

Irritable Bowel Syndrome in Children: Is There an Association with Infantile Colic in Infants?

Abdelrazak Mansour Mohamed Ali,
Mohamed Abdelrahman Mohamed

Keywords: Helicobacter Pylori, Rome III Criteria, Infantile, Stool Antigen Test, Childhood

Objectives: To determine whether irritable bowel syndrome is associated with impressing history of early infantile colic. **Design:** A retrospective case controlled study. **Setting:** Local tertiary hospital in Muhayel Aseer Abha district (Saudi Arabia), Rural area in Abo Hareez, Sharkia Governorate (Egypt) and Al Hussein University Hospital(Cairo, Egypt) from April, 2010 to June, 2012. **Participants:** Four hundred and fifty cases of irritable bowel syndrome (IBS) that meet the Rome III criteria and one hundred control, aged 7-17 years old. **Main outcome Measures:** Irritable bowel patients diagnosed on the basis of Rome III criteria for IBS. Complete stool analysis including Helicobacter pylori (H pylori) stool antigen test and occult blood in addition to urea breath test if necessary. **Results:** Of the total 450 irritable bowel syndrome cases, 195(43.3%) had reported infantile colic at age 0- 4 months compared to 7% in control group, and family history was evident in 179 (91.8%) of combined colic -irritable bowel cases and in 406 (90.2%) irritable bowel cases. H pylori was present in 41.7% of IBS cases compared to 8% in control. **Conclusion:** Our findings provide a new correlation between childhood irritable bowel syndrome and past history of infantile colic. Moreover, a significant association was found between irritable bowel syndrome and H pylori infection.

Background

Irritable bowel syndrome (IBS) is a common disorder that may affect over

15 percent of the general population. It is sometimes referred to as spastic colon, spastic colitis, mucous colitis or nervous stomach. IBS should not be confused with other diseases of the bowel such as ulcerative colitis or Crohn's disease. IBS is a functional disorder where the function of the bowels may be abnormal but no structural abnormalities exist.^[1] Diarrhea or constipation may predominate, or may alternate (classified as IBS-D, IBS-C or IBS-A, respectively). Historically, it is a diagnosis of exclusion. The diagnosis of IBS can now be made on the basis of symptoms alone, in the absence of alarm features such as age of onset greater than 50 years, weight loss, gross hematochezia, systemic signs of infection or colitis, or family history of inflammatory bowel disease^{(2),(3)}. Onset of IBS is more likely to occur after an infection (post-infectious, IBS-PI),^[4] or a stressful life event,^[5] but varies little with age.^[6] The American Gastroenterological Association published a set of guidelines for the tests to be performed to rule out other causes for these symptoms. These include gastrointestinal infections, lactose intolerance, and celiac disease.^[7] Although there is no cure for IBS, there are treatments that attempt to relieve symptoms, including dietary adjustments, medication and psychological interventions. Patient education and a good doctor-patient relationship are also important.^[8] Several conditions may present themselves as IBS, including celiac disease, mild infections, and parasitic

infestations like Giardiasis^[9], several inflammatory bowel diseases, bile acid malabsorption, functional chronic constipation, small intestinal bacterial overgrowth, and chronic functional abdominal pain. In IBS, routine clinical tests yield no abnormalities, although the bowels may be more sensitive to certain stimuli, such as balloon insufflation testing. The exact cause of IBS is unknown. The most common theory is that IBS is a disorder of the interaction between the brain and the gastrointestinal tract, although another common theory is that, in IBS there are abnormalities in the gut flora which results in inflammation and altered bowel function.^[10] IBS is unlike other health problems in that there are no clear-cut diagnostic tests or laboratory findings that pinpoint what is going wrong. Although a direct cause may not be identified, problems with visceral hypersensitivity and colon motility seem to be at play. There are several theories may be behind these dysfunctions, so it may be a good idea to be acquainted with those theories to better understand what could be behind the child's symptoms^[11]. Medical history questions focus on bowel habits, diet, exercise, and stress. Physical examination looks for other causes of GIT problems, as well as other body system diseases. Complete blood count and blood chemistries may be ordered to look for anemia or other abnormalities such as an allergy to gluten. Testing for blood in the stool, endoscopy of the GI tract and biopsy may be taken to exclude the

possibility of cancer, celiac disease, or other inflammatory bowel disease^[11]. IBS occurs in both children and adults. Almost 14% of high school students and 6% of middle school students complain of IBS-like symptoms. There is no known gene that causes IBS, but the disorder does seem to occur more often in families where either a child or a parent has the disorder^[12]. IBS has no direct effect on life expectancy. It is, however, a source of chronic pain, fatigue, and other symptoms^[13]. Several intestinal disorders have symptoms that are similar to irritable bowel syndrome. Examples include malabsorption, inflammatory bowel disease, Celiac disease, *Helicobacter pylori*, parasites and microscopic colitis^[14-17].

