

ARTICLE INFORMATION

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Enterocutaneous fistula et cause abdominal tuberculosis in community: An emergency diagnosis challenge

Siusanto Hadi*, Pieter David Adriaan Ferdinandus, Minarni Wartiningsih, Billy Daniel Messakh, Purwakaning Purnomo Agung, Cempaka Harsa Sekarputri, Vincent Aurelius Gonaldy

Universitas Ciputra

Corresponding author: *E-mail: siusanto.ciputra@gmail.com

Abstract

Background: A fistula is defined as an abnormal connection that connects two hollow spaces of the body. Fistula are divided into two categories, internal and external. Abdominal TB can mimicks other diseases including Enterocutaneous fistula that occur due to chron's disease, malignancy, typhoid or radiation exposure. Tuberculosis is a rare cause of enterocutaneous fistula increasing the needs of clinicians to diagnose TB in an emergency manner.

Purpose: To assess clinical manifestation of enterocutaneous fistula in patient with abdominal tuberculosis, and to determine the best emergency diagnosis tools in the progress of diagnosing abdominal tuberculosis.

Method: This literature review is guided by the PICOS framework, encompassing materials published from 2000 to 2024. Data were obtained from diverse sources such as PubMed Central, Google Scholar, Science Direct, Elsevier (SCOPUS), scientific journals, articles, and books. The analysis proceeded through three stages: data reduction, presentation, and formulation of conclusions. Studies fulfilling the inclusions criteria were selected.

Results: Patient with TB could have enterocutaenous fistula as one of its clinical manifestations, therefore. This study concludes that multiplex PCR shows an outstanding result for its specificity making it highly effective in ruling out non-tubercular diseases with minimum false positive.

Conclusion: Enterocutaneous fistula in intestinal tuberculosis often presents without clear thoracic imaging of pulmonary TB, complicating diagnosis. Abdominal TB's non-specific symptoms can mimic other diseases, making CT scans and ultrasonography useful, though not definitive. Laparoscopy, combined with histological examination, remains the most reliable diagnostic tool. Laboratory tests like ADA levels, PCR, and culture are essential in confirming the diagnosis. A diagnostic algorithm and early anti-tubercular therapy can help when test results are inconclusive.

Keywords: Abdominal Tuberculosis; Enterocutaneous Fistula; Literature Review; Multiplex PCR.

INTRODUCTION

Fistula is a common complication in surgery, in other cases fistula could form due to infection or inflammation (Crohn's disease), cancer in gastrointestinal tract, radiation therapy, and congenital defect. The epidemiology of fistulas vary depending on the type of underlying causes; the most common type of fistula are anal fistulas with an estimated prevalence of 1.2-2.8 per 10.000 people and found more in men than women (Almadi, Ghosh, & Aljebreen, 2009).

The second most common type of fistulas is enterocutaneous fistulas even though this type of enterocutaneous fistulas occur more rarely, it is often associated with complications of abdominal surgery, with few percentages caused by inflammatory diseases such as abdominal tuberculosis, diverticulitis, etc (Gefen, Garoufalia, Zhou, Watson, Emile, & Wexner, 2022).

Enterocutaneous fistula is an abnormal connection that develops between the intestinal tract or stomach and the skin, which causes contents leakage of the intestine through the skin (University of California San Francisco, 2019). Tuberculosis (TB) was one of the top diseases which caused numerous deaths worldwide (Dahale, Puri, Sachdeva, Agarwal, Kumar, Dalal, & Saxena, 2021). Abdominal tuberculosis includes various forms of tuberculosis affecting extrapulmonary system, including gastrointestinal TB also known as intestinal TB, Peritoneal TB, abdominal lymph nodes TB, and other organs such as the liver and spleen (Maulahela, Simadibrata, Nelwan, Rahadiani, Renestein, Suwanti, & Anggraini, 2022). Indonesia is a tropical country and is known for its high prevalence of Tuberculosis (TB) infection. Number of reported TB cases has increased by 75 %, from 330 729 in 2015 to 578 987 in 2019 (Van Hoving, Griesel, Meintjes, Takwoingi, Maartens, & Ochodo, 2019).

