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Research Article

Study on Abdominal Tuberculosis Detecting in Ascitic Fluid with ADA Analysis in A Tertiary Care Hospital in Bangladesh

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Abstract

Background: Abdominal tuberculosis is a type of extrapulmonary tuberculosis which involves the abdominal organs such as intestines, peritoneum and abdominal lymph nodes. In patients with disseminated tuberculosis, it can either occur in isolation or along with a primary focus. And ascites is the pathologic accumulation of fluid within the peritoneal cavity. Since many diseases can cause ascites, in particular cirrhosis. Ascitic fluid are commonly analyzed in order to develop a differential diagnosis.

Objective: The purpose of this study was to determine whether ADA helps in detecting Abdominal Tuberculosis.

Methods: This cross-sectional study was conducted in Gastroenterology department of Dhaka Medical College Hospital in collaboration with National Tuberculosis Reference Laboratory, NIDCH, Mohakhali, Dhaka from May 2015 to April 2016. A total of 73 patients with abdominal TB who met the selection criteria and attended in Gastroenterology department of DMCH either through admission or referral were enrolled in this study.

Results: The mean age of the study subject was 33.90 ± 15.14 years. Majority of the patients (53.2%) were in between 18-30 year's age group followed by 18.8% were in between 31-40 year's age group and lastly 28% were in between 41 to 70 year's age group. Most common symptoms were weight loss (96.9%), abdominal pain (75%), fever (75%), loss of appetite (68.8%), night sweats (34.4%), swelling of abdomen (31.3%,), diarrhea (25%), cough and sputum (21.8%), constipation (25%), vomiting (15.6%). MTB DNA was detected in 9 (45%) patients. Diagnostic yield of Gene Xpert to detect MTB DNA on colonoscopic biopsy specimen found in 42.1% and Ultrasound guided biopsy of the L/N in 100% of patients. Histolopathogy showed epithelioid cell granulomas with or without caseation in 37.5% patients, Positive AFB on culture of tissue sample in 9.4% patients, ADA value in ascitic fluid (Cutoff >40 IU/L) in 25% patients and good clinical response to therapeutic trial anti-TB treatment found in 18.7% patients. Beside 18.7% patients were diagnosed on the basis of combination of various tests. Gene Xpert detected cases had a higher above-normal ADA level (92.2%) than Gene Xpart negative patients (14.7%).

Conclusion: We can conclude that extrapulmonary TB patients had significantly higher ADA levels. Ascitic fluid ADA can be used as a standard test in the diagnosis of tuberculosis since it is a simple, inexpensive, specific, and sensitive biomarker for disease diagnosis.

Keywords: Abdominal Tuberculosis; Ascitic Fluid; ADA; Gene Xpert; MTB DNA; Histolopathogy

Introduction

Tuberculosis (TB) is still a significant global health issue. It is one among the top ten causes of death worldwide, affecting around 10 million people each year. Peritoneal tuberculosis affects 5% of persons with Mycobacterium TB infection over the world [1,2]. In Rwanda, about 6000 cases of tuberculosis were reported in 2015, with pulmonary tuberculosis accounting for 84 percent of the occurrences. According to the 2017 Global Tuberculosis Report, the incidence of tuberculosis in Rwanda was 56 per 100,000 persons, with a death rate of 3.8 per 100,000 [3]. Bangladesh has a high tuberculosis endemic zone. Tuberculosis can affect any region of the gastrointestinal tract, and it is the sixth most common extrapulmonary source of infection. In Bangladesh, 12 percent of people have abdominal tuberculosis. Extrapulmonary tuberculosis affects about 20% of tuberculosis patients, and up to 12% of those with abdominal tuberculosis have peritoneal involvement [4]. There is a 30% chance of having active pulmonary TB and abdominal TB at the same time. Reactivation of latent tuberculosis foci causes the majority of tuberculosis peritonitis. Wet TB with ascites, dry tuberculosis with adhesions, and fibrotic tuberculosis with omental thickening and loculated ascites are the three types of peritoneal tuberculosis. Enlarged and matted mesenteric lymph nodes, omental thickening, and numerous yellow-white peritoneal tubercles describe the gross pathology. Peritoneal TB is difficult to diagnose since it is difficult to distinguish from other intra-abdominal diseases that cause ascites. Furthermore, because mycobacterial cultures grow slowly, bacteriologic confirmation is difficult to get in a situation where many patients are unable to follow up on culture results after they leave the hospital [5,6]. Adenosine deaminase (ADA) is a purine-degrading enzyme that catalyzes irreversible adenosine deamination, creating inosine in the process. Several studies have shown that ADA can be used to diagnose tuberculosis in other fluids such as meningeal, pleural, and pericardial fluids, implying that increasing ADA activity is related to the intensity of stimulation and lymphocyte maturation due to the immune cellular response against Mycobacterium tuberculosis [7]. Because of the description of fast determination methods, such as the technique described by Giusti in 1981 [8], which is the most extensively described in the literature and is one of the most used in clinical practice among countries with high prevalence of TB, ADA level measurement in body fluids has emerged as an appealing alternative for the diagnosis of TB.

