



Original Research Article

A Survey of Intestinal Lesions with Special Reference to Intestinal Tuberculosis in and Around Uttar Pradesh, India

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ABSTRACT

Tuberculosis is a big challenge in India. In our country there is still lot of ignorance towards vaccination and lack of knowledge for proper treatment and its follow up leading to development of resistance to anti-tubercular drugs. Due to late clinical presentation in case of intestinal tuberculosis as compared to pulmonary tuberculosis, this type poses even more problem, resulting in extensive morbidity and burden on health services. Tuberculosis can involve any part of the gastrointestinal tract and is the sixth most frequent site of extra pulmonary involvement. Both the incidence and severity of abdominal tuberculosis are expected to increase with increasing incidence of HIV infection. To study the occurrence of intestinal tuberculosis in and around Uttar Pradesh and to know its disease burden amongst all other frequently encountered intestinal lesions. This retrospective study was conducted on 304 intestinal biopsies and resection specimens to determine the spectrum of intestinal diseases, especially intestinal tuberculosis. The pathological findings were correlated with the clinical findings and supportive investigations. Majority of the lesions were categorised as inflammatory (non-specific) and malignancy. Tuberculosis was found to be the most common cause of enteritis amongst the cases of infective etiology. Intestinal tuberculosis remains a significant cause of subacute intestinal obstruction in our setup. In some cases definite pathological findings may not be observed, hence clinicoradiological findings and microbiological investigations should be taken into consideration to reach an appropriate diagnosis.

Keywords

Intestinal tuberculosis, spectrum, diagnosis, microbiological investigation

Introduction

Tuberculosis (TB) is a big challenge in India. It is a highly contagious disease caused by the bacillus *Mycobacterium tuberculosis*, responsible for ill health among millions of people each year. It poses a big challenge in India due to lack of

awareness, knowledge and infrastructure for timely and accurate diagnosis, as well as proper treatment and follow-up leading to resistance of anti-tubercular drugs which poses a looming threat. According to (World Health Organization Global TB, 2014)

report it has been estimated that there were 9.0 million new TB cases in 2013 worldwide and 1.5 million TB deaths. India stands among the 22 high TB burden countries; accounting for approximately one quarter (26%) of all TB cases worldwide. India reported the largest number of incident cases of 2.2 million in 2012 with 2,70,000 mortality per year (RNTCP report, 2012). This heavy toll in India could be due to lack of awareness, knowledge and infrastructure for timely and accurate diagnosis, as well as proper treatment and follow-up leading to resistance of anti-tubercular drugs which poses greatest threat to its control.

TB can involve any part of the gastrointestinal tract and is the sixth most frequent site of extra-pulmonary involvement (Sharma MP 2004). The Extra pulmonary tuberculosis (EPTB) constitutes (10–15%) of total TB cases amongst which abdominal tuberculosis (ATB) accounts for 1–3% (Sharma, 2004). The incidence of EPTB is upto 50% in HIV positive patients (Singhal *et al.*, 2005, Butt *et al.*, 2001). There is a resurgence in the incidence and severity of intestinal tuberculosis (ITB) due to the rise of HIV infection in the developing countries.

The principal causative organism of ITB is *Mycobacterium tuberculosis*. ITB could be a primary infection, or secondary following reactivation from a primary pulmonary focus. Unpasteurized or contaminated milk and dairy products, ingestion of infected sputum, lymphatic spread or direct spread from adjacent viscera (Sharma, 2004) are some of the other mode of transmission of ITB.

Ileocaecal region (52%–85%) is the most common site involved by the ITB (Khan *et al.*, 2001). The latter is broadly classified into three main forms i.e. ulcerative, hypertrophic or ulcerohypertrophic, and

fibrous stricturing form (Shaikh *et al.*, 2007). The hypertrophic form is the most common type and patients usually presents with features of intestinal obstruction such as colicky abdominal pain, borborygmi and vomiting (Khan *et al.*, 2001).

