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Original Article

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Yield of gene Xpert in diagnosing patients with pleural tuberculosis presenting to a tertiary care Hospital

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ABSTRACT

BACKGROUND & OBJECTIVE: Pleural tuberculosis is a common type of extrapulmonary tuberculosis and remains a common problem for pulmonologists. Early detection of tuberculosis is a global priority for TB control. Gene Xpert is a real-time PCR, which can reveal Mycobacterium tuberculosis within 2 hours. This study will bridge the gap and help the pulmonologist for deciding on the use of Gene Xpert as diagnostic tool for pleural tuberculosis. Our objective is to find the frequency of positive Gene Xpert among patients of pleural tuberculosis presenting to tertiary care hospital.

METHODOLOGY: A Cross-sectional study was conducted in the Department of Pulmonology, Aziz Fatima Hospital, Faisalabad from 26 February 2022 to 25 March 2022. Total 187 patients ages between 15-80 years having pleural tuberculosis diagnosed during last 6 months were included in the study. Patients already taking anti-tuberculosis therapy were excluded. Pleural fluid was processed in Aziz Fatima Hospital, Faisalabad laboratory for Gene Xpert immediately. Reports were collected next day and noted in the proforma. Positive Gene Xpert as per operational definition. Data was stratified for variables like age, gender, comorbidities (like diabetes mellitus, and smoking status). Chi-square test was applied taking p-value ≤ 0.05 as significant.

RESULTS: Out of 187 patients, mean age was 43.71±14.93 years. 95(50.8%) patients were male and 92(49.2%) patients were females. Positive Gene Xpert was found in 49(26.2%) patients. Out of 72 diabetic patients, 23(31.9%) patients had positive Gene Xpert and out of 115 non-diabetic patients, 26(22.6%) patients had positive Gene Xpert with p-value = 0.158. Out of 82 smoker patients, 27(32.9%) had positive Gene Xpert and out of 105 non-smoker, 22(21%) had positive Gene Xpert with p-value=0.065.

CONCLUSION: Gene Xpert can be used as a reliable investigation for detection of pleural tuberculosis and timely initiation of treatment.

KEY WORDS: Pleural Tuberculosis, Gene Xpert, Anti-Tuberculosis Therapy.

INTRODUCTION

Tuberculosis (TB) remains a global health problem, with 8.7 million new cases reported in 2011 [1]. Pulmonary TB is the most common type of TB but the disease burden of extrapulmonary TB increases to ~50% in high HIV prevalence areas [2]. Pleural TB is a common type of extrapulmonary TB and remains a common problem for pulmonologists. The diagnosis of pleural aspirate requires time consuming and painful procedures. To obtain quick results, nucleic acid amplification tests are increasingly used worldwide for the rapid detection of tuberculosis.

Gene Xpert is a real-time PCR, which has been introduced into high burden areas and is able to detect Mycobacterium tuberculosis within 2 hours [3]. Gene Xpert has been introduced by the WHO as a rapid test for both smear positive and smear-negative respiratory samples [4].

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One study demonstrated about 58.2% of the patients having extrapulmonary tuberculosis were detected positive by Gene Xpert [5] while other study found that about 47% of the patients with pleural tuberculosis were detected positive by Gene Xpert [6].

Another study showed even a lower frequency of pleural tuberculosis patients as positive by Gene Xpert i.e. 22.5%[7]. Thus the data regarding the sensitivity of Gene Xpert for detection of pleural tuberculosis shows considerable variation. Moreover, the reliability of these results is doubtful because of limited sample size and a difference in prevalence of tuberculosis that varies throughout the world while no local data is available. The diagnosis of pleural tuberculosis is difficult and available tests are usually expensive and time-consuming taking days to weeks for diagnosis[8].

The Aim of this study is to find the role of Gene Xpert [9] in detecting patients with pleural tuberculosis presenting to the tertiary care hospital of Faisalabad. This will help the pulmonologist for making decision regarding use of Gene Xpert as diagnostic tool for pleural tuberculosis.