Objective

The purpose of this study was to determine whether ADA helps in detecting Abdominal Tuberculosis.

Methods

- **Types of study:** This study was a cross sectional study.
- **Place of study:** This Study was conducted in Gastroenterology department of Dhaka Medical College Hospital in collaboration with National Tuberculosis Reference Laboratory, NIDCH, Mohakhali, Dhaka.
- **Duration of study:** This study was conducted from May 2015 to April 2016.
- **Study population:** All consecutive patients with abdominal TB who met the selection criteria and attended in Gastroenterology department of DMCH either through admission or referral were enrolled in this study.
- **Sample size:** This study was conducted on 73 patients.
- **Data collection:** Patient's demographic profile, clinical features associated with other medical illnesses, family and past history of TB was recorded. Laboratory tests, Mantoux skin test, chest and abdominal imaging results, histopathology findings, Gene Xpert, acid fast bacilli (AFB) staining by LED fluorescence microscope and culture (MGIT 960) reports, ascitic fluid analysis including ADA, findings of upper gastrointestinal endoscopy, colonoscopy with or without ileostomy, laparotomy were collected by structured questionnaire.
- **Data analysis:** Clean coded data was input into Microsoft Excel and exported to SPSS version 22 for further analysis. The descriptive statistical analysis was described using sentences, graphs, tables, frequencies, percentages, and mean and standard deviation. The frequencies of the variables were used in a descriptive analysis, and the 95 % confidence intervals (CIs) were produced. The statistical analysis was omitted from questionnaires that were incomplete. In multivariable logistic regression, statistically significant was considered at $p < 0.05$.

Results

It is a Cross sectional hospital based observational study carried out among 73 adult patients with diagnosis of abdominal TB (Based on positive microbiology, histopathology, ascitic fluid ADA report and clinical response to trial anti TB drugs) who met the selection criteria and attended in Gastroenterology department of DMCH

either through admission or referral. The mean age of the study subject was 33.90 ± 15.14 years. Majority of the patients (53.2%) were in between 18-30 year's age group followed by 18.8% were in between 31-40 year's age group and lastly 28% were in between 41 to 70 year's age group.

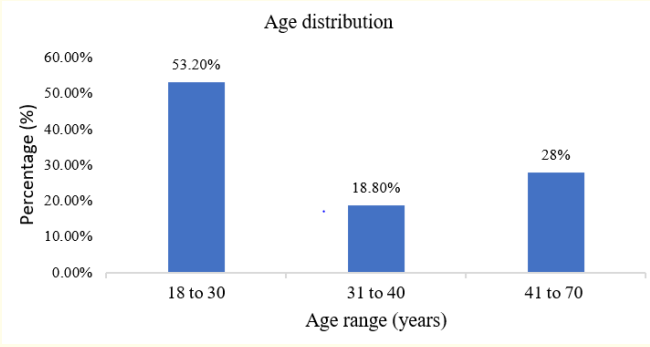

Figure 1: Age distribution of the patients.

