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Original Research Article

Clinico-radiological profile of abdominal tuberculosis in HIV/AIDS patients-a study from rural central India

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ABSTRACT

Background: One of the major challenge of present era is dual epidemic of HIV/AIDS and tuberculosis. With immunosuppression, risk of opportunistic diseases increases in these patients and tuberculosis is most common opportunistic infection. The prevalence of abdominal tuberculosis seems to be rising, particularly due to increasing prevalence of HIV infection. The diagnosis of abdominal tuberculosis can often be difficult and it remains underdiagnosed, in view of its nonspecific manifestations. The investigations involved in its diagnosis are expensive and time consuming, however, ultrasonography (USG) is an affordable, non-invasive and widely available modality which can be of help in the diagnosis of abdominal tuberculosis. Therefore, this study was undertaken to evaluate clinical and USG finding among Abdominal Tuberculosis patients with HIV/AIDS.

Methods: After informed consent, patients underwent thorough history taking and clinical examination followed by high quality USG abdomen and other biochemical and haematological tests including CD4 count. Follow up USG abdomen was done at time of completion of course of ATT and data was analysed.

Results: 45 were found to have abdominal tuberculosis. Of these patients, 31(68.9%) were male and 14 (31.1%) were female. Mean age of HIV-abdominal TB was 34.27±9.66 years. most common symptoms were weight loss 41(91.1%), loss of appetite 38(84.4%), fever 32(71.1%), generalized weakness 30(66.7%) and abdominal pain 27(60.0%). On USG abdomen, intraabdominal lymphadenopathy was most common finding found in 44(97.8%). Average size of enlarged lymph node was 3.1+-1.0 cm. Mesenteric lymphnodes were enlarge in 40(88.89%), paraaortic 8(17.78%), retroperitoneal 4(8.89%) while peripancreatic and porta hepatic in 3(6.67%). splenomegaly was noted in 14(31.1%) cases. Hepatomegaly was found in 6 cases, who all were male. Ascites was evident in 5(11.1%) patients. Extensive involvement, defined as involvement of two or more intraabdominal sites, was found 24(53.3%) cases. There was no statistically significant difference found among these USG findings and CD4 count.

Conclusions: The findings of lymphadenopathy (size>15mm) and hypoechoic/necrotic echotexture, hepatosplenomegaly with hypoechoic lesions in ultrasonography are suggestive of abdominal tuberculosis in HIV infected patients with unexplained nonspecific symptoms and low CD4 count. However, above findings are not standardized and inability to confirm the diagnosis of tuberculosis by direct microscopy and culture is the limitation of this study. Ultrasonography is an affordable, widely available, non-invasive imaging modality which may be optimally utilized for the diagnosis of abdominal tuberculosis in HIV infected patients, especially in the rural setup where microbiological and other sophisticated radiological investigations have limited availability.

Keywords: Abdominal tuberculosis, CD4 count, Extrapulmonary tuberculosis, HIV/AIDS, Rural

INTRODUCTION

One of the major health challenge of the present era is the impact of dual epidemic of HIV and Tuberculosis especially in countries like India. According to WHO total number of HIV/AIDS cases in 2015 were 36.7 million of which 2.1 million were reported in the year 2015.[1] According to National AIDS Control Organization (NACO) total number of people living with HIV/AIDS was estimated to be around 2.12 million in the year 2015 in India.[2] Globally, there were 10.4 million new cases of tuberculosis diagnosed in the year 2015, of which People living with HIV accounted for 11%. Out of 10.4 million cases India shares 2.2 million cases, making it highest burden country worldwide.[3]

HIV leads to immunosuppression, which put these patients at increased risk for infection with less virulent organisms in addition to increased severity of common infections. As immunosuppression from HIV infection progresses, the overall incidence of opportunistic disease increases; however, the risk for individual opportunistic illnesses varies with the specific degree of immunosuppression.[4]

