

Clinical Manifestations and Etiology of Liver Abscess in Children in Tertiary Care Hospital

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ABSTRACT

Background: The liver is a major metabolic organ with a dual blood supply, hence vulnerable to infection. The liver abscess (LA) is a space-occupying lesion in the liver parenchyma filled with pus caused by bacteria, parasites, or fungus.

Objective: To determine the clinical manifestations and etiology of liver abscess among children presenting at a tertiary care hospital.

Methodology: This cross-sectional study was conducted at the medical department of the National Institute of Child Health, Karachi, Pakistan from July 2022 to December 2022. A total of 147 children of either gender aged below 12 years with liver abscesses were analyzed. At the time of enrollment, demographic features, clinical features, characteristics, and etiological agents of LA. The cause of the liver abscess was confirmed by pus culture, blood culture, and indirect haemagglutination assay (IHA). Aspiration was performed among cases who had LA>5cm and liquefaction of abscess.

Results: Of a total of 147 children with LA, 96 (65.3%) were boys. The mean age was 7.08±2.61 years. Socioeconomic status of 112 (76.2%) children was poor. In terms of frequency of presenting features/complaints, pyrexia (100%) and abdominal pain (98.6%) were the most commonly found whereas hepatomegaly (98%) and right hypochondrium tenderness (97.3%) were the commonest signs. The right hepatic lobe was involved in 120 (81.6%) LA cases and the majority of LA were solitary (93.2%). The size of the liver in 57 (38.8%) LA cases was between 3-6 cm while 93 (63.3%) cases were aspirated. The etiological diagnosis revealed that bacterial involvement was found in 36 (24.5%) LA cases while amoebic presence was noted in 75 (51.0%) cases. No cases of fungal involvement were found.

Conclusion: A predominance of male gender and low socioeconomic status was found among children with LA presenting at a tertiary care hospital in Karachi, Pakistan. The most frequent presenting complaints were pyrexia and abdominal pain. Amoebic presence was the most common etiological agent behind LA.

Keywords: *Amoeba, blood culture, hepatomegaly, liver abscess, pyrexia.*

INTRODUCTION

The liver abscess (LA) was first described by Hippocrates and dated back to 400 BC, however, the fundamental review of it was first published by Ochsner and colleagues in 1938 [1]. The LA is a space-occupying lesion in the liver parenchyma filled with pus caused by bacteria (pyogenic liver abscess [PLA]), parasites (amoebic liver abscess [ALA]), or fungus [2]. The liver is a major metabolic organ with a dual blood supply, hence vulnerable to infection. The literature has reported the incidence of LA to be 25-79 cases per 100,000 paediatric admissions [3, 4].

The vast majority of cases of PLA are idiopathic while perforated appendicitis, *Ascaris* infestation, infected hydatid cyst, penetrating trauma, etc. might be a few of the predisposing causes with immunodeficiency, malnutrition as associated factors [5, 6]. The cause of ALA is *Entamoeba histolytica*, a parasite, common in third-world countries where the sanitation environment is compromised [7]. Trophozoites and cysts both pass through faeces by the organism in the intestine.

Trophozoites cannot survive in an external environment whereas cysts being covered by refractile walls ingested through contaminated food (faeco-oral route) release a large number of trophozoites in the caecum where they colonize and cause amoebic colitis [8]. From the colon these get absorbed in portal circulation and lodge in the liver; thus causing liver abscess. The ALA consists of a wall of degenerated liver cells and has a liquefied center of brownish pus which contains leucocytes, erythrocytes strands of connective tissue, and debris [9]. Worldwide literature shows the majority of cases of LA are pyogenic in origin (80%) while the rest are amoebic [10]. The fungal abscess is very rare and affects mainly those populations who are immunosuppressed [11].