The most frequent presenting symptoms in this study were weight loss (71,96.9%), abdominal pain (55,75%), fever (55,75%), loss of appetite (50,68.8%), night sweats (25,34.4%), swelling of abdomen (23,31.3%,), diarrhea (18,25%), cough and sputum (16,21.8%), constipation (18,25%), vomiting (11,15.6%).

Variables	Frequency (n)	Percentage (%)
Weight loss	71	96.9
Abdominal pain	55	75
Fever	55	75
Loss of appetite	50	68.8
Night sweats	25	34.4
Swelling of abdomen	23	31.3
Diarrhea	18	25
Vomiting	11	15.6
Constipation	18	25
Cough and sputum	16	21.8

Table 1: Common symptoms of the patients (N = 73).

Table 2 showed Gene Xpert MTB/RIF test was performed in 50 patients. MTB DNA was detected in 22 (45%) patients. Diagnostic yield of Gene Xpert to detect MTB DNA on colonoscopic biopsy specimen found in 20/48 (42.1%) and Ultrasound guided biopsy of the L/N in 2/2 (100%) of patients.

Gene Xpert	Frequency (n)	Percentage (%)	
MTB detected	22	45.0	
MTB undetected	28	55.0	
Biopsy material	Patients in which investigations performed (n)	Yield of diagnostic test	
		Frequency (n)	Percentage (%)
Colonic tissue by colonscopic biopsy	48	20	42.1
Lymph node by USG guided biopsy	2	2	100.0

Table 2: Distribution of patients according to Gene Xpert MTB/RIF test findings (n = 50).

Table 3 showed the basis of diagnosis in abdominal tuberculosis. Histolopathogy showed epithelioid cell granulomas with or without caseation in 27 (37.5%) patients, Gene Xpert of tissue sample showed MTB DNA in 21 (28.1%) patients, Positive AFB on culture of tissue sample in 7 (9.4%) patients, ADA value in ascitic fluid (Cutoff >40 IU/L) in 18 (25%) patients and good clinical response (on the basis of Weight gain and general improvement in wellbeing) to therapeutic trial anti-TB treatment in 14 (18.7%) patients. Beside these 14 (18.7%) patients were diagnosed on the basis of combination of various tests.

Variables	Frequency (n)	Percentage (%)
Histopathology	27	37.5
Gene Xpert	21	28.1
AFB culture	7	9.4
ADA value in ascitic fluid (>40 IU/L)	18	25.0
Combined tests	14	18.7
Anti-tubercular trial	14	18.7

Table 3: Basis of diagnosis in abdominal tuberculosis, (N = 73).

The relationship between ADA level and Gene Xpert of the patients is shown in table 4. Gene Xpert detected cases had a higher above-normal ADA level (92.2%) than Gene Xpart negative patients (14.7%), whereas Gene Xpart negative cases had a higher normal ADA level (85.3%) than Gene Xpert detected cases (7.8%).

Gene Xpert for MTB	ADA level		p-value
	Normal	Above normal	
Detected 22	2 (7.8%)	20 (92.2%)	0.001
Undetected 28	24 (85.3%)	4 (14.7%)	

Table 4: Relationship between ADA level and Gene Xpert (n = 50).

