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Diagnostic accuracy of BAL Gene Xpert compared to BAL AFB staining in Sputum negative Pulmonary Tuberculosis Suspects

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ABSTRACT

Tuberculosis has stood the test of time over the millennia and still wreaks havoc on human life all over the world. We have studied the role of bronchoscopy in smear negative PTB suspects and have compared the results of BAL Gene Xpert with BAL AFB staining among the study population. We have also determined the microbiological profile in cases who are MTB negative. We retrospectively reviewed the respiratory samples (sputum and BAL) of 82 sputum negative PTB suspects from july 2018 – july 2019 for ZN stain and Gene Xpert. 25 cases were detected by Gene Xpert additionally to the 11 cases detected by BAL afb staining alone. Out of the 36 cases detected on gene Xpert 3(8%) were RIF resistant. These 5 samples which were positive on BAL AFB and negative on Gene Xpert, are suspected to be NON TB mycobacteria. Out of the remaining 41 samples, non TB culture results showed 8 Acinetobacter, 10 pseudomonas, 12 klebsiella, 2 e.coli, 2 candida, 7 no growth on culture. According to our study, the bronchoscopic samples when subjected to Gene Xpert detect a higher number of cases which would go undetected otherwise compared to BAL AFB staining. Hence, bronchoscopy must be performed on such smear negative suspects and Gene Xpert could replace smear microscopy as initial diagnostic testing. It also helps in detecting first line drug resistance in addition.

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INTRODUCTION

Tuberculosis, an important preventable and treatable cause of death, is a major health issue worldwide. Detecting cases with pulmonary tuberculosis is an important component in starting early appropriate treatment and interrupting the chain of transmission in such cases. Although sputum smear is a low cost test implemented by RNTCP, Gene Xpert has emerged as a highly specific and sensitive test in detecting pulmonary tuberculosis within a matter of hours (Agrawal *et al.*, 2016). Whereas mycobacterial culture take about 6-8 weeks time (Evans, 2011) during which valuable time is lost in initiating treatment. Bronchoscopy is one of the newer methods in obtaining samples from "sputum smear negative PTB" (Bachh *et al.*, 2010). Reasons for sputum smear negativity include poor quality of sputum sample, deficient preparation or staining, or examination or very low bacterial load. Although persons with smear negative TB have less bacterial load their potential to transmit disease is higher in the long run as they have the propensity to go undetected for a longer duration. Conversely, correct prediction of persons who are unlikely to have TB is important

as well to limit the expense and potential toxicity of empiric therapy.

Aim

1. To study the role of bronchoscopy in smear negative PTB suspects
2. To compare the result of BAL Gene Xpert with BAL AFB staining among study population
3. To determine the microbiological profile in cases who are MTB negative.

MATERIALS AND METHODS

This is a Retrospective study conducted in the department of Pulmonary medicine, Saveetha medical college and hospital, Chennai between period of July 2018- july 2019. The study population included all sputum negative cases/ sputum scarce patients suspected radiologically and / or clinically to have pulmonary tuberculosis. Bronchoscopy was done and BAL was subjected to AFB staining, Gene Xpert, and Non TB culture and results were recorded. Outcome measures of the study was to compare the results of Gene Xpert over AFB staining of the Bal samples so that the suspected cases are initiated on early treatment thus reducing morbidity and mortality and hence reducing undue spread. Graph development and percentage calculation was done using spreadsheets .

Bal AFB and non TB culture was done in the department of microbiology, Saveetha medical college. Gene Xpert of the BAL samples were sent to Hitech labs poonamalee for reporting in a sterile falcon tube and transported in a cold chain box.

Inclusion Criteria

Patients with clinical suspicion of Pulmonary tuberculosis including symptoms of cough with or without expectoration for >2 weeks, weight loss, fatigue , hemoptysis and loss of appetite with/ without radiological lesions like non homogenous opacities, nodules, hilar enlargement or consolidation with air bronchogram. Subjects must have had no sputum production or two sputum AFB samples negative and ,must have been subjected to Flexible optic bronchoscopy and samples sent for AFB staining, Gene Xpert, non TB culture.