The exact incidence of LA is not properly reported in Pakistan because of the paucity of literature. This study aimed to determine the clinical manifestations and etiology of children presenting with LA at a tertiary care hospital. The results of this study were thought to guide the timely identification and treatment of LA.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at the medical department of the National Institute of Child Health, Karachi, Pakistan from July 2022 to

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December 2022. Approval from “Institutional Ethical Committee” was obtained. Informed and written consent was acquired from the parents/guardians of study participants. Inclusion criteria were children of either gender aged below 12 years with liver abscesses. Unwillingness to participate in the study by parents/guardians or comorbidities in the children like diabetes, tuberculosis, etc. (based on medical history and record) were excluded.

EPI info sample size calculator was used for the estimation of sample size taking a confidence interval of 95%, and a margin of error of 4% considering the reported frequency of fever in children with LA as 94.7 % [9]. The minimum estimated sample size came out to be 121. At the time of enrollment, demographic and clinical features along with characteristics (site, size, and number of LA) and etiological agents of LA were noted. LA was diagnosed by clinical features, laboratory investigations, and imaging modalities like ultrasound and CT scan. The cause of the liver abscess was confirmed by pus culture, blood culture, and indirect haemagglutination assay (IHA). IHA is sensitive and specific for *the Entamoeba histolytica* parasite. The treatment of LA was done with antibiotics alone or antibiotics with either aspiration or pigtail catheter insertion. Aspiration was performed among cases who had LA>5cm and liquefaction of abscess. Socio-economic status was labeled as low if monthly family income was below PKR.30000, medium if between PKR.30000-60000, and high if above PKR. 60000.

Data analysis was performed using “Statistical Package for Social Sciences (SPSS)”, version 26.0. Qualitative data was presented as frequency and percentages while quantitative data was shown as mean and standard deviation (SD). The chi-square test was used to compare categorical variables while analysis of variance (ANOVA) was applied to compare means. P-value < 0.05 was taken as significant.

RESULTS

In a total of 147 children with LA, 96 (65.3%) were boys and 51 (34.7%) girls representing a boys-to-girls ratio of 1.9:1. The mean age was 7.08±2.61 years ranging between 2 to 12 years while 43 (29.3%) children were aged below 5 years and remaining 104 (70.7%) were aged between 6-12 years. The mean body weight was calculated to be 16.25±5.55 kg ranging between 6 to 35 kg. Socio-economic status of 112 (76.2%) was poor and 35 (23.8%) belonged to middle socio-economic status. In terms of frequency of presenting features/complaints, pyrexia (100%) and abdominal pain (98.6%) were the most commonly found whereas hepatomegaly (98%) and right hypochondrium tenderness (97.3%) were the commonest signs. The frequency of presenting symptoms and clinical features is shown in **Fig. (1)**.

The right hepatic lobe was involved in 120 (81.6%) LA cases and the majority of LA were solitary (93.2%). The

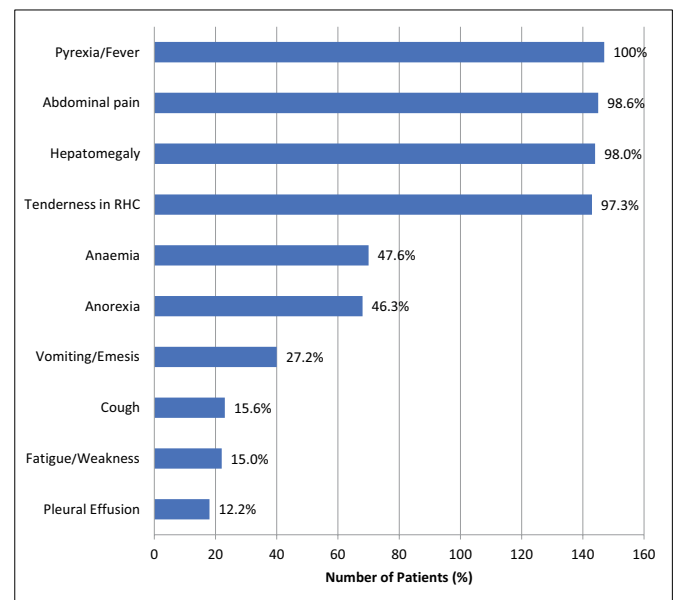


Fig. (1): Frequency of Presenting Symptoms and Clinical Features (n=147).

size of the liver in 57 (38.8%) LA cases was between 3-6 cm while 93 (63.3%) cases were aspirated. The details of clinical and laboratory parameters are shown in **Table 1**.