ITB is difficult to diagnose in the early stages because of its non-specific symptoms and variable manifestations and lack of specific diagnostic test. It progresses slowly and presents late with complications, especially acute or sub-acute obstruction due to mass (tuberculoma), stricture formation in the ileocaecal region or perforation leading to peritonitis (Shaikh *et al.*, 2007). The major diagnostic dilemma ITB poses is its differentiation from Crohn's disease (Almadi *et al.*, 2009), although ITB mimics other conditions like colonic malignancy, or other gastrointestinal infections (Khan *et al.*, 2001) and may present as an acute abdomen, malabsorption or perforation.

Microscopy is the most rapid diagnostic tool but it is very insensitive, yielding only 10-30% of culture-positive samples, especially in severely immunocompromised individuals (Sinkala *et al.*, 2009). Culture is sensitive, but may take four weeks to obtain conclusive results even with enhanced culture systems. Therefore, other potential diagnostic markers are needed. The criteria for diagnosing ITB on biopsy are the presence of caseating granuloma with acid fast bacilli stained by Ziehl-Neelsen technique. Tubercular granulomas initially form in the mucosa or Peyer's patches, whilst ulcers are relatively superficial, with a different appearance from those in Crohn's disease. Clinical chemistry, immunology and nucleic acid amplification techniques are not used routinely in the resource poor countries. Therefore, other potential diagnostic markers are required to explore (Donoghue and Holton, 2009).

ITB is widely prevalent in our country but often goes under-diagnosed to its diverse and non-specific features as well as lack of specific diagnostic test. The present study was undertaken to document the percentage of ITB cases amongst intestinal biopsies sent for histopathology and health burden related to it in our population, so that early diagnosis and treatment can be rendered to avoid its late complications.

Materials and Methods

Around 304 intestinal biopsies and resection specimens were reviewed retrospectively to study the spectrum of intestinal diseases especially of intestinal TB. Initial diagnosis was made on the basis of history, physical examination and ancillary investigations. The clinical impression was confirmed by histological examination of tissue specimens. The Haematoxylin and Eosin stained sections were examined carefully for presence of granulomas and necrosis. Acid-fast stains were utilized wherever necessary to support or exclude tubercular infection. The results were analysed carefully to determine the frequency of intestinal tuberculosis, and the accuracy of routine histological diagnosis.

Result and Discussion

A total of 304 intestinal biopsies and resection specimens (including omental biopsies and mesenteric lymphnodes) were covered in this study. The ages of the patients ranged from 1 month to 85 years. There were 168 males and 136 females in our study, resulting in a slight male predominance, with a male to female ratio of 1.24:1. Majority of the patients belonged to lower middle class strata of the population. Majority of the lesions (138 cases-48%) were diagnosed as inflammatory (non-specific enteritis/colitis). A confirmatory

diagnosis of intestinal tuberculosis was rendered in 28 cases (9.2%). Out of these, 14 were intestinal specimens while omentum and mesenteric lymph nodes were received from 4 patients undergoing laparotomy. In 8 samples, a definite histopathological diagnosis of tuberculosis could not be made since characteristic lesions were not detectable even after repeated examinations. In these patients, correlation with ancillary tests was advised. 37 patients (12%) were found to be suffering from intestinal malignancies, of which the most common was adenocarcinoma. Inflammatory bowel disease was found in 17 patients (5.5%) was also an important clinical diagnosis requiring biopsy of the intestinal tract. Other miscellaneous samples constituted about 60 cases (20%), which included Hirschsprung's disease and Coeliac disease (amongst pediatric age group), Meckel's diverticulum, worm infestation, and polyps (8 cases). A subset of cases (4%) does not yield any result due to inadequate biopsy. The breakup of cases is shown in the pie chart 1.

