

## CLINICOPATHOLOGICAL PROFILE OF GASTROINTESTINAL TUBERCULOSIS PATIENTS AT A TERTIARY CARE HOSPITAL

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### ABSTRACT

#### BACKGROUND

Abdominal tuberculosis represents the sixth most frequent form of extra-pulmonary tuberculosis after lymphatic, genitourinary, bone and joint, miliary and meningeal tuberculosis. It can affect gastrointestinal, lymphatic and pancreatobiliary system.

#### AIMS

To study clinicopathological features of biopsies and resected abdominal specimens diagnosed as TB.

#### METHODS AND MATERIAL

It is a cross-sectional study and include 135 patients diagnosed histopathologically as GITB between January 2004 to June 2015 in a Tertiary Health Care Centre. Analysis of various intestinal tuberculous lesions in relation to age, gender, socioeconomic class, clinical signs and symptoms, basic hematological parameters, histopathological findings etc. was done.

#### RESULTS

Out of total 135 cases, 75(55.56%) were males and 60(44.44%) were females with male:female ratio being 1.25:1. Maximum incidence of GITB was seen in 21-30 years age group. Maximum number of GITB cases belonged to low (Lower and upper lower) socio-economic class, i.e. 58.52%. Abdominal pain (95.56%) was the most common presenting symptom and abdominal tenderness (67.41%) was most common clinical sign. Ileo-caecal junction (38.52%) was the most common site involved in GITB. AFB positivity in tissue was reported in 16.3% cases out of total 135 GITB cases.

#### CONCLUSION

The diagnosis of GITB is difficult and careful approach to the patients and supportive investigation data are necessary to make the final diagnosis. Neither clinical features nor laboratory findings are conclusive of GITB, histopathological findings by themselves provide a gold standard in the diagnosis.

#### KEYWORDS

Gastrointestinal Tuberculosis, Abdominal Tuberculosis, Intestinal Lesions, Tuberculosis.

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#### INTRODUCTION

Tuberculosis detected as far back as 10000 BC, still remain a major public health problem worldwide.<sup>1</sup> It ranks as the second leading cause of death from an infectious disease worldwide, after the Human Immunodeficiency Virus (HIV).<sup>2</sup> Hence called as "The Captain of all men of death." According to World Health Organization (WHO), worldwide there were 9.6 million new TB cases in 2014 and 1.5 million TB deaths (1.1 million among HIV-negative people and 0.4 million among HIV-positive people). India, Indonesia and China had the largest number of cases (23%, 10% and 10% of the global total respectively).<sup>3</sup> TB mortality is unacceptably high given that most deaths are preventable if people can access health care for a diagnosis and the correct treatment is provided. Abdominal tuberculosis represents the sixth most frequent form of extra-pulmonary tuberculosis after lymphatic, genitourinary, bone and joint, miliary and meningeal tuberculosis.<sup>4</sup>

Abdominal TB accounts for 2% of all cases of tuberculosis.<sup>5</sup> and about 12% of extrapulmonary TB.<sup>6</sup> It can affect gastrointestinal, lymphatic and pancreatobiliary system.<sup>7</sup> Most of the cases of Gastrointestinal Tuberculosis (GITB) are due to *M. tuberculosis*. *M. bovis* earlier accounted for a substantial number of cases worldwide, is now less frequently encountered due to widespread pasteurization of milk. Clinical manifestations of GITB are often non-specific and to be confused with many other diseases, specially Crohn's disease, intestinal neoplasms, amoebiasis and yersinia infection.<sup>8</sup>

Laboratory and radiological findings are also non-conclusive. There is no single feature, which is diagnostic for GITB. A combination of symptomatology and diagnostic tools is used, but histopathology still remains the gold standard for the diagnosis of GITB in routine practice. Many cases of GITB present with complications due to delayed diagnosis. The associated mortality and morbidity demand prospective research to find out the ways and procedure to reduce this.

The present study aims at a fresh look into GITB and a better understanding of its clinical manifestations and histopathological diagnosis.

