Comparative diagnostic efficacy of Gene Xpert MTB/RIF, AFB Smear and Culture in the diagnosis of Tuberculous Pleural Effusion

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MKC RI conceived idea, MKC AH drafted the study, RI AH collected data, AH MKC did statistical analysis & interpretation of data, MKC RI critical reviewed manuscript, All approved final version to be published.

Declaration of conflicting interests

The Authors declares that there is no conflict of interest.

Abstract

Background: Tuberculosis is a life-threatening disease worldwide whereas pleural effusion is second common presentation as regard to extrapulmonary TB. Present study was conducted to see the efficacy of Gene Xpert MTB/RIF, AFB smear by microscopy and culture to diagnose tuberculous pleurisy.

Methodology: This cross-sectional study was conducted at institute of chest medicine/PHRC King Edward Medical University during the period January 2017 to January 2019. Inclusion criteria consist, no gender distinction, no age limit, patients who have never taken ATT and exudative, lymphocytic predominant with high adenosine deaminase (ADA) level >40 IU/L in pleural effusion. Informed consent was taken to get the sample of 120 cc pleural fluid from each patient. A 20cc fluid from each patient was analyzed for biochemistry, cytology and ADA level. The remaining (100cc) sample was processed by PHRC lab for Gene Xpert MTB/RIF, ZN staining and culture. The data was processed by SPSS.

Results: A total number of 150 cases of exudative lymphocytic with high ADA level in pleural effusion were included, of which 104 were males, and 46 were females. Age range was between 18 - 79 years with mean age of 37.1 ± 16.5years for males and for females it was between 16 - 70 years with mean age of 32.3 ± 14.3 years. ZN staining was positive in 12 (8%) patients and culture was positive in 18 (12%) cases, MTB was detected by Gene Xpert in 28 (18%) and RIF resistance was positive in 4 (50% of each were male and female) patients.

Conclusion: Diagnostic efficacy of both smear and culture is low as compared to Gene Xpert but these techniques are of great use in the confirmation of diagnosis of tuberculous pleurisy.

Key Words: Xpert MTB/RIF; Pleural Effusion; Rifampicin Resistance

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Introduction

Tuberculosis is a common infectious disease which can lead to death. It is one of the top ten causes of deaths globally.[1] Pulmonary TB is the most common presentation of Tuberculosis while pleural effusion is the second common presentation as regards extra pulmonary TB.[2] Diagnosis of Tuberculous pleural effusion depends mainly on detection of Mycobacterial tuberculosis in the Pleural fluid or microbiological culture or histopathology of pleura. These methods are invasive, laborious, time consuming and insensitive.

Demonstration of Acid fast bacilli by microscopy and culture is a traditional method which is in use for many years. Pleural fluid is a paucibacillary sample. The

sensitivity of pleural fluid microscopy is about 10% and of culture is about 20% respectively.[3]

Gene Xpert MTB/RIF assay is a new technique, which is an automated cartage based nucleic acid amplification test for MTB. This technique has the capability to detect not only mycobacterium tuberculosis nucleic acid but also resistance to Rifampicin in less than two hours. WHO has recommended this technique for the diagnosis of Pulmonary and extrapulmonary TB for initial screening of suspects having MDR resistance and HIV coinfection.[4] Most of the times sputum is used for screening and there are relatively scares studies using other types of samples like pleural fluid and CSF etc.

Studies using Xpert MTB/RIF in the diagnosis of tuberculous effusion have variable sensitivity and specificity ranging from 13 to 100%.[5,6]

The purpose of this study is to compare the efficacy of Gene Xpert MTB/RIF, AFB microscopy and culture in the diagnosis of Tuberculous pleural effusion.