Tuberculosis is still most common OI among HIV patients and it also continues to be most common cause of death among HIV patients.[5] TB incidence continues to rise especially in countries most affected by HIV epidemic, compounded by poverty, political turmoil, migration, unemployment and IV drug abuse. The risk of developing TB is estimated to be between 12-20 times greater in people living with HIV than those without HIV infection.[6] In general one third of world population is latently infected with M. tuberculosis.[7] Approximately 10% of M. tuberculosis infected individuals are thought to develop overt clinical disease.[8] The lifetime risk of developing active tuberculosis in immunocompetent adult is 5%-10%, but in HIV positive individuals this risk is increased to 5%-15% annually.[9] The depletion of CD4 cells, one of the important feature of AIDS, is most important contributor to increased susceptibility to new TB infection and reactivation of latent tuberculosis.

The prevalence of abdominal tuberculosis seems to be rising, particularly due to increasing prevalence of HIV infection.[10] The diagnosis of abdominal tuberculosis can often be difficult and it remains underdiagnosed, in view of its nonspecific manifestations. The investigations involved in its diagnosis are expensive and time consuming like CT scan of abdomen, laparoscopy and others. However, ultrasonography (USG) is an affordable, non-invasive and widely available modality which can be of help in the diagnosis of abdominal tuberculosis.[11] If we know the frequent clinical presentations among this subset of patients then we can suspect this earlier and institution of early therapy will not only improve the outcome in these patients but also prevent emergence of drug resistance. There are very few studies addressing this issue in the past and as per literature search there is no study from rural population.

Rural population is different from urban population in life style and cultural customs which make this population at higher risk of tuberculosis. Availability and access to health services are poor among rural areas which accounts for late presentation and non-specific complaints further contribute to delay in diagnosis. This study was done to address this issue and generate clinic-epidemiological data among HIV patients with abdominal tuberculosis which, help clinician to suspect abdominal tuberculosis early and institute therapy earlier.

METHODS

Uttar Pradesh University of Medical Sciences is located in Etawah district, which caters to the referral tertiary care needs of Etawah district and its neighboring district of Mainpuri with cumulative area and population of 5071 sq. km and 23.5 lakh respectively.[12] This was a prospective study done at the ART center of UPUMS and approved by institutional ethical committee.

Inclusion criteria

- Age >18 years
- Abdominal tuberculosis in HIV positive patients.

Exclusion criteria

- Patients not willing to give consent.

The study group consisted of subjects who were diagnosed to be infected with HIV by NACO guideline 2007. All HIV positive patients were selected as per inclusion and exclusion criteria and informed consent was obtained. Detailed history and examination was done and patients with persistent fever more than 2 weeks, abdominal pain or distension, altered bowel habit or diarrhea which could not be attributed to any other cause underwent USG abdomen at Department of Radiology. The following features on USG were considered suggestive of abdominal tuberculosis as demonstrated by other studies.[13-15]

- Enlarged lymph nodes predominantly hypoechoic/necrotic. Size of lymph nodes greater than 15 mm was considered tubercular.[14] Hypoechoic nodes means that hilar echogenicity of the nodes are lost.
- Visceral involvement may be seen as organomegaly or as multiple small abscesses/hypoechoic lesions in the organs.
- Bowel wall thickening (especially in the Ileocecal junction), peritoneal nodules, mesenteric thickening or ascites.
- Presence of more than one of the above findings was considered as extensive abdominal involvement.

Apart from clinical details and USG abdomen, demographic variables, routine blood chemistry and CD4 count were recorded. Ascitic fluid cytology was done and diagnosis of tubercular ascites was made on the basis of USG and supportive evidence. All these patients were started on antitubercular therapy for a duration of 9 months comprising four drugs (rifampicin, isoniazid, pyrazinamide and ethambutol) for 3 months and 3 drugs (rifampicin, isoniazid and ethambutol) for 6 months.

Antiretroviral therapy was initiated 2-4 weeks after start of antitubercular therapy as per guidelines of the National AIDS Control Organization (NACO).[16] Clinical responses were monitored monthly during routine ARTC visits. Subsidence of presenting complaints of fever, abdominal pain, distension, altered bowel habits at the end of antitubercular regimen was considered as clinical improvement. Ultrasonography was repeated at the end of antitubercular therapy and compared with the prior findings to assess improvement. Resolution of adenopathy, hypoechoic lesions in spleen and liver, bowel wall thickening and ascites was considered as ultrasonographic improvement. The patients who did not show clinical or ultrasonographic improvement were excluded during data analysis.