METHODOLOGY

Total 187 patients ages between 15-80 years having pleural tuberculosis diagnosed during last 6 months between 26 February 2022 to 25 March 2022 were included in the study after taking ethical approval (IEC/171-22). Patients already taking anti-tuberculosis therapy were excluded. Sample size of 187 cases is calculated with 95% confidence level, 5% margin of error and taking expected percentage of positive Gene Xpert as 22.5%.

Pleural tap was done using aseptic techniques undertaking standard protocol by the researcher himself and processed in Aziz Fatima Hospital Faisalabad laboratory for Gene Xpert[10] immediately. Reports were collected next day and the results were noted in the proforma. Positive Gene Xpert as per operational definition and Confidentiality of data ensured. Pleural tuberculosis was defined as patients showing one or more caseating granulomas on pleural biopsy report or raised ADA level [11] as having pleural tuberculosis.

Gene Xpert is a real-time PCR used to detect mycobacterium tuberculosis. A report showing any detection of mycobacterium tuberculosis RNA polymerase (rpoB) gene (Qualitative) on pleural fluid sample done with the help of WHO approved Gene Xpert machine, was labeled as positive Gene Xpert. Data entered and analyzed using SPSS v25.0. Numerical variable i.e. age was summarized as mean and standard deviation. Qualitative variables like sex and positive Gene Xpert were presented in the form of frequency and percentages. Data was stratified for variables like age, gender, comorbidities (like diabetes mellitus, and smoking status). chi-square test was applied taking p-value ≤ 0.05 as significant.

RESULTS

Total 187 patients having ages between 15-80 years of either gender already diagnosed pleural tuberculosis during last 6 months were included in the study 95(50.8%) patients were male, while 92(49.2%) patients were females table-I. Out of 187 patients, mean age of the patients was 43.71±14.93 years. Minimum age was 15 years while maximum age was 80 years. Out of 187 patients, 25(13.4%) patients had ages between 15-25 years ,44(23.5%) patients had ages between 26-35 years, 28(15%) patients had ages between 36-45, 33(17.6%) patients had ages between 46-55 and 57(30.5%) patients had age >55 years Table-II.

Out of 187 patients, 49(26.2%) had positive Gene Xpert Table-III. Among patients, 72(38.5%) patients had diabetes mellitus, 82(43.9%) patients were smokers. Maximum number of patients with positive Gene-Xpert were seen in 26 to 35 years of age group (i.e 29 %), while minimum number with positive Gene-Xpert was seen in above 55 years of age group (i.e 14%) out of 95 male patients, 25(26.3%) had positive Gene Xpert and out of 92 female patients, 24(26.1%) patients had positive Gene Xpert with p-value = 0.972 Table-V.

Out of 72 diabetic patients, 23(31.9%) had positive Gene Xpert and out of 115 non-diabetic patients, 26(22.6%) patients had positive Gene Xpert with p-value = 0.158 Table-VI.

Out of 82 smoker patients, 27(32.9%) patients had positive Gene Xpert and out of 105 non-smoker patients, 22(21%) had positive Gene Xpert with p-value=0.065 Table-VI.

Table-I: Frequency distribution of gender.

Gender	n (%)
Male	95(50.8)
Female	92(49.2)
Total	187

Table-II: Frequency distribution of age.

Age groups	n (%)
15 to 25	25 (13.4)
26 to 35	44 (23.5)
36 to 45	28 (15)
46 to 55	33 (17.6)
Above 55	57 (30.5)

Table-III: Frequency distribution of positive Gene Xpert.

Positive Xpert MTB/RIF assay	n (%)
Yes	49(26.2)
No	138(73.8)
Total	187

Table-IV: Table of association among the age and Gene Xpert.

		Positive Result		Total
		Yes	No	
Age	15 to 25	7	18	25(13.4%)
	26 to 35	13	31	44(23.5%)
	36 to 45	9	19	28(15.0%)
	46 to 55	12	21	33(17.6%)
	Above 55	8	49	57(30.5%)
Total		49	138	187(100%)

Chi-square value = 6.933 **p-value = 0.139**

Table-V: Table of association among the gender and Gene Xpert.