Sections from specimens of intestinal TB showed the presence of caseating and non caseating granulomas surrounded by chronic inflammatory cells and epithelioid cells (Figure 1a). However, out of these, only one demonstrated acid-fast bacilli on Ziehl – Neelsen staining (3.6%). (Figure 1b) Cases with histopathological suspicion of tuberculosis showed only vague granulomas without necrosis (Figure 2a). These were AFB –negative (Figure 2b). The major differential diagnoses were Inflammatory bowel disease, and foreign body granulomas (Figure 3a, b).

India has the highest burden of TB in the world, an estimated 2 million cases annually, and accounting for approximately one-fifth of global incidence. It is estimated

that about 40% of the Indian population is infected with TB bacteria, the vast majority of whom have latent rather than active TB disease (RNTCP report, 2012). The economically productive age is mainly the victim of this disease leading to a huge socio-economic impact. In concordance with other studies (Shaikh *et al.*, 2007; Niaz and Ashraf, 2010), the majority of patients in our study came from poor families in the rural areas. Gastrointestinal system ranks amongst the sixth-leading site of extra-pulmonary tuberculosis, followed by nodal, genitourinary, bone and joint, miliary and meningeal locations. Although it affects almost every tissue of abdominal cavity, but ileocaecal region remains the most favoured site (Kumar *et al.*, 2008). The incidence and severity of abdominal tuberculosis is increased in HIV-positive patients, by reactivation of latent TB and new infections (Mehta *et al.*, 1999).

Abdominal Tuberculosis does not have any age predilection but is more common in adolescence and economically productive age group (Khan *et al.*, 2005). The ages of the patients in this study ranged from very young to very old, majority were in between second and third decade which is consistent with other studies also (Rajpoot *et al.*, 2005; Gondal *et al.*, 2000). The male to female ratio in this study is 1.24: 1, as opposed to other series which report slight female predominance (Khan *et al.*, 2008; Chandir *et al.*, 2010).

Most patients in the study presented late with development of potentially fatal complications, such as intestinal obstruction and bowel perforation with peritonitis. In resource-poor countries like India, lack of primary healthcare infrastructure and poor socioeconomic conditions usually result in delayed and inadequate medical treatment. Another possible reason may be failure of

response to therapy in drug defaulters or multidrug resistant cases.

Biopsy is probably the most important investigation for a definitive diagnosis of abdominal tuberculosis. In our study, histopathology was the basis of diagnosis in 11.8% of patients; however a typical granuloma with caseation was found only in 9.2% of patients in our series. Similar histopathological pattern was reported by (Khan *et al.*, 2006).

The majority of patients in our study had ileocaecal region involvement. This is in agreement with other surveys on abdominal tuberculosis (Donoghue and Holton, 2009), the latter is mainly due to either physiological stasis, large surface area of this part of the intestine, complete digestion of food and abundant lymph nodes in this region.

As has been well documented in published literature, AFB staining cannot be relied upon for a confirmatory diagnosis as the sensitivity is very low (Jain, 1996). As such, the mainstay of diagnosis remains clinic-radiological evidence of tubercular infection along with demonstration of definitive histological changes. However, as observed in the study, a comparatively small percentage of patients may be diagnosed on histopathology. This may be because in a substantial number of cases, treatment may be started on an empirical basis and continued if there is adequate clinical response. Another possible reason may be the presence of a percentage of cases which were given false negative diagnoses due to lack of definite clinicopathological changes.