Statistical analysis

The data was analysed using the Statistical Package for Social Sciences version 21 (SPSS v21, USA) software. Categorical variables were expressed as absolute number and percentage and continuous variables were expressed as mean and standard deviation (SD). The USG findings were also categorized into non-overlapping groups and one way ANOVA was applied to see relation with CD4 counts.

RESULTS

Of total 101 patients of HIV-TB co-infection, 45 were found to have abdominal tuberculosis. Of these patients, 31(68.9%) were male and 14 (31.1%) were female. Mean age of HIV-abdominal TB was 34.27±9.66 years. Mean age among female was 35.57±10.94 years and that among male was 33.68±9.15 years. Average BMI of patients' was 17.69±3.37. BMI of females was 17.03±2.89 while that of males was 17.99±3.57. Other epidemiological characteristics are given in Table 1.

Laboratory parameters of patients were given in Table 2. Mean haemoglobin was lower in female than male (9.23 vs. 10.12). Mean ESR was 41.76±18.83. Mean CD4 among HIV-abdominal tuberculosis infected patients was 163.23.

Symptoms and sign of presentation of co-infected patients is given in Table 3. Overall, most common symptoms were weight loss 41 (91.1%), loss of appetite 38 (84.4%), fever 32 (71.1%), generalized weakness 30 (66.7%) and abdominal pain 27 (60.0%).

Among female patients, common symptoms were weight loss 12 (85.7%), loss of appetite 12 (85.7%), abdominal pain 11 (78.6%) and generalized weakness 10 (71.4%) while that among male were weight loss 29 (93.5%), loss of appetite 26(83.9%), fever 24 (77.4%), abdominal pain 16 (51.6%), night sweats 13 (41.9%) and chronic diarrhea 12 (38.7%).

Table 1: Epidemiological parameters of HIV-abdominal TB co-infected patients.

Variable	Category	Frequency (%)
Gender	Female	14 (31.1)
	Male	31 (68.9)
Age	18-27 Years	10 (22.2%)
	28-37 Years	19 (42.2
	38-47 Years	12(26.7)
	>47 Years	4(8.9)
Education	Graduate	2(4.4)
	Illiterate	13(28.9)
	Primary	15(33.3)
	Secondary	15(33.3)
Occupation	Farmer	4(8.9)
	House wife	12(26.7)
	Labourer	11(24.4)
	Others	8(17.8)
	Trader	5(11.1)
	Truck driver	5(11.1)
Marital status	Married	33(73.3)
	Unmarried	7(15.6)
	Widowed/Widower	5(11.1)
Risk/route of exposure to HIV	Blood transfusion	1(2.2)
	Heterosexual	41(91.1)
	IDU	1(2.2)
	MTCT	2(4.4)

On USG abdomen, intraabdominal lymphadenopathy was most common finding found in 44 (97.8%), of them 27 (61.36%) of cases showed loss of central hilar echogenicity. Average size of enlarged lymph node was 3.1+-1.0 cm. Mesenteric lymphnodes were enlarge in 40 (88.89%), paraaortic 8 (17.78%), retroperitoneal 4 (8.89%) while peripancreatic and porta hepatic in 3 (6.67%). splenomegaly was noted in 14 (31.1%) cases. Hepatomegaly was found in 6 cases, who all were male. Ascites was evident in 5 (11.1%) patients of which 3 were female and 2 were male.

Extensive involvement, defined as involvement of two or more intraabdominal sites, was found 24 (53.3%) cases of which 7 (50.0%) were female and 17 (54.8%) were male (Table 4).

