

# Pancreatic Tuberculosis: A Rare Type of Extra Pulmonary Tuberculosis

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## **ABSTRACT**

*Tuberculosis is a serious health problem not only in Indonesia, but worldwide. Each year, it occurs in nearly 9.7 million people and claims about 2 million lives worldwide. Pancreatic tuberculosis is a rare type of extra pulmonary tuberculosis that only occur less than 4.7% worldwide. The most common symptoms is abdominal pain and most of the patients shows abdominal tenderness on palpation. Diagnosis of pancreatic tuberculosis consist of tuberculin skin test, ultrasonography, computed tomography-scan, magnetic resonance imaging and biopsy. Diagnosing pancreatic tuberculosis is a challenge because of its rarity and it has similar symptoms as more common pancreatic condition such as pancreatic malignancy. Understanding of pancreatic tuberculosis will increased the clinical awareness that may guide clinicians to avoid unnecessary diagnostic or therapeutic procedures and early diagnosis.*

**Keywords:** *tuberculosis, pancreatic tuberculosis, abdominal tuberculosis, abdominal pain*

## **ABSTRAK**

*Tuberkulosis adalah masalah kesehatan serius dimana tidak hanya di Indonesia, tetapi di seluruh dunia. Setiap tahun, tuberkulosis terjadi pada hampir 9,7 juta orang dan menyebabkan kematian sekitar 2 juta jiwa di seluruh dunia. Tuberkulosis pankreas adalah jenis tuberkulosis ekstrapulmoner langka yang hanya terjadi kurang dari 4,7% di seluruh dunia. Gejala yang paling umum adalah nyeri perut dan sebagian besar pasien terdapat nyeri perut saat palpasi. Diagnosis tuberkulosis pankreas adalah dengan tes kulit tuberkulin, ultrasonografi, computed-tomography scan, magnetic resonance imaging dan biopsi. Mendiagnosis tuberkulosis pankreas merupakan tantangan karena kelangkaannya dan memiliki gejala yang mirip dengan kondisi pankreas yang lebih umum seperti keganasan pankreas. Memahami tuberkulosis pankreas akan meningkatkan kewaspadaan klinis dokter untuk menghindari prosedur diagnostik atau terapeutik yang tidak perlu dan diagnosis dini.*

**Kata kunci:** *tuberkulosis, tuberkulosis pankreas, tuberkulosis abdomen, nyeri perut*

## **INTRODUCTION**

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*.<sup>1,2</sup> Tuberculosis is a serious health problem not only in Indonesia, but worldwide.<sup>1</sup> In 2003, it is estimated that 9.0 million people developed TB and 1.5 million died from the disease, and each year it occurs in nearly 9.7 million

people and claims about 2 million lives worldwide, with the highest incidence occur in Asia, South America, eastern Europe, and most sub-Saharan African countries.<sup>1,2</sup>

Pulmonary TB is the most common presentation of disease. Other than pulmonary TB, there is extra pulmonary TB (EPTB). Extra pulmonary TB occurs in

20% of all cases of TB in immunocompetent hosts and nearly 50% in patient with human immunodeficiency virus (HIV).<sup>1,2</sup> Extra pulmonary TB means the occurrence of TB at sites other than the lung, and it can occur in almost any organ system, including abdominal organs.<sup>2</sup>

Abdominal TB is the sixth most common site for EPTB and includes infection anywhere in the gastrointestinal tract, peritoneum, and intraabdominal organs such as spleen, liver, and pancreas.<sup>1,3,4</sup> Abdominal TB happens in 5-12% of patients with TB.<sup>1,3</sup> Pancreatic TB is rare even in the endemic countries, with incidence report to be less than 4.7% worldwide.<sup>1,2</sup> However lately cases are increasingly reported, probably due to further advancements in diagnostic.<sup>5</sup> Pancreatic TB first reported in 1944 by Auerbach that found only 14 cases with pancreatic involvement from 1,656 TB patients.<sup>6</sup>

