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Study of the diagnostic yield of sputum CBNAAT in HIV-positive clinically suspected pulmonary tuberculosis

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Abstract
The main reason for this high mortality is the lack of proper diagnosis at the right time. This is particularly important in patients with HIV and TB co-infection; especially with extra pulmonary TB as the detection rates are low. There is an urgent need to implement newer diagnostic modalities for the detection of TB especially in highly HIV prevalent areas. Patients satisfying inclusion criteria i.e. HIV positive patients clinically and/or radiologically suspected of pulmonary tuberculosis whose sputum AFB is reported negative were subjected for CBNAAT. This was done with the intention of identifying yield of CBNAAT over microscopy. Among patients with abnormal chest x-ray, 84.6% had positive CBNAAT while in those with normal chest X-ray, 81.1% had negative CBNAAT. Hence majority of patients with abnormal chest X-ray findings had positive CBNAAT while majority of those with normal chest x-ray had negative CBNAAT.
Keywords: CBNAAT, Hiv-positive, pulmonary tuberculosis

Introduction

Tuberculosis (TB) is a leading cause of morbidity and mortality, and is currently listed as the fourth most common cause of death among communicable diseases worldwide[1].There are about 9 million global cases of newly detected tuberculosis every year, out of which 24% is from India. Being one of the most common opportunistic infections in HIV, prevalence of TB in HIV patients in India stands at around 17%. The mortality in HIV due to TB is increasing, and was reported to be at 36 million deaths worldwide in 2019.

The main reason for this high mortality is the lack of proper diagnosis at the right time. This is particularly important in patients with HIV and TB co-infection; especially with extra pulmonary TB as the detection rates are low. There is an urgent need to implement newer diagnostic modalities for the detection of TB especially in highly HIV prevalent areas. It is high time that a test is selected which can detect pulmonary TB in HIV patients rapidly and with maximum reliability[2].

Conventionally, sputum microscopy is used to detect tuberculosis in India. CBNAAT is a newer technique using real-time PCR for tuberculosis detection and rifampicin resistance. WHO first introduced CBNAAT in 2010, and in India, the RNTCP program introduced CBNAAT in 2013.

MDR tuberculosis is defined as tuberculosis resistant to isoniazid and rifampicin. WHO reports estimate that 51% of MDR TB cases are underdiagnosed in India in 2019, which could be attributed to the lack of appropriate facilities. CBNAAT also known as GeneXpert, simultaneously detect TB and rifampicin resistance in <2 hours with minimal biosafety and training requirement[3].

In developing countries like India, the availability of test and cost-effectiveness should be taken into consideration. Although sputum culture is considered to be the gold standard in pulmonary tuberculosis, the time taken for the culture results cause the treatment to be delayed. Another problem in HIV patients with pulmonary tuberculosis is that due to the

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lesser caseation, the amount of sputum produced is less as well. The concentration of bacilli in sputum of HIV patients with pulmonary TB is also less[4].
The accurate points of care diagnostic test should be one or a combination of some, which are affordable to the nation. It should also be able to detect the burden of tuberculosis with good sensitivity and specificity, without compromising the time delay in diagnosis and hence, treatment. Therefore, it is important to assess the diagnostic yield of newer techniques like CBNAAT over conventional microscopy.

Methodology

Source of data

A total of 50 patients from those attending medicine OPD and getting admitted under medicine wards were taken for study considering the inclusion and exclusion criteria.

Sample size: 50.

Study method: Prospective Study.

Sample technique: Simple Random Sampling.

Method of collection of data

The data was collected from the patients by the detailed clinical history, clinical examination of the patients and relevant investigation in a specially designed proforma.

Case history

1. Patients were assigned a case number, and their name, age, sex, weight and height were noted. BMI was also calculated.
2. Detailed history of the presenting complaints was noted.
3. Total duration on ART treatment.
4. History of pulmonary tuberculosis in the past.

