


Abdominal Tuberculosis in Children

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ABSTRACT

Objective: To provide an insight into the presentation, diagnosis and management of gastrointestinal tuberculosis in children.

Methods: We reviewed the medical records of children who were diagnosed with gastrointestinal tuberculosis, between October 2013 and October 2023. The analysis was performed using descriptive statistics.

Results: During the study period, 11 of 76 tuberculosis pediatric patients (14.5%) were diagnosed with gastrointestinal tuberculosis. Six of 11 patients (54.5%) were female. The median age of the patients was 60 months (51-205 months). Eight of 11 patients had intra-abdominal lymph node involvement, 3 of 11 patients had intestinal tuberculosis and 2 of 11 patients had also active pulmonary tuberculosis. Multiple intra-abdominal areas were involved in 6 patients. Mean duration of symptoms before admission was 60 days (5-180 days). The most common symptoms were abdominal pain (63.7%), weight loss (63.7%) and weakness/fatigue (54.5%). Acid-fast bacilli and tuberculosis PCR were positive in only two patients. Tuberculosis culture positivity was detected in two patients, both of them showed *M. bovis* growth. Necrotizing granulomatous inflammation was the most frequently observed histopathological finding. Anemia was detected in 6 patients. There was elevated ESR in 8 patients and elevated CRP in 6 patients. In one patient, recurrent obstruction symptoms developed due to stenosis of terminal ileum. Clinical cure was achieved with supportive treatment.

Conclusion: Diagnosis of gastrointestinal tuberculosis is very difficult due to non-specific clinical and radiological features. Microbiological confirmation of the disease is often challenging. Making a definitive diagnosis requires reliance on strong clinical suspicion, imaging and histopathological findings, microbiological tests, and/or response to treatment.

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INTRODUCTION

According to the World Health Organization, an estimated 10.6 million people worldwide contracted tuberculosis in 2021, of whom 1.2 million were children. In total, 1.6 million people died from tuberculosis.¹

Extrapulmonary tuberculosis is defined as a disease that affects structures outside the lung parenchyma. Extrapulmonary tuberculosis occurs through mucosal or lymphohematogenous spread of *Mycobacterium tuberculosis*. Tuberculosis involvement of any of the intra-abdominal organs is defined as gastrointestinal tuberculosis. Sites of involvement can be any part of the gastrointestinal tract from the mouth to the anus, the omentum, peritoneum, mesentery and lymph nodes, and other solid intra-abdominal organs such as the liver, spleen and pancreas. Infection occurs due to ingestion of infected material resulting from lung disease or hematogenous spread to the abdominal organs and subsequent involvement of adjacent structures.²

Gastrointestinal tuberculosis accounts for 3-10% of all tuberculosis patients.² Children constitute only 10-20% of gastrointestinal tuberculosis. Therefore, the data mostly belong to adult studies.³ It has been reported that 0.3-4% of tuberculosis patients in childhood are gastrointestinal tuberculosis cases.⁴

The symptoms of gastrointestinal tuberculosis are often nonspecific and can mimic any other gastrointestinal system (GIS) disease. Common symptoms include abdominal pain, abdominal distension, fatigue, weight loss, fever, anorexia, constipation, vomiting, bloody stool and edema.⁵⁻⁸

Moreover, diagnosis of gastrointestinal tuberculosis is very difficult due to non-specific clinical and radiological features. There is no single test that is sufficient for the diagnosis of digestive tuberculosis in all patients. Mild anemia and increased erythrocyte sedimentation rate (ESR) are often detected.^{6,9} In addition to clinical, radiological, endoscopic and histopathological features, Tuberculin skin test (TST), *M. tuberculosis* polymerase chain reaction (PCR) and *M. tuberculosis* culture results, and even good response to antituberculosis treatment play an important role in providing a differential diagnosis.⁶⁻⁹ Most patients respond well to antituberculosis therapy and only a minority of patients require surgical intervention.^{7,9}

In this study, we evaluated the clinical, routine laboratory, microbiological, histopathological and

radiological features and results of pediatric patients with gastrointestinal tuberculosis in order to raise awareness.

