Research Article

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Journal of Infectious Diseases and Treatment
ISSN 2472-1093

2016
Vol. 2 No. 1: 10

DOI: 10.21767/2472-1093.100015

Diagnostic Accuracy of Xpert MTB/RIF Assay in Diagnosis of Pulmonary Tuberculosis

Nwachukwu O Ndubuisi[1], Onyeagba R Azuonye[1], Nwaugo O Victor[1], Ononiwu A Happiness[1] and Okafor C Daniel[2]

1 Department of Microbiology, Abia State University, Uturu, Nigeria
2 Chukwuemeka Odimegwu Ojukwu University Teaching Hospital, Awka, Nigeria

Corresponding author:
Nwachukwu O Ndubuisi

nwachukwundubuisi82@yahoo.com

Department of Microbiology, Abia State University, Uturu, Nigeria.

Tel: +2348033561693

Citation: Ndubuisi NO, Azuonye OR, Victor NO, et al. Diagnostic Accuracy of Xpert MTB/RIF Assay in Diagnosis of Pulmonary Tuberculosis. J Infec Dis Treat. 2016, 2:1.

Abstract

Objectives/Background: The objectives of this study are to assess diagnostic of Xpert MTB/RIF assay for pulmonary tuberculosis (PTB) diagnosis and to compare it with microscopy (Ziehl-Neelsen staining) in the detection of pulmonary TB in Anambra state, Nigeria.

Methods: A total of 1500 individuals with presumptive PTB participated. Participant's age ranged from 15 years and above. Two sputum specimens were submitted on-the spot (S-S) within an hour interval. Sputum specimens were processed directly from Xpert MTB/RIF test according to manufacturer's protocol whereas sputum smears were stained using Ziehl-Neelsen technique.

Results: Xpert MTB/RIF test detected *Mycobacterium tuberculosis* (MTB) in 389 (25.9%) out of 1500 sputum specimens while microscopy detected only 237 (15.8%). Xpert MTB/RIF thus detected all the 237 smear positive cases of microscopy in addition to 152 (12.0%) positive cases among 1263 smear negative cases. Among 389 specimens with MTB detected by Xpert, Rifampicin resistance was seen in 12 (3.1%) cases. Most of the PTB patients were young men whose occupation was trading.

Conclusion: Xpert MTB/Rif assay is an accurate method for rapid diagnosis of PTB. It outperformed microscopy and detected MTB in smear negative cases. It could therefore be used as an initial diagnostic test for PTB detection and rifampicin resistance in Anambra and Nigeria in general.

Keywords: Xpert MTB/RIF; Pulmonary tuberculosis; Diagnostic accuracy; Ziehl-Neelse

Received: June 16, 2016; **Accepted:** June 25, 2016; **Published:** June 30, 2016

Introduction

The inadequate ability to rapidly and accurately diagnose active pulmonary tuberculosis in developing countries remain a major obstacle in global control of the disease [1] Millions of pulmonary tuberculosis (PTB) cases therefore go undiagnosed each year. Accurate and rapid detection of PTB and drug resistance facilitates therapeutic interventions and community transmission [2].

In most countries including Nigeria the conventional microscopy (Ziehl-Neelsen technique) is the cornerstone of tuberculosis diagnosis. Microscopy lacks sensitivity, it can only detect 10-75% of PTB cases [3]. The cultural methods which are highly sensitive takes as long as 2 to 6 weeks to produce results and require special materials and laboratories [4].

In other to obtain results in a short period of time, nucleic acid amplification test are increasingly used worldwide for rapid diagnosis of tuberculosis [5]. In December 2010, the WHO endorsed GeneXpert MTB/RIF (Xpert) (Cepheid Inc., New Jersey, USA) for *Mycobacterium tuberculosis* detection in settings with high burden of tuberculosis and HIV [6-8].

The Xpert MTB/RIF is a cartridge-based, automated diagnostic test that can identify *Mycobacterium tuberculosis* (MTB) DNA and resistance to rifampicin (RIF) by nucleic acid amplification techniques (NAAT) in less than 2 hours [9,10].

Results from field demonstration studies found that a single Xpert MTB/RIF test can detect MTB in 99% of patients with smear positive PTB and more than 80% in patients with smear negative pulmonary tuberculosis [4]. Following sample loading, all steps in the assay are completely automated and self-contained. In addition, the assay's sample reagent (SR) used

to liquefy sputum has potent tuberculocidal properties and so largely eliminate biosafety concerns during test procedure [11]. The assay can be performed directly from a clinical sample or from a decontaminated sputum pellet. These features allow the technology to be taken out of reference laboratory and used nearer to the patient.

Nigeria is one of the 22 tuberculosis high burden countries in the world with an estimated prevalence of 322 per 100,000 population and incidence of 338 per 100,000 population of all forms of tuberculosis [12]. Xpert MTB/RIF assay for the diagnosis of MTB and RIF resistance was introduced in Nigeria in 2012. Xpert programme in Nigeria is largely implemented by the KNCV TB Foundation in partnership with Government of Nigeria and support from US Agency for International Development (USAID).

We therefore aimed this work at assessing the diagnostic accuracy of Xpert MTB/RIF for pulmonary tuberculosis diagnosis and compared it with microscopy in the detection of pulmonary tuberculosis cases.

Materials and Methods

Study area

This prospective study was carried out at Nnamdi Azikwe University Teaching Hospital, (NAUTH) Nnewi, Nigeria. NAUTH is a tertiary hospital with specialist care and referral centre for other hospitals.

Study participants: Individuals aged 15 years and older who were presumptive pulmonary TB cases