

Amoebic Liver Abscess: A Complete Overview in Tertiary Care Centre

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ABSTRACT

Introduction: Amoebiasis is defined as human infection with protozoan parasite, *Entamoeba histolytica* regardless of the clinical outcome. It commonly resides in large intestine but can invade to other organs. Amoebic Liver Abscess (ALA) is the most common complication of invasive amoebiasis.

Aim: To study various aspects of ALA like demographic profiles, clinical features, radiological and laboratory findings and treatment.

Materials and Methods: A cross-sectional study was performed in the Department of Microbiology, Maulana Azad Medical College, New Delhi, India, from October 2012 to April 2014. Pus, blood and stool samples were taken from each patient after taking informed consent and examined for trophozoite by microscopy, IgG antibody and antigen of *Entamoeba histolytica* by ELISA respectively. The results were presented as mean for quantitative variables and percentages for qualitative data. Calculations were done using Microsoft Excel software.

Results: Total 65 patients with age more than 18 year were

enrolled in the study out of which 39 cases (60%) were diagnosed as ALA. The age ranged from 18 to 90 years (mean age 37.1 year). Male patients were dominated over female. About 74.3% patients were addicted to alcohol. Most patients had acute presentation. Pain in abdomen and fever were the most common symptoms observed (97.4% and 94.8% respectively). The right lobe was involved in 76.9% cases. Solitary abscess was found in 82.0% cases out of which 64.1% were in right lobe. Volume of abscess ranged between 70 cc and as much as 1200 cc. Volume less than 300 cc was seen in 17 cases (43.5%) and more than 300 cc was seen in 22 cases (56.5%). Pleural effusion and intra peritoneal rupture were the two complications (28.2% and 10.2%) found in this study. All patients were treated successfully with or without help of percutaneous intervention.

Conclusion: ALA presents itself through various non specific symptoms and signs. Confirmation of diagnosis is made possible with the help of radiological and microbiological methods. Prompt diagnosis and treatment can markedly reduce the complication and mortality.

Keywords: ELISA test, Right lobe, Solitary abscess

INTRODUCTION

Liver is the most common organ which is prone to development of abscess, contributing about 48% of all visceral abscess and 13% of all intra-abdominal abscess [1]. Liver abscess fall broadly into two categories- amoebic and pyogenic. Pyogenic Liver Abscess (PLA) is more common in developed world, while Amoebic Liver Abscess (ALA) is more common in developing world.

ALA is the commonest extraintestinal manifestation of amoebiasis which arises due to spread of *Entamoeba histolytica* from the large bowel to the liver via the portal vein [2]. *Entamoeba histolytica* infects 10% of world population, out of which 10% develop invasive amoebiasis and 1-10% of them develop ALA [3]. Most of the infected persons reside in tropical and subtropical countries like tropical Asia, Africa, Mexico, Central and South America [4].

In developing countries, amoebiasis is more common due to poor sanitary conditions and lower socioeconomic status. Other

predisposing factors for ALA are alcoholism, homosexuality and individuals with AIDS or immunosuppression. In developed countries, amoebic liver abscess is rare and is found almost exclusively in travellers and immigrants.

ALA presents itself more commonly with fever and right upper quadrant pain. There may be uncommon manifestations due to rupture of abscess in neighbouring cavities like pleura, pericardium and peritoneum, compression of tubular structures in hepatic hilum and distant embolic dissemination. Ultrasonography is the method of choice for diagnosis of liver abscess [3]. ALA should be further confirmed by microscopic examination of pus for amoebic trophozoites and detection of serum anti-amoebic IgG antibody by Enzyme Linked Immunosorbent Assay (ELISA). Although, the presence of amoebic trophozoites in aspirated pus is confirmatory for ALA, it is not a sensitive method of diagnosis [5]. So, detection of serum anti-amoebic antibody is the most frequently used for its diagnosis. Early diagnosis and treatment of ALA is essential

as it results in low morbidity and mortality.

This study was carried out to look for various aspects of ALA like demographic profile, clinical presentations, association with intestinal disease, radiological and laboratory findings, treatment modalities and complications.

