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Research Article

Comparison Between Gene Xpert MTB and Colonoscopic Biopsy Findings Detecting Abdominal Tuberculosis in a Tertiary Care Hospital in Bangladesh

Mostofa Showkat Imran[1]*, Arunangshu Raha[2], Ashfaque Ahmed Siddique[2], Moshfiqur Rahman Chowdhury[3], Syeda Meherunnesa[4], Alamgir Haider[5], Md Reaz Uddin Chowdhury[6] and Taslima Zaman[7]

[1]Assistant Professor, Department of Gastroenterology, Ibn Sina Medical College and Hospital, Dhaka, Bangladesh

[2]Assistant Professor, Medical Gastroenterology, Sheikh Russel National Gastroliver Institute and Hospital, Dhaka, Bangladesh

[3]Registrar, Medical Gastroenterology, Sheikh Russel National Gastroliver Institute and Hospital, Dhaka, Bangladesh

[4]Registrar, Department of Obstetrics and Gynecology, Ad Din Medical College and Hospital, Dhaka, Bangladesh

[5]Assistant Professor, Department of Anaesthesia, Aichi Medical College and Hospital, Uttara, Dhaka, Bangladesh

[6]Consultant, Department of Internal Medicine, Abdul Malek Ukil Medical College and Hospital, Noakhali, Bangladesh

[7]Associate Consultant, Department of Gastroenterology, United Hospital Ltd. Dhaka, Bangladesh

***Corresponding Author:** Mostofa Showkat Imran, Assistant Professor, Department of Gastroenterology, Ibn Sina Medical College and Hospital, Dhaka, Bangladesh. E-Mail ID: imranssmc@gmail.com

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Abstract

Background: GeneXpert MTB/RIF assays for diagnosing tuberculosis have been performed in the body secretions with excellent results. But the diagnosing intestinal tuberculosis is challenging due to the limited yield of diagnostic modalities like CT scan, and colonoscopy with blind ileal biopsies.

Objective: To compare the Gene Xpert *Mycobacterium tuberculosis* and colonoscopic biopsy findings detecting abdominal tuberculosis in a tertiary care hospital in Bangladesh.

Methodology: This cross-sectional hospital-based observational study was carried out among 73 adult patients in the Gastroenterology department of DMCH through admission or referral from May 2015 to April 2016. Laboratory tests, abdominal colonoscopic imaging results, Gene Xpert, colonoscopy with or without ileostomy, etc. were noted.

Result: 21 (28.1%) patients had no abnormality in the colonoscopic finding test. Abnormal findings showed there were colonic mucosal ulcerations in 34 (46.8%), mucosal macronodular lesions in 14 (18.75%), mucosal nodules in 11 (15.6%), colonic strictures in 11 (15.6%), deformed ileocaecal valve in 9 (12.5%), deformed caecum in 7 (9.4%) and polypoid mucosal lesion in 3 (3.1%) patients. Gene Xpert MTB DNA was detected in 33 (45.2%) patients. Diagnostic yield of Gene Xpert to detect MTB DNA on colonoscopic biopsy specimen was found in 29 out of 69 (42.1%) and Ultrasound-guided biopsy of the L/N in 4 out of 4 (100%) patients.

Conclusion: The result of this study highlighted the alternative approach of Gene Xpert diagnoses *Mycobacterium tuberculosis* that shows rapid results with good diagnostic accuracy.

Keywords: *Abdominal Tuberculosis; Gene Xpert MTB/RIF Assay; Colonoscopy; Biopsy*

Abbreviations

TB: Tuberculosis; MTB: *Mycobacterium tuberculosis*; ATB: Abdominal Tuberculosis; RIF: Rifampin; MDR: Multidrug Resistant

