# A CLINICOPATHOLOGICAL STUDY OF ABDOMINAL TUBERCULOSIS*

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*Summary.* In a prospective study, 99 patients with possible diagnosis of abdominal tuberculosis underwent endoscopy with biopsy or cytological examination for histopathological and bacteriological confirmation of the presumptive diagnosis. The gastrointestinal tract was predominantly involved in 77 patients, the peritoneum in 12 and mesenteric glands in 10. Small intestine was the most frequently affected site (42) in gastrointestinal tract followed by ileocaecal region (17), colon (10) and duodenum (4). Stomach, oesophagus and rectum were other sites of tubercular involvement. Endoscopic biopsies were available in 37 patients with gastrointestinal disease and 25 (67.5%) of them revealed granulomas on histology. *M. tuberculosis* was isolated in 16 (43%) patients on culture. The diagnosis of tuberculous peritonitis was confirmed in 3 patients on peritoneal biopsy obtained through laparoscope and in 2 patients on positive culture of ascitic fluid. Fine needle aspiration of mesenteric lymph nodes demonstrated cytological features consistent with tuberculosis in 8 of 10 patients. The diagnosis of tuberculosis was confirmed in 45 (76%) of 59 patients on the basis of positive histopathology and/or bacteriology. However, because of inability to obtain biopsies in most patients with small intestinal disease, the overall diagnostic yield was 45% (45/99).

## Introduction

Though abdominal tuberculosis is a common disease in developing countries of the world, the diagnosis of this condition is difficult and often remains obscure as the symptoms and signs are vague and the laboratory investigations are not helpful. Radiology is still the most important investigation for establishing the diagnosis but it suffers from lack of specificity[1]. Several studies have shown the inaccuracy of diagnosis of abdominal tuberculosis made on the basis of clinical and laboratory investigations[23]. Das and Shukla[4] found in a study that a correct pre-operative diagnosis of tuberculosis was made in only 50 percent of cases. The diagnosis of abdominal tuberculosis needs histologic or bacteriologic confirmation which, in the past, usually required laparotomy. However, with the introduction of fiberoptic endoscopes, a large portion of gastrointestinal tract can be visualised and tissue obtained for confirmation of the disease[5]. Bhargava et al[6] performed colonoscopy in 11 suspected cases of ileocaecal tuberculosis and in 7 of them the diagnosis was confirmed on positive histology or positive culture. Similarly, in patients with intra-abdominal masses the diagnosis of tuberculosis can be established on examination of material obtained by fine needle aspiration. However, there is paucity of reports on the yield of these procedures in establishing the diagnosis of abdominal tuberculosis. The present study describes our experience with endoscopy, biopsy and fine needle aspiration cytology in the diagnosis of abdominal tuberculosis.

## Material and Methods

Over a period of three years (1987-90), 113 patients with presumptive diagnosis of abdominal tuberculosis, attending the gastroenterology clinic of G.B. Pant Hospital, New Delhi were selected for the study. Two patients were subsequently excluded as one of them was found to have adenocarcinoma of jejunum and the other pseudo-obstruction of bowel. Another twelve patients dropped out for various reasons leaving ninety nine patients who were classified into 3 categories according to dominant involvement of organ

system *(a)* tuberculosis of gastrointestinal tract, (£>) tuberculosis of peritoneum and (c) tuberculosis of abdominal lymphnodes. The diagnosis of abdominal tuberculosis was based on clinical features, radiological findings, endoscopy, biopsy .and tissue culture for mycobacterium. The radiological investigations included X-ray of chest and abdomen, conventional barium contrast study of gastrointestinal tract and tube enema of small bowel. The radiological features of contrast study of small intestine and colon included stricture(s) of small bowel or colon (Fig. 1 & Fig. 2), obliteration of ileocaecal valve, deformity and retraction of caecum (Fig. 3) and ascending colon and various filling defects. Fixation of small bowel loops and spiculation of intestinal wall were the other features. Obstruction in the bowel was associated with secondary megacolon or megaileum. Patients with gastric tuberculosis showed narrowing of gastric antrum and filling defects. One patient with oesophageal disease showed irregularity of mucosal wall.