Table 1: Clinical and Biochemical Parameters (n=147).

Clinical and Biochemical Parameters		Frequency (%)
Site of liver abscess	Right lobe	120 (81.6%)
	Left lobe	25 (17.0%)
	Both lobes	2 (1.4%)
Size of liver abscess (cm)	1-3	6 (4.1%)
	3-6	57 (38.8%)
	6-9	55 (37.4%)
	>9	29 (19.7%)
Number of liver abscesses	Single	137 (93.2%)
	Multiple	10 (6.8%)
Aspiration of liver abscess	Yes	93 (63.3%)
Positive Indirect Haemagglutination Test		92 (62.6%)
Pus culture causative agent	Bacterial	50 (34.0%)
	None	97 (66.0%)
Blood C/S causative agent	Bacterial	44 (29.9%)
	no growth	103 (70.1%)
Diagnosis	Bacterial	36 (24.5%)
	Amoebic	75 (51.0%)
	Both	16 (10.9%)
	None	20 (13.6%)

The etiological diagnosis revealed that bacterial involvement was found in 36 (24.5%) LA cases while amoebic presence was noted in 75 (51.0%) cases, both bacterial and amoebic in 16 (10.9%) whereas the remaining 20 (13.6%) cases were not identified to have any causative agents involvement. No cases of fungal involvement were found. **Table 2** is showing the distribution of socio-demographic, presenting symptoms, and clinical features concerning the involvement of etiological agents. Vomiting/emesis (p=0.019), cough

Table 2: Distribution of Socio-demographic, presenting symptoms, and clinical features/complaints with regards to etiological diagnosis.

Study Variables		Bacterial n(%)	Amoebic n(%)	Both n(%)	None n(%)	p-value
Gender	Boys	23 (63.9%)	48 (64.0%)	10 (62.5%)	15 (75.0%)	0.808
	Girls	13 (36.1%)	27 (36.0%)	6 (37.5%)	5 (25.0%)	
Age	≤5 years	13 (36.1%)	25 (33.3%)	3 (18.8%)	2 (10.0%)	0.119
	6-12 years	23 (63.9%)	50 (66.7%)	13 (81.3%)	18 (90.0%)	
Socio-economic status	Poor	29 (80.6%)	55 (73.3%)	14 (87.5%)	14 (70.0%)	0.519
	Middle	7 (19.4%)	20 (26.7%)	2 (12.5%)	6 (30.0%)	
Frequency of Presenting Features/ Complaints	Fever	36 (100%)	75 (100%)	16 (100%)	20 (100%)	-
	Abdominal pain	35 (97.2%)	75 (100%)	16 (100%)	19 (95.0%)	0.288
	Vomiting/emesis	5 (13.9%)	27 (36.0%)	6 (37.5%)	2 (10.0%)	0.019
	Diarrhea	1 (2.8%)	11 (14.7%)	3 (18.8%)	-	0.062
	Cough	3 (8.3%)	10 (13.3%)	7 (43.8%)	3 (15.0%)	0.010
	Fatigue/weakness	3 (8.3%)	8 (10.7%)	9 (56.3%)	2 (10.0%)	<0.001
	Anorexia	13 (36.1%)	37 (49.3%)	13 (81.3%)	5 (25.0%)	0.004
	Weight loss	-	2 (2.7%)	-	-	0.584
	Respiratory distress	1 (2.8%)	2 (2.7%)	5 (31.3%)	5 (25.0%)	<0.001
	Anaemia	11 (30.6%)	37 (49.3%)	15 (93.8%)	7 (35.0%)	<0.001
	Jaundice	1 (2.8%)	1 (1.3%)	1 (6.3%)	3 (15.0%)	0.048
	Hepatomegaly	34 (94.4%)	75 (100%)	16 (100%)	19 (95.0%)	0.172
	Tenderness in the right upper quadrant	33 (91.7%) (92.0%)	75 (100%)	16 (100%)	19 (95.0%)	0.065
	Pleural effusion	2 (5.6%)	8 (10.7%)	5 (31.3%)	4 (20.0%)	0.052