Post Covid-19 pandemic shows that the prevalence of TB per 100.000 in Indonesia was 759 with Sumatra ranked 1st. TB has contributed to a significant disease burden and economic loss worldwide (Jha, Pathiyil, & Sharma, 2023). TB was a widespread infectious disease caused by the bacterium *Mycobacterium tuberculosis* (Abu-Zidan, & Sheek-Hussein, 2019). Even though Indonesia strives to eliminate TB, persistent and organized efforts are still needed to achieve the target. TB are able to occur outside of the lungs, also known as extrapulmonary TB. Extrapulmonary TB accounted for 14% of the 6.4 million incident cases worldwide. The incident of enterocutaneous fistula as a complication of intestinal tuberculosis is quite rare but doesn't mean impossible, hence we provide presentation of enterocutaneous fistula that was proven to be from intestinal tuberculosis.

RESEARCH METHOD

In this study, the method is a literature review guided by the PICOS Framework, encompassing materials published from 2018-2024 with the attempt to summarize studies of enterocutaneous fistula to determine their etiology, diagnosis, treatment. Data for this literature were obtained from diverse sources such as pubmed central, the cochrane registry, and other sources.

Researchers independently examined the relevance of all references by title, abstract, and aim focusing on the last six years. The journals were categorized based on inclusion and exclusion criteria.

A reviewer independently evaluated risk of bias in each article using Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool for observational studies.

