

## Research Article

# Clinical profile of 128 HIV positive cases with abdominal tuberculosis

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## ABSTRACT

**Background:** Tuberculosis and HIV co-infection remains a major public health challenge throughout the world. An extra 25% of deaths among TB patients are attributable to co-infection with HIV according to the WHO 2009 TB report. TB is often the first opportunistic infection and a leading cause of death in HIV infected persons. The main objective was to study the clinical profile of the patients co-infected with HIV and abdominal tuberculosis in Government Medical College, Aurangabad.

**Methods:** Patients co-infected with HIV and abdominal tuberculosis were included in this observational study. Patients were either HIV positive and later diagnosed to have abdominal tuberculosis or diagnosed to be HIV positive when investigations were done after the diagnosis of abdominal TB. The common presenting symptoms were weight loss, fever, loss of appetite, pain in the abdomen and chronic diarrhoea. Ultrasound and routine chest X-ray were done along with other routine blood investigations including CD4 count.

**Results:** We studied 407 cases of HIV-TB co-infected patients out of whom 248 (61%) were of extra-pulmonary tuberculosis. Out of 248, 128 cases (51.6%) were diagnosed to have abdominal tuberculosis which was the commonest type of extra pulmonary tuberculosis in HIV –TB co- infected patients. They had higher morbidity, but we found that 96.06% patients completed anti-tubercular treatment and responded. Mortality rate of abdominal TB was lowest (3.94%) among all types of extra-pulmonary and also pulmonary TB in HIV co -infected patients. So we can conclude that HIV TB co infected patients show good response to anti- tubercular treatment if we diagnose this condition early.

**Conclusions:** Abdominal tuberculosis is the commonest type of extra pulmonary tuberculosis in HIV patients. On ultrasonography, the common abnormalities seen were intra-abdominal lymphadenopathy, splenic abscesses, ascites etc. All the patients who were diagnosed within few weeks of symptoms recovered with anti tubercular therapy, similar to HIV negative patients.

**Keywords:** AKT, Splenic abscesses, Lymphadenopathy

## INTRODUCTION

Tuberculosis and HIV co-infection remains a major public health challenge throughout the world. An extra 25% of deaths among TB patients are attributable to co-infection with HIV according to the WHO 2009 TB

report. TB is often the first opportunistic infection and a leading cause of death in HIV infected persons.

HIV infection is the primary reason for the failure to meet tuberculosis control targets (at least 85% cure rate among new sputum smear positive TB cases) in countries with high HIV infection. HIV-infection leads to diagnostic

challenges and delays in identifying TB that profoundly impacts treatment outcome. Studies and reports elsewhere have demonstrated a high TB treatment death rate in TB/HIV co-infected patients when compared to HIV negative TB patients, as high as 35%.

Estimates by the World Health Organization (WHO) indicate that there are more than 9 million new active cases of TB and close to 2 million deaths per year and that 2.6 million new cases of HIV infection and 1.8 million AIDS-related deaths occur per year. Some 14 million individuals worldwide are estimated to be dually infected. TB is the largest single cause of death in the setting of AIDS, accounting for about 26% of AIDS-related deaths, 99% of which occur in developing countries. Both TB and HIV have profound effects on the immune system, as they are capable of disarming the host's immune responses through mechanisms that are not fully understood. HIV co-infection is the most powerful known risk factor for progression of M. tuberculosis infection to active disease, increasing the risk of latent TB reactivation 20-fold. Likewise, TB has been reported to exacerbate HIV infection.

**METHODS**

We studied 407 cases of HIV-TB co-infected patients out of whom 248 (61%) were of extra pulmonary tuberculosis. Abdominal tuberculosis was the most common form of extra pulmonary tuberculosis observed by us in 128 cases (51.61%). Though mortality rate was low (3.94%), the morbidity was high, especially in cases who were diagnosed after a few weeks of illness.

**RESULTS**

The total number of HIV-TB co-infected patients was 407, of these 159 were pulmonary (39%) and 248 (61%) were extra pulmonary TB cases (Table 1).

