

Intestinal Amebiasis: A Concerning Cause of Acute Gastroenteritis Among Hospitalized Lebanese Children

Amal Naous, Ziad Naja, Nour Zaatari, Raymond Kamel, Mariam Rajab

Department of Pediatrics, Makassed General Hospital, Beirut, Lebanon

Abstract

Background: Intestinal amebiasis is an important public health problem worldwide. More severe disease is associated with young age, malnutrition and immunosuppression. **Aim:** The aim of this study is to evaluate the prevalence and characteristic nature of intestinal amebiasis among pediatric population, and compare it with other causes of gastroenteritis. **Materials and Methods:** This is a retrospective comparative study conducted at Makassed General Hospital between January 2008 and December 2012, including all pediatric patients between birth and 15 years of age, who presented with symptoms of acute gastroenteritis. **Results:** One thousand three hundred ninety-five patients were included in the study, and were divided into four groups: Group I (*Entameba histolytica* group = 311 cases, 22.3%), group II (Rotavirus group = 427 cases, 30.6%), group III (bacterial group = 107 cases, 7.7%), group IV (unidentified group = 550 cases, 39.4%). Significant leukocytosis, neutrophilia and positive C-reactive protein were found among more than 50% of admitted *Entameba histolytica* cases with a picture of severe invasive disease in young infants. **Conclusion:** *Entameba histolytica* can be an emerging serious infection, especially when it finds suitable environmental conditions and host factors, so we should be ready to face it with effective preventive measures.

Keywords: Intestinal amebiasis, *Entameba histolytica*, *E. histolytica*, Gastroenteritis

Address for correspondence: Dr. Amal Naous, Department of Pediatrics, Makassed General Hospital, Beirut, Lebanon.
E-mail: amalnaous@hotmail.com

Introduction

Amebiasis caused by the intestinal parasite *Entameba histolytica*, is a disease of global health importance, especially in developing countries.^[1,2] It has an estimated worldwide prevalence of 50 million cases of symptomatic disease and is responsible for 40000-110000 deaths annually. It is the third leading parasitic cause of death worldwide.^[2-4] Amebiasis is defined as an intestinal or extraintestinal disease due to the parasite *E. histolytica*.^[5-7] *E. histolytica* is transmitted via the fecal-oral route. The infection causes a variety of clinical presentations, from asymptomatic colonization

to invasive amebic dysentery and extra-intestinal amebiasis.^[8]

E. histolytica has a two-stage life cycle, existing as resistant infective cysts in the environment and potentially pathogenic trophozoites in the human colon. The more common path is commensal colonization, where trophozoites inhabit the gut lumen and feed on enteric bacteria by phagocytosis.^[9,10] The less common path leads to invasive amebiasis. Virulence factors allow the parasite to cause pathogenic amebiasis. The cysts transform to trophozoites which degrade the colonic mucosal layer and bind to host epithelial cells. The trophozoites trigger pathology in the host tissues, promoting penetration and infection.^[10-13]

The rate of infection by *E. histolytica* differs among countries, socio-economic and sanitary conditions, and populations. It is highly endemic throughout poor and socio-economically deprived communities in the tropics and subtropics.^[2,14,15] In developing countries, parasitic diseases represent a social and economic

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problem with more severe disease associated with young age, malnutrition, and immunosuppression.^[2,16] In industrialized nations, on the other hand, populations at greatest risk for severe intestinal protozoan infections include immunocompromised patients.^[17]

Previous study done in Lebanon showed that *E. histolytica* is more prevalent in adults than in children.^[17] In view of lack of information concerning intestinal amebiasis and its impact among Lebanese children, we decided to conduct this study to assess the prevalence, characteristic nature and risk factors for intestinal amebiasis necessitating hospitalization in infants and children, and in comparison with other hospitalized children with non *E. histolytica* gastroenteritis (GE).

Materials and Methods

Patient selection

This is a retrospective comparative study that was carried out at Makassed General Hospital, Beirut, Lebanon, which is a tertiary referral medical center. Infants and children between birth and 15 years of age with acute GE, who necessitated hospitalization or Emergency Department (ED) management, were enrolled in the study, during the period from January 2008 through December 2012. This study was approved by the research and ethical committee of the hospital institutional review board. For better comparative analysis and characterization of *E. histolytica* cases, a cross-sectional comparative study was conducted as all acute GE cases were divided into four main groups: Group I (confirmed *E. histolytica* cases), group II (confirmed Rotavirus (RV) cases), and group III (confirmed bacterial gastroenteritis), group IV (GE with unidentified enteropathogens).

