Indian tubercular belly: A prospective study of 140 patients of abdominal tuberculosis and their outcomes

Monika Keena[1], Gopal Chawla[2], Ujjwal Sonika[3], Nupur Abrol[4], Shrikant Hiremath[5], Virender Kumar Meena[6]

[1]Department of Pulmonary Medicine, Consultant, Railway Hospital, Jodhpur, Rajasthan, [2]Department of Pulmonary Medicine and Critical Care, Metro Centre of Respiratory Disease, Noida, UP, [3]Department of Gastroenterology, GB Pant Institute of Post Graduate Medical Education and Research, New Delhi, [4]Department of Anaesthesia, Max Super Speciality Hospital, Shalimar Bagh, New Delhi, [5]Department of Pulmonary Medicine, SDM College of Medical Sciences, Sattur, Dharawad, Karnataka, [6]Department of Radiology, Geetanjali Medical College and Hospital, New Delhi, India

Abstract

Background: Abdominal tuberculosis is an important yet ignored entity in the spectrum of tuberculosis which has been dominated by pulmonary tuberculosis. Diagnosis and treatment are often delayed due to nonspecific symptoms. In this study, we aimed to highlight the clinical features, diagnostic methods and outcomes of abdominal tuberculosis. **Methods:** A prospective study was conducted in tertiary referral centre where all patients referred to drug distribution centres (DOTS centre) for abdominal tuberculosis were identified. Their demographic clinical and radiological profile was evaluated. These patients were followed-up for their treatment course for complications and outcomes. **Results:** A total of 140 patients who were labelled abdominal tuberculosis over a period of 2 years were reviewed at tuberculosis drug distribution centre (DOTS). Mean age of study population was 35.42 ± 12.53 years and majority of the population were males, 58.6% (82). The most common presenting symptom was abdominal pain which was seen in 82.8% (n = 116) of the patients, followed by feverin 65.6% (n = 92); 22.8% (n = 32) were seropositive for HIV and 44.2% (n = 62) had luminal tuberculosis of which ileocecal was the most common site. Peritoneum was second most common site which was involved in 26.4% (n = 37) of the patients followed by mixed tuberculosis involving more than one type. Confirmed diagnosis was achieved in 74 patients (52.8%), while the remaining 66 patients (47.14%) were diagnosed clinically. During follow-up, 12 patients were lost to follow-up; 113 (80.7%) had complete response, while 3 (2.14%) patients died during treatment. **Conclusion:** Abdominal tuberculosis usually presents with nonspecific complaints which require high index of suspicion. Most patients require only medical therapy which has good results.

Keywords: Abdominal Koch, abdominal pain, extra pulmonary tuberculosis, HIV

Introduction

Tuberculosis (TB) has been a major cause of ill health since centuries and is one of the leading causes of death from a single infectious agent. It typically affects the lungs but can also affect other sites. Indian subcontinent accounts for almost 45% of global TB burden. Extrapulmonary TB constitutes (EPTB) approximately 15% of the total TB cases.[1] EPTB can present in many forms, can cause significant ill-health and lasting disability. Abdominal TB mostly present with nonspecific complaints often leading to delay in treatment which can be a cause of morbidity and life altering complications.[2] Most of the resources for research, diagnosis and management are

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diverted toward pulmonary TB, as it is a major public health concern and cause of mortality leaving EPTB and in particular abdominal TB[2,3]

Swallowing infected sputum, hematogenous spread from a pulmonary focus, lymphatic spread from infected lymph nodes and contiguous spread from adjacent organs are the important modes of infection in the cases of abdominal TB.[4] Symptoms of abdominal TB are related to the infected site such as abdominal pain, and diarrhoea are seen in luminal TB while ascites and abdominal distension are commonly seen with peritoneal TB, general physician as primary care giver are at unique position in determining fate of these patients.[5]

Therefore, to evaluate the burden of abdominal TB and response to treatment, the study was conducted to study the clinical profile, risk factors and various modalities of diagnosis and outcomes of abdominal TB.