The non-overlapping USG findings in 45 patients lymphadenopathy with organomegaly was found in 18 (40.0%) with CD4 count of 179.89±152.39 count/µL, lymphadenopathy only in 22 (48.9%) cases with CD4

count of 153.09±115.21 count/µL and only ascites in 5 (11.1%) with CD4 count of 148.00±74.47 count/µL. There was no statistically significant difference found among these USG findings and CD4 count Table 5.

Table 2: Biochemical parameters of HIV-abdominal TB co-infected patients.

Parameter	Overall		Female		Male	
	Mean	(±SD)	Mean	(±SD)	Mean	(±SD)
Hb (gm/dl)	9.84	(±1.93)	9.23	(±1.93)	10.12	(±1.89)
TLC (/uL)	6526.36	(±2591.49)	5766.57	(±2511.81)	6869.48	(±2593.23)
ESR (mm/hr)	41.76	(±18.83)	46.29	(±17.72)	39.71	(±19.24)
S. Albumin (gm./dl)	4.10	(±5.82)	3.21	(±0.71)	4.51	(±6.99)
S. total protein (gm./dl)	6.77	(±1.27)	6.51	(±1.40)	6.88	(±1.22)
A/G ratio	1.15	(±1.92)	0.82	(±0.36)	1.29	(±2.29)
S. total bilirubin (mg/dl)	0.60	(±0.70)	0.73	(±1.10)	0.54	(±0.42)
SGOT (IU/L)	54.44	(±37.72)	55.29	(±43.21)	54.06	(±35.74)
SGPT (IU/L)	39.60	(±23.14)	35.50	(±22.14)	41.45	(±23.70)
ALP (IU/L)	171.56	(±109.50)	166.86	(±101.76)	173.68	(±114.39)
S. Creatinine (mg/dl)	0.95	(±0.30)	0.86	(±0.19)	1.00	(±0.33)
S. Urea (mg/dl)	30.69	(±13.85)	28.14	(±8.41)	31.84	(±15.70)
CD4 count (count/µL)	163.24	(±126.50)	198.93	(±140.171)	147.13	(±118.72)

Table 3: Sign and symptoms of HIV-abdominal TB co-infected patients.

Symptoms/Signs	Overall (N=45)	Gender	
		Female (N=14)	Male (N=31)
Fever	32 (71.1%)	8 (57.1%)	24 (77.4%)
Abdominal pain	27 (60.0%)	11 (78.6%)	16 (51.6%)
Abdominal distension	7 (15.6%)	2 (14.3%)	5 (16.1%)
Vomiting	5 (11.1%)	1 (7.1%)	4 (12.9%)
Chronic diarrhoea	19 (42.2%)	7 (50.0%)	12 (38.7%)
Weight loss	41 (91.1%)	12 (85.7%)	29 (93.5%)
Night sweats	19 (42.2%)	6 (42.9%)	13 (41.9%)
Generalized weakness	30 (66.7%)	10 (71.4%)	20 (64.5%
Loss of appetite	38 (84.4%)	12 (85.7%)	26 (83.9%)
Pallor	20 (44.4%)	9 (64.3%)	11 (35.5%)
Lymphadenopathy	6 (13.3%)	0 (0.0%)	6 (19.4%)
Jaundice	1 (2.2%)	0 (0.0%)	1 (3.2%)
Palpable organomegaly	3 (6.6%)	0 (0.0%)	3 (9.6%)
Ascites	3 (6.7%)	2 (14.3%)	1 (3.2%)

Table 4: Ultrasonographic findings of HIV-abdominal TB co-infected patients.

Ultrasonographic findings	Overall (N=45)	Gender	
		Female (N=14)	Male (N=31)
Intraabdominal lymphadenopathy (mesenteric>paraaortic>retroperitoneal >peripancratic and porta hepatis)	44 (97.8%)	14 (100%)	30 (96.8%)
Splenomegaly with Hypoechoic infiltrations	14 (31.1%)	4 (28.5%)	10(32.2%)
Hepatomegaly	6 (13.3%)	0 (0.0%)	6(19.4%)
Bowel thickening	1 (2.2%)	0 (0.0%)	1(3.2%)
Ascites	5 (11.1%)	3 (21.4%)	2(6.4%)
Extensive involvement (involvement of >2 sites)	24 (53.3%)	7 (50.0%)	17(54.8%)

Table 5: Relationship between non-overlapping USG findings and CD4 count among HIV-Abdominal TB co-infected patients.

