Original Research Article

A Hospital Based Study to Compare GENE XPERT (CB-NAAT) and Cytochemical Analysis of Pleural Fluid in Diagnosis of Tuberculosis in Exudative Pleural Effusion at a Tertiary Care Center in Western Rajasthan

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Abstract

Background: Pleural fluid analysis is the most useful test in differentiating possible causes and directing further investigations. Pleural fluid Adenosine Deaminase (ADA) levels are high in pleural tuberculosis, although an elevated value is non-specific and may occur in other infection and malignancy. The aim of this study to compared GENE XPERT (CB-NAAT) and cytochemical analysis in patients with exudative pleural effusion in diagnosis of tuberculosis.**Materials & Methods:** Present study was a hospital based cross-sectional study. All the patients with pleural effusion at our department were undergone diagnostic thoracocentesis. As per Light's criteria; Patients with transudative pleural effusion were excluded from study. Total 50 patients were eligible as per the inclusion and exclusion criteria and were included in the study. We also recorded detailed history including socio-demographic profile, smoking habits, history of anti-tubercular treatment, occupational history, along with detailed respiratory and other systemic examinations in a pre-structured proforma.**Results:** Age ranges from 18 to 78 years. Male to female ratio was 3.16:1. 20 (40%) patients had history of addiction and out of which 16 were smokers, 3 were alcoholic and 1 had dual (alcoholic and smoker) addiction. The pleural effusion sensitivity of CB-NAAT was 10% and specificity were 90% in study population. It means positive predictive value in study were only 10 cases sensitive in population.**Conclusion:** We concluded that CB-NAATs have high specificity and could be used alongside ADA (or interferon-gamma) to increase sensitivity for ruling out disease and NAAT for high specificity to rule it in.

Keywords: CB-NAAT, Pleural Effusion, Fluid, Tuberculosis, ADA.

Introduction

The accumulation of fluid in the pleural space is a common manifestation of a wide range of diseases, and frequently presents to general physicians. The pleural space normally contains 0.1–0.2 ml/kg body weight of fluid, filtered from systemic capillaries down a small pressure gradient[1].Pleural effusions are classified as transudates or exudates according to biochemical criteria. Transudates are the result of changes in hydrostatic forces, with capillary permeability remaining normal[2]. Exudates involve increased capillary permeability and lymphatic obstruction[3].Pleural fluid analysis is the most useful test in differentiating possible causes and directing further investigations. Therefore, aspiration should be performed in all cases of radiologically confirmed pleural effusion, with the exception of cases where the clinical context is suggestive of a transudative process. The differential cell count in pleural aspirates can aid in narrowing the differential diagnosis A lymphocytic pleural effusion is most often the result of tuberculosis or malignancy. However, up to 10% of tuberculosis effusions are polymorph predominant[4].The use of biochemical markers such as adenosine deaminase (ADA) in pleural fluid may be of benefit in the early diagnosis of tuberculous pleurisy[5]. Pleural fluid ADA levels are high in pleural tuberculosis, although an elevated value is non-specific and may occur in other infection and malignancy. In areas where tuberculosis is prevalent, an elevated ADA value is both highly sensitive and specific, especially in young patients in whom empyema has been excluded, and treatment without pleural biopsy may be considered[6].An elevated ADA level is less useful in the elderly and in regions where tuberculosis is uncommon, as the possibility of an alternative diagnoses is increased [5], however, a low ADA value may still be informative as it makes tuberculosis unlikely. Although tuberculous pleural effusions typically resolve spontaneously over several months, treatment is recommended as 65% of untreated patients develop active pulmonary tuberculosis within 5 years. The aim of this study to compared gene xpert and cytochemical analysis in patients with exudative pleural effusion in diagnosis of tuberculosis.

Materials & Methods

After taking permission from the institutes ethical committee the study was conducted in the department of respiratory medicine of

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PDU Medical College, Churu. The study was a hospital based cross-sectional study. All the patients who were presents with pleural effusion at our department were undergone diagnostic thoracocentesis and pleural fluid cytochemical analysis after obtaining written consent. As per Light's criteria; Patients with transudative pleural effusion were excluded from study.

Inclusion Criteria

1. Patient willing for participation in the study and gave consent
2. All exudative pleural effusions not falling in exclusion criteria.

