

Evaluation of Gene Xpert versus Pleural Biopsy in Diagnosis of Suspected Cases of Tuberculous Pleural Effusion.

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INTRODUCTION

Tuberculosis is a prominent cause of illness and mortality. It is a common public health illness with one third of world's population infected with it. Pleural TB occurs in up to 30% of patients concomitantly with pulmonary TB and represents a major portion of TB.¹

For its paucibacillary character, the disease goes undetected in a significant percentage of cases. The gold standard for diagnosis is culture on solid and liquid media, but in resource-constrained places, the longer turnaround time combined with the quite high cost of infrastructure development remains a concern.²

Rapid diagnosis in patients with tuberculous Pleural effusion is needed to reduce morbidity, the newer serological tests like interferon gamma release assays do not differentiate between active and latent TB infection.³

ABSTRACT

Background: Due to the low sensitivity of current diagnostic tests and increasing medication resistance; Diagnosing and treating tuberculous pleural effusion are difficult. Gene Xpert is a completely automated real-time nucleic acid amplification test that identify Mycobacterium tuberculosis besides rifampicin resistance within short time.

Aim of the work: to assess the diagnostic role of Gene Xpert in the diagnosis of suspected cases of tuberculous pleural effusion and compare it's results with pleural biopsy results obtained by Abraham's needle and Thoracoscope.

Patients and Methods: The present study was conducted on 60 patients who have strong suspicion of tuberculous pleural effusion after recording a written consent in Abasia chest hospitals at the period from November 2017 to May 2020.

Result: 7 patients out of 60 (11.7%) were diagnosed with Gene Xpert, while 42 patients (70%) were diagnosed with tissue biopsy. As regard the second group, 25 patients of them diagnosed through thoracoscope and 17 of them diagnosed through Abrams needle biopsy, there was significant variance between these two methods of biopsy ($P > 0.05$).

Conclusion: We concluded that, the Gene Xpert test has a restricted diagnostic capacity for pleural fluid samples of TB origin, which prevents its widespread application in this setting.

Keywords: Gene Xpert; Tuberculous pleural effusion; Thoracoscope; Abrams needle.

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More fast tests, such as nucleic acid amplification, can diagnose pleural tuberculosis quickly and definitively. Gene Xpert is a completely automated real-time nucleic acid amplification test that identifies Mycobacterium tuberculosis in less than three hours.⁴

Gene Xpert is a promising invention having high sensitivity, specificity and rapid result.⁵

Therefore, this research was designed to evaluate the possibility of using the Gene Xpert in diagnosing tuberculous pleural effusion cases and clarify the extent to which this test can be widely used.

The goal of this study is to assess the diagnostic role of Gene Xpert in the diagnosis of suspected cases of tuberculous pleural effusion and compare its results with pleural biopsy results obtained by Abraham's needle and Thoracoscope.

PATIENTS AND METHODS

This study was done at Abbaseia Chest Hospital at the period from November 2017 to May 2020.

Study design: A prospective study for evaluation of efficacy as determined by the diagnostic yield and safety of Gene Xpert in comparison to Pleural Biopsy.

Patients: sixty patients who have strong suspicion of tuberculous pleural effusion (exudative, predominantly lymphocytic and highly positive tuberculin skin test) were included in this study.

Inclusion criteria: patients with high suspicion of exudative tuberculous pleural effusion based on clinical signs and symptoms of tuberculosis confirmed with Light’s criteria in addition to radiological proof of a pleural effusion considered large enough for a pleural biopsy, also highly positive tuberculin skin test and absence of other causes of pleural effusion.

Exclusion criteria: any patient received anti-TB treatment within two months prior to the study or any patient with positive test for acid fast bacilli in sputum or patient with any contraindications to pleural biopsy procedure and patients with any chronic disease rather than tuberculosis.

Statistical Analysis of data

The Statistical Program for Social Science (SPSS) version 15.0 was used to examine the data. Quantitative data were stated as mean± standard deviation (SD). Frequency and percentage were used to express qualitative data.

The following tests were done:

Independent samples t-test of significance: was used when assessing between two means.

Probability (P-value)

- P-value < 0.05 was considered significant.
- P-value < 0.001 was considered as highly significant.
- P-value > 0.05 was considered irrelevant.

RESULTS

		Studied patients (N = 60)	
Cytology	Exudate	60	100%
	Transudate	0	0%
Gene Xpert	Negative	53	88.3%
	Positive	7	11.7%

Table 1: Description of pleural fluid examination results in all studied patients.