The mortality rate in HIV-TB co-infected patients who had pulmonary TB was 11.95%. In co-infected patients with extra pulmonary TB, it was 8.47%. Amongst HIV-EPTB co-infected patients, mortality in abdominal tuberculosis was 3.94% whereas for other forms of EPTB, it was 13.22%.The data is statistically significant, i.e. deaths are more common in HIV-pulmonary TB co-infected cases compared to extra pulmonary TB (Table 1A). Also, deaths were significantly higher in extra pulmonary tuberculosis other than abdominal tuberculosis as compared to abdominal tuberculosis.

In this study, the youngest patient was 8 years old and eldest was a 60 years female. The majority, 68.50%, of patients belonged to the age group of 21 to 40 years (Table 2). 73.22% patients of abdominal tuberculosis were males and 26.77 % were females (Table 3).

Patients who were already HIV positive presented with weight loss and fever as the common presenting symptom

followed by loss of appetite, weakness, chronic diarrhoea, pain in abdomen (Table 4). Majority of patients presented with the collective symptoms of weight loss, loss of appetite, fever, loose motions and pain in abdomen.18 patients had cervical lymphadenopathy along with other presenting symptoms and only two patients had only cervical lymphadenopathy as the presenting complaint and were diagnosed to have abdominal TB on investigations. Also, there was only one patient with haemoptysis as the presenting symptom along with other complaints (Table 5).

125 out of 127 (98.42%) presented with weight loss as their initial presenting complaint followed by loss of appetite, fever, pain in abdomen, loose motions (Table 6). Diarrhoea was also a common presenting complaint and 49 cases presented as loose motions along with other features (Table 7). Majority i.e. 81.9% patients had symptoms of abdominal TB for 2 to 4 weeks. 9.45% had symptoms for less than 2 weeks and 4.72% had symptoms for more than 2 months (Table 8). In 50.39% of cases, the CD4 count less than 200, in 17.32%, it was 201 to 350 and in 31.49% it was more than 350 i.e. in 49.61% it was more than 200 (Table 9).

**Table 1: Total HIV-TB co-infected patients and their distribution according to pulmonary and extra pulmonary TB.**

HIV-TB co-infected patients	No of cases	Percentage
Extra Pulmonary TB	248	61%
Pulmonary TB	159	39%
Total	407	100%

**Table 1A: Mortality rate in HIV-TB coinfectd patients.**

HIV-TB Coinfectd patients	No. of cases	Deaths	Survival	Percentage of death
Extra Pulmonary TB	248	21	227	8.47%
Pulmonary TB	159	19	140	11.95%
Total	407	40	367	9.83%

**Table 2: Age wise distribution.**

Age in years	No. of cases	Percentage
1-10	6	4.72
11-20	4	3.14
21-30	27	21.26
31-40	60	47.24
41-50	21	16.54
51-60	9	7.08
Total	127	100

**Table 3: Male female sex ratio.**

Sex	No. of cases	Percentage
Male	93	73.22%
Female	34	26.77%
Total	127	100%

**Table 4: Initial presentation in HIV patients.**

Symptoms	No. of Cases
Weight loss	90
Fever	61
Loss of appetite	52
Cough	10
Weakness	39
Chronic Diarrhoea	49
Asymptomatic (on screening)	19
Pain in abdomen	40
Breathlessness	1
Oral ulceration	4
Difficulty in swallowing	1
Vomiting	1

**Table 5: Syndromic presentation.**

Syndromic presentation	No. of cases
Weight loss, Loss of appetite, pain in abdomen	11
Weight loss, Loss of appetite, pain in abdomen, Fever	26
Weight loss, Loss of appetite	12
Cough, Weight loss, pain in abdomen, Fever	11
Weight loss, Loss of appetite, pain in abdomen, Fever, Lymphadenopathy	18
Weight loss, Fever, Haemoptysis	1
Lymphadenopathy	2
Weight loss, Loss of appetite, Fever	46
<b>Total</b>	<b>127</b>