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Universitas Ciputra

Corresponding author: *E-mail: siusanto.ciputra@gmail.com

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RESEARCH RESULTS

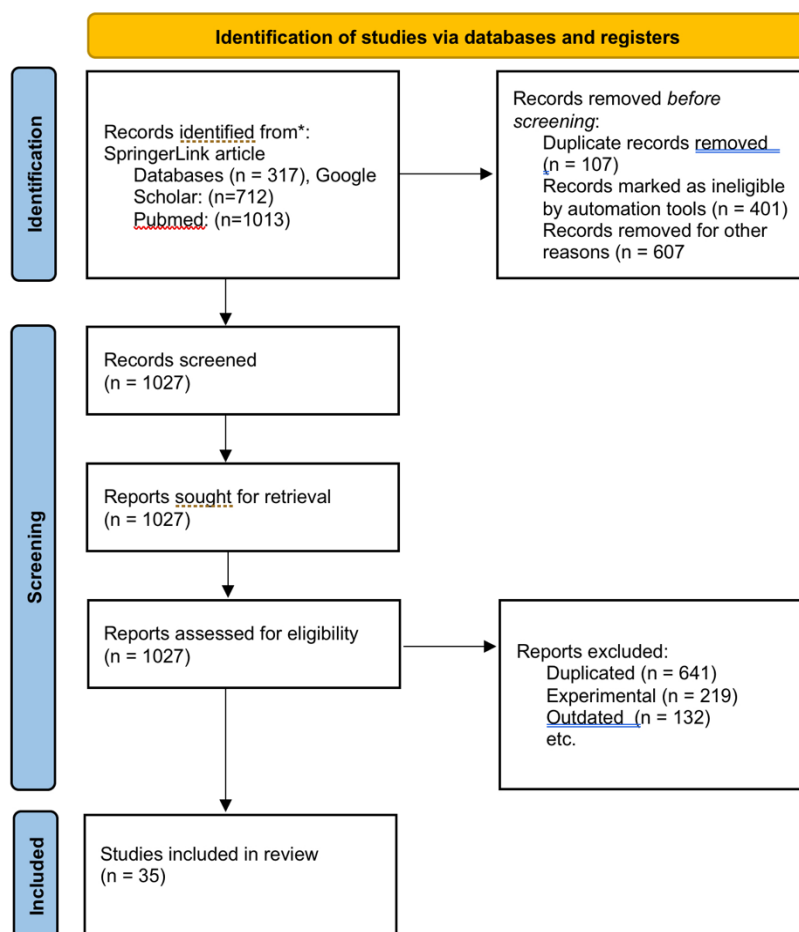


Figure PRISMA Flow Chart

The researcher found 36 studies from 2000-2024. Enterocutaneous fistula is defined as an abnormal communication between the gastrointestinal tract and the skin. Enterocutaneous fistulas are one of the rare sequelae of chron's disease that commonly occurs spontaneously or postoperatively (Iglay, Bennett, Kappelman, Reynolds, Aldridge, Karki, & Cook, 2022). The best diagnosis modality for fistula is by using the Computed Tomography (CT) that provides overall survey of surroundings fistula anatomy that can be augmented by using the water-soluble contrast in many ways, including through the fistula tract itself when the source of the fistula is in question. The use of CT fistulography is done through a case-by-case basis. MRI and MR fistulography can also be used although MRI is generally used to evaluate fistulas in the perianal region.

The treatment of enterocutaneous fistula is decided according to the specific etiology for the patient itself. There are various treatments to treat Enterocutaneous fistula but all treatments have the same aims, to focus on; 1. Sepsis control, 2. Nutrition support, 3. Surrounding anatomy of the fistula, 4. Developmental of surgical procedure.

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Universitas Ciputra

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Table 1. Enterocutaneous Fistula Etiology

Author, year	Classification	Etiology
Kate, 2024	Postoperative	1. Disruption of anastomosis 2. Inadvertent enterotomy 3. Inadvertent small-bowel injury 4. Complication of restorative proctocolectomy 5. Gastroduodenal fistulas
	Traumatic	1. Iatrogenic 2. Accident/ trauma to the gut
	Spontaneous	1. Malignancy 2. Radiation enteritis 3. Intra-abdominal sepsis 4. IBD (Chron disease) 5. Intestinal Tuberculosis 6. Ulcerative colitis
(Cowan, & Cassaro, 2023)	Postoperative	1. Enterotomies 2. Intestinal anastomotic dehiscence
	Systemic Disease	1. Chron's disease 2. Radiation enteritis 3. Malignancies 4. Trauma 5. Ischemia

Table 2. Characteristics of Paper Included in Systematic Review

Author, Year (Country)	Inclusion Criteria	Exclusion Criteria	Postoperative or Spontaneous EF	Interventions	ROBINS-I
(Shah, & Wani, 2017) (Saudi Arabian)	Sequale of Chron's Disease	Dit not specif Enterocutaneous Fistula Subtype	Spontaneous	Anti tubercular Treatment	Moderate
(Cowan, & Cassaro, 2023) (California)	Chron's disease, radiation enteritis, malignancies, trauma, or ischemia.	Post surgery	Spontaneous	Stabilization, electoryle corrections, sepsis prevention	Moderate
(Limengka & Jeo, 2018) (Indonesia)	Surgical, Laparotomy	—	Post operative	Negative pressure Wound Therapy	Moderate

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Author,Year (Country)	Inclusion Criteria	Exclusion Criteria	Postoperative or Spontaneous EF	Interventions	ROBINS-I
				Intermittent pressure of 70 mmHG (5 min of negative pressure and 2 mins of rest) for 1 months	
(Kate, 2024) (Edinburgh)	–	–	Boath	Conservative therapy Laser Ablation for chronic ECF after failed conservative therapy	Moderate
(Iswara, Karera, & Saksana, 2023) (Indonesia)	–	–	Post Operative	Conservative therapy (Electrolytes correction, sepsis treatment, fistula output control, wound care, psychological support).	Moderate
(Tan et al., 2020) (China)	–	–	Post Operatif	Surgery, antimicrobial therapy	Moderate
(Khalid, et al., 2021). (Nigeria)	Digestive tuberculosis	Pulmonary TB	Spontaneous	Anti tuberculousis therapy	Moderate