Methods

Study design

A prospective cohort study.

Study populations

Between January 2014 and January 2016, a total of 140 consecutive adult patients aged >18 years who were diagnosed with abdominal TB and began treatment with anti-TB drugs at our centre who gave consent to be a part of the study were enrolled. Demographic, socioeconomic data along with clinical features, HIV status, diagnostic method, drug resistance and clinical outcome were noted. Patient's mobile phone number along with contact number of their immediate relatives were also noted to strengthen the follow-up.

Definitions and classification

Abdominal TB was defined as infection of gastrointestinal tract or peritoneum or intrabdominal lymph node or any solid abdominal organ with mycobacterium TB.

Diagnosis of abdominal TB was made in any of the following ways:
- Histopathological: Demonstration of caseous granulomas on biopsy specimens or Fine Needle Aspiration Cytology (FNAC) of lymph node.
- Microbiological: Positive Mycobacterium culture with tissue specimen or ascites. Positive Acid Fast Bacilli (AFB) smear or positive Cartridge Based Nucleic Acid Amplification test (CBNAAT) for mycobacterium TB (Cartridge-based Nucleic acid amplification test), that is, GeneXpert (Cepheid Inc., Sunnyvale, CA, USA) or culture from ascites, biopsy specimen (microbiologic diagnosis) or from Lymph node aspirate were considered as confirmed cases.
- Clinical: Clinical symptoms with radiological features favouring abdominal TB like involvement of ileocecal region

or typical presentation and good response to anti-TB agents. When peritoneal TB could not be diagnosed on biopsy, the high ascitic adenosine deaminase (>33 IU/L) criteria was used for clinical diagnosis.[6,7]

All patients were evaluated for pulmonary TB with chest X-ray and sputum for AFB.

Patients were classified into 5 groups: (1) luminal, (2) nodal, (3) peritoneal, (4) visceral and (5) mixed. Luminal TB was further divided into esophageal, gastric, duodenal, jejunal, ileocecal and colorectal. Peritoneal TB was divided into 2 types: the wet and dry type (fixed fibrotic and dry plastic type). Nodal TB was divided into mesenteric, porta hepatitis, celiac axis, peripancreatic and combined. Visceral TB was divided into hepatic, splenic and combined.[8]

Clinical outcomes

Abdominal TB outcomes were defined as follows
(1) Complete response: Gain in weight and relief of symptoms were considered as markers for response to treatment. Complete relief from symptoms along with microbiological sterility in the form of negative culture or smears for AFB, in those who were earlier positive.
(2) Partial response: partial resolution of symptoms or partial healing of lesions on endoscopy at the end of treatment;
(3) No response: No relief from symptoms or persistence of AFB on smear or culture or persistence of active TB lesions on relook colonoscopy at the end of treatment;
(4) Lost to follow-up: treatment defaulters for more than 2 consecutive months;
(5) Death: death from any cause during treatment;
(6) Recurrence: endoscopic or radiologic documentation of new lesions after a complete response.

All diagnosed were given Anti Tubercular Treatment (ATT) according to the guidelines, first lines for 6 months and second line for 9 months and were followed-up monthly over a period of 6 months for adverse drug effects, complications and relief of symptoms.[6] Those who did not have complete response after 6 months were given ATT for 3 more months and evaluated, and if still there is partial response, 3 more months of ATT was given and after 1 year of start of treatment, they were labelled no response or partial response. All those who had complete response after 6 months were followed-up till 1 year since the start of treatment for recurrence. Final outcome was labelled only after patient has been followed-up for 1 year.

Study size

This prospective study was planned over 1-year recruitment period followed by follow-up for 1 year. Ours is a tertiary care hospital that caters 5 cities and 15 villages, where total population is about 18 lakhs and number of new TB cases every year was around 21,000.[9] Considering prevalence of abdominal TB in the country to be 4%,[10,11] sample size calculated was 102 at

99% confidence level.[12] In view of attrition and losses during follow-up, sample size of 140 was taken.

Statistical methods

Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. Data were checked for normality before statistical analysis using Shaipro–Wilk test.