MATERIALS AND METHODS

This retrospective study was approved by the Selçuk University Faculty of Medicine Ethics Committee (Approval number 2023/568). We reviewed the medical records of 76 children who were diagnosed with tuberculosis at the Department of Pediatric Infectious Disease at the Selçuk University Faculty of Medicine in Konya, Türkiye, between October 2013 and October 2023. Gastrointestinal tuberculosis was diagnosed according to the following criteria: 1. Positive acid-fast bacillus [AFB] smear or culture; 2. Histopathology showing tubercular granuloma (with or without caseation); 3. Radiological features compatible with tuberculosis; and 4. Patients who have clinical findings compatible with tuberculosis and a negative diagnostic examination, but who respond well to antituberculosis drug treatment (5). Children under the age of 18 who met the diagnostic criteria for gastrointestinal tuberculosis were included in the study. Patients who met the diagnostic criteria for gastrointestinal tuberculosis but had missing data were excluded from the study. Epidemiological data on gender, age, clinical data, site of disease, and exposure data, laboratory, microbiological (AFB staining, *M. tuberculosis* PCR, and *M. tuberculosis* culture) histopathological and radiological findings, treatment and outcome were obtained. For microbiological tests and histopathological examination, tissue biopsies were taken during open surgery in patient 3, during lower endoscopy in patient 6, and under ultrasound guidance in the others. Additionally, all patients were screened for pulmonary tuberculosis: sputum from patients who could produce sputum and fasting gastric fluid from patients who could not produce sputum were taken for EZN staining, *M. tuberculosis* PCR and *M. tuberculosis* culture. Real-time-PCR method was performed using the Artus® *M. tuberculosis* RG PCR kit (Qiagen, Germany) on the Rotor-Gene® Q device (Qiagen, Germany) in accordance with the company's recommendations. Loewenstein-Jensen-medium was used for the conventional cultivation as well as the automated liquid media system Bactec MGIT 960 (Becton-Dickinson). TST results were obtained in 10 patients. Since all our patients were Bacillus Calmette-Guerin vaccinated, the TST test positivity limit was accepted as 15 mm endurance. The

Quantiferon-TB Gold test was performed when available in our hospital.

All children had an abdominal ultrasound. After a 2-way chest radiography was performed on all patients, low-dose contrast-enhanced thorax computerized tomography (CT) was performed on all patients because it provides more reliable information and is easily accessible in our country. Other imaging examinations, especially abdominal MRI, were performed depending on clinical necessity.

Predisposing factors such as malnutrition, HIV status, primary immunodeficiencies and immunocompromised conditions were also evaluated. The analysis was performed using descriptive statistics.

RESULTS

We collected data from 76 pediatric patients with tuberculosis. During the study period gastrointestinal tuberculosis is diagnosed in 11 patients (14.5%). Of the 11 patients 6 were female (54.5%). The median age was 60 months (51-205 months).

Mean duration of symptoms before admission was 60 days (5-180 days). The most common symptoms were abdominal pain (63.7%), weight loss (63.7%), weakness/fatigue (54.5%), fever (27.3%) and night sweats (27.3%) (**Table 1**). Menstrual irregularity was seen in two adolescent girl patients.

Routine laboratory tests were generally normal. Leukocytosis was detected in 2 patients, anemia in 6 patients, erythrocyte sedimentation rate (ESR) elevation in 8 patients, C-reactive protein elevation in 6 patients, and procalcitonin elevation in 1 patient. Only one ascites fluid sample was tested for adenosine deaminase (ADA) and found to be normal (17.4 U/L) (normal value is <40 U/L). TST test positivity was seen in 5 patients. Quantiferon-TB Gold test was performed in 4 patients and found positive in all of them (**Table 1**).

Abdominal lymphadenopathy, the most common radiological finding, was detected in 9 patients (81.8%). Hepatosplenomegaly, terminal ileitis, intra-abdominal mass lesion were the other findings (**Table 1**).