To understand abdominal tuberculosis better it is essential for physician to understand the clinical features of abdominal tuberculosis typical manifestations of abdominal TB are abdominal pain, intestinal swelling, intestinal obstruction, hematochezia, a palpable abdominal mass, fever, weight loss, and night sweats (Park, Kansara, Victoria, Boma, & Hong, 2021). A comparison table of the clinical findings according to literatures are summarized in Table 2.

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Table 3. Abdominal Tuberculosis Clinical Features

mClinical Features	Fei et al. 89 person (Hongkong)	Tanoglu et al. 104 patients (Multicenter)	Cheng et al. 85 patients (China)
Abdominal pain	76 (85.4%)	80 (76.9%)	75 (88.2 %)
Fever	43 (48.3%)	69 (66.3%)	44 (51.8 %)
Diarrhea	46 (44.2 %)	25 (24 %)	30 (35.3 %)
Abdominal Mass	6 (5.8 %)	Not mentioned	15 (17.6 %)
Intestinal bleeding	4 (3.8%)	11 (10.5 %)	Not mentioned
Bowel Fistula	2 (1.9%)	Not mentioned	1 (1.2 %)
Bowel perforation	2 (1.9 %)	Not mentioned	21 (24.7 %)

The clinical manifestation of abdominal tuberculosis vary and may not be specific, hence making it a challenge for physicians to diagnose and to give proper treatment. The most clinical features are Abdominal pain, and fever, while the most common complications found in abdominal tb are intestinal bleeding, fistula, and perforations (Shi, Zhang, Zhang, Liu, & Fei, 2016).

In order to help physicians diagnose abdominal tuberculosis, compilation of laboratory test analysis is compiled below. The first laboratory diagnosis is Adenosine deaminase levels where ADA levels significantly elevates in patient with abdominal tuberculosis. Other laboratory diagnosis will also be shown below.

Table 4. Baseline Data Regarding ADA in Patient with Abdominal TB

Laboratory diagnostic	Samples	Cut-off (IU/L)	Sensitivity (%)	Specificity (%)
Dahale et al.	Ascites	41.1	95	93
Sun et al.	Ascites	21	83.3	95.2
He et al.	Ascites	24.06	90	96.77
Kumabe et al.	Ascites	40	100	96

Table 5. Baseline Data of GeneXpert in Diagnosis of Abdominal Tuberculosis

Study	Sensitivity (%)	Specificity (%)
Singh et al	88	91
Kumar et al	91	100
Lowbridge et al	95.7	100

GeneXpert is a cutting-edge, and cartridge-based nucleic acid amplification test (NAAT). Genexpert is used to help physicians in diagnosing abdominal tuberculosis, and to help physicians determine whether a Tuberculosis is rifampicin resistance. PCR detect specific DNA sequences associated with *M.tuberculosis*. Main function of Genexpert in clinical use is to diagnose both pulmonary TB and extrapulmonary TB, including intestinal tuberculosis, by detecting DNA of *M. TB* in various secretions of the body including, sputum, ascitic fluid, and stool.

IGRA have been progressively been used as a substitution of tuberculin skin test. IGRA has been used as an instrument in diagnosis of tuberculosis. Numerous study shows that IGRA has a much higher sensitivity if compared to tuberculin test, the same goes for IGRA specificity compared to the tuberculin test. Currently there are two commercial techniques of IGRA which is "QUANTIFERON-TB GOLD IN TUBE" and T-Spot. IGRA principle is to recognize interferon gamma via enzyme linked immunosorbent assay.

