Clinical, Laboratory, Colonoscopic and Management Profile in Patients of Liver Abscess from Northern India

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Abstract
Problem: To study the clinical profile, microbiological aetiologies, colonic involvement & management in patients with liver abscess. **Approach**: 155 participants were involved in a retrospective observational study that was carried out over a year. Records of the history, examination, and laboratory tests were noted. Ultrasound guided aspiration was done and samples were investigated. All participants with an amoebic liver abscess underwent colonoscopy to evaluate the colonic involvement. Chi-square test and multivariate regression analysis were performed. **Findings:** The mean age of subjects was 40.3 years. Most of them (60%) belonged to a lower socioeconomic class and 76% of them were alcoholics. Majority of abscesses were solitary (62%), involving commonly the right lobe (68%). 72% were amoebic, 20% pyogenic, 1 %tubercular, 2 %fungal and 5 % mixed liver abscess. Colonic involvement was seen in 75% of amoebic liver abscess (ALA) patients with most commonly isolated cecal involvement (60%). Small ulcerations were significantly higher among cases of multiple ALA compared to solitary ALA (P=0.0003). In 80% of patients, percutaneous needle aspiration was performed; in 15% pigtail drainage and in 5%, surgical intervention. Overall mortality was 2 %, all reported in surgical group. **Conclusion:** The frequent presentation was solitary amoebic liver abscess mainly involving right lobe in a young alcoholic male, of low socioeconomic class. Three fourth of the patients with an amoebic liver abscess had colonic ulcers, especially those who presented with diarrhoea. Appropriate use of minimally invasive drainage techniques reduces mortality.
Keywords: colonic ulcers, clinic-etiological profile, liver abscess.

Introduction

Liver abscess (LA) is characterised by accumulation of pus in liver due to varying aetiologies namely bacterial, fungal, parasitic or mixed infection. In developing countries about two-third of cases are as a result of entamoeba histolytica, while three-fourths of cases are pyogenic in origin [1].

In the tropical and subtropical areas, amoebiasis is common, that affects around 12% of the population [2]. 85% of amoebic infections are asymptomatic while 10% cases presents with dysentery secondary to amoebic liver abscess (ALA) [2]. Poor hygiene, diabetes mellitus, steroid misuse, chronic alcoholism, and human immunodeficiency virus infection are risk factors for the development of ALA. Pyogenic and tubercular abscesses are the closest differentials of the ALA [2]. Alcoholism, immunodeficiency,

inappropriate antibiotic use, and the advent of drug-resistant bacteria have all contributed to an increase in the frequency of tubercular liver abscess (TLA) [3].

LA usually presents with fever, anorexia and abdominal pain. Amoebiasis primarily affects the colon, which frequently presents as diarrhoea. The parasite is typically transported to the liver from the large bowel through the portal venous system, making the liver the most frequently affected extraintestinal organ [4]. However, colon involvement in most ALA patients is asymptomatic. In a study by Aikat et al. 59% of liver abscess cases had extensive intestinal ulceration [5]. Colonic involvement was also found in 58% of ALA cases by Sachdev and Dhol [6]. Colonic ulcerations were present in 55% of ALA cases in study by Mishra. They found colonic involvement were more when active diarrhoea was present [7]. However, evidence regarding an association between the site of the colonic lesions and location of abscesses in the liver is scarce.

Previously the mainstay of management of liver abscess was surgical. However, in contrast the conservative therapy such as percutaneous drainage has demonstrated a good outcome with a shorter average length of hospital stay.

With this background we conducted this study to assess the evolving patterns in the clinical characteristics, microbiological causes, and therapeutic outcomes of patients with LA. We also studied the correlation between colonic involvement in solitary and multiple amoebic liver abscesses.

Material and Methods

This was a retrospective observational study conducted over a period of 1 year from Jan 2022 to Jan 2023 in the gastroenterology department of a tertiary care centre in Northern India. Approval of institutional ethics committee was taken. After obtaining informed written consent, we enrolled 155 participants whose ultrasonography results demonstrated a liver abscess.