USG Finding	Frequency (Percentage)	CD4 count (count/µL) Mean±SD	p-value using one way ANOVA	Range of CD4 count
Lymphadenopathy with organomegaly	18 (40.0%)	179.89±152.39	P=0.77	16-566
Lymphadenopathy only	22 (48.9%)	153.09±115.21		12-395
Ascites	5 (11.1%)	148.00±74.47		71-250
Total	45 (100.0%)	163.24±126.50		12-566

The non-overlapping USG findings in 45 patients lymphadenopathy with organomegaly was found in 18(40.0%) with CD4 count of 179.89±152.39 count/ lymphadenopathy only in 22 (48.9%) cases with CD4 count of 153.09±115.21 count/µL and only ascites in 5 (11.1%) with CD4 count of 148.00±74.47 count/µL. There was no statistically significant difference found among these USG findings and CD4 count Table 5.

Of 45 total patients, 1 lost follow up (not attended antiretroviral therapy centre for consecutive 3 months) and 1 expired. USG evaluation was done in remaining 43 patients at the end of 9 months of antitubercular therapy. Resolution of lesion was found in 40 (93.0%) and residual changes were seen in 3 (6.9%) patients. Clinical improvement was observed in all 43 patients.

DISCUSSION

In our study, males were found to be affected more than female which consistent with other studies1.[17,18] Some studies also reported female predominance19. Clinical symptoms were very vague and nonspecific, which is in consensus with other studies.[18,20] Most common presenting symptoms were weight loss, loss of appetite, fever, generalized weakness and abdominal pain, so any patient with unexplained these symptoms should be suspected of having tuberculosis and should be evaluated for the same.

Abdominal tuberculosis has varied findings on ultrasonography, involving the gastrointestinal tract, lymph nodes, peritoneum, and solid organs. Tuberculosis of the abdomen in non-HIV patients most commonly affects the ileocaecal region of the bowel where it causes circumferential ulcers with multiple strictures and sometimes involves the draining lymph nodes.[21] Another common presentation is tubercular peritonitis with ascites.[17] However, bowel wall involvement and ascites were quite low in our subjects which is similar to Agarwal D et al.[18]

In our study most common ultrasonographic finding was enlargement of abdominal lymphnode which is similar to other studies on abdominal tuberculosis in HIV patients.[18,22,23] Splenic involvement in tuberculosis in immunocompetent patients is a very rare entity, only few cases have been reported in literature.[24,25] In our study splenomegaly with hypoechoic infiltrate is seen in a large number of cases as observed in other studies.[18,22,26] In view of rare presentation of splenic tuberculosis in immunocompetent patients, its presence in a patient carries a high suspicion of HIV infection. There was no statistically significant difference found between ultrssonographic finding and CD4 count. Agarwal D et al has shown significantly higher CD4 count among patient with only lymphadenopathy.[18]

Institution of anti-tubercular therapy lead to clinical improvement in the majority of patients along with ultrasonographic resolution suggesting that USG can be used for diagnosis, treatment and follow up of HIV patients with abdominal tuberculosis. The persistent lesion on completion of ATT could be due to HIV itself and needs further evaluation.

CONCLUSION

In conclusion, the findings of lymphadenopathy (size >15mm) and hypoechoic/necrotic echotexture, hepatosplenomegaly with hypoechoic lesions in ultrasonography are suggestive of abdominal tuberculosis in HIV infected patients with unexplained nonspecific symptoms and low CD4 count. However, above findings are not standardized and inability to confirm the diagnosis of tuberculosis by direct microscopy and culture is the limitation of this study. Ultrasonography is an affordable, widely available, non-invasive imaging modality which may be optimally utilized for the diagnosis of abdominal tuberculosis in HIV infected patients, especially in the rural setup where microbiological and other sophisticated radiological investigations have limited availability.

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