Diagnosis of intestinal tuberculosis: A systematic review and meta-analysis

Pubet Weeranawin[1], Tanawat Geeratragool[1], Wanruchada Katchamart[2], Julajak Limsrivilai [1]
[1]Division of Gastroenterology, Department of Medicine
[2]Division of Rheumatology, Department of Medicine
Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Diagnosis of intestinal tuberculosis (TB) is challenging. Histopathology and microbiological examination remain gold standard diagnostic methods, but previous studies show varied diagnostic performance of the tests. We aimed to systematically evaluate the accuracy of tests to diagnose intestinal tuberculosis in both conventional and novel methods.
Methods: We searched MEDLINE and EMBASE from inception to August 2023. All studies enrolling at least 10 patients with reported information regarding the diagnosis of intestinal tuberculosis based on endoscopic biopsy specimens, stool tests, and blood tests were included. Most studies used positive tissue AFB, presence of caseous granuloma on histopathology, positive tissue polymerase chain reaction (PCR) for TB, mycobacterial culture, and response to empirical anti-TB treatment as the reference standards. We performed meta-analysis using a random-effects model to estimate each test's pooled sensitivity, specificity, and summary receiver operating characteristic (SROC) curve. Risk of bias was assessed using the QUADAS-2.
Result: Of 3,308 abstracts reviewed, 57 studies with 5,946 participants met the inclusion criteria (Figure 1). As shown in Table 1, endoscopic tissue biopsy samples for AFB, the presence of caseous granuloma on histopathology, PCR for TB, mycobacterial culture, and GeneXpert showed pooled sensitivity of 11% (95%CI 7-17), 17% (95%CI 11-26), 58% (95%CI 44-71), 24% (95%CI 11-44) and 29% (95%CI 17-46), respectively. The pooled specificities of these tests were 100%, except the tissue PCR for TB of which pooled specificity was 98%. For mycobacterial culture, the liquid medium culture showed higher sensitivity than conventional Löwenstein–Jensen medium [32% (95%CI 26-39) and 6% (95%CI 3-13)]. Pooled sensitivity and specificity of stool PCR for TB were 73% (95%CI 43-90) and 95% (95%CI 79-99), respectively. Additionally, pooled sensitivity and specificity of interferon-gamma release assay (IGRA) were 85% (95%CI 79-89) and 86% (95%CI 82-89); the T-SPOT TB test showed slightly higher sensitivity with lower specificity compared to the QuantiFERON-TB GOLD test (Table 1). Most studies have low risk of bias.

Conclusion: Endoscopic tissue biopsy samples had limited sensitivity in diagnosing intestinal TB; combining them may increase the sensitivity but need more data. IGRA showed good accuracy and may be used in conjunction with other methods to improve the diagnostic yield. Stool PCR also demonstrated a high sensitivity; however, the results should be interpreted with caution due to a limited number of included studies and potentially false positive results from pulmonary tuberculosis.

Table 1: Pooled diagnostic performance

Diagnostic Test	N of Study	n	Heterogeneity	Pool Diagnostic Performance					
			I^2	Pool Sensitivity	Pool Specificity	Pool PLR	Pool NLR	Pool DOR	SROC-AUROC
1. Tissue									
1.1 AFB	20	1,941	0.01	0.11 (0.07-0.17)	1.00 (0.00-1.00)	N/A	N/A	N/A	N/A
1.2 Pathology	22	1,817	0.00	0.17 (0.11-0.26)	1.00 (0.97-1.00)	N/A	N/A	N/A	N/A
1.3 PCR	18	1,316	54.08	0.58 (0.44-0.71)	0.98 (0.94-0.99)	25.9 (9.8-68.2)	0.43 (0.31-0.59)	60 (19-188)	0.96 (0.94-0.98)
1.4 Culture									
a. Total	15	1,531	0.00	0.24 (0.11-0.44)	1.00 (0.00-1.00)	N/A	N/A	N/A	N/A
b. LJ medium	4	308	0.00	0.06 (0.03-0.13)	1.00 (0.00-1.00)	N/A	N/A	N/A	N/A
c. Liquid medium	6	406	0.00	0.32 (0.26-0.39)	1.00 (0.00-1.00)	N/A	N/A	N/A	N/A
1.5 GeneXpert	7	837	0.31	0.29 (0.17-0.46)	1.00 (0.75-1.00)	N/A	N/A	N/A	N/A
2. Stool									
2.1 PCR	4	403	43.57	0.73 (0.43-0.90)	0.95 (0.79-0.99)	N/A	N/A	N/A	N/A
3. Serum									
3.1 IGRA									
a. Total	26	3,242	70.66	0.85 (0.79-0.89)	0.86 (0.82-0.89)	6.0 (4.6-8.0)	0.18 (0.12-0.25)	34 (20-59)	0.92 (0.89-0.94)
b. T-SPOT	11	1,651	62.72	0.88 (0.83-0.92)	0.83 (0.74-0.90)	5.2 (3.2-8.6)	0.14 (0.09-0.22)	36 (15-86)	0.92 (0.90-0.94)
c. QFT	11	849	41.17	0.75 (0.60-0.86)	0.88 (0.84-0.91)	6.2 (4.4-8.7)	0.28 (0.17-0.48)	22 (10-48)	0.90 (0.87-0.92)

AFB; acid fast bacilli, AUROC; area under receiver operating curve, DOR; diagnostic odds ratio, NLR; negative likelihood ratio, PCR; polymerase chain reaction, PLR; positive likelihood ratio, LJ; Löwenstein–Jensen medium, IGAR; interferon gamma releasing assay, T-SPOT; T-SPOT TB, QFT; QuantiFERON-TB Gold, SROC; summary receiver operating characteristic

Figure 1: Study disposition