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## AIMS AND OBJECTIVES

The objectives of present study are:

- To study the demographic factors associated with Gastrointestinal Tract Tuberculosis (GITB) like age, sex and socioeconomic status.
- To find out the common organ and site of involvement in cases of GITB.
- To study clinical and hematological findings in cases of GITB.
- To study gross and microscopic features of biopsies and resected abdominal specimens diagnosed as TB.
- To apply Ziehl Neelsen stain and find out incidence of Acid Fast Bacilli (AFB) positivity in cases of GITB.

## MATERIAL AND METHODS

It is a cross-sectional study and include 135 patients diagnosed histopathologically as GITB between January 2004 to June 2015 in a Tertiary Health Care Centre.

### Inclusion Criteria

- All patients diagnosed histopathologically as GITB on biopsies/resected surgical specimens.

### Exclusion Criteria

- All clinically suspected TB patients, but not diagnosed as TB on histopathological examination of biopsies/resected surgical specimens were excluded from the study.
- Autolysed specimens.
- Visceral form of abdominal TB involving solid organs (Liver, Spleen and Pancreas) without definitive involvement of GI tract.

A detailed information including age, gender, history of pulmonary TB, socioeconomic status, history of contact with TB patient's, etc. clinical signs and symptoms, basic hematological parameters were recorded in the proforma.

For retrospective cases, slides and paraffin blocks of previously diagnosed cases of GITB were retrieved from Surgical Pathology Department and reviewed. Additional sections were cut to prepare fresh slides wherever required, stained and studied.

For prospective cases, all biopsies and resected surgical specimens of GIT clinically suspected as TB were received in 10% neutral buffered formalin in the Department of Surgical Pathology. The details of gross examination findings of biopsies and resected specimens were noted. Tissues were processed, sections were cut by microtome and evaluated after staining by Haematoxylin and Eosin technique. Zeihl Neelson staining was done to demonstrate Acid fast Bacilli.

We selected one of the following two criteria for the diagnosis of GITB in present study:

1. Histological demonstration of characteristic epithelioid granulomas with or without caseation either in the biopsies/resected bowel or regional lymph nodes.
2. Demonstration of acid fast bacilli in the Zeihl Neelson sections of biopsies/resected bowel or regional lymph nodes.

Analysis of various intestinal tuberculous lesions in relation to age, gender, socioeconomic class, clinical signs and symptoms, basic hematological parameters, histopathological findings, etc. was done.

## RESULTS

Out of total 135 cases, 75(55.56%) were males and 60(44.44%) were females with male:female ratio being 1.25:1. Maximum incidence of GITB was seen in 21-30 years age group in females and 31-40 years age group in males. Overall, maximum incidence (28.89%) of GITB was seen in 21-30 years age group. Youngest patient in the present study was of 2 years while oldest one was of 78 years (Mean age 32.97 years). Table

1 shows age and gender-wise distribution of GITB cases. Maximum number of GITB cases belonged to low (Lower and upper lower) socio-economic class, i.e. 58.52%. Middle socio-economic class constitute 39.26% and Upper socio-economic class constitute only 2.22% of total 135 cases.

Abdominal pain (95.56%) was the most common presenting symptom followed by anorexia (74.81%) and altered bowel habits (65.92%). Cough was present in 31.85% of total cases, although past history of pulmonary tuberculosis was given by 84 patients (62.22%). Table 2 shows common presenting symptoms of GITB reported in the present study.

Abdominal tenderness (67.41%), cachexia (65.92%) and pallor (62.22%) were common clinical signs. Table 3 shows various clinical signs reported in GITB cases in present study. Laboratory investigations revealed low haematocrit (Less than 41% in male and less than 36% in female) in 73.33% cases of GITB, but haemoglobin (Hb) was low in only 34.07% of cases. Leucocytosis with lymphocytosis was seen in 38.52% and monocytosis in 33.33% of GITB cases. Erythrocyte Sedimentation Rate (ESR) was raised (more than 30mm at the end of first hour) in 57.78% of GITB cases. Mantoux test was positive (More than 10mm of induration and erythema) in 71.85% cases of GITB. Acid Fast Bacilli (AFB) were detected in sputum in 26.21% cases out of 103 GITB cases; 4.44% cases of GITB were reactive for Human Immunodeficiency Virus (HIV). Ileo-caecal junction (38.52%) was the most common site involved in GITB cases followed by ileum (35.56%), caecum (9.63%), colon (5.92%), appendix (5.18%), rectum/anal canal (2.96%), jejunum (1.48%) and stomach (0.74%).

