td>
<td>14 (100%)</td>
<td>0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Type C</td>
<td>11 (33.33%)</td>
<td>22 (66.67%)</td>
<td></td>
</tr>
<tr>
<td>Type D</td>
<td>12 (50.00%)</td>
<td>12 (50.00%)</td>
<td></td>
</tr>
<tr>
<td>Type M</td>
<td>2 (40.00%)</td>
<td>3 (60.00%)</td>
<td></td>
</tr>
<tr>
<td>Type U</td>
<td>4 (100%)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

(p1compared no IBS with type C, p2compared no IBS with type D, p3compared no IBS with type M, p4compared no IBS with type U, p5 compared with type C &D, p6compared with type C &M, p7compared with type C &U, p8 compared with type D&M, p9 compared with type D&U, p10 compared with type M &U)

Comparison among grades of IBS as regard H. pylori:

<table>
<thead>
<tr>
<th>Grades of IBS</th>
<th>Mean ± SD Median (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No IBS</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>0.08±0.09 0.07 (0-0.4)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Grade 2</td>
<td>0.14±0.18 0 (0-0.5)</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.35±0.25 0.45 (0-0.9)</td>
<td></td>
</tr>
</tbody>
</table>

(p1compared no IBS with grade 1, p2compared no IBS with grade 2, p3compared no IBS with grade 3, p4compared grade 1 & 2, p5 compared with grade 1 & 3, p6compared with grade 2 & 3)

Discussion

IBS is a substantial medical challenge to society, and the development of a novel treatment for this disease is frustrated by the lack of insight into its etiology and pathogenesis. In the present study we explored the potential association between H. pylori and IBS. Previous basic studies have suggested that the systemic inflammation provoked by CagA (cytotoxin-associated gene A) and VacA (vacuolating cytotoxin) of H. pylori may link this bacterium to the pathogenesis of IBS (1) starting to test this hypothesis through a cross sectional analysis of the effects of H. pylori infection inpatient population attending Sohage University Hospital internal medicine outpatient clinic and gastro intestinal...
tract out patient clinic. Numerous obstacles hamper the study of the relation between *H pylori* infection and IBS. Most cases of *H pylori* infection are silent and, although abdominal symptoms are commonplace, not all dyspeptic patients seek medical advice.\(^2\)\(^,\)\(^3\) Symptom assessments must be meticulous as *H pylori* infection may induce some abdominal symptoms while other symptoms may not be associated with the infection. Moreover, to assess the association between *H pylori* infection and IBS, *H pylori* related organic disease must be ruled out. Whereas the sensitivity of the SAT used in this study was high, the specificity was relatively low. The low specificity would, however, mask a possible effect of *H pylori* on gastrointestinal symptomatology as symptoms caused by *H pylori* may also be reported by people who tested SAT. The diagnostic accuracy of commercially available serology kits varies considerably between different laboratories.\(^4\) The specificity of the present assay, however, was only slightly lower than that which could be obtained with commercially available detection kits in this study population. The main aspect in our study is to detect the pattern of *H pylori* infection among patients with irritable bowel syndrome. And so we made comparison between those without and with IBS according to *H. pylori* SAT and we found that big partition of IBS cases were SAT positive (65%) and 35% were SAT negative, and among patients without IBS criteria 30% of cases were SAT positive this was near the results of many studies like (Ford AC, Moayyed P, Jarbol DE et al. Meta-analysis: *H. pylori* 'test and treat' compared with empirical acid suppression for managing dyspepsia. Aliment Pharmacol Ther 2008; 28: 534 – 44). revealed only 50% were SAT positive and 50% were SAT negative infected patients this may be explained by difference in dietary habits as we mentioned above socioeconomic state as this study revealed that constipation was predominant. Differences between both studies this may be explained by different number of cases and change in locality as *H. pylori* infection is more common in local countries like Egypt as *H. pylori* is more prevalent among older adults, African, and lower socioeconomic groups as the main route of transmission of this bacterium is fecooral route so bad hygiene and low socioeconomic state in our locality affect morbidity of infection by this bacterium.

So we should mention that Rovell and Ford conducted meta-analysis on the study of the epidemiology of IBS (Rovell Rm, Ford Ac, global prevalence and risk factors for irritable bowel syndrome metaanalysis clin gastroenterol hepatol 201210:72-721) the study revealed that socioeconomic state affect the prevalence of IBS, this study was done on 300 patient suffering from manifestations of irritable bowel syndrome and fulfilling the Rome criteria for its diagnosis, those patients of various socioeconomic state and various locality. Upper endoscopy and tissue biopsy was done for those patients. Percentage of *H pylori* positive patients was more among low socioeconomic state patients. Another item which is important in description of the pattern of *H pylori* infection among patients with irritable bowel syndrome is to compare different types of IBS according to severity of *H pylori* infection which can be detected by stool antigen titer. Our study revealed constipation predominant IBS have the highest records of *H pylori* SAT (41%) then diarrhea predominant have the 2nd
level (30%) while mixed and unclassified cases have the lowest records. This result was near many studies like (McCune A, Lane A, Murray L et al. Reduced risk of atopic disorders in adults with Helicobacter pylori infection. Eur J Gastroenterol Hepatol 2013; 15: 637 – 40) which revealed that the two most common subtypes are diarrhea predominant (45%) and constipation predominant (35%) but the difference from this study is that the most common subtype is diarrhea predominant not constipation predominant as in our study but unclassified and mixed have higher results and may be explained by deficient number of these cases in my study and affected by dietary habits, psychical treatment, support and follow up which is deficient in our locality (5, 6) according (Yuka, Yomataka et al) IBS, and its subtypes prevalence is affected by age sex, bowel habits, ibs may be more common among H. Pylori infected patients. This may be explained by difference in dietary habits as we mentioned above socioeconomics state as this study revealed that constipation predominant Differences between both studies this may be explained by different number of cases and change in locality as H. Pylori infection is more common in local countries like Egypt as H. Pylori is more prevalent among older adults, African, and lower socioeconomic groups as the main route of transmission of this bacterium is fecooral route so bad hygiene and and low socioeconomic state in our locality affect morbidity of infection by this bacterium.

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The last aspect we want to explore in our study is to compare severity of IBS with the severity of H.pylori infection and we found that there highest records of H.pylori SAT was grade 111 sever the lowest records was grade 1. This was like many results like (10)

It is interesting to observe how patients with visceral hypersensitivity also exhibit H. pylori infections. This fact suggests that this bacterium may be involved in triggering abdominal pain in IBS patients (11)

Such association between H. pylori and IBS can be partially explained by the presence of different types of H. pylorivirulence factors, in addition to host genetic predisposition and environmental factors; moreover, the clinical outcomes are determined by the interplay of these factors (12, 13)

**Conclusion** In this study revealed positive relationship between H. Pylori infection and irritable bowel syndrome as regard types of irritable bowel syndrome, the incidence of H. Pylori infection was more with constipation predominant patients and as regard severity of irritable bowel syndrome, H. Pylori infection more common in grade 3

**Recommendation** This study affected by limited number of cases, specificity and sensitivity of SAT ELISA APPARATUS, more researches are need to be done to explore this relation, and to explore the effect of H. Pylori

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eradication therapy on improvement of symptoms of irritable bowel syndrome which may help in adding TTT of H. Pylori infection as a line of management of IBS

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