MATERIALS AND METHODS

A cross-sectional study was planned and conducted at the Department of Microbiology and Department of Surgery, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi, India, from October 2012 to April 2014. Ethical clearance was taken from institutional ethical committee. All radiologically confirmed liver abscess cases which were above 18 years of age were considered for the study. Immunosuppressed patients, cases of bleeding diathesis and hydatid cyst were excluded from the study. Informed consent was taken from all subjects prior to their inclusion into study. All patients underwent physical examination, hematological, biochemical and radiological investigations. Pus, blood and stool samples were collected and processed in the Microbiology laboratory as follows.

Pus and Blood Culture

Direct microscopic examination of pus was done to visualize the presence of trophozoites of *Entamoeba histolytica*. Direct Gram's stain was performed to look for pus cells and bacterial agents. Bacteriological culture was done aerobically using 5-10% sheep blood agar and McConkey's agar at 37°C for 18-24 hours and anaerobically using cooked meat broth and Brucella blood agar with hemin and vitamin K1 (HiMedia, Mumbai) at 37°C upto 7 days.

About 5 to 10 mL blood sample was collected from each patient in blood culture bottle and incubated at 37°C. Subcultures were made on 5-10% sheep blood agar and McConkey's agar on 2nd and 5th day and incubated at 37°C.

Serology

Two mL blood sample was collected in plain Vacutainer® vials (Becton, Dickinson and Company, USA). It was allowed to clot for 30 minutes and centrifuged at 2000 to 3000 revolutions per minute for 10 minutes to separate serum and examined for the presence of antibodies to *E. histolytica* by ELISA (IVD Research Inc., Carlsbad, California).

Stool Investigations

Stool sample was examined macroscopically for color, consistency, presence of mucus, blood, worms and microscopically for presence of trophozoites of *Entamoeba histolytica* or any other parasite. It was also examined for presence of antigen of *Entamoeba histolytica* by ELISA (IVD Research Inc., Carlsbad, California).

STATISTICAL ANALYSIS

The results were presented as mean for quantitative variables and percentages for qualitative data. Calculations were done

using Microsoft Excel software.

RESULTS

A total of 65 clinically and ultrasonographically confirmed cases of liver abscess were initially included in the study, out of which 39 cases were diagnosed as ALA on the basis of positive serum IgG ELISA for *E. histolytica* and absence of bacterial growth in pus and blood cultures. These 39 patients were further investigated and described underneath.

Demographic Profile

The age of the study subjects ranged between 18 years to 90 years, with the mean age being 37.1 years [Table/Fig-1]. The young age group (20-40 years) comprised the maximum cases (64.1%). The ratio of male to female was 8.7:1. About 74.3% patients were presented with history of alcoholism.

| Variables | Number (n=39) | Percentage (%) |
|------------------------------|---------------|----------------|
| Age Groups (in years) | | |
| 18-20 | 1 | 2.5 |
| 21-30 | 12 | 30.7 |
| 31-40 | 13 | 33.3 |
| 41-50 | 10 | 25.6 |
| 51-60 | 2 | 5.1 |
| >60 | 1 | 2.5 |
| Sex | | |
| Male | 35 | 89.7 |
| Female | 4 | 10.3 |
| Education Status | | |
| Uneducated | 14 | 35.8 |
| Till primary school | 9 | 23.0 |
| Till higher secondary | 13 | 33.3 |
| Graduate | 3 | 7.6 |
| Post-graduate | 1 | 2.5 |
| Occupation | | |
| Salaried | 11 | 28.2 |
| Self-employed | 13 | 33.3 |
| Laborer/Daily wage worker | 8 | 20.5 |
| Others | 2 | 5.1 |
| Unemployed | 5 | 12.8 |
| Marital Status | | |
| Married | 35 | 89.7 |
| Unmarried | 4 | 10.3 |
| Alcohol Intake | | |
| Regular (≥3 times/week) | 23 | 58.9 |
| Occasional (≤3 times/week) | 6 | 15.4 |
| Never | 10 | 25.6% |

[Table/Fig-1]: Socio-demographic profile of patients with ALA.

