



CHANGING TRENDS IN AMOEBIC LIVER ABSCESS AMONG HIV AND NON HIV PATIENTS: A TEN YEAR EPIDEMIOLOGICAL STUDY FROM INDIA.

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ABSTRACT Human Immunodeficiency Virus(HIV) has been gripping the immune system of the world steadily at an escalating rate. With a wide spectrum of Clinical manifestations of HIV infection involvement of the gastrointestinal tract, predominantly Liver as a organ has been rising. A detailed study of the clinical manifestations of Amoebic Liver abscess in patients not infected with HIV and infected with HIV is of importance to understand the variations & severity of signs & symptoms.

KEYWORDS : Amoebic liver abscess, HIV, Non HIV, changing trends, Epidemiological study, India

INTRODUCTION

The epidemic of Acquired Immunodeficiency Syndrome (AIDS) sweeping the world cuts across the conventional boundaries of nationality and age. The human Immunodeficiency virus (HIV) has infected millions of men, women and children all over the world including developing countries. The incidence of liver abscess (pyogenic or amoebic), which is a commonly encountered tropical gastrointestinal disorder is on the rise with the increasing incidence of HIV. To the best of our knowledge there has not been any study comparing the clinical presentations of amoebic liver abscess (ALA) in HIV and non HIV patients. Hence this study was carried out to study the epidemiology of amoebic liver abscess in HIV and non HIV patients.

AIMS AND OBJECTIVES

To study the epidemiology of HIV amongst patients with amoebic liver abscess in terms of incidence, age and sex, clinical features, investigations, their correlation with CD4 cell count and various management modalities.

METHODS

A prospective study was conducted at Grant Medical College and Sir JJ group of Hospitals, which is a tertiary teaching institute and referral centre, Mumbai between May 2003 and May 2013. It is a state run public hospital providing state of art health care facilities to the poor, free of cost. Since the beginning of HIV epidemic in the country, Sir J. J. hospital is providing treatment to HIV/AIDS patients. The National AIDS Control Organisation (NACO), New Delhi has designated this hospital as "Center of Excellence" for treatment of HIV/AIDS.

Inclusion criteria:

1. Diagnosed cases of amoebic liver abscess (diagnosed on the basis of demonstration of trophozoites of *E. histolytica* or a positive test based on Polymerase chain reaction (PCR) of the aspirated pus).
2. Patients of any sex above 12 years of age
3. Patients consenting to be a part of the study.

Exclusion criteria:

1. Children below the age of 12 years
2. Pregnant females
3. Abscesses other than amoebic in etiology
4. Patients not consenting to be a part of the study.

Patients presenting with symptoms suggestive of liver abscess (or diagnosed with liver abscess) were investigated with ultrasound or computed Tomography (CT) scan of the abdomen for the presence of liver abscess. Pus specimen/necrotic liver bits obtained from all cases of liver abscess were submitted for bacterial culture/isolation of trophozoites/ Polymerase chain reaction (PCR). The pus aspirate was negative for gram positive/negative organisms, and for acid fast

bacilli. The trophozoites of *E. histolytica* was identified on giemsa and per iodid acid (PAS) stain and later was confirmed on iron haematoxyline stain. Isolation of trophozoites of *E. Histolytica* in the pus aspirate or a positive test on Polymerase chain reaction (PCR) for definitive diagnosis of *E. Histolytica* from the aspirated pus were diagnosed as case of amoebic liver abscess. HIV status of the individuals were obtained by using enzyme linked immuno sorbent assay (ELISA) technique after voluntary pre as well as post test counseling for both HIV-1 and HIV-2 antibodies. All the sera reactive by above test kits were further tested using enzyme linked immunosorbent assay(ELISA) technique after voluntary pre as well as post test counselling for both HIV1 and HIV2 bispot test kits. Patient who were positive for both the tests were labelled as HIV positive. All patients included in the study were positive for HIV1 antibodies and none for HIV2 antibodies. CD4 counts were evaluated in patients diagnosed with HIV infection. Patients with a CD4 count of less than 200 cells/mm³ were included as AIDS. Patients positive for HIV infection with AIDS were provided with highly active retroviral therapy (HAART). The patients with amoebic liver abscess were divided into following 3 categories of amoebic liver abscess:

- 1) Amoebic liver abscess without HIV infection
- 2) Amoebic liver abscess with HIV infection (CD4 cell count above 200cells/microL)
- 3) Amoebic liver abscess with AIDS