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Table 6. Diagnostic Accuracy of IGRA

Study	Sample	Techniques	IGRA	
			Sensitivity	Specificity
Zhao et al.	Blood	-	88	74
Chen et al.	Blood	T-SPOT.TB or QFT- GIT	74	87
	Average		81 %	80.5 %

A study by Zhao starts with gaining information of patients that was suspected with Crohn's diseases which at that time were admitted to the hospital, the patients were later given a diagnostic test of IGRA to help physicians determine whether those patients which were a suspect of Crohn's disease is in fact Crohn's disease or tuberculosis.

The study results are quite shocking where patients with IGRA levels of > 100 pg/ml indicate a higher possibility of tuberculosis infections, the study provides results of 88% sensitivity and 74 % specificity by using IGRA as diagnostic tools in diagnosing abdominal tuberculosis. The study reveals that not all 56 patients admitted have IGRA levels above 100 pg/ml, in fact only 33 patients out of 56 have IGRA levels > 100 pg/ml. Out of all 33 patients with IGRA levels above 100 pg/ml only 25 received anti tuberculosis therapy. All 25 patients whom received anti tuberculosis therapy had been reported to have improvement. Patients with anti tuberculosis therapy shows significant results after undergoing therapy for 2-3 months.

Further study concludes that IGRA level of minimum 100 pg/ml indicates a higher possibility of abdominal tuberculosis compared to Crohn's diseases. Clinical study of intestinal tuberculosis shows that not all patients diagnosed with intestinal tuberculosis shows tuberculosis symptoms out of 15 patients only 8 of them shows weight loss symptoms.

The study comes to a final conclusion that IGRA may also be used to detect severity of abdominal tuberculosis but further research needs to be done due to small group of sample being researched. 2 literatures included in this research discussed the effectiveness of IGRA by using a blood samples, with 81 % sensitivity of IGRA and average specificity of 80.5 %. Before considering whether a patient is diagnosed with abdominal tuberculosis, it is very important to consider whether a patient is also diagnosed with gastrointestinal tuberculosis, Solid organ Involvement in TB, Lymphadenopathy or peritonitis.

Colonoscopy plays an important role in diagnosing gastrointestinal tuberculosis, and dry peritonitis in suspected TB patient. The main rule must not be forgotten not all patient with abdominal tuberculosis shows a symptom of pulmonary tuberculosis vice versa. Endoscopic Techniques in diagnosing gastrointestinal tract tuberculosis includes the use of colonoscopy, mucosal biopsy, and endoscopy.

Table 7. Sensitivity and specificity of Colonoscopy

Study	Sample	Techniques	Colonoscopy	
			Sensitivity	Specificity
Krishna, 2023	108 patients	Acid-Fast Stain	82.8 %	92 %
Sudcharoen, 2023	116 patients	Acid-Fast Stain	62 %	87 %

Although colonoscopy is considered to be a diagnosis tool in diagnosing gastrointestinal TB, the moderate sensitivity of the diagnostic tools shows that some cases may be missed, primarily due to subtle or not well defined tissue lesions. But the high specificity of the diagnostic means positive findings shows likely indicative of true disease, during colonoscopy biopsies should also be taken. Biopsies are considered to be one of the best procedure to confirm diagnosis through histopathological examination but is not quick enough to be considered as an emergency diagnosis tool. Clinicians should consider other parameters alongside clinical findings and other diagnostic tests to make sure that comprehensive evaluation of the patient has been done and to ensure that the patient is managed thoroughly in a case of suspected abdominal tuberculosis.

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DISCUSSION

TB is still one of the many endemic sickness in developing countries, few tropical countries such as Indonesia and India is susceptible to multi drug resistance TB (MDR-TB). *World Health Organization* has concluded that TB prevalence is greater in some areas in Indonesia and India due to poverty and migration. Although TB is an endemic disease the involvement of gastrointestinal system is very rare, fewer than 5% of patients have extrapulmonary manifestations and only 1 % of patients had their gastrointestinal system affected (World Health Organization, 2020; Tan, Porter, Guo, Pan, Yang, & Zhang, 2020).

