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A Clinicopathological Study and Management of Abdominal Tuberculosis

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Abstract: ***Abdominal tuberculosis is a tricky clinical problem that a physician will come across. A lack of specific signs and symptoms poses a diagnostic challenge and mimics many other conditions leading to diagnostic delay and development of complications. Therefore, a high index of suspicion is required for anearly diagnosis. Tuberculous bacteria can involve any part of the gastrointestinal tract, spreadby hematogenous route from infected focus in the lung or cervical lymph nodes,by contagious spread from infected lymph nodes or fallopian tubes, and ingestion of infected sputum.The gross pathology is characterized by transverse ulcers, fibrosis, thickening and strictures of the bowel wall, enlarged and matted mesenteric lymph nodes, omental thickening, and peritoneal tubercles. Sometimes, presents to emergency with proximal perforation or intestinal obstruction. Early diagnosis and initiation of anti-tuberculous therapy and surgical treatment are essential to prevent morbidity and mortality. Most of the patients respond very well to standard antitubercular therapy and surgery required only in a minority of cases if detected early.A retrospective study was done on 38 patients with proven abdominal tuberculosis.***

Keywords: Tuberculosis (TB), Extra Pulmonary tuberculosis (EPTB), Abdominal Tuberculosis (ATB), Intestinal Tuberculosis (ITB), Peritoneal tuberculosis (TBP)

1. Background

Tuberculosis continues to be a major killer disease worldwide, which can affect any organ system. Globally, an estimated 10.0 million people fell ill with TB in 2019.[1] Tuberculosis infects around 30% of the global population, more so in lower and middle-income countries and tropical countries like India, Indonesia, and China.[2] Majority of people who develop the disease are adults in the 3rd and 4th decade, with more cases among men than women.[1] The development of TB is associated with five risk factors: undernutrition, HIV infection, alcohol abuse, smoking (more among men), and diabetes.[1] Abdominal tuberculosis (ATB) accounts for 12.8% (11-16%) of all EPTB cases.[2] It is the 6th most common type of EPTB.[3] ATB can occur either alone or in association with pulmonary tuberculosis. Abdominal tuberculosis is described as EPTB that involves the various organs of the abdominal cavity like the small or large intestines, peritoneum, and lymph nodes, either alone or in combination[2]. The tuberculous Involvement of the genitourinary systems are considered as a separate entity, not a part of Abdominal tuberculosis.[2]

Pathology and Pathogenesis

Mycobacterium tuberculosis is responsible for most of the cases of ATB. The spread of abdominal tuberculosis can occur in multiple ways.

Previously, primary infection used to occur with ingestion of food contaminated with M.Bovis in unpasteurized milk. Present times it is due to reactivation of infection during childhood. secondary infection occurs by hematogenous spread from a focus in lungs or nodes in the neck, or ingestion of infected sputum from active pulmonary disease, contiguous spread from an infected organ-like female genital tract, and lymph nodes in the abdomen.

The mucosal glands of the GI tract get infected with bacilli, which initiates an inflammatory reaction leading to epithelioid tubercles formation in the lymphoid tissue of submucosa. After 2 to 4 weeks, it undergoes caseous necrosis. submucosal tubercles enlarge with edema and endarteritis causing ischemia, leading to ulceration of overlying mucosa causing spread into deeper layers, adjacent lymph nodes, and peritoneum. The spread of bacilli via lymphatics causes lymphatic obstruction of the mesentery and bowel leading to mass formation. Rarely, these bacilli can enter the portal circulation or the hepatic artery to involve solid organs like the liver, pancreas, and spleen. Swallowed bacteria travel through the payer's patches in intestinal mucosa and are carried by macrophages to mesenteric lymph nodes where they remain dormant. Reactivation of the disease in these nodes occurs in patients with immunocompromised states like diabetes, renal failure, HIV infections, steroid usage, and malignancy.[4]

Clinical Presentation

The disease in the majority has an insidious chronic course over a long period. The presenting symptoms vary depending on the site and the type of lesion. Symptoms vary from a chronic mild abdominal pain with constitutional symptoms to acute or acute on chronic presentation of Intestinal obstruction and/or perforation. The constitutional symptoms of tuberculosis include fever, night sweats, loss of weight, and appetite.

