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Research Article

A COMPARATIVE STUDY BETWEEN CBNAAT AND SPUTUM MICROSCOPY TO DETECT TUBERCULOSIS IN HIV INFECTED PATIENTS

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ABSTRACT

Introduction: With an estimated global incidence of 9.6 million cases per year Tuberculosis (TB) counts for the one of the most common infectious disease of the world, India being at the top. There are various methods to detect pulmonary tuberculosis having various limitations of each test, the newest in this line is Cartridge Based Nucleic Acid Amplification Test (CBNAAT). Sputum microscopy is the simplest and one of the older one to detect TB but it has many limitations especially in Patients Living With HIV (PLHIV) who have scarce production of sputum, so we aim to compare the efficacy of CBNAAT to Sputum Microscopy in detecting TB in PLHIV.

Materials and Methods: In this observational descriptive study we studied 161 subjects infected with HIV and having various symptoms suggestive of Pulmonary Tuberculosis. We did both CBNAAT, Sputum microscopy and Sputum culture as gold standard test for diagnosis of TB.

Results: The most common clinical features was cough (71.42%) followed by fever (70%) & loss of appetite (64.28%), with most cases (44.99%) had CD4 count below 200 cells/cumm and 13.57% cases had seen more than 500 cells/cumm CD4. The prevalence of sputum culture positive Tuberculosis in our study was 88/140 (62.85%). The sensitivity, specificity, PPV, NPV, PLR, NLR of Sputum microscopy were 21.59%, 78.85% ,63.33% , 37.27%, 1.020, 0.994(0.674-1.437) respectively. The sensitivity, specificity, PPV, NPV, PLR, NLR of CBNAAT were 81.82% (72.16-89.24), 90.38%, 93.51%, 74.60%, 8.509, 0.2011 (0.0823-0.7823) respectively. There was significantly higher test accuracy for CBNAAT compared to Sputum microscopy [0.95 vs 0.72, mean diff 0.23 (0.096-0.37), $p<0.001$).

Conclusion: We concluded that CBNAAT is a better modality than sputum microscopy for diagnosis of pulmonary tuberculosis in specially HIV infected patients.

INTRODUCTION

Tuberculosis (TB), with an estimated global annual incidence of 9.6 million with 2.2 million cases in India[1] making it one of the most prevalent infectious disease here, which is caused by Mycobacterium Tuberculosis a bacteria. Thus, 23% of global annual TB incidents occur in India which is the highest case burden overall.[1]

Tuberculosis remains the most common opportunistic infection among PLHIV, and HIV-TB co- infected individuals have more mortalityrates.[2] Standard sputum based methods to detect pulmonary tuberculosis include sputum microscopy and culture. However, in PLHIV, the sputum production is very scarce, lack of caseous necrosis leads to decreased bacilli in sputum, and also there is higher incidence of various non-tubercular mycobacterial infections in these patients. All these factors decrease the statistical significance of sputum microscopy as a diagnostic tool for tuberculosis in general population and in PLHIV.

however to overcome this problem sputum culture can be used, but it has limitations of its own, it takes 4-6 weeks to grow the bacteria, it is not widely standardized , and also not cost effective to be used as a screening test. This delays initiation of anti-tubercular treatment especially for drug-resistant forms of TB, increases risk of transmission of (drug-resistant) TB in the community and increases the risk of spread to extra-pulmonary sites within the patient.[3]

A recently introduced polymerase chain reaction (PCR) based method for detection of TB that is Cartridge-based nucleic acid amplification test (CBNAAT) has promising results. As, it simultaneously targets the rpoB gene of mycobacteria thus helpful in detecting the rifampicin resistance in particular sample. CBNAAT is an automated, cartridge based nucleic acid amplification assay using real-time PCR and provides

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results within 100 minutes. It uses 3 specific primers and 5 unique molecular probes to target the rpoB gene, which is the critical gene associated with rifampicin resistance, making this a highly specific test for diagnosis of M.Tuberculosis bacteria and various other implications.