Exclusion criteria

Patients more than 15 years, patients with chronic diarrhea, patients with immunodeficiency, or having any extraintestinal infection at the time of hospitalization were excluded from the study. Patients with diarrheal illness who had received antibiotics in the preceding 1 month that might be related to *Clostridium difficile*-associated diarrhea or antibiotic-associated pseudomembranous colitis, and patients who had combined gastrointestinal infection with more than one organism were also excluded from the study.

Methodology

Medical records of all patients, from birth to 15 years of age with acute GE, who necessitated Emergency Department management or hospitalization, during the period from January 2008 through December 2012 were subjected to thorough review and analysis.

The following data on admission for all patients in pediatric ED: Age, gender, residency, season and year of admission, duration of stay, complete history and physical examination were recorded. However, data about type of nutrition were not documented in the ED medical charts, and laboratory investigations with stool sampling were not routinely done for every case of acute GE presenting to ED.

On the other hand, complete data were recorded in the medical charts of hospitalized patients. All infants and children hospitalized for acute GE were subjected to thorough history taking, anthropometric measurements, systemic examinations including degree of dehydration (according to Vesikari Clinical Severity Score), socioeconomic status, type of nutrition, and laboratory investigations (CBC including total and differential leukocyte count, C-reactive protein (CRP), and stool examination). Leukocytosis and neutrophilia were defined according to age-related specific values for each individual case.^[18] Imaging investigations (abdominal and pelvic ultrasound, abdominal X-ray, CT scan of abdomen and/or pelvis and barium enema) were performed when needed on case-by-case basis.

Our protocol of treatment for all cases of acute GE included oral or intravenous rehydration as clinically indicated. Metronidazole, either orally or by intravenous infusion, was used to all confirmed *E. histolytica* cases. Third generation cephalosporin, either orally or by intravenous infusion, was used for acute GE cases with clinical (high grade fever and toxic state) and/or laboratory (leukocytosis and positive CRP) evidence of invasive gastroenteritis or possible unrevealed coinciding bacterial infections that are associated with *E. histolytica* infection.^[19,20] Blood cultures were also done for these cases to detect possible associated bacteremia. The patient course of illness, follow-up, and response to treatment were recorded in medical charts for each admitted case with acute GE.

Sampling and laboratory techniques

Fresh stool samples were collected in sterile containers and sent within a maximum period of 2 h to the hospital laboratory.

Examination of feces for protozoa and helminthes

Stool specimens were examined for intestinal parasites within 30 min of collection. The examination took place in the parasitology section at the Department of Pathology and Laboratory Medicine at MGH. Stool specimens were first grossly checked for the presence of complete or part of adult parasites then by light microscopy using a concentration technique according to the manufacturer's

instructions (Fecal Parasite Concentrator (FPC), Evergreen Scientific, Los Angeles, CA, USA).

One spoonful of stool specimen was mixed with 9 ml of 10% formalin in a 15 ml sterile tube. The mixture was kept at room temperature for 30 min for fixation. Three drops of Triton X-100 (surfactant) were added, followed by 3 ml of ethyl acetate to dissolve fat and reduce the bulk of stool.

The mixture was transferred to a 15 ml centrifuge tube through the FPC strainer attached to the tube. This FPC strainer has a precision molded filter matrix (0.6×0.6 mm² holes) that allows helminthes eggs and larvae, protozoan cysts, and coccidian oocytes to pass but will retain the coarse particulate matter (excess fecal debris). After completing this filtration step, the tube was capped and centrifuged at 2000 ppm for 10 min. The supernatant was decanted, and 3 drops of 10 ml of 10% formalin were added and mixed with the sediment. Part of the latter was transferred to a slide and examined for parasites under the light microscope. In addition "watery stool" was also examined microscopically without concentration looking for trophozoites of parasites. Coccidian parasites, *e.g.* *Cryptosporidium* and *Cyclospora* were looked for using modified acid fast stain.^[21]

Examination of feces for viruses

Rotavirus was detected after collecting sufficient quantity of feces (1-2 g or 1-2 ml) in a clean dry container and the fecal specimen was analyzed by Omega Virotest Rota (Omega Diagnostics, Omega House, Hill foots Business Village, AlvaFK12 5DQ, Scotland, United Kingdom). It is a rapid latex slide test (qualitative test) for detection of RV in human feces with a relative sensitivity of 97.2% and relative specificity of 97.1%.^[22]

Examination of feces for bacterial enteropathogens

Stool cultures for enteric bacteria were mainly limited to *Salmonella*, *Shigella spp* and Shiga toxin producing *Escherichia coli* as *E. coli* serotype 0157:H7 based on the ability of such enteropathogens to cause dysentery-like illness such as *E. histolytica*, the previous epidemiologic prevalence of these enteropathogens in stool cultures of our locality, and the availability of their diagnostic tests. *Shigella* and *Salmonella* were identified by standard bacteriologic methods with primary isolation on MacConkey, XLD (xylose lysine deoxycholate) agar, and *Salmonella-Shigella* agar to inhibit the growth of normal flora and growth amplification of *Salmonella* in celenite broth.^[23,24] Further biochemical or serological identification was done for the detected *Salmonella* and *Shigella* species.