Intestinal TB (ITB)

Common site of infection in GIT is the Ileo-caecal region which is involved in 64% of cases.[5] The reasons for predisposition of the ileocecal area are physiological stasis of food, alkaline media, lack of digestive enzyme activity, the broad surface area of absorption, high resorption of fluid, and abundant lymphoid tissue.[6] Isolated jejunal involvement is rare and if present may mimic Crohn's disease. ITB presents as ulcerative, hypertrophic, nodular, ulcero-hyperplastic, and stricture-type lesions. The symptom complex depends on dominant local pathology. The ulcerative form is characterized by pain abdomen, chronic diarrhea, and malabsorption, while the clinical picture of hypertrophic or stricture presents as abdominal pain and episodes of sub-acute or acute intestinal obstruction. In the chronic stage, the ileocaecal valve appears fixed, rigid, and incompetent. The caecum appears conical, shrunken in size, and pulled up away from the right iliac fossa due to fibrotic changes in the mesocolon. It may mimic lymphoma or a carcinoma where carcinoma usually does not extend beyond the ileo-caecal junction. Intestinal obstruction and GI tract perforation are acute presentations that may need surgery. Bowel obstruction occurs due to hyperplastic mural thickening, stricture formation, or due to adhesion and bands. The most common complication is sub-acute intestinal obstruction, although acute-on-chronic abdominal pain may indicate a perforation. Tubercular perforations are single and proximal to a stricture.

Colon involvement is next to ITB. Segmental or isolated colonic TB occurs (5%) in the right side of the colon without ileocaecal involvement. Haematochezia which is presenting symptom with pain and change in bowel habit.

Anorectal involvement presents with abscess, multiple fistula, fissure, or mass.

Oesophageal, Gastro-duodenal involvement by Tuberculosis is rare (<1%). Oesophageal involvement is usually secondary to mediastinal lymph nodes infiltrating or compressing the esophagus. Clinical presentation may include dysphagia and/or hematemesis apart from constitutional symptoms. Gastroduodenal TB is another uncommon site of tuberculosis and the presence of gastric acid having bactericidal properties, scarcity of lymphoid tissue, and rapid emptying of gastric contents seems to play a protective role[3].

Peritoneal TB (TBP)

It could be acute or chronic in presentation. Three types of peritoneal lesions are described. They are wet ascitic type, dry adhesive type, fibrotic fixed type with loculated ascites and thickening of the omentum, and the mesentery with nodularity.[7] A rare combination of mixed type of these three lesions is seen as Abdominal cocoon,[7] characterized by the formation of a membranous sac around clumped bowel loops (sclerosing encapsulating peritonitis).[2] Rolled-up omentum presents as a mass.

Lymph nodes involved are mesenteric, para-aortic, periportal, and retroperitoneal groups. They can be caseating, hyperplastic or calcified types. Often mesenteric lymph nodes are affected with caseation and or cold abscess leading to inter bowel adhesions.

Visceral Tuberculosis

Solid visceral tuberculosis of the liver, spleen, pancreas, gall bladder, and biliary tract are rare but have been reported. Isolated involvement of abdominal solid organs is relatively uncommon and occurs in 15% to 20% of all patients with abdominal TB.[8] Hepatic tuberculosis could be miliary or localized. The localized TB hepatitis is associated with larger lesions, known as tuberculoma which could be calcified or present as liver abscess. Pancreatic tuberculosis is very rare. It could be due to the primary involvement of the pancreas or peripancreatic lymph nodes. Gall bladder tuberculosis is usually diagnosed histologically after cholecystectomy.