Inclusion & Exclusion criteria:

All patients with liver abscesses who required intervention, such as those with (a) left lobe abscesses (b) abscesses larger than 5 cm (c) impending rupture (<1 cm liver tissue between abscess and liver margin) [8-10].

Patients under the age of 18, those with organized abscesses, abscesses in close proximity to large vessels in liver and pregnant women were excluded.

Procedure:

On a predesigned proforma, thorough history, clinical findings, and laboratory profile, including colonoscopy findings, were documented. Alcoholism was defined in accordance with the CAGE questionnaire. Patients were categorized into categories such as non-drinkers, occasional drinkers (those who consume alcohol less than three times per week), and frequent drinkers (those who consume alcohol more than three times per week) [11]. Modified Kuppuswamy's socioeconomic status scale was used to classify the patients into upper, middle, and lower socioeconomic classes [12]. The complete hemogram, a liver function test (LFT), a kidney function test (KFT), and a coagulation profile (PT/INR) were performed on all patients. Cultures of blood and urine were also sent. Serologies for HIV, hepatitis B, hepatitis C viruses and entamoeba histolytica were performed. Chest radiographs, sputum for CBNAAT and the mantoux test were administered to all patients with chronic cough with expectoration, or radiological abnormalities to rule out pulmonary Koch's disease.

All subjects who met the inclusion criteria underwent ultrasound-guided liver abscess aspiration using a pigtail catheter or a percutaneous needle after taking informed written consent. Interventions were carried out only after correction of coagulopathy (INR below 1.4). In a single, large (>10 cm), deeply seated, and partially liquefied abscess, we employed a pigtail catheter. While those multiple, tiny (5-10 cm), superficial, and totally liquefied abscesses were treated with percutaneous catheters. The aspirate was promptly sent to the microbiology department for microscopic evaluation of the wet mount for entamoeba trophozoites, gram's staining, and ZN staining for AFB. In aerobic, anaerobic, and fungal culture

mediums, samples were plated. Patients received nitromidazoles and intravenous antibiotics until a pus culture result was obtained.

All patients with amoebic liver abscess (ALA) underwent colonoscopy at admission or within 48 hours after beginning anti-amoebic therapy. On colonoscopy, mucosal lesion with erythema and ulceration was recorded. If ulceration was evident, information on the ulcers' size, location, and surrounding inflammation was noted. Size of less than 3 cm was regarded as a small ulcer, and that of more than 3 cm was regarded as a large ulcer. Multiple biopsy specimens were taken from the ulcer margins and sent for histopathological examination. The resolution of the presenting complaints along with hemodynamic stability was the criteria for discharge.

All data were entered in an MS-Excel spreadsheet and analyzed with SPSS software version 24.0 for Windows (SPSS, Chicago, IL, USA). For continuous variables, the mean, median, and standard deviation were computed. For the test of association, the chi-square test and multivariate regression analysis were used. The statistical significance level for all comparisons was set at p 0.05 for two-tailed analyses.

Results

155 patients with hepatic abscess were analyzed. The patient's age ranged from 21 to 76 years, with a mean of 40.3 years. The ratio of male to female was 1.5: 1. 60% and 35% of cases were from lower and middle socioeconomic class respectively, while only 5% belonged to upper class. (Table 1)

Out of 155 subjects of LA, 72% (n = 111) were of an amoebic origin, 20% (n = 31) were pyogenic, 5% (n = 8) were mixed amoebic and pyogenic, 1% (n = 2) were tubercular, and 2% (n = 3) were caused by fungal infections. (Table 2)

Ultrasonographic findings suggested that right lobe was the most commonly involved (68%; n= 105) while amongst the segment it was found to be segment VII most commonly involved (n=50, 32%). Solitary abscesses were more common and seen in 62% of all the cases. Multiple abscesses were commonly pyogenic in origin while solitary abscesses were more frequently associated with amoebic and tubercular abscesses (p = 0.001). The mean abscess volume was 217 ml. At the time of presentation, 4% of the patients exhibited typhlitis symptoms. (Table 3 & 4)

The most prevalent symptom was abdominal pain (97%; n = 150). The most frequent examination finding was tender hepatomegaly (91%; n = 141). 25% (n = 38) of the patients had pleural effusions, which were more common on the right side (20%; n = 31). However, 2% of the patients had left-sided effusions, and 3% had bilateral effusions. When evaluated for alcohol consumption, it was found that ALA patients were more likely to be alcoholics (p = 0.013) and had more weight loss (p = 0.008). None of the subjects tested positive for hepatitis B and C while 2% were HIV positive. (Table 5)

The complete laboratory data of the patients were presented in Table 6.