Acid-fast bacilli and *M. tuberculosis* PCR were detected positive in appendectomy specimen taken third month of the antituberculosis treatment in patient 3 and in ileal biopsy materials taken during

ileocolonoscopy in patient 6. Tuberculosis culture positivity was detected in only two patients, both of whom showed *M. bovis* growth; in the sputum of patient 4 and in the ileum tissue culture of patients 6 (**Table 1**).

Histopathologic investigation was performed in all patients. Biopsies were taken during surgery in patient 3, during ileocolonoscopy in patient 6, and under ultrasound guidance in patient 3 and other 9 patients. Necrotizing granulomatous inflammation was observed in the lymph node examination of 7 patients, non-caseating granulomatous inflammation was observed in the liver biopsy sample of patient 2 and ileum/colon biopsy of patient 6 and, necrotizing granulomatous inflammation was observed in the pelvic mass including tubal tissue biopsy of patient 11 (**Table 1**).

In pulmonary CT scan, changes due to active pulmonary tuberculosis were observed in 2 patients, and sequelae changes due to previous tuberculosis were observed in 2 patients (**Table 1**). A cranial MRI performed on patient 6 due to persistent projectile vomiting revealed cerebral and cerebellar tuberculomas.

Ileocolonoscopy was performed in only patient 6 and the ileum entrance was observed to be edematous, hyperemic and narrowed. Intestinal obstruction attacks due to intestinal stricture were seen in the same patient, he recovered only with supportive treatment.

Patient 1 required surgery due to acute abdomen at first admission, and patient 3 required surgery due to tuberculous appendicitis in the 3rd month of anti-tuberculosis treatment.

As for the final diagnosis, 8 of 11 patients had intra-abdominal lymph node involvement, 3 of 11 patients had intestinal tuberculosis, and 2 of 11 patients had active pulmonary tuberculosis (**Table 1**).

In all patients except one, four antituberculosis drugs were used in the intensive phase (isoniazid, rifampicin, pyrazinamide, and ethambutol or streptomycin, then isoniazid and rifampicin for the next 7-10 months. Treatment was well tolerated except for patient 4 with rifampicin allergy, which develops as a widespread rash on the whole body, conjunctival hyperemi, facial edema and fever. He was treated with multidrug resistant infection. All patients completed the drug therapy. Pyrazinamide resistance was detected in two patients with *M. bovis*

infection, as expected. Two patients needed surgical intervention (18.1%) (patients 1 and 3).

Family history of tuberculosis was positive in 2 patients. There was no known consumption of unpasteurized dairy products in all patients. Malnutrition was observed in a total of 3 patients (27.3%), one each with mild, moderate and severe malnutrition. None of the patients had HIV positivity, immunosuppression, or other predisposing factors. No mortality was documented.

DISCUSSION

This study reported 11 children with gastrointestinal tuberculosis with a median age of 60 months. The most common symptoms were abdominal pain (63.7%), weight loss (63.7%) and weakness/fatigue (54.5%). Routine laboratory tests were not helpful in diagnosis. Abdominal lymphadenomegaly was the most common radiologic finding. The diagnosis was confirmed histopathologically in all patients and by microbiological tests in 3 patients (27.2%). The most common type of gastrointestinal tuberculosis was intra-abdominal lymph node involvement (72.7%). All patients, except one, were treated with four antituberculosis drugs for a minimum of 6 months. No patient died.

Gastrointestinal tuberculosis is rare in young children. Lancella et al. reported that 5 of 216 (2.3%) pediatric tuberculosis patients had gastrointestinal tuberculosis (10). In a multicentric study, gastrointestinal tuberculosis was detected in 23 (4.3%) of 539 children diagnosed with tuberculosis in a 12-year period in Türkiye.¹¹ The rate of gastrointestinal tuberculosis among pediatric tuberculosis patients was reported as 2.3% in Italy and 4.3% in Türkiye.^{10,11} We found that 11 of 76 (14.4%) tuberculosis patients had gastrointestinal tuberculosis. While the ages of the patients ranged between 1.3-12 years, the highest number of patients were observed in the 6-9 age group (33.04%).⁶ In the study of Kılıç et al., the mean age of the patients was reported as 9.77±4.36 years (6 months-16 years).⁵ The median age of our patients was 60 months (51-205 months).