Patients clinical details were recorded as per the proforma outlined, and subsequently routine blood investigations and stool samples were also analysed for co existing amoebic colitis. Patients were given metronidazole 30mg/kg/day in 3 divided doses along with ciprofloxacin 20mg/kg in 2 divided doses along with analgesics, antipyretics and antacids. All patients with abscess value of more than 100cc or more on ultrasound with liquefaction were subjected to either aspiration or catheter drainage of abscess. Patients who presented with ruptured abscess with signs of peritonism underwent surgery. Patients were followed up till the time of discharge during their stay in the hospital or death and assessed as

- 1) cured
- 2) patient asymptomatic but residual disease (assessed by Ultrasonography for the status of the liver abscess) or recurrence and
- 3) death

Data was analysed using open epi software. Continuous variables were analysed using analysis of variance (ANOVA). Quantitative data was analysed using mid p exact values and odds ratio was determined.

Results:

Patient Demographics:

A total of 177 patients were included in the study, which comprised of 160 males, 12 females and 5 homosexuals. 53 of 177 patients (29.94%) were HIV infected (22 AIDS and 31 HIV infection). Liver abscess was noted in age group of 41-50 years in all the 3 groups (Table 1).

Clinical Features:

Clinically the most common complaint was fever which was seen in all the patients, however, high grade fever was seen in 33.0% of non HIV patients, 29.0% of HIV positive patients and 27.27% of AIDS patients. Pain in the right upper abdomen was seen with 100% of non HIV patients, 93.54% of HIV positive patients and 68.18% of patients with AIDS. A clinically significant finding was that 67.7% of HIV positive patients and 77.27% of AIDS suffered from pleural effusion, whereas 42.74% of non HIV patients suffered from pleural effusion (Tab 2). Co existing colitis was seen in 13.17% of non HIV patients, 3.2% of HIV positive patients and 4.5% of AIDS patients.

Laboratory Investigations: The average WBC count in non HIV patients was 12,555 c/mm³ (range 4000- 15000 c/mm³), 9,430 (range 4000-13000 c/mm³) in HIV positive patients and 9,013 (range 4000-13000 c/mm³) in AIDS patients. The average cell CD4 count in HIV positive patients was 273 cells/microL and in AIDS group was 90 cells/microL. However, there was no correlation between the CD4 count and the severity of the illness. Trophozoites were seen in 3 of 31 HIV positive patients, 16 of 124 non HIV patients and 3 of 22 AIDS patients [Fig 1]. The rest of the patients (155) were diagnosed on the basis of PCR

Imaging Modalities: On ultrasonography, it was seen that the right lobe of the liver was involved in more than 80% of the cases. Involvement of both the liver lobes were seen in 9.69% of non HIV patients, 12.9% of HIV positive patients and 18.18% of AIDS patients. Multiple abscesses were seen in 21.77% of non HIV patients, 41.9% of HIV positive patients and 45.45% of AIDS patients [Fig 2].

Treatment Modality: Medical management was carried out in 37.9% of non HIV patients, 54.83% of HIV positive patients and 59.0% of patients with AIDS. Ultrasound guided pig tailing of the liver abscess was carried out in 49.1% of non HIV patients, 32.2% of HIV positive patients and 22.7% of AIDS patients. Open surgery was performed in 12.9% of non HIV patients, 12.9% of HIV positive patients and 18.18% of AIDS patients who presented with ruptured abscess. Recurrence was seen in 2.41%, 3.2% and 4.1% in the 3 groups respectively. Mortality rate was 5.6% in non HIV patients, 6.4% of HIV positive patients and 9% of AIDS patients succumbed to their illness.

DISCUSSION

At the cataclysmic moment in history, millions of years after earth's crust had solidified, atoms of hydrogen, oxygen, nitrogen and carbon came together to constitute life. One of the first forms of this life to develop was the amoeba. In the waters of earth, it waited, through millenniums, for the advent of man! Man evolved, roamed the earth, drank its waters and sometimes developed amoebiasis, occasionally an amoebic liver abscess. As more advanced facilities for investigating and treating liver abscess are now available, a more concrete picture of amoebic liver abscess is evolving. However, with the emergence of HIV as the modern age plague, the epidemiology, presentation and treatment of this disease appears to change rapidly.

Today, with the rise of AIDS as the modern day pandemic, it is clear that every physician in every country will be required to have some degree of familiarity with the work up, diagnosis, management, and specific treatment of HIV infected individuals [1]. Today an estimated 36 million people are living with HIV/AIDS [2].

