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The Relation of Parasitic Infection and Growth States in Pediatric Patients with Irritable Bowel Syndrome

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ABSTRACT

Background: Irritable bowel syndrome (IBS) is a group of diseases of the gastrointestinal tract (GIT) with a heterogeneous pathophysiology and unclear role for intestinal parasitic infections. **Objective:** The aim of the current study was to detect the relationship of parasitic infection with malnutrition among cases of IBS.

Patients and methods: A cross sectional study was conducted and included 120 children in age from 5 to 15 years old attending the outpatient clinics in October 6 University Hospital and Primary Healthcare centers with GIT symptoms suggesting IBS. All cases subjected to medical evaluation, anthropometric assessment and stool analysis. **Result:** The study revealed that 68/120 (56.7%) of IBS cases had parasitic infection (Group A) with *Giardia lamblia* stages is the most frequent one (25/68 samples, 36.7% of group A, and 20.8% of total IBS case). IBS- diarrheic type (IBS-D) was the predominant subtypes (54/120, 45%) and associated with parasitic infection (*P-value <0.05*) that wasn't observed in other subtypes. The most frequent form of malnutrition according to the Egyptian Z score was overweight (19/120, 15.8%) of IBS cases and no cases with undernutrition or obesity. No significant relation between parasitic infection and malnutrition in IBS (*P-value* >0.05) for all parameters. **Conclusion:** Parasitic infection is common among cases of IBS and associated with diarrhea. Overweight is the most frequent form of malnutrition in cases of IBS even in presence of parasitic infection that revealed no association of parasitic infection with undernutrition in cases of IBS.

Keywords: Egypt, Children, Irritable bowel syndrome, Parasites, Anthropometric measurement.

INTRODUCTION

Functional dyspepsia, abdominal migraine, irritable bowel syndrome (IBS), and functional abdominal pain not otherwise described are among the pediatric functional abdominal diseases [(1)].

More than 50% of kids who visited a pediatric GI clinic for the first time had at least one functional gastrointestinal disease (FGID) [(2)]. The prevalence of FGID varies by geography, age, and sex and is estimated to be between 3% and 16%. IBS is a functional gastrointestinal disorder (FGID) with a prevalence ranging from 1.2% to 5.4% depending on the region. It is characterized by chronic abdominal pain, bloating, passage of mucus or straining during bowel movements, a feeling of incomplete evacuation following bowel movements, or a sense of urgency to move the bowels [(3)]. Heterogeneous factors, such as abnormal gastrointestinal motility, excessive intestinal gas, altered visceral perception or intestinal microbial flora, an exaggerated neurohormonal stress response, and disturbed central processing of visceral stimuli, may contribute to the pathophysiology of IBS [(4)].

Intestinal parasite infection is a significant global public health issue, especially in poor nations where it is more prevalent in children under the age of five [(5)].

As a result of cognitive impairment, anemia, malnutrition, and greater susceptibility to other illnesses, these parasite diseases have a variety of negative effects on children's health [(6)].

Particularly in some tropical regions where both IBS and intestinal parasitism are more prevalent, the function of intestinal parasitic infections in IBS is unclear. Additionally, Blastocystis hominis infection, one of the parasitic infections, has been linked to an increased risk of developing IBS-D in adolescents [(7, 8)].

Although malnutrition and FAPDs have been linked in a number of studies conducted in clinic settings, there is no clear connection between the particular forms of malnutrition and FAPDs [(9)]. In many investigations, both obesity and underweight have been identified as risk factors for various forms of FAPDs [(10)]. An American research that utilized the Rome III classification to classify children in a general pediatric clinic revealed a relationship between both functional abdominal pain syndrome and IBS and being obese/overweight [(11)].

Our study aimed to identify the relationship between parasitic infection and IBS and evaluate the effect of IBS and parasitic infection on the nutritional status of cases of IBS among children.

PATIENTS AND METHODS

A cross sectional study was conducted from April 2022 to the end of January 2023. The study included 120 children ranging in age from 5 to 15 years old of both sexes attending outpatient clinics in October 6 University Hospital and Primary Healthcare centers who were diagnosed as having IBS according to ROME criteria (III or IV) [(3)], and were not receiving treatment for parasitic infection for one month before the study and they have no abnormality in abdominal ultrasound were included in the study.