Methods

This retrospective study included patients younger than 18 years [mean age(SD)=11.7±(1.7)], who had symptoms that met Rome III criteria. Exclusion criteria included those had not symptoms that met Rome III criteria and had taken antibiotics or gut cleansing medications before. Potential participants were identified and recruited from Local Tertiary Hospitals in Muhayel Aseer Abha district (Saudi Arabia), *Abo Hareez* Rural area in Sharkia Governorate (Egypt) and Al Hussein University Hospitals (Cairo, Egypt) from April 2010 to June 2012. Eligible cases were enrolled from outpatient clinics as well as inpatient admissions after informed consent obtained from a parent or guardian. The study was approved by the medical ethical review board of the medical centers. Printed records were collected to verify inclusion criteria, medications given, clinical review, family and past histories and test results. Participants meet the Rome III criteria for IBS if their symptoms began at least 6 months ago, have had abdominal pain or discomfort at least 3 days each month in the last 3 months, and at least two of the following statements are true, 1-The pain is relieved by having a bowel movement. and/ or 2.Onset associated with a change in frequency

of stool; and/or 3.Onset associated with a change in the appearance of stool. In addition to the above criteria, no evidence of an inflammatory, parasitic (*Giardia*), anatomic, metabolic, or neoplastic process that explains the subject's symptoms.^{(18),(19)}

The more recent Rome III Process was published in 2006. Physicians may choose to use one of these guidelines. The algorithm may include additional tests to guard against misdiagnosis of other diseases as IBS such as "red flag" symptoms that include weight loss, gastrointestinal bleeding, anemia, or nocturnal symptoms. However, researchers have noted that red flag conditions may not always contribute to accuracy in diagnosis; for instance, as many as 31% of IBS patients have blood in their stool.^[20] The history of infantile colic was identified and defined according to modified Wessel criteria for infantile colic, which criteria mean that a well thriving infant cried for 3 hours daily for more than 3 days every week for more than 3 weeks.^[21,22] Eligible controls with mean age (SD) =12.1 ± (1.2) were selected from the same population and matched to cases by country of origin, age, sex, and race. The study controls were identified as having no IBS or history of IBS (i.e not fulfill Rome III criteria of irritable bowel syndrome), and no severe distressing illness or abnormalities.

The case and control groups were investigated for H pylori using a stool antigen test. This one-step test is a chromatographic immunoassay for the qualitative detection of H pylori infections (Alcon Laboratories Inc). It is a relatively simple, reliable, more applicable, and noninvasive test of H pylori infections in children.^[23,24,25] *Helicobacter pylori* fecal antigen has shown a high degree of sensitivity, specificity, and positive and negative predictive values.^[25] The Urea Breath Test (UBT), was advocated to certain patients who can swallow capsule (containing 14 C-Urea) with 50ml water, and if the result of H pylori stool antigen test was weak positive. Peak time is typically 10–30 minutes. This test has been shown to be an extremely accurate method of

detecting H pylori infection because it has the advantage of evaluating the gastric mucosa as a whole. Multiple studies have shown that (UBT) has both high sensitivity and high specificity for diagnosing active H pylori infection in children^[26]

All analyses were performed using SPSS (SPSS Inc). The demographic characteristics of cases and controls were compared using the Fisher exact test, and Odds Ratios and 95% CIs were calculated.

Results

Between April, 2010 and June, 2012; 450 patients (56% Girls) were eligible for inclusion and 100 (55% Girls) for control according to the Rome III criteria for the diagnosis of irritable bowel syndrome (IBS). Characteristics of the study population are presented in Table 1., where most variables evaluated were not confounders, the common sociodemographic variables such as gender, ethnicity, socioeconomic status, etc, were included except the education which did not differ significantly among the study population groups. Although the number of the known potential confounders are likely limited because of (1) lack of association between IBS and many commonly known sociodemographic factors and (2) the small number of known risk factors^{[27],[28]} H pylori documentation was relatively increased to 192(41.7%) in IBS cases then markedly decreased to 8% in control. Family history was approximately similar in both irritable bowel and infantile colic cases (70% and 75% respectively). Table 2 shows that of the total 450 irritable bowel syndrome cases, 195 (43.3%) had a reported infantile colic at age 0-4 months compared to 7% in control. Having history of infantile colic is more than 10-fold increase for those who have irritable bowel syndrome than those who don't have the syndrome. A high significant association between irritable bowel and infant colic cases is evident. (95% confidence interval=4.6087-22.3967, P value<1%). Fig 1, can illustrate and summarize the results.