Ultrasound and computerised tomography (CT) scan were done to detect peritoneal and nodal involvement. Sonographic features suggestive of tuberculosis were presence of ascites with anechoic masses in the retroperitoneum. The CT findings included irregular soft tissue densities in the omentum, low density masses surrounded by thick solid rims and high density ascites[7].

Patients showing radiological changes suggestive of tuberculosis of oesophagus, stomach and duodenum underwent upper gastrointestinal endoscopy using Olympus GIF XQ 10 instrument. Fiberoptic enteroscopy (with $SIF_{10}$ instrument) was performed in patients showing involvement of proximal jejunum. Patients with involvement of rectum, colon, ileocaecal region and terminal ileum underwent colonoscopy (with $P_{10}L$ instrument). All fiberoptic endoscopic procedures were performed using standard techniques. In certain cases with strong clinical suspicion, endoscopy was done even if radiological studies did not suggest tuberculosis. Multiple pinch biopsies were obtained from the target lesions and the specimens were processed for histopathology and bacteriology.

Paracentesis was done in patients with ascites. The ascitic fluid was examined for protein content, cell count and AFB culture. Nearly one third of patients in whom the diagnosis of tuberculosis was

not definite on ascitic fluid examination and radiological investigations underwent laparoscopy. The diagnosis of adhesive peritonitis was based on clinical features, radiological investigations ultrasound and CT scan; laparoscopy was not attempted in these patients because of risk of complications.

The diagnosis of mesenteric lymphadenitis was based on ultrasound and CT findings coupled with cytological and microbiological study of the material obtained from intra-abdominal mass by fine needle aspiration.

*Biopsy Processing*

Biopsy specimens were fixed in 10% neutral buffered formalin and partially serial sectioned by the usual method. The sections were stained with Hematoxyline and Eosine. Two to three slides each containing at least 5 sections were examined. The biopsies were also stained with Ziehl Neelsen staining and modified staining using prior oxidation followed by silver impregnation for demonstration of mycobacterium[8].

*Microbiological Study*

Tissue specimens obtained through the endoscope were preserved in sterile normal saline. The tissue was finely ground and cultured on Lowenstein Jensen medium. Colonies of mycobacteria were identified by colonial character and biochemical tests. The material obtained through fine needle aspiration was mixed, with a small amount of saline and processed in a similar manner.

**Results**

There were 56 males and 43 females with M:F ratio 1.3:1. The mean (±SD) age of patients was 31.6 ± 13.6 years with a range of 13-te- 65 years. There was wide variation in duration of symptoms; it ranged from 17 days to 12 years. However, in about half the patients the duration of symptoms was less than 1 year.

The symptoms given by patients are listed in Table 1. Pain in the abdomen was the most common symptom followed by weight loss and anorexia. Physical examination revealed an abdominal mass in 24 patients and free abdominal fluid in 9 patients.

Thirty four of 99 patients had evidence of tuberculosis elsewhere in the body. Thirty patients

Table 1. *Symptoms and physical findings at presentation in patients 'with abdominal tuberculosis*

| | |
|---|---|
| Abdominal Pain | 83 |
| Weight Loss | 70 |
| Anorexia | 53 |
| Abdominal distension | 50 |
| Fever | 45 |
| Vomiting | 40 |
| Constipation | 30 |
| Diarrhoea | 29 |
| Abdominal mass | 24 |
| Ascites | 9 |
| Total | 99 |

had x-ray evidence of pulmonary tuberculosis, three had histologically confirmed tuberculosis of cervical lymphnodes and one had tuberculosis of endometrium.

Seventy seven of 99 patients had involvement of gastrointestinal tract. Twelve had tuberculous peritonitis (9 had ascitic variety and 3 were of adhesive type) and 10 patients had mesenteric lymphadenitis (Table 2). Amongst the patients with gastrointestinal tract tuberculosis, small intestine was the most commonly affected site (42 of 77 patients). The other sites of involvement in order of frequency were ileocaecal region, colon, duodenum, stomach, oesophagus and rectum.