2. Investigations

Xpert MTB/RIF is a nucleic acid amplification test (NAAT) that rapidly detects the Mycobacterium tuberculosis complex and resistance to rifampicin simultaneously. It is an automated test that has emerged as an important diagnostic test for MTB.[9]Xpert MTB/RIF is a heminested real-time PCR test that utilizes a nucleic acid hybridization probe to identify the Beta subunit of RNA polymerase (rpoB) gene of the organism. Mutations in the rpoB gene of MTB account for 95% 0f Rifampicin resistance. This test requires minimal expertise and can be used in unprocessed samples. There is a possibility of false positive detection of rifampicin resistance in a small number of patients [10]. Xpert MTB/RIF has been recommended as an adjunct for rapid diagnosis of lymph node, meningeal and pleural tuberculosis [11]. Truenat TB test is a portable and battery-operated test using the same molecular testing. This has an advantage over the Xpert MTB/RIF test which needs a fully equipped laboratory. WHO currently recommends only the XpertMTB/RIF for the diagnosis of TB. A positive Xpert result can rapidly identify positive cases, but a negative test does not rule out TB.

The tubercular ascitic fluid is straw colored with cobweb formation on standing and has protein > 3g/dL, with a total cell count of 150-4000/µL predominantly of lymphocytes, serum ascitic albumin gradient is <1.1 g/dL[12]. Ascitic fluid adenosine deaminase (ADA) levels are elevated in tubercular ascites with 33 u/L taken as cut-off value with sensitivity and specificity of 100% and 97% respectively. Hematological findings are nonspecific and include raised ESR, anemia, hypoalbuminemia.

The various radiological studies are used for the diagnosis of abdominal TB. Plain radiographs may show enteroliths, perforation, and features of intestinal obstruction. Ultrasound is useful in the evaluation of extraintestinal lesions of peritoneal, ascitic fluid, lymph nodes, and solid organs. It also shows peritoneal thickening, rolled up omental with nodules, and bowel wall thickening. The thickening is uniform and concentric as opposed to the eccentric thickening at mesenteric border found in Crohn's disease and the variegated appearance of malignancy.[13] Pseudo kidney sign involvement of ileocaecal region which is pulled up to subhepatic position [13].

Barium meal follow-through is the best diagnostic test for intestinal TB.it shows intraluminal changes like ulcers, strictures of intestines, and also thickened mucosal folds, luminal stenosis, or multiple stenoses with segmental dilatation of bowel loops. Barium enema shows conical shrunken caecum which is pulled up due to contraction and fibrosis of mesocolon.

CT has almost replaced barium studies. Lymph node enlargement is the most common finding followed by ascites, bowel wall thickening, bowel dilatation, omental thickening, mesenteric thickening. MRI helpful for evaluation of abdominal TB and detects more strictures than barium study, but no added advantage over CT.

Colonoscopy determines the site and pattern of involvement and also provides tissue biopsies from the colon. Laparoscopy is also useful for diagnosis and taking a tissue biopsy.

DIAGNOSIS -Logan modification of the Paustian's criteria for diagnosis were suggested as 1] clinical manifestations suggestive of TB. 2] imaging evidence indicative of abdominal TB. 3] histological or microbiological evidence of TB. 4] Therapeutic response to treatment

Management of Abdominal Tuberculosis

Recent evidence suggests that standard ATT for six months is effective for patients with abdominal tuberculosis. [14,15] Standard ATT with Rifampicin, Isoniazid, Ethambutol, and pyrazinamide is recommended for intestinal and peritoneal tuberculosis. The treatment of lymph nodes and solid organs may need prolonged therapy. Endoscopy should be done 2-3 months after initiation of ATT. In the case of non-healing ulcers, the possibility of drug-resistant ITB or other diagnoses should be considered.[2] The culture and drug sensitivity should be performed in patients with non-healing mucosal lesions, those with a history of previous treatment of ATT, and in patients with HIV.[2] In peritoneal TB follow up USG findings of improvement of ascites is a good prognostic factor. Multiple strictures are less likely to respond to ATT than a single stricture.[14] The colonic strictures are more likely to persist and may need an endoscopic or surgical intervention. ATT remains the first line of treatment.[14] There is a higher failure rate of medical therapy in strictures and often requires surgical excision and anastomosis.