Cases of celiac disease, gastrointestinal malignancies, inflammatory bowel disease, were

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excluded by history, examination, and investigations done before the study. All patients were subjected to a full detailed medical history taking concerning their main gastrointestinal symptoms, nutritional history and complete clinical examination.

Nutritional assessment includes anthropometric measurements (height and weight) adhering to standard procedures [(12)].

The height was measured to the closest centimeter (cm) using a tape meter set on a wood board (150cm) put vertically on the wall by adequately qualified medical staff. Each kid was told to stand barefoot with their heads in the Frankfurt plane, which is where their ear canals' upper margins and orbital margins are closest to being parallel to the ground. The youngster was weighed while wearing light clothing and bare feet on a scale that had been calibrated to the closest kilogram (kg).

Anthropometric indices were calculated using the Egyptian Z score for weight for age for detection of underweight (WFZ), height for age (HFZ) for detection of stunting and body mass index (BMZ) for detection of underweight, overweight and obesity for the studied children by using anthropometry software for Egyptian charts [(13)].

Children were considered to be undernourished (stunting, underweight, and wasting) if their Z Scores were less than -2 standard deviation units ((<−2 Z Scores) from the median reference values for WFZ. HFZ, BMZ respectively according to the ages and sex. Overweight was defined as BMI ranging from +1:+2 standard deviation, while obesity was greater than 2 (>2 SD) above the median reference values of BMI for age and sex [(5)].

After collecting of the clinical data sheets, the cases that met the ROME III/ IV criteria for IBS was asked to collect a single stool sample that were sent to the laboratory for examination. Stool analysis was done macroscopically and microscopically by direct wet mount and concentrated technique for detection of helminthic stages and protozoal stages [(14)]. Each sample was examined before and after staining with Lugol iodine solutions [(15)].

Ethical approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, October 6 University. Written informed consent was obtained from parents/guardians of all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 18 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD), and independent sample t-test was used for comparison between groups. P value ≤0.05 was considered to be statistically significant.

RESULTS

Results are illustrated in tables 1, 2, 3, 4, 5 and 6. The cases were divided according to the presence of parasites in stool analysis into groups (A) that included 68 cases with parasitic infection and group (B) that included 52 cases without parasitic infection.

The study population was comprised of 69 (57.5%) boys and 51 (42.5%) girls. The mean age of the study population was 7.8 (SD 2.5). The mean age of cases in group A was 8 (SD 2.5) and in B was 7.6 (SD 2.4). Difference in age and sex distribution between the groups were found to be statistically insignificant (P value >0.05) (Table 1).

Table (1): Demographic data of studied children of IBS.

Variable	Group A (n=68)		Group B (n=2)		Total (n=120)		P value
Age in years	**Frequency**	**Percentage**	**Frequency**	**Percentage**	**Frequency**	**Percentage**	0.08
5	15	22.1%	12	23.1%	27	22.50%	
6-11	44	64.7%	34	65.3%	78	65%	
12-15	9	13.2%	6	11.5%	15	12.50%	
Sex							
Male	41	60.3%	28	53.8%	69	57.5%	0.6
Female	27	39.7%	24	46.2%	51	52.5%	
Residency							
Urban	52	76.5%	32	61.5%	84	70%	0.0091
Rural	5	7.3%	17	32.7%	22	18.3%	
Suburban	11	16.2%	3	5.8%	14	11.7%	

Group A included 68/120 (56.5% of cases of IBS) with parasitic infection with the most frequent parasites species were *Giardia lamblia (G.lamblia)* cysts/ trophozoite in 25 (36.6%) samples, followed by *Entameba.histolytica (E.histolytica)* cyst / trophozoite in 19 (27.9%) (Table 2).

Table (2): Detected intestinal parasites in stool samples of cases.