### Endoscopy

The lesions in gastrointestinal tract were classified in four groups on gross endoscopic appearance : *(a)* hypertrophic *(b)* ulcerohypertrophic, (c) ulcerative and *(d)* ulcero-constrictive. The hypertrophic lesion was characterised by thickening and cobblestoning of mucosa. Presence of ulcer(s) with hypertrophied mucosa was labelled as ulcerohypertrophic. In the ulcerative type, the ulcers were single or multiple, of variable shapes and sizes, usually covered with slough. A few of the ulcers were placed circumferentially. In ulceroconstrictive lesions the narrowed segment of the intestine had ulcers too

Seven patients with presumptive diagnosis of tuberculosis of upper gastrointestinal tract involving oesophagus (1 patient), stomach (2 patients) and duodenum (4 patients) had upper G.L endoscopy. In the patient with ocsophageal disease

the endoscopy revealed an oval ulcer covered with necrotic slough in the middle part of the oesophagus; another had nodular lesion involving whole of antral region and another had marked narrowing of gastric antrum. Amongst patients with duodenal disease the lesion was present in post bulbar region (2 patients), in the middle part of descending duodenum (1) and in the 3rd part of duodenum (1). The lesions were ulceroconstrictive.

### Enteroscopy

Enteroscopy located the stricture in upper jejunum in only two patients. In other patients, the lesions were presumably too distal for the enteroscope to reach.

### Colonoscopy

Colonoscopy was performed on 17 patients with ileocaecal tubeorculosis, 10 with tuberculosis of colon and 1 with rectal tuberculosis.

The commonest lesion in the ileocaecal region was either hypertrophic (8) or ulcerohypertrophic (4). An ulcerative lesion was seen in 2 patients whereas ulceroconstrictive lesions were present in the remaining 3 patients.

In the colon, hepatic flexure was the most common site of tubercular involvement (4), followed by ascending colon (3), splenic flexure (2), and mid transverse colon (1). Compared to ileocaecal region the most common lesion in colon was ulceroconstrictive (5) or ulcerative (3). In the

Table 2 *Distribution of types of tuberculosis*

| Type of Tuberculosis | No. of Patients | |
|---|---|---|
| a. Gastrointestinal | 77 | |
|     Small intestine | | 42 |
|     Ileocaecal | | 17 |
|     Colon | | 10 |
|     Duodenum | | 4 |
|     Stomach | | 2 |
|     Oesophagus | | 1 |
|     Rectum | | 1 |
| b. Peritoneal | 12 | |
|     Ascitic | | 9 |
|     Adhesive | | 3 |
| c. Abdominal lymphnodal | 10 | |