**Table 6 : Symptoms in Tuberculosis patients.**

Presenting symptoms	No. of cases
Weight loss	125 (98.42%)
Loss of appetite	113 (88.97%)
Fever	102 (80.31%)
Loose motion	49 (38.58%)
Pain in abdomen	66 (51.96%)
Cough	11 (8.66%)
Haemoptysis	2 (1.57%)
Lymphadenopathy	2 (1.57%)

Once extra pulmonary tuberculosis (EPTB) is diagnosed, the case of HIV is considered to be in Clinical stage 4. In the 127 cases in this study, at the time of diagnosis of HIV, 34 (26.77%) were in stage 1, whereas majority (65.35%) were in Clinical stage 4 and co-infection with

HIV was diagnosed when they presented for symptoms of TB abdomen (Table 10).

**Table 7: Syndromic presentation.**

Syndromic presentation	No. of cases
Weight loss, Loss of appetite, pain in abdomen, loose motion	10
Weight loss, Loss of appetite, pain in abdomen, Fever, loose motion	12
Weight loss, Loss of appetite, loose motion	1
Cough, Weight loss, pain in abdomen, Fever, loose motion	7
Weight loss, Loss of appetite, pain in abdomen, Fever, Lymphadenopathy, loose motion	3
Weight loss, Fever, Haemoptysis, loose motion	1
Weight loss, Loss of appetite, Fever, loose motion	15

**Table 8: Duration of symptoms of tuberculosis.**

Duration	No. of cases	Percentage
< 2 weeks	12	9.45
2-3 weeks	64	50.40
3-4 weeks	40	31.50
< 2 months	5	3.94
>2 months	6	4.72
Total	127	100

**Table 9: CD4 count.**

CD4 count	No. of cases	Deaths	Percentage of deaths
< 200	64 (50.39%)	3 (2.36%)	2.36
201-350	22 (17.32%)	0	0
>350	40 (31.49%)	1 (0.78%)	0.78
Not done	1	1 (0.78%)	0.78
Total	127	5 (3.94%)	3.94

**Table 10: Clinical stage of HIV.**

Stage	No. of cases	Deaths	Percentage
1	34	0	0
2	8	1	0.78
3	2	0	0
4	83	4	3.14
Total	127	5	3.94

**Table 11: Sputum positive patients in abdominal TB HIV co-infection.**

Patients type	No. of cases
Sputum Positive	1
Sputum Negative	127
Total	128

**Table 12: ART regime.**

Regime	No. of cases	Percentage
TLE	45	35.43
ZLE	32	25.19
ZLN	16	12.60
SLE	7	5.51
SLN	4	3.15
TLN	3	2.36
Second line	4	3.15
Pre Art	16	12.60
Total	127	100

**Table 13: USG findings and their percentage.**

Ultrasound findings	No. of cases	Percentage
Abdominal lymphadenopathy	106	83.47%
Splenic micro abscess	60	47.2%
Ascites	16	12.6%
Ileocaecal kochs	12	9.44%

**Table 14: AKT category.**

Category	No. of cases	Percentage
1	106	83.46
2	14	11.03
4	0	0
Non dots	7	5.51
Total	127	100

**Table 15: Outcome of tuberculosis.**

Outcome	No. of cases	Percentage
AKT completed	105	82.68
Deaths	5	3.94
On AKT	17	13.39
Total	127	100

**Table 16: Mortality due to tuberculosis in HIV patients.**

Type	No. of cases
Abdominal Koch's'	3.94%
Pulmonary kochs'	11.94%
Other extra pulmonary	13.22%

Only one patient was also sputum positive. 83.47% patients had abdominal lymphadenopathy as ultrasound finding (106 out of 127), 60 patients (47.2%) had splenic micro abscesses, 16 patients (12.6%) had ascites and 12 patients (9.44%) had intestinal strictures (Table 13). 83.46% patients received Cat I regime, Cat II regimen of AKT (11.03%). No patient required Cat 4 regimen (Table 14).