Most common finding on gross examination of resected specimens was ulcer (81%) followed by strictures (49.42%), band and adhesions (20.74%), perforation (17.78%), hypertrophic mass (15.55%), tubercles over surface (9.63%) and ulcero-hypertrophic lesion (8.15%). Table 4 shows macroscopic findings of GITB cases. Most common finding on microscopic examination was tuberculous granuloma (97.03%) followed by Langhan's type giant cells (95.56%), caseous necrosis (79.26%) and foreign body giant cells (15.56%). AFB positivity in tissue was reported in 16.3% cases out of total 135 GITB cases.

## DISCUSSION

When the results of the present study are analyzed against the backdrop of the available literature, many results are concordant with the previous studies, but few disparities are also noticeable.

### Age-Wise Distribution of GITB Cases

In the present study, maximum incidence of GITB was seen in 21-30 years age group followed by 31-40 years (25.18%). These results are consistent with the findings of Darbari A et al.<sup>2</sup> (58%), Krishnanand et al.<sup>9</sup> (54.8%), Tripathi PB et al.<sup>10</sup> (55.4%), Zea MI et al.<sup>11</sup> (64%), Saaq M et al.<sup>12</sup> (61.37%), Shimy GG et al.<sup>13</sup> (45.56%), Islam MB et al.<sup>14</sup> (75%) and Rabbi ANMA et al.<sup>15</sup> (54.54%).

Abdominal tuberculosis like tuberculosis elsewhere in the body affects the young people at the peak of their productive life. This fact has serious impact on the national economy and production, as working and productive class of community is replaced by sick and ill individuals.

### Gender Wise Distribution of GITB Cases

In the present study out of total 135 cases, 55.56% were males and 44.44% were females with M:F ratio being 1.25: 1. Sharma YR et al.<sup>16</sup> (2.57:1), Darbari A et al.<sup>2</sup> (1.3:1) and Shimy GG et al.<sup>13</sup> (M:F = 1.25:1) have reported male preponderance in GITB cases. On the contrary, Lal V et al.<sup>17</sup> (M:F = 1:1.38),

Sankpal J et al.<sup>18</sup> (M:F = 1:1.6) and Shrestha S et al.<sup>19</sup> (M:F = 1:2.2) have reported female preponderance in their studies.

Tripathi PB et al.<sup>10</sup> have reported equal incidence of GITB in both gender. So conclusion cannot be drawn and we can say that GITB can affect both genders without any predilection. Differences may be due to geographical variation and catchment of health services.

### Socio-Economic Class

Various authors have reported GITB cases in low socio-economic class ranging from 60% (Islam MB et al.<sup>14</sup>) to 83% (Niaz K et al.<sup>20</sup>) We have reported 58.52% of GITB cases belonging to low socioeconomic class in our study. As undernutrition, unhygienic environment and overcrowding are commonly associated with low socio-economic class, this may be the reason of maximum incidence of GITB in this class.

### Clinical Presentation

Abdominal pain was the most common presenting symptom reported by most of the previous authors. It ranged from 51.2% (Uygur Bayramicli O et al.<sup>21</sup>) to 100% (Shimy GG et al.<sup>13</sup> Lal V et al.<sup>17</sup> Sankpal J et al.<sup>18</sup>) of GITB cases in various studies. Abdominal pain in GITB may be due to intestinal obstruction, perforation or peritonitis. Similarly altered bowel habits in GITB are due to intestinal ulcers, strictures and subacute obstruction.

Association of Pulmonary Tuberculosis (PTB) with GITB cases as reported by various authors ranges from 8.91% (Sankpal J et al.<sup>18</sup>) to 50% (Tripathi PB et al.<sup>10</sup>) in previous studies. In the present series, association of PTB was reported in 34.81% of GITB cases. Abdominal tenderness (67.41%) was found as most common clinical sign in the present study, which is consistent with the studies of Sharma YR et al.<sup>16</sup> (48%), Ibrahim M et al.<sup>22</sup> (74%), Shimy GG et al.<sup>13</sup> (81.1%) and Lal V et al.<sup>17</sup> (64%). Abdominal tenderness may be due to intestinal obstruction, perforation or peritonitis.

