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Role of diagnostic laparoscopy in suspected abdominal tuberculosis

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ABSTRACT

Background: The difficulty in confirming the diagnosis, morbidity and mortality associated with laparotomy in patients with abdominal Tuberculosis (TB) has generated interest in laparoscopy to obtain specimens for histological and microbiological assessment. **Aims and Objectives:** Difficulty in sample procurement, paucibacillary load and non-specific clinical, biochemical, and radiological features makes early diagnosis difficult in abdominal TB. Diagnostic laparoscopy with peritoneal biopsy can provide rapid and correct diagnosis of abdominal TB and reduce significant morbidity and mortality. **Materials and Methods:** Laparoscopy with umbilical port enabled direct inspection of peritoneum, intra-abdominal organs and facilitated obtaining biopsy specimens, cultures, and aspiration. **Results:** Diagnostic laparoscopy has an important role not only in diagnosing abdominal TB, but also to rule out TB in certain cases. In our study, mesenteric lymphadenopathy was present in 85% of cases, tubercles in 63% and adhesions in 73%. An alternative diagnosis was established in 6 suspected abdominal TB patients (20%) who were microbiologically confirmed TB negative. **Conclusion:** The study showed the feasibility of diagnostic laparoscopy in diagnosis of abdominal TB by sampling macroscopically visible pathological tissue with a low complication and conversion rate in most patients with suspected TB, and also providing an alternative diagnosis.

Key words: Tuberculosis; Acid fast bacilli; Bacillus-calmette guerin; Computed tomography; Abdominal tuberculosis; Diagnostic laparoscopy

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INTRODUCTION

Tuberculosis (TB) is a life-threatening disease affecting almost all the organs of the body.[1] There were an estimated 10 million new cases (incidence) of TB. Abdominal TB may occur in four forms: gastrointestinal TB, tuberculous peritonitis, mesenteric and retroperitoneal lymph nodes (tuberculous adenitis) and solid organs, for example, liver, spleen, kidney, and pancreas.[2,3] The difficulty in confirming the diagnosis, morbidity and mortality associated with laparotomy in patients with abdominal TB has generated interest in laparoscopy to obtain specimens for histological and microbiological assessment.

Gold standard diagnosis of TB rests on microbiological confirmation through acid-fast smear microscopy and growth on various solid and liquid culture medias. Since the early 1980's a diagnostic model has been widely used in South Africa to make the diagnosis of abdominal TB; the model included hard and soft criteria.[4,5]

The hard criteria include (i) Microbiological or histological evidence of *Mycobacterium tuberculosis* (ii) Granulomas with caseous necrosis (iii) Successful culture of *M. tuberculosis* from the tissue specimen (iv) Evidence of TB at a distant site (v) Typical operative findings in conjunction with macroscopic caseation and caseating granulomas with or without acid-fast bacilli (AFB) on histology and (vi) Clinical

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diagnosis at autopsy. These hard criteria generally required an operative procedure with tissue resection or colonoscopic examination to provide histological or microbiological evidence of TB. The soft criteria include (i) Clinical features, (ii) Radiological features, and (iii) Response to chemotherapy without recurrence.

Until recently, laparotomy was the only available diagnostic procedure to obtain adequate tissue to make a definitive diagnosis of abdominal TB, but complications of laparotomy such as anastomotic leak and fistula, difficulty in confirming the diagnosis, considerable morbidity and mortality associated with laparotomy in patients with abdominal TB, and the reluctance to embark on poorly defined empirical therapy have generated interest in the use of laparoscopy to visually inspect the abdominal cavity and obtain specimens for histological and microbiological assessment with minimal morbidity.[6-8] Laparoscopy has its own complications involving iatrogenic injury to major vessels or to hollow viscera but by safely inducing a pneumoperitoneum and introducing operative ports, the risk is <0.05%.[9]

Diagnosis of abdominal TB is difficult due to suboptimal, non-invasive access to the intraperitoneal pathology. Laparoscopy with peritoneal biopsy provides rapid and correct diagnosis and should be performed early in suspected cases. The macroscopic diagnosis rate by laparoscopy was reported to be 78% in one study. It has been reported that up to 5% of TB patients may have abdominal TB and of these, 25–60% may have peritoneal involvement.[10]

In the present study, we have performed clinical analysis to evaluate the role of diagnostic laparoscopy in cases of suspected abdominal TB, for the intraperitoneal findings and evaluated visceral biopsies for Microbiological and HPE confirmation of abdominal TB.