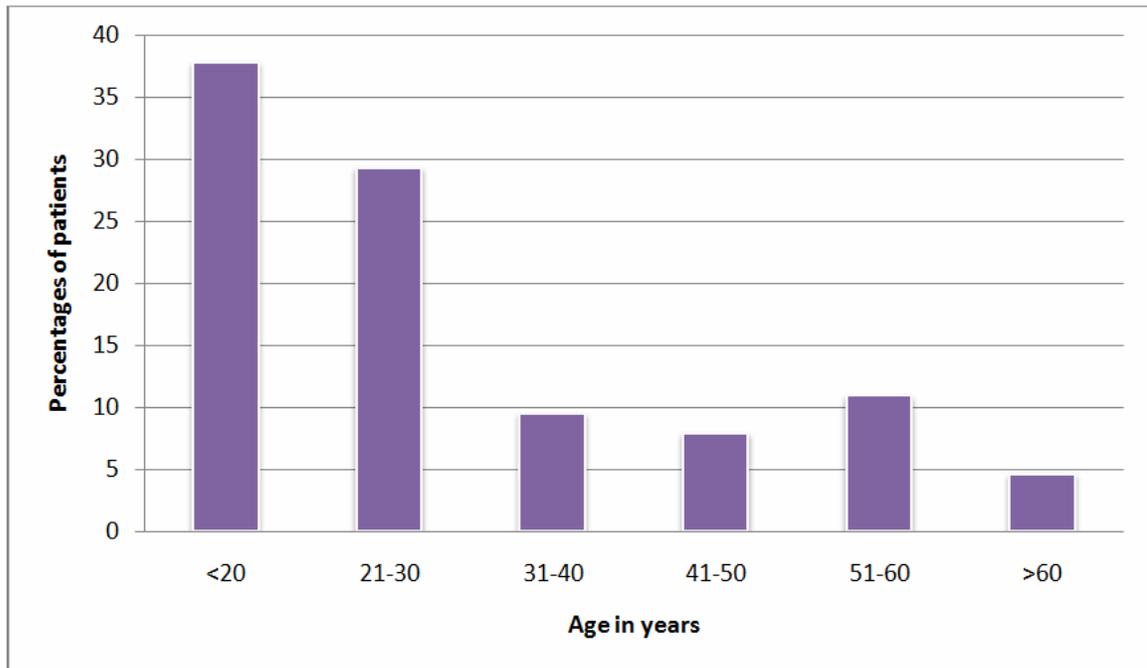
Serological tests for diagnosis like Enzyme Linked Immunosorbent assay (ELISA) lack high sensitivity and specificity (Bhargava *et al.*, 1992) and can yield only a probable

diagnosis. The need for a highly sensitive and specific test can be overcome by the use of Polymerase Chain Reaction (PCR) which has the benefit of being faster than cultures and more sensitive than immunohistochemical analysis and in situ hybridization (Park *et al.*, 2003). However, cost constraints are a major obstacle to its routine use in all cases in our country, as most of the patients belong to low and middle class socioeconomic strata. As such, in the current scenario, there is an urgent need for development of better diagnostic modalities in order to minimize false negative diagnoses and enable higher diagnostic accuracy.

Intestinal tuberculosis remains a significant cause of subacute intestinal obstruction and

perforation in our setup. Presence of granuloma with caseous necrosis in an intestinal biopsy specimen is probably the most important finding for a definitive diagnosis of abdominal tuberculosis. However, in some cases definite pathological findings may not be observed; hence, clinical findings and microbiological investigations should be taken into consideration for appropriate diagnosis. There is a very urgent need for development of cost-effective diagnostic modalities which have high sensitivity and specificity, in order to minimize false negative results and reduce the burden of disease in developing countries.