The specificities and sensitivities of the polymerase chain reaction (PCR) based diagnostic tests are quite variable.[4,5] Further, these tests involve multiple manual steps and long turn-around time, making them unsuitable for decentralized deployment. A series of meta-analyses have shown that cartridge based nucleic acid amplification test (CBNAAT)/ Xpert MTB/ RIF have a high specificity with variable sensitivity in different type of specimens for diagnosing tuberculosis.[6-8] CBNAAT, a tool with a quick turn-around time, which simultaneously detects TB and rifampicin resistance, offers a promising solution to achieve the global objective of early TB case detection, improved TB care and controlling the disease.[9]

Diagnosing tuberculosis (TB) in people living with HIV/AIDS (PLHIV) is very challenging as sputum microscopy is negative in more than half of the patients due to lack of caseous necrosis. Sputum culture however, reliable but is a slow method which takes around 4 - 8 weeks to grow mycobacteria. While delaying the treatment for TB in PLHIV is well known to be associated with increased mortality, the role of a newly launched cartridge based nucleic acid amplification test (CBNAAT) with a potential to diagnose TB and rifampicin resistance within 2 hours in PLHIV can't be over emphasized. But the role of CBNAAT in diagnosing TB particularly in PLHIV patients has not been widely studied here in India. This study was carried out to evaluate the role of CBNAAT in early diagnosis of TB in PLHIV and simultaneously comparing its efficacy against the conventional sputum microscopy to detect pulmonary TB.

MATERIAL & METHODS

This is a hospital based observational, descriptive study on 161 subjects who were diagnosed as HIV infected by ELISA rapid and simple (ERS) test according to NACO guidelines bet ween June 2017 to November 2018, Presented to the Department of General Medicine, S.M.S Hospital & Attached Group of Hospitals, Jaipur with history of productive cough for 2 weeks and/or chest X-ray findings suggestive of pulmonary tuberculosis.

Inclusion Criteria

A HIV positive patient with

1. Fever
2. Cough > 2 weeks
3. Weight loss
4. Night sweats

Exclusion Criteria

1. Age <18 years
2. Pregnant female
3. Extra pulmonary involvement

History and examination

All patients included in the study underwent a detailed history and clinical examination. History of presenting complaints, past illnesses, mode of transmission of HIV and high-risk behaviour was taken. Clinical history regarding current complaints of fever, cough, sputum production, hemoptysis, weight loss was taken. History regarding previous treatment for tuberculosis was also taken into consideration. All patients were evaluated for presence of headache, seizures, chest pain, breathlessness and neck swelling or any other evidence of extra-pulmonary tuberculosis. Radiological evaluation and chest X-ray was done by a radiologist who was blended to patient clinical status. Standard comparison of radiological finding was used.

Immune status assessment

CD4 lymphocyte counts of all the patients were determined by flow cytometry.

Sputum analysis

We assessed HIV positive adults referred to with pulmonary sy mptoms suggestive of tuberculosis by sending two sputum samples for microscopy using ZN stai, one sputum sample for CBNAATand one sputum sample for BACTEC based culture in each patient's sample. Adequacy and quality of sputum collection was observed.

Sputum Microscopy

Sputum smears after Ziehl-Neelsen staining was examined under oil immersion microscopy. A minimum of 1 slide positive even for single AFB/100 fields were taken as positive for *Mycobacterium tuberculosis* and a minimum of two sputum samples negative for AFB evaluated for 100 fields were declared as negative.

Sputum for CBNAAT

One sputum sample of 1 ml was collected in a sterile container and was analyzed by CBNAAT on *Xpert® MTB/RIF* manufactured by Cepheid, endorsed by WHO (2010). The sample was diluted with three times the reagent, incubated at room temperature and loaded into the cartridge for automated analysis with results in 100 minutes. Detection of mycobacteria and rifampicin resistance was carried-out in the same setting.

Rifampicin resistant samples were further analyzed by LPA(Li ne Probe Assay). The three steps for LPA test included DNA extraction, multiplex polymerase chain reaction (PCR) amplification and reverse hybridization.

Sputum Culture

Using BACTEC culture positive as gold standard, we determined comparative sensitivity, specificity, Positive Predictive Value, Negative Predictive value, Positive Likelihood Ratio and Negative Likelihood Ratio of CBNAAT and sputum microscopy using SPSS 15.0 software. Definitive diagnosis of tuberculosis is based on culture or nucleic acid amplification. Specimens are cultured on egg or agar medium (e.g. Löwenstein –Jensen (LJ) or Middlebrook) and incubated at 37°C. As the Mycobacteria are slow growers, 4-8 weeks were required for growth to be detected.