In the present study intestinal obstruction was reported in 47.41% of total 135 GITB cases. Previous authors have reported intestinal obstruction ranging from 9.3% (Ibrahim et al.<sup>22</sup>) to 66.65% (Krishnanand et al.<sup>9</sup>). Intestinal obstruction occurs mainly due to narrowing of the lumen by hyperplastic caecal tuberculosis by strictures of the small intestine, which are commonly multiple or by adhesions. Various authors have reported peritonitis ranging from 6% (Darbari et al.<sup>2</sup>) to 35.7% (Shimy GG et al.<sup>13</sup>) in their studies. In present study, we found signs of peritonitis in 17.78% of 135 GITB cases. Acute tubercular peritonitis may be due to perforation. Acute tubercular peritonitis without perforation is usually an acute manifestation of peritoneal disease, but may be due to ruptured caseating lymph nodes.

### Laboratory Investigations

In the present study, anaemia was reported in 73.33% of total 135 cases. Various authors have reported anaemia ranging from 30% (Darbari A et al.<sup>2</sup>) to 77.36% (Miah AR et al.<sup>23</sup>) in previous studies. Anaemia in abdominal tuberculosis may be due to nutritional deficiency as malabsorption is commonly associated with subacute intestinal obstruction. Malabsorption is due to bacterial overgrowth and bile salt deconjugation in the upper small intestine.

ESR was raised in 57.78% of GITB cases in the present study. Previous authors have reported raised ESR in 46% (Ibrahim M et al.<sup>22</sup>) to 90% (Shreshtha S et al.<sup>19</sup>) of GITB cases.

As Mantoux test is a non-specific test, reported positive in 19.2% (Uygur Bayramicli O et al.<sup>21</sup>) to 85.57% (Islam MB et al.<sup>14</sup>) cases by various authors in their studies; 71.85% cases have positive Mantoux test in the present study. Negative Mantoux test may be due to GI loss of protein and anorexia leading to hypoalbuminemia.

### Anatomic sites Involved in GITB

Ileocaecal junction was the most common site involved in GITB cases in the present study, which is in concordance with the studies done by Sharma YR et al.<sup>16</sup> (28%), Islam MB et al.<sup>14</sup> (51.6%), Ibrahim M et al.<sup>22</sup> (38.46%), Tripathi PB et al.<sup>10</sup> (50.9%), Rabbi ANMA et al.<sup>15</sup> (56.52%) and Zea MI et al.<sup>11</sup> (72.22%). The exact explanation for more frequent involvement of the ileocaecal region is unknown, but it may be due to a variety of factors such as increased rate of fluid/electrolyte absorption, abundance of lymphoid tissue in the form of Peyer's patches, physiological stasis and minimal digestive activity at the ileocaecal region.

In the present study, mesenteric lymphadenopathy was reported in 31.11% of total 135 GITB cases. Zea MI et al.<sup>11</sup> reported mesenteric lymph node involvement in all (100%) cases. Tripathi PB et al.<sup>10</sup> reported in 65.5% cases, Islam MB et al.<sup>14</sup> in 53.3% cases, Lal V et al.<sup>17</sup> in 48% cases, Shrestha S et al.<sup>19</sup> in 18.7% cases, Uygur-Bayramicli O et al.<sup>21</sup> in 16.8% cases, Ibrahim M et al.<sup>22</sup> in 12% cases, Saaq M et al.<sup>12</sup> in 11.58% cases, Sankpal J et al.<sup>18</sup> in 10.45% cases and Sharma YR et al.<sup>16</sup> in 8% cases.

### Macroscopic Findings

Ileocaecal TB is conventionally classified into ulcerative, ulcero-hypertrophic and hypertrophic lesion.