Chart.1 Distribution of patients according to age group



Pie Chart 2

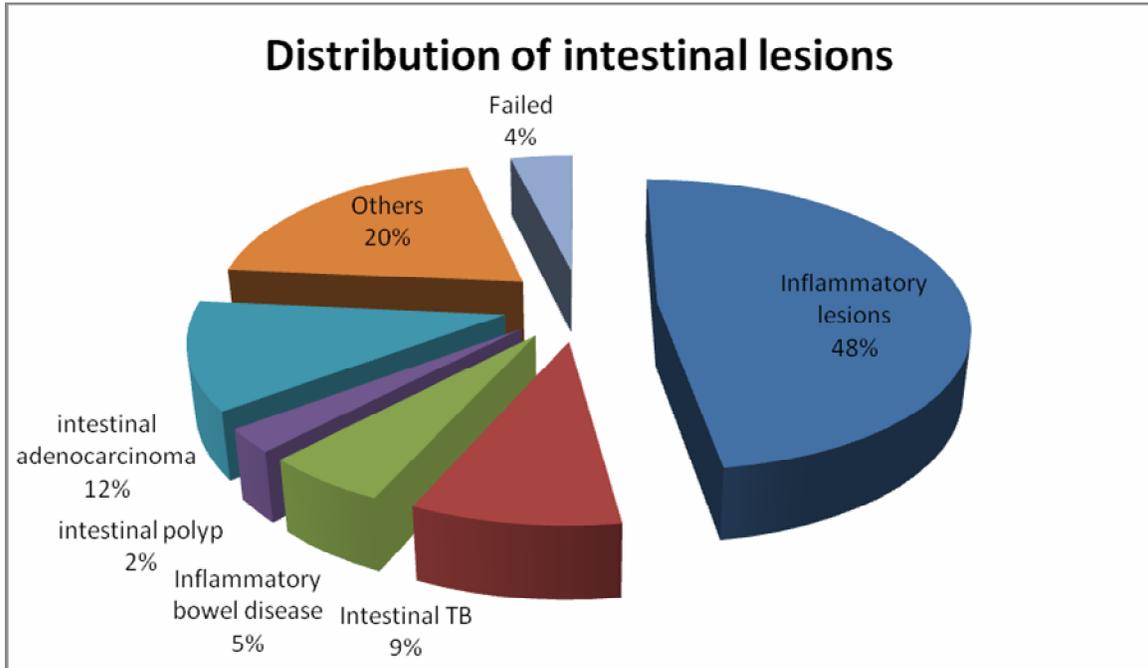


Fig 1(a) H&E shows tubercular granuloma with caseous necrosis

Fig1(b) Ziehl-Neelsen staining showing Acid fast bacilli (AFB) positivity

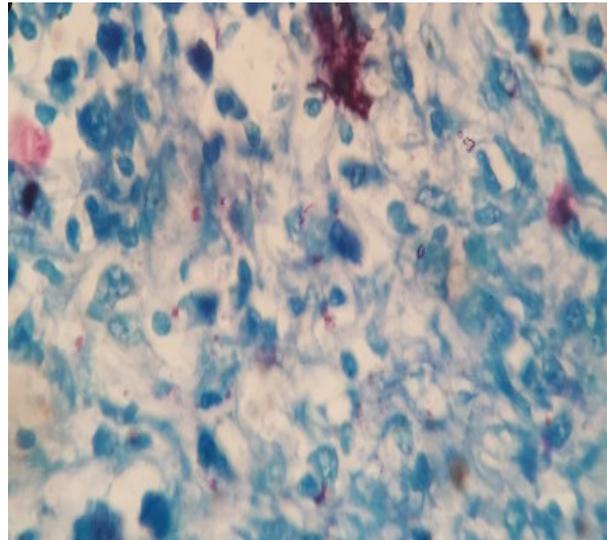
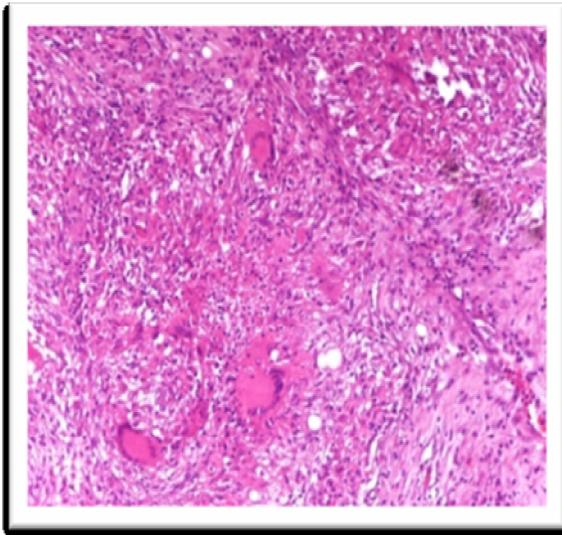