This table shows the description of pleural fluid examination results in all studied patients. As regard cytology, all studied patients (100%) revealed exudate. As regard gene expert, it was negative in 53 patients (88.3%) and positive in 7 patients (11.7%).

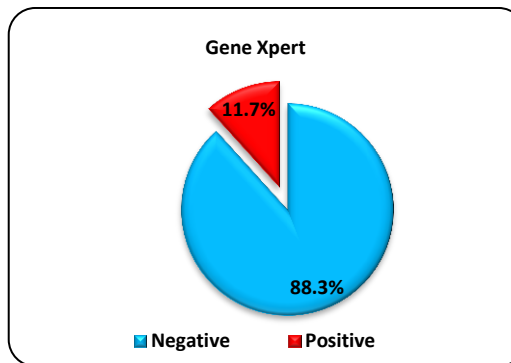


Fig. 1: Description of gene expert results in all studied patients.

		Biopsy method		Stat. test	P-value
		Abrams (N = 30)	Thoracoscope. (N = 30)		
Biopsy results	Negative	13	43.3%	X ² = 5.07	0.024 S
	Positive	17	56.7%		

Table 2: Comparison of biopsy results as regard biopsy method.

X²: Chi-square test; S: p-value < 0.05 is counted significant.

This table displays statistically significant difference (p-value < 0.05) between biopsy methods as regard biopsy results.

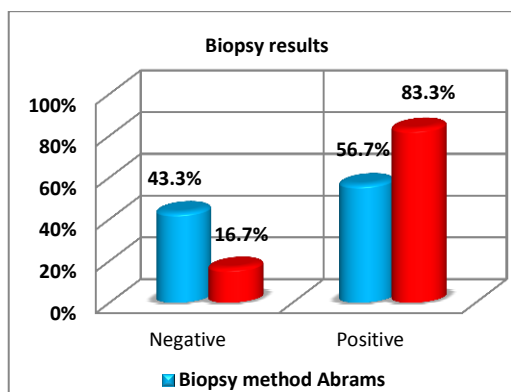


Fig. 2: Comparison of biopsy results as regard biopsy method.

DISCUSSION

On analysis of data in this study most cases were middle age adults ranged from 43 years to 62 years with mean age 52.3 ± 6.9 years. with male predominance: 42 patients out of 60 (70%) among all patients participating in the study (Table 1).

This outcome relatively matches to Omar et al, study which mentioned that the mean age of studied cases was 37.7±15.3 years. With male predominance: 9 patients out of 15 (60 %) among studied groups of research. ⁶

Also, according to Anushree et al, study, there were 57 male and 18 female patients, with a mean age of 36 years ± 13 years. ⁷

And in *Mona Mansour et al*, study Most patients were males (74.65%) with mean \pm SD age of approximately 29.23 \pm 9.48 years.⁸

In analysis of common complains of patients, fever represent the major symptom which present in 52 patients (86.7%), then shortness of breath which present in 45 patients (75%) and finally cough noted in 36 patients (60%).

These results are parallel to *Omar et al*, study results, which states that night fever present in 86% of patients, dyspnea present in 73%, and cough present in 33.3% of patients, also it mentioned that there was anorexia in all patients of study, chest pain in 80% of patients and night sweating in 86% of them.⁶

On other hands, *Anushree et al*, study mentioned that Cough was the most common symptom in the studied patients, appearing in 67 of 75 cases (89 %), only 14 (18.6%) of the participants had minor expectoration, while 53 (81.4%) had a dry cough, 46 (61%) of the patients had chest pain, 42 (56%) had dyspnea, and 57 (76%) of the patients had a fever. Patients reported losing their appetite and weight in 31 (41%) and 28 (37%) cases, respectively.⁷

If we take a look about chest X-Ray results in our study in all studied patients. As regard side and amount of effusion we could figure that it was on the right side in 38 patients (63.3%) and on the left side in 22 patients (36.7%).

And it occupies approximately one hemithorax in 9 patients (15%), two third of it in 34 patients (56.7%) and one third of it in 17 patients (28.3%).

Our results agree with *Muhammad Khalid et al*, study that founds Chest radiology represented right sided pleural effusion in 73%, left sided pleural effusion in 25% and bilateral effusion in 2% of total cases.⁹

Also, *Omar et al*, study give similar results and according to the study, the effusion was on the right side in 7 patients (46.7 %) and the left side in 5 patients (33.3 %), with effusion covering more than half of the hemithorax in 2 patients (13.3 %) and less than half of it in 13 patients (86.7 %).⁶

When we come to the results of our study about pleural fluid examination by Gene Xpert to detect tuberculous pleural effusion, we will observe that it shows negative result in 53 patients (88.3%) and positive in 7 patients (11.7%). On other hands, as regard pleural biopsy results, it was negative in 18 patients (30%) and positive in 42 patients (70%).