Results

In a prospective study conducted in tertiary hospital with drug distribution centre, 920 new TB patients visited, out of which 196 (21.2%) were referred for abdominal TB; 56 patients refused to participate in the study. A total of 140 patients (82 males, 58.6%) with an average age of 35.42 ± 12.53 years were enrolled, youngest being 13 years and oldest being 75 years. Median duration of symptoms was 142 (IQR 45–106) days. Abdominal TB was more common amongst office workers followed by housewives and students. The most common presenting symptom was abdominal pain which was seen in 82.8% (n = 116) of the patients followed by fever in 65.7% (n). Abdominal distension was present in 40% of the patients primarily due to ascites; 34.2% (n = 48) had concomitant respiratory complaints, 22.8% (n = 32) were seropositive (HIV +) and 77.14% (n = 108) were seronegative. Only 12.8% (n = 18) had a past history of TB, out of which 12 patients were previously treated for pulmonary TB, while 6 had EPTB (3 tubercular pleural effusion, 1 inguinal lymphadenopathy, 1 Potts spine and 1 TB meningitis). Only 60 (42.8%) patients had positive Mantoux test. All patients were evaluated for concomitant pulmonary TB and chest X-ray was normal in 102 patients, while 20 showed active infection in the form of infiltration, consolidation or military shadow. Twelve showed pleural effusion, while eight had right-sided pleural effusion and 1 had bilateral effusion. Sputum for AFB was done in all and for those who could not produce sputum, sputum induction with 3% saline was done. Sputum was positive in 22 (15.8%) patients; 16 (72.7%) out of 22 patients produced sputum only on induction. HIV was the most common risk factor seen in 32 patients (22.8%) followed by young age and alcohol [Table 1].

Ultrasonography (USG) abdomen and CT abdomen was done in all 140 patients. USG screening was positive in 84 (61.4%) patients. Most common finding was ascites which was seen in 40 patients followed by intestinal wall thickening in 19 and enlarged lymph nodes in 14 patients. Twelve patients out of 40 had complex ascites either with septations, debris or both. CT abdomen showed positive findings in 96.4%, luminal gastro intestinal (35%) was most common followed by peritonitis (32.14%) and lymph nodes (15%) [Table 2 and Figure 1].

A total of 40 patient who had ascites underwent ascitic fluid examination; all were lymphocytic predominant, mean ^ Serum Ascites Albumin Gradient (SAAG) 0.72 ± 0.41, mean protein content was 3.8 ± 0.96 and mean adenosine

Table 1: Demographic and clinical parameters of study population

	No. of patients	%age
Age group		
13-20	30	21.4
21-30	36	25.7
31-40	30	21.4
41-50	24	17.1
51-60	12	8.7
61-70	6	4.3
71-80	2	1.4
Gender		
Male/Female	82/58	58.6/41.6
Professional Status		
Labourer/Farmer	23	16.4
Businessman/Vendors	29	20.7
Office	48	34.2
Retired/service	4	2.4
Housewives	36	24.3
Educational Status		
Uneducated	52	37.1
Primary	41	29.3
Matric	37	26.4
Graduate	10	7.1
Presenting Symptoms		
Abdominal pain	116	82.8
Fever	92	65.7
Vomiting	54	38.5
Bowel disturbances	52	37.14
Abdominal distension	56	40
Anorexia	90	64.28
Weight loss	86	61.4
Respiratory symptoms	24	17.14
Acute Surgical problem Intestinal obstruction/perforation	26	18.6
Examination Findings		
Pallor	48	34.2
Ascites	56	40
Abdominal mass	3	2.14
Hepatomegaly	6	4.28
Splenomegaly	6	4.28
Hyperperistaltic bowel sounds	22	15.7
Guarding	36	25.7
Rigidity	22	15.7
Past history of TB		
Present	18	12.8
Tuberculin skin test		
Positive	60	42.8
Chest X-ray		
Normal	102	72.8
Infiltration	14	10
Consolidation	4	2.9
Pleural effusion	12	8.6
Miliary	2	1.4
Old fibrotic calcified lesion	4	2.9
Fibrocavitatory lesion	2	1.4
Risk factors		
HIV	32	22.8

Contd...

