

## Abdominal Tuberculosis: Analysis of Clinical Features and Outcome of Adult Patients in Southern Taiwan

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**Background:** Abdominal tuberculosis remains a serious health threat. This retrospective report aimed to analyze patients after the development of the tuberculosis control program by the Center of Disease Control (Taiwan) in January 2000. The study was conducted at the Chang Gung Memorial Hospital-Kaohsiung, Taiwan.

**Methods:** Between January 2000 and December 2006, we evaluated 14 adult patients with abdominal tuberculosis by reviewing their clinical information, therapeutic methods and outcomes. Diagnosis of abdominal tuberculosis was made based on clinical features of abdominal infection with microbiological results from culture, acid-fast bacilli stain and polymerase chain reaction for *Mycobacterium tuberculosis* and/or histopathological confirmation from biopsy and ascites.

**Results:** Tuberculous peritonitis and intestinal tuberculosis were the most common type of infections followed by hepatic tuberculosis, and intra-abdominal tuberculoma. 35.7% of these patients had the coexistence of extra-abdominal infection. The most common clinical symptoms and signs were abdominal pain, abdominal distension, ascites and body weight loss. Fever was found in 35.7% of patients and peritoneal signs were noted in 7.1%. Immunocompromised states and old age are relevant to adult abdominal tuberculosis. Overall, patients were diagnosed by bacteriology (35.7%), biopsy materials from laparotomy (42.8%), liver biopsy (14.3%), and biopsy materials from colonoscopy (7.2%). Patients were cured after taking antituberculous drugs for at least 6 months without relapse during regular follow-up for at least 2 years. However, three patients died of sepsis and decompensated liver cirrhosis during treatment.

**Conclusion:** Extra vigilance in dealing with patients who present with unexplained abdominal conditions is the key to the diagnosis of abdominal tuberculosis. Early diagnosis, early antituberculous therapy and surgical treatment of the associated complications are essential for the survival of the patient.

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**Key words:** abdominal tuberculosis, *Mycobacterium tuberculosis*, tuberculous peritonitis, intestinal tuberculosis

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Abdominal tuberculosis (ATB) is defined as an infection in the gastrointestinal tract, peritoneum, or intra-abdominal solid organs of *Mycobacterium tuberculosis* (*M. tuberculosis*). It constitutes about 12% of extra-pulmonary tuberculosis and 1-3% of all cases of tuberculosis (TB).<sup>(1-3)</sup> ATB is relatively uncommon in Taiwan as compared with pulmonary tuberculosis, but it still remains a serious health threat.<sup>(4,5)</sup> With the emergence of the human immunodeficiency virus (HIV) infection and the use of immunosuppressive therapy, its incidence has also been increasing in low-income and middle-income societies.<sup>(6-8)</sup>

The diagnosis of abdominal TB is difficult to make due to the nonspecific presentation of symptoms and signs. In addition, it can mimic many diseases and conditions such as malignancy, bacterial infectious disease, and inflammatory disease.<sup>(4,9)</sup> Delayed diagnosis or misdiagnosis is directly related to poor outcome in patients who are not able to receive early treatment.<sup>(4,5,9)</sup> The World Health Organization estimates that one-third of the world's population is infected with *M. tuberculosis*, with the highest prevalence of TB in Southeast Asia.<sup>(10)</sup> Moreover, the emergence of drug-resistant tuberculosis has become a cause for concern in many parts of the world,<sup>(7)</sup> including Taiwan.<sup>(11)</sup> The incidence of TB might have been underestimated in Taiwan before the strict policy of circulating notices to the public after every new case was diagnosed. This system was established through the tuberculosis control program of the Center of Disease Control (CDC) (Taiwan) in January 2000.<sup>(12)</sup> Therefore, in this retrospective study, we only dealt with patients from after the notice system was conducted by the CDC in order to minimize any possible underestimating of TB patients. We analyzed clinical, laboratory and imaging studies and therapeutic outcomes of 14 adult patients with abdominal TB as reported to the Center of Disease Control of Taiwan by our hospital.