Fig. 1    Barium contrast study showing stricture in
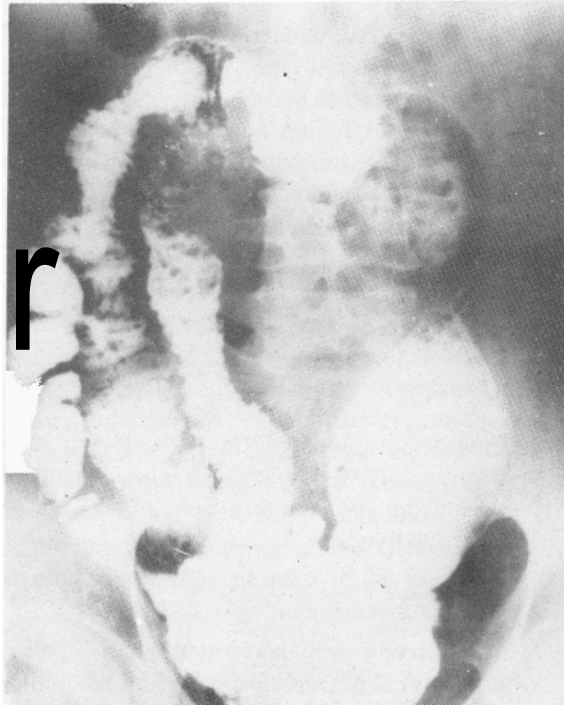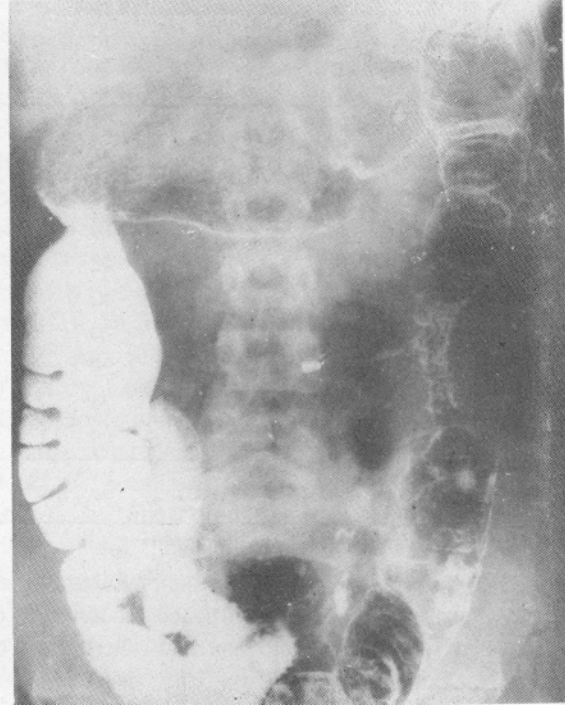
Fig. 2    Barium enema showing stricture in transverse



colon

other 2 patients with colon disease and in one patient with rectal tuberculosis, the lesion was ulcerohypertrophic.

*Histology*

Endoscopic biopsies were obtained from target lesions in 37 patients (Table 3). Biopsy specimens usually contained mucosa and muscularis mucosae and seldom submucosa (3/37). Microscopic examination revealed granulomas (Fig. 4) consisting of epithelioid cells and Langhans' giant cells in 25 (67,5%) cases (Table 3). The granulomas were usually single and discrete in 19 but confluent in the remaining 6 cases. In 5 cases, the granulomas had central caseation. In addition, mucosa showed predominant infiltration by chronic inflammatory cells. The biopsies obtained from colon and rectum also showed distorted cryptic glands in 7 and crypt abscesses in 4 cases. The frequency of positive histology in relation to number of biopsy specimens obtained was quite variable; on an average one out of 4 biopsy specimens was positive for granuloma. Ziehl

**Table 3** *Positive endoscopic biopsy and tissue culture in patients with gastrointestinal tuberculosis*

| Site of Involvement | No. of Patients | Histo-patho-logy | Tissue culture |
|---|---|---|---|
| Oesophagus | 1 | 1 | 0 |
| Stomach | 2 | 2 | 1 |
| Duodenum | 4 | 2 | 2 |
| Jejunum | 2 | 0 | 0 |
| Caecum/ Ileocaecal region | 17 | 12 | 7 |
| Colon | 10 | 8 | 5 |
| Rectum | 1 | 1 | 1 |
| Total | 37 | 25 (67.5%) | 16 (43%) |