Parasite stage	Group A (n=68)	
	No	%
Giardia lamblia cyst/trophozoite	25	36.7%
Entamoeba histolytic cyst/trophozoite	19	27.9%
Blastocystis hominis	14	20.6%
Mixed protozoal infection	4	5.9%
Egg of Enterobius vermicularis	3	4.4%
Egg of Hymenolepis nana	3	4.4%

The mean weight of the whole cases was 25, Height 122.6 and BMI 16.5. The mean of group A was 26.5 for weight, 123 for height, and 16.6 for BMI and in group B was 24.8, 121, 16.2 for weight, height and BMI, respectively (Table 3).

Table (3): The mean values of anthropometric parameters for cases of IBS.

Parameters	Mean ± SD
Weight	25.6 ± 8
Height	122.6 ± 15.4
BMI	16.5 ± 1.5
WAZ	-0.16 ± 0.87
HAZ	-0.5 ± 0.86
BMZ	0.08 ± 1.1

The mean values of anthropometric parameters by Z score (WFZ, HFZ) of the total study population were found to be -0.16,-0.5 below Egyptian reference median for each parameter respectively and 0.08 above it for BMZ. There was no significant difference among both groups regarding those parameters (Table 4).

Table (4): Comparison of mean values of anthropometric measurement between group (A and B).

Means of parameters	Group A	Group B	P value
Weight	26.5±24	24.8±7	0.4
Height	123±15.7	121±14.8	
BMI	16.6 ±1.5	16.2 ±1.5	
WAZ	-0.13±0.8	-0.19±0.8	0.3
HAZ	-0.47±0.9	-0.52±0.7	
BMZ	0.13±1.0	0.01±1.2	

According to Egyptian Z score median values, there were no cases detected with undernutrition (≤2) among both groups. 19 (15.8%) cases was over weigh (between +1and +2 SD), distributed as following 8 (11.7%) in group A and 11 (21.2%) in group B with no significant relation between parasitic infection and measured parameters for malnutrition among IBS cases as shown in table 5.

Table (5): Comparison between group (A and B) with IBS regarding anthropometric growth parameters using Egyptian Z score.

Z Score	Groups		P- value
	Group A (n=68)	Group B (n=52)	
WAZ At risk (-2:-1) Within normal range (-1:+2)	7 (10.3%) 61(89.7%)	7 (13.5%) 45 (86.5%)	0.6
HAZ At risk (-2:-1) Within normal range (-1:+2)	17(25%) 51(75%)	10(19.2%) 42(80.8%)	0.4
BMZ At risk(-2:-1) Within normal range (-1:+1) Overweight (+!:+2)	9(13.2%) 51(75%) 8(11.8%)	8(15.4%) 33(64.5%) 11(21.2%)	0.3

According to **Kanazawa *et al.* (2016)**, the IBS sub classified into 4 subtypes IBS-D, IBS-C, IBS-M and IBS-U. The IBS-D was the most frequent (54/120, 45%), followed by IBS-U (46/120, 38.3%) and IBS-C in 20/120 (16.7%). No IBS-M detected. Other GIT symptoms of IBS included abdominal pain which was the main symptom in all cases (114/120, 95%) followed by gaseous abdominal distention and bloating (70/120, 58.3%. As shown in **table 6**, there are association between IBS-D and parasitic infection with p value of 0.04. However, there were no significant statistical differences regarding other IBS subtypes and symptoms.

Table (6): Comparison between group (A and B) with IBS regarding gastrointestinal tract symptoms.

Groups	Group A (n=68		Group B (n=52)		Total (120)		P – value
	No.	%	No.	%	No.	%	
IBS-D	36	52.9%	18	34.6%	54	45%	*0.04
IBS-C	11	16.2%	9	17.3%	20	16.7%	0.8
IBS-U	21	30.9%	25	48.1%	46	38.3%	0.05
Abdominal pain	65	95.6%	49	94.2%	114	95%	0.7
Abdominal distension	36	52.9%	34	65.4%	70	58.3%	0.1

DISCUSSION

IBS is a functional gastrointestinal illness (FGID) that is characterized by defecation issues and stomach pain or discomfort [(3)]. The exact etiology of IBS is still unsettled. Although it has been hypothesized, there is no proof that an infectious origin is a contributing component. One of hypothesis is that a parasitic infection can be a triggering factor for the exacerbation [(16)]. Due to its suspected etiological factor in IBS and its possible impact on growth of children in general, this research was designed to detect the

parasitic infection and the nutritional status of diagnosed cases of IBS and their relations.