## METHODS

Between January 2000 and December 2006, 14 adult patients were admitted to Chang Gung Memorial Hospital-Kaohsiung, Taiwan and subsequently reported to the CDC with the diagnosis of abdominal TB. We retrospectively evaluated these 14 adult patients by reviewing their clinical information,

therapeutic methods and outcomes from the database. Abdominal TB is defined as *M. tuberculosis* infections in the gastrointestinal tract, peritoneum, or intra-abdominal solid organs.<sup>(13,14)</sup> Diagnosis of abdominal TB was made based on clinical features of abdominal infection and at least one of the following criteria:<sup>(4,15)</sup> (1) positive culture of *M. tuberculosis* from abdominal organ tissue or peritoneal fluid; (2) positive acid-fast bacilli (AFB) stain from the tissue biopsies; (3) histopathological demonstration of typically caseating granulomatous necrosis; or (4) positive polymerase chain reaction (PCR) for *M. tuberculosis* on abdominal organ tissue or peritoneal fluid. The clinical information, including age, sex, medical history, symptoms and signs, physical findings, laboratory and image findings (radiography and sonography), therapeutic methods and outcomes were reviewed and analyzed. Eleven patients received antituberculous treatment for at least 6 months and were then followed up at out-patient clinics for at least 2 years after treatment.

## RESULTS

This study recruited 14 patients (6 males and 8 females) with the diagnosis of abdominal TB. Their ages ranged from 20 to 60 years with a mean of  $57.8 \pm 18$  years of age. More than half of our patients (57.1%) were older than 60 years. The clinical characteristics of the 14 patients are shown in Table 1. The co-morbidity of a single or multiple underlying diseases was identified in all but two patients: liver cirrhosis (n = 5), hypertension (n = 5), chronic renal failure (n = 4), diabetes mellitus (n = 3), chronic hepatitis C (n = 3), iatrogenic Cushing's syndrome (n = 2), old stroke (n = 2), alcoholism (n = 1) and cancer (n = 1). Five patients (Patients 2, 3, 9, 10 and 12) had a coexisting infection of pulmonary TB while patient 3 had concomitant pulmonary TB and TB meningitis.

The anatomical locations of abdominal TB are listed in Table 2. TB peritonitis and intestinal TB were the most common types of infection followed by hepatic TB and intra-abdominal tuberculoma. One patient (Patient 12) suffered from coexisting intestinal TB and TB peritonitis. The clinical manifestations in these 14 patients were abdominal pain (71.4%), abdominal distension (57.1%), ascites (50%), body weight loss (42.9%), fever (35.7%),

**Table 1.** Demographic Characteristics in 14 Adult Patients with Abdominal Tuberculosis

Patient	Age (years) /Sex	Type of infection	Underlying diseases	Clinical manifestations*	Therapy	Outcome
1	62/F	TB peritonitis	DM, CRF, HTN, hepatitis C, LC	1, 2, 3, 5, 10	Anti-TB agents	Died
2	70/F	TB peritonitis, pulmonary TB	HTN, LC	1, 2, 3, 4, 6, 10	Anti-TB agents	Died
3	74/M	TB peritonitis, pulmonary TB, TB meningitis	Stroke, CRF, HTN	1, 8	Anti-TB agents	Cured
4	31/F	Small intestinal TB with perforation, abscess formation	–	1, 4, 5, 6	Surgical resection Anti-TB agents	Cured
5	74/F	TB peritonitis	Hepatitis C, LC, TB meningitis	1, 2, 3, 4, 5	Anti-TB agents	Cured
6	51/M	Hepatic TB	Bladder cancer	4, 5	Anti-TB agents	Cured
7	73/M	TB peritonitis	DM, CRF, HTN, LC	2, 3, 4, 7, 10	Anti-TB agents	Died
8	20/F	Intra-abdominal tuberculoma	–	1, 6	Surgical excision Anti-TB agents	Cured
9	53/M	TB peritonitis with intestinal obstruction, pulmonary TB	CRF, HTN, stroke, Cushing's syndrome	1, 9	Surgical resection Anti-TB agents	Cured
10	61/M	TB peritonitis, pulmonary TB	Alcoholism, LC	2, 3	Anti-TB agents	Cured
11	47/F	Colonic TB	Cushing's syndrome	1, 2, 7	Right hemicolectomy Anti-TB agents	Cured
12	80/F	Small intestinal TB, TB peritonitis, pulmonary TB	DM	1, 2, 3, 7	Anti-TB agents	Cured
13	72/F	TB peritonitis	–	1, 2, 3, 4	Anti-TB agents	Cured
14	41/M	Hepatic TB	Hepatitis C	5	Anti-TB agents	Cured

**Abbreviations:** F: female; M: male; TB: tuberculosis; DM: diabetes mellitus; CRF: chronic renal failure; HTN: hypertension; LC: liver cirrhosis; Anti-TB: antituberculous; \*: Clinical manifestations: 1. abdominal pain, 2. abdominal distension, 3. ascites, 4. body weight loss, 5. fever, 6. abdominal mass, 7. constipation, 8. bloody stool, 9. peritoneal sign, 10. sepsis.

abdominal mass (21.4%), constipation (21.4%), sepsis (21.4%), bloody stool (7.1%) and peritoneal signs (7.1%).