Discussion

Abdominal TB is a complex disease and has diverse symptomatology that is non-specific. The patients included in this study were presented with multiple symptoms at the time of admission. The most frequent presenting symptoms were weight loss (71,96.9%), abdominal pain (55,75%), fever (55,75%), loss of appetite (50,68.8%), night sweats (25,34.4%), swelling of abdomen (23,31.3%,), diarrhea (18,25%), cough and sputum (16,21.8%), constipation (18,25%), vomiting (11,15.6%). Our finding is compared to a previous study [9] where the most frequent symptoms were abdominal pain (194, 93%), fever (134, 64%), night sweats (99, 48%) and weight loss (98,47%). Also coincide with the study result [10] where abdominal pain and weight loss appeared to be the most frequent symptoms. In the present study Gene Xpert MTB/RIF test was performed in 50 patients. MTB DNA was detected in 22 (45%) patients. Diagnostic yield of Gene Xpert to detect MTB DNA of colonic tissue by colonoscopic biopsy specimens found in 20/48 (42.1%) and Ultrasound guided biopsy of the L/N in 2/2 (100%) of patients. Our study results are in line with a previous study [10] showed that the Xpert test has true diagnostic potential with moderate sensitivity (63 to 73%) for tissues, lymph nodes. Another study [11] showed that the sensitivity of Xpert test to detect TB in extra pulmonary site is 53-95%. This study shows basis of diagnosis in abdominal tuberculosis were follows: histolopathogy showed epithelioid cell granulomas with or without caseation in 27(37.5%) patients, Gene Xpert of tissue sample showed MTB DNA in 21 (28.1%) patients, positive AFB on culture of tissue sample in 7 (9.4%) patients, ADA value in ascitic fluid (cut off value >40 IU/L) in 18(25%) patients and good clinical response to therapeutic trial of anti-TB treatment in 14 (18.7%) patients. Beside these 14 (18.7%) patients were diagnosed on the basis of combination of various tests (Histopathology, Gene Xpert, AFB culture and ADA value in ascitic fluid). Among them the basis of diagnosis of both Gene Xpert and histopathology were in 7(9.4%) patients, both AFB culture and histopathology were in 2(3.1%) patients, both Gene Xpert and ADA value in ascitic fluid were in 2(3.1%) patient and combination of all tests (Histopathology, Gene Xpert, AFB culture and ADA value in ascitic fluid) were in 2(3.1%) patients. Basis of diagnosis in abdominal tuberculosis in a previous study [10] were: histolopathogy showed epithelioid cell granulomas with or without caseation in 42% patients, Positive AFB on culture of tissue sample in 2.9% patients and good clinical response to therapeutic trial of anti-TB treatment in 2.3% patients. Another study [12] showed 8.1% patients had positive response to anti tubercular trial. In the literature up to 40% patients were given therapeutic trial of anti TB drugs [13]. Gene Xpert detected cases had a greater above-normal ADA level 20(92.2%) than Gene Xpert negative cases 4(14.7%), and this difference in ADA level and Gene Xpert detection was significant (p=0.001). In one study, overall sensitivity was found to be 94.29 %, specificity 92.16 %, positive predictive value 89.00 %, and negative predictive value 95.92 % in extrapulmonary disease, and sensitivity was found to be 92.80 %, specificity 90.00 %, positive predictive value 92.86 %, and negative predictive value 90.00 % in pulmonary disease, and they were found to be significantly associated [14].

Conclusion

Despite the availability of effective chemotherapy, tuberculosis (TB) remains a common health problem in the developing countries like Bangladesh. It is becoming a worldwide problem due to its drug resistance. From the study observations, abdominal TB was mostly found in third to fourth decade with male preponderance and had diverse and nonspecific symptomatology. No single test was adequate for diagnosis of abdominal tuberculosis in all patients. A high index of clinical suspicion was required along with the help of multiple adjuvant diagnostic tools for diagnosis of ATB. The diagnostic yield of various investigation modalities for diagnosis of ATB were variable. In conclusion, the result of this study emphasized the diagnostic yield of various investigation modalities, particularly Gene Xpert, culture sensitivity in Bactec MGIT 960 and basis of diagnosis in abdominal TB. This study also unwavering the MTB culture positivity from tissue biopsies in patients with abdominal TB. It validated drug-resistant MTB in culture-confirmed abdominal TB. High ascitic fluid ADA (>40) correlates with positive

Gene Xpart test of biopsy materials. So high ascitic fluid ADA is a strong diagonistic test to select abdominal TB.

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