Malik AK et al.<sup>24</sup> (77.5%), Tripathi PB et al.<sup>10</sup> (66.4%) and Lal V et al.<sup>17</sup> (60%) have reported ulcerative lesion in maximum cases of GITB. Even in the present study, ulcerative lesion was reported in maximum cases (60%) of GITB. Ulcer in GITB is transverse to the long axis of ileum. Hypertrophic mass reported in GITB cases by various authors ranged from 2.5% (Malik AR et al.<sup>24</sup>) to 48.3% (Islam MB et al.<sup>14</sup>). In the present study, hypertrophic mass (15.55%) was reported as a second most common finding, while it was reported as a most common finding in the study by Islam MB et al.<sup>14</sup> It occurs due to fibrotic thickening of intestinal wall and sometimes it may mimic malignancy.

In the present study, band and adhesions were reported in 20.74% of total 135 GITB cases, which is in concordance with the studies of Sankpal J et al.<sup>18</sup> (22.39% cases), Jamal S et al.<sup>25</sup> (22.73% cases) and Saaq M et al.<sup>12</sup> (23.78% cases).

Tubercles over the serosal surface were reported in 7.46% (Sankpal J et al.<sup>18</sup>) to 70% (Islam MB et al.<sup>14</sup>) cases by various authors in their studies. In the present study tubercles were reported in 9.63% of GITB cases. Tubercles in GITB are due to secondary involvement of intestine by hematogenous spread of mycobacteria.

Strictures were seen in 16% (Darbari A et al.<sup>2</sup>) to 69.5% (Saaq M et al.<sup>12</sup>) cases by various authors in their studies. In the present study, strictures were reported in 49.62% cases, which is in concordance studies of Arbo A et al.<sup>26</sup> in 46.7% cases and Lal V et al.<sup>17</sup> in 42% cases. In the present study, in few cases multiple strictures were reported. And in few cases combination of perforation with strictures and perforation with bands/adhesions were also reported. The chronic inflammation of TB is a transmural inflammation and heals by fibrosis resulting in strictures.

Authors have reported perforation in GITB cases ranging from 3.3% (Islam MB et al.<sup>14</sup>) to 68.2% (Jamal S et al.<sup>25</sup>) cases. In the present study perforation in GITB cases was reported in 44.44% cases. Tuberculosis is the second common cause of perforation after typhoid. Perforation may be near strictures due to obstruction. An increased incidence of perforation has also been observed with HIV infection, low immunity and failed antitubercular therapy. Perforation in GITB is usually found in ileum and rarely at any other sites. In the present study caecal perforation was reported in 4 cases of GITB, which is unusual site.

### Microscopic Findings

Tuberculous granuloma, the most common microscopic finding in cases of GITB reported by various authors ranged from 67.5% to 100% cases. Vij JC et al.<sup>27</sup> have reported tuberculous granulomas in 67.5% cases, Ibrahim M et al.<sup>22</sup> in 84% cases, Sharma YR et al.<sup>16</sup> in 92.86% cases, Chao CH et al.<sup>28</sup> in 95% cases and Malik AK et al.<sup>24</sup> Tripathi PB et al.<sup>10</sup> and Lal V et al.<sup>17</sup> reported in 100% cases. In the present study, tuberculous granulomas were reported in 97.03% of total 135 GITB cases. Though the hallmark of diagnosing GITB is demonstration of caseating granulomas on histologic examination, non-caseating granulomas may be seen in some cases due to low virulence of the organism or high resistance of the host or due to previous anti-tubercular therapy.

In the present study, four (2.96%) out of total 135 GITB cases, tubercular granulomas were present in the mesenteric lymph nodes and absent in intestinal lesions.

Langhan's type giant cells were reported by various authors ranged from 55% to 95.56% cases in their studies. Malik AK et al.<sup>24</sup> have reported Langhan's type giant cells in 55% cases, Vij JC et al.<sup>27</sup> in 67.5% cases and Chao CH et al.<sup>28</sup> in 80% cases. Langhan's type giant cells were reported in 95.56% cases of GITB in the present study. Various authors have reported caseous necrosis in their studies ranged from 13.51% to 92.86% cases. Vij JC et al.<sup>27</sup> have reported caseous necrosis in 13.51% cases, Lal V et al.<sup>17</sup> in 59% cases, Tripathi PB et al.<sup>10</sup> in 61.8% cases, Chao CH et al.<sup>28</sup> in 75% cases, Malik AK et al.<sup>24</sup> in 80% cases and Sharma YR et al.<sup>16</sup> in 92.86% cases. In the present study, caseous necrosis was reported in 79.26% of total 135 GITB cases. Foreign body giant cells in GITB cases were reported by Malik AK et al.<sup>24</sup> in 17.5% cases in their study, while in the present study it was reported in 15.56% of total 135 GITB cases.