Neelsen staining as well as modified staining method failed to show AFB in any biopsy specimen.
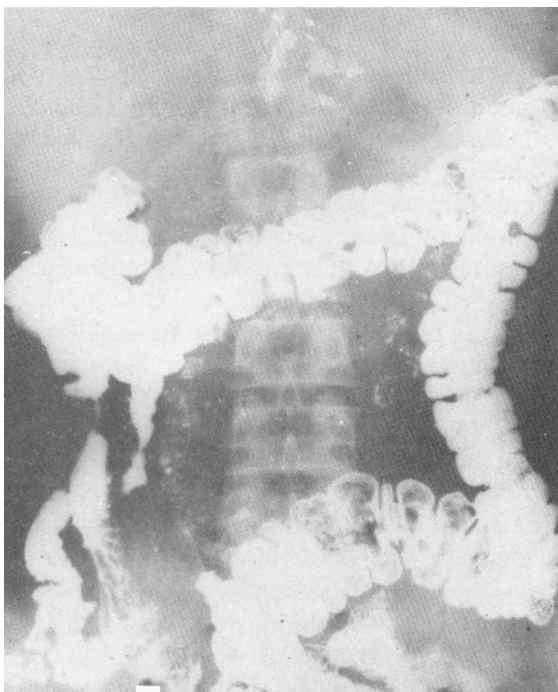
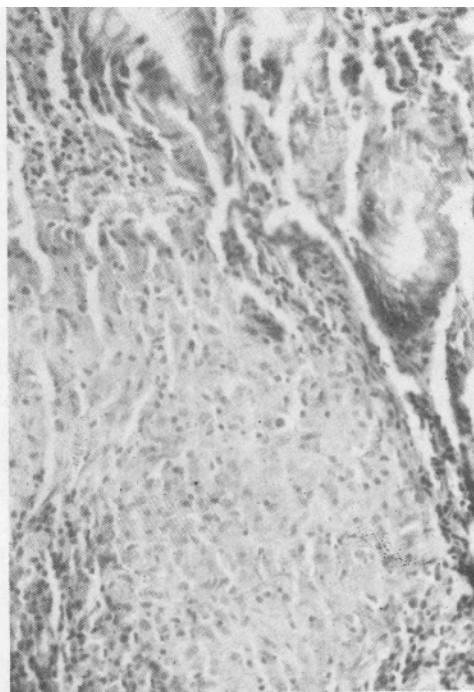Fig. 3 Ileocaecal tuberculosis-deformity and retraction of caecum

Fig. 4 Histopathology of intestinal tuberculosis showing a granuloma consisting of epithelioid cells and Langhans' giant cells

*Bacteriology*

Of the 37 biopsy specimens, 16 (43%) yielded positive culture on Lowenstein Jensen Medium (Table 3) and all the organisms were identified as *M. tuberculosis* on the basis of colony characters and biochemical tests. In 9 patients, both histology and bacteriology were positive. In 7 patients the tissue culture was positive for *M. tuberculosis* but histology did not show a granuloma.

**Peritoneal tuberculosis**

Of the 9 patients with ascitic type of peritonitis, the diagnosis in 3 patients was confirmed on histological changes in the biopsy obtained through the laparoscope and in 2 patients on positive culture of ascitic fluid. Remaining 4 patients had characteristic changes such as raised protein content and increased lymphocytes in ascitic fluid and they all showed excellent response to antituberculosis therapy. The diagnosis of adhesive peritonitis (3 cases) was based on CT findings and good response to chemotherapy.

**Tuberculous mesenteric lymphadenitis**

The diagnosis was confirmed in 8 patients on the basis of cytological changes consistent with tuberculosis in the material obtained by fine needle aspiration. In 3 of them aspirated material also yielded positive culture of *M. tuberculosis*. In the remaining 2 patients, CT scan showed changes suggestive of central necrosis in lymphnodes and fine needle aspiration yielded only caseous material. Both showed good response to chemotherapy.

**Discussion**

In this study the alimentary tract proper was the most common site of tuberculous involvement followed by involvement of- peritoneum and mesenteric lymph nodes. The reported occurrence of tuberculosis in these sites varies from series to series and from country to country. The ten percent occurrence of mesenteric lymphadenitis in our study is comparable to that reported by other workers but that of gastrointestinal involvement

(77%) is more and of peritonitis (12%) less than that reported in these series. This difference, seemingly, is related to the type of patients-referred to our Centre.