Exclusion Criteria

1. Patients age below 18 years and above 80 years
2. Patients with transudative pleural effusion
3. sputum smear positive patients with pleural effusion

Total 50 patients were eligible as per the inclusion and exclusion criteria and were included in the study. Plural fluid was further tested by CBNAAT at our department. We also recorded detailed history including socio-demographic profile, smoking habits, history of anti-tubercular treatment, occupational history, along with detailed respiratory and other systemic examinations in a pre-structured proforma.

Statistical analysis: Data were analyzed using SPSS version 17. Proportion and percentages were calculated for categorical variables and mean± SD were calculated for continuous variables. Sensitivity and specificity of CBNAAT were calculated in comparison with ADA and Lymphocytes for the diagnosis of pleural tuberculosis.

Results

Total 50 patients were enrolled in the study and their age ranged from 18 to 78 years. Male to female ratio was 3.16:1. 20 (40%) patients had history of addiction and out of which 16 were smokers, 3 were alcoholic and 1 had dual (alcoholic and smoker) addiction. (table 1).Out of 50 patients, 23 patients were presented with right sided and 27 patients with left sided pleural effusion. 56% of study participants had moderate plural effusion. (table 1).The mean value of biochemical analysis such as RBC, Serum protein and Serum albumin was 96.13±14.30, 6.487±0.7256 and 3.472±0.5123 respectively. The mean value of TLC was 2756± 1438 (Range= 200-8900 per cu mm), mean value of Lymphocyte was 82.86±8.290 (range=70-98%) and mean value of polymorphs was 17.25±8.23 (range=2-30%) (table 2).The sensitivity of CB-NAAT was 10% and specificity was 90% in diagnosis of plural tuberculosis. It means positive predictive value in study was only 10% (table 3).

Table 1: Demographic profile of patients

Demographic profile		No. of patients (N=50)	Percentage
Age (yrs) (Mean±Sd)		46.23±6.53	
BMI (Kg/m2)		21.57±3.62	
Sex			
Male		38	76%
Female		12	24%
Addiction			
No addiction		30	60%
Addiction (N=20)	Only smoking	16	32%
	Only alcohol	3	6%
	Alcohol+Smoking	1	2%
Site of pleural effusion			
Right		23	46%
Left		27	54%
Effusion of pleural fluid			
Mild		14	28%
Moderate		28	56%
Massive		8	16%

Table 2: Biochemical & Cytochemical Analysis of plural fluid in Study Population

Analysis	Mean Value	SD
RBC	96.13	14.30
Serum protein	6.487	0.7256
Serum albumin	3.472	0.5123
Blood sugar	62.53	22.92
TLC	2756	1438
Lymphocyte	82.86	8.290
Polymorphs	17.25	8.23
ADA	91.22	62.56

Table 3: Comparison of prevalence of pleural effusion by ADA & Lymphocyte and CB-NAAT test

Prevalence of Pleural effusion	No.	%
ADA & Lymphocyte	50	100%
CB-NAAT	5	10%
Sensitivity of CB-NAAT	10%	
Specificity of CB-NAAT	90%	
Positive predictive value (PPV)	10%	
% False Negative rate (FNR)	90%	

Discussion

Tuberculous pleurisy may occur during primary infection, when it tends to affect younger individuals in areas with a high prevalence of tuberculosis, or it may be recognized as a manifestation of disease reactivation, particularly affecting older patients. Pleural fluid is usually a serous exudate, and pleural fluid glucose and pH values are lowered in a minority of patients. Pleural effusions usually occur in adults. However, they appear to be increasing in children, often in the setting of underlying pneumonia. Fetal pleural effusions have also been reported and under certain circumstances may be treated prior to delivery[6-8].Our study showed than mean value of age was 46.23 years. There are reasons for the vulnerability of older people: those living in nursing homes and similar facilities are in close contact with others who may be infected. The aging process itself may weaken the