Aims and objectives

We aim to evaluate intraperitoneal findings on diagnostic laparoscopy for features suggestive of abdominal tuberculosis and evaluate visceral biopsies for microbiological and HPE confirmation of abdominal tuberculosis.

MATERIALS AND METHODS

Our study titled "role of diagnostic laparoscopy in suspected abdominal TB" was a prospective interventional cohort study, and the data were collected from each patient during the pre-, peri- and post-operative period in the Department of General Surgery VMMC and Safdarjung hospital from October 2017 to March 2019. The study was pre-approved by the Institutional Ethics Committee for the final permission.

An observational study of the use of diagnostic laparoscopy in 30 patients with suspected abdominal TB was conducted. The investigating team assessed all patients with clinically suspected but histologically or microbiologically unconfirmed abdominal TB. Patients diagnosed with TB by another procedure, for example, sputum analysis or peripheral lymph node biopsies were excluded from this study cohort.

Pre-operative strategies

Pre-operative body weight, hemoglobin (Hb) %, and CRP levels were recorded in all patients to compare with post-operative response to treatment. (i) Laparoscopy was done under GA, after pre-anesthetic check-up. (ii) 10 mm trocar was introduced infraumbilically with verres needle. Second and third trocars were introduced under direct vision (iii) Whole abdominal cavity was inspected: Free fluid was aspirated, abnormal looking tissues such as enlarged lymph nodes, mass, omentum, peritoneum, or liver tissues were biopsied and sent for histological examination and microbiological cultures (iv) Trocar sites were closed with non- absorbable sutures.

Laparoscopic strategies

The laparoscopic findings in abdominal TB were grouped into three categories: (i) thickened peritoneum with tubercles (ii) thickened peritoneum without tubercles (iii) fibro adhesive peritonitis with markedly thickened peritoneum and multiple thick adhesions fixing the viscera (Figures 1-5).

Sample isolation and study design

Patient study was conducted in the Department of Surgery, VMMC and Safdarjung Hospital for 18 months. Biopsies were taken from peritoneum, thickened omentum, any involved organ and ascitic fluid samples were sent in saline filled sterile containers for microbiological cultures and formalin filled containers for histopathological analysis.

A detailed pro forma was designed taking into consideration all aspects of the study that is clinical, laboratory, and epidemiological data. The study is a prospective cohort study, and data were collected from each patient during the pre-, peri-, and post-operative period.

Clinical assessment signs and UGC/CECT findings

Following signs and symptoms were considered for clinical assessment of patients: pain in abdomen, fever with anorexia, weight loss, night sweats, abdominal distension, abdominal mass, diarrhea, obstipation, constipation, general physical examination, abdominal examination, nourishment, lymph node enlargement, anemia, weight and height.

Figure 1: Mesenteric Lymphadenitis

Figure 2: Dissection of Mesenteric Lymph node for sampling.

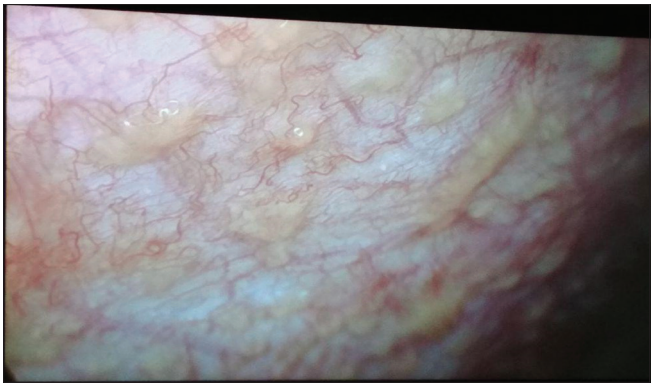


Figure 3: Peritoneum studded with Tubercles.

USG/CECT findings suggestive of abdominal TB

Following features, for example, ascites, peritoneal thickening and nodules, bowel nodules, enlarged mesenteric lymph nodes, bowel strictures, thickening of terminal ileum and ileo-cecal junction, white "military nodules"/plaques ("violin-string" fibrinous strands), stalactic bands (omental thickening/omental caking), mesentric lymphadenopathy, liver, and spleen tubercles were observed which indicated the presence of abdominal TB.