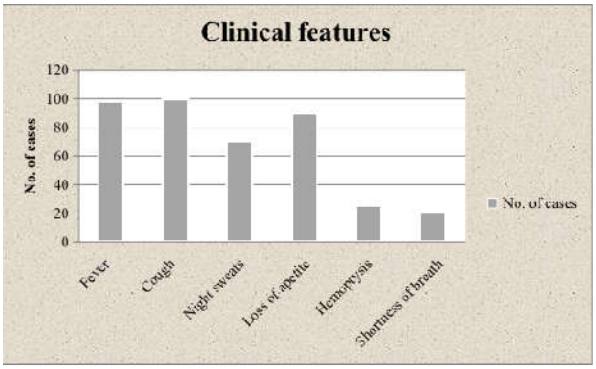
RESULTS

Our study showed that Out of 160 screened patients, 140 included with adequate sputum volume for diagnosis of HIV infected pulmonary tuberculosis for CBNAAT. The majority of cases were seen in 31-50 years of age groups and the mean age of patients was 39.21 years (table 1).

Table 1 Age Wise Distribution of Cases

Age (yrs)	No. of cases	Percentage
18-20 yrs	3	2.14%
21-30 yrs	27	19.28%
31-40 yrs	53	37.85%
41-50 yrs	45	32.14%
51-60 yrs	9	6.42%
>60 yrs	3	2.14%
Total	140	100%

The most common clinical features was cough (71.42%) followed by fever (70%) & loss of appetite (64.28%) (graph 1). The most cases (44.99%) had below 200 cells/cumm CD4 count and 13.57% cases had seen more than 500 cells/cumm CD4 count (table 2).



Graph 1 Clinical features of cases

Table 2 Distribution of CD4 in cases

CD4/cumm	No. of Cases	Percentage
<200	63	44.99%
201-300	20	14.28%
301-400	22	15.72%
401-500	16	11.42%
>500	19	13.57%
Total	**140**	**100%**

The prevalence of sputum culture positive Tuberculosis in our study was 88/140 (62.85%). The sensitivity, specificity, PPV, NPV, PLR, NLR of Sputum microscopy were 21.59% (1 3.53-31.65), 78.85% (65.3-88.94), 63.33% (43.86-80.07), 37.27% (28.24-47.01), 1.020 (0.667-3.126), 0.994 (0.674-1.437) respectively (table 3).

Table 3 Results: Sputum microscopy

Sensitivity= a/a+c	21.59%	95% CI 13.53% to 31.65%
Specificity=d/d+b	78.85%	95% CI 65.30% to 88.94%
Positive likelihood ratio= sensitivity/ 100-specificity	1.020	95% CI 0.667% to 3.126%
Negativelikelihoodratio=100-sensitivity/ specificity	0.994	95% CI 0.674% to 1.438%
Disease Prevalence =a+b/a+b+c+d	62.85%	95% CI 32.68% to 88.56%
PPV =a/a+b	63.33%	95% CI 43.86% to 80.07%
NPV =d/d+c	37.27%	95% CI 28.24% to 47.01%

a=True positive, b=False positive, c=False negative, d= True negative

The sensitivity, specificity, PPV, NPV, PLR, NLR of CBNAAT were 81.82% (72.16-89.24), 90.38% (78.97-96.80), 93.51% (85.49-97.86), 74.60% (62.06-84.73), 8.509 (4.526-18.89),0.2011(0.0823-0.7823) respectively (table 4).

The Test accuracy as represented by AUROC (Area under receiver operator characteristics) was significantly higher for CBNAAT compared to Sputum microscopy [0.95 vs 0.72, mean diff 0.23 (0.096-0.37), p<0.001).

Table 4 Results – CBNAAT

Sensitivity= a/a+c	**81.82%**	**95% CI 72.16% to 89.24%**
Specificity=d/d+b	90.38%	95% CI 78.97% to 96.80%
Positive likelihood ratio= sensitivity/ 100-specificity	8.509	95% CI 4.526% to 18.89%
Negative likelihood ratio = 100-sensitivity/ specificity	0.2011	95% CI 0.0823% to 0.7823%
Disease Prevalence =a+b/a+b+c+d	62.85%	95% CI 32.68% to 88.56%
PPV =a/a+b	93.51%	95% CI 85.49% to 97.86%
NPV =d/d+c	74.60%	95% CI 62.06% to 84.73%

a=True positive, b=False positive, c=False negative, d= True negative

DISCUSSION

Tuberculosis has been a major challenge in countries suffering with a high load of HIV co- infection along with a resource-limited socio-economic scenario.[10] These risks are further increased manifold due to increased probability of presence of multi-drug resistant tuberculosis. To address these challenges, there is a critical need for rapid and authentic screening for TB and detection of drug resistance for early initiation of appropriate treatment.

