

Amoebic vs pyogenic liver abscesses: A comparative study in a tertiary care hospital

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ABSTRACT

Background and Objectives: Liver abscess is a potentially life-threatening condition with a majority of cases being amoebic in tropical countries. In India, poor sanitary conditions and low socioeconomic status contribute to the endemicity of amoebiasis. As treatment modalities are different for amoebic and pyogenic liver abscesses (ALA and PLA, respectively), it is necessary to differentiate them. Facilities for amoebic culture are not available and microscopy is nondiscriminatory, hence serological tests are greatly relied upon for the identification. No studies have been done so far in our region on patients admitted with liver abscess. The aims of this study were to find the aetiology of liver abscess in admitted patients and to know the proportion of amoebic liver abscess using serological techniques. **Materials and Methods:** The study was done for 6 months and the sample size was 50. The ultrasonography (USG)-guided aspirates were subjected to microscopy and aerobic and anaerobic cultures on appropriate media. Serum samples of all patients were examined for *Entamoeba histolytica* immunoglobulin G (IgG) antibodies by enzyme-linked immunosorbent assay (ELISA) along with 35 control samples. **Results:** Of the 50 patients, 34 were diagnosed as amoebic by (ELISA) (68%), 11 as pyogenic (22%) and five as indeterminate (10%). Alcohol was found to have a higher association with ALA than with PLA. Of the 34 amoebic liver abscesses, only four (8.8%) showed motile trophozoites. The mortality rate was only 2.2%. **Conclusion:** Rapid diagnosis with serology and prompt treatment can result in reduced hospital stay in cases of ALA.

Key words: Amoebic, enzyme-linked immunosorbent assay (ELISA), *Entamoeba histolytica*, liver abscess, pyogenic

INTRODUCTION

Liver abscess, a potentially life-threatening intra-abdominal infection, falls broadly into two categories: Amoebic liver abscess (ALA) and pyogenic liver abscess (PLA). In tropical and subtropical countries, 50-70% of cases of liver abscess are amoebic in origin.^[1] ALA accounts for 3-9% of all cases of amoebiasis.^[2] The incidence of PLA ranges 1.1-2.3 cases per 1,00,000 population every year. They are frequently polymicrobial, with *Klebsiella pneumoniae*, *Escherichia coli*, *Streptococcus milleri* and *Bacteroides fragilis* being the most common isolates.^[3] About one-fourth of cases are cryptogenic. In 25% of patients, abscesses are sterile, probably due to antibiotic treatment.^[4] The differentiation of ALA from PLA is greatly assisted by amoebic serology, as liver function tests and microscopy are non-discriminatory, facilities for amoebic culture are lacking and the positivity rate of bacterial culture is often affected by prior antibiotic therapy. The enzyme-linked

immunosorbent assay (ELISA) test, which determines the anti-lectin immunoglobulin G (IgG) antibody, is the most frequently used serological test.^[5]

At our institution in central Kerala, India, patients with liver abscess are treated successfully with percutaneous drainage, blanket therapy of antibiotics and anti-amoebic drug combinations, but the exact prevalence of invasive amoebiasis with liver abscesses remains undetected due to non-availability of serological diagnostic tests for routine screening of ALA. This study aims to find out the aetiology of liver abscess in patients admitted with specific predisposing factors, if any, and to know the proportion of ALA using the IgG ELISA test.

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MATERIALS AND METHODS

The study was carried out at Government Medical College, Thrissur, Kerala. The study protocol was approved by the Institutional Research Committee. The study period was 6 months: From June 2012 to November 2012.

Inclusion criteria

Patients with clinical features, laboratory investigations and ultrasonographic (USG) evidence of liver abscess who were admitted to the Surgery unit were included in this study.

Exclusion criteria

Patients aged less than 18 years, those with organized abscess and pregnant females were excluded.

Informed consent was obtained from all the subjects involved. Detailed history, symptoms, signs, therapeutic interventions and laboratory data on admission and during the clinical course were recorded. USG-guided abscess aspirates were subjected to microscopy (wet film for trophozoites of *Entamoeba histolytica*, Gram stain for bacteria and acid-fast stain for *Mycobacterium tuberculosis*), aerobic (MacConkey and blood agar) culture and anaerobic culture (Anaerocult, Merck diagnostics, Darmstadt, Germany) for bacteria. The isolates were identified by standard methods.^[6] Blood samples (5 mL) were collected from all patients, serum was separated and all the samples were tested for hepatitis B surface antigen (HBsAg) and antibodies to human immunodeficiency virus (HIV), hepatitis A, hepatitis C and hepatitis E by ELISA to rule out other causes of hepatic infections, before testing the samples for anti-amoebic IgG antibodies using a commercially available ELISA kit (Novalisa™ *Entamoeba histolytica* IgG ELISA, ENTG0140, NovaTec Immunodiagnostic GMBH, Dietzenabach, Germany). Thirty-five age, sex and locality matched control samples with no history of liver disease were also tested for anti-amoebic IgG antibodies.