The diagnosis of diarrheagenic *E. coli* infection was made by initial isolation of the bacteria from stool cultures,

and based on biochemical criteria (*e.g.* fermentation patterns). Enterohemorrhagic *E. coli* (EHEC or O157:H7) was suggested by the failure to ferment sorbitol on MacConkey sorbitol medium.^[25] *Campylobacter species* were not cultured due to lack of specific medium at our laboratory.

Statistical analysis

Analysis was done using statistical package for social science program version 19. Data were reported as mean standard deviation (SD), or number of patients (percentage). *T*-test (two-tailed) and Chi-square test were used to assess any significant difference between the groups. $P < 0.05$ were considered statistically significant.

Results

Three thousand one hundred ninety-six patients presented to MGH due to acute GE between January 2008 and December 2012. One thousand six hundred ninety-six patients were excluded from the study due to incomplete documentation in their medical charts, and one hundred five patients were also excluded because they failed to fulfill the inclusion criteria: Presence of simultaneous or combined infections. The most common combined infection associated with *E. histolytica* was *Salmonella* infection (in 43 cases) and they were also among the excluded cases in the study.

One thousand three hundred ninety-five pediatric patients hospitalized for acute GE were included in the study, and were subsequently divided into four main groups: Group I (*E. histolytica* group = 311 cases), group II (RV group = 427 cases), group III (bacterial group = 107 cases), group IV (unidentified group = 550 cases). The bacterial group comprised cases of gastroenteritis due to the following bacteria: *Salmonella* species (70 cases, 65.5%), enteropathogenic *E. coli* (33 cases, 30.8%) and *Shigella* (4 cases, 3.7%).

The most prevalent identified enteropathogen was RV (30.6%), followed by *E. histolytica* (22.3%) and then enteric bacteria (7.7%), however, the majority of the enteropathogens were unidentified (39.4%). The percentage of cases under 1 year of age was significantly higher in RV group than in other 3 groups ($P < 0.0001$) [Table 1]. However, when considering the frequency of *E. histolytica* among different age groups, it shows that *E. histolytica* was more frequent below 1 year of age (25.7%) and this frequency decreases as age increases [Figure 1]. No statistically significant difference was found between the four studied groups regarding gender, but *E. histolytica*, RV and unidentified enteropathogens were significantly prevalent in the low

socio-economic group. Regarding residency, *E. histolytica* was significantly prevalent in patient coming from the north (50%) ($P = 0.024$) [Table 1].

Cases were admitted with acute GE due to *E. histolytica* because of any or combination of the following symptoms: High grade fever, vomiting, abdominal pain, bloody or mucoidy diarrhea and varying degrees of dehydration. Table 2 shows the comparison of the various clinical manifestations and laboratory findings of *E. histolytica* between three different age groups (<1 year, 1-5 years and 6-15 years). The group of infants under 1 year presented with significantly higher degrees of dehydration than the 1-15 years age group ($P = 0.008$). The 1-15 years group had significantly higher presentation with abdominal pain, vomiting, and neutrophilia on laboratory findings than the group of infants less than 1 year ($P < 0.0001$). ($P < 0.0001$). CRP was significantly positive in all age groups ($P < 0.0001$). No statistically significant difference was detected among the 3 age groups regarding symptoms of fever, bloody, and mucoidy diarrhea [Table 2].

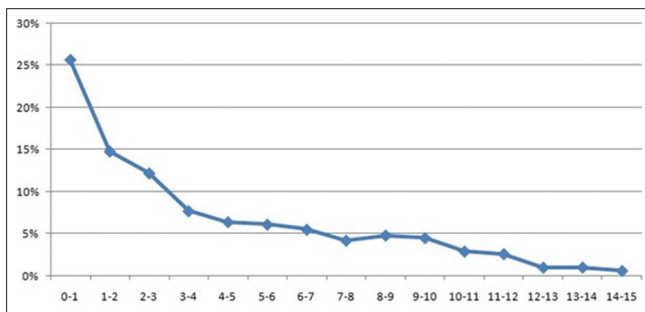


Figure 1: Different age group frequency among *E. histolytica* group

The risk factors for acute GE were also studied among the four studied groups. Significantly higher percentage of *E. histolytica* cases was observed among breastfed infants and children compared to RV cases ($P1 < 0.0001$). Bottle feeding displays a significant risk factor of acute GE among the four studied groups ($P1 = 0.029$, $P2 = 0.047$ and $P3 < 0.0001$). There was no significant difference regarding the nutritional status of infants and children among the four studied groups [Table 3].