There are two type of pancreatic TB patients, first, patients with other organ's involvement as a consequence of miliary TB or EPTB with involvement of other organs in addition to pancreas; and second, primary pancreatic TB which is an isolated involvement of pancreas by *Mycobacterium tuberculosis* in the absence of involvement of any other organ or previously identified TB. Isolated pancreatic TB is rare, and predominantly observed in patient who reside in endemic tuberculous zones, patients in areas of widespread TB dissemination such as a military setting and developing countries, and patients who are immunocompromised.<sup>1</sup>

Diagnosing pancreatic TB is a challenge because of its rarity and it has similar symptoms as more common pancreatic condition such as pancreatic malignancy.<sup>1</sup> Understanding of pancreatic TB will increased the clinical awareness that may guide clinicians to avoid unnecessary diagnostic or therapeutic procedures and early diagnosis.<sup>2,7</sup>

## **PATHOGENESIS**

The pathogenesis of pancreatic TB is not known for certain because of its rarity, but several possible mechanisms for pancreatic involvement in TB have been reported: (1) Ingestion of infected material from an active pulmonary lesion is on. Ingestion the bacilli will gain access to the gastrointestinal tract where necrotizing granulomas may develop and then spread to the lymphatics affecting any organ in the gastrointstinal tract, including hepatobiliary and pancreatic tissue; (2) Lymphohematogenous

dissemination from pulmonary disease, and it seems to be the most common mechanism; (3) Reactivation of latent tuberculosis in the pancreatic focus; (4) Direct spread from an adjacent organ.<sup>1,2,3</sup>

The rarity of pancreatic TB occurs due to retroperitoneal location of pancreas as well as pancreatic enzymes including lipase that interfere with the colonization, seeding and proliferation of the bacteria.<sup>1,3,8</sup> Pancreatic secretions also showed to have an antitubercular effect in vitro, thus a large intrapancreatic inoculum of *Mycobacterium tuberculosis* is required to cause pancreatic TB.<sup>1</sup>

## **CLINICAL MANIFESTATIONS**

We searched PUBMED, Medline and Google Scholar database for english language case report of pancreatic tuberculosis since January 2016. We only included case reports with full text available and 14 cases were found (Table 1). Of these patients, 7 were male (50%) and age range from 16 to 95 years old. Only one patient has a pulmonary TB, and it shows that pancreatic TB can occur without pulmonary involvement. The most common location for pancreatic TB has been reported in the head (10- 71.4%), followed by the neck (3-21.4%) and the body (2-14,2%). Same as our findings, Wintraub et al stated that the most common location of pancreatic TB as a mass has been reported in the head.<sup>6</sup> The most common symptoms found is abdominal pain (14-100%), followed by weight loss (9-64.3%), loss of appetite (5-25.7%), fever (7-35.7%) and jaundice (3-21.4%). Faria et al and Shahrokh et al stated that abdominal pain is the most common symptoms follows by fever, weight loss, appetite loss, and jaundice that were obstructive in nature.<sup>1,9</sup> Singhai et al stated that the three most common presenting complaints were abdominal pain, jaundice and weight loss. Pancreatic TB also can manifest as night sweats, back pain, and gastrointestinal hemorrhage secondary to splenic vein thrombosis.<sup>2,10</sup> Most of the patient will show abdominal tenderness, especially upper abdominal on palpation. Patients may present with pancreatic mass that is clinically indistinguishable from a pancreatic neoplasm.<sup>10</sup> Most of the patient also had lymphadenopathy.