ALA was defined with sterile bacterial cultures, the presence of the trophozoite of *Entamoeba histolytica* in wet film microscopy and/or positive ELISA test for anti-amoebic antibodies.^[1] PLA was defined by positive bacterial cultures/infection or abdominal pathology in the distribution of the portal vein and negative amoebic serology.^[1,3] Those patients with liver abscess who did not fall under either of the two groups were termed indeterminate.

Control sample size was calculated using the formula, $(Z \alpha + Z \beta)^2 \times p_1 q_1 / d^2$

where p = proportion = $p_1 + p_2/2$ (p_1 = proportion of ALA in diseased and p_2 = proportion of ALA in endemic

areas in normal individuals, $q = 100 - p$, $d = p_1 - p_2$, and $(Z \alpha + Z \beta)^2 = 7.14$, a constant; $p_1 = 50$, $p_2 = 10$

Data entry and data analysis were done using Microsoft EXCEL (Washington, USA) and Epi info (CDC, Atlanta, Georgia, USA). A P value less than 0.05 was considered statistically significant when comparing the two groups with liver abscess.

RESULTS

Of the 50 patients with liver abscess studied, 34 (68%) were diagnosed as amoebic, 11 (22%) as pyogenic and five (10%) as indeterminate. The age range was 24-85 years and 49 (98%) of the patients were males. The personal histories of the 50 patients are shown in Table 1.

Several demographic, behavioural, clinical and laboratory parameters were compared between the two main groups (ALA and PLA) to find out whether we can distinguish between the two, as their treatment and prognoses differ [Tables 2 and 3]. There was a higher association of alcohol intake with ALA compared to PLA. Findings from USG of patients with ALA and PLA are shown in [Table 4].

All the 50 cases tested for HBsAg, antibodies against HIV, and hepatitis A, C and E turned out to be negative.

Table 1: Main factors in the personal history of 50 patients admitted with liver abscess

Factors	N [%]
Alcohol	40 [80]
Smoking	24 [48]
Diabetes mellitus	11 [22]
Hypertension	2 [4]
Trauma	2 [4]

Table 2: Comparison of demographic, behavioural and clinical parameters in patients with amoebic and pyogenic liver abscess

Parameters analysed	Amoebic abscess [34 cases]		Pyogenic abscess [11 cases]		P value
	N	Percentage (%)	N	Percentage (%)	
Age >50 years	21	61.7	7	63.6	NS
Age <50 years	13	38.3	4	36.4	NS
Alcohol	31	91.1	6	54.5	.01
Smoking	19	55.8	3	27.2	NS
Diabetes mellitus	7	20.5	3	27.2	NS
Fever	32	94.1	10	90.9	NS
Abdominal pain	30	88.2	11	100	NS
Jaundice	14	41.1	6	54.5	NS
Vomiting	5	14.7	4	36.3	NS
Diarrhoea	1	2.9	2	18.2	NS

NS: Not significant

While 34/50 (68%) cases were positive for anti-amoebic IgG antibodies by ELISA, 4/34 (8.8%) of ALA showed motile trophozoites of *Entamoeba histolytica* on wet film examination. Among the 35 age-, sex- and locality-matched control samples tested, with no history of liver disease, four (11.4%) were positive for anti-amoebic antibody by ELISA.

Out of 50 cases, 11 (22%) cases were defined as PLA. One patient had a history of trauma with injury to the abdomen and had had surgical intervention 2 years back. Another gave a history of chronic pancreatitis. Samples from six cases of PLA out of 11 (54.5%) yielded bacterial isolates by aerobic culture. Polymicrobial infection (*Escherichia coli* and *Enterococcus faecalis*) was diagnosed in one patient (9%), and none of the cases showed anaerobic growth [Table 5]. Three of the five culture-negative PLA cases were complicated by ruptured liver abscesses. One of them developed pelvic abscess and another had appendicitis.

Five cases of liver abscess (10%) could not be grouped into either of the two major groups. They were negative

for amoebic serology and their culture was sterile. No predisposing abdominal pathology could be found in these cases.