Amoebic IgM antibodies were positive in 70% (n = 100) of patients. 13.5% (n = 21) of pus cultures were positive for gram-negative bacteria, with E. coli (6%; n = 8) being the most frequently isolated organism. However blood cultures were positive in only 2% of the cases. (Table 7)

In patients with ALA, colonic involvement in the form of erythema and ulceration was seen in 75% (n =83) patients. Amongst these, cases of multiple ALA had significantly more colonic involvement (90% vs 70%; p= 0.03). Overall 60% patients had isolated cecum involvement followed by lesions involving both right colon with transverse colon (22%). 15% had isolated ascending colon involvement and 3% cases had isolated transverse colon involvement.

In patients with solitary ALA, there was significantly more isolated cecal involvement 56% versus 10 % in multiple ALA (p=0.0001). Isolated ascending colon and transverse colon were also more involved in solitary ALA but results were not statistically significant. However there was statistical significant involvement of the right and transverse colon in cases of multiple ALAs compared to solitary ALA (81% vs 15%, p= 0.0001). (Tale 8)

On histological examination flask-shaped ulcers and acute inflammatory cells were frequently observed, but only 18% (n=15) of the patients had trophozoites that invaded the lamina propria. 78% of ALA cases had small colonic ulcers (< 3 cm), while 22% of patients had large ulcerations (>3 cm). Small ulcerations were seen in the cecum, ascending colon or hepatic flexure without any surrounding hyperemia. Small ulcerations were significantly higher among cases of multiple ALAs compared to solitary ALA

(P=0.0003). Large colonic ulceration were also more commonly associated with multiple compared to solitary ALA but results were not statistically significant (40% versus 25%; p= 0.18).

Abscess drainage with percutaneous needle aspiration were done in 80% (n = 124) cases. 15% (n = 23) underwent pigtail drainage. Open surgical intervention was required for managing rupture in 5% (n= 8) patients (Table 9). Out of them, 3 died; with overall mortality of 2 %.

Multivariate regression analysis showed that volume of abscess was directly proportional to the levels of serum alkaline phosphatase (p = 0.03). While the length of hospitalisation was proportional to duration of fever (p = 0.03), values of ESR (p = 0.03), and INR (p = 0.02). It was inversely related to serum albumin (p = 0.03).Mortality was higher among females (p = 0.001), those with longer duration of fever (p = 0.001), icterus (p = 0.001) and ascitis (p = 0.004) (Table 10)

Discussion

Liver abscess (LA) is common condition in the tropical areas. E. histolytica (amoebic), bacterial, and fungi are the most frequent causes of LA. In developing nations like India, ALA is the leading cause of LA. They typically have an impact on younger people, particularly males. Abdominal pain, fever, and weight loss are frequent presenting complaints in patients with LA.

In our study we found ALA accounted for about 72% of cases. Solitary ALA were predominant with right lobe predilection, similar to studies by Sharma et al and Mukhopadhyay et al. [10,13]. Similar to the previous studies, the majority of patients in our study were young alcoholic males (with mean age of 40 years) of lower socioeconomic class. These results can be explained by the high alcohol use among young males and the fact that alcohol inhibits the liver's Kupffer cells, which play a critical role in amoeba clearance. Additionally, the high iron level of liquor makes regular drinkers more susceptible to invasive amoebiasis. [14]. According to a study by Reddy and Thangavelu, the females are less affected as menstrual cycle lessens the likelihood of hepatic abscess formation by preventing hepatic congestion [15].