Symptoms and Signs

Total 32 patients (82.1%) presented with acute signs and symptoms (within 14 days), (5/39) 12.8% patients had sub-acute (within 15-30 days), while (2/39) 5.1% patients had chronic presentations (> 30 days).

Fever 37 (94.8%) and upper abdominal pain 38 (97.4%) were the most common symptoms [Table/Fig-2]. Hepatomegaly (>14 cm) was seen in 34 (87.1%) cases.

Radiological findings: Right lobe was involved in 30 (76.9%) cases, left lobe in 7 (17.9%) cases and both the

| Variables | Number (n=39) | Percentage (%) |
|----------------------|---------------|----------------|
| Symptoms | | |
| Fever | 37 | 94.8 |
| Upper abdominal pain | 38 | 97.4 |
| Nausea/Vomiting | 11 | 28.2 |
| Anorexia | 10 | 25.6 |
| Diarrhoea | 6 | 15.3 |
| Signs | | |
| Fever (>38°C) | 37 | 94.8 |
| Abdominal Tenderness | 38 | 97.4 |
| Hepatomegaly | 34 | 87.1 |
| Jaundice | 4 | 10.2 |
| Ascites | 7 | 17.9 |
| Complications | | |
| Pleural Effusion | 11 | 28.2 |
| Intrapleural Rupture | 4 | 10.2 |

[Table/Fig-2]: Symptoms, signs and complications ALA.

lobes were involved in 2 (5.1%) cases [Table/Fig-3]. Most of the abscess 32 (82.0%) solitary in nature and out of which right lobe was involved in 64.1% cases. Volume of abscess ranged between 70 cc and as much as 1200 cc. Volume less than 300 cc was seen in 43.4% cases and more than 300 cc was seen in 56.4% cases.

Laboratory findings: Anemia was the most common hematological finding seen in 36 (92.3%) cases, followed

| Variables | Number (n=39) | Percentage (%) |
|----------------------------|---------------|----------------|
| Single | 32 | 82.0 |
| Right lobe* | 30 | 76.9 |
| Left lobe | 7 | 17.9 |
| Multiple | 7 | 17.9 |
| Both lobe | 2 | 5.1 |
| Size of the Abscess | | |
| <6 cm | 6 | 15.4 |
| 6-10 cm | 11 | 28.2 |
| >10 | 22 | 56.4 |

[Table/Fig-3]: Type and size of abscess in ALA.

* Out of 30, in 25 (64.1%) cases of abscess were solitary in nature.

by leukocytosis in 31 (79.4%) cases [Table/Fig-4]. Increased Alkaline Phosphatase (ALP) was seen in 82.0% cases.

All ALA patients were also examined for *Entamoeba histolytica* antigen in stool samples by ELISA, which was positive in 20.5% cases.

| Parameters | Number (n=39) | Percentage (%) |
|------------------------------------|---------------|----------------|
| Laboratory Investigations | | |
| Anaemia | 36 | 92.3 |
| Leukocytosis | 31 | 79.4 |
| Thrombocytopenia | 0 | 0 |
| Prolonged PT | 0 | 0 |
| Low Hematocrit | 30 | 76.9 |
| Urea | 5 | 12.8 |
| Creatinine | 2 | 5.1 |
| ALP | 32 | 82.0 |
| ALT | 27 | 69.2 |
| AST | 29 | 74.3 |
| Hypoalbuminaemia | 30 | 76.9 |
| ↑ Total Bilirubin | 3 | 7.6 |
| Treatment | | |
| Only Drug Therapy | 6 | 15.4 |
| Needle Aspiration and Drug Therapy | 11 | 28.2 |
| Pigtail Drainage and Drug Therapy | 22 | 56.4 |

[Table/Fig-4]: Management (Laboratory investigations and treatment) of the ALA patients.