Abdominal sonography was performed in 11 patients. Non-specific liver parenchymal changes were found in 7 patients (Patients 2, 3, 5, 6, 7, 12 and 13), ascites in 7 (Patients 1, 2, 5, 7, 10, 12 and 13), liver cirrhosis in 5 (Patients 1, 2, 5, 7 and 10), abdominal cystic lesion in 1 (Patient 8) and an abdominal mass in 1 (Patient 2). Abdominal computed tomography (CT) was performed in 7 patients and revealed ascites with thickening of the peritoneum in 4 patients (Patients 5, 7, 12 and 13), abdominal cyst in 1 (Patient 8), lobulated abscess in 1 (Patient 4) and thickening of the ascending colon wall in 1 (Patient

11). In addition, peritoneal carcinomatosis was initially suspected in 4 patients (Patients 2, 3, 5 and 12).

Different diagnostic methods were used in detecting abdominal TB in these 14 patients: diagnostic laparotomy and biopsy, ascites culture or AFB stain, endoscopy with biopsy, ultrasound-guide liver biopsy (Table 3). All specimens obtained from such procedures underwent TB culture, AFB stain, TB PCR, and/or histopathological examination to confirm the diagnosis. In the current study, only 7 patients were initially suspected of having TB infection because of the presence of massive ascites or as a result of computed tomography image studies that revealed a thickened peritoneum before the final diagnosis was actually confirmed. On the other hand,

**Table 2.** The Anatomical Locations of Abdominal Tuberculosis (TB)

Location	n (%)
Peritoneum	9 (60.0%)
Intestine	3 (20.0%)
Terminal ileum	2
Ascending colon	1
Liver	2 (13.3%)
Intra-abdominal tuberculoma	1 (6.7%)

One patient (Patient 12) had coexisted with intestinal TB and TB peritonitis.

**Table 3.** Diagnostic Methods in 14 Patients with Abdominal Tuberculosis (TB)

Diagnostic methods	n (%)
Ascites culture or AFB stain	5 (35.7%)
TB culture	3
AFB stain positive	2
Laparotomy and biopsy	6 (42.8%)
Pathology with caseous necrosis, AFB stain positive	3
Pathology with caseous necrosis, AFB stain negative	2
Positive polymerase chain reaction for TB	1
Ultrasound-guide liver biopsy (Pathology with granulomatous caseous necrosis)	2 (14.3%)
Colonoscopy and biopsy (Pathology with granulomatous caseous necrosis, AFB stain positive)	1 (7.2%)

**Abbreviation:** AFB: Acid-fast bacilli

seven patients were found to have TB infection by accident either during an operation for gastrointestinal bleeding (Patient 3), a laparotomy with biopsy (Patient 4, 8, 9), liver biopsy (Patient 6, 14) or colonoscopy with biopsy (Patient 11). Overall, patients were diagnosed by bacteriology (35.7%), biopsy materials from laparotomy (42.8%), from liver biopsy (14.3%), and biopsy from colonoscopy (7.2%).

Four patients received surgical intervention for the abdominal TB infections. The operative proce-

dures are shown in Table 1. There were no significant postoperative complications or mortality in these 4 patients. All patients had received antituberculous therapy. However, a regime of at least 6 months of antituberculous drugs was only completed in 11 patients and they remained disease-free during regular follow-up. Three patients died during the course of antituberculous therapy. The major cause of death in these patients was due to concomitant sepsis and septic shock instead of TB itself. The overall crude mortality rate was 21.4%.

## DISCUSSION

The introduction of milk pasteurization has reduced the incidence of abdominal infection with *M. tuberculosis*. In Taiwan, the government's strict policy of Bacillus Calmette-Guérin vaccination at birth, pre-employment chest X-ray screening programs and the advent of effective antituberculous medications has reduced the incidence of TB in the past.<sup>(11,16)</sup> However, the resurgence of TB and its persistently high rate of mortality have recently become an important public health issue in Taiwan.<sup>(11)</sup> In the past, the incidence of TB might have been underestimated in Taiwan. One of the main reasons put forward, was the lack of a strict system that could notify the public about TB outbreaks among the various districts on the island. To avoid such discrepancy and possible bias, this study only dealt with patients after CDC had started the reporting system in 2000.<sup>(12)</sup>

Abdominal TB tends to affect a population in the third and fourth decades of life.<sup>(13,17,18)</sup> The ages of most of our patients (60%) were older than 60 years. Moreover, 80% of our patients had underlying diseases that included liver cirrhosis, chronic renal failure, diabetes mellitus, chronic hepatitis, iatrogenic Cushing's syndrome, alcoholism and cancer. This implies that old age and a compromised immune system are important predisposing factors for adult abdominal TB. Whereas female predominance has been reported in some large series,<sup>(19,20)</sup> gender is not significantly different in this study.