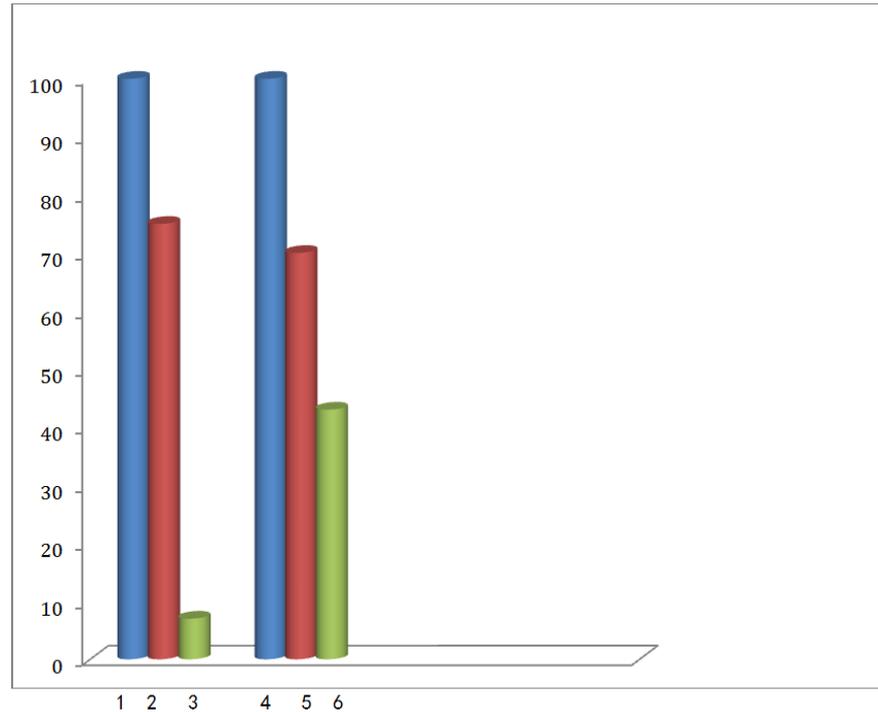


Fig 1. A diagrammatic representation of the study groups, family history in both cases(irritable bowel syndrome and infant colic) and control;1.Control group, 2.Family history of infant colic, 3.Past history of colic in control, 4.Irritable bowel cases, 5.Family history of irritable bowel syndrome, 6.History of infant colic in irritable bowel cases.

Table 1. Characteristics of the study population.

	Irritable bowel syndrome group. (No=450)	Control group (No=100)
Ethnicity		
- Egyptian	210(46.7%)	48 %
-Saudian	240(53.3%)	52 %
Age ,Mean(SD)	11.7(1.7)	12.1(1.2)
Gender		
- Male	198 (44%)	45%
-Female	252(56%)	55%
Socioeconomic status,		
- Low	121 (26.9%)	29%
-Mid	279(62.0%)	58 %
-High	50(11.1%)	13%
Hospitalized	53(11.8%)	9%
Non	397(88.2)%	91%
Colic history,		
-Yes	195(43.3%)	7%
- Non	255(56.7%)	93%
Family history,		
- Yes	315(70%)	10%
-No	135(30%)	90%
H pylori,		
-Yes	192(42.7%)	11%
-No	258(57.3%)	89%

socio-demographic variables did not differ significantly among the study population groups.

Table 2. Distribution of the study population according to the presence of irritable bowel syndrome.

	Cases with Irritable Bowel Syndrome. No. (percentage)	Cases without Irritable Bowel Syndrome No.(percentage)
History of infantile colic	195(43.3%)	7(7%)
No history of infant. Colic	255(56.7%)	93(93%)
Total	450	100

Odds ratio=10.16 i.e the odds of having history of infantile colic is more than ten greater for those who have irritable bowel syndrome than those who don't have the irritable bowel syndrome (95% confidence interval=4.6087-22.3967.P value <1%).