Investigation

1. Sputum AFB.
2. Sputum CBNAAT.
3. Chest X-ray.
4. CD4 count.

Inclusion criteria

1. Age group between 15 to 40 years.
2. HIV positive cases.
3. History of fever, cough with expectoration more than two weeks, hemoptysis, significant weight loss.
4. Radiological features suggestive of pulmonary tuberculosis.
5. Cases with negative sputum microscopy.

Exclusion criteria

1. Age <15yrs.
2. Sputum microscopy AFB positive cases.
3. Extrapulmonary tuberculosis.

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Patient evaluation

Patients satisfying inclusion criteria i.e. HIV positive patients clinically and/or radiologically suspected of pulmonary tuberculosis whose sputum AFB is reported negative were subjected for CBNAAT. This was done with the intention of identifying yield of CBNAAT over microscopy.

Sputum sample, spot sample was utilized for the Xpert MTB/RIF assay using the GeneXpert MTB/RIF version G4.

The sputum samples were treated with a sample reagent (SR) containing sodium hydroxide and isopropanol. The SR was added to the sample in a ratio of 2:1 and incubated at room temperature for 15 min. The treated sample is then manually transferred to the cartridge which is loaded into the GeneXpert instrument. A printable test result was obtained after 1hour 45 minutes.

Results

Table 1: Distribution based on CBNAAT results

Distribution of study subjects based on CBNAAT results		
CBNAAT	**Frequency**	**Percent**
Negative	37	74
P-low	6	12
P-medium	5	10
P-high	2	4
Total	50	100

Table 2: Distribution of patients with positive CBNAAT results

Distribution of patients with positiveCBNAAT results		
Positive	**Frequency**	**Percent**
Low	6	46.2
Medium	5	38.5
High	2	15.4
Total	13	100

Among the patients tested positive for sputum CBNAAT, the majority (46.2%) were in the low category based on CT values while 15.4% reported as high.

Table 3: CBNAAT versus CD4 count

CBNAAT1 versus CD4 count among the patients					
CBNAAT1	**CD4ct (1-200)**		**CD4 ct (201-2000)**		**P Value**
	Frequency	**Percent**	**Frequency**	**Percent**	
Negative (n=37)	3	8.1	34	91.9	<0.0001
Positive (n=13)	10	76.9	3	23.1	
Total (n=50)	13	26.0	37	74.0	

In this study, among CBNAAT negative patients, majority of the cases -91.9%, had CD4 counts above 200, while in CBNAAT negative patients majority cases -76.9%, had CD4 counts below 200 and this was statistically significant with p value of <0.0001.

Hence a positive correlation between lower CD4 counts and CBNAAT positivity was found.

Table 4: CBNAAT versus chest x-ray

CBNAAT versus Chest X ray among the patients					
CBNAAT1	**CXR abnormal**		**CXR normal**		**P Value**
	Frequency	**Percent**	**Frequency**	**Percent**	
Negative (n=37)	7	18.9	30	81.1	<0.0001

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Positive (n=13)	11	84.6	2	15.4	
Total (n=50)	18	36.0	32	64.0	

Among patients with abnormal chest x-ray, 84.6% had positive CBNAAT while in those with normal chest X-ray, 81.1% had negative CBNAAT.
Hence majority of patients with abnormal chest X-ray findings had positive CBNAAT while majority of those with normal chest x-ray had negative CBNAAT.