		Positive Result		Total
		Yes	No	
Gender	Male	25	70	95(50.8%)
	Female	24	68	92(49.2%)
Total		49	138	187(100%)

Chi-square value = 0.001 **p-value = 0. 972**

Table-VI: Table of association among the diabetic, smokers, HIV patients and Gene Xpert.

Variables	Positive Result		Total	Chi–Square value	p-value
	Yes	No			
Diabetic	23	49	72(38.50%)	1.996	0.158
Non-Diabetic	26	89	115(61.50%)		
Smokers	27	55	82(43.85%)	3.414	0.065
Non-Smokers	22	83	105(56.15%)		

DISCUSSION

Tuberculosis (TB) is a major health problem worldwide. Pleural TB is the second most common type of extrapulmonary Tuberculosis [12]. Diagnosis of pleural TB is made with examination of pleural fluid and/or biopsy specimens using ZN staining, AFB culture, PCR, evaluation of pleural fluid characteristics, and/or histopathology. However, these methodologies are time taking and have different sensitivities. There is a great need for a rapid detecting technique.

In December 2010, the World Health Organization (WHO) introduce GeneXpert for the rapid diagnosis of TB and multidrug-resistant TB (MDR-TB) [13]. Gene Xpert is capable of detecting the Mycobacterium tuberculosis and detecting rifampicin resistance in <2 h. Several studies have assessed the Gene Xpert in pulmonary TB and a meta-analysis of 16 studies gave combined sensitivity of 90% and specificity of 98%.

Results of study revealed mean age of the patients was 43.71±14.93 years. Most of the patients (30.5%) had age >55 years. There were 50.8% males and 49.2% females. Positive Gene Xpert was found in 26.2% patients. Positive Gene Xpert was equally common among all age groups (p-value = 0.139), both gender (p-value=0.972), diabetic patients (p-value =0.158) and smokers (p-value=0.065).

One study showing comparison of same day diagnostic tools including Gene Xpert and unstimulated IFN-γ for the evaluation of pleural tuberculosis. According to their results, positive Gene Xpert was found in 22.5%[7,14].

Other study conducted on rapid diagnosis of pleural tuberculosis by Gene Xpert using pleural biopsy and pleural fluid samples. Positive Gene Xpert was present in 85.7%[15]. They concluded that Gene Xpert on pleural biopsy specimens may provide an accurate diagnosis of pleural TB.

Another study conducted on Gene Xpert for diagnosis of pleural tuberculosis. The results of their study showed that 25% patients had positive Gene Xpert[16]. They concluded that Gene Xpert on pleural fluid is feasible but has low sensitivity and is linked to a positive pleural fluid culture.

One Pakistani study conducted on Gene Xpert–diagnostic role in tuberculous pleurisy [17]. The results of their study showed that 12% patients had positive Gene Xpert. They concluded that Gene Xpert is a useful new rapid technique to diagnose tuberculous pleurisy[17].

CONCLUSION

Gene Xpert is a simple test which provides results in just 2 hours as compared to other diagnostic tests which takes time from days to weeks. Gene Xpert MTB/RIF can be used as a reliable investigation for diagnosing pleural tuberculosis and initiation of treatment leading to decrease in time of diagnosis on a resource limited country.

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REFERENCES

1. World Health Organization: WHO: Global Tuberculosis Report 2012. Geneva, Switzerland: WHO. 2012:100.
2. Light RW: Update on tuberculous pleural effusion. Respirology. 2010;15(3):451–458.
3. Theron G, Peter J, Van Zyl-Smit R, Mishra H, Streicher E, Murray S, et al. Evaluation of the Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in a high HIV prevalence setting. American Journal of Respiratory and Critical care Medicine. 2011;184(1):132-140.
4. World HealthOrganization: Report of the Tenth Meeting WHO Strategic and Technical Advisory Group for Tuberculosis (STAG-TB). Geneva: World Health Organization. 2010:27–29.