Table 1: Contd...		
	No. of patients	%age
Diabetes	8	5.7
Chronic renal disease	6	4.3
Chronic liver disease	12	8.6
Young age <20 years	26	18.6
Prolonged steroid use (>1 month)	10	7.1
Alcohol	12	15.7

Table 2: Radiological features of patients of abdominal tuberculosis		
	Number of patients	%
USG feature		
No significant Finding	56	40
Ascites *n*=40		
Simple	28	20
Complex (Septate, Debris)	12	8.6
Omental thickening	4	2.8
Intestinal bowel thickening	19	13.6
Lymph nodes	14	10
Hepatomegaly	3	2.14
Splenomegaly	5	3.6
Hepatic foci	3	2.14
CT abdomen features		
No significant finding	5	3.6
Peritonitis *n*=45		
Wet/Ascites	40	28.6
Dry	5	3.6
Lymphadenopathy, *n*=21		
Peri portal	7	5
Mesenteric	5	3.6
Para aortic	4	2.8
Diffuse	6	4.3
Luminal gastro intestinal involvement *n*=49		
Stomach (ulcer)	1	
Duodenum	3	2.14
Jejunum	6	4.3
Ileocecal	39	27.8
Colorectal	3	2.14
Hepatic foci	9	6.4
Splenic abscess	4	2.8
Splenic foci	2	1.4

deaminase was 45.53 ± 16.8 units. CBNAAT detected mycobacterium in 6 patients (15%) and Rifampicin resistance was seen in 2 out 6. Mycobacterium culture was positive in 9 patients and out of that 4 showed resistance to first line agents [Table 3].

In total, 25 patients underwent colonoscopy and 7 had Upper Gastrointestinal (UGI) endoscopy, while laparoscopy was performed in 19 patients [Figures 1e, 1f and 2a]. Twenty (14.28%) patients presented with acute intestinal obstruction and required surgery [Figure 2b, 2c and Table 4], providing tissue sample for histopathology and microbiology [Figure 1e, 1f]. However, culture of tissue specimens yielded positive growth in 36 (50.7%) cases while pathological diagnosis was made in 52 (73.2%) cases. In 34 patients, both histology and bacteriology were positive. In

16 patients, organisms were isolated on culture but the histology did not reveal the granuloma. Thus, the diagnosis of TB was made in 70 on basis of tissue specimen reports. (34 on histology, 18 on microbiology and 18 both culture and histology). Three out of 36 patients for whom microbiology was positive showed resistance to first line agents.

According to the types of abdominal TB, luminal TB (44.2%) was dominant pattern followed by peritoneal TB (26.4%). Ileocecal junction (n = 43) was the most commonly involved area followed by jejunum (n = 6), colorectum (n = 6) and duodenum (n = 5); 15% had mixed abdominal TB [Table 5].

When patients were followed-up, 17 (12.14%) had side effects to ATT, warranting stopping of it. Nine patients out of 17 required changes in a regimen, while in rest 8, it was reintroduced. Most common side effect were gastrointestinal (n = 8) side effects followed by drug-induced hepatotoxicity (n = 5), thrombocytopenia (n = 2) and Steven Johnson syndrome (n = 1). Monthly follow-up was strictly ensured with regular phone calls if patient did not turn up. Despite best efforts, 12 patients were lost to follow-up. Out of 113 patients who showed complete response to ATT, 88 (77.8%) patients showed complete response in 6 months, 19 (16.8%) showed in 9 months and 6 (5.3%) in 12 months. Two patients had recurrence in the form of new symptoms like new onset abdominal pain and laparoscopic biopsy was positive for AFB bacilli. All the 3 patients who expired had concomitant pulmonary TB, and of these 2 were seropositive for HIV [Table 6].