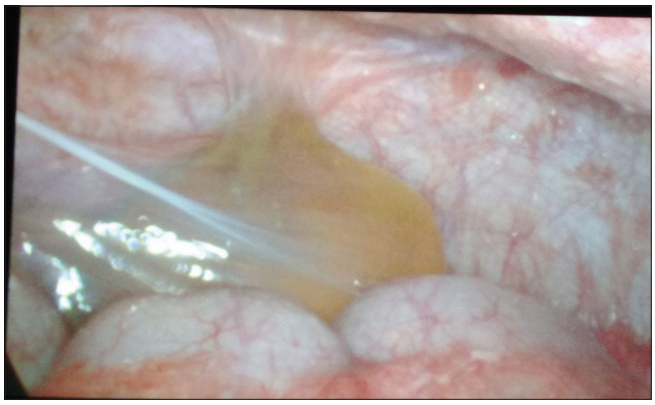


Figure 4: Loculated fluid collection seen intra-operatively highly suggestive of abdominal TB.

Figure 5: Stretched adhesions easily seen on creation of pneumoperitoneum along with tubercles on parietal peritoneum

Inclusion and exclusion criteria

Following were the inclusion criteria: All suspected cases more than 12 years of age, of abdominal TB on clinical, laboratory or radiological tests attending surgery department. Following were the exclusion criteria: patients not fit for GA; patients with histologically or microbiologically confirmed TB on ATT; acute abdomen requiring emergency surgery; suspected TB of retroperitoneal organs.

The sample size from 30 patients was calculated using formula P=92.0 and l=10% S=4pq/l^2 and obtained the value 29.4 patients (confidence interval=90%). Written consent was taken from all the patients participating in this study after explaining the study details. Approval was sought from the Institutional Ethics Committee before starting the present study.

Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean±SD and median. Inter-rater kappa agreement was used to find out the strength of agreement between HPE+MICRO and other findings. Diagnostic test was used

to calculate sensitivity, specificity, PPV, and NPV. P<0.05 was considered statistically significant. The data were entered in MS EXCEL spreadsheet, and analysis was done using Statistical Package for Social Sciences version 21.0.

RESULTS

Abdominal TB is a diagnostic challenge due to difficulty in sample procurement, paucibacillary load and non-specific clinical, biochemical, and radiological features make early diagnosis difficult. Rapid molecular tests such as Gene Xpert, AMTDT, and Real time PCR have gained much attention for diagnosing of abdominal TB.

In our study, we evaluated the role of diagnostic laparoscopy in selected patients for diagnosis of abdominal TB. Our study has shown that diagnostic laparoscopy has an important role not only in diagnosing abdominal TB, but also to rule out TB in certain cases as suggested by clinico-radiological and biochemical investigations. The mortality of tuberculous peritonitis is almost 50% if untreated, mainly because of delayed or missed diagnosis.[4,11]

Signs and symptoms

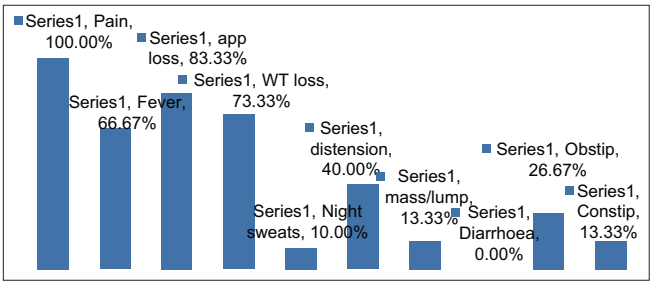
The most common presentation was abdominal pain (100%), followed by appetite loss (83%) and weight loss (73%), which is similar in other series including the gastrointestinal symptoms.[12] Fever was less common in our series (67%).[12] Ascites was present in 90% of patients in some of the series in the past and in 65% of patients in some of the recent series,[7] in comparison none of our patients had clinical evidence of ascites and they presented with plastic (dry) type (Graph 1).