All the patients included in this study group had undergone percutaneous drainage. PLA was treated with broad-spectrum antibiotics, drainage and surgery with peritoneal lavage in three cases of ruptured liver abscess. There was no mortality in the pyogenic cases. The average duration of hospital stay in this group was 11 days. ALA cases were also treated with broad-spectrum antibiotics including Metronidazole and Ciprofloxacin for 10 days. One patient died in this group (2.9%) with rupture of the liver abscess into the peritoneal cavity. The average duration of hospital stay for ALA patients was 9.75 days.

DISCUSSION

Amoebiasis is a protozoan disease that affects 10% of the world population, with a high prevalence in Mexico, South Africa, some areas in the Middle East, South Asia, Southeast Asia and parts of West Africa and South America.^[3]

Of the 50 cases of liver abscess studied, 34 (68%) were found to be amoebic in origin by serology and 16 (22%) were pyogenic. This reinforces the findings of previous studies conducted in the tropical countries which showed higher incidence of ALA in this area compared to PLA.^[1,7] ALA has a predilection for middle-aged men and is less common at extremes of age, whereas PLA is often seen in individuals >50 years.^[3,8] In the present study, no significant difference could be seen between the two types of liver abscess in the age group, as 61.7% of ALA and 63.6% of PLA occurred in patients >50 years. This upward shift in the age range has been observed in earlier reports.^[9,10] With the development of better diagnostic techniques, early antibiotic administration, and the improved survival of the general population, the demography has shifted towards the sixth and seventh decades of life. Male preponderance to both diseases has been reported in various studies.^[3,11] The difference in gender incidence could reflect differences in environmental exposure related to occupation, although the precise underlying explanation remains unknown.

Diabetes mellitus as a risk factor for PLA has been mentioned in various studies.^[7,12] However, in the present study no significant difference could be seen for diabetes as a risk factor between the two diseases under discussion. Alcohol suppresses the functioning of Kupffer cells in the liver and is a direct hepatotoxin. A high content of iron in the diet, often from country liquor in habitual drinkers, predisposes to invasive amoebiasis.^[12,13] In the present study,

Table 3: Comparison of laboratory parameters in patients with ALA and PLA

Parameters analysed	ALA [34 cases]		PLA [11 cases]		P value
	N	Percentage (%)	N	Percentage (%)	
Leucocytes >12,000 µ/L	27	85.2	10	90.9	NS
Bilirubin >1 mg	19	55.8	6	54.5	NS
ALT [U/L] >2N	16	47	6	54.5	NS
AST [U/L] >2N	27	79.4	11	100	NS
Serum albumin <3 gm/d	19	55.8	4	36.3	NS

NS: Not significant; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase

Table 4: Type and intra-hepatic location of abscesses by USG

Distribution	Amoebic [34 cases]		Pyogenic [11 cases]		P value
	N [%]	N [%]	N [%]	N [%]	
Single abscess	14 [41.2]		8 [72.7]		NS
Multiple abscess	20 [58.8]		3 [27.3]		NS
Right lobe	27 [79.5]		7 [63.6]		NS
Left lobe	1 [2.9]		1 [9.1]		NS
Both lobes	6 [17.6]		3 [27.3]		NS

NS: Not significant

Table 5: Bacterial isolates in 11 cases of pyogenic abscess

Bacteria	N
<i>Klebsiella pneumoniae</i>	2
<i>Escherichia coli</i>	2
<i>Pseudomonas aeruginosa</i>	1
<i>Acinetobacter baumannii</i>	1
<i>Enterococcus faecalis</i>	1

consumption of alcohol, especially toddy, was found to be high in both groups (ALA 91.1% and PLA 54.5%). There is a higher proportion of alcohol intake in ALA when compared to PLA in our study.

Blood parameters for both types of abscesses are similar, with increased erythrocyte sedimentation rate (ESR), leucocytosis with shift to left and slight changes in liver function tests. In cases secondary to biliary tract infection, bilirubin levels are often raised. In our study, 85.2% of ALA and 90.9% of PLA cases showed leucocytosis with no significant difference. Bilirubin, liver enzymes and alkaline phosphatase levels were all raised in both groups, with no statistically significant difference. This is comparable to various other studies.^[3,7]

USG and computed tomography (CT) scanning have proved particularly useful for demonstration and drainage of abscesses. However, it is observer-dependent, and the sensitivity is 92-97%.^[7,11,13] ALA usually occurs in the right lobe of the liver and is solitary in 30-70% of cases. Multiple liver abscesses occur in 4-42%, and 20-35% have abscess in the left lobe.^[1,2,8] The predilection of ALA in the right lobe is because that lobe receives most of the blood draining from the right colon, the primary site of intestinal amoebiasis. Diseases of the colon, e.g., appendicitis or diverticulitis, predisposing to PLA are also very common in this region. Another factor is that the volume of blood flow is more in the right lobe and the biliary canaliculi are denser, thus leading to more congestion.^[13] The present study did not find any correlation between the presence of either single or multiple lesions, the site of the lesion and the underlying disease. Similar results were obtained by various other studies.^[3,7,14]