In an autopsy study including 48 patients with fatal gastrointestinal tuberculosis, co-morbidity was detected in 29.16% of the patients. The most frequently detected co-morbidities were alcohol use disorders and the presence of malignancy.¹² Other, co-morbidities that predispose to gastrointestinal

tuberculosis like chronic liver disease, Asian ethnicity, HIV co-infection, immunosuppression, diabetes, female gender and peritoneal dialysis were not detected in any of our patients.^{13,14} Only, malnutrition was observed in 3 of our patients.

Clinical findings in gastrointestinal tuberculosis vary widely depending on the site of involvement and mimic many other diseases. Early diagnosis is difficult because the clinical presentation is nonspecific. The most frequently reported complaints were abdominal pain (34.5%), abdominal distension (21%) and fever (11.5%). Interestingly, 22.3% of the patients had no complaints at the time of admission.⁷ Basu et al. reported that abdominal pain was the most common symptom (90.43%); followed by fever, weight loss, abdominal distension, anorexia, and alteration of bowel habits, vomiting and cough (73.04%, 68.70%, 66.96%, 60.87%, 52.17%, 26.96%, 25.22%, respectively).⁶ Lal et al. reported that the most common symptoms in their series, in which they shared data from 218 patients, were abdominal pain (81%), fever (76%) and weight loss (74%).⁸ This triad was present in 118 (54%) patients. The most common symptoms are reported as abdominal pain (44-100%), abdominal distension (35-92%), fever (34-90%), weight loss or growth retardation (30-78%) and malnutrition (28-90%). Also, abdominal mass, ascites, diarrhea or constipation, and peripheral lymphadenopathy may be observed.³ Interestingly, 22.3% of the patients had no complaints at the time of admission.⁷ The triad of abdominal pain, fever, and weight loss was present in half of the patients.⁸ Weight loss, abdominal pain and weakness/fatigue were the most common symptoms in our patients. Fever, night sweats, diarrhea, nausea/vomiting, abdominal distention, and menstrual irregularity were the other symptoms. Cheng et al. found malnutrition in 50.6% of 85 patients with intestinal tuberculosis.⁹ Malnutrition was observed in 3 of our patients (27.3%). The frequent observation of nonspecific symptoms such as weight loss, abdominal pain, fever, diarrhea and constipation has been associated with late diagnosis (7-24 weeks)¹² Mean duration of the complaints was reported as 109 days (10 days-3 years) by Kılıç et al. 5, and 54 days (7 days-9 months) by Talwar et al. ¹³. It was 60 days (5-180 days) in our patients. Regardless of the duration of abdominal complaints, tuberculosis should be kept in mind in the differential diagnosis.

Table 1. Clinical, laboratory, and outcome features of Children with abdominal tuberculosis