Immunological and hematological

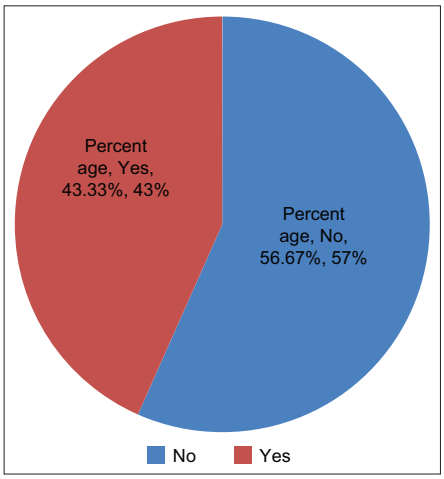
Immunological and Hematological investigations such as Hb, ESR, CRP, and Mantoux are controversial in diagnosis of abdominal TB. Our results were found to be consistent with earlier studies.[12] Histology/culture for TB was positive in 89% of patients with high ESR. CRP has been used both as diagnostic and prognostic tool for TB.[13-15] The newer MTB/RIF test can detect TB in 72% of smear-negative and 98% of smear-positive pulmonary TB.[16] The biggest limitation of this test is the high cost of the equipment, test cartridges and the maintenance of the machines (Graphs 2-4).

Imaging

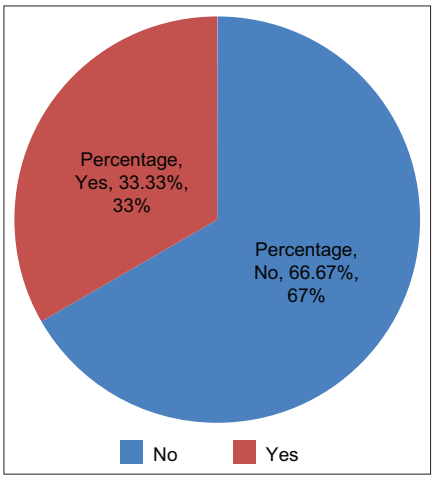
Evidence of TB in a chest X-ray supports the diagnosis, but a normal chest X-ray does not rule it out. X-rays were positive in patients with acute complications (80%). USG abdomen was suggestive of TB in 63.3% patients, compared to CT, which was suggestive in 93.3% cases. The



Graph 1: Depicting the symptomatology in patients suspicious of abdominal Tuberculosis, well noted here are pain, appetite loss and weight loss seen in majority patients



Graph 2: Depicting that only 43% patients suspected of clinically having abdominal Tuberculosis had anemia (Hb<10)



Graph 3: Depicting that only 33% patients of our study group had raised ESR values

sensitivity and specificity of CT scan in the diagnosis of TB abdomen were 92% and 95%, respectively, in one study, although the sample size was small[17] and the sensitivity was only 69% in another study.[18]

However, when both USG+CT were collaborated, this showed slightly better results (94%) but histology/

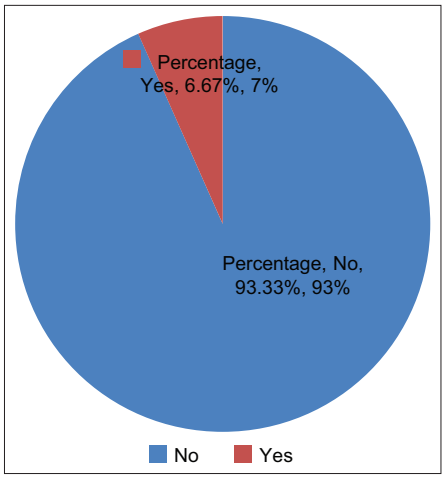
culture results were positive in 60% patients. Although the sensitivity of CT scan was high, the specificity was very low in our series. Caseating lymph nodes with hypodense centers and peripheral rim enhancement along with calcification are highly suggestive of TB.[12,19] Radiology is a primary screening tool with a high inter and intra-observer variability. In our study, radiology reports were available for all patients and 94% showed radiological findings suggestive of TB (Graphs 5 and 6).

Previously, mesenteric lymphadenopathy was not the most common findings in abdominal TB. Nafeh et al.,[12] did not have any patients with mesenteric lymphadenopathy, while Clarke et al., had 23% of their patients with mesenteric lymphadenopathy. In contrast, mesenteric lymphadenopathy was a common finding in our series and all these mesenteric lymph nodes were biopsied and results were highly histology positive (>85%). Tubercles were present in 63% of our patients, whereas Nafeh et al.,[12] had 58% of their patients with tubercles. Adhesions were present in 22 patients (73%), in our series, which was more than in the series by Nafeh et al., (42%)[12] (Table 1 and Graph 7).