Table 4 shows the percentages of variable clinical manifestations, laboratory findings, imaging studies, and medications among the four studied groups. Symptoms such as abdominal pain with bloody and mucoidy diarrhea were significantly higher in *E. histolytica* group more than other 3 groups ($P1 < 0.0001$, $P2 < 0.0001$ and $P3 < 0.0001$, respectively). High grade fever was significantly frequent in *E. histolytica* and bacterial groups ($P1 < 0.0001$ and $P2 < 0.0001$), whereas vomiting was a more frequent symptom in *E. histolytica* and RV groups ($P2 < 0.0001$ and $P3 < 0.0001$). The severity of dehydration was higher in both *E. histolytica* and bacterial groups than in RV and unidentified groups ($P1 < 0.0001$ and $P3 = 0.001$). However, there was no significant difference in the mean duration of symptoms and hospital stay among the four studied groups [Table 4]. Laboratory findings and imaging studies of all hospitalized GE cases were also studied among the four main groups. Laboratory findings presented significantly higher percentages of leukocytosis with neutrophilia for age in both *E. histolytica* and bacterial groups than the other 2 groups ($P1 < 0.0001$

Table 1: Comparison of the demographic characteristics among the 4 studied groups

Character	<i>E. histolytica</i> group I (n=311) (%)	RV group II (n=427) (%)	Bacterial group III (n=107) (%)	Unidentified group IV (n=550) (%)	Total (1395)	P values
Age						
<1 year	80 (17.0)	190 (40.3)	31 (6.8)	170 (35.9)	471	<0.0001
1-5 years	128 (18.4)	226 (32.5)	59 (8.4)	283 (40.6)	696	
6-15 years	103 (45.2)	11 (4.8)	17 (7.9)	97 (42.1)	228	
Gender						
Male	192 (24.4)	233 (29.6)	51 (6.5)	311 (39.5)	787	0.057
Female	119 (19.6)	194 (31.9)	56 (9.2)	239 (39.3)	608	
Residency						
Beirut	260 (22.4)	356 (30.7)	91 (7.9)	452 (39.0)	1159	0.024
Bekaa	5 (23.8)	6 (28.6)	0 (0.0)	10 (47.6)	21	
North	9 (50)	6 (33.3)	1 (5.6)	2 (11.1)	18	
South	18 (17.8)	22 (21.8)	11 (10.9)	50 (49.5)	101	
Mountain	19 (19.8)	37 (38.5)	4 (4.2)	36 (37.5)	96	
Socioeconomic						
High	9 (11.5)	27 (34.6)	13 (16.7)	29 (37.7)	78	<0.0001
Medium	142 (19.4)	187 (25.5)	55 (7.5)	349 (47.6)	733	
Low	160 (27.4)	213 (36.5)	39 (6.7)	172 (29.5)	584	

Significant $P < 0.05$. Extremely significant $P < 0.0001$. Data presented as frequency (%)

Table 2: Clinical manifestations, laboratory findings and imaging studies of hospitalized cases of *E. histolytica* among the three main age groups

	Age <1 year (%)	Age 1-5 years (%)	Age 6-15 years (%)	P value
Frequency	80 (25.7)	128 (41.2)	103 (33.1)	
Clinical manifestation				
Fever	72 (90.0)	121 (94.5)	100 (97.1)	0.123
Vomiting	54 (67.5)	116 (90.6)	97 (94.2)	<0.0001
Abdominal pain	31 (38.8)	82 (64.1)	82 (79.6)	<0.0001
Bloody diarrhea	44 (55.0)	77 (60.2)	67 (65.0)	0.385
Mucoidy diarrhea	71 (88.0)	106 (82.8)	94 (91.3)	0.143
Dehydration				
Mild	0 (0.0)	12 (9.4)	15 (14.6)	
Moderate	70 (87.5)	103 (80.5)	82 (79.6)	0.008
Severe	10 (12.5)	13 (10.2)	6 (5.8)	
Laboratory findings				
Leukocytosis	27 (33.8)	47 (36.7)	42 (40.8)	0.612
Neutrophilia	13 (16.3)	61 (47.7)	87 (84.5)	<0.0001
Bands	15 (18.8)	39 (30.5)	23 (22.3)	0.128
Positive CRP	64 (81.0)	124 (96.9)	95 (92.2)	<0.0001
Imaging studies	35 (33.7)	24 (23.1)	45 (43.3)	
Abdominal X-ray	1 (2.9)	10 (41.7)	11 (24.4)	<0.0001
CT	0 (0.0)	1 (4.2)	2 (4.4)	
US	14 (40.0)	11 (45.8)	25 (55.6)	
Barium enema	13 (37.1)	0 (0.0)	1 (2.2)	
Combined imaging	7 (20.0)	2 (8.3)	6 (13.3)	