The term "abdominal TB" emphasizes the involvement of any or multiple parts of the gastrointestinal system with the most frequently involved sites being the peritoneum and intestine.<sup>(4,13,14)</sup> The involvement of the appendix and jejunum is uncommon while mention of TB of the ascending colon,

esophagus, stomach, duodenum, rectum, and anus is distinctly rare in literature. In our current study, we also found that the peritoneum is the most common site of infection with more than half of the patients with abdominal TB having TB peritonitis. This finding is quite consistent with other reports.<sup>(4,13-15)</sup> Chu et al reported that laparoscopic observation in combination with a biopsy could establish the cause of ascites of unknown origin (86.0%) among which 20.2% belonged to tuberculous peritonitis.<sup>(21)</sup>

On the other hand, gastrointestinal TB is a diagnostic challenge, particularly in the absence of evidence of pulmonary infection. It may mimic many other abdominal diseases such as other infectious processes, tumors, and Crohn's disease. In the absence of any positive laboratory and radiologic tests, the diagnosis is often established by obtaining a surgical specimen. Lin et al emphasized that colonoscopy with biopsy is also a useful diagnostic tool for early diagnosis and in avoiding unnecessary morbidity and mortality associated with exploratory laparotomy in colonic TB.<sup>(22)</sup> The colonoscopic appearance may include the following: ulcerated lesions, sessile firm polyps, masses, and small diverticula, ranging from 3 to 5 mm in diameter. Infection of 1 or 2 (Table 2 is 1) patients with intestinal TB was located in the specific ileocecal area. The ileocecal valve is a common site of intestinal infection owing to the presence of rich lymphoid tissue.<sup>(23)</sup> However, the difficulty in differentiating segmental tuberculosis intestinal disease from Crohn's disease is always a challenge.<sup>(24)</sup> The similarities in both diseases are the colonic skip lesions, particularly the ileocecal involvement and granulomas on the histological features. Macroscopic distinction between the two is usually very difficult. Therefore, a critical review based on other evidence such as clinical, radiographic, and pathologic information is usually mandatory in the diagnosis of the two diseases.

The clinical presentation of abdominal TB is usually non-specific<sup>(13,14)</sup> and, therefore, often results in diagnostic delay and hence the development of complications.<sup>(14)</sup> There are many vague presentations that will challenge the diagnosis of this life threatening infectious disease. From our observation, the most common clinical symptoms and signs in patients with abdominal TB were abdominal pain, abdominal distension, ascites and body weight loss. Fever was found in 35.7% of patients and peritoneal

signs were only noted in 7.1%. Two patients with hepatic TB experienced only low grade fever, body weight loss and abnormal liver functions. Although abdominal CT and ultrasonography are useful in making the diagnosis of abdominal TB,<sup>(13,25)</sup> peritoneal carcinomatosis was initially suspected by abdominal CT in 4 patients. Our results demonstrated that PCR testing and the AFB stain of biopsy tissue and ascites allow the rapid diagnosis of abdominal TB. The AFB stains were performed on biopsy tissues and fluid from ascites from 13 patients. Six of them showed positive results. TB-PCR was performed for patient 3 with a positive result. Microbiological and/or histopathological confirmation may also establish the diagnosis. Nevertheless, exploratory laparotomy has been suggested in cases suspected of abdominal carcinomatosis without definite diagnosis.<sup>(5)</sup>

Undiagnosed and untreated abdominal TB can result in a mortality rate of 50-60%.<sup>(26)</sup> However, this disease is usually curable after proper treatment. Chang et al.<sup>(4)</sup> and Chen et al.<sup>(5)</sup> reported that the mortality rate of treated abdominal TB were 13.2% and 14.8% respectively. In our study, the overall mortality rate was 20% due to sepsis and septic shock. All three of these patients had TB peritonitis and underlying liver cirrhosis. Thus, sepsis and liver cirrhosis may be strongly associated with therapeutic failure in TB peritonitis.