Our study showed that the majority of cases with tuberculosis in HIV were seen in 31-50 years of age groups. The mean age of patients was 39.21±9.830 years. R Dewan *et al* (2015)[11] found that the mean age of the study population was 35 ± 9 years. Most patients (69%) were in the age group of 20 to 40 years.

Our study had majority of male participants(75%) with Male to female ratio was 3:1. The mean CD4 count of the patients was 267.9±190.2 cells/mm. Mostly cases (44.99%) had <200 cells/mm CD4 count. R Dewan *et al* (2015)[11] found that the majority (76%) of the patient were males, there were 21% women and three transgenders. The mean CD4 count of the subjects was 230 cells/ml. Thirty two patients had CD4 count less than 100 cells/ml, which is consistent with our results.

Our study showed that the most common clinical features was cough (71.42%), in X-ray findings, Reticulo-nodular infiltration was seen in 35.71% of cases and only 1.42% case had mediastinal widening. Similar to study done by Padyana M[12] as they found that out of 54 sputum positive patients had infiltration on X-ray in 18 of them (39%), followed by consolidation in 14 (30%), Cavity and cardiomegaly were present in 5(11%) each. All of these patients had CD4 count <200.

In the present study out of 140 screened patients considering sputum culture as the gold standard for diagnosis of tuberculosis, Only 30 patients were found to be sputum positive for AFB by direct microscopy and 110 cases were missed and reported as sputum smear negative, which was statistical non significant (p=1.000). This indicated that sputum microscopy is not a very useful method in diagnosing pulmonary tuberculosis in HIV patients. The consequences of this can be several, including delayed or misdiagnosed cases, contributing to delayed treatment with increased morbidity and mortality rates and continued spread of TB to contacts.

Our study showed that the sensitivity, specificity, PPV, NPV, PLR, NLR of Sputum microscopy were 21.59% (13.53-31.65), 78.85% (65.3-88.94), 63.33% (43.86-80.07), 37.27% (28.24-

47.01),1.020 (0.667-3.126), 0.994 (0.674-1.437) respectively. From Africa, Cattamanchi *et al*[72] have also reported that the sensitivity of sputum microscopy in HIV infection ranged from 43 to 51percent, and in Tanzania, Matee *et al*[73] found it to be only 55%.

WhereasIndian studies show varying degree of sensitivity of sputum microscopy range from 11% to61.5% in study of R Devan *et al*[11] 11%, Prem Prakash Gupta *et al*[13] 26.66%, Sowjanya D *et al*, Vizianagaram[14] 52.68%, and Anupam Kumar Singh *et al*[15] 61.5% which are compatible to our study. Out of 161 screened patients, 140 were included with adequate sputum volume, of these 77 were CBNAAT positive and 63 were CBNAAT negative. Thus, tuberculosis detection rate increased by more than double using CBNAAT as compare to sputum microscopy, which was statistical significant (p<0.0001***). The prevalence of sputum culture positive Tuberculosis in our study was 88/140 (62.85%). The sensitivity, specificity, PPV, NPV, PLR, NLR of CBNAAT were 81.82% (72.16-89.24), 90.38% (78.97-96.80), 93.51% (85.49-97.86), 74.60% (62.06-84.73), 8.509 (4.526-18.89), 0.2011 (0.0823-0.7823) respectively.