Patient No. Age (Year)/ Gender	Symptoms	TST/IGRA	Microbiology	Radiology	Histopathology	Primary Disease Site	Treatment	Outcome
1 14.42/M	Abdominal pain	20 mm/ND	Fasting gastric fluid EZN staining: (-) Fasting gastric fluid <i>M. tuberculosis</i> PCR: (-) Fasting gastric fluid <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Ascending colonic dense lesion with calcifications Chest x-ray: Normal Thorax CT: Right hilar LAP Abdominal CT: Calcified LAP in the right lower quadrant, one millimetric calcification in the spleen.	Mesenteric lymph node biopsy: Necrotizing granulomatous lymphadenitis	Intestinal, mesenteric lymphadenitis	HRZE 9 months	Cured
2 12.33/F	Fever	0 mm/ND	Fasting gastric fluid EZN staining: (-) Fasting gastric fluid <i>M. tuberculosis</i> PCR: (-) Fasting gastric fluid <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Splenomegaly Chest x-ray: Normal Thorax CT: Millimetric calcified lesions in both lung parenchymas. Abdominal MRI: Multiple hepatic microabscesses, splenic millimetric nodular lesions, hepatosplenomegaly	Liver biopsy: Non-caseating granuloma	Hepatic, splenic	HRZE 9 months	Cured
3 11.58/F	Abdominal pain	10 mm/ND	Appendix biopsy EZN staining: (+1) Appendix biopsy <i>M. tuberculosis</i> PCR: (+) Appendix biopsy <i>M. tuberculosis</i> culture: (-) Fasting gastric fluid EZN staining: (-) Fasting gastric fluid <i>M. tuberculosis</i> PCR: (-) Fasting gastric fluid <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Conglomerated mesenteric LAPs. Chest x-ray: Normal Thorax CT: Normal. Abdominal CT: Conglomerated, centrally necrotic mesenteric LAPs.	Mesenteric lymph node biopsy: Necrotic granulomatous inflammation	Appendix, mesenteric lymph nodes	HRZE 10 months	Cured
4 16.25/M	Abdominal pain, weight loss	22 mm/ND	Sputum EZN staining: (-) Sputum <i>M. tuberculosis</i> PCR: (-) Sputum <i>M. tuberculosis</i> culture: <i>M. bovis</i>	Cervical USG: Bilateral cervical LAPs. Abdominal USG: Right paraaortic LAP, hepatomegaly Chest x-ray: Normal Thorax CT: Right hilar calcified lymph node. Abdominal MRI: Mesenteric LAPs, hepatosplenomegaly	Mesenteric lymph node biopsy: Necrotizing granulomatous lymphadenitis	Mesenteric lymph nodes	HEMA 20 months	Cured
5 4.25/M	Abdominal pain	12 mm/(+)	Sputum EZN staining: (-) Sputum <i>M. tuberculosis</i> PCR: (-) Sputum <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Paraaortic necrotic conglomerated LAPs. Chest x-ray: Normal Thorax CT: Normal.	Paraaortic lymph node biopsy: Necrotizing granulomatous inflammation	Paraaortic lymph nodes	HRZE 9 months	Cured
6 16.17/M	Abdominal pain, diarrhea, vomiting, night sweats, fever, weight loss, weakness, fatigue.	0 mm/(+)	Sputum EZN staining: (-) Sputum <i>M. tuberculosis</i> PCR: (-) Sputum <i>M. tuberculosis</i> culture: (-) Ileal biopsy EZN staining: (+2) Ileal biopsy <i>M. tuberculosis</i> PCR: (+) Ileal biopsy <i>M. tuberculosis</i> culture: <i>M. bovis</i>	Abdominal USG: Intraabdominal disseminated LAPs, terminal ileitis, hepatosplenomegaly Chest x-ray: Bilateral reticulonodular opacities Thorax CT: Cavitory lesions and tree-in-bud lesions. Abdominal CT: Whole colonic diffuse wall thickening, paraaortic and mesenteric LAPs, ascites, hepatomegaly. Brain MRI: Cerebral and cerebellar nodular lesions.	Ileum and colon biopsies: Non-caseous granulomatous inflammation.	Intestinal, brain, lung	HRZE 11 months	Cured