Surgery in ATB is mainly due to Intestinal obstruction due to strictures, adhesions, and cocoon formation. Free perforation is 2nd common indication. Localized perforation with abscess or fistula formation is also common. GI bleeding is rare and may need surgical intervention. surgical procedures needed are adhesiolysis, resection and anastomosis, stricturoplasty, perforation closure, and stoma creation. Multiple small bowel strictures are treated with stricturoplasty rather than major resections.[4] Limited ileocaecal resection for obstructing Ileo-caecal TB with adjuvant ATT gives better results.[4] Short strictures accessible to endoscopy may be treated with endoscopic dilatation or stenting.It is recommended to start ATT if there is a high index of suspicion for ileocecal TB based upon clinical, radiologic, and endoscopic findings, despite nondiagnostic histological and/or bacteriological studies of biopsies.[15]

3. Materials and Methods

This is a retrospective study of patients diagnosed with abdominal tuberculosis from May 2016 to February 2020 in a tertiary care center. 38 cases were diagnosed as abdominal tuberculosis on basis of clinical history, physical examination, investigations, and those confirmed by histopathology. Patients whose histopathology was negative for TB were excluded from the study. All patients with abdominal tuberculosis were started on antitubercular therapy as per the RNTCP (Revised National Tuberculosis Controlled Program) and were regularly followed on an outpatient basis.

4. Results

The observations based on the analysis of the data of 38 cases of ATB and summarized as follows:

Age

Age	No. of Cases	Percentage
<20	5	13.1
20 to 30	16	42.1
30 to 40	9	23.7
40 to 50	3	7.9
50 to 60	2	5.3
>60	3	7.9

In the present study the age of the patient ranged between 15 years to 75 years, the maximum number of cases were found to be in the age group of 20 years to 30 years (42.1%), followed by 30 years to 40 years age group with 9 cases (23.7%).

Sex Distribution

Sex	No. of Cases	Percentage
Males	23	60.5%
Females	15	39.5

The slight male preponderance (60% Vs 40%) was noted in this study. The gender difference has remained variable. Some authors have reported the predominance of the disease in females in developing countries, while some studies show male predominance. However, no significant reason could be found for this gender difference. The male to female ratio is 1.5:1.

Signs and Symptoms

Symptoms	No. of Cases	Percentage
Pain Abdomen	35	92.1
Fever	16	42.1
Vomitings	10	26.3
Distension	15	39.4
Loss of Weight	9	23.6
Loss of Appetite	**14**	**36.8**
Altered Bowel Habits	**7**	**18.4**
Cough	**5**	**13.1**
Mass Abdomen	**8**	**21**
Peritonitis	**21**	**55.2**

The most common complaint is abdominal pain (92.1%) followed by fever (42.1%). The patients with pulmonary symptoms of cough are low (13.1%) in this study. In the present study, abdominal tenderness is the most common sign, followed by guarding and rigidity which is suggestive of peritonitis (55.2%).

Associated Pulmonary Tuberculosis:

TB	No. of Cases	Percentage
Present	9	23.6
Absent	29	76.3

Only 9 out of 38 cases were found to have coexisting pulmonary tuberculosis.

Hematological Investigations:

Category	Parameters			
	Hemoglobin		ESR	
	Cases	%	Cases	%
Low	27	71	-	-
Normal	11	28.9	7	18.4
High	-	-	31	81.5

Anaemia with Hb% level low <10gm/dl is seen in 27 patients (71%) and high erythrocyte sedimentation rate > 20mm in 1st hour in 31 patients (81.5%).

Radiological Investigations

Radiological Investigations and Findings		
Investigation	No. of Findings	Percent
XRay Chest	9	23.6
Erect XRay Abdomen	17	44.7
USG	35	92.1
CT Abdomen	27	71

USG of abdomen and pelvis shows 35 cases (92.1%) with abnormal findings such as ascites (16), mesenteric lymphadenopathy (15), subacute intestinal obstruction (12), thickened bowel loops (10), omento-peritoneal thickening (4), small bowel stricture (3), and tubercles on bowel surface (1).