**Table 1. Summary of reported cases of pancreatic tuberculosis since January 2016**

Author	Age	Sex	HIV/AIDS	Pulmonary TB	Location	Presenting symptoms	Physical examination	Laboratory values	Lymph nodes
Wright et al <sup>11</sup>	20	male	(-)	(-)	head	abdominal pain, weight loss, fever, night sweats	mild epigastric tenderness	normal hepatic transaminase, normal amylase lipase	(+)
Kaur et al <sup>12</sup>	25	male	(-)	(-)	head	abdominal pain, weight loss, loss of appetite, fever	mild epigastric tenderness	normal hepatic transaminase, high bilirubin	(+)
Waintraub et al <sup>8</sup>	31	male	(-)	(-)	head	abdominal pain, weight loss, loss of appetite, fever	not described	high amylase lipase	(+)
Rana et al <sup>13</sup>	42	female	(-)	(-)	head	abdominal pain, weight loss	not described	normal hepatic transaminase, normal amylase lipase	(+)
Kumar et al <sup>14</sup>	57	female	(-)	(-)	head	abdominal pain, loss of appetite, fever	mild epigastric tenderness	normal hepatic transaminase, normal amylase lipase	not described
Singhai et al <sup>2</sup>	16	male	(-)	(-)	head	abdominal pain, weight loss, loss of appetite, fever	mild midepigastric tenderness	normal hepatic transaminase, normal amylase lipase	(+)
Zhu et al <sup>15</sup>	23	male	(-)	(-)	neck	abdominal pain, weight loss, loss of appetite	upper abdominal tenderness	normal hepatic transaminase	(+)
Yadav et al <sup>16</sup>	23	female	(-)	(-)	head	abdominal pain, jaundice, high coloured urine, clay coloured stool	not described	high hepatic transaminase, high bilirubin total and bilirubin direct	(+)
Abbaszadeh et al <sup>17</sup>	23	female	(-)	(-)	head	abdominal pain, weight loss	upper abdominal tenderness	high hepatic transaminase, normal amylase lipase	not described
Sreevathsa et al <sup>19</sup>	45	male	(-)	(-)	head	abdominal pain, weight loss, fever, jaundice	not described	high hepatic transaminase, high bilirubin	not described
Kohan et al <sup>18</sup>	52	female	(-)	(-)	head	abdominal pain, jaundice	not described	high bilirubin total and direct	(+)
Sreevathsa et al <sup>19</sup>	68	female	(-)	(-)	body	abdominal pain, weight loss	not described	normal hepatic transaminase	(-)
Duarte-Chavez et al <sup>20</sup>	95	male	(-)	(-)	neck and body	abdominal pain	mild andominal tenderness	not described	(+)
Najdi et al <sup>21</sup>	46	female	(-)	(+)	neck	abdominal pain	right upper quadrant tenderness	high amylase lipase, high bilirubin total and bilirubin direct	(+)

## DIAGNOSIS

If pancreatic TB is suspected, preliminary testing such as tuberculin skin test can be done.<sup>2</sup> Tuberculin skin test have sensitivity around 58–100% in patients with abdominal TB, but has a false-negative rate of 10%-25%.<sup>7</sup> We found that most pancreatic TB can shows normal hepatic transaminase (7-70%), normal amylase and lipase (5-71.4%), but high bilirubin.<sup>5</sup>

Pancreatic TB can be classified radiologically into 3 groups: mass-forming (with or without diffuse pancreatic enlargement), a diffuse form and a small nodular form. The mass-forming is the most common form that accounts for 94.4% of cases.<sup>1</sup> Ultrasonography (USG) is non-invasive, simple, readily available and cost-effective; thus, it is usually used as an initial diagnostic tool for patients presenting with abdominal pain.<sup>1</sup> On USG, pancreatic TB can appear as well-defined hypoechoic lesion and shows lymph node involvement.<sup>3</sup> Around 90.9% patients show involvement of lymph node. Shahrokh et al stated that, in pancreatic TB, common bile duct and the pancreatic duct appear normal in images, even if the mass is localized centrally in the head of the pancreas. Contrary to pancreatic TB, in pancreatic adenocarcinoma the pancreatic duct is dilated in the tumors that are positioned centrally in the head region.<sup>1</sup>