Discussion

In the present study of 50 PTB with HIV co-infection, 52% were males, 48% were females. The male-predominance noted in the present study was similar to that observed in other studies. In a study by Patel.*et al*. [5], 82% of the patients were male and 18% were female and in the study by Praveen Kumar *etal*.[6], male patients were 90.5% and female were only 9.5%. But Purushottam*et al*. [7]observed that male patients were 58% and female were 42%. The study conducted by Christopher *etal*.[8]in Nigeria that of those co-infected with HIV-TB, 57.4% of the participants were females while 42.6% of the participants were male.
In the present study, CBNAAT was positive in 13 out of 52 cases (26%) which were sputum negative and clinically and/or radiologically suspected pulmonary tuberculosis with HIV. Unlike other studies given below, our study considered only those PLHIV patients who were smear negative yet suspected of pulmonary tuberculosis.
In the study by R Dewan *etal*. [9],11 out of 100 (11%) were positive by sputum microscopy for acid-fast bacilli and 40 (40%) were positive by CBNAAT. In the S. Subbarao *et al*. [10]study, 7 out of 191 PLHIV patients (3.66%) were positive by sputum microscopy for acid-fast bacilli and 54 (28.2%) were positive by CBNAAT. In the Gabriella *etal*. [10]study, among the sample size of 131 patients, 45 (34.4%) had TB. CBNAAT detected 44 out of 45 cases and smear microscopy detected 31 out of 45 cases. Two patients had false positive CBNAAT, one of them was also smear-positive. So total CBNAAT detected were 46 (35.11%) and microscopy detected were 32 (24.43%) cases. In Prem Parkash Gupta *etal*.[11]study, LED Fluorescent Microscopy for AFB detected 8 (26.67%) cases and CBNAAT detected 17 (56.67%) cases out of 30 PLHIV patients.
CBNAAT helps in increased case detection to diagnose pulmonary tuberculosis in PLHIV ascompared to conventional sputum microscopy. Thus, this helps to diagnose tuberculosis early and initiation of anti-. Tuberculosis treatment. Therefore, CBNAAT is to be indicated as a primary diagnostic test in PLHIV with presumptive pulmonary tuberculosis.
In the present study, we got a higher detected CBNAAT positivity of 85.71% in patients with CD4 count up to 100 cells/ml, when compared to the R. Dewan *et al*. study[9],where it was 43.75%. In patients with CD4 count of 101-200 cells/ml, CBNAAT positivity was 71.42% when compared to the R. DEWAN *et al*. study it was 41.67%. In patients with CD4 count of 201-350 cells/ml, CBNAAT positivity was detected 8.3% in the present study when compared to R. DEWAN *et al*. study it was 37.5%.
Also in our study among the 13 cases detected by sputum CBNAAT, 6 cases (46.15%) patients have CD4 counts below 100, followed by 5 cases (38.46%) with CD4 counts between 100-200. Higher proportions of tuberculosis is seen in PLHIV patients with CD4 count <200/µl. Therefore, low CD4 counts can also be used as a marker for suspicion of severe forms of tuberculosis.
Monitoring of CD4 cell count is still important, soon after an HIV positive diagnosis, before beginning HIV treatment. It provides important information about disease progression and the immune system.
In the present study, CBNAAT detected 1 (7.69%) rifampicin resistant cases out of 13 CBNAAT positive cases. In the R.Dewan *etal*. study[9],CBNAAT detected 10 (25%) rifampicin resistant cases out of 40 CBNAAT positive cases. In the Gabriella *etal*. [10]study, CBNAAT detected 3 (6.52%) rifampicin resistant cases out of 46 CBNAAT positive cases. In the Prem Parkash Gupta *etal*.[11]study, CBNAAT detected 2 (11.76%) rifampicin resistant cases out of 17 CBNAAT positive cases[12].

Conclusion

In our study among the 13 cases detected by sputum CBNAAT, 6 cases(46.15%) patients have CD4 counts below 100, followed by 5 cases (38.46%) with CD4 counts between 100-200. Higher proportions of tuberculosis is seen in PLHIV patients with CD4 count <200/µl. Therefore, low CD4 counts can also be used as a marker for suspicion of severe forms of tuberculosis.