### CONCLUSION

To conclude, our study showed that GITB is commonly seen in young males of lower socioeconomic status with ileocaecal junction being most common anatomical site involved. Patients of GITB most commonly presents with abdominal pain & tenderness may be associated with altered bowel habits and cachexia although varied mode of clinical presentation has been reported. History of pulmonary tuberculosis and cough may or may not be associated. Most patients of GITB are anaemic with high Erythrocyte Sedimentation Rate (ESR) mostly associated with lymphocytosis and monocytosis. Ulcerative lesions are most commonly seen in resected specimens of GITB. Histologically presence of caseating tuberculous granulomas is the gold standard for diagnosis of GITB as acid fast bacilli are detected in very few cases.

The diagnosis of GITB is difficult and careful approach to the patients and supportive investigation data are necessary to make the final diagnosis. Neither clinical features nor laboratory findings are conclusive of GITB, histopathological findings by themselves provide a gold standard in the diagnosis.

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Sl. No.	Age Group	No. of Cases			Percent age
		Male	Female	Total	
1	0-10	5	1	6	4.44
2	11-20	10	12	22	16.29
3	21-30	15	24	39	28.89
4	31-40	19	15	34	25.18
5	41-50	9	3	12	8.89
6	51-60	11	3	14	10.37
7	61-70	5	1	6	4.44
8	71-80	1	1	2	1.48
<b>Total</b>		<b>75 (55.56%)</b>	<b>60 (44.44%)</b>	<b>135 (100%)</b>	<b>100</b>

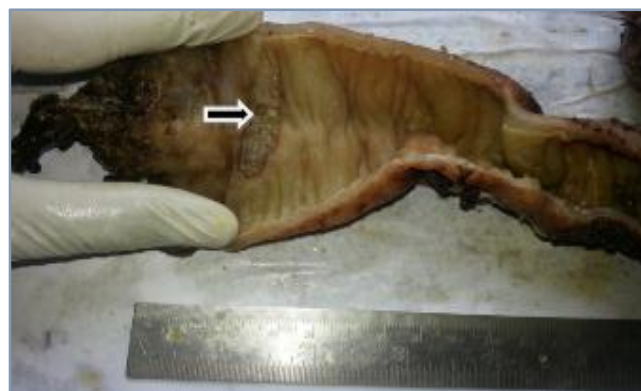
**Table 1: Age and Gender-wise distribution of GITB cases**

Sl. No.	Macroscopic Findings	No. of Cases	%
1	Ulcer	81	60
2	Ulcerohypertrophic lesion	11	8.15
3	Hypertrophic (mass) lesion	21	15.55
4	Bands & Adhesions	28	20.74
5	Tubercles over surface	13	9.63
6	Strictures	67	49.62
7	Perforation	24	17.78

**Table 4: Macroscopic findings observed in resected specimens of GITB**

Sl. No.	Symptoms	No. of Cases	Percentage
1	Abdominal pain	129	95.56
2	Fever	84	62.22
3	Weight Loss	89	65.92
4	Anorexia	101	74.81
5	Nausea/Vomiting	73	54.07
6	Altered bowel habits	89	65.92
7	Melena	04	2.96
8	Night sweats	31	22.96
9	Abdominal Distension	87	64.44
10	Abdominal Lump	12	8.89
11	Cough	43	31.85

**Table 2: Common presenting symptoms reported in GITB cases**



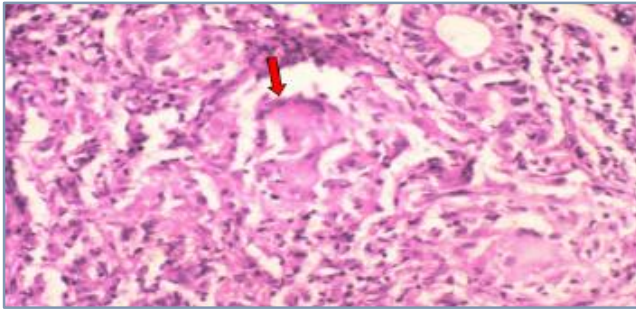
**Fig. 1: Photograph showing transverse ulcer (↑) in mucosa of small intestine**