Discussion

In this study, we studied the patients with abdominal TB who were referred to drug distribution centre in western India and we followed-up them for 1 year for response assessment. We tried to confirm diagnosis either microbiologically or pathologically but was limited by availability of tests and patient's willingness to go for the procedure. Microbiological diagnosis had poor sensitivity. We had good treatment results with ATT in prescribed 6 months, while few required extended treatments. We had rigorous follow-up plan where patients were followed-up even if they had complete response.

Maximum number of the patients referred for drug distribution centre belonged in the 3rd decade with average age being 35.42 ± 12.53 years which was comparable to earlier study of 300 patients. According to Bhansali *et al.*,[13] this pattern has not changed in almost 50 years which was seen in Udgirkar *et al.*[14] As pulmonary TB is also more common in this age group, chances of abdominal TB are also higher in this group. This could be due to high requirement of nutrition which is not met by low socioeconomic individuals leading to malnutrition and decreased immunity. Males were predominantly involved in our study as was in study by Vij *et al.*[15] In agreement with previous studies, most common symptom of presentation was abdominal pain.[13,14,16] Mostly, patient presents with chronic symptoms while some
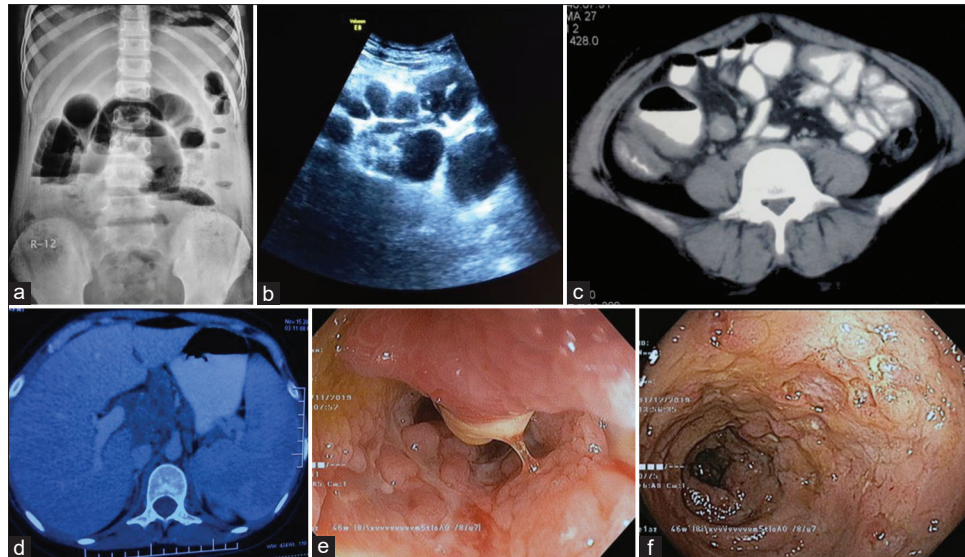
Figure 1: (a) Abdominal X-ray shows multiple air fluid levels suggestive small bowel obstruction, (b) USG abdomen showing necrotic conglomerated retroperitoneal lymphnodes, (c) CT abdomen showing ileocecal thickening, (d) CT abdomen showing nodes along with vascular encasement, (e) Colonoscopic image showing ulceronodular mucosa of ileocecal junction and (f) Ulceronodular mucosa of colon

Table 3: Diagnostic method in patients with abdominal tuberculosis

	Number of patients	%
Pathologically	65	46.4
Surgical biopsy	20	30.7
Laparoscopic biopsy	18	27.7
Upper GI endoscopic biopsy	2	3.07
Colonoscopic biopsy	12	18.5
Lymph node cytology	13	20
Microbiologically	54	38.5
Surgical biopsy culture	12	21.4
Laparoscopic biopsy culture	9	16.1
Upper GI endoscopic biopsy culture	5	8.9
Colonoscopic biopsy culture	10	17.8
Ascites microbiology	9	16.1
Lymph node FNAC CBNAAT	9	16.1
Clinically	66	47.1
Symptoms	10	15.1
Clinico-radiologically	28	42.4
Paracentesis (L%, ADA)	28	42.4