As shown in demographic data, most of children with IBS were at middle age childhood with mean of age 7.8, this is in accordance to **Khan *et al.* [17] and Devanarayana *et al.* [18]** regarding the likelihood of acquiring IBS declining with age in Sri Lankan schoolchildren.

Rajindrajith *et al.* [19] showed that the prevalence of both constipation and fecal incontinence peaked at age 10 and declined with age, most likely as a result of maturity, which improves control over body processes, including bowel habits. In contrast, several epidemiological studies have found that the prevalence of IBS increases with age **[20,21,22].**

Concerning sex distribution of our included patients of IBS, there were male predominance as 69 (57.5%) were male and 51(42.5%). **Rajindrajith *et al.* [19]** reported that in study among pediatric patients with IBS, diarrhea-predominant IBS was more prevalent in 69% in boys while constipation-predominant IBS was prevalent in 62% in girls that is with our finding as the most predominant type of IBS in our study was IBS-D (45%) that lead to overall male predominance.

In contrast with these findings, **Morgan *et al.* [23]** have noted that IBS is more frequent in women, with diarrhea-predominant IBS and mixed-type IBS being the most prevalent types.

Although, these studies attributed that to effects of female hormones on GIT and brain-gut interactions, The gender difference among children with FGID cannot entirely be attributed to the effects of female sex hormones because the majority of the children included in prior research are young and have not yet developed a completely mature hormonal profile of a female **[24].**

Regarding residency, urban residency was the predominant in all cases (70%) of studied cases with statistical significance difference with other areas that may have impact on the socioeconomic status of patients. **Rajindrajith *et al.* [25]** stated that sociocultural factors have a role in the emergence and persistence of a number of FGIDs and showed that children from lower socioeconomic backgrounds are more likely to experience defecation problems including functional constipation. However, our research study not studied the full socioeconomic aspects of patient with IBS to detect the exact correlation and this predominance among urban area may be due to the location of the study.

Concerning evaluation of parasitic infection in IBS cases, our study found that the overall percentage of any parasitic infection (protozoan or helminthic) was 56.5% that is in agreement with documentation of **Tungtrongchitr *et al.* [26]** about parasitic infection in IBS patients and that it is significantly more likely than in control subjects and in consistent with the report of **Giacometti *et al.* [27]** about the prevalence of B. hominis in IBS, which was 11.1%, compared with 6.1% in non-IBS patients. However, **Morgan *et al.* [23]** discovered no connection between IBS and parasite infection in the environment of underdeveloped countries.

The most frequent parasite species in IBS cases were *Giardia lamblia* stages in 25 samples (36.6% of group A, 20.8% of total IBS cases), and *Entamoeba histolytica* stages was the second frequently detected parasite in 19 samples (27.9%, 15.8% of total cases) and *Blastocystis hominis* was detected in 14 samples (20.5%, 11.7% of total IBS cases). *Hymenolepis nana* eggs and *Enterobius vermicularis* eggs were detected in only three samples for each (4.4%). Moreover, mixed parasitic infections were found in 4 (5.8%) samples and showed *Entamoeba histolytica* cysts *and Blastocystis hominins.*

Similarly, **D'Anchino *et al.* [16]** studied the association between parasitic infection and IBS and reported that 82/100 patients with symptomatic giardiasis were also affected by IBS and were not cured by antiparasitic treatment. Additionally, higher prevalence of *Entamoeba spp* (20.2%) than other protozoa while the most prevalent helminthic infection were mainly *A. lumbricoide (* 6%) and *T. trichiura* (1.8%) among IBS as observed by **Morgan *et al.* [23].**

This is quite different to study of **Tungtrongchitr *et al.* [26]** where *B. hominis*was the predominant parasitic stages in IBS cases (8/59, 13.6 %) and *Giardia lamblia* cyst was only (1/59, 1.7%). This variation in species predominance among the studies may be related to several factors like different geographic areas with difference in prevalence of parasitic species and seasonal variation.