Sl. No	Sign	No. of Cases	Percentage
1	Abdominal tenderness	91	67.41
2	Abdominal Mass	32	23.70
3	Ascites	52	38.52
4	Cachexia	89	65.92
5	Hepatomegaly	15	11.11
6	Splenomegaly	06	4.44
7	Intestinal Obstruction	64	47.41
8	Pallor	84	62.22
9	Oedema	10	7.40
10	Peritonitis	24	17.78

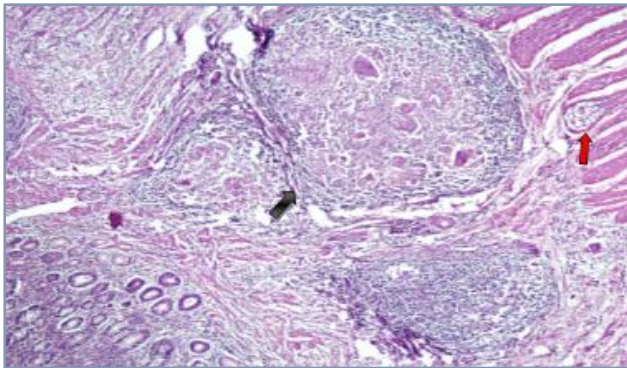
**Table 3: Common Clinical Signs Reported In GITB Cases**



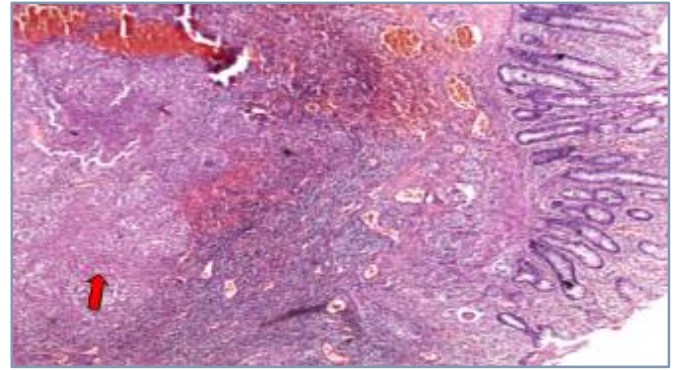
**Fig. 2: Photograph showing thickened caecal wall (↑) in a case of hyperplastic tuberculosis**



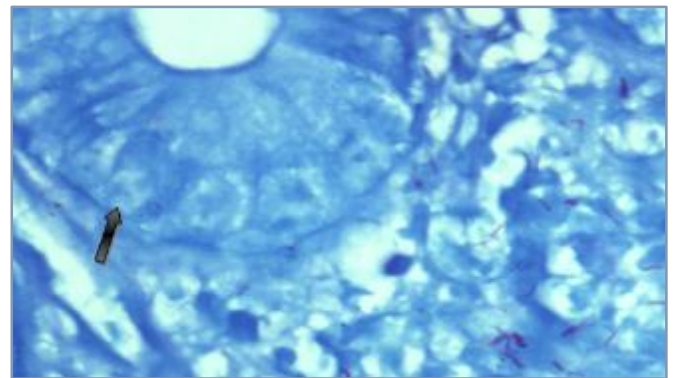
**Fig. 3: Microphotograph showing gastric gland (↑) and epithelioid granuloma with Langhan's type of giant cell (↑). (H&E, 400X)**



**Fig. 4: Microphotograph showing ileal wall with chronic inflammatory cell infiltrate and caseating epithelioid granulomas in submucosa (↑) and muscle layer (↑). (H&E, 40X)**



**Fig. 5: Microphotograph of colon showing caseous necrosis in the submucosa with congested blood vessels and epithelioid cell granulomas (↑). (H&E, 40X)**



**Fig. 6: Microphotograph showing multiple beaded acid fast bacilli and mucous gland (↑) in a section of ileum.**