Table 4: Various causes of surgeries

Site and type of lesion	No. of patients	Percentage
Jejunal strictures	2	2.9
Jejunal perforation	1	1.4
Ileum band and adhesions	5	7.1
Ileal perforation	4	5.7
Hypertrophic	1	1.4
Ascending colon stricture	1	1.4
Intestinal obstruction	8	11.4

had acute presentation in the form of intestinal obstruction. Proportion of patients presenting with intestinal obstruction or perforation was 18.6% which is far more than any other Indian study probably, as ours is a tertiary centre and have more of

referral patients.[17]

There were a variety of risk factors which we studied and HIV was found to be most important risk factor which is in concordance with other studies.[14,18,19]

Concurrent pulmonary infection in our study was 15.8%, though 12.8% had past history of pulmonary TB. This was similar to various studies in India and abroad, where they have shown rate of 15% to 25%.[4,20]

USG and CT abdomen showed positive features in 60% and 96.4%, respectively, which was similar to the study by Udgirkar *et al.*[14] Ultrasonography being readily available is now a screening procedure for all patients suspected to have abdominal TB, as it accurately demonstrates small quantities of fluid, retroperitoneal lymph nodes and helps in picking up intestinal involvement.[21] CT abdomen had better yield in our study as majority were referral cases. In a study by Das *et al.*,[22] correct clinical diagnosis of abdominal TB could be made in approximate 50% of cases, whereas Hoon *et al.* reported accuracy of 34% in diagnosis based on clinical features.[22,23] In our study set, 47.14% of patients were started ATT without microbiological or histopathological examination either on basis of symptoms or radiological supporting features or paracentesis examination; 42.12% of these patients had paracentesis which was lymphocytic, high ADA and low SAAG, this percentage is more than other developed nations[19] and 52.8% had microbiological or histopathological diagnosis consistent with abdominal TB. Classically, the TB is confirmed when caseating granuloma are seen, but there may be number of granulomas which may not show caseation. Patients on chemotherapy may also not show caseation in the granuloma.[24] Demonstration of these granulomas help in differentiating abdominal TB from Crohn's disease. In histopathology, the presence of granuloma in biopsy supported
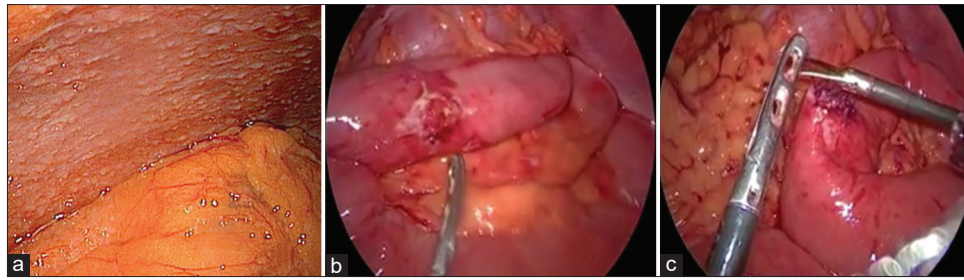
Figure 2: (a) Laparoscopic image showing studded mesentery and omentum, (b) image showing perforation of jejunum and (c) laparoscopic repair of jejunal perforation

Table 5: Site of involvement in abdominal tuberculosis	
Site	No. of patients
Luminal	62 (44.3%)
Esophagus	2
Gastric	1
Duodenum	5
Jejunum	6
Ileocaecal	43
Colorectal	5
Peritoneal	37 (26.4%)
Dry	3
Wet	34
Nodal	8 (5.7%)
Visceral	12 (8.6%)
Liver	6
Spleen	6
Mixed	21 (15%)
Luminal and peritoneal	5
Luminal and nodal	4
Luminal, peritoneal and nodal	7
Peritoneal and visceral	1
Nodal and visceral	2
Peritoneal, visceral and nodal	2

with clinical and radiological features along with excellent therapeutic response to ATT is considered diagnostic of TB.[25]

