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# The Diagnosis of Serous Forms of Extra pulmonary Tuberculosis: Is PCR Definite Answer?

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**Abstract**
**Objectives:** *To study the evaluation the use of polymerase chain reaction (PCR) in patients of serous form of extra pulmonary tuberculosis.*
**Methods**: *We studied all patients of serous form of extra pulmonary tuberculosis with high suspicion of index in our hospital from July 2014 to June 2017 in department of medicine, FHMC and Hospital, Etmadpur, Agra. All patients were subjected for detailed clinical examinations, investigations and PCR study and statistically analysed.*
**Results:** *A total of 320 patients were included in study. 230 patients were suspected as tubercular and 90 patients were non tubercular on the ground of clinical and cytobiochemical analysis. Among 230 patients, only 85 patients were PCR positive (41.38%) for tuberculosis while out of 90 non tubercular patients, none was PCR positive (100%). Thus PCR study showed that sensitivity was 41.38% and specificity was 100%.*
**Conclusion:** *PCR is a rapid diagnostic technique having high degree of specificity for the detection mycobacterium tuberculosis in the serous forms of extra pulmonary tuberculosis.*

## Introduction

The serous forms of extra pulmonary tuberculosis is not uncommon and its incidence is 10-15 percent of total tuberculosis cases.[2]To establish the diagnosis of serous form of extra pulmonary tuberculosis is still eniagma and depends largely upon clinical features, cytobiochemical picture of fluid and biopsy of serous membrane due to low yield of bacilli.[7]The polymerase chain reaction (PCR) has emerged as important diagnostic tool in rapid and definite diagnosis of tuberculosis.PCR is highly sensitive(70%) and specific 100% (positive specific value 100% and negative specific value 86.95%),[2,15] PCR is molecular biological technique for isolating and exponentially amplifying a fragment of DNA via enzymatic replication without using living organism. This method detects mycobacterial DNA in clinical sample within 24-48 hours by amplification.[6] PCR represents a rapid and sensitive method for detection of extra pulmonary tuberculosis. The present study was conducted to evaluate the use of

PCR in patients of extra pulmonary tuberculosis with high suspicious of index

**Material and Methods**

The study was conducted over the period of two years from July 2014 to June 2017 in the department of medicine, F.H.M.C and Hospital, Etmadpur, Agra. A total of 320 patients were included in the study. All the patients having clinical and cytobiochemical suspicion of serous forms of extra pulmonary tuberculosis were included in study.Patients were subjected for the detailed clinical history and physical examination. The investigations like routine blood tests, chest skiagram, CT head, ECG, 2D Echo, cytobiochemical examination of serous fluid (peritoneal, pleural, pericardial and CSF) and DNA-PCR were considered for final diagnosis due to low culture yield from serous fluid. The result of PCR was compared with the final diagnosis of tuberculosis made on the basis of clinical and cytobiochemical parameters and significance was determined by Z test.

The sensitivity was calculated as

$$\left[\frac{T_P}{T_P + F_N}\right] \times 100$$

The specificity was calculated as

$$\left[\frac{T_N}{T_N + F_P}\right] \times 100$$

True positive (TP); True negative (TN)

False positive (FP); False negative (FN)

**Results**

A total of 320 patients were included in this study. Out of 320 patients, 85 patients had pleural effusion, 85 patients had miningitis, 90 patients had ascites and 60 patients had pericardial effusion. There were 190 male patients (59.39%) and 130 female (40.61%) patients with mean age 37-66 years. Majority of patients were in 10-40 years age group.

Presenting symptoms in patients of pleural effusion (85 patients) were dyspnea 88.29% (75), chest pain 64.70% (55), fever 47% (40), cough (47% (40), anorexia 35.29% (30) and malaise 29.4% (25). Cytobiochemical changes in these patients were suggestive of tuberculosis in 70 patients (protein >3.0 gm/dl, blood sugar low < 60 mg/dl, total leucocyte count >500 $mm^3$ and lymphocytosis >50%) while 15 patients were suggestive of non-tuberculosis.

Presenting signs and symptoms in 85 patients of meningitis were headache (100%), low grade fever 88.23% (75), vomiting 47% (40), altered sensorium 35.29% (30), neck rigidity 41.17% (35), Kernig's sign 35.26% (30), raised ICT 70% (60), hydrocephalus 35.29% (30), cranial nerve palsy 23.52% (20) and vasculitis 11.70% (10) in patients. Cytobiochemical analysis showed raised protein >4.5 gm/dl, blood sugar > 40 mg/dl, total leucocyte count <3.0/ $mm^3$ and lymphocytosis >50% in 50 patients and suggestive of tubercular meningitis.

There were 90 patients of Ascites, presented with clinical feature of distension of abdomen 100%, fever 83.33% (75), abdominal pain 50% (45) and anorexia in 77.78% (70) patients.

Cytobiochemical profile showed protein >2.5 gm/dl, sugar <60 mg/dl, total leucocyte count > 300/$mm^3$ and lymphocytosis >50% in 65 patients suggestive of tuberculosis.