References

1. Hirsh AE, Tsolaki AG, DeRiemer K, Feldman MW, Small PM. Stable association between strains of *Mycobacterium tuberculosis* and their human host populations. Proc. Natl. Acad. Sci. USA. 2004;101:4871-6.
2. Rothschild BM, Martin LD, Lev G, Bercovier H, Bar-Gal GK, Greenblatt CL, *et al*. *Mycobacterium tuberculosis* Complex DNA from an Extinct Bison Dated 17,000 Years before the Present. Clin. Infec. Dis. 2001;33:305-11.
3. Migliori GB, Loddenkemper R, Blasi F, Raviglione MC. 125 years after Robert Koch's discovery of the tubercle bacillus: the new XDR-TB threat. Is "science" enough to tackle the epidemic? Eur. Respir J. 2007;29(3):423-7.
4. Global tuberculosis control:epidemiology, strategy, financing: World Health Organization Report, 2009. Available from: http://apps. Who. Int/iris/bitstream/10665/44035/1/9789241563802_eng.pdf.
5. Patel AK, Thakrar SJ, Ghanchi FD. Clinical and laboratory profile of patients with TB/HIV coinfection: A case series of 50 patients. Lung India: official organ of Indian Chest Society. 2011 Apr;28(2):93.
6. Kumar P, Sharma N, Sharma NC, Patnaik S. Clinical profile of tuberculosis in patients with HIV infection/AIDS. Indian Journal of Chest Diseases and Allied Sciences. 2002 Jul;44(3):159-64.
7. Giri PA, Deshpande JD, Phalke DB. Prevalence of pulmonary tuberculosis among HIV positive patients attending antiretroviral therapy clinic. North American journal of medical sciences. 2013 Jun;5(6):367.
8. Affusim CC, Kesieme E, Abah VO. The pattern of presentation and prevalence of tuberculosis in HIV-seropositive patients seen at Benin City, Nigeria. ISRN Pulmonology, 2012 Mar 12.
9. Dewan R, Anuradha S, Khanna A, Garg S, Singla S, Ish P*et al*. Role of cartridge-based nucleic acid amplification test (CBNAAT) for early diagnosis of pulmonary tuberculosis in HIV. Journal, Indian Academy of Clinical Medicine, 2015 April-June, 16(2).
10. Carriquiry G, Otero L, Gonza´lez-Lagos E, *et al*. A Diagnostic Accuracy Study of XpertHMTB/RIF in HIV-PositivePatients with high Clinical Suspicion of Pulmonary Tuberculosis in Lima, Peru. PLoS ONE. 2012;7(9):e44-626. Doi:10.1371/journal.pone.0044626. 14.
11. Gupta PP, Mynalli AB, Yadav A. Diagnostic Role of Cartridge Based Nucleic Acid Amplification Test in Diagnosing Tuberculosis in Patients Co-infected with Human Immunodeficiency Virus. Journal of medical science and clinical research.
12. Combs DL, O'Brien RJ, Geiter LJ. USPHS Tuberculosis Short-Course Chemotherapy Trial 21: effectiveness, toxicityand acceptability. The report of final results. Ann Intern Med. 1990; 112:397.
13. Dr. AarushiKataria, Dr. Naveen Nandal and Dr. Ritika Malik, Shahnaz Husain -A Successful Indian Woman Entrepreneur, International Journal of Disaster Recovery and Business ContinuityVol.11, No. 2, (2020), pp. 88–93
14. Kumar, S. (2020). *Relevance of Buddhist Philosophy in Modern Management Theory*. *Psychology and Education*, Vol. 58, no.2, pp. 2104–2111.

15. Roy, V., Shukla, P. K., Gupta, A. K., Goel, V., Shukla, P. K., & Shukla, S. (2021). Taxonomy on EEG Artifacts Removal Methods, Issues, and Healthcare Applications. Journal of Organizational and End User Computing (JOEUC), 33(1), 19-46. http://doi.org/10.4018/JOEUC.2021010102
16. Shukla Prashant Kumar, Sandhu Jasminder Kaur, Ahirwar Anamika, Ghai Deepika, MaheshwaryPriti, Shukla Piyush Kumar (2021). Multiobjective Genetic Algorithm and Convolutional Neural Network Based COVID-19 Identification in Chest X-Ray Images, Mathematical Problems in Engineering, vol. 2021, Article ID 7804540, 9 pages. https://doi.org/10.1155/2021/7804540
17. Aarushi, Naveen Nandal, Parul Agrawal. AN EXPLORATORY RESEARCH IN PRODUCT INNOVATION IN AUTOMOBILE SECTOR. JCR. 2020; 7(2): 522-529. doi:10.31838/jcr.07.02.98