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Entamoeba histolytica cyst as a causative pathogen of bloody diarrhea in children below 5 years

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Abstract:

Background: *Bloody diarrheas continue to be one of the most common causes of morbidity and mortality among young children in developing countries. Knowledge of the specific pathogens that cause bloody diarrhea and their epidemiology is critical for the implementation of specific strategies.*

Objective: *To demonstrate possible cause of bloody diarrhea in children below 5 years.*

Patients and methods *A descriptive study of 1366 children their age below 5 years with bloody diarrhea who were attended outpatient clinic of Al-kadhimiya Teaching Hospital, AL-kadhimiya Hospital for pediatrics and two primary health care centers in Baghdad during the period between14th of September 2009 to 27th of august 2013. All the patients were investigated by general stool examination twice (fresh stool) and stool culture were done to all of them and they receive drug that act on Entamoeba histolytica cyst (furamide) until complete recovery occur.*

Results: *The incidence of the disease was nearly equal in male and female 705 (52 %), 661 (48%) respectively, the number of the patients according to age group were 29 (0.2%) below twelve months, 785 (57.5%) between 12 and 24 months, 338 (24.7 %) between 25 and 36 months, and 214 (17.6%) of them between 37 and 60 months. Regarding the response to treatment, 1134 (83 %) of them respond to antiprotozoal drug after first course, 198 (14 %) respond after second course and 34 (3 %) responding after third course.*

Conclusion: *Entamoeba histolytica cyst could be one of the causes of bloody diarrhea in children below 5 years of age.*

Key words: *Entamoeba histolytica*, cyst, bloody diarrhea, developing countries, descriptive.

1. Introduction

Bloody diarrhea in young children is usually assign of invasive enteric infection that carries substantial risk of serious morbidity and mortality and among important cause of bloody diarrhea is a parasitic infection caused by the protozoon *Entamoeba histolytica* which is the third leading cause of death worldwide (1). The genus *Entamoeba* contains many species, some of which (i.e., *E histolytica, Entamoeba dispar, Entamoeba moshkovskii, Entamoeba polecki, Entamoeba coli,* and *Entamoeba hartmanni*) can reside in the human interstitial lumen. Of these, *E histolytica* is the only one definitely associated with disease; the others are considered nonpathogenic (2). Amebiasis is caused by *Entamoeba histolytica,* a protozoan that is found worldwide. The highest prevalence of amebiasis is in developing countries where barriers between human feces and food and water supplies are inadequate (3, 4, 5). Approximately 50 million cases of invasive *E. histolytica* disease occur each year, resulting in as many as 100000 deaths. This represents the tip of the iceberg because only 10%-20% of infected individuals become symptomatic (6, 7, 8). The incidence of amebiasis is higher in developing countries (9). The parasite has 2 forms: a motile form, called the trophozoite, and a cyst form, responsible for the person-to-person transmission of infection. The trophozoite of *E. histolytica* inhabits the large intestine to produce lesions of amebic colitis (10). *E. histolytica* is transmitted primarily through the fecal-oral route. Infective cysts can be found in fecally contaminated food and water supplies and contaminated