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7 13.92/F	Weight loss, anorexia, weakness, fatigue.	20 mm/(+)	Fasting gastric fluid EZN staining: (-) Fasting gastric fluid <i>M. tuberculosis</i> PCR: (-) Fasting gastric fluid <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Hepatomegaly. Chest x-ray: Normal Thorax CT: Milimetric parenchymal nodules. Abdominal MRI: Conglomerated LAP in the right lower quadrant.	Abdominal LAP biopsy: Necrotizing lymph node inflammation	Abdominal lymph nodes	HRZE 12 months	Cured
8 17.08/F	Weakness, fatigue, nausea, dyspnea, night sweats, weight loss.	21 mm/ND	Fasting gastric fluid EZN staining: (-) Fasting gastric fluid <i>M. tuberculosis</i> PCR: (-) Fasting gastric fluid <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Parailiac conglomerated LAPs. Chest x-ray: Radiopaque space-occupying lesion in the hilus of the right lung Thorax CT: Hilar LAP, tree-in-bud lesions, consolidation, pleural effusion. Abdominal MRI: Splenic nodular lesion, intraabdominal disseminated necrotic LAPs, omental and peritoneal thickening, ascites.	Abdominal LAP biopsy: Necrotizing granulomatous inflammation	Abdominal lymph nodes, lung, spleen, periton	HRZE 8 months	Cured
9 15.42/F	Abdominal pain, hemoptysis, weakness, fatigue, night sweats, weight loss.	17 mm/(+)	Sputum EZN staining: (-) Sputum <i>M. tuberculosis</i> PCR: (-) Sputum <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Disseminated LAPs. Chest x-ray: Normal Thorax CT: Normal. Abdominal MRI: Numerous cystic necrotic conglomerated LAPs, terminal ileal thickening.	Mesenteric lymph node biopsy: Necrotizing granulomatous lymphadenitis	Intestinal, mesenteric lymph nodes	HRZE 12 months	Cured
10 12.75/M	Abdominal pain, weight loss, weakness, fatigue.	8 mm/ND	Fasting gastric fluid EZN staining: (-) Fasting gastric fluid <i>M. tuberculosis</i> PCR: (-) Fasting gastric fluid <i>M. tuberculosis</i> culture: (-) Urine EZN staining: (-) Urine <i>M. tuberculosis</i> PCR: (-) Urine <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Right nephromegaly, multiple LAP in front of right ureter, right renal pelvicalyceal dilatation, splenomegaly Chest x-ray: Normal Thorax CT: Normal. Abdominal CT: Parailiac, adjacent to the right ureter solid mass lesion, hepatosplenomegaly. MR Urography: Cystic necrotic lesion (10x7 cm) Abdominal MRI: 3x2 cm LAP in the right paraaortic area.	Abdominal lymph node biopsy: Granulomatous inflammation	Abdominal lymph nodes	HRZE 6 months	Cured
11 17.08/F	Diarrhea, vomiting, anorexia, abdominal distension, weight loss, fever, weakness, fatigue.	No info/ND	Sputum EZN staining: (-) Sputum <i>M. tuberculosis</i> PCR: (-) Sputum <i>M. tuberculosis</i> culture: (-)	Abdominal USG: Massive ascites, ovarian cyst, hepatosplenomegaly. Chest x-ray: Normal Thorax CT: Pleural effusion, atelectasia. Abdominal CT: Right 6.5x8 cm adnexal cyst, 2x3 cm mass. Abdominal MRI: Mid abdominal line mass lesion (6x8x12 cm), ascites, ovarian cystic lesion.	Mass lesion biopsy: Diffuse granulomatous inflammation involving the tuba wall. Citology: Mesenteric granulomatous inflammation	Tuboovarian, mesenteric lymph nodes	HRZE 10 months	Cured

A, Amikacin; CNS, central nervous system; CT, computerized tomography; E, ethambutol; EZN, Ehrlich-Ziehl-Neelsen; F, female; H, isoniazid; IGRA, interferon-gamma release assays; M, moxifloxacin; M, male; MRI, magnetic resonance imaging; LAP, lymphadenopathy; ND, not done; PCR, Polymerase Chain Reaction; S, Streptomycin; R, rifampicin; TST, tuberculin skin test, USG, ultrasonography; Z, pyrazinamide;

Although, gastrointestinal tuberculosis may involve the gastrointestinal tract, peritoneum, lymph nodes, and/or solid organs, most commonly involved areas are peritoneum, intestine, and/or lymph nodes.¹⁴ Cho et al. reported that of 139 patients diagnosed with gastrointestinal tuberculosis, 49.6% had luminal tuberculosis, 20.1% peritoneal tuberculosis, 5.0% nodal tuberculosis, 16.5% visceral tuberculosis and, 8.6% mixed tuberculosis.⁷ In a study by Al Karawi et al., where they examined 130 gastrointestinal tuberculosis patients, 8.5% of the patients had the upper gastrointestinal tract, 33.8% had the small intestine, 22.3% had the large intestine, 30.7% had the peritoneum and 14.6% had the liver involvement.¹⁵ Kılıç et al. found that out of 35 children with gastrointestinal tuberculosis, 29 had tuberculous peritonitis, five had intestinal tuberculosis, and one had pelvic tuberculosis.⁵ Of our 11 patients with gastrointestinal tuberculosis, 9 had nodal tuberculosis, three had intestinal involvement, two had spleen involvement, one had liver involvement, one had peritonitis and one had tubo-ovarian involvement (**Table 1**).