Treatment: Ultrasonographically, the size of abscess was in the range of 6 cm to 16 cm [Table/Fig-3]. About 15.4% patients had abscess size less than 6 cm and were treated by drug therapy only (800 mg metronidazole three times in a day). In all, 11 (28.2%) patients with abscess size of 6 cm-10 cm were treated by needle aspiration and drug therapy. Remaining 56.4% patients with abscess size more than 10 cm, were treated with pigtail drainage and drug [Table/Fig-4]. Pleural effusion and intra peritoneal rupture were seen in 28.2% and 10.2% cases respectively.

DISCUSSION

Liver abscess is a collection of pus in the liver parenchyma. It is usually amoebic or pyogenic, and rarely tubercular or fungal in origin [6]. ALA can be suspected in any person of endemic region who presents with fever, pain abdomen and liver tenderness [2].

Most studies prove that amoebic liver abscess affects commonly middle-aged man and uncommonly seen at extreme of ages [7,8]. Our study is in accordance with these studies as 64.1% (25 out of 39) cases were between 20 to 40-year age group. Highest number of cases were in individuals between 31 and 40 years of age (33.3%); as has been reported previously [3,9]. Mean age was around 37.1

years which is comparable to other studies [2,10].

Males were predominantly affected, ratio of male: female ratio being 8.7:1. Almost all studies show the male preponderance. Das J et al., showed 77.5% male cases of ALA [11]. Mukhopadhyay M et al., found male to female ratio 11:1 [3]. Blessman J et al., found male to female ratio 7:1 [12]. Male preponderance may be due to heavy outdoor activity and alcoholism [12]. In the present study, 74.4% cases were alcoholic. Alcohol predisposes to hepatitis and trauma and makes liver more susceptible to infections by lowering body resistance, suppressing liver functions and causing malnutrition [13]. Furthermore, iron is important for invasive amoebiasis and this is provided in diet of habitual drinkers [14]. Low iron levels in females belonging to low socioeconomic families, have inhibitory effect to *Entamoeba histolytica* growth [15]. Some studies also found that complement mediated killing was more common in female and failure to produce early cytokine like IFN- γ in male mouse model [16].

All cases in this study belonged to low to lower middle socioeconomic status as per Kuppaswamy's socioeconomic status scale [17]. Most individuals were uneducated or received only basic education, while very few were graduates [Table/Fig- 1]. Such people show poor personal hygiene so more prone to *Entamoeba histolytica* infection. Our study is in agreement with previous studies by Das J et al., and Alam et al., [11,16].

In the present study, most of the cases (82.0%) cases presented within two weeks of onset of symptoms as reported by other studies [2,18]. Abdominal pain and fever are the common presenting symptoms in most of the studies [2,3,16]. The present study noted upper abdominal pain and fever in 97.4% and 94.8% cases, respectively. Nausea and vomiting (28.2%) and anorexia (25.6%) were the third and fourth symptoms in this study as in the study by Singh R et al., [9]. Active intestinal infections are generally not seen in ALA; hence, diarrhoea is a less common symptom. In our study, it was seen in only 15.3% of the cases. Various studies have reported it in the range of 4% to 33% [2,3,9,19].

Hepatomegaly was seen in 87.1% cases in this study. Our study is in agreement with previous studies like Mukhopadhyay M et al., Hai AA et al., and Ghosh S et al., which reported 81.9%, 85% and 89% respectively [3,13,14]. Sharma N et al., reported less number of cases with hepatomegaly (16%) which may be due to less number of alcohol consuming persons (46%) [2]. Two other signs ascites (17.9%) and jaundice (10.2%) was also seen in this study. Ascites is associated with compression on inferior vena cava or decompensated liver disease [13]. In previous studies from India, jaundice has been reported in as many as 45%-50% of cases [13]. However, due to improved therapy available, it is seen with much lower frequency now.

There are many complications which are associated with ALA like pleuropulmonary, intraperitoneal rupture, ascites, jaundice, elevated right hemidiaphragm, sub-phrenic abscess, pericardial rupture etc. We also found two types of

complications-right sided pleural effusion and intraperitoneal rupture. Pleural effusion was present in 28.2% cases which are in accordance with reported incidence of 25-42% [3]. Intraperitoneal rupture was seen in 10.2% of cases in our study. All the intraperitoneally ruptured abscesses were managed conservatively with the help of percutaneous drainage as surgical exploration is used mainly in hemodynamically unstable patients [2].