Fig.2(a) H&E section shows caseating granluoma

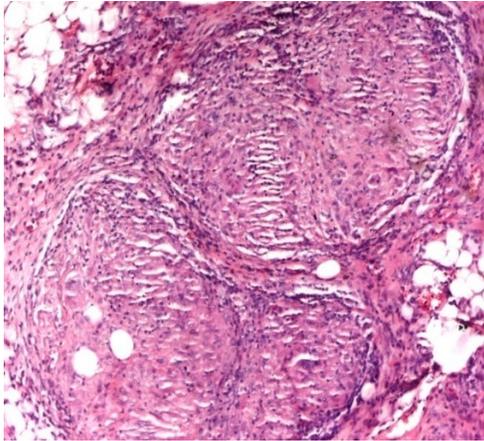


Fig.2(b) Ziehl-Neelsen staining showing AFB non-negativity suspicious of TB

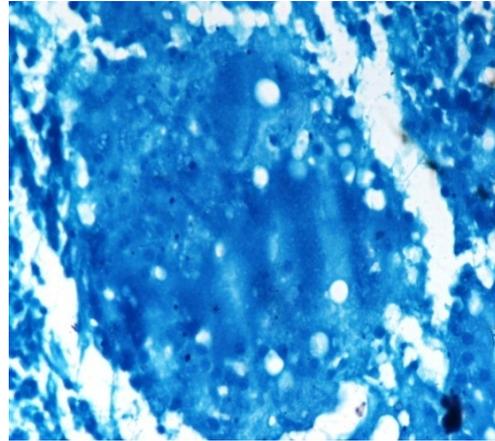


Fig.3(a) H &E crohn's disease

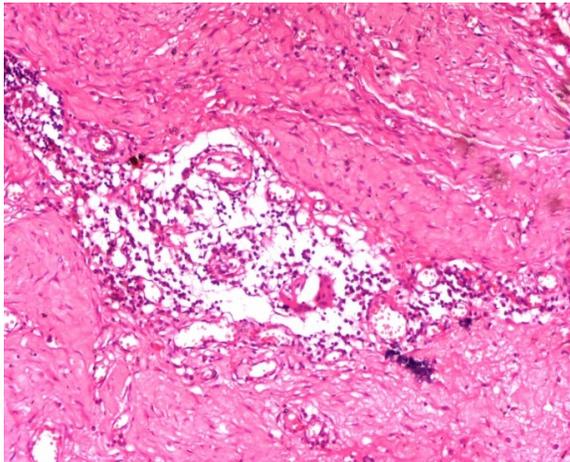
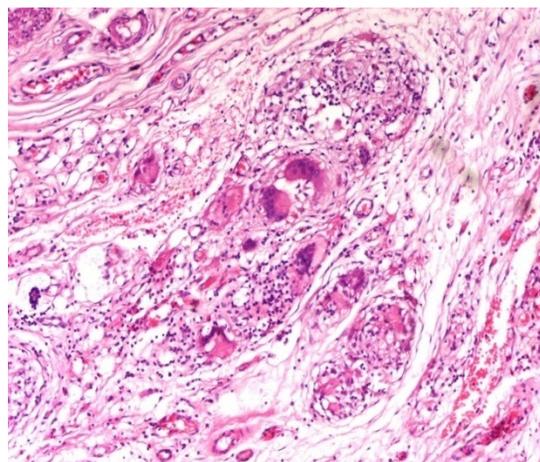


Fig.3(b) Foreign body granuloma in the Serosa of small intestine



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