body's immune system, which is then less able to ward off the tubercle bacillus. Finally, bacteria that have lain dormant for some time in elderly persons may be reactivated and cause illness. Accumulation of pleural fluid is not a specific disease but reflects an underlying pathological process. A thorough occupational history from school-leaving age should be elicited. This should include the dates and amount of exposure to asbestos, circumstances and environment (e.g. ventilation, use of respiratory protection) and details of the employer (to aid subsequent compensation claims). High-risk occupations for asbestos exposure include construction, insulation, electrical repair, carpentry, plumbing, ship-building and petrochemical plant work[9]. In India common causes of pleural effusion are tuberculosis, bacterial pneumonias, malignancies, congestive heart failure, renal failure, connective tissue disorders and pulmonary embolism.Alcoholics and intravenous drug abusers are also at increased risk of contracting tuberculosis. Until the economic and social factors that influence the spread of tubercular infection are remedied, there is no real possibility of completely eliminating the disease.The prognosis in pleural effusion varies in accordance with the condition's underlying etiology. However, patients who seek medical care earlier in the course of their disease and those who obtain prompt diagnosis and treatment have a substantially lower rate of complications than do patients who do not.In present study observed the left side pleural effusion (54%) more as compared to right side (46%) of chest in radiograph in tuberculosis patients. The erect PA chest radiograph is usually abnormal once >200 ml of fluid is present, whereas a lateral film will show blunting of the posterior costophrenic angle with as little as 50 ml[10].Pleural thickening can be distinguished from fluid by using a lateral decubitus film, as the freely moving fluid gravitates to the dependent part of the lung[11]. Exudative effusions with loculation and fibrous septa may appear as mass lesions on the chest radiograph as fluid climbs into the fissure; ultrasound is helpful in this case. There may be difficulty identifying pleural effusions in the intensive care setting; supine films are less sensitive, and hazy opacification of one lung field or thickening of the minor fissure may be the only clues.The use of biochemical markers such as adenosine deaminase (ADA) in pleural fluid may be of benefit in the early diagnosis of tuberculous pleurisy.An elevated ADA level is less useful in the elderly and in regions where tuberculosis is uncommon, as the possibility of an alternative diagnoses is increased;[5] however, a low ADA value may still be informative as it makes tuberculosis unlikely.In 1990, D. K. Gupta et al[12]in their study of 53 cases of pleural effusion found that the mean ADA level in those of tuberculous origin was 77.7 U/L in contrast to 14.5 U/L in cases of malignant effusion. In present study the sensitivity of CB-NAAT was 10% and specificity was 90% in study population. Porcel JM et al (2013)[13] conducted study in 67 patients with pleural effusions, of whom half had tuberculous pleuritis, Xpert yielded 15% sensitivity and 100% specificity in the detection of tuberculosis (TB). In our results contrast with Christopher DJ et al (2013)[14], Friedrich SO et al (2011)[15] and Jinghui Du et al (2015)[16].Christopher DJ et al (2013)[14] studied gene Xpert on pleural fluid, detected 4 out of 25 patients with confirmed TB resulting in a sensitivity of 16.0%, specificity was 100%.Friedrich SO et al (2011)[15] investigated the diagnostic utility of the Xpert MTB/RIF (Mycobacterium tuberculosis/rifampin [RIF] resistance) assay in 20 cases with confirmed tuberculous pleural effusion. The sensitivity and specificity of the Xpert assay in pleural fluid were 25% and 100%, respectively.Jinghui Du et al (2015)[16]to investigate the diagnostic accuracy of the Xpert MTB/RIF (Xpert) (Cepheid, Sunnyvale, CA) assay using pleural biopsy and pleural fluid specimens in patients. The sensitivity of the Xpert assay using pleural biopsy specimens for the diagnosis of pleural TB was 85.5%, and specificity was 97.2%.

The sensitivity and specificity of the Xpert assay in pleural fluid were 43.6% and 98.6%, respectively.Rajendra Prasad et al (1992) studied 47 cases of pleural effusion and found that at 30 U/L cut off value the sensitivity and specificity of ADA for diagnosing Tubercular plural effusion was 100%, which was consisted with our results[17].

Conclusion

We concluded that CB-NAATs have high specificity and could be used alongside ADA (or interferon-gamma) to increase sensitivity for ruling out disease and NAAT for high specificity to rule it in. The study highlights the limited sensitivity of Xpert. Further research on the optimisation of sample processing should be considered to enhance the sensitivity of the test. In summary, our findings suggest that Xpert is of limited use in the diagnosis of pleural TB.

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