Comment

To our knowledge, this is the first study to assess the direct association between irritable bowel syndrome and infantile colic. Theoretically, both disorders are closely similar in various aspects; these are; 1. Both are functional disorder, 2. Family history is the rule in both, 3. both have nocturnal nature, and 4. Both have repeated bouts.^[19,28,29,30] Recent studies suggest that irritable bowel syndrome (IBS) is associated with low-grade inflammation and has demonstrated the marked distribution of *Helicobacter pylori* cytotoxin-associated gene A (*cagA*) and vacuolating cytotoxin A (*vacA*) alleles (e.g., *s1* and *s2*) in patients with diarrhoea-dominant IBS (IBS-D) as the latter causes vacuolation in colonic epithelial cells *in vitro*.^(16,31) It varies greatly internationally, both within and between countries. A worldwide community prevalence of between 3% and 22%, with wide variations between countries, ranging from 3.5% to, 30% has been reported.^[28,32] Revising the community prevalence and distribution patterns of *Helicobacter pylori* and infantile colic, they seem a nearly similar to that of irritable bowel syndrome.^[29,30] Taken together the forementioned information and the results of other studies done by Yakoob et al.(2012)^[31] and Su et al.(2000)⁽¹⁶⁾ that revealed an association between H pylori infection and the functional dyspepsia in patients with irritable bowel syndrome, we can build up a convincing evidence that both infantile colic and irritable bowel are closely related functional disorder, and commonly associated with H pylori infection. Our results demonstrate that high significant correlation has been found between colic in infancy and irritable bowel

syndrome in childhood-adolescence age, and family history is substantially significant in both. The results of our study are potentially supported by many recent studies which recommend usage of Lactobacillus and Bifidobacterium probiotics to treat and alleviate symptoms of infantile colic, irritable bowel, and other inflammatory gastrointestinal disorders. These symptomatic responses were associated with A-Normalization of the ratio of an anti-inflammatory to a proinflammatory cytokines^[16], B- Compete for receptors in endothelial cells,C- Produce antimicrobial compounds,D- Competition with other organisms for nutrients,E- Affect modification of the receptors for bacterial toxins, and,I- Promoting production of IL-10 with consequent proliferation of CD4⁺ CD25 T-cell receptors suggesting an immune-modulating role for this probiotic organism^[33-39]. However, a study done by Su et al⁽¹⁶⁾, associates symptoms of Irritable bowel syndrome (IBS)with H. pylori infection, female gender, and perceived stress, but the small sample size of that study may influence its strength. The current study has several methodological strengths that enhanced the validity of the new findings; First, its design substantially reduces the likelihood of potential biases associated with the participation influenced by the presence of outcomes. Second, both the exposure risk(infant colic)and the outcome(diagnosis of IBS)in this study were measured objectively without the knowledge of each other, thus reducing the concern of recall bias associated with the ascertainment of exposure and outcome variables .It is clear that irritable bowel syndrome and other GIT functional disorders may potentially affect genetically susceptible individuals with an exaggerated response to a variety of physiological and non-physiological gastrointestinal stimuli that include H pylori infection and probably other infectious agents with particular emphasis on H pylori organism.

Basically, the results of our study are in agreement with the findings of another recent study which found that H pylori infections may be the etiologic pathogenic organism of infantile colic⁽²⁹⁾. While some researchers see that there is evidence that IBS is related to an undiscovered agent, others believe that IBS patients suffer from overgrowth of intestinal flora(small intestinal bacterial overgrowth), and the antibiotics are effective in reducing this overgrowth.^[40] Other researchers have focused on a possible unrecognized protozoal infection such as blastocystosis as a cause of IBS^[10] as certain protozoal infections occur more frequently in IBS patients.^[41,42] *Dientamoeba fragilis* has also been considered a possible organism to study, though it is also found in people without IBS.^[43]

In short, the functional GIT disorders (Infantile Colic and IBS),could be simplified and virtually formulated in the form of four-sided square, with the following sides,1.Genetic susceptibility, 2.Gut microfloral system,3.Host immune system, and 4.H pylori organism or probably another organism to be identified.

Conclusion .Our study findings provide a new correlation between childhood irritable bowel syndrome and past history of infantile colic. Moreover, a high significant association was found between irritable bowel syndrome and H pylori infection.■

Abdelrazak Mansour Mohamed Ali

Assistant Professor of Pediatrics, Al Azhar University, Cairo, Egypt;
Address, 9 Mahmoud Ali street, from Abdelsamea, Faisal, Giza, Cairo, Egypt
abdelrazak_ali@yahoo.com

Mohamed Abdelrahman Mohamed

Consultant of family medicine,
Ministry of health, Egypt
muhammad.abdalrahman@yahoo.com

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