Significant $P < 0.05$. Extremely significant $P < 0.0001$. Data presented as frequency (%). CRP: C-reactive protein; CT: CT scan abdomen and pelvis; US: Ultrasound abdomen

Table 3: Comparison of the risk factors among the 4 studied groups

	<i>E. histolytica</i> group I (<i>n</i> =311) (%)	RV group II (<i>n</i> =427) (%)	Bacterial group III (<i>n</i> =107) (%)	Unidentified group IV (<i>n</i> =550) (%)	P value
Breast feeding					
Adequate	115 (39.8)	104 (24.5)	38 (40.0)	234 (45.7)	$P_1 < 0.0001$
In adequate	69 (23.9)	53 (12.5)	27 (28.4)	116 (22.7)	$P_2 = 0.591$
No	105 (36.3)	267 (63.0)	30 (31.6)	162 (31.6)	$P_3 = 0.244$
Formula feeding					
Yes	257 (82.6)	377 (88.3)	97 (90.7)	503 (91.5)	$P_1 = 0.029$
No	54 (17.4)	50 (11.7)	10 (9.3)	47 (8.5)	$P_2 = 0.047$
					$P_3 < 0.0001$
Nutritional status					
Appropriate	268 (86.2)	368 (87.5)	94 (87.9)	504 (91.6)	$P_1 = 0.997$
Inappropriate	43 (13.8)	59 (13.8)	13 (12.1)	46 (8.2)	$P_2 = 0.660$
					$P_3 = 0.011$

Data are presented as frequency (%); P_1 group I versus group II; P_2 group I versus group III; P_3 group I versus group IV; RV: Rotavirus

and $P_3 < 0.0001$), however, the presence of bands and positive CRP were significantly higher in *E. histolytica* group than the other 3 groups ($P_1 < 0.0001$, $P_2 < 0.01$ and $P_3 < 0.001$, respectively) [Table 4]. Imaging studies showed statistically high percentages in *E. histolytica* group compared with the other 3 groups, as 33.4% (104 cases/311) of *E. histolytica* group were exposed to imaging compared to 6% (6 cases/427) of RV group, 14% (15 cases/107) of bacterial group, and 5.6% (31 cases/550) of unidentified group ($P_1 < 0.0001$,

$P_2 < 0.0001$, and $P_3 < 0.0001$, respectively). These imaging studies included: Ultrasound abdomen which was done in 48.1% (50 cases/104) of *E. histolytica* group, abdominal X-ray was done in 21.2% (22 cases/104) of *E. histolytica* group and CT scan of abdomen was performed in 2.9% (3 cases/104) of *E. histolytica* group, but the most striking imaging studies were barium enema and combined imaging which were done in 13.5% (14 cases/104) and 14.4% (15 cases/104) of *E. histolytica* group, respectively, and were performed mostly in the age group of infants

Table 4: Comparison of the clinical manifestations, laboratory findings, imaging studies, and medications among the 4 studied groups