Evidence of extra intestinal tuberculosis was present in 34 patients, the commonest site (30) being the lung. The frequency of associated pulmonary tuberculosis has been changing over the years. In the past when no specific treatment existed, about 90% of fatal cases of pulmonary tuberculosis had intestinal involvement. With the advent of chemotherapy more and more cases of abdominal tuberculosis without active pulmonary tuberculosis are being found and majority of patients with lung involvement have radiographic evidence of healed pulmonary tuberculosis. In a collective analysis of seven series on abdominal tuberculosis from different parts of the world, 700 out of 935 (75%) chest roentgenograms were negative.[9]

The clinical characteristics of patients with abdominal tuberculosis are non specific. In a study[4] based on surgical findings, a correct clinical diagnosis of abdominal tuberculosis could be made only in 50% of cases. Iloon[10] reported 34% accuracy of diagnosis based on clinical features. Majority of patients with gastrointestinal tuberculosis in our scries presented with symptoms suggestive of subacute obstruction which were intermittent and chronic. The obstruction involved pylorus, duodenum, small bowel or large bowel. Similarly, most patients with tuberculous peritonitis presented with abdominal pain and abdominal distension. The common presenting symptoms in patients with mesenteric lymphadenitis were pain in the abdomen and palpable abdominal mass. Bowel disturbances, fever, weight loss and anorexia were other common features. In this series about one fourth of total patients had palpable abdominal mass. All patients with mescnteric lymphadenitis presented with intra-abdominal mass whereas 10 of 17 patients with ileocecal tuberculosis and 2 of 10 cases with colonic tuberculosis had a palpable mass which is usually due to hypcrplastic bowel or lymphadenitis or a combination of both. Two patients with peritoneal tuberculosis also had mass in the abdomen.

The preopcrative diagnosis of abdominal tuberculosis is difficult. Routine haematological and biochemical tests are of no diagnostic value.

The diagnosis of tuberculosis can only be confirmed by the typical histopathological picture and demonstration of acid fast bacilli on culture. In the past, numerous reports in the literature have stressed the need for surgical intervention to establish the diagnosis[11]. However, with the advent of fiberoptic endoscopes, large parts of gastrointestinal tract can now be examined and targeted biopsies obtained, which is helpful not only in establishing the diagnosis of tuberculosis but also helps in excluding other diseases such as malignancy, Crohn's disease, amoeboma, etc.

Endoscopic appearances of tuberculous lesions are fairly characteristic though not diagnostic. Aoki *et al*[5] were first to describe the endoscopic features of tuberculous lesions. They found transverse and linear ulcers with necrotic bases and oedematous borders in addition to strictures and inflammatory polyps in patients with colonic tuberculosis. Bhargava *et al*[6] observed in patients with ileocaecal tuberculosis contracted caecum and hypcrtrophic as well as pseudopolypoid folds in caecal wall besides oedematous and deformed ileocaecal valve. In gastrointestinal tract the type of endoscopic lesion had some relationship with the site of involvement. In this study, all the patients with tuberculosis of duodenum, jejunum and majority of patients with colonic tuberculosis had ulceroconstrictive/ulcerative type of lesion whereas majority of patients with ileocaecal tuberculosis had hypertrophic or ulcero-hypertrophic lesion. One patient with gastric tuberculosis had modularity of mucosa and another had infiltrative lesion mimicking malignancy. Distal jejunum and proximal ileum were the most difficult sites for establishing a firm diagnosis since these regions could not be approached endoscopically. Unless subjected to surgery, the diagnosis in such patients was mainly based on

Table 4 *Comparison of frequency of site of involvement in patients with abdominal tuberculosis in various studies*

|  | Das & Shukla[4] (1976) (n=182) | Jakubowski[21] etal(1988) (n = 82) | Present Study (n = 99) |
|---|---|---|---|
| G.I. Tract | 93  (54%) | 33  (40%) | 77 (77%) |
| Peritoneum | 68  (37%) | 41  (50%) | 12 (12%) |
| Abdominal Lymphnodes | 21  (12%) | 8  (10%) | 10 (10%) |