The spread of HIV infection in India has been uneven. The first cases of HIV were diagnosed among commercial sex workers (CSW) in Chennai in 1986. Since then the country has evolved from "low" to "concentrated" epidemic. In 2005 an estimated 2.4 million people were living with HIV. Slightly lower than 2.5 million were reported in 2007. However, India remains just behind the African subcontinents in numbers of persons living with AIDS [3].

India has the third largest number of people living with HIV/AIDS. As per the 2008/09 HIV estimates, there are an estimated 2.3 million people currently living with HIV/AIDS in India with an adult prevalence of 0.31% in 2009 [3]. A more recent investigation by the

million death study collaborators in the British Medical Journal 52 53 (2010) estimates the population to be between 1.4-1.6 million [4].

Mumbai, the capital city of Maharashtra state, the fourth most populous place in the world is home to more than 13.7 million people. In the initial studies conducted by Rathi [5] Amrapur [6] and Lanjewar [7] in the city of Mumbai, the incidence of amoebic liver abscess was just 1.75-2.7%. However, with the increasing incidence of HIV infection, the incidence of ALA in HIV positive patients in certain geographical areas, is increasing (28.81%). Studies by Park [8] supports our finding wherein the incidence of ALA is on the rise in HIV positive patients. It was seen that the mean age of patients with AIDS presenting with ALA was younger when compared to HIV and NON HIV patients (41.6 years, 42.9 years and 46.9 years), which could probably be due to the underlying immunosuppression.

The previous studies conducted by Park and Kwang choon lee et al [9] reported amoebic liver abscess as an exclusive male disease in HIV positive patients. However, with changing trends of the disease 5 of the 53 HIV positive patients in the present study (including AIDS patients) were females.

Clinically fever and abdominal pain are the most common complaints. High grade fever which took twice the time to defervescence was seen in HIV positive patients than the NON HIV patients. Studies by Seeto [10] and Park [8] also provided similar results. In comparison with NON HIV patients, HIV positive and AIDS patients had decreased perception of pain. (93.54%) of HIV patients and 68.18% of AIDS patients). This decreased perception of pain could be attributed to decreased inflammatory response in HIV positive patients. 70.58% of the HIV patients presented with pleural effusion. This figure was comparable to the study by Park [8] 50% and Myoung don [11] 60% which showed that most of the HIV positive patients presented with right sided pleural effusion.

The average CD4 counts of HIV positive patients was 275 c/microL (range 90-620). Park [8] in his study of 31 patients with 10 HIV positive patients had average CD4 count of 279 cells/microL with a range of 40-370 cells/microL, while the patients in Myoung Don [11] Study had a mean CD4 count of 275 cells/microL with a range of 220-370 cells/microL.

More than 80% patients presented with a right side abscess while 5.8% of the patients having a left lobe abscess. An interesting finding was that 12.9% of the HIV positive patients and 18.18% of AIDS patients presented with liver abscesses involving both lobe of the liver, which is usually a feature of pyogenic liver abscess. While 21.77% of the NON HIV patients had multiple liver abscesses, the HIV group had almost double the number of patients 41.9% and the AIDS group had 45.45% presented with multiple liver abscesses. Comparing the present study with Park [8] and Myoung don [11], the incidence of multiple liver abscesses in their study was 20% of HIV patients.

Amoebic liver abscess, undiagnosed and untreated has a very high mortality rate [12]. With early diagnosis and prompt institution of specific therapy, the prognosis is excellent and mortality extremely low [13]. Treatment is based on the principles given by Oschner and Debakey [14].

- 1) Every case of amoebic liver abscess should be given a course of amoebicidal drug therapy before any procedure is used, unless rupture of the abscess appears imminent
- 2) If evacuation of the pus is necessary, aspiration and preliminary administration of amoebicidal drugs is the procedure of choice
- 3) Open drainage of the abscess should be reserved for the relatively few cases of secondarily infected abscesses.

Every case of liver abscess should ideally be hospitalized as continuous observation is required for early recognition of the complications.