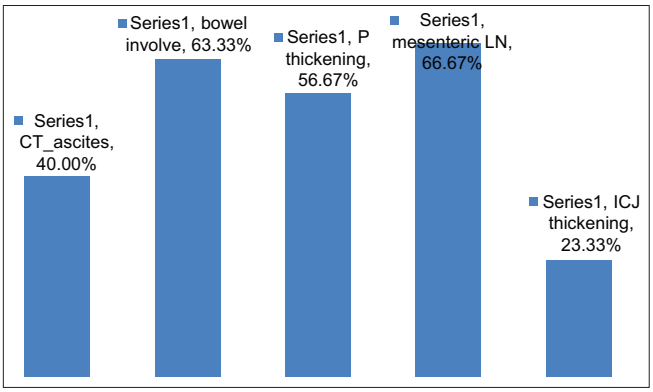
Out of 18 TB positive specimens, 6 of them had caseating granuloma (30%), 4 had non-caseating granuloma (22%). Our findings were little different from that of Nafeh et al.,[12] who had caseating granuloma in 34% and non-caseating granuloma in 56% cases. However, they did not mention about presence of AFB in their ascitic fluid specimens.

Alvares et al.,[20] in his study, demonstrated well-formed granulomas in 23 patients (54%). 14 of the patients (61%) had caseation and 11 (48%) had confluence of the granulomas. AFB was present in the biopsies from two patients (5%). 6 patients had alternative diagnosis as described in Chart 4.

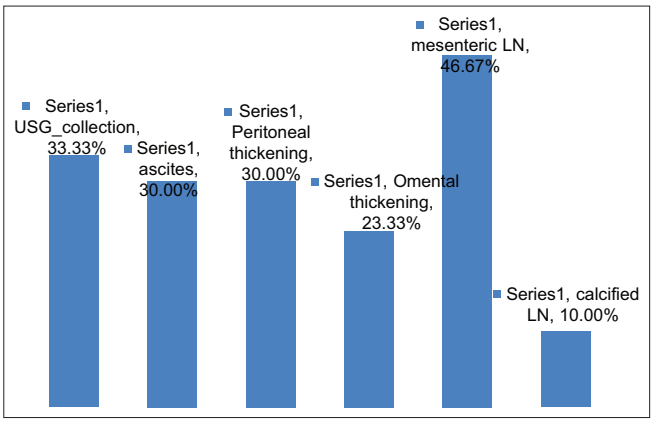
Our main concern was the 6 patients (20%) who were TB negative with no other alternative diagnosis and had non-specific chronic inflammation. Nafeh et al., had 3% of their patients with non-specific chronic inflammation and 7% with unsatisfactory biopsy.



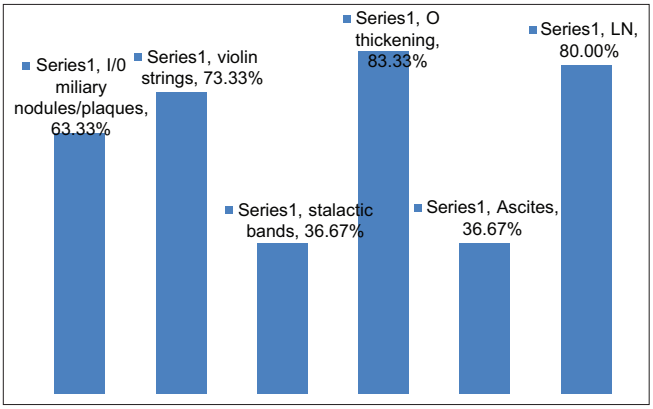
Graph 4: Depicting only 6.67% patients of our study group had raised CRP. CRP: C-reactive protein



Graph 6: Break up and incidences of various findings in CT reports suggestive of Tuberculosis



Graph 5: Break up and incidences of various findings in USG reports suggestive of Tuberculosis



Graph 7: Incidence of various intra-operative macroscopic features suggesting Tuberculosis