In our study, 105 patients (82.68%) of tuberculosis abdomen completed antituberculosis therapy, 5 patients (3.94%) died and 17 patients are still on antituberculosis therapy (Table 15). Abdominal TB contributed only 3.94% of deaths in HIV patients whereas other extra pulmonary TB contributed 13.22% of death (Table 16).

## DISCUSSION

Diagnosis of TB on the whole is difficult in HIV infected patients because of masking of constitutional symptoms, sputum negativity, atypical chest radiograph and resemblance to other opportunistic infections. Due to involvement of inaccessible and uncommon sites in EPTB, diagnosis of EPTB becomes especially challenging.

In this study, the sites of EPTB were, abdomen in 128 (51.2%), cervical lymph nodes in 59 (23.6%), pleura in 48 (19.2%), meninges in 9 (3.6%), spine in 3 (1.2%), pericardium in 1 (0.4%). Two patients had military TB (0.8%). We did not get any case of scrofuloderma genitourinary TB.

The presenting symptoms in this study were-weight loss in 125 (98.42%), loss of appetite in 113 (88.97%) fever in 102 (80.31%) loose motions in 49(38.58%), pain in abdomen 66 (51.96%), cough in 11 (8.66%), haemoptysis 2 (1.57%) and lymphadenopathy in 2.

Tuberculosis can involve any part of the gastrointestinal tract and is the sixth most frequent site of extra pulmonary involvement. Tuberculosis bacteria reach the gastrointestinal tract via haematogenous spread, ingestion of infected sputum, or direct spread from infected contiguous lymph nodes and fallopian tubes. The gross pathology is characterized by transverse ulcers, fibrosis, thickening and stricturing of the bowel wall, enlarged and matted mesenteric lymph nodes, omental thickening, and peritoneal tubercles. Peritoneal tuberculosis occurs in three forms: wet type with ascites, dry type with adhesions, and fibrotic type with omental thickening and loculated ascites. The most common site of involvement of the gastrointestinal tuberculosis is the ileocaecal region. Ileocaecal and small bowel tuberculosis presents with a palpable mass in the right lower quadrant and/or complications of obstruction, perforation or malabsorption especially in the presence of stricture. Rare clinical presentations include dysphagia, odynophagia and a mid-oesophageal ulcer due to oesophageal tuberculosis, dyspepsia and gastric outlet obstruction due

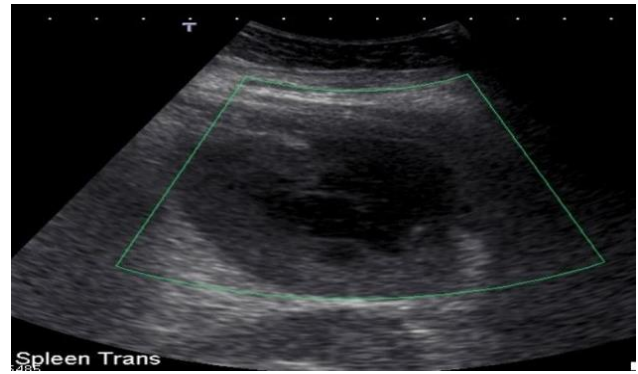
to gastroduodenal tuberculosis, lower abdominal pain and haematochezia due to colonic tuberculosis, and annular rectal stricture and multiple perianal fistulae due to rectal and anal involvement. Useful modalities for investigating a suspected case include ultrasonography, computed tomographic scan and colonoscopy. Ascitic fluid examination reveals straw coloured fluid with high protein, serum:ascitis albumin gradient less than 1.1 g/dl, predominantly lymphocytic cells, and adenosine deaminase levels above 36 U/l. Laparoscopy is a very useful investigation in doubtful cases. Management is with conventional antitubercular therapy for at least 6 months.

The clinical presentation tends to be non-specific, with abdominal pains and general complaints, and the differential diagnosis will often include inflammatory bowel disease, malignancy or some other infection.<sup>1,2</sup> Prompt diagnosis allows an early start to anti-TB therapy, with advantages for the patient and savings to the health system.<sup>1</sup>

Maximum number of patients, i.e. 47.2% belonged to the age group of 31 to 40 years. 85% of the patients were between 21 to 50 years of age, which is in accordance of the age group in which HIV infection and AIDS occurs commonly.