The hallmark of gastrointestinal tuberculosis in both adults and children is lymphadenopathy, which occurs in 55-66% of cases. The most commonly involved nodal regions are peripancreatic/periportal, mesenteric/omental and paraaortic/pericaval regions.¹⁶ We detected predominantly mesenteric lymphadenopathies in our patients.

In a study of 85 adult patients with intestinal tuberculosis 67.1% of patients had coexisting pulmonary TB.⁹ Children (20-60%) with gastrointestinal tuberculosis have evidence of current or past pulmonary tuberculosis on chest radiographs, whereas 23% of children with culture-confirmed pulmonary tuberculosis have evidence of gastrointestinal tuberculosis on ultrasound.¹⁶ Active pulmonary involvement was seen in two patients in our study, while Basu et al. reported that the evidence of primary focus in chest radiographs was found in 40% of patients.⁶

Although tuberculosis is one of the most common causes of hepatic granulomas, liver tuberculosis is rare and is usually reported as a case report. However, Al Karawi et al. reported a 14.6% rate of liver involvement.¹⁵ The liver may be involved in the form of miliary liver disease or isolated liver disease and may present with hepatomegaly, fever, respiratory symptoms, abdominal pain, and weight loss.¹⁴ The diagnosis of

miliary liver tuberculosis was made in patient 2. Although the patient's TST result was 0 mm and there was no microbiological evidence, antituberculosis treatment was started because of the histopathological examination of the liver biopsy showing non-caseating granuloma, presence of calcifications in both lung parenchyma related to previous tuberculosis and presence of active liver tuberculosis in her sister.

Although routine laboratory tests are not specific and diagnostic, anemia, leukocytosis, high ESR levels and hypoalbuminemia are frequently observed due to chronic inflammation.^{5, 6, 9, 14} As in our patients, high ESR values were reported in 60-86.7% of the patients.⁹ Although ADA in peritoneal fluid is a sensitive and highly specific test for tuberculous peritonitis (93% and 95%, respectively), only one ascites fluid sample tested for ADA and found normal (17.4 U/L).¹³

In the diagnosis of patients with gastrointestinal tuberculosis, abdominal ultrasound is requested as the first examination. In case of suspicion of gastrointestinal tuberculosis, abdominal ultrasonography is requested as the first examination. It shows enlarged intra-abdominal lymph nodes, ascites, fibrin networks and loculations, thickening of intestinal walls, omental masses, focal lesions in the liver and spleen, and psoas abscesses.³ Performing an ultrasound-guided biopsy enabled rapid diagnosis. Abdominal CT or magnetic resonance imaging (MRI) is more successful in showing intra-abdominal lymphadenopathies and characteristic rim-sing.³ CT or MRI can also provide information about adjacent structures as well as thickening of the peritoneum or bowel wall and loss of regular wall stratification of the loops.¹⁰ After seeing abnormalities in abdominal ultrasound in our patients, we especially preferred abdominal MRI as a further test (**Table 1**). While peritoneal or mesenteric thickening, abdominal lymphadenopathy, thickened bowel wall, ascites were reported in other studies^{5,6,17}, abdominal lymphadenopathies were the most common radiologic finding in our study.

Biopsy samples can be taken by laparoscopy, endoscopy and ultrasound-guided interventions, etc. Biopsy options should be evaluated based on individual circumstances, including the predominant site of involvement and associated risks and benefits.¹⁴ Biopsies were taken during open surgery in patients 1 and 3, during ileocolonoscopy in patient

6, and under ultrasound guidance in patients 3 and the others. In patient 3, necrotic granulomatous inflammation was detected in the ultrasound-guided biopsy taken from the mesenteric lymph node, and antituberculosis treatment was started. Acute appendicitis developed in the 3rd month of treatment. AFB and *M. tuberculosis* PCR were detected positive in the appendectomy specimen, but there was no growth in culture.