Enterocutaneous Fistulae alongside with intestinal tuberculosis is very rare and typically affects ileocecal segments. Enterocutaneous fistulae with intestinal tuberculosis is usually found to co-exist alongside pulmonary TB or extrapulmonary TB. Source of infection in spontaneous enterocutaneous fistula with intestinal TB includes swallowing infected sputum, hematogenous or contiguous spread from contaminated food. Some cases mimicks chrons-like lesions such as intestinal inflammation with ulcers, hypertrophic lesions and ulcers (Singh, Gupta, Moses, & Jain, 2009).

Enterocutaneous fistula associated with intestinal tuberculosis does not always present in its full-blown stages. Most cases show an unlikely diagnosis of pulmonary TB on thorax imaging (Khan, Abid, Jafri, Abbas, Hameed, & Ahmad, 2006). The biggest challenge in managing patients with abdominal tuberculosis is the lack of specific diagnostic tools due to the imprecise clinical manifestations and the fact that abdominal TB is often mistaken for other diseases (Maulahela et al., 2020).

Imaging such as CT scans can support the diagnosis of enterocutaneous fistula caused by abdominal TB, with findings like lymphadenopathy and duodenal wall thickening (Nagi, Lal, Gupta, Kochhar, & Sinha, 2015). Ultrasonography, though less commonly used, identifies lymphadenopathy and splenic lesions but has a specificity of only 68% when tuberculosis is confirmed through culture (Van Hoving, et al., 2019). CT scans play a larger role, showing features like ileocaecal involvement and para-aortic lymphadenopathy (Jha et al., 2023).

A systematic review found CT scans to have a higher specificity for peritoneal thickening (84%) but a lower sensitivity (59%) (Jha et al., 2023). While both imaging techniques improve diagnostic accuracy, neither is 100% accurate (Jha et al., 2023), and patients may present asymptotically (Patel & Yagnik, 2018).

Laparoscopy, with a diagnostic yield of 92%, is the best imaging tool when combined with histological confirmation. Laboratory tests such as ADA levels, PCR, culture, and histological examination should also be used, especially where abdominal TB is suspected (Jha et al., 2023). Elevated ADA levels in ascitic fluids have 100% sensitivity and 97% specificity for diagnosing peritoneal TB (Oey, Van Buuren, & De Man, 2016). PCR on biopsy specimens can also be effective but may not always be available, though its specificity can reach 95% (Almadi, 2009). Culture of tissues remains the gold standard for diagnosis, and histological examination can detect acid-fast bacilli or caseating granulomas (Almadi, 2009).

A diagnostic algorithm that categorizes clinical and radiological findings into five categories is recommended. If diagnostic tests are inconclusive, initiating anti-tubercular therapy and monitoring the patient's response can help confirm the diagnosis (Jha et al., 2023).

CONCLUSIONS

Physicians should adopt a comprehensive approach that combines various diagnostic tools for abdominal tuberculosis. While ultrasonography may help, CT scans should be prioritized due to their higher specificity. Laparoscopy should be used in more difficult cases, as it has proven highly effective when combined with histological confirmation. Physicians should also utilize laboratory tests such as ADA levels, PCR, culture, and histology to strengthen diagnostic accuracy. In peripheral healthcare settings, increasing the availability of diagnostic tools like colonoscopy and multiplex PCR would improve detection and treatment. When diagnostic results are unclear, initiating anti-tubercular therapy and observing the patient's response can help establish a probable diagnosis. Furthermore, using a diagnostic algorithm that categorizes findings will assist in making a more accurate diagnosis.

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Universitas Ciputra

Corresponding author: *E-mail: siusanto.ciputra@gmail.com

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Universitas Ciputra

Corresponding author: *E-mail: siusanto.ciputra@gmail.com

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