Introduction

After lymphatic, genitourinary, bone and joint, miliary, and meningeal tuberculosis, abdominal tuberculosis is the fourth most prevalent extrapulmonary tuberculosis location [1]. Abdomen tuberculosis affects 11% to 16% of patients with extrapulmonary tuberculosis [2,3]. The ileocaecal area is the most common site of involvement, followed by the ascending colon, jejunum, appendix, duodenum, stomach, esophagus, sigmoid colon, and rectum, in order of decreasing incidence [2]. Although less frequent in Western countries, abdominal TB is a severe public health problem in underdeveloped countries, with significant morbidity and mortality. Tuberculosis in the abdomen can be a primary infection or a secondary infection after reactivation from a primary pulmonary focus [4]. Because of its restricted diagnostic modalities and yield, confirming the diagnosis of *Mycobacterium tuberculosis*, where it is a leading presentation, can be difficult [5]. Because *Mycobacterium tuberculosis* can mimic Crohn's disease or intestinal cancers, ultrasound abdomen, Barium investigations, and CT scans are used to help with diagnosis [6]. Many individuals decline invasive treatments such as colonoscopy with blind Ileal biopsies, which are thought to be involved in 84 percent of *Mycobacterium tuberculosis* cases [7]. Due to the limited availability of colonoscopy, access to higher-up involvement of the jejunum and other parts of the ileum is also not available. As a result, a non-invasive, readily available diagnostic test with a satisfactory diagnostic yield is required. Because of the lack of particular symptoms, low yield of acid-fast bacilli (AFB) on smear and culture due to the paucibacillary lesion, and varying presentations depending on the anatomical placement of the disease, abdominal TB is difficult to diagnose [8]. Traditionally, histological, microbiological, and culture confirmation of *Mycobacterium tuberculosis* are required to diagnose abdominal tuberculosis [9]. Imaging (ultrasound, barium X-rays, and CT scan) and the Mantoux test have merely a supporting role to play [10]. In Bangladesh, the therapy for abdominal tuberculosis is an entire standard course of anti-tubercular medications for at least 6 months, including an initial 2 months of rifampicin, isoniazid, pyrazinamide, and ethambutol, followed by 4 months of rifampicin and isoniazid [11]. Multidrug-resistant tuberculosis (MDR-TB) is a rapidly growing public health concern worldwide. After culture conversion (without any positive culture), a total treatment duration of at least 18 months is recommended, including an initial phase of at least 6 months with pyrazinamide, kanamycin, ofloxacin, ethionamide, cycloserine, and a continuation phase of at least 13 months with the same drugs except kanamycin [12]. When one or more of the following criteria are met, along with supportive clinical characteristics, abdominal tuberculosis is diagnosed: (1) Epithelioid cell granulomas with or without caseation on histology; (2) Positive AFB on smear or culture of a tissue sample; and (3) High index of clinical suspicion and non-diagnostic histology; but the good clinical response to anti-TB medication in a therapeutic trial [13]. In high-burden countries, inexpensive and rapid diagnostic methods are constantly needed for early treatment initiation [14]. The Gene Xpert MTB/RIF (Xpert) assay is an automated molecular test for *Mycobacterium tuberculosis* (MTB) and rifampin resistance (RIF). It uses a semi-nested real-time polymerase chain reaction (PCR) assay to amplify an MTB-specific sequence of the rpoB gene, then probed with molecular beacons for mutations within the rifampin [15,16]. The sensitivity and specificity of the Xpert assay were 81 and 99%, respectively, among 547 patients with suspected extrapulmonary TB in India and 1068 patients in Europe [17,18]. WHO guideline from 2013: For testing specified non-respiratory materials (lymph nodes and other tissues) from patients suspected of having extrapulmonary TB, Xpert MTB/ RIF may be used as a substitute test for standard practice (including conventional microscopy, culture, or histopathology) (conditional recommendation, inadequate- quality evidence) [2]. GeneXpert Tuberculosis is a NAAT (Nucleic Acid Amplification Test) that can now be conducted in sputum and other body fluids with greater sensitivity and specificity, as well as the added benefit of detecting Rifampicin Resistance in as little as two hours [14]. A study found that the Xpert test had the real diagnostic potential for tissues and lymph nodes, with intermediate sensitivity (63 to 73 percent) [19]. According to another study, the Xpert test has 53 - 95 percent sensitivity for detecting TB in extrapulmonary sites [20].

Objectives of the Study

To compare the Gene Xpert *Mycobacterium tuberculosis* and colonoscopic biopsy findings detecting abdominal tuberculosis.

Methodology

A total of 73 patients were referred with a confirmed diagnosis of abdominal tuberculosis or admitted or referred to the Gastroenterology department of Dhaka Medical College Hospital (DMCH)in collaboration with the National Tuberculosis Reference Laboratory, NIDCH, Mohakhali, Dhaka, Bangladesh were included in the study. Patients were recruited from May 2015 until April 2016. All patients with abdominal tuberculosis any adult patients.