Table 3: Distribution of liver abscess-related characteristics and laboratory parameters with regards to etiological diagnosis.

Study Variables		Bacterial n(%)	Amoebic n(%)	Both n(%)	None n(%)	p-value
Site of liver abscess	Right lobe	28 (77.8%)	67 (89.3%)	12 (75.0%)	13 (65.0%)	0.144
	Left lobe	7 (19.4%)	8 (10.7%)	4 (25.0%)	6 (30.0%)	
	Both lobes	1 (2.8%)	0(0)	0(0)	1 (5.0%)	
Size of liver abscess (cm)	1-3	2 (5.6%)	3 (4.0%)	0(0)	1 (5.0%)	0.123
	3-6	15 (41.7%)	34 (45.3%)	2 (12.5%)	6 (30.0%)	
	6-9	13 (36.1%)	27 (36.0%)	6 (37.5%)	9 (45.0%)	
	>9	6 (16.7%)	11 (14.7%)	8 (50.0%)	4 (20.0%)	
Number of liver abscesses	Single	31 (86.1%)	70 (94.6%)	16 (100%)	19 (95.0%)	0.229
	Multiple	5 (13.9%)	4 (5.4%)	0(0)	1 (5.0%)	
Aspiration of liver abscess (positive)		23 (63.9%)	39 (49.3%)	15 (93.8%)	18 (90.0%)	<0.001
Positive Indirect Haemagglutination Test		1 (2.8%)	75 (100%)	16 (100%)	0(0)	<0.001
Pus culture causative agent	Bacterial	28 (77.8%)	0(0)	10 (62.5%)	12 (60.0%)	<0.001
	None	8 (22.2%)	75 (100%)	6 (37.5%)	8 (40.0%)	
Hemoglobin (g/dl)		9.34±1.59	9.11±1.50	7.76±1.40	8.80±1.90	0.008
Total leucocyte count (/uL)		14050±4192	14728±6033	19187±5729	16835±5933	0.010
C-Reactive protein (mg/L)		23.64±18.41	15.75±12.84	16.31±7.95	22.45±10.5	0.020

($p=0.010$), fatigue/weakness ($p<0.001$), anorexia ($p=0.004$), respiratory distress ($p<0.001$), anaemia ($p<0.001$) and jaundice ($p=0.048$) were having significant association with types of etiological agents.

Aspiration of liver abscess ($p<0.001$), positive indirect haemagglutination test ($p<0.001$), pus culture containing causative agent ($p<0.001$), types of pathogens ($p<0.001$), hemoglobin levels ($p<0.001$), hemoglobin ($p=0.008$), TLC ($p<0.001$) and CRP ($p=0.011$) were revealed to have a significant association with the distribution of causative agent related to LA (**Table 3**). The most common bacterial agent turned out to be *Staphylococcus aureus* ($n=16$), *Burkholderia* ($n=12$), and *Pseudomonas* ($n=4$).

DISCUSSION

The LA is an uncommon entity in developed countries, unlike developing countries where low socioeconomic conditions, and poor sanitary environments where amoebiasis is endemic play a major role [12, 13]. In our study, the mean weight of children with LA was 16.25 ± 5.55 kg while the mean age was noted to be 7.08 ± 2.61 years. Kumar *et al.* reported moderate to severe malnutrition in 27% of patients of LA [4].