There are only a few studies on CBNAAT from India available in literature. A study done in 2011 in Hyderabad showed incremental case detection of 10.8% when CBNAAT was used to diagnose tuberculosis over and above fluorescent microscopy.[16] However, HIV status of the patients was not evaluated in the study. A multicentre assessment at five trial sites in Peru, Azerbaijan, Cape Town, Durban and India by Boehme *et al* Among culture positive PTB, the sensitivity of the CBNAAT was 97.6%. For smear and culture positive patients, the sensitivity was 99.8, smear negative culture positive, it was 90.2%, which was compatible to our study. The sensitivity with CBNAAT was compared between HIV positive (98.4%) and negative individuals (93.9%), but there were no statistically significant co relation.[17]

In Indian study sensitivity of CBNAAT ranges from 40% to 82.7%. R Dewan *et al*[11] 40%, Prem Prakash Gupta *et al*[13] 56.66%, Sowjanya D *et al*[14] 70.24% and Anupam Kumar Singh *et al*[15]82.7% which was compatible with our study.

Tortolli and colleague's assessed the performance of the Xpert system in diagnosing EPTB in a low incidence setting. They found, in comparison with a reference standard consisting of combination of culture and clinical diagnosis of TB, an overall sensitivity and specificity of81.3% and 99.8% for Xpert, while the sensitivity of microscopy was 48%. Although the role of culture remains central in the microbiological diagnosis of EPTB, the sensitivity of Xpert in rapidly diagnosing the disease makes it a much better choice compared to smear microscopy. The ability to rule out the disease still remains suboptimal. [18]

Ligthelm *et al* demonstrated that the excellent diagnostic accuracy of the Xpert MTB/RIF test in patients with tuberculous lymphadenitis. The test sensitivity and specificity were 96.7% (95% confidence interval [CI], 86.6 to 100%) and 88.9% (95% CI, 69.6 to 100%), respectively, and it correctly identified 6/6 (100%) of the cytology smear-negative/culture-positive cases and 1 of 2 (50%) rifampin-resistant cases.[19]

HIV-TB co-infection has been shown to substantially decrease the sensitivity of sputum microscopy (to 47%), but it does not significantly affect CBNAAT performance.[20] Studies from high HIV endemicity areas in Peru have also shown that HIV status does not affect the performance of CBNAAT.[21] Sensitivity and specificity of CBNAAT were reported to be > 95%.

Our study showed that the combination of smear microscopy and CBNAAT had a significantly better sensitivity than smear microscopy alone in patients infected with HIV with a CD4 countless than 200 cells/ml (64.3% vs 34.5%; p, 0.0478). which was consistent with a study from CapeTown, South Africa, the combination of smear microscopy and CBNAAT had a significantly better sensitivity than smear microscopy alone in patients infected with HIV with a CD4 count less than 200 cells/ml (69.6% vs 39.1%; p, 0.05).[63] Thus CBNAAT was found to be additive over microscopy alone.

The WHO policy guidance on the use of CBNAAT was issued in December 2010. The recommendations were that it should be used as the initial diagnostic test in individuals at risk of having MDR-TB or HIV-associated TB (strong recommendation), and that it could be used as a follow-on test to microscopy in settings where MDR and/or HIV is of lesser concern, especially in smear-negative specimens (this was a conditional recommendation, recognizing major resource implications). This recommendation applied to the use of CBNAAT in sputumspecimens only, as data on its performance (sensitivity and specificity) for testing of extra-pulmonary specimens at that time were limited.[22]

This molecular technique of GeneXpert assay is relatively more expensive than traditional culture methods; however, it makes an important contribution to the modern-day detection of TB with higher sensitivity and provides a more rapid diagnosis than culture and histology.

CONCLUSION

We concluded that CBNAAT performs better than sputum microscopy in diagnosis of pulmonary tuberculosis in HIV patients at multiple levels. Also CBNAAT is an important add-on in diagnosis of pulmonary TB in HIV negative, smear negative cases as well.

References

1. https://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=4569&lid = 3174.
2. Corbett EL, Watt CJ, Walker N *et al*. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. *Arch Intern Med* 2003; 163 (9): 1009-21.
3. Swaminathan S, Ramachandran R, Baskaran G *et al*. Risk of development of tuberculosis in HIV-infected patients. *Int J Tuberc Lung Dis* 2000; 4 (9): 839-44.
4. Raj A, Singh N, Mehta PK. Gene Xpert MTB/RIF Assay: A New Hope for Extra- pulmonary Tuberculosis. IOSR J Pharm Biol Sci.2014; 2(1): 083-089.
5. Bianchi L, Galli L, Moriondo M, Veneruso G, Becciolini L, *et al*. Interferon-gamma release assay improves the diagnosis of tuberculosis in children. Pediatr Infect Dis J.2009; 28(6): 510-514.
6. Pai M, Flores LL, Pai N, Hubbard A, Riley LW, *et al*. Nucleic acid amplification tests in the diagnosis of tuberculous pleuritis: a systematic review and meta-analysis. BMC Infect Dis.2004; 4: 6.