Exclusion Criteria

1. Samples for which gene Xpert was not done.

2. Patient diagnosed with other lung conditions like lung malignancies

3. Samples for which history not available.

RESULTS AND DISCUSSION

Out of the total 82 subjects, 56(68%) were males, 26(32%) were females (Figure 1) Out of the total samples 16(20%) were BAL AFB positive (Figure 3). Out of the 66(80%) BAL negative samples, 25 were positive for MTB on gene xpert. Out of total 82 subjects gene xpert was positive in 36(44%) and Mtb not detected in 44(54%),1 (1%)invalid, 1(1%) error (Figure 2).

Hence 25 cases were detected by agent Xpert in addition to the 11 cases detected by BAL afb staining alone (Figure 4). Out of the 36 cases detected on gene xpert 3(8%) were rif resistant (Figure 5).

5 samples were positive on BAL AFB and MTB not detected on gene expert. These 5 samples are suspected to be NON TB mycobacteria. Out of the remaining 41 samples , non TB culture results showed 8(20%) Acinetobacter, 10(24%) pseudomonas, 12(29%) klebsiella, 2(5%) e.coli,2(5%) candida, 7(17%) no growth on culture (Figure 6). Out of the 36 cases detected on gene xpert 16(44%) had non homogenous opacities ,9(25%) had homogenous opacities with air bronchograms, 6(17%) had cavities,3(8%) had nodules,2(6%) had hilar enlargement on chest skiagram (Figure 7).

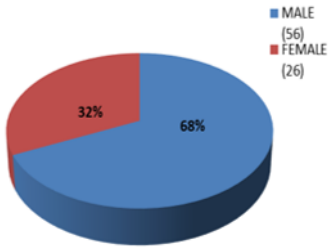

Figure 1: Gender Distribution of Study Population

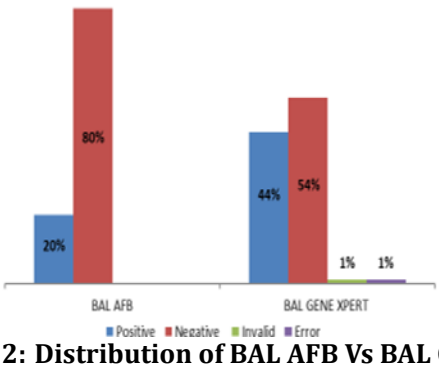

Figure 2: Distribution of BAL AFB Vs BAL Gene Xpert

The aim of this study is to determine the diagnostic superiority of gene xpert over traditional stain-