Table 1: Incidence of various intra-operative macroscopic features suggesting TB

DIAGNOSTIC LAPAROSCOPY
A: Visual appearance
B: HPE+MICRO
C: PCR
A: Visual appearance

	Frequency	Percentage
Miliary nodules/plaques	19	63.33
Violin strings	22	73.33
Stalactic bands	11	36.67
Omental thickening	25	83.33
Ascites	11	36.67
Lymph node	24	80.00

DISCUSSION

Diagnosis of abdominal TB has remained difficult ever since because of its nonspecific clinical presentation, despite improvement in the technology and diagnostic tools. Due to the growing burden of disease, emergence of drug resistance, Human Immunodeficiency Virus co-infection and the complexities of integrated drug therapy, it is important to make a definitive early diagnosis and spare the misery of patients without TB of having to suffer unnecessary and long-term anti-TB therapy with all its potential side effects. The use of diagnostic aids and syndromic diagnosis of TB have largely been developed and validated in the context of pulmonary TB but have huge lacunae in the same for abdominal TB. The patient profile in our study was completely different from those of many other studies of the past; luminal gastrointestinal disease and clinical ascites were uncommon. As luminal and fluid samples were not available by simple means to establish the diagnosis, laparoscopy as the only way to take adequate tissue biopsies and make definitive diagnosis.

Laparoscopy with peritoneal biopsy provided rapid and correct diagnosis of abdominal TB and should be performed early in suspected cases. Three types of peritoneal TB are described, the wet, dry and plastic types.[21] Therapeutic trial with anti-tubercular therapy, though recommended is not really justified.[22] Furthermore, anti-tubercular therapy, given for 4–6 weeks, can alter the histological picture so much that subsequent differentiation from Crohn's disease becomes difficult.[23] Semenovski et al., consider laparoscopy as the most specific diagnostic test for abdominal TB[24,25] with its advantage of histological confirmation.

In another study conducted by Safarpor, et al., at Department of Surgery, Guilan University of Medical Sciences, Iran, they suggested that laparoscopic visualization along with tissue biopsy provided rapid and correct diagnosis of abdominal TB.[26] The macroscopic diagnosis rate by laparoscopy was reported to be 78% in one study. It has been reported that up to 5% of TB patients may have abdominal TB and of these, 25–60% may have peritoneal involvement.[26] Concomitant active pulmonary TB associated with abdominal TB has been reported to range from 20% to 50%.[27]

Limitations of the study

Drawbacks of this study are that only patients with no age-matched controls were included due to the limitation of time, cost and feasibility. All patients in this study had initial clinical suspicion of TB therefore creating a positive selection bias. Increasing the number of subjects would have improved validity of the findings. Thus, multicentric larger studies including controls conducted as a randomized control trial would greatly add value to creating a diagnostic algorithm for abdominal TB patients. Moreover, laparoscopy is an invasive procedure and has its associated surgical and anesthetic risks involved.

There were other limitations as well in our study. Laparoscopic specimens were not diagnostic for every patient. In our study, only the specimens with macroscopic features suggestive of TB were collected for further tests and investigations. It is unclear if extending the biopsies to routine sampling of all accessible tissues would further enhance the sensitivity and specificity of diagnostic laparoscopy and sampling. Specimens were divided into two parts, one for histological and the other for microbiological examinations.

CONCLUSION

This study has shown the feasibility of laparoscopy in most of the patients with suspected TB with a low complication and conversion rate. It has a high yield to establish the diagnosis of abdominal TB by sampling macroscopically visible pathological tissue, utilizing fresh biopsy specimens for analysis by newer molecular techniques and also providing an alternative diagnosis. The subgroup of patients who were TB negative but still symptomatic with non-specific chronic inflammation needs further evaluation before we can abandon the strategy of empiric therapy in such patients. To avoid the morbidity and mortality associated with laparotomy, and unnecessary long-term therapy, diagnostic laparoscopy and tissue sampling is a viable and reliable strategy in patients with suspected abdominal TB.

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Authors Contribution:
AG- Concept and design of the study; **NP-** Patient study, coordination, statistical analysis and compilation; **VS-** Prepared first draft of manuscript, statistical analysis and interpretation; **ND-** Reviewed the literature; **ID-** Patient study and coordination

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