Study procedures

The study was conducted in a prospective observational style. Patients with diagnosis of abdominal tuberculosis (based on positive AFB culture, Gene Xpert, histopathology, ascitic fluid ADA report and response to anti TB trial) attended in Gastroenterology department of DMCH either through admission or referral. Consecutive patients referred with a diagnosis of abdominal tuberculosis were recruited. The patients were investigated to confirm a diagnosis of abdominal tuberculosis.

Molecular diagnostic methods

A molecular diagnostic technique was performed using an automated molecular test, Gene Xpert *Mycobacterium tuberculosis* (MTB), and resistance to rifampin (RIF) assay. RIF resistance determination in a single cartridge and Xpert MTB/RIF integrates DNA extraction, genomic amplification, semi-quantitative detection of MTB complex. To the rpo B "core" region (81 bp), determining RIF resistance, detection consisted of the hybridization of the amplicon with five overlapping probes complementary [21]. RIF resistance is considered a surrogate marker for MDR-TB, as < 10% of RIF resistance has been reported to be monoresistance [22].

Statistical analysis

All analyses were performed using MS Excel 2016 and the Statistical Package for the Social Sciences (SPSS) Version 25.0 (SPSS Inc, Chicago, IL, USA).

Results

Table 1 shows the colonoscopic/USD or CT guided results, which were performed on all patients. Abnormal findings showed there were colonic mucosal ulcerations in 34 (46.8%), mucosal macronodular lesions in 14 (18.75%), mucosal nodules in 11 (15.6%), colonic strictures in 11 (15.6%), deformed ileocaecal valve in 9 (12.5%), deformed caecum in 7 (9.4%) and mucosal polypoid lesion in 7 (9.4%) patients, USD or CT guided was 4 (5.1%) patients.

Colonoscopy/USD or CT guided	Frequency (n)	Percentage (%)	P-value
Colonic mucosal ulcerations	34	46.8%	1.00
Mucosal ulceronodular lesion	14	18.75%	
Mucosal nodules	11	15.6%	
Colonic strictures	11	15.6%	
Deformed ileocaecal valve	9	12.5%	
Deformed caecum	7	9.4%	
Mucosal polypoid lesion	7	9.4%	
USD or CT guided	4	5.1%	

Table 1: *Colonoscopic/USD or CT guided findings among the adult respondents in a tertiary care hospital in Bangladesh.*

Figure 1 shows distribution of patients according to Gene Xpert MTB/RIF test findings and biopsy materials.

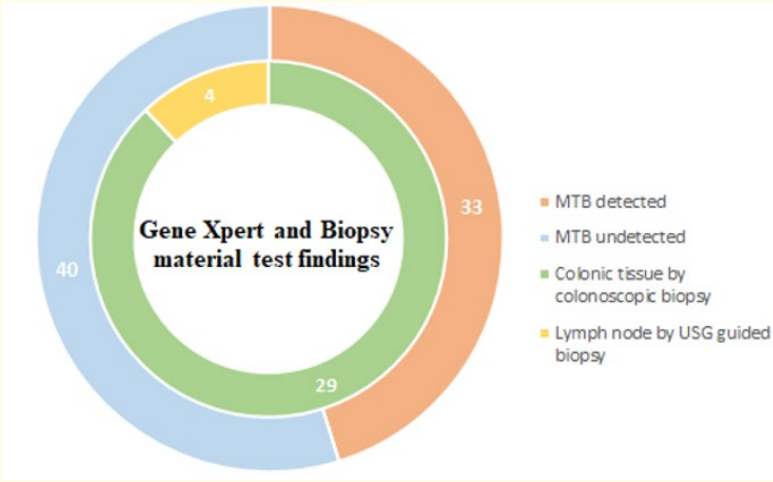

Figure 1: *Illustrates the Gene Xpert MTB/ RIF test was performed in 73 patients. MTB DNA was detected in 33 (45.2%) patients. Diagnostic yield of Gene Xpert to detect MTB DNA on colonoscopic biopsy specimen found in 29 out of 69 (42.1%) and ultrasound-guided biopsy of the L/N in 4 out of 4 (100%) of patients.*

