Bangladesh Med Res Counc Bull 2014; 40: 89-91

Role of ascitic fluid adenosine deaminase (ADA) and serum CA-125 in the diagnosis of tuberculous peritonitis

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Abstract

This cross sectional study was carried out in the department of gastroenterology, BIRDEM, Dhaka from January 2010 to May 2011 to determine the role of ascitic fluid ADA and serum CA-125 in the diagnosis of clinically suspected tubercular peritonitis. Total 30 patients (age 39.69±21.26, 18M/12F) with clinical suspicion of tuberculosis peritonitis were included in this study after analyzing selection criteria. Laparoscopic peritoneal biopsy with 'histopathological diagnosis' was considered gold standard against which accuracics of two biomarkers (ADA & CA-125) were compared. Cut off value of ADA and CA-125 are 24 u/l, 35 U/ml respectively. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ADA as a diagnostic modality in tuberculos peritonitis were 87.5%, 83.33%, 95.45%, 62.5% and 86.67% respectively where as CA-125 was found to have 83.33% sensitivity, 50% specificity, 86.9% positive predictive value, 42.85% negative predictive value and 76.6% accuracy. Both biomarkers are simple, non-invasive, rapid and relatively cheap diagnostic test where as laparoscopy is an invasive procedure, costly & requires trained staff and not without risk and also not feasible in all the centre in our country. So ascitic fluid ADA and serum CA-125 are important diagnostic test for peritoneal tuberculosis.

Introduction

Bangladesh is a high endemic zone of tuberculosis. Tuberculosis can involve any part of the gastrointestinal tract and is the sixth most frequent site of extra-pulmonary involvement. Prevalence of abdominal tuberculous in Bangladesh is 12%. About 20% of tuberculosis patients may have extra-pulmonary & up to 12% abdominal tuberculosis and of these 25-60% may have peritoneal involvement.[1] Concomitant active pulmonary TB associated with abdominal TB is 30%. Majority of tuberculos peritonitis result from reactivation of latent tuberculos foci. Peritoneal tuberculosis occurs in three forms: wet type with ascites, dry type with adhesions, and fibrotic type with omental thickening and loculated ascites. The gross pathology is characterized by enlarged and matted mesenteric lymph nodes, omental thickening and multiple yellow-white peritoneal tubercles. Diagnosis of tuberculous peritonitis is sometimes difficult. High index of clinical suspicion is necessary for the diagnosis of tuberculous peritonitis as missing the diagnosis can result in significant morbidity & mortality. Laparoscopic peritoneal biopsy is the gold standard in the diagnosis of tuberculous peritonitis but it is invasive, costly and not feasible in all the centre. Adenosine deaminase activity is increased in chronic inflammatory response eg. tubercular pleural effusion, tuberculous peritonitis. The ADA activity is significantly higher in the tuberculous peritonitis. Tuberculosis is virtually excluded if the value is very low. High level of ADA (cut off value 24 U/L) gave the test sensitivity of 93% and specificity 96%.[2-4] The CA-125 is a tumor marker associated with ovarian carcinoma. The CA-125 is also significantly higher in tuberculous peritonitis. So ovarian malignancy is must be excluded before diagnosis of peritoneal tuberculosis. High level of CA-125 (cut off value 35 U/ml) gave the test sensitivity of 98.4% and specificity 95.9%.[5] There is a significant correlation between ADA & CA-125 in patients with tubercular peritonitis.[6] Both biomarkers are simple, rapid, non-invasive & relatively cheap diagnostic test for tuberculous peritonitis. So establish as a new biochemical marker of ADA and CA-125 are time demanding for the diagnosis of peritoneal tuberculosis. The aim of this study is to evaluate ADA and CA-125 as diagnostic tools for tuberculous peritonitis.

Materials and Methods

This cross sectional study was carried out in the department of gastroenterology in BIRDEM Hospital, Dhaka from January, 2010 to May, 2011 on the patients with clinical suspicion of tuberculos peritonitis. Total 30 patients were selected purposively meeting the following inclusion & exclusion criteria. Clinically suspected cases of tubercular peritonitis presenting with abdominal pain, fever, ascites, weight loss, history of contact of TB patients or past history of TB were included in this study and those admitted in this hospital and those refused to be included in the study, Pregnant or lactating mother, known case of cirrhosis of liver, CKD, heart failure or intra-abdominal malignancy were excluded. Taking detailed clinical history, Physical examination, relevant investigations (eg. CBC, S. Creatinine, RBS, liver function tests, chest x-ray PA view, ECG, USG of W/A, urine R/M/E) were done in all cases. Endoscopy and colonoscopy were done in few cases for exclusion of intra-abdominal malignancy. Serum CA-125 and ascitic fluid study (including ADA, SAAG and malignant cell) were done in all patients. All patients were underwent laparoscopic peritoneal biopsy by experienced and skill surgeon after taking informed written consent from every patient and histopathology report of tissue samples were collected. Ethical clearance was taken from the institutional ethical committee of BIRDEM hospital. Sample were interviewed with a specific pre-designed and pre-tested questionnaire and other information were gathered by document review. Collected data was cleaned, edited and analyzed with the help of software SPSS. P value <.05 was considered to be significant.