Analysing the present study, percutaneous drainage 49.1% of the liver abscess via a pig tail catheter was the mainstay in the treatment of NON HIV cases, while medical management with metronidazole was the most commonly performed modality adopted in HIV and AIDS (54.83% and 59.0%). The second most common treatment modality for HIV patients was percutaneous drainage with pigtail catheter 32.2%. The increased usage of medical management amongst HIV cases can be attributed to high frequency of multiple abscesses along

with involvement of both lobes or good response to anti amoebicidal drugs. In addition to the treatment of ALA, patients with AIDS also received highly active antiretroviral therapy (HAART). Patients who responded to HAART had a progressive increase in their CD4 count and had a better prognosis than their counterparts. As more advanced facilities for investigating and treating liver abscess are now available, a more concrete picture of amoebic liver abscess is evolving. The story has not ended; rather a new page has been opened in this story.

Conclusion:

Amoebic liver abscess remains an important tropical gastrointestinal disorder. The 2nd highest number of HIV cases in the world are seen in the Indian subcontinent. HIV patients show relative immunosuppression and are more susceptible to infection including liver abscesses. The disease pattern of ALA among HIV patients is different as compared to non-HIV with even female patients being affected and is no longer a truly "Male disease". Findings of atypical multiple amoebic liver abscess or involvement of both lobes of liver in a patient should raise the suspicion of a compromised immune status. Most patients with HIV and amoebic liver abscess can still be managed by non surgical intervention with metronidazole, simple aspiration or pig tailing.



Figure 1. Showing
 a) Clinically evident Liver abscess
 b) Pus aspirated for analysis
 c) Ruptured Hepatic abscess
 d) Histopathology study showing Trophozoites

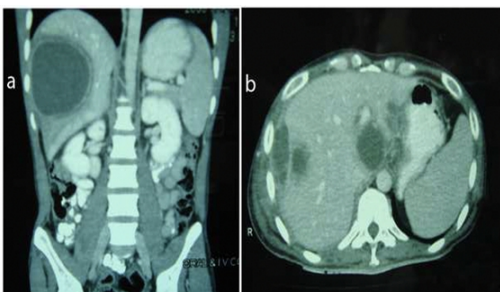


Figure 2. Contrast enhanced CT showing Liver abscess (Solitary & Multiple)

Table 1

Variable	Non HIV Patients(%)	HIV Positive Patients(%)	AIDS Patients (%)	Total (%)
Number	124(70.5)	31(17.5)	22(12.4)	177
77Males	116(65.5)	28(15.8)	16(9.03)	160(90.4)

Variable	Non HIV	HIV	Mid P exact and Odds Ratio between Non HIV & HIV	Mid P exact & odds ratio between HIV Positive without AIDS and with AIDS
Females	07(3.9)	02(1.1)	03(1.7)	12(6.8)
Homosexual(M)	01(0.5)	01(0.5)	03(1.7)	05(2.8)
Homosexual(F)	00	00	00	00
Mean age	46.9	42.9	41.6	43.8
High grade fever	41(33)	09(29)	06(27.2)	56(31.6)
Abdominal pain	124(100)	29(93.5)	15(68.2)	168(94.9)
Colitis	17(13.1)	01(3.2)	01(4.5)	19(10.7)
Mean WBC count	12470	9350	9100	10306
Mean CD4 count	Not done	275	90	-
Bilobe lesion	12(9.6)	04(12.9)	04(18.2)	20(11.3)
Multiple abscess	27(21.7)	13(41.9)	10(45.4)	50(28.2)
Ruptured abscess	16(12.9)	04(12.9)	04(18.2)	24(13.5)
Medical treatment	47(37.9)	17(54.83)	13(59)	77(43.5)
Percutaneous drainage	61(49.1)	10(32.2)	05(22.7)	76(42.9)
Surgical drainage	16(12.9)	04(12.9)	04(18.9)	24(13.5)
Recurrence	03(2.4)	01(3.2)	01(4.5)	05(2.8)
Mortality	07(5.6)	02(6.4)	02(9)	11(6.2)
High Grade fever	41	15	0.271/0.8	0.44/0.9
Abdominal pain	124	44	0.000005	0.011
Colitis	17	02	0.023/0.24	0.415/1.4
Bilobe inv	12	08	0.156/1.65	0.3/1.48
Multiple abscess	27	23	0.023/2.73	0.40/1.1
Ruptured abscess	16	08	0.34/1.19	0.3/1.48
Medical Management	47	30	0.012/2.12	0.38/1.18
Per cutaneous drainage	61	15	0.005/0.4	0.23/0.6
Surgical drainage	16	08	0.34/1.19	0.3/1.48
Recurrence	03	02	0.31/1.58	0.41/1.42
Mortality	07	04	0.32/1.36	0.37/1.44

Table 2

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