There were 60 patients of pericardial effusion and signs and symptoms were dyspnea 83.33% (50) cases followed by chest pain 75% (45), cough 58.34% (35), fever 54.34% (35), pain in abdomen 25% (15), palpitation 91.67% (55), raised JVP 15% (45), muffled heart sound 58.34% (35), hepatomegaly 41.66% (25), oedema 41.66% (25), hypotension 33% (20), pulsus paradoxus 25% (15) and tachycardia were seen in 25% (15) patients respectively. Cytobiochemical profile showed protein >2.5 gm/dl, sugar level <60 mg/dl, leucocytosis >500./$mm^3$ and lymphocytosis >50% in 45 patients suggestive of tuberculosis.

PCR results in 85 patients of pleural effusion showed positive PCR results in 16 patients (28.57%) out of 70 suspected cases of tuberculosis while all non-tuberculosis (15 patients) were PCR negative. Thus sensitivity and specificity was

28.57% out of 100% respectively in pleural effusion cases. In cases of meningitis, out of 50 suspected for tuberculosis only 20 patients were PCR positive while non tubercular patients none was the positive. Thus sensitivity and specificity in meningitis was found 40% and 100% respectively. PCR results in patients of suspected tubercular ascites were positive in 25 cases out of 65 patients while none was positive in non tubercular cases (n=25). Thus PCR sensitivity and specificity was 38.46% and 100% respectively in abdominal ascites. PCR results in suspected tubercular pericardial effusion cases (n=45) were positive in 30 patients while negative in all non-tubercular cases (n=15). Thus sensitivity and specificity in pericardial effusion cases was 66.67% and 100% respectively.

Thus, out of 320 patients 230 patients were suspected as tubercular and 90 patients were non tubercular. Among 230 patients, only 85 patients were PCR positive (41.38%) for tuberculosis while out of 90 non tubercular cases none were PCR positive (100%). Thus, PCR study showed that sensitivity was 41.38% and specificity was 100%.

**Discussion**

IN India and other developing countries, serous forms of extrapulmonary tuberculosis is not uncommon and at time it may present as medical emergencies leading morbidity and mortality too. Thus, requires timely definitive diagnosis of the disease and its management to prevent morbidity and mortality.

The diagnosis of serous form of extrapulmonary tuberculosis is still eluding and largely depend upon clinical and cytobiochemical study. The demonstration of tubercular bacilli in culture have very low yield due to paucibacillary. Estimation of ADA is still not very helpful in the definitive diagnosis. PCR is based on amplification of mycobacterium necleic acid and has shown high sensitivity and specificity.[7] In our study PCR was done in all the samples and results were compared with clinical and cytobiochemical study in serous form of extra pulmonary tuberculosis. Previous study have shown variable results of sensitivity (31.42% to 75%) and specificity (61 to 100%) respectively.[1,2,3,5,8,10,11,15]

Dil Afrose et al evaluated the 82 patients of pelural effusion (48 patients confirmed tubercular pleural effusion and 34 patients nontubercular pleural effusion) and did not find any false positive result by PCR, specificity worked out to be 100% while sensitivity was 67%.

In our study, a total of 320 patients were included and 230 patients were diagnosed as serous form of extra pulmonary tuberculosis while 90 patients as non tubercular etiology. Out of 230 suspected tubercular patients 85 patients were PCR positive (41.38%) while all non tubercular patients (n=90) were PCR negative (100%). This sensitivity and specificity in our study were 41.38% and 100% respectively. We also observed highest sensitivity (66.67%) in pericardial effusion and least (28.57%) in pleural effusion but specificity 100% in all cases. None of the sample was positive for AFB due to very low yield in serious fluid which is comparable to previous studies.[4]

Cegi.. JP et al[4] compared PCR to culture and histopathology for diagnosis of serous form of extra pulmonary tuberculosis and osberved that sensitivity of PCR was higher in tissue specimen (80%) as compared to fluid (15%) (p=0.002). Thus, over all accuracy of PCR is superior over ADA and other conventional method.

The polymerase chain reaction (PCR) is a molecular biological technique for isolating and exponentially amplifying a fragment of DNA via enzymatic replication without using a living organism such as E.coli or yeast. PCR is an invitro technique and can be performed without restriction on the form of DNA. It can be extensively modified to perform a wide array of genetic manipulations.[9,12,13,14] AFB screening has very low sensitivity and ADA estimation has both low sensitivity and specificity. While, PCR represents a rapid and sensitive method for detection of mycobacterium DNA is serous form of extra pulmonary tuberculosis. Therefore PCR

merits higher in list of conventional investigations in terms of specificity. Thus, in cases high index of suspicion of tuberculosis clinically, PCR may be of added benefit and should be included in armamentarium of investigations as it is highly specific test.

**Conclusion**

PCR is rapid diagnostic technique having high degree of specificity for detection of the mycobacterial tuberculosis complex group of organisms from serosal fluids.

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