Other than USG, computed tomography-scan (CT-scan) is commonly used and the investigation of choice for pathologies of pancreas because of its high sensitivity.<sup>1</sup> CT findings include hypodense lesions with irregular borders usually in the head of the pancreas, diffuse enlargement of the pancreas or enlarged peripancreatic lymph nodes.<sup>10</sup>

Magnetic resonance imaging (MRI) findings of focal pancreatic TB include sharply delineated mass usually located in the pancreatic head, showing heterogenous enhancement, hypointense on fat-suppressed T1-weighted images and show a mixture of hypo/hyperintensity on T2-weighted images.<sup>10</sup>

It should be noted that there are no pathognomonic radiological features of pancreatic TB, and since pancreatic TB may present as cystic or solid pancreatic masses, abscesses, lymphomas, pseudocysts or acute or chronic pancreatitis, cytological or histopathological is necessary for the diagnosis of pancreatic tuberculosis.<sup>1,2,10</sup> Techniques for pancreatic biopsy include CT or USG-guided percutaneous biopsy, surgical biopsy, or endoscopic ultrasound-(EUS-) guided fine needle aspiration (FNA).<sup>2</sup>

EUS-guided FNA is known to be quite effective in diagnosis and staging of pancreatic carcinoma,

and emerged as a reliable and cost effective way of diagnosing pancreatic TB.<sup>3</sup> EUS-FNA has been noted to be 76% to 95% accurate for diagnosis of pancreatic cancer and 46% for focal inflammation.<sup>10</sup> It is also preferred for tissue biopsy because of less chances of needle tract dissemination especially when the mass seems malignant. In EUS-FNA, the samples are evaluated by staining, cytology, and culture. The microscopic features of tuberculosis are granuloma, caseation necrosis (seen in 75-100% of cases) and presence of acid fast bacilli (identified in 20-40% of cases).<sup>1</sup> Bacterial culture, although requiring a prolonged incubation, has proven to be the most specific diagnostic modality to reveal pancreatic TB.<sup>2</sup>

## MANAGEMENT

Once the diagnosis of pancreatic TB has been made, standard antituberculin therapy appears to be successful in management of this infection.<sup>2,4</sup> A minimum of 6 months of antituberculin therapy is often indicated to achieve resolution of pancreatic lesions and alleviation of symptoms.<sup>2</sup> Antituberculin therapy regimen including isoniazid, rifampicin, pyrazinamide, and ethambutol or streptomycin for 6-12 months.<sup>1</sup> Follow-up CT imaging after antituberculin therapy may guide clinicians regarding duration of therapy.<sup>2</sup> Pancreatic TB has mortality rate of 10.8%, but death can easily avoided with antituberculin treatment.<sup>1</sup>

However for those patients whose tuberculous pancreatic mass is enlarged and causes symptoms even after therapy for a reasonable period of time, we should consider minimally invasive procedures such as endoscopic internal drainage, percutaneous catheter drainage or biliary stenting. Percutaneous drainage is preferably used in patients with no pancreatic duct strictures and pancreatic duct-pseudocyst communications and in those with immature or infected pseudocysts, or when the patient is at high surgical risk, or exhibits malnourishment.<sup>1</sup>

## CONCLUSION

Pancreatic TB is a rare type of extrapulmonary TB. Because of its rarity and have similar symptoms as more common pancreatic condition such as pancreatic malignancy, diagnosing pancreas TB proven to be challenging. The most common symptoms is abdominal pain and most of the patients shows abdominal tenderness on palpation. Diagnosis of pancreatic TB consist of tuberculin skin test, USG, CT-Scan, MRI, and biopsy. Due to absence of

pathognomonic feature of radiology and various form of pancreatic lesions can occur, it is necessary to do cytological/histopathological examination using material taken with EUS-FNA. Pancreatic TB responds well to antituberculin therapy.

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