So, when we evaluate the diagnostic performance of Gene Xpert in relation to biopsy results, while total studied patients were 60 patients, there were 7 patients (11.7%) true positive, 18 patients (30%) true negative and 35 patients (58.3%) false negative. Thus, Gene Xpert had the sensitivity of 16.7%, specificity of 100%, PPV of 100%, NPV of 33.9% and accuracy of 41.7%.

On comparison of this results to other similar studies we will find that there are close results to our study.

For example, *Porcel et al*, study states that Gene Xpert test in pleural fluid was positive in five patients out of A total of 33 patients with tuberculous pleuritis (21 men and 12 women; mean age 33 years), yielding a test sensitivity of 15% (95% confidence interval [CI] 7–32), a specificity of 100% (95% [CI] 88–100), a positive LR of 11.3 (95% [CI] 0.65–197) and a negative LR of 0.85 (95% [CI] 0.73–0.99) in the detection of TB.¹⁰

In addition, *Galal El-din et al*. found that one patient out of 46 confirmed tuberculous pleuritis cases had a positive Gene Xpert test in pleural effusion (2.2 %), 42 pleural biopsies were found to be positive (91.3%). Meanwhile, pleural tissue Gene Xpert yielded a superior result, detecting 16 positive results (34.8 percent).¹¹

In comparison to other tests, the sensitivity of both the pleural fluid and tissue Gene Xpert tests was poor (2.17 percent for pleural fluid and 36.78 percent for pleural biopsy). Pleural fluid/biopsy mycobacterial culture and pleural biopsy histopathology, on the other hand, have higher sensitivity (>80%) for the diagnosis of tuberculous pleural effusion.¹¹

While, in *Mona Mansour et al*, study 63 of 71 cases were positive for TB pleurisy with respect to the gold standard histopathology report, but the GeneXpert identified positive results in only 16 of 71 cases. The Gene Xpert had higher specificity performance (75%), whereas its sensitivity power was lower (22.2%). The PPV of that test was greater (87.5%), but the NPV was very low (10.9%), and the accuracy of that test in assessing TB pleurisy was also quite low (28.6%) compared with the thoracoscopic biopsy.⁸

In another study, in which there was a comparison between the performance of Gene Xpert and ZN stain in detection of tuberculous pleural effusion with reference to histopathological examination as a gold slandered test, *Omar et al*, study mentioned that out of a total of 27 patients of suspected tuberculous pleural effusion were included in that work, histopathological examination of the patients' pleural biopsies revealed that 15 (55.6%) were positive for tuberculosis and 12 (44.4%) were negative.⁶

With regard to microbiological examination of the pleural fluid samples obtained from the studied patients, they found that, in all patient with negative pleural biopsy for TB, ZN and Gene Xpert examinations were negative. But in those with positive histopathology for TB, only four patients (26.7%) had positive Gene Xpert for TB and two patients (13.3%) had a positive smear examination for TB.⁶

So, Gene Xpert had 26.7% sensitivity and 100% specificity in identifying tuberculous pleural effusion. ZN examination, on the other hand, had 13.3% sensitivity and 100% specificity in identifying tuberculous pleural effusion.⁶

As regard the pleural biopsy results, we found that the biopsy was obtained by either Abrams needle or via medical thoracoscope.

When we observe the results, we will find that for the Abram's needle biopsies only 17 patients out of 30 (56.7%) showed positive results while in biopsies taken by medical thoracoscope there were 25 positive results out of 30 (83.3%), these results show statistically significant difference (p-value < 0.05) between both biopsy methods.

These findings are similar to those of *Diacon et al.*, who found that out of 51 patients with exudative pleural effusion, 42 (82%) had TB, five (10%) had malignancy, and four (8%) had idiopathic exudative pleural effusion. ¹²For Abram's needle biopsy, histology, culture, and combined histology/culture sensitivity were 66 percent, 48 percent, and 79 percent, respectively, and for thoracoscopy, 100 percent, 76 percent, and 100 percent. ¹²

CONCLUSION

Although Gene Xpert is a useful rapid method to diagnose tuberculous pleural effusion, it has a low sensitivity and poor results, also, at present, it has limited availability.

Also, the use of the medical thoracoscopy to obtain pleural tissue biopsy for histopathological examination, gives more positive results than using the Abrams needle.

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