Study by Ochsner et al. found pyogenic liver abscesses (PLA) was more common in young male patients with intra-abdominal infections [1]. Usually PLA is predisposed by illnesses such as acute cholecystitis, choledocholithiasis, biliary-enteric bypass surgeries, chronic pancreatitis, diverticulitis, colonic perforation, appendiceal abscess, malignant obstruction of the common bile duct, cholangiocarcinoma, pancreatic carcinoma, and colonic carcinoma. However, the prevalence of cryptogenic PLA without a known cause is rising [16]. In our study, PLA accounted for about 16% of cases. Majority of cases had multiple abscesses involving the right lobe. Mean age of PLA was similar to overall average (42 years compared to 40 years overall). However our findings were contrasting to Pang et al. and Heneghan et al. where average age of presentation was 65 and 60.3 years, respectively. E.coli was the most common gram negative pathogen organisms similar to previous studies [17,18].

In our study incidence of tubercular liver abscess was 1 % in comparison to Essop et al where 0.34% of patients presented with hepatic tuberculosis [19]. Incidence of tubercular liver abscess (TLA) is low as liver is unfavorable for growth of tubercular bacilli due to low oxygen levels. In our patients all cases of TLA were solitary. All the cases were AFB positive and were associated with ascitis. Fungal abscesses were the rarest cause of LA in our study. 3 fungal abscess cases were found in our study and all of them were positive for Candida and HIV. One of them had history of diabetes mellitus.

Abdominal pain and fever were the most prevalent LA symptoms seen in 97% and 93% of cases, respectively. This was comparable to findings from other studies, which ranged from 62 to 94% and 6 to 77%, respectively [10,13]. Diarrhoea was present in 28% of LA patients compared to previous studies that reported range of 4% to 33% [10]. This could be due to intestinal amoebiasis involving the colon. Cough was rare symptom seen in 12% versus 3.5–24% reported in previous studies [10]. Pleural effusion and collapse of the lung parenchyma were the two most common causes of cough in patients of LA. As pleural effusion spontaneously resolved after treating the abscess, this was typically caused by reactive pathology. Jaundice and ascites were uncommon signs of LA. Icterus usually develops as a result of damage bile ducts and hepatic veins due to intrahepatic biliary obstruction because of enlarging abscess or biliovascular fistula due to hepatic necrosis [20]. However, in our study no cases of biliovascular fistula were found. In comparison to the other studies that found 45- 50% of subjects to have icterus, our study showed an

incidence of 30%. Yoo et al. found a decrease in incidence of jaundice from 25% to 7% after antimicrobial treatment, which is similar to our study [21].

With a sensitivity of 92 to 97%, abdominal ultrasonography is the preferred diagnostic method for hepatic disorders like liver abscess. The sagittal plane scan aids in localizing the precise section affected by locating the abscess relative to the hepatic circulation [22].The right lobe's sixth and seventh segments were the most frequently affected in our study. The right lobe is more frequently involved because it receives the majority of blood from the right colon, which is the main location of intestinal amoebiasis. Additionally, the right lobe has a higher blood flow volume and denser biliary canaliculi, which increases congestion [23].

In our study, 75% of ALA patients had colonic ulcerations. Patients who had multiple ALA were substantially more likely to develop these lesions (90% vs. 70%, P=0.03). Colonic involvement was detected in 58% of ALA patients according to Sachdev and Dhol, whereas 55% of cases according to Mishra et al [6,7].When compared to solitary ALA, multiple ALA were more likely to have small ulcerations (<3cm) (P=0.0003). Similar to Goswami et al we found that colonic involvement was commonly seen proximal to the hepatic flexure. The most often affected area was the cecum (70%) followed by the right colon with transverse colon (38%) and the isolated ascending colon (25%). When compared to solitary ALA, those with multiple ALAs had a significantly higher involvement of the transverse colon as well as the right colon (P=0.0001). [24] This is due to the streamlined portal blood flow, in which the left lobe of liver received blood from the spleen and colon and the right from the small intestine [25].