TST positivity was seen in %50 of our patients, while it was reported as 24-40% before (5, 6, 18).

Because microbiological confirmation is the gold standard for the diagnosis of gastrointestinal tuberculosis, all tissue by surgery or ileocolonoscopy should be directed to microbiological evaluation.⁷ Culture positivity not only confirms the diagnosis of tuberculosis but also allows testing of the drug sensitivity of the isolated strain, allowing for appropriate treatment. AFB staining is extremely low for intestinal tuberculosis. Culture positivity was generally reported as less than 50% (7-79%).^{9,12} Only, 2 of our patients had culture positivity and 2 of positive for AFB staining.

Most of the cases are due to *M. tuberculosis*, while *Mycobacterium bovis* infection is seen rarely. Gastrointestinal TB may develop as a result of consuming dairy products infected with *M. bovis*, especially in rural areas where pasteurization is not easily achieved.¹⁸ Livestock farming is very common in our region. In rural areas, dairy products, especially cheese, are produced without boiling or pasteurization. We made a definitive diagnosis of gastrointestinal tuberculosis with culture positivity in only 2 patients. We detected *M. bovis* growth in these patients. Both of them had multiorgan involvement. There was no known consumption of unpasteurized dairy products in both patients.

The Xpert Mtb/Rif test has been reported to have low sensitivity (23%) and high specificity (100%) in the diagnosis of intestinal tuberculosis (20). Unfortunately, we could not perform the Xpert Mtb/Rif test on any of our patients.

Intestinal obstruction, ulcerations, intussusception, abscess, and intestinal perforation may be observed as complications.^{7,9} Intestinal obstructions can be caused by the inflammatory process, strictures or adhesions. In a meta-analysis of 1969 patients with gastrointestinal tuberculosis, the overall prevalence of intestinal strictures was 0.12. While 0.77 of the patients responded clinically to

antituberculosis treatment, 0.21 required surgical intervention and 0.14 required endoscopic dilatation.²¹ Only in patient 6, recurrent obstruction symptoms developed due to stenosis of the terminal ileum. Clinical cure was achieved with supportive treatment.

Although, six months of antituberculosis therapy is sufficient in most cases.¹⁹ However, it is observed in the literature that longer treatment periods are preferred (5, 7, 8, 9), ideally, total duration of the therapy must be decided on a case-to-case basis.¹² We gave antituberculosis treatment to our patients for varying periods of time depending on the severity of their clinics (**Table 1**). Mortality was reported as 1.4-20% before.¹⁰ None of our patients died.

Limitations

First of all, our retrospective single-center study has a very small sample size. Due to the limited number of cases, advanced statistical tests could not be performed. Microbiological evidence of tuberculosis disease was obtained in a minority of our pediatric patients.

Conclusion

Gastrointestinal tuberculosis can affect many tissues/organs within the abdomen. Depending on the organ involved, the presenting symptoms may vary greatly. So, a high suspicion index must be required for early diagnosis. Early diagnosis plays an important role in preventing both morbidity and mortality. Performing an ultrasound-guided biopsy enabled rapid diagnosis and therefore rapid initiation of treatment. Further studies are needed to clarify the management of gastrointestinal TB cases.

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Authors' contributions:

Melike Emiroglu: Substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; and drafting the article and revising it critically for important intellectual content.

Gulsum Alkan: Substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; and revising it critically for important intellectual content.

Meltem Kıymaz: Substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; and revising it critically for important intellectual content.

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We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Ethics approval: The study protocols were approved by Selçuk University Faculty of Medicine ethics committee (2023/568)

Consent to participate: We confirm that the manuscript has been read and approved by all named authors and that there are no other people who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

Consent for publication: All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. Manuscript is not under publication or consideration for publication elsewhere.

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