Laparoscopy was performed in 22 of the 140 patients and was diagnostic in 20 (90.9%). Remaining two laparoscopies were unsuccessful because of adhesions and could not be completed. It was not routinely performed as majority of patients did not give consent and was done as last investigation as reported in other study. But given the choice, it is the investigation for diagnosis with highest yield.[16,26]

Drug resistance was seen in 6.4% (n = 9) patients diagnosed either on CBNAAT of ascites (n = 2) or mycobacterium culture of ascitic fluid and tissue specimen (n = 7), which was less as compared with other Indian study where it was 9.4%.[27] There is sparse data on drug resistance in abdominal TB as compared with pulmonary TB. In endemic country like ours, most of the patients are started on clinico-radiological basis and very few like peritoneal TB and culture positive patients undergo drug resistance testing.[14,24]

We were able to achieve complete response in 77.8% patients in 6 months, while other required continuation of treatment to 9 or 12 months. Extended course has not shown to be superior but in our study, 17.8% (n = 25) were given extended treatment who showed complete response. These patients had continuation of clinical symptoms which had decreased but were still present. So, 17 of these patients underwent repeat FNAC or relook colonoscopy. None of peritoneal TB required extended treatment. Mixed (n = 15), nodal (n = 4) and intestinal TB (n = 6) required extended treatment. Longer treatment is required may be due to malabsorption in abdominal TB and thus limited bioavailability or because adverse drug effects forcing to stop treatment for a while or modifying it.[28] No response was seen in 2 of those who were presumed to have ileocecal TB on clinical suspicion and on colonoscopy turned out to be having inflammatory bowel disease which is often the chronic mimicker of it.[25]

Strengths of our study were that it was a prospective study with enough sample size to be representative of western India abdominal TB burden. We followed-up patients for response out come along with recurrences, drug effects and complications. There were some limitations that it was the single centre study. Another limitation is that only a fraction of patients with ileocecal TB underwent colonoscopy but this is a common practice in India where colonoscopy facilities are not easily available to every patient. We had many patients diagnosed without microbiological or histopathological evidence but considering TB to be endemic in India, high index of suspicion was warranted. Very few patients were verified for complete response microbiologically and histopathologically as majority of patients did not give consent when they were feeling fine.

Role of family physicians
Abdominal TB has a significant effect socially, economically and mentally, apart from physical symptoms. Diagnosis is often difficult and gets delayed resulting in increased morbidity but patients can be cured if they have access to diagnosis and treatment with anti-TB drugs in time.

Conclusion
Abdominal TB though may be the 4th common in list of EPTB is a cause of high morbidity and complications. High index of

Table 6: Follow up in 140 patients with abdominal tuberculosis		
Characteristics	Number of Patients	Percentage of Patients
Significant side effects to ATT	17	12.14
Gastro-intestinal Side effects	8	5.7
Thrombocytopenia	2	1.4
SJ syndrome	1	0.07
Drug induce hepatitis	6	4.3
Drug resistance	9	6.4
Treatment regimen		
First line ATT	127	90.7
Modified regimen	4	2.8
Second line ATT	9	6.4
Outcome		
Lost to follow-up	12	8.5
Complete response *n*=113		
6 months	88	77.8
9 months	19	16.8
12 months	6	5.3
Partial response	8	5.7
No response	2	1.4
Recurrence	2	1.4
Death	3	2.14

suspicion coupled with radiology often helps in identifying the patients with abdominal TB. The established microbiological and molecular methods of diagnosis have poor sensitivity in abdominal TB. Therefore, majority of patients are treated on clinic-radiological suspicion which is going to remain the standard practice in near future.

Take home message

Medical therapy has excellent results and against the common belief, only a few require surgery. Drug resistance is low. Peritoneal TB is easy to diagnose and has better response to 6-month ATT. Complete response can be achieved in majority provided right treatment is started without any delay and keeping drug resistance in consideration. We need to have better record keeping of abdominal TB and involve various disciplines for achieving diagnosis and effective treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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