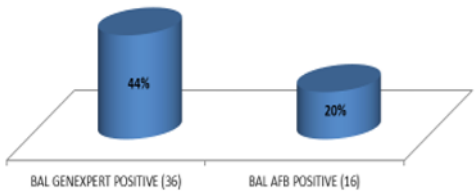

Figure 3: Comparison of BAL GenexpertVS BAL AFB

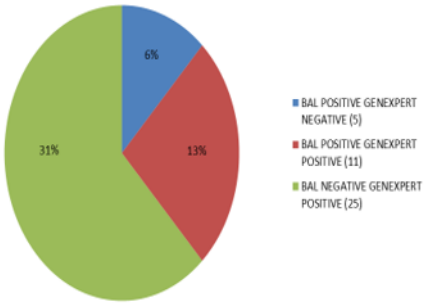

Figure 4: Comparison of BAL Genexpert Vs BAL AFB

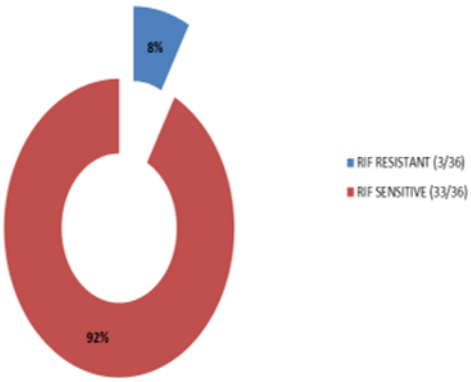

Figure 5: Rifampicin Resistance Vs Sensitivity

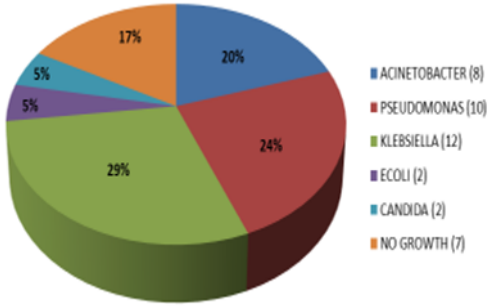

Figure 6: Distribution of Microbiological Culture of BAL AFB Negative Samples

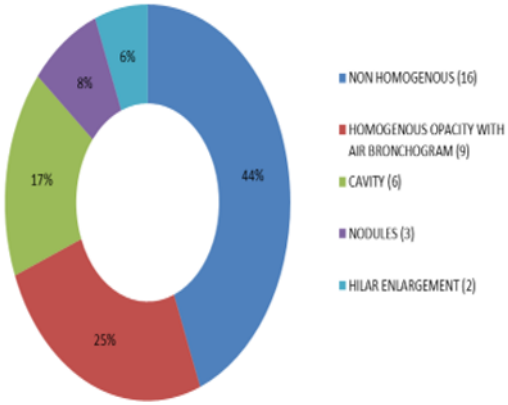

Figure 7: Radiological Profile Among PTB Cases Detected by Gene Xpert

ing methods like AFB. The recent guidelines recommend gene xpert in all sputum positive cases (Xpert, 2013). But through this study we recommend gene xpert in highly suspicious cases (either clinically or radiologically) to detect more cases.

The results of our study show that Gene Xpert has higher yield than AFB smear in sputum negative / sputum scarce pulmonary tuberculosis cases. The conventional AFB staining can miss sputum with low bacterial load as microscopy needs at least 10,000 bacilli/ml for direct microscopy to show a positive result (Mavenyengwa *et al.*, 2017).

Gene Xpert is a simple assay which can be performed with minimal training and results can be obtained in a couple of hours (Khalil *et al.*, 2015). Gene Xpert has helped us in identifying such cases which tend to go undetected and hence have the propensity to go untreated. Such cases can continue spreading TB in the community in the long run. By doing a FOB wash we also detect cases earlier than the time when they eventually turn to be sputum positive. These cases, before detection, have the probability to spread the disease to a few contacts.

Among the BAL samples 25 cases (31%) were detected by Gene xpert while it was missed by AFB staining. This is comparable to a study by Iyer VN et al who also had similar percentage of TB cases detected from BAL gene Xpert testing (Iyer *et al.*, 2011).

Another important factor, RIF resistance was found among 3(8%) of the PTB positive cases. This is comparable to a study by H.Y Lee et al, where they had demonstrated Rif resistance in 2 of the 35 positive cases (Lee *et al.*, 2013).

According to a study by Y.MOK et al in Singapore, BAL gene xpert also lessens the requirement for invasive like procedures Transbronchial biopsy to prove TB affliction. The same proved true for our

study subjects who underwent bronchoscopy due to PTB suspicion (Mok *et al.*, 2016).

Out of the remaining samples which were negative for PTB both by Gene Xpert and AFB smear, we followed up the non-Tb culture results and found Klebsiella(29%) to be the most common organism grown in culture followed by pseudomonas(24%)and Acinetobacter (20%) respectively.

We also analysed the radiological profile among the 36 cases detected on Gene Xpert and found that 44%had non homogenous opacity, 25 % had homogenous opacity with air bronchogram, 17% had cavitation, 8% had nodules and 6 % had hilar enlargement. In a study done by Deependra k rai et al patchy infiltrates and cavitation was observed in sputum positive compared to sputum negative cases, but in our study we could not make that comparison as we have studied only sputum negative PTB suspects (Rai *et al.*, 2019).

Bronchoscopy contraindications are relative and if performed by an experienced bronchoscopist the risks of bleeding, injury and discomfort to patient etc can be minimized and benefits will outweigh the risks.

Limitations

Tb Culture was not performed to rule out possibility of false positive results, however Xpert / MTB/RIF have shown specificities above 95%in previous studies (Policy statement, 2011).

CONCLUSIONS

FOB should be advised in clinically/ radiologically suspected PTB cases and the BAL should be subjected to Xpert MTB/RIF assay along with AFB staining. We have showed in our study, that Xpert MTB/RIF assay has helped us detect PTB in 31% of the suspects, which went undetected by BAL AFB staining alone. This is particularly helpful in detecting patients who could go untreated for a long period of time but meanwhile continue spreading TB in the community.

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The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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