hands of food handlers. Poor nutrition, through its effect on immunity, has been found to be a risk factor for amebiasis (11). Humans and perhaps nonhuman primates are the only natural hosts. Ingestion of *E. histolytica* cysts from the environment is followed by excystation in the terminal ileum or colon to form highly motile trophozoites. Upon colonization of the colonic mucosa, the trophozoite may encyst and is then excreted in the feces, or it may invade the intestinal mucosal barrier and gain access to the bloodstream, whereby it is disseminated to the liver, lung and other sites. Excreted cysts reach the environment to complete the cycle. Disease may be caused by only a small number of cysts, but the processes of encystation and excystation are poorly understood (12, 13). The incubation period can range from a few days to months or years with 2-4 weeks being the most common. Transitions from one type of intestinal syndrome to another can occur and intestinal infections can give rise to extraintestinal infections. The majority of individuals diagnosed with *E. histolytica* exhibits no symptoms or has vague and nonspecific abdominal symptoms. This state can persist or progress to a symptomatic infection. Symptomatic nondysenteric infections exhibit variable symptoms ranging from mild and transient to intense and long lasting Cysts will tend to predominate in formed stools and trophozoites in diarrheic stools (14). Asymptomatic intestinal amebiasis occurs in 90% of infected individuals. However, only 4%-10% of individuals with asymptomatic amebiasis who were monitored for 1 year eventually developed colitis or extraintestinal disease. Laboratory diagnosis of amebiasis is made by demonstrating the organism or by employing immunologic techniques. In addition to standard blood tests, other laboratory studies employed for diagnosis include microscopy; culture, serologic testing, and polymerase chain reaction (PCR) assay (2). Case-fatality rates associated with amebic colitis range from 1.9% to 9.1%. Amebic colitis evolves to fulminant necrotizing colitis or rupture in approximately 0.5%

of cases; in such cases, mortality may exceeds 40% or even, according to some reports, 50% (15). With the introduction of effective medical treatment, mortality has fallen below 1% for patients with uncomplicated amebic liver abscess. However, amebic liver abscess can be complicated by sudden intraperitoneal rupture in 2-7% of patients, and this complication leads to a higher mortality (16). Several drugs are available for the treatment of amebiasis and the choice of drug(s) depends on the clinical stage of the infection. The prognosis following treatment is generally good in uncomplicated cases. In cases where *E. histolytica* is confirmed, asymptomatic cyst passers should be treated to prevent the progression to severe disease and to control the spread of the disease. However, in many endemic areas, where the rates of reinfection are high and treatment is expensive, the standard practice is to only treat symptomatic cases. Metronidazole or tinidazole (if available) is recommended for all symptomatic infections. This treatment should be followed by or combined with lumenal antiamoebic drugs as described for asymptomatic patients (17). Prevention and control measures are similar to other diseases transmitted by the fecal-oral route like wash hands thoroughly with soap and hot running water after using the toilet or changing a baby 's diaper, and before handling food. Clean bathrooms and toilets often pay particular attention to toilet seats and taps (18).

2. Patients and methods

Across sectional descriptive study was conducted on 1366 patients attending the outpatient clinic in Al-kadhimiya Teaching Hospital, AL-kadhimiya Hospital for pediatrics and two primary health care centers in Baghdad during the period from 14th of September 2009 to 27th of august 2013. All of them bellow 5 years of age and the total number of children coming to these medical places complaining from diarrhea were 21438,

and those who getting bloody diarrhea were 4415 (20.6%), and those patients who their general stool examinations according to (19) (fresh stool) which were performed twice (inside and outside the hospital, or primary health care centers) show cyst of *E. histolytica* were 1366, for them stool culture were done, any patient presented with bloody diarrhea and his stool culture show any type of bacteria which could be a cause of bloody diarrhea were excluded from the study also other possible causes of bloody diarrhea were excluded from the study, so all patients included in this study had bloody diarrhea with negative stool culture and their stool show only cyst of *E. histolytica*, they were divided into four groups according to their age.

Group A their ages were below one year (< 12 months).
Group B their age group between 12 months and 24 months.
Group C their age group between 25 months and 36 months.
Group D their age group between 37 months and 60months.

Also all patients had been given antiprotozoal drugs that act on cyst of *Entamoeba histolytica* (Furamide 20 mg / k/day) for 7 days duration for each course without given any antibiotics that act on bacterial infections, any patient not responding to treatment after three course also excluded from the study.

3. Results

Males were slightly more than females 705 (52 %), 661 (48 %) respectively and males to females ratio was 1:0.7 as shown in (Table 1).

Total number of patients in group A were 29 (0.2 %), in group B were 785 (57.5 %), in group C were 338 (24.7 %) and in group D were 214 (17.6 %) as shown in (Table 1). All patients who are below two years (814) were bottle fed or on mixed feeding with bad sterilization.