Children with LA have a unique set of signs and symptoms that must be addressed properly. Most common clinical features in our study were fever (100%), abdominal pain (98.6%), hepatomegaly (98%), and tenderness in the right hypochondrium (97%) which are quite similar to a study conducted by Waghmare *et al.* [14]. The frequency of other features like anorexia, nausea,

vomiting, jaundice, respiratory distress, etc. has also been described both other researchers among patients of LA [15]. Among cases of LA, respiratory distress is mainly due to pleural effusion and anemia whereas pleural effusion occurs because of the proximity of liver and lungs.

It was found that 81% of LA cases occurred in the right lobe of the liver and the majorities were solitary (93%). This is in contrast to a study done by Kumar *et al.* [4] in which 66% of LA occurred in the right lobe and 75% of cases were solitary; however, the predominance of the right hepatic lobe can be associated with the volume of right portal vein flow and also that the right portal vein continues in the direction of the common portal vein, whereas the left portal vein takes a more horizontal direction [9, 16].

In our study, the majority of cases were amoebic 51.0%, bacterial 24.5%, or both amoebic and bacterial involvement was observed in 13.6%. This is in contrast to literature where PLA constitutes 80% of cases [10]. The most probable reason for this might be endemicity of *Entamoeba histolytica*. ALAs are uncommon in children with occurrence influenced mostly by endemic factors. The reported incidence of ALAs for children varies, such as 7% (n=1/15), 30% (n=9/30), 35% (n=9/26), and 50% (n=10/20) from studies in Taiwan, Côte-d'Ivoire, Senegal, and Spain [9, 17-19].

The commonest organisms were *Staphylococcus aureus* and *Burkholderia* in this study. These results are similar to the study by Waghmare *et al.* [14]. The next most common organisms in their study were *Escherichia Coli*, *Pseudomonas*, *Klebsiella*, *Enterobacter*, and anaerobes. We also found similar trends however *Pseudomonas* was mentioned as a separate entity and the rest were placed in gram-negative rods and mixed organisms group.

In the present study, 65.3% of children with LA were boys. Yeh, *et al.* in their study revealed that 66% of children were male which is almost identical to the present findings [9]. We also noted that 76.2% of children with LA belonged to poor socio-economic status. Kannathasan *et al.* from Sri Lanka also shared that low socio-economic status was one of the major epidemiological factors among patients of LA [20].

The mainstay of treatment in LA cases is antibiotics and aspiration [16, 21]. Antibiotics must be a broad spectrum for PLA covering both gram-positive and gram-negative organisms as well as anaerobes. For ALA, metronidazole and diloxanide furorate are first-line choices as these are systemic and intestinal amoebicides respectively [11, 22]. Aspiration of the abscess cavity is necessary for effective penetration of antibiotics, hence quick recovery; however, aspiration size should be more than 4 cm and the abscess must be liquefied [10]. In our study, we aspirated 63.3% of cases.

The present study is among the first research performed in Pakistan showing details and descriptions of various LA aspects and laboratory parameters which gives strengths to the findings of this study. Single center study design, relatively small sample size, and inability to record outcomes among LA cases in this study were some of the limitations.

CONCLUSION

A predominance of male gender and low socioeconomic status was found among children with LA presenting at a tertiary care hospital in Karachi, Pakistan. The most frequent presenting complaints were pyrexia and abdominal pain. Amoebic presence was the most common etiologic agent behind LA.

ETHICS APPROVAL

Ethical approval was obtained from the IERB of the National Institute of Child Health, Karachi, Pakistan as IERB No: IERB-37/2021, dated: 07-12-2021. All procedures performed in studies involving human participants were following the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the parents/guardians of all the participants.

AVAILABILITY OF DATA

The authors confirm that data supporting the results of this study are available upon request to the corresponding author.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

AUTHORS' CONTRIBUTION

All authors contributed significantly to the study.

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