CECT abdomen was performed in 27 cases (71) and all of them have positive findings such as mesenteric lymphadenopathy followed by ascites, small bowel stricture, and pulled-up caecum.

Abnormal findings in chest x-ray were seen in 9 cases (23.6%) and had findings of patchy opacities in 7 cases and 2 cases with bilateral pleural effusion with pulmonary consolidation with fibrosis. X-ray of erect abdomen was taken in all cases and 17 cases (44.7%) had abnormal findings such as dilated bowel loops, multiple air-fluid levels, gas under diaphragm.

Site of Involvement

Site of Involvement		No. of Cases	Percentage
Peritoneal/Ascites		16	42.1
Lymph Nodes		9	23.7
GIT	Ileocecal Region	7	18.4
	Colon	2	5.3
	Small Intestine	2	5.3
Multiple Sites	Peritoneum & Intestines	4	10.5
	Peritoneum, Intestines & Lymph Nodes	2	5.3

In the present study peritoneal tuberculosis was more involved in 16 cases (42.1%) followed by GIT with 11 cases (28.9%) and lymphadenopathy with 9 cases (23.7%). In GIT most commonly involved site was the ileocecal region seen in 7/11 cases (63.6%). No solid organ involvement was seen in our study.

Mode of Treatment

Treatment	No. of Cases	Percent
Conservative	23	60.5%
Surgery	15	39.5%

Out of 38 patients, 23(60.5%) were treated conservatively with ATT. 15 (39.5%) patients needed surgical intervention.

Surgical Procedures

Total cases 15

Procedure	No. of Cases	Percentage
Resection And Stoma	5	33.33
Resection & Primary Anastomosis	3	20
Biopsy	3	20
Stricturoplasty	2	13.33
Primary Closure Of Perforation	2	13.33

Intestinal resection with ileostomy was the most frequent surgical procedure performed in 5 cases (33.33%).

Postoperative Complications:

Postop Complication	No. of Cases	Percentage
Wound Infection	2	13.33
Wound Dehiscence	1	6.66
Enterocutaneous Fistula	1	6.66

4/15 (26.67%) cases had complications in the postoperative period. 2 cases (13.33%) had wound infection and 1 case each (6.66%) had wound dehiscence and enterocutaneous fistula.

5. Discussion

Tuberculosis is a worldwide disease and a major health problem in developing countries. [15] With the emergence of HIV, it has become a resurgent problem. Abdominal tuberculosis is a common disease that poses a diagnostic challenge. The nonspecific features of the disease lead to a delay in diagnosis and development of complications. This condition is a great mimicker of other abdominal pathology. The spread of the disease is further aided by poverty, overcrowding, and drug resistance. Abdominal tuberculosis usually presents late, mostly in surgical emergencies with obstruction and peritonitis.

The mean age was found to be 24.5 years with the youngest patient being fifteen years old and the oldest being 75 years old. This finding was consistent with other studies that have reported peak incidence of tuberculosis in the 2nd to 4th decades [16]. However, in the developed world, abdominal tuberculosis is mostly seen in older, immunocompromised patients or immigrants from endemic areas [17]. The peak incidence of abdominal tuberculosis in the productive years of life puts a great impact on the economy of the family and the society as a whole.

The slight male preponderance (60:40%) was noted in this study. The gender difference had remained variable. Some authors have reported the predominance of the disease in females in developing countries, while some studies show male predominance [18] However, no significant reason could be found for this gender difference.

In developing countries like India incidence of tuberculosis is very high because of overcrowding, poor living conditions, poor hygiene, and illiteracy.

In the present study maximum, no of cases were seen in low socioeconomic status with 85% in the Below Poverty Line strata. This correlates with findings of previous studies like Arunima M [19] et al 2014 who reported 92% occurrence in low socioeconomic status respectively.