In our study, pronounced weight loss and abdominal pain were the predominant presenting complaints, followed by loss of appetite, nausea, vomiting and diarrhoea. 81% of our patients had symptoms since 2 to 4 weeks. The findings of the present study confirm earlier reports on the difficulties of diagnosis, including non-specific presenting features, unhelpful laboratory tests, negative results with tuberculin skin tests and Ziehl-Neelsen staining and false-negative ultrasound and CT scans.<sup>3,4</sup> Others studies have found CT scan of the abdomen, used commonly as a follow-on from ultrasound, only marginally more specific for abdominal TB than ultrasound.<sup>7,8</sup>

Abdominal tuberculosis comprises of tuberculosis of gastrointestinal tract, peritoneum, omentum, mesentery and its lymph nodes and other abdominal organs such as liver, spleen and pancreas. Extra pulmonary tuberculosis is common amongst HIV-infected patients. (248 patients out of 407 i.e. 61% in our series of HIV TB co infected patients had EPTB). In various series, extra pulmonary tuberculosis alone or in association with pulmonary disease has been documented in 40-60% of all cases with HIV co-infected individuals.<sup>6</sup>



**Figure 1: Ultrasonographic picture of splenic microabscesses in abdominal TB and HIV co-infection**

Abdominal tuberculosis can occur primarily or it can be secondary to a tubercular focus elsewhere in the body. Infection by *Mycobacterium tuberculosis* causing abdominal tuberculosis is acquired in following ways; (1) Dissemination of primary pulmonary tuberculosis in childhood; (2) Swallowing of infected sputum in active pulmonary tuberculosis; (3) Hematogenous dissemination from a focus of active pulmonary tuberculosis or miliary tuberculosis; (4) *Mycobacteria* can spread from infected adjacent organs like fallopian tubes; (5) Intestinal infection can occur by lymphatic spread from infected mesenteric lymph nodes; (6) *Mycobacteria* can also get disseminated through bile from tubercular granulomas of the liver. Sites of Involvement in Abdominal Tuberculosis as following ; (1) Gastrointestinal tract; (2) Peritoneum, e.g. ascites; (3) Lymph nodes; (4) Solid organs, e.g. liver, spleen and pancreas.<sup>3</sup> Gastrointestinal tuberculosis constitutes 70-78% cases of abdominal tuberculosis.<sup>4</sup> Ileocaecal area is the most commonly involved site due to the abundance of lymphoid tissue (Peyer's patches) followed by the colon and jejunum. Rarely tuberculosis may also involve stomach, duodenum and oesophagus. Strictures are usually produced as a result of cicatricle healing of ulcerative intestinal lesions. Most cases of gastrointestinal tuberculosis have associated lymph node and peritoneal involvement. Peritoneal involvement occurs in 4-10% patients of extra pulmonary tuberculosis (EPTB).<sup>6</sup> Tubercular peritonitis follows either the direct spread of tuberculosis from ruptured lymph nodes and intra-abdominal organs or haematogenous seeding. Peritoneal involvement may be in the form of peritoneal adhesions or exudative fluid in the peritoneal cavity (ascites). The coexistence of cirrhosis in patients with tubercular peritonitis complicates the diagnosis. Tubercular lymphadenitis accounts for about 25% cases of extra pulmonary tuberculosis. The lymph nodes disease is particularly frequent in younger age groups and more frequent in HIV-infected patients. The nodal involvement in abdominal tuberculosis is mainly mesenteric (tabes mesenterica) or retro-peritoneal.<sup>5</sup> The lymph nodes may show caseation or calcification. Intestinal, nodal and peritoneal tuberculosis may also occur in varying permutations and combinations. The involvement of liver

and spleen in tuberculosis occurs as a part of disseminated and miliary tuberculosis and is usually granulomatous. The macronodular form of hepatosplenic tuberculosis is an uncommon form of disseminated tuberculosis<sup>7</sup>. Gastric tuberculosis though rare but is commoner than oesophageal, duodenal, appendicular and anal tuberculosis.<sup>6</sup> In order of frequency, abdominal tuberculosis manifests as tubercular lymphadenitis, peritonitis and hepatosplenic or pancreatic tuberculosis. The disease may present at any age but commonly seen in young adults.<sup>8</sup> In children, peritoneal and nodal form of tuberculosis is more common than intestinal tuberculosis.<sup>9</sup>