	<i>E. histolytica</i> group I (n=311)	RV group II (n=427)	Bacterial group III (n=107)	Unidentified group IV (n=550)	P value
Clinical manifestation					
Fever	293 (94.2%)	207 (48.5%)	95 (88.8%)	396 (72.0%)	P1<0.0001 P2=0.061 P3<0.0001
Vomiting	267 (85.9%)	356 (83.4%)	63 (58.9%)	409 (74.4%)	P1=0.359 P2<0.0001 P3<0.0001
Abdominal pain	195 (62.7%)	95 (22.2%)	33 (30.8%)	99 (18.0%)	P1<0.0001 P2<0.0001 P3<0.0001
Bloody diarrhea	188 (60.5%)	3 (0.7%)	42 (39.3%)	21 (3.8%)	P1<0.0001 P2<0.0001 P3<0.0001
Mucoidy diarrhea	271 (87.1%)	19 (4.4%)	74 (69.2%)	155 (28.2%)	P1<0.0001 P2<0.0001 P3<0.0001
Dehydration					
Mild	27 (8.7%)	83 (19.4%)	4 (3.7%)	95 (17.3%)	P1<0.0001
Moderate	255 (82.0%)	319 (74.7%)	93 (86.9%)	419 (76.2%)	P2=0.240
Severe	29 (9.3%)	25 (5.9%)	10 (9.3%)	36 (6.5%)	P3=0.001
Duration of symptoms					
Mean (days)	1.80	2.11	2.21	2.18	P=0.070
Duration of stay					
Mean (days)	3.16	3.72	3.84	3.29	P=0.092
Laboratory findings					
Leukocytosis	116 (37.3%)	24 (5.6%)	43 (40.2%)	87 (15.8%)	P1<0.0001 P2=0.596 P3<0.0001
Neutrophilia	161 (51.8%)	81 (19.0%)	50 (46.7%)	161 (29.3%)	P1<0.0001 P2=0.368 P3<0.0001
Bands	77 (24.8%)	4 (0.9%)	13 (12.1%)	4 (0.7%)	P1<0.0001 P2=0.006 P3<0.0001
Imaging studies	104 (33.4%)	6 (1.4%)	15 (14%)	31 (5.6%)	P1<0.0001
Medications					P2<0.0001 P3<0.0001
3 rd generation cephalosporin	38 (12.2%)	0 (0.0%)	16 (14.9%)	2 (0.003%)	P1<0.0001 P2<0.0001 P3<0.0001

Data are presented as frequency (%); P1 group I versus group II; P2 group I versus group III; P3 group I versus group IV; RV: Rotavirus

less than 1 year ($P < 0.0001$) [Table 2]. Almost all cases of *E. histolytica* showed favorable response to our protocol of treatment that included oral or intravenous rehydration with metronidazole, with regression of symptoms within a mean duration of 2-3 days, however, 12% (38 cases/311) of patients with *E. histolytica* infection received 3rd generation cephalosporin, in addition to metronidazole [Table 4]. The frequency of *E. histolytica*

as a cause of acute GE among children is increasing throughout years as its frequency doubled from year 2008 (14.9%) to year 2012 (28.9%) [Figure 2]. Regarding seasonal variation of the studied enteropathogens, it seems that *E. histolytica* infection has a specific seasonal pattern. It is prevalent all over the year with peak prevalence during summer and autumn, whereas, RV infection has the opposite seasonal pattern [Figure 3].

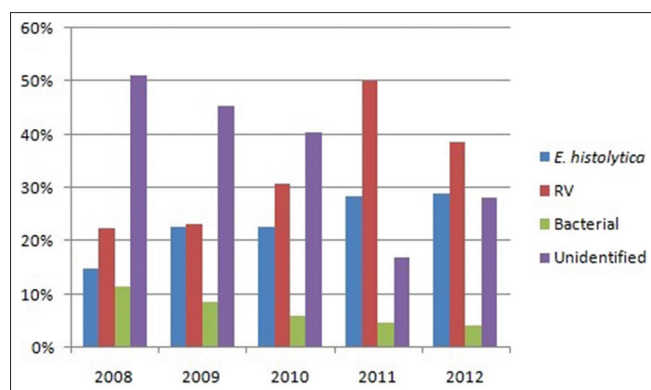


Figure 2: Yearly variation in the prevalence of enteropathogens

Discussion

In this study, admitted cases of GE at MGH, during the period between January 2008 and December 2012, were found to be 1395 cases out of 3196 total pediatric GE case presented to our hospital during the same period. Cases admitted with *E. histolytica* (311) constituted 22.3% of total admitted cases of GE. The diagnosis of *E. histolytica* infection was based on detection of *E. histolytica* trophozoites or cysts in several fresh stool samples sent for Fecal Parasite Concentrator, which is an efficient device to concentrate parasites and protozoa,^[21] as the *E. histolytica* antigen detection test was not available at our locality. Moreover, these hospitalized *E. histolytica* cases had symptoms of parasitic GE.

This study showed that the prevalence of *E. histolytica* is 22.3% of all hospitalized pediatric GE cases, which corroborates previous studies from Asia and East Africa as the prevalence of *E. histolytica* among pediatric GE cases was 20.0% in Saudi Arabia,^[2] 18.0% in Tanzania,^[26] 17.1% in Yemen^[27] and 25.9% in Tajikistan.^[28] In Lebanon, two previous studies were conducted by Araj *et al.*, at American University of Beirut Medical Center, and Hamze *et al.*, at North Lebanon. Both studies reviewed the parasitology records of the general population, regardless of correlation with clinical manifestations, and both showed that the prevalence of *E. histolytica* infection is 2% in the age group below 15 years, and 4.57% in adults, respectively.^[17,29] In our study, the increased prevalence of *E. histolytica* infection among inpatient pediatric GE cases may be attributed to concerning risk factors. Moreover, there was a considerable number of inpatients under 1 year infected with *E. histolytica* (80/311, 25.7%), which is an unusual presentation in this age group because *E. histolytica* is usually transmitted via fecal oral route with contaminated food and water, so young infants are less likely to develop intestinal amebiasis very often.^[16] This increased frequency of *E. histolytica* infection in this small age group, may be linked to the formula feeding, with inappropriate sterilization techniques of bottles,