Methodology

This cross-sectional study was conducted at institute of chest medicine/PHRC King Edward Medical University during the period January 2017 to January 2019. A total 150 cases were included in this study. Amongst these 104 were males and 46 were females with mean age of 36.4 years and 32.3 years of males and females respectively. Informed consents was taken to get the sample of 120cc pleural fluid from each patient. 20cc fluid was sent for biochemistry, cytology and ADA. The remaining sample was divided into two and sent to PHRC lab for processing by Genexpert MTB/RIF, ZN staining and culture on LJ media. Only those cases of pleural fluid were included in the study who have exudative pre-dominantly lymphocytic with high ADA level (>40IU/L). The data was processed by SPSS.

Results

Study comprised of 150 cases of pleural effusion. Amongst these 104 were males and 46 were females Figure 1 gender distribution. The mean age was 37.1±16.5 years and 32.3±14.3 years of males and females respectively. Initial diagnosis of Tuberculous Pleural Effusion was made by pleural fluid analysis that include biochemistry cytology and ADA level which is shown in table 1 & 2.

Figure 1: Gender Distribution of study subjects

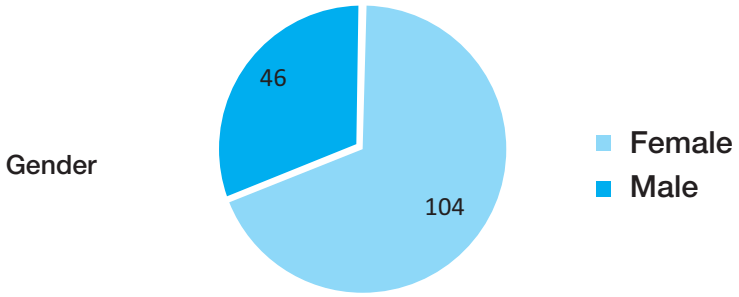

Table 1: Biochemistry of Pleural fluid

1	Protein	3.2 to 7.4 g/DL
2	LDH	320-700U/l
3	ADA	>40IU/L

Table 2: The cytology of pleural fluid among study cases

Lymphocyte Count	No. of Cases
90 - 100%	58 %
80 - 89%	42 %
70 - 79%	25 %
60 - 90%	15 %
55 - 59%	10 %

Out of total 150 cases, 12 (8%) were positive for AFB by ZN staining, amongst AFB positive cases 8 (75%) were males and 4 (25%) were females. The culture was positive in 18 (12%) cases. Amongst culture positive patients were 12(75%) males and 6 (25%) were females. All smear positive cases were culture positive table 3.

Gene Xpert MTB/RIF detected mycobacteria Tuberculosis in 28 (18%) cases. Amongst these 28 cases 18 (64%) were males and 10 (36%) were females. Rifampicin resistance was detected in 4 (2.6%) cases. Amongst 4 (14.8%) rifampicin resistance detected cases 2(50%) of each were male and female as in table 3.

Table 3: Finding of study cases

Parameter	Male N (%)	Female N (%)	Total N(%)
ZN Smear Positive	8 (75)	4 (25)	12 (8)
AFB Culture Positive	12 (75)	6 (25)	18 (12)
MTB Detected by Gene Xpert	18 (64)	10 (36)	28 (18)
Rif Resistant In Gene Xpert Detected	2 (50)	2 (50)	4 (14.8)

Discussion

Tuberculous pleurisy is one of the most common type of extrapulmonary TB which is about one fourth of all extra pulmonary TB cases. It may occur either as primary or reactive disease.[7] Initially it was thought that TB pleurisy is a delayed hypersensitivity reaction but now it is believed that it is due to direct infection of pleura with mycobacterial tuberculosis which results in lymphocytic derived immunological response. This concept has increased the importance of detection of Mycobecteria tuberculosis in the pleural fluid and pleural tissue. So detection of Mycobacteria tuberculosis in the pleural fluid and pleural biopsy by either microscopy or culture or by Gene Xpert MTB/RIF and histopathology of the pleura are the gold standard for diagnosis of Tuberculous pleurisy. Gene Xpert MTB/RIF is relatively new technique which not only detects the MTB but also resistance to Rifampicin. Drug resistance TB is a new emerging issue for the treatment of tuberculosis.