Table 1. Distribution of patients according to sex and age group.

Age group	Male		Female		Total		
	NO.	%	NO.	%	NO.	%	
Group A	16	0.2	13	1.9	29	0.2	X^2=0.52
Group B	401	56.9	384	58.1	785	57.5	
Group C	179	25.4	159	24.1	338	24.7	df=3
Group D	109	17.5	105	15.9	214	17.6	
Total	705	100	661	100	1366	100	P=0.91

Regarding the response to treatment that act on cyst of Entamoeba Histolytica (absence of bloody diarrhea and negative stool examination for cyst twice) the study show that 1134 (83 %) patients responding to treatment after first course, 198 (14%) were responding after two course and 34 (3 %) were responding after three courses as shown in (Table 2).

Table 2. Distribution of patients according to response to treatment.

Response to treatment	Number of patients	%
1st course	1134	83
2nd course	198	14
3rd course	34	3
Total	1366	100

Males are nearly equal to females in their response to treatment as shown in table 3.

Table 3. Response to treatment according to sex.

Sex	Response to treatment								
	1st course		2nd course		3rd course		Total		X^2=11.055
	No.	%	No.	%	No.	%	No.	%	
Male	592	84	105	15	8	1	705	100	df=2
Female	542	82	93	14	26	4	661	100	
Total	1134	83	198	14	34	3	1366	100	P=0.004

Also the study shows no significant difference in response to treatment regarding age group as shown in (Table 4).

Table 4. Response to treatment according to age group.

Age group	Response to treatment								
	1st course		2nd course		3rd course		Total		
	No.	%	No.	%	No.	%	No.	%	
Group A	21	72	6	21	2	7	29	100	X^2=69.2
Group B	695	89	74	9	16	2	785	100	
Group C	234	69	92	27	12	4	338	100	df=6
Group D	184	86	26	12	4	2	214	100	
Total	1134	83	198	14	34	3	1366	100	P=0.00001

4. Discussion

Bloody diarrhea which is commonly present in developing countries as shown in many study such that in Bangladesh which show that preschool children experienced 0.09 episodes of bloody diarrhea each year (20). Also in United Arab Emirate the infection rates were 15.7% and 3.2% among the native and expatriate population respectively (21). While in our study sample the bloody diarrhea was found in 20.6 %. This meaning that the problem of bloody diarrhea is a big problem need to be investigated carefully and good planning to treat and prevent this problem should be taken seriously.

The study show that some cases presented below one year, this explained by increased frequency of using bottle feeding in our society (Iraq) which was 63.8 % as recorded in study done in 2008 (22). This study show slight increase number of males than females which is similar to other studies that show similar incidence of disease in both sex but one of these studies show increase incidence of complications in males than females like amebic liver abscess which was found to be 7-12 time more common in male (4), the reason for this disparity is unknown, though hormonal effects may be implicated. Most of the patients had good response to treatment in first course in both sex which is statistically significant indicating good compliance of mothers in giving the treatment.

Till now there is no study show that *Entamoeba histolytica* cyst can cause bloody diarrhea in children or even in

adult so this study is the first in exploring this new cause of bloody diarrhea and this could be explain by:

1. Change in virulence of *Entamoeba histolytica* cyst so it can invade the mucosa of large intestine and produce bloody diarrhea.
2. Allergic reactions that occur due to presence of cyst of *Entamoeba histolytica* in intestine that cause bloody diarrhea look like inflammatory reaction that occur in cow's milk allergy.
3. This bloody diarrhea could be due to unusual bacteria which were not identifying by usually used culture and it is sensitive to drug used to treat *Entamoeba histolytica*.

So this finding need further studies to support this new cause of bloody diarrhea or find another new causes.

5. Conclusion

Entamoeba histolytica cyst can be accusative pathogen in patients with bloody diarrhea so in empirical treatment of bloody diarrhea one can give drugs that act on cystic form of *Entamoeba histolytica*. Also it need further studies to document or reject this new cause of bloody diarrhea.

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