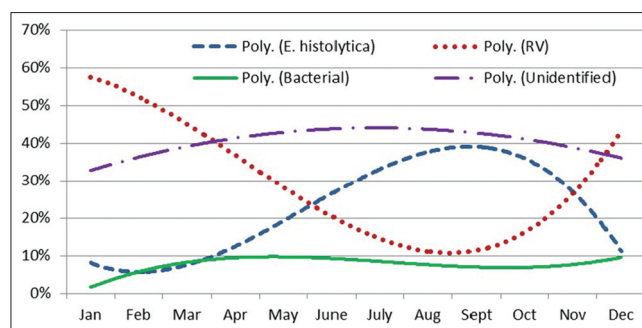


Figure 3: Seasonality of enteropathogen

and the use of unimproved drinking water for formula preparation, all reflecting that hygiene plays a very important role in the spread of *E. histolytica* infection.

Low socio-economic status was the most significant demographic factor associated with high prevalence of *E. histolytica* among infants and children, and this is probably due to low level of public and individual hygienic conditions.^[7] Regarding residency, despite majority of inpatient pediatric GE cases were from the capital Beirut, almost 50% of hospitalized GE cases coming from North Lebanon had *E. histolytica* infection. However, this cannot be relied on, due to the small number (18 cases) of GE cases presenting from the North. Otherwise, gender and residency had no statistically significant effect on the prevalence of *E. histolytica* infection [Table 1].

Taking into consideration the various clinical manifestations associated with intestinal amebiasis, infants less than 1 year of age presented with more severe degrees of dehydration. Besides we had two cases admitted to intensive care units: The first case was 14 days old infant admitted for GE and was found to have *E. histolytica* infection, and the second one was 28 days old infant admitted for severe dehydration and was diagnosed to have *E. histolytica* infection. This implies that infants under 1 year presented with moderate to severe dehydration secondary to *E. histolytica* infection and could be protected by exclusive breastfeeding and improved hygienic practices. On the other hand, symptoms such as fever, vomiting, mucoidy and bloody diarrhea were noticed similarly among all age groups of *E. histolytica* GE. The group of children above 1 year of age had significantly higher presentation with abdominal pain than the group of infants less than 1 year ($P < 0.0001$). This may be related to developmental maturity of this age group to express their feelings much better than younger infants who presents more with irritability and inconsolable crying as an expression of their pain.^[2]

Regarding risk factors to acquire *E. histolytica* infection, breast feeding did not have an effect on decreasing the

rate of *E. histolytica* infection in our study, while it was protective against RV infection [Table 3]. Despite this, it is known that colostrum and mature human milk have significant lethal effect on *E. histolytica*, which is accomplished by bile salt-stimulated lipase in human milk that kills both *Gardia lamblia* and *E. histolytica*.^[30,31] This may be attributed to inadequate maternal hygiene or associated improper feeding practices as unapproved herbal remedies for infantile colic. Moreover, all studied enteropathogens were significantly prevalent in bottle-fed infants [Table 3], and this may be due to inadequate or non-sterilization of bottles. This spots the light on the importance of awareness for exclusive breastfeeding and avoidance of improper feeding practices, in addition to adequate personal hygiene and proper techniques of sterilization of bottles.

When comparing the clinical manifestations among the four studies groups, significantly high percentages of symptoms such as high grade fever, abdominal pain, vomiting, bloody or mucoidy diarrhea, and moderate to severe degrees of dehydration were found in *E. histolytica* group compared to the other groups, and this can be attributed to the fact that we are dealing with only severe *E. histolytica* cases that required admission and not outpatient *E. histolytica* cases. Regarding the laboratory studies in our *E. histolytica* cases, a significant number (>50%) of cases had leukocytosis, with neutrophilic shift, positive CRP, as well as the presence of significant numbers of band cells, which were significantly higher than both RV unidentified groups, but approximately similar to that of the bacterial group, suggesting similar presentation of intestinal amebiasis to an invasive bacterial disease.