Ultrasonography is the method of choice for diagnosing liver abscess due to low cost, greater availability and high accuracy. It is helpful in assessing site, number, size and also complications like pleural or peritoneal rupture.

Most of the ALA abscess are located in right lobe and solitary in nature [3,13,20,21]. More involvement of right lobe as it receives most of the blood from intestine through portal system [3]. In our study, 30 (76.9%) cases had abscess in right lobe, 7 (17.9%) in left lobe and 2 (5.1%) cases in both lobes. Similarly, 32(82%) cases were with solitary abscess out of which 64.1% in right lobe, 17.9% in left lobe and multiple abscess in 17.9% (12.8% in right lobe and 5.1% in both lobes).

Various studies show anemia and leukocytosis in various proportions of patients. Sharma N et al., Mukhopadhyay M et al., and Nari GA et al., found anemia in 62%, 52.7% and 56.2% cases, respectively, while leukocytosis was noted in 68%, 80.5% and 87.5% cases, respectively [2,3,22]. Our study found anemia in 92.3% cases and leukocytosis in 79.4% cases. More cases of anemia in our study may due to more number of cases with alcoholism which causes negligence of food habit and folate deficiency. Increased ALP consistently noted by many studies [3,13]. 82% patients showed increased ALP in our study. However, Sharma N et al., and Amarapurkar and colleagues reported fewer cases with raised liver enzymes which may be due to earlier detection of ALA [2,18].

Microscopic examination of pus sample is not a sensitive method as suggested by various studies. Trophozoites have been seen in aspirated pus in 11-25% caeses [23]. Parija and Khairnar found trophozoites of *E. histolytica* in pus in 7.2% cases [24]. Haque R et al., confirmed 11% aspirated pus positive for trophozoite of *E. histolytica* [25]. Stool microscopy or antigen detection are not much helpful for diagnosis; less than 10% of patients have identifiable amoebae in stool [24]. Our study showed 20.5% cases with stool antigen positive for *E. histolytica* by ELISA but it could not find any case with trophozoite of *Entamoeba histolytica* on microscopy of stool or pus.

Systemic amoebicidal drug like metronidazole, tinidazole along with luminal amoebicide like paramomycin, diloxanide furoate is the mainstay of drug therapy. Indications for aspiration include lack of response to medical therapy, abscess >6 cm or volume >300 mL, impending rupture, multiple abscess, left side abscess, compression symptoms like inferior vena cava obstruction [9]. Gupta SS et al., suggested percutaneous drainage of abscess is better than percutaneous aspiration when abscess size >10 cm [26]. In our study, 15.4% cases

with abscess size less than 6 cm were treated by only drug therapy, 28.2% cases with abscess size 6 to 10 cm treated by needle aspiration and drug and 56.4% with abscess size more than 10 cm treated by pigtail drainage and drug therapy. So, most of the patients in our study were assisted with percutaneous intervention which resulted in rapid recovery with no residual complication. Singh R et al., also found that intervention combined with anti-amoebic therapy hasten the recovery [9].

Most of the patients in our study were presented with uncomplicated liver abscess. Complicated cases and patients with large abscesses were immediately managed by percutaneous intervention. So, no mortality was seen in this study.

LIMITATION

As small number of cases were included in this study therefore it is difficult to develop a general idea especially regarding complications. Patients were observed as long as they stayed in hospital so post treatment or long-term outcome cannot be discerned. The ELISA used for stool antigen detection was common for both *Ehistolytica*/dispar so exact correlation between ALA and intestinal amoebiasis cannot be concluded. Histological aspects were not included in this study.

CONCLUSION

In endemic countries, ALA should always be diagnosis of exclusion particularly in a male patient of low socioeconomic status presenting with abdominal pain, fever and hepatomegaly. Right lobe is involved in most of the cases. Immediate proper management must be done to prevent morbidity and mortality. Although, primary focus of infection in ALA is intestine, few cases present themselves with active intestinal infection.

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