Percutaneous needle aspiration was performed in the majority of patients (80%) [26]. 5% of the patients required surgical intervention due to abscess rupture. However inaccessible anatomical locations, failure to respond to treatment after conservative therapy, and complications such as peritonitis and biliary-enteric fistulisation were other reasons for surgical intervention. The overall mortality rate was 2%, which was comparable to previous studies reporting 2- 15% [27]. Average age in this group was 65 years (range: 43 to 78 years) compared to overall average of 45 years. 2 of these patients were female: 2 ALA, 1 PLA. All of them had icterus and hepatomegaly, while two patients also had pallor and one had ascites. In addition, they showed higher laboratory abnormalities such as ESR of 35mm in the first hour, haemoglobin of 8 gm/dL, TLC of 35000/uL, urea of 150mg/dL, bilirubin of 5.6 g/dL, albumin of 2.2 g/dL, SGOT of 250 IU/L, SGPT of 223 IU/L, ALP of 1400 IU/L, and INR of 1. On ultrasound, 2 of 3 abscesses were found to be solitary mainly involving the right lobe with a mean volume of 388 cc. The average hospital stay among those who died was 14 days (3–18 days). The presence of icterus and ascites, longer duration of fever prior to presentation, and female gender were associated with mortality.

Conclusion

In our study, solitary amoebic liver abscess, involving the right lobe was the most frequent pattern. The young alcoholic male from a lower socioeconomic category were most commonly affected, with the average age of 40 years. However patients in their sixth decade had a greater fatality rate. Colonic involvement was most commonly seen in amoebic liver abscess, with nearly all patients having involvement of the cecum and ascending colon. In multiple amoebic liver abscesses, the colonic involvement extended beyond hepatic flexure. The fact that all patients received etiology-specific antimicrobials and minimally invasive draining procedures contributed to the overall low mortality. Mortality was higher among patients undergoing surgical intervention for rupture.

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Table: 1 Demographic Characteristics of liver abscess patients.

Parameters	N =155
Age, Median(IQR)	40.3 (21,76)
MALE % (n)	60 (93)
Male : Female	1.5:1
Socioeconomic status, % (n)	

Upper class	5% (8)
Upper middle class	13% (20)
Lower middle class	22% (34)
Upper lower class	29% (45)
Lower class	31 %(48)

Table: 2 Aetiological classification of liver abscess patients.

Aetiology	% (n)
Amoebic liver abscess (ALA)	72%(111)
Pyogenic liver abscess (PLA)	20% (31)
Tubercular liver abscess (TLA)	1% (2)
Fungal liver abscess	2% (3)
Mixed (amoebic & pyogenic)	5% (8)

Table: 3 Ultrasonographic findings for liver abscess patients.

	Parameters	Percentage (n)
Lobe	Right	68% (105)
	Left	21% (33)
	Bilateral	11% (17)
Number	Solitary	62% (96)
	Few (≤3))	12% (18)
	Multiple (>3)	26% (41)
Typhlitis		4%
Abscess volume in ml Mean (SD)		217(124)
	VII	32% (50)

Segment involved	VI VIII V IV Rest	27% (42) 11% (17) 8% (13) 10% (15) 12% (18)

Table 4: Comparision of anatomical involvement of liver in various liver abscess patients

Parameters	Solitary liver abscess	Multiple liver abscess	P value
Amoebic liver abscess (ALA)	70 (63%)	30 (27%)	0.001
Pyogenic liver abscess	8 (25%)	23 (75%)	0.0001
Tubercular liver abcess	2 (100%)	0 (0)	0.0001

Table: 5 Clinical profile of Liver Abscess patients.

	Parameters	Percentage (n)	P value
Symptoms	Pain abdomen	97% (150)	
	Fever	93% (144)	
	Anorexia	91% (141)	
	Nausea/vomiting	47% (72)	
	Diarrhoea	28% (43)	
	Cough	12% (19)	
	Weight loss Amoebic liver abscess Pyogenic liver abscess Tubercular liver abscess	45% (69) 33% (52) 10% (16) 0.6% (1)	0.008
Risk Factors	Alcoholic Amoebic liver abscess Pyogenic liver abscess Tubercular liver abscess	76% (117) 57% (89) 17%(27) 0.6%(1)	0.002

	Diabetic	12% (19)	
	HIV positive	2% (3)	
	HbsAg & HCV	0 (0)	
Signs	Pallor	40% (62)	
	Jaundice	30% (46)	
	Tender Hepatomegaly	91% (141)	
	Splenomegaly	11% (17)	
	Ascitis	10% (15)	
	Pleural effusion Right sided pleural effusion Left sided pleural effusion Bilateral pleural effusion	25% (38) 20%(31) 2%(3) 3%(4)	

Table: 6 Laboratory investigations in Liver abscess patients.