Also a significant number of cases with *E. histolytica* GE underwent imaging studies of the abdomen (104/311, 33.4%) due to initial presentation with clinical picture of severe abdominal pain mimicking surgical abdomen. Moreover, 14 infants (13%), of whom 13 were below 1 year of age, presented with an initial clinical picture of intussusceptions (irritability, bloody stool, and hypoactivity) necessitating barium enemas to be performed and turned to be normal, and this severe clinical picture was due to *E. histolytica* infection. Besides, 12.2% (38 cases/311) of *E. histolytica* GE cases were started, upon initial presentation, on 3rd generation cephalosporin as their clinical manifestations and laboratory findings were mimicking invasive bacterial GE [Table 4]. The combination of these laboratory findings, together with the severity of clinical presentation, have been described usually with amebic liver abscess, the commonest from of invasive amebiasis, and not with intestinal amebiasis,^[3,32,33] and rarely with severe amebic colitis in young children when the colon was found to be necrotic with several perforations leading to peritonitis.^[34,35]

However, this unusual presentation in our patients, especially in infants, was associated only with intestinal amebiasis without the disseminated diseases mentioned above, and this was proved by the improvement of patients after initiation of metronidazole treatment within a mean of 2-3 days, and a significant number of patients underwent imaging studies such as ultrasound of abdomen and pelvis, and CT scan of abdomen, and none of these imaging studies revealed any abscess, perforation or severe colitis, this indicates the aggressive nature of *E. histolytica* infection in our patients, and that an early invasive disease could occur, unless if the *E. histolytica* infection was diagnosed early and appropriately treated.^[2] This invasive nature was more common than expected or previously reported in the literature, and even more severe than our inpatients with GE due to other enteropathogens.

These findings were similar to a study conducted in Saudia Arabia, raising the issue that a more virulent strain of *E. histolytica* is responsible for such serious manifestations in the Middle East, and need to be investigated as Petri suggested that genetically distinct strains of *E. histolytica* might exist and are more virulent than others.^[2,36] Besides this aggressive presentation of *E. histolytica* in our cases may also need further evaluation to reveal a possible underlying immunologic mechanism that might be responsible for such severe *E. histolytica* cases at our country and in Saudi Arabia.^[2] Regarding the mean duration of hospitalization, cases with *E. histolytica* GE had mean duration of hospital stay of 3 days, similar to other groups, with average cost of 1800\$ for each case.

Finally, *E. histolytica* infection is increasing throughout years as its prevalence doubled from year 2008 (14.9%) to year 2012 (28.9%), and this reflects deterioration in both public and individual hygienic standards, besides unimproved drinking water plays a contributing role in such increase in *E. histolytica* infection. Besides, *E. histolytica* GE is prevalent all over the year, but it seems to have its highest prevalence during summer and autumn seasons, opposite to Rotavirus infection, which makes *E. histolytica* in our locality, on the top of list of differential diagnosis for acute GE among children in these two seasons.

Limitation of the study

This study was a retrospective one, some of the data were not fully available, and however, we relied on every single documentation in the patients' medical charts. This study included one tertiary care referral center in Beirut, but it would have been better if it could include more medical centers in various regions of Lebanon, to be a multicenter study and to provide more informative data regarding the prevalence and nature of *E. histolytica* infection.

However, the number of pediatric patients admitted to our hospital represents a sufficient sample to be studied in our region. Another limitation is unavailability of *E. histolytica* antigen detection test to confirm and increase the yield for diagnosis of *E. histolytica* infection. Besides, there was no specific medium for *Campylobacter spp.* in the microbiology section at the Department of Laboratory Medicine at our hospital. Despite this, all hospitalized *E. histolytica* cases had typical manifestations of amebic gastroenteritis, and moreover, they responded well to the treatment with metronidazole.

Recommendations

This study raises the issue of a public health problem which reflects deterioration in hygienic measures in our country, with predominance in low socio-economic status, and for sure the presence of contaminated water supplies.

Health care providers should advice for better hygiene, especially in the low socioeconomic group, with education for better sterilization techniques of water and bottles especially in infants under 1 year of age.

Improved water and food supplies by the government should be applied, including protection and mandatory inspection measures to reduce the rate of infection with *E. histolytica*.

Conclusions

The prevalence of *E. histolytica* infection is increasing throughout years. It is accompanied with severe manifestations, and unusual presentation in infants and children.

Severe clinical manifestations and laboratory findings suggestive of a severe invasive disease (leukocytosis, neutrophilia, positive CRP, presence of bands) were found in almost more than 50% of patients with *E. histolytica* infection in our hospital.

This denotes that *E. histolytica* infection is an emerging serious disease, not only a simple gastroenteritis, especially in low socio-economic and poor hygienic conditions. And it is an important cause of hospitalization and financial burden in our country.

So we must be ready for this serious infection with more effective and powerful preventive measures.

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