Results

Result of the study was analyzed by comparison between ADA, CA-125 and histopathology of peritoneal tissue. Baseline clinical data and investigations findings were also observed. Mean age of the study subjects was 39.69±21.26 (SD). In ascitic fluid study, 22 patients (73.3%) of ADA level was found high (>24 u/l) and rest of the 8(26.7%) patients of ADA level was found low (<24 u/l). Among the study subjects, 23(76.7%) patients of serum CA-125 level was found high (>35(U/ml)) and rest of the 7 (23.3%) patients of CA-125 was found low (<35 U/ml). According to histopathological reports, 24(80%) patients was found tubercular granuloma and non-tubercular was in 6 (20%). In this study, 22 patients of high level of ADA (>24 u/l) was found histopathologically tubercular in 21(87.5%) patients and rest 1 patient was found non-tubercular. On the other hand, 8 patients of low level of ADA (<24 u/l) was found histopathologically tubercular in 3 (12.5%) patients and rest of the 5 patients were found histopathologiclly non-tubercular. (P<.05, χ^2=12.31df=1, CI 95%). This relation was highly significant (P value 0.001). In present study, 23 patients of high level of CA-125 (>35 U/ml) were found histopathologically tubercular in 19(79.2%) patients and rest of the 4 patients were found histopathologically non-tubercular. On the other hand, 7 patients of low level of CA-125 (<35 U/ml) was found histopathologically tubercular in 5(20.8%) patients and rest of the 2 patients were found histopathologically non-tubercular. This association was not statistically significant. P value =.051, (χ^2 .419, df 1 CI 95%). Relation of ADA with CA-125 was mentioned in table I. Sensitivity and specificity were described in table II.

Table I: Relation of ADA with CA-125 (N-30)

			ADA (u/l)		Total	P Value
			<24	>24		
CA-125 (u/ml)	<35	number	2	5	7	
		%	28.6%	71.4%	100.0%	.896
	>35	number	6	17	23	
		%	26.1%	73.9%	100.0%	

Table II Sensitivity and specificity (N-30):
(a): Sensitivity and specificity of ADA.

Test	Gold standard test Tubercular	Non-Tubercular	Total
Test Positive (ADA >24)	21	1	22
Test Negative (ADA<24)	3	5	8
Total	24	6	30

Performance of Diagnostic Test

PPV	NPV	Accuracy	Sensitivity	Specificity
95.45%	62.5%	86.67%	87.5%	83.33%

(b) Sensitivity and specificity of CA-125 (N-30)

Test	Tubercular	Non-tubercular	Total
Test positive (CA-125 >35)	19	4	23
Test negative (CA-125 <35)	5	2	7
Total	24	6	30

Performance of diagnostic test

PPV	NPV	Accuracy	Sensitivity	Specificity
86.9%	42.85%	76.6%	83.33%	50%

Discussion

High index of clinical suspicion is necessary to diagnose peritoneal tuberculosis.[8] In this study male is predominant possibly due to increase risk of exposure to infecting agent. One third of the patients had history of contact with TB patients (33.33%). Past history of tuberculosis was in 4 patients (13.4%). Muneef et al found 30% of the patients either gave past history of TB or presented with active TB.[9] Clinical presentations and baseline investigations data were consistent with other published data.[9] Twenty two patients (73.3%) had

high ADA level (>24 u/l). Among the study subjects 23(76.7%) patients had high serum CA-125 (>35 U/ml). Low serum CA-125 were in 7 patients (23.3%). Uygur-Bayramicli O et al also pointed diagnostic value of ascities fluid ADA and CA-125 in tuberculous peritonitis. Present study is comparable with this study. All study patient underwent laparoscopic biopsy and histopathology consistent with TB was found in 24(80.0%). Bhargava et al did Laparoscopy in 3 cases and revealed tubercle on the peritoneum and intestine with omental thickening which are histopathologicaly proved (100%).[11] In this study 22 patients had high ADA level (>24 u/l). Among high ADA level, 21 patients had histopathologicaly proved TB. On the other hand, among 8 patients of low ADA, 3 patients was histopathologicaly consistent with tuberculosis and 5 patients was non-tubercular ($P<.05$, $\chi^2=12.31df=1$, CI 95%). This relation was highly significant. In this study, 23 patients had high CA-125 value (>35 U/ml). Among them 19 patients had histopathologicaly consistent with TB and 4 patients had non-tubercular. On the other hand, among the 7 patients of low CA-125 value, 5 patients had histopathlogicaly consistent with TB and 2 patients were non-tuberculer. In case of ADA, sensitivity was 87.5% and specificity was 83.33%. In case of CA-125, sensitivity was 83.33% and specificity was 50%. Mean±SD of ADA was 65.67±34.12 in tubercular patients and mean±SD of ADA was in 13.27±7.17 in non-tubercular patients, confirmed by biopsy. The association between two groups was statistically significant (P value <.05). In case of tubercular patients, CA-125 (Mean±SD) was in 223.83±159.17 and non-tubercular of CA-125 (Mean±SD) was in 155.67±181.49. This difference was statistically not significant. Binder HJ et al found that six of seven studies outside the United States have reported 100% sensitivity for the diagnosis of peritoneal tuberculosis, with specificities in the range of 92-100%.[12] In another study pointed that the diagnostic sensitivity of adenosine deaminase for tuberculous peritonitis was in 94.2%, and its positive predictive value was in 75%.[10] In this study PPV was 95.45%, acuracy was 86.67%. It is concluded that measurement of ADA in ascitic fluid and serum CA-125 is a fast and accurate test for diagnosis of peritoneal tuberculosis. It has enough discriminatory power to either confirm or rule out the diagnosis of peritoneal tuberculosis in most cases. The beginning of empirical treatment when a patient has a high value of both ADA and CA -125 to be good approach while we waiting for the results of mycobacterial culture or biopsies.

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