7. Dinnes J, Deeks J, Kunst H, Gibson A, Cummins E, *et al*. A systematic review of rapid diagnostic tests for the detection of tuberculosis infection. Health Technol Assess. 2007; 11(3): 1-196.
8. Pai M, Nathavitharana R. Extrapulmonary Tuberculosis: New Diagnostics and New Policies. Indian J Chest Dis Allied Sci.2014; 56(2): 71-73.
9. https://tbcindia.gov.in/WriteReadData/TB%20India%202017.pdf
10. Kranzer K, Houben RM, Glynn JR, Bekker LG, Wood R, Lawn SD. Yield of HIV- associated tuberculosis during intensified case finding in resource-limited settings: a systematic review and meta-analysis. Lancet Infect Dis. 2010;10(2):93-102.
11. R Dewan, S Anuradha, A Khanna, S Garg, S Singla, P Ish, S Agarwal, A Narayana H, M Hanif, H Singh, S Uppal. Role of cartridge-based nucleic acid amplification test (CBNAAT) for early diagnosis of pulmonary tuberculosis in HIV. JIACM 2015; 16(2): 114-7
12. Padyana M, Bhat RV, Dinesha M, Nawaz A. HIV-Tuberculosis: A Study of Chest X-Ray Patterns in Relation to CD4 Count. *N Am J Med Sci*. 2012;4(5):221-5.
13. Prem Parkash Gupta, Adarsh B Mynalli, Aparna Yadav. Diagnostic Role of Cartridge Based Nucleic Acid Amplification Test in Diagnosing Tuberculosis in Patient s Co-infected with Human Immunodeficiency Virus. JMSCR Volume 05 Issue 05 May 2017; page no. 21841-21848.
14. Sowjanya D, Behera G, Reddy VR, Praveen J. CBNAAT: a Novel Diagnostic Tool For Rapid And Specific Detection Of Mycobacterium Tuberculosis In Pulmonary Samples.
15. Singh, Anupam & Karmakar, D & Jha, Ratnakar. Compa rative Accuracy of CBNAAT and Sputum microscopy in diagnosis of Pulmonary Tubercul osis and Meta-analysis ofexisting literature. The Journal of the Association of Physicians of India. 2014.
16. Gerardo A, Jose M, Manoranjan M *et al*. Rapid diagnosis of pulmonary and extra pulmonary TB in HIV-infected patients, comparison of LED flurescent microscopy and gene expert MTB/RIF assay in a district hospital in India. *Tuberc Res Treat* 2012; article ID932862, do I;10.1155/2012.
17. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, *et al*. Rapid molecular detection of tuberculosis and rifampin resistance. New England Journal of Medicine. 2010;363(11):1005-15.
18. Tortoli E, Russo C, Piersimoni C, Mazzola E, Dal Monte P, Pascarella M, Borroni E, Mondo A, Piana F, Scarparo C, Coltella L. Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis. European Respiratory Journal. 2012 Aug 1;40(2):442-7.
19. Ligthelm LJ, Nicol MP, Hoek KG, Jacobson R, van Helden PD, Marais BJ, *et al*. Xpert MTB/RIF for rapid diagnosis of tuberculous lymphadenitis from fine-needle-aspiration biopsy specimens. Journal of clinical microbiology. 2011;49(11):3967-70.
20. Van Rie A, Page-Shipp L, Scott L *et al*. Xpert(®) MTB/RIF for point-ofcare diagnosis of TB in high-HIV burden, resource-limited countries: hype or hope? *Expert Rev Mol Diagn* 2010; 10: 937-46.
21. Carriquiry G, Otero L, Gonza´lez-Lagos E *et al*. A Diagnostic Accuracy Study of XpertHMTB/RIF in HIV-Positive Patients with high Clinical Suspicion of Pulmonary Tuberculosis in Lima, Peru. *PLoS ONE* 2012; 7 (9): e44626. doi:10.1371/ journal.pone.0044626.
22. WHO Policy statement: automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system 2011. Available at: http://www.who.int/tb/ laboratory/en/.

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