The sensitivity and specificity of conventional microscopy in diagnosis of *Entamoeba histolytica* are less than optimal, with only 11-25% of motile trophozoites visible.^[1,5] In the present study, only 8.8% of ALA cases revealed motile trophozoites on wet film examination of the liver aspirate. There are several factors that adversely affect the results of microscopy. Lack of well-trained personnel; delayed deliveries to the lab; difficulty in differentiation between non-motile trophozoites, neutrophils, macrophages and tissue cells; inadequate collection conditions; and interfering substances such as antibiotics are the factors that make microscopic diagnosis quite inadequate.

The absence of serum antibodies to *Entamoeba histolytica* after 1 week of symptomatic liver disease is strong evidence against a diagnosis of invasive amoebiasis. They are detected in 85-95% of all patients with

invasive amoebiasis.^[5,8] The indirect haemagglutination (IHA) test has been replaced by commercially available ELISA kits for serodiagnosis of amoebiasis. ELISA is relatively simple, easy to perform, rapid, inexpensive, and more sensitive. Of the recommended serological tests, those that detect the presence of anti-lectin IgG antibodies are the most frequently used for diagnosis.^[5] In the present study, after eliminating HIV and hepatitis A, B, C and E, 34 of the 50 cases (68%) with liver abscess that were sterile by bacterial culture were positive for anti-amoebic IgG antibodies. As antibodies persist for many years, ELISA or IHA cannot distinguish acute from remote infection in areas of endemicity such as ours. This may be the reason for the positivity of the four control samples (11.4%) without USG-proved liver abscess.

Of the 11 cases defined as pyogenic, which were negative for IgG anti-amoeba antibody, in six cases bacterial isolates were obtained from aerobic culture (54.5%) with both *Klebsiella pneumoniae* and *Escherichia coli* in two samples each. This is similar to the findings of another study.^[3] In one patient (9%), polymicrobial infection was diagnosed with both *Escherichia coli* and *Enterococcus faecalis*. This is less when compared to other studies.^[1,3] In five cases of PLA, culture was sterile, which may be partly due to the early antibiotic treatment. Lack of anaerobic agents may be due to lack of a good transport system, delay in processing, and early antibiotic treatment.

The treatment of ALA consists of intra-luminal and systemic administration of amoebicides as soon as possible.^[1,3] Guided percutaneous drainage is performed in cases of large abscess >5 cm, those in the left lobe, and when no response to medical treatment occurs.^[2,3] There is no indication for routine aspiration in ALA. A combination of USG findings with positive serology in an appropriate clinical setting is adequate to start drug treatment. In our study, all the cases of ALA underwent percutaneous drainage. They were treated with Metronidazole and Ciprofloxacin for 10 days. Open surgical drainage is rarely indicated in ALA. It is done only when the abscess has ruptured into the adjacent viscera or the peritoneum. In our study, one patient with ALA had a rupture for which exploratory laparotomy with peritoneal lavage was done. The mortality rate was 2.2% as one patient with rupture into the peritoneal cavity could not undergo surgery due to poor general condition. The rest of the patients were discharged, with an average of 9.75 days' hospital stay. After the clinical cure, the sonographic abnormality takes several months to disappear. Therefore, clinical criteria rather than USG should be used to monitor the results of the treatment.^[8]

The treatment of choice for PLA, i.e., percutaneous drainage and antibiotics, cures 72-90% of patients.^[1] In the present study, all patients with PLA had percutaneous drainage and were treated with broad-spectrum antibiotics. Surgery with peritoneal lavage was done in three cases of rupture with no mortality.

CONCLUSION

Our area is endemic for amoebiasis, thus ALA is predominant here. Alcohol intake was found to have a higher association with ALA when compared to PLA. No single clinical or biochemical parameter could be obtained to differentiate between the two diseases. No significant difference could be seen between ALA and PLA in the distribution of abscesses. Amoebic serology was found to be useful in diagnosing ALA along with clinical and radiological findings, even though the presence of remote infection could not be ruled out. As ALA is a potentially life-threatening infection, rapid diagnosis is mandatory so that prompt treatment can follow, resulting in rapid recovery. As the sensitivity of microscopy is poor, with little or no available culture, serodiagnosis in patients with suspected amoebic abscess is often an important tool in clinical decision-making. This is a pilot study with a relatively small number of cases, but it is the first of its kind in our setting and it emphasises the need to conduct further studies.

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Conflicts of interest

There are no conflicts of interest.

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