clinical and radiological features. Therefore, they can be best categorised as "most probably tuberculosis". Based on endoscopic features, it may not be possible to differentiate tuberculosis from Crohn's disease, malignancy and lymphoma. However, histopathologic examination of biopsies is helpful in confirming the diagnosis.[12] The reported yield of endoscopic biopsies is very variable. Hoshino et a/[13] on reviewing several small series found 50% positive yield for endoscopic biopsies utilising both histology and culture. On the other hand, Bhargava et al[6] found positive histology in only 3 of 11 patients. In our study, granulomas were present in 25 of 37 (67.5%) cases. This difference in various studies may be related to the number of biopsies obtained and location of the lesion. Breiter and Haggar[14] found in a patient with colonic tuberculosis six of 12 biopsy specimens positive for tuberculosis when they obtained biopsies from deeper portion of ulcer bed and margins of the lesion. It is difficult to say with conviction as to how many biopsies are needed to obtain positive result. In our study, on an average, one out of 4 biopsies showed granuloma but it is preferable to obtain at least 6 biopsies for reasonably good yield. The exact cause of negative histology is not known. It may be related to the deeper location of granulomas[15,16] or to the fact that tubercular changes may be found in the draining lymph nodes and the intestine may show only non specific change[10,17].

Classically, the diagnosis of tuberculosis is based on the demonstration of caseating granuloma, but a significant number of granulomas may not show caseation. Several workers[11,15] have reported non caseating granuloma in patients with tuberculosis. Patients who have received chemotherapy may also not show caseation in the granuloma.[18] In Bhargava's series[6], only one out of 11 patients with ileocaecal tuberculosis showed caseating granuloma. In tropical countries where Crohn's disease is very rare, the presence of granuloma in biopsy specimens in association with clinical and radiological features along with excellent therapeutic response to chemotherapy may be considered diagnostic of tuberculosis.

Attempts to demonstrate acid fast bacilli (AFB) microscopically in biopsy specimens by staining techniques were uniformly unsuccessful : Ziehl Neelsen staining as well as modified staining using prior oxidation followed by impregnation of silver[8] failed to show the organisms in biopsy specimens. The exact reason for this is not clear. However, culture of tissue specimens yielded positive growth in 16 (45%) cases. In 9 patients, both histology and bacteriology were positive. In 7 patients, organisms were isolated on culture but the histology did not reveal a granuloma. Thus, the diagnosis of tuberculosis was made in 32 (25 on histology and 7 on bacteriology) of 37 (86%) patients. Isolation of organisms was not related to associated pulmonary disease.

In patients with ascites, the presence of straw colour fluid with increased protein content (> 2.5 g/dl), predominance of lymphocytes and absence of malignant cells on abdominal paracentesis suggest tuberculous peritonitis. Confirmation is achieved by histological demonstration of tuberculous lesion in peritoneal biopsy obtained through the laparoscope or by Cope's needle. Levine[19] reported 100% success rate for obtaining peritoneal biopsy by Cope's needle while Singh et al[20] had only 64% success. In the present study, 9 patients had ascitic and 3 adhesive type of peritonitis. All the 9 patients had characteristic ascitic fluid changes. The confirmation was obtained in 2 cases on the basis of positive culture and in 3 cases on histology in peritoneal biopsy obtained through the laparoscope and in the remaining 4 patients on the basis of excellent response to antituberculosis therapy. The diagnosis of mesenteric lymphadenitis was confirmed by typical cytological changes in 8 to 10 patients. In the remaining 2 patients, caseous necrotic material was obtained by aspiration without other evidence suggestive of tuberculosis. However, both the patients showed good response to antituberculosis treatment.

**In summary, a positive diagnosis of tuberculosis was made in 45 out of 59 patients (75%) in whom biopsy specimens obtained through the endoscope or aspirated material/ ascitic fluid was availablefor histological and/ or bacteriological confirmation. However, of the total patients with abdominal tuberculosis, the diagnosis of tuberculosis could be established in 45% (45/99) and the overall low positivity was mainly due to the inability to**

**obtain biopsies from the involved region in the small bowel.**

## Acknowledgement

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