Discussion

After lymphatic, genitourinary, bone and joint, miliary, and meningeal tuberculosis, abdominal tuberculosis is the fourth most prevalent extrapulmonary tuberculosis location [9]. While the frequency of abdominal tuberculosis is steadily increasing, particularly in developing countries, symptoms are frequently misdiagnosed due to their similarities to those of other infectious diseases. When patients do not have clinical and test evidence of lung disease, it is difficult to make a confirmed diagnosis. Due to the low yield of imaging and endoscopic procedures for confirming intestinal tuberculosis, a test to detect this curable condition quickly is needed. With the Gene Xpert assay, it is now possible to diagnose tuberculosis early by detecting rifampicin resistance in sputum and extrapulmonary tissues with higher sensitivity and specificity. PCR tests and Gene Xpert have been used in tissues in various research studies (biopsy specimens) [23,24]. In two different investigations, the Xpert test was done on mucosal biopsy specimens collected during colonoscopy with a lower sensitivity but 100% specificity [25,26]. In the intestinal variation of tuberculosis, the colon and terminal ileum are the most prevalent sites of involvement, and colonoscopic pictures and biopsies are considered a rapid and effective diagnostic tool in this regard [10]. All of the patients in this research had a colonoscopy. Colonic mucosal ulcerations were seen in 34 (46.8%), mucosal macronodular lesions in 14 (18.75%), mucosal nodules in 11 (15.6%), colonic strictures in 11 (15.6%), deformed ileocaecal valve in 9 (12.5%), impaired caecum in 7 (9.4%), and polypoid mucosal lesion in 7 (9.4%) patients. These findings are nearly identical to those of a prior study that found no abnormalities in 8 of 20 patients (40 percent) [19]. These patients had ulcers in 9 (45%), nodules in 2 (10%), and stricture, polypoid lesions, granulomatous abnormalities in the terminal ileum, and rectal fistula in one (5%) of the cases. Deformed caecum in 32 (91%) patients, the abnormal ileocaecal valve in 28 (80%), colonic mucosal ulcerations in 28 (80%), mucosal nodules in 11 (31%) patients, and colonic strictures in 6 (17%) patients were all found in another investigation [10]. The Gene Xpert MTB/ RIF test was performed on 73 individuals in this investigation. MTB DNA was found in 33 (45.2%) of the patients. The diagnostic yield of Gene Xpert to detect MTB DNA on colonoscopic biopsy specimens was seen in 29 of 69 (42.1%) patients, and ultrasound-guided biopsy of the L/N was found in 4 of 4

(100%) patients. In comparison, a prior study found that the Xpert test offers real diagnostic potential for tissues and lymph nodes, with intermediate sensitivity (63% to 73%) [19]. According to another study, the Xpert test has 53-95 percent sensitivity for detecting TB in extrapulmonary sites [20].

Conclusion

GeneXpert testing offers an alternative approach to diagnose *Mycobacterium tuberculosis* that shows rapid results with fairly good diagnostic accuracy. Although these tests cannot replace the conventional AFB smear, culture identification, or histopathological observations, they contribute significantly for an early diagnosis of abdominal tuberculosis and positively impact the early diagnosis management of the disease. The limitation of this study is that the biopsy specimen was not tested for GeneXpert or AFB culture, which may have given a better yield in diagnosing *Mycobacterium tuberculosis*. We recommend that in patients with radiological suspicion of TB and in whom colonoscopy biopsy shows nonspecific colitis or non-caseating granulomas, we can have this test for GeneXpert to have a confirmed diagnosis of intestinal TB.