5. Özkütük N, Sürücüoğlu S. Evaluation of the Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary Tuberculosis in an Intermediate-Prevalence Setting. Mikrobiyol Bul. 2014;48(2):223-232.
6. Scott LE, Beylis N, Nicol M, Nkuna G, Molapo S, Berrie L, et al. Diagnostic accuracy of Xpert MTB/RIF for extrapulmonary tuberculosis specimens: establishing a laboratory testing algorithm for South Africa. Journal of Clinical Microbiology. 2014;52(6):1818-1823.
7. Meldau R, Peter J, Theron G, Calligaro G, Allwood B, Symons G, et al. Comparison of same day diagnostic tools including Gene Xpert and unstimulated IFN-γ for the evaluation of pleural tuberculosis: a prospective cohort study. BMC Pulmonary Medicine. 2014;14(1):1-0. Doi:10.1186/1471-2466-14-58
8. Elbrolosy AM, El Helbawy RH, Mansour OM, Latif RA. Diagnostic utility of GeneXpert MTB/RIF assay versus conventional methods for diagnosis of pulmonary and extra-pulmonary tuberculosis. BMC Microbiology. 2021;21(1):1-0. Doi:10.1186/s12866-021-02210-5
9. Liang Q, Pang Y, Yang Y, Li H, Guo C, Yang X, et al. An improved algorithm for rapid diagnosis of pleural tuberculosis from pleural effusion by combined testing with GeneXpert MTB/RIF and an anti-LAM antibody-based assay. BMC Infectious Diseases. 2019;19(1):1-8. Doi:10.1186/s12879-019-4166-1
10. Enas M, Mona I, Abdelrahman M, Doaa Y. Utility of GeneXpert MTB/RIF assay for the diagnosis of pulmonary and extra-pulmonary tuberculosis, A report from Egypt. Novel Research in Microbiology Journal. 2021;5(1):1146-1161.
11. MacLean E, Kohli M, Weber SF, Suresh A, Schumacher SG, Denkinger CM, et al. Advances in molecular diagnosis of tuberculosis. Journal of Clinical Microbiology. 2020 ;58(10):e01582-01519.
12. Mechal Y, Benaissa E, Benlahlou Y, Bssaibis F, Zegmout A, Chadli M, et al. Evaluation of GeneXpert MTB/RIF system performances in the diagnosis of extrapulmonary tuberculosis. BMC Infectious Diseases. 2019;19(1):1-8. Doi:10.1186/s12879-019-4687-7
13. Rahman H, Khan SU, Khan MA, Qasim M, Jabbar A, Noor S, et al. Molecular detection of rifampicin resistance by GeneXpert® assay among treated and untreated pulmonary tuberculosis patients from Khyber Pakhtunkhwa, Pakistan. Journal of global antimicrobial resistance. 2017;9:118-120. Doi:10.1016/j.jgar.2017.02.013
14. Du J, Huang Z, Luo Q, Xiong G, Xu X, Li W, et al. Rapid diagnosis of pleural tuberculosis by Xpert MTB/RIF assay using pleural biopsy and pleural fluid specimens. Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences. 2015;20(1):26-31.
15. Friedrich SO, Von Groote-Bidlingmaier F, Diacon AH. Xpert MTB/RIF assay for diagnosis of pleural tuberculosis. Journal of clinical microbiology. 2011;49(12):4341-4342. Doi: 10.1128/JCM.05454-11
16. Ch MK, Saeed MS, Iqbal R, Ali A. Gene Xpert MTB/RIF–Diagnostic Role in Tuberculous Pleurisy. Annals of King Edward Medical University. 2016;22(1):78-78. Doi:10.21649/akemu.v22i1.803
17. Shaw JA, Diacon AH, Koegelenberg CF. Tuberculous pleural effusion. Respirology. 2019;24(10):962-971. Doi: 10.1111/resp.13673

Author's Contribution:

Awais Aslam: Made concept & study design, analysed data, revisited critically and made final approval of version.
Istikhar Ali Sajjad: Analysed data.
Abdul wajid khan: Made concept & study design, revise critically and made final approval of version.
Hafiz Muhammad Taha Waqas: Made concept & study design, revisited critically and made final approval of version.
Zara Saleem: Revised critically and made final approval of version.
Hina Imtiaz: Analysed data, revisited critically and made final approval of version.

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