The clinical manifestations depend on the site and type of involvement. The symptomatology mainly includes (i) constitutional symptoms in about one-third of patients (fever, malaise, anemia, night sweats, loss of weight, weakness), and (ii) local symptoms and signs referable to the site involved. Ultrasonography (USG) is most beneficial in extra intestinal (peritoneal, lymph nodes) tuberculosis. The USG of abdomen may show a mass of matted loops of small bowel with thickened walls, rolled up or diseased omentum, and loculated ascites. Fine septae (complete or incomplete), echogenic debris (seen as fine strands and particulate matter) may be seen within tubercular ascites. These septae are due to high fibrin content of the exudative ascitic fluid. Peritoneal thickening and nodularity are the other ultrasonographic findings of peritoneal tuberculosis. Interloop ascites due to localized collection of fluid between radially-oriented bowel loops named as Club sandwich or sliced bread sign may be observed.

Small bowel mesenteric thickening (15 mm or more) with increased echogenicity combined with mesenteric lymphadenitis is a characteristic ultrasonographic feature of early abdominal (mesenteric) tuberculosis. Omental thickening with altered echogenicity has also been reported. Dilated small bowel loops, bowel wall thickening showing a hypoechoic halo measuring >5 mm is suggestive of intestinal tuberculosis.

The following features on USG were considered suggestive of abdominal tuberculosis as obtained from other studies in HIV patients.<sup>4-6</sup> Enlarged lymph nodes predominantly hypoechoic/ necrotic, size of lymph nodes greater than 15 mm. 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 at the ileocaecal junction), peritoneal nodules, mesenteric thickening or ascites are also suggestive. Presence of more than one of the above findings was considered as extensive abdominal involvement.

A high degree of suspicion combined with proper use of diagnostic modalities will help in the timely diagnosis of the disease.

In our study, abdominal (mesenteric/retroperitoneal), lymphadenopathy with predominantly hypoechoic/necrotic echo-texture was seen in 106/127 (83.47%) patients. Splenic micro-abscesses were seen in 60 patients (47.2%). Ascites was seen in 12 patients (9.44%), small bowel wall thickening in 16 (12.6%). Loculated ascites was not seen in any case. Splenic micro-abscesses appeared to be far commonest in HIV positive cases as compared to negative, though we do not have exact data about HIV negative cases.

82.6% cases showed clinical recovery after completing conventional treatment (83.6% cases received CAT1; whereas 11.03% received CAT-2. 5.51% patients received daily therapy.) 17 are still on treatment and improving. There were no defaulters as these patients are also on ART, come regularly for follow up and medicines to the ART centre and are rigorously counselled there. 5 of the 127 patients died (mortality 3.94 %). These patients were seriously ill at the time of presentation and died during hospitalization or soon after discharge. This emphasizes the need to diagnose abdominal tuberculosis at an early stage, especially in HIV positive patients.

## CONCLUSION

Abdominal tuberculosis is the commonest type of extra pulmonary tuberculosis in HIV infected patients. The common presenting features are weight loss, abdominal pain, diarrheal and loss of appetite. On ultrasonography, the common abnormalities seen were intra-abdominal lymphadenopathy, splenic abscesses, thickening of the bowel wall and ascites. All the patients who were diagnosed within few weeks of symptoms recovered with anti-tubercular therapy, similar to HIV negative patients. Compliance of the patients to treatment was very good as they were supervised regularly in the ART clinic. Clinical features and sonography together diagnose abdominal TB in HIV positive cases very effectively

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