Presenting symptoms in abdominal tuberculosis vary widely and are nonspecific. Studies from India in the last 3 decades have shown that pain is the most common presenting symptom and is present in about 80 to 100% of patients. [20] Our study show pain is the most common symptom (92.1%) inconsistent with other studies. The mode of presentation depends upon the site of involvement. Peritoneal involvement generally presents with abdominal distension and pain, while the intestinal variant presents with pain and features of subacute intestinal obstruction. Bowel disturbances were seen in most cases of right ileac fossa mass which can be explained by hypertrophic tuberculosis seen among the exposed population with increased resistance to the organism. Hepatic tuberculosis presents with pyrexia of unknown origin (PUO) and jaundice with raised ALP levels.

Only nine patients (23.6%) had a concomitant pulmonary tuberculosis and 29 (76.4%) had primary abdominal tuberculosis. Studies done in developing countries have shown similar results while in developed countries, primary abdominal tuberculosis is rare. However, no logical explanation could be drawn for such differences [21].

In the present study peritoneal tuberculosis was most common, seen in 16 cases (42.1%) which includes ascites, adhesions and omental tuberculosis followed by ulcero-sclerotic gastrointestinal tuberculosis, hyperplastic gastrointestinal tuberculosis

In agreement with the other studies, the ileocecal region was the most commonly involved region in GIT tuberculosis in this study (63.6%) [22]. Similar figures have been provided in previous studies studying acute presentations of abdominal tuberculosis with ileal strictures being the most prevalent pathology [22]. This could be explained by the abundance of Peyer's patches in the ileal segment, which leads to uptake of mycobacterium tuberculosis by lymphoid cells in this region and proliferation of lymphoid tissue. Moreover, stasis and increased physiological exchange of fluid and electrolytes lead to increased contact time of pathogens with ileal mucosa rendering this region vulnerable to the development of intestinal tuberculosis [23].

Routine haematological investigations revealed anaemia [Hb <10gm%] in 27 cases [71%]. Anemia was reported in 64% of patients in a study from Nepal [24]. Various pathogeneses have been suggested in TB-associated anemia, but most studies have shown the suppression of erythropoiesis by inflammatory mediators as the cause of the anemia [25].

Another routine haematological investigation, ESR, was evaluated in 31 patients in the present study and was found to be elevated in 81.5% of the cases. A 77% prevalence, comparable to ours was reported by Niaz and Muhammad [26]. ESR is a nonspecific significant parameter that is raised in almost all patients with chronic ailments, as well as, in abdominal TB. Both of these parameters are considered nonspecific changes useful in validating other pathological and clinical findings.

Most of the positive findings were recognized in ultrasonography followed by an erect x-ray abdomen. CECT was performed only in cases in which diagnosis is doubtful.

The most commonly performed procedure was resection anastomosis and ileostomy. Although no statistically significant difference was noted in patients who underwent stoma formation compared to those who underwent primary anastomosis, comparison cannot be properly drawn because no randomization was observed in selecting patients for either primary anastomosis or stoma formation. Stoma needs proper patient education for handling and prolongs hospital stay [27]. Moreover, a second surgery is required to restore the intestinal continuity once the disease is cured with a significantly increasing morbidity. Hence, randomized controlled trials are needed to establish whether primary anastomosis is superior to the stoma in the management of intestinal tuberculosis presenting as acute abdomen. Moreover, experience has shown that stoma prevents significant morbidity in moribund patients presenting with more than 48 hours of peritonitis. The presence of intra-abdominal sepsis in a malnourished patient increases the chances of anastomotic breakdown, however, evidence-based data is lacking in such cases.[4]

The commonest complication was wound infection, which occurred in 13.33% of our patients. Rajput et al also reported surgical site infection as the most common postoperative complication [28]. SSI was observed in this study because most of our patients were undernourished and, hence, had reduced healing ability in addition to decreased immune function.

6. Conclusion

Abdominal tuberculosis is a major public health concern of low-income countries. It remains a diagnostic dilemma for healthcare providers because of diverse presentations and unequivocal signs and symptoms. It is seen in under nourished people of relatively younger age group. Delayed presentation remains the hallmark of this disease in our setting. Hence, disease surveillance strategies need to be implemented to ascertain early diagnosis and prompt treatment. Moreover, more randomized controlled-trials need to be conducted to establish evidence-based guidelines on the surgical management of acute abdomen due to abdominal tuberculosis.

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