Bibliography

1. Arif AU., *et al*. "The frequency and management of intestinal tuberculosis a hospital-based study". *Journal of Postgraduate Medical Institute (Peshawar-Pakistan)* 22.2 (2011): 152-156.
2. Rathi P and Gambhire P. "Abdominal tuberculosis". *Journal of the Association of Physicians of India* 64.2 (2016): 38-47.
3. Aston NO. "Abdominal tuberculosis". *World Journal of Surgery* 21.5 (1997): 492-499.
4. Saaiq M., *et al*. "Abdominal tuberculosis: epidemiologic profile and management experience of 233 cases". *Journal of the Pakistan Medical Association* 62.7 (2012): 704-707.
5. Baloch NA., *et al*. "A study of 86 cases of abdominal tuberculosis". *Journal of Surgery Pakistan (International)* 13.1 (2008): 30-32.
6. Mukewar S., *et al*. "Colon tuberculosis: endoscopic features and prospective endoscopic follow-up after anti-tuberculosis treatment". *Clinical and Translational Gastroenterology* 3.10 (2012): e24.
7. Patel B and Yagnik VD. "Clinical and laboratory features of intestinal TB". *Clinical and Experimental Gastroenterology* 11 (2018): 97-103.
8. Almadi MA., *et al*. "Differentiating intestinal tuberculosis from Crohn's disease: a diagnostic challenge". *The American Journal of Gastroenterology* 104.4 (2009): 1003-1012.
9. Al-Quorain AA., *et al*. "Abdominal tuberculosis in Saudi Arabia: a clinicopathological study of 65 cases". *American Journal of Gastroenterology* 88.1 (1993): 75-79.
10. Khan R., *et al*. "Diagnostic dilemma of abdominal tuberculosis in non-HIV patients: an ongoing challenge for physicians". *World Journal of Gastroenterology* 12.39 (2006): 6371.
11. NTP. National Tuberculosis Control in Bangladesh. Annual Report 2007. National Tuberculosis Control Programme, DGHS, MOH & FW. Dhaka: 2-5.
12. NTP. Treatment strategy for MDR TB, Jan-2009. Operational manual for the management of MDR-TB, First edition, National Tuberculosis Control Programme, DGHS, MOH & FW. Dhaka: 467-468.
13. Lazarus AA and Thilagar B. "Abdominal tuberculosis". *Disease-a-Month* 53.1 (2007): 32-38.

14. Hillemann D., *et al*. "Rapid molecular detection of extra pulmonary tuberculosis by the automated Gene Xpert MTB/RIF system". *Journal of Clinical Microbiology* 49.4 (2011): 1202-1205.

15. Welday SH., *et al*. "Stool as appropriate sample for the diagnosis of *Mycobacterium tuberculosis* by Gene Xpert test". *Open Journal of Respiratory Diseases* 4.3 (2014): 83.

16. Dasgupta A., *et al*. "Abdominal tuberculosis: a histopathological study with special reference to intestinal perforation and mesenteric vasculopathy". *Journal of Laboratory Physicians* 1.2 (2009): 56-61.

17. Vadwai V., *et al*. "Xpert MTB/RIF: a new pillar in diagnosis of extrapulmonary tuberculosis?" *Journal of Clinical Microbiology* 49.7 (2011): 2540-2545.

18. Tortoli E., *et al*. "Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis". *European Respiratory Journal* 40.2 (2012): 442-447.

19. Vadwai V., *et al*. "Xpert MTB/RIF: a new pillar in diagnosis of extrapulmonary tuberculosis?" *Journal of Clinical Microbiology* 49 (2011): 2540-2545.

20. Lawn., *et al*. "Xpert® MTB/RIF assay: development, evaluation and implementation of a new rapid molecular diagnostic for tuberculosis and rifampicin resistance". *Future Microbiology* 6.9 (2011): 1067-1082.

21. Moure R., *et al*. "Rapid detection of *Mycobacterium tuberculosis* complex and rifampicin resistance in smear-negative clinical samples by use of an integrated real-time PCR method". *Journal of Clinical Microbiology* 49.3 (2011): 1137-1139.

22. Drobniewski FA and Pozniak AL. "Molecular diagnosis, detection of drug resistance and epidemiology of tuberculosis". *British Journal of Hospital Medicine* 56.5 (1996): 204-208.

23. Chien HP., *et al*. "Comparison of the BACTEC MGIT 960 with Löwenstein-Jensen medium for recovery of mycobacteria from clinical specimens". *The International Journal of Tuberculosis and Lung Disease* 4.9 (2000): 866-870.

24. Berney T., *et al*. "Duodenal tuberculosis presenting as acute ulcer perforation". *The American Journal of Gastroenterology* 93.10 (1998): 1989-1991.

25. Danish MI. "Short textbook of medical diagnosis and management". 5th edition. Karachi: Johar Publications (2004): 53-55.

26. Das P and Shukla HS. "Clinical diagnosis of abdominal tuberculosis". *British Journal of Surgery* 63.12 (1976): 941-946.

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