Our study shows positive smear microscopy in 12 (8%) cases with male to female proportion of 2:1. Culture was positive in 18 (12%) cases with male to female proportion 2:1. Comparing with the results of the study conducted by Diacon AH et al. where smear positivity was 10% and culture was 20% respectively.[3] Another study conducted by Qing Zhang et al. shows AFB smear positivity of 3.1% and culture positivity of 17.8%.[8] If we compare the results of these studies with our study the yield of microscopy and culture is match-able with our results.

As regards Gene Xpert results of our study, there are 28 (18%) cases with male to female proportion of 64% and 36%. The drug resistance (RR) was detected in 14.8% with male to female proportion of 50% and 50% respectively from MTB detected cases. The pooled sensitivity shown in the study by Inderpaul Singh Sehgal et al. is 22.7%.[9] Another study conducted by Zhen-YU Huo et al. in which pooled sensitivity of Gene Xpert MTB/RIF was 30% on the basis of meta-analysis of 23 studies.[10] Comparing with the above mentioned studies, it is obvious that the yield of Gene Xpert MTB/RIF is low but it has advantage that it indicates the drug resistance also which is an emerging issue of the present era and the results available with two hours.

Comparing the results of pleural fluid microscopy, culture and Gene Xpert MTB/RIF we can conclude that diagnostic efficacy of both these investigations is low but these techniques are of great use in the confirmation of diagnosis of tuberculous pleurisy. They are also useful in the sense that they are minimally invasive techniques and are easily available at different centers of developing world, moreover drug resistance is detected in addition to diagnosis of MTB.

Conclusion:

Each of the three procedures have its own importance but for fast and initial diagnostic process Gene Xpert is of much importance as by use of Gene Xpert treatment of patients start as soon as possible and this procedure play important role in achieving the successful outcome.

References

1. WHO TB Key facts sheet. [updated18 September 2018, Cited August 2019] Available from URL:[https://www.who.int/news-room/fact-sheets/detail/tuberculosis].
2. Light RW. Update on Tuberculous Pleural effusion. Respirology 2010;15;451-458.doi 10.1111/j.1440-1843.2010.

3. Diacon AH, Van de Wal BW, Wayser C, Smedema JP,Bezuidenhout J, et al. Diagnostic tools in tuberculous pleurisy: a direct comparative study. Eur Respir J 2003:589-591.

4. World Health Organization. Automated real-time mucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system/2011. 26 May 2018

5. Causse M, Ruiz P, Gutiérrez-Aroca JB, Casal M. Comparison of two molecular methods for rapid diagnosis of extrapulmonary tuberculosis. Journal of clinical microbiology. 2011 Aug 1;49(8):3065-7.

6. Wang D, Chen Z, Chen Q, Zhang G. Evaluation of GeneXpert MTB/RIF assay for diagnosis of tuberculous pleurisy and detection of rifampin resistance. Int J Respir. 2015;35:1071-3.

7. Kian HJ, Lee HJ, Kwon SY, Yoon HI, Chung HS, Lee CT, Han SK, Shim YS, Yim JJ. The prevalence of pulmonary parenchymal tuberculosis in patients with tuberculous pleuritis. Chest. 2007;131:1125-32

8. Zhang Q, Zhou C. Comparison of laboratory testing methods for the diagnosis of tuberculous pleurisy in China. Scientific reports. 2017 Jul 3;7(1):4549.

9. Sehgal IS, Dhooria S, Aggarwal AN, Behera D, Agarwal R. Diagnostic performance of Xpert MTB/RIF in tuberculous pleural effusion: systematic review and meta-analysis. Journal of clinical microbiology. 2016 Apr 1;54(4):1133-6.

10. Huo ZY, Peng L. Is Xpert MTB/RIF appropriate for diagnosing tuberculous pleurisy with pleural fluid samples? A systematic review. BMC infectious diseases. 2018 Dec;18(1):284.