Parameters	Mean (SD)	Out of range cut off	Out of range percentage
ESR (mm 1st hr)	43 (28)	>20	75%
Hb(gm/dl)*	10.5 (1.6)	<11	42%
TLC (per uL)#	21000 (8560)	>11000	88%
INR	1.38(0.22)	>1.2	78%
Bilirubin (mg/dL)	2.50(1.87)	>1.2	25%
SGOT(IU/L)$	90(36)	>50	42%
SGPT(IU/L)@	76 (32)	>50	46%
Alkaline phosphatises(IU/L)	720 (223)	300	80%
Albumin (g/dL)	2.9(0.45)	<3.5	78%
Urea (mg/dL)	42(18)	>45	22%
Calcium(mg/dL)	8.2(0.8)	<8	30%

*Hb- haemoglobin, #TLC- total leukocyte count, $SGOT- Serum glutamic-oxaloacetic transaminase, @ SGPT- Serum glutamate-pyruvate transaminase

Table: 7 Etiological analysis in liver abscess patients.

	Parameter	Percentage (*n*)
Appearance	Anchovy sauce Purulent	68% (105) 15% (23)
Amoebic serology Positive		70% (100)
AFB positivity on pus		1% (2)

Fungal culture on pus	*Candida*	2% (3)
Positive cultures on pus		13.5% (21)
Etiological agents in positive pus culture	*E.coli* *Klebsiella* *Pseudomonas* *Acinetobacter* *Staphylococcus* *Enterococcus* *Citrobacter*	6% (8) 3.5% (5) 1% (2) 1% (2) 1% (2) 0.5% (1) 0.5% (1)
Blood culture positive		2% (3)

*AFB- Acid Fast Bacilli

Table 8: Colonic involvement in amoebic liver abscesses (ALAs)

Colon segment	% (n) 72% (111)	Solitary ALA, % (n) 63% (70)	Multiple ALAs % (n) 27% (30)	P Value
Colon lesion (involved)	75% (83)	70% (44)	90% (27)	**0.03**
Isolated cecum	60% (50)	56% (25)	10% (3)	**0.0001**
Isolated ascending colon	15% (12)	22% (10)	7% (2)	0.18
Isolated transverse colon	3% (3)	6% (3)	0 (0)	
Transverse colon + right colon	22% (18)	15% (6)	81% (22)	**0.0001**
Colonic lesions (cm) <3 (small) >3 (large)	83(100) 78% (64) 22% (10)	44 (100) 60% (26) 40% (18)	30 (100) 75% (23) 25% (7)	 **0.0003** 0.18

Table: 9 Management outcomes in liver abscess patients.

	Parameters	Percentage (*n*)
Abscess drainage	Percutaneous needle aspiration Pigtail drainage Open surgical	80% (124) 15% (23) 5% (8)

Change of antimicrobials required		22% (34)
Duration of Mean(SD)	Hospitalisation Treatment	12(4.5) 35 (10)
Surgical intervention		5% (8)
Mortality		2% (3)

Table: 10 Multivariate analysis of abscess size and duration of hospitalisation and Mortality with various clinical and laboratory variables.

	Parameter	Correlation coefficient	P value
Abscess volume	Anemia Alkaline phosphatise	−0.31 0.34	0.004 0.03
Duration of hospitalisation (morbidity indicators)	Duration of Fever ESR INR Albumin	 0,17 0.23 -0.25	 0.03 0.03 0.02 0.03
Mortality	Females Duration of fever Icterus Ascites		0.02 0.001 0.001 0.004