Regarding nutrition status of cases with IBS , in spite of mean weight-for-age, height-for-age, of the study population were lower than the median Egyptian reference value while BMI-for-age of the study population were above it ,there were no cases of undernutrition detected in patients with IBS either those infected or not infected with intestinal parasites by Z score and the only observed form of malnutrition among whole population of study was overweight (19/120, 15.8%) with higher frequency of overweight cases in group B that not had parasitic infection (11/52, 21.1% versus 8/68, 11.7% in group A) according to Z score. however, no statistical significant difference among both groups. Based on previous findings, Chi-square test revealed no statistical relation between parasitic infections.

This is in consistent with the documentation of **Pawłowska *et al.* [10]** about the prevalence of excessive body weight (overweight and obesity) in the total sample of cases of FGID as excessive body weight was detected in 15/102, 14.7%, and it proved to be the greatest in children with IBS (8/102, 7.8%, one case obese and 7 cases overweight).

Furthermore, **Fifi *et al.* [28]** found that Rome IV criteria-diagnosed functional abdominal disorders (FGIDs) in school children did not significantly differ

from healthy controls in the community in terms of nutritional status, and it was noted that FGIDs were not frequently associated with "red flag" symptoms like weight loss, underweight, or short stature, which is consistent with our findings. In contradictory, multiple studies showed association with parasitic infection and malnutrition [29]. For example, **Hegazi *et al.*** [30] illustrated significantly lower z-score values of WAZ and WHZ among Egyptians preschool children with parasitic infection compared to those without infection. Also they report that stunting was found in 44.1% of infested children, underweight in 39.1%, wasting in 11.5. This difference may be due to difference in the type of the enrolled cases and age group of population in both study and sample size. Also the **Hegazy *et al.*** [30] used WHO Z-scores [31], but our study used Z-scores for Egyptians [13].

Furthermore, one of important possible cause of this contradict between our observations and other studies showing undernutrition associated parasitic infection is that our study conducted among children diagnosed as IBS which is tend to be more in obese and overweight children as noted in our study, beside that the chronicity of parasitic infection and their reflection on nutrition status that mostly occur in chronic untreated infection that not investigated in our study. Owing to previous observation, the effect of parasites that leads to undernutrition as it common in literature not obvious in our study of IBS cases. Concerning the frequency of IBS subtypes according to the predominant symptoms within last month (diarrhea, constipation, or non), the IBS-D was the most frequent (54/120, 45%), followed by IBS-U (46/120, 38.3%) and IBS-C in 20/120 (16.7%) . other GIT symptoms of IBS, abdominal pain was the main symptoms in all cases (114/120, 95%) followed by gaseous abdominal distention and bloating (70/120,58.3%).

Also, **Kanazawa *et al.*** [8] reported the IBS-D in higher percentage than IBS-C, However IBS mixed type was the predominant type as he documented that 2.8 % met the criteria for IBS-C, 4.5% for IBS with diarrhea (IBS-D) and 8.2% for mixed IBS (IBS-M) that not detected in our study. The high percentage of cases of IBS that had gaseous abdominal distention and bloating is in agreement of the study of **Ringel *et al.*** [32] who showed that bloating symptoms were the third most important reason to seek medical care.

Concerning the relation of parasitic infection and predominant IBS subtypes and related GIT symptoms, our we found that significant relation between parasitic infection and IBS-D where diarrhea is predominant symptom as 52.9% of cases with diarrhea was associated with parasitic infection while 34.5% weren't associated with parasitic infection with a significant p value <0.05. However, there were no significant relation with other types and symptoms. This supports the idea that IBS symptoms may be related to non-resident microbiota colonization and resident microbiota expansion in the small intestine, a generally sterile area of the gut. Also, **Kay *et al.*** [1] found that evidence suggests that the protozoan *Blastocystis hominis* is connected to the IBS-D subtype.

CONCLUSIONS AND RECOMMENDATIONS

Parasitic infection is a common finding among cases of IBS with significant association with IBS-D, yet, it is not associated with malnutrition when assessing the Z score for Egyptian children. Based on our finding, it is recommended to check for parasitic infection in cases of IBS especially if associated with diarrhea and provide frequent follow up of nutrition parameters of cases of IBS with parasitic infection even if having normal growth parameters to detect early malnutrition.

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