Earlier reports from Taiwan provide evidence that pulmonary TB can be found in 70-80% of patients with abdominal TB.<sup>(4,5)</sup> The high frequency of the coexistence of pulmonary TB and abdominal TB may be related to lower socioeconomic circumstances.<sup>(5)</sup> By contrast, Western studies<sup>(26-28)</sup> show that less than half of the patients with abdominal TB coexisted with pulmonary TB. In this study, we found that only 5 patients (35.7%) had pulmonary TB and 1 patient had pulmonary TB and TB meningitis. This phenomenon may be related to geographic factors and recent improvements in the socioeconomic conditions in Taiwan. However, the presence of pulmonary TB or TB meningitis did not influence the prognosis of our patients.

The pathogenesis of abdominal TB in patients remains speculative. There are four different possible pathways for intra-abdominal *M. tuberculosis* infection: hematogenous spread from primary pulmonary TB, ingestion of infected milk products, ingestion of

infected sputum from pulmonary TB and the direct invasion from an adjacent organ.<sup>(27-30)</sup> After the ingestion of infected food or sputum, *M. tuberculosis* may spread via lymphatics from infected lymph nodes.<sup>(13,14)</sup> Peritoneal TB is usually secondary to the hematogenous spread from a primary lung focus.<sup>(31)</sup> In patients with chronic renal failure undergoing continuous ambulatory peritoneal dialysis, Lui and colleagues<sup>(32)</sup> proposed that infection is acquired by direct contamination via the peritoneum. Latent TB may reactivate during peritoneal dialysis, resulting in clinical peritonitis.<sup>(33)</sup> In rare cases, the mycobacteria may enter the peritoneal cavity from an infected bowel or fallopian tube.<sup>(34)</sup>

The recommended treatment for abdominal TB is conventional anti-TB therapy for a minimum of 6 months.<sup>(13)</sup> Surgical intervention may be required to establish the diagnosis if medical treatment fails or to treat complications of abdominal TB.<sup>(13,14)</sup> In this study, 11 patients were successfully treated medically. Apart from the anti-TB therapy, 4 patients received surgical therapy to relieve an obstruction, repair a perforation and stricture, or remove space occupying lesions. Consequently, prompt treatment after early diagnosis can improve the morbidity and mortality rate of abdominal TB.

In conclusion, extreme vigilance in patients with unexplained abdominal conditions is the key to the successful diagnosis of abdominal TB. Early diagnosis, early antituberculous therapy and surgical treatment of the associated complications are essential for survival.

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## 腹部結核：成年病患的臨床表現與預後分析

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**背景：**近年來在台灣，結核病的重現是公共衛生的重要課題。腹部結核約佔所有結核感染病例的1-3%，且對健康造成嚴重威脅。本回溯性研究乃高雄長庚醫院自2000年衛生署開始執行通報機制後，腹部結核病患的臨床分析研究報告。

**方法：**自2000年1月至2006年12月，我們共通報14位患有腹部結核的成年病患。藉由回溯性的研究分析臨床表徵、治療方法與治療結果。診斷腹部結核的方法是藉由腹部感染的症狀與微生物學的方法（結核菌的培養、抗酸菌染色與聚合酶鏈鎖反應）或組織與腹水的組織病理學切片確認。

**結果：**腹膜結核與腸道結核是最常見的感染，其次依序為肝臟結核與腹腔內結核瘤。35.7%病患合併有腹腔外結核，包括肺結核與結核性腦膜炎。臨床症狀並不典型但最常見的為腹痛、腹脹、腹水及體重減輕。有35.7%病患患有發燒的症狀，7.1%病患患有腹膜炎症狀。有4位病患經由腹部電腦斷層檢查懷疑有腹膜轉移的現象。在所有的病患中，35.7%病患經由細菌學確診，42.8%病患經由開腹手術檢體確診，14.3%病患經由肝切片確診，7.2%病患經由大腸鏡切片確診。在此研究中，免疫不全與年長者較容易得到腹部結核。除了3位因敗血症與肝硬化而死亡的病例，其餘病患服用6個月以上的抗結核藥物皆可以成功治癒。

**結論：**基於腹膜結核無特異性的症狀而不易診斷，台灣又是結核病的流行地區，我們對於不明原因的腹痛病患要有高度的警戒心。早期診斷與早期治療，包含抗結核菌藥物與手術，以期增加病患之治癒率和存活率。

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**關鍵詞：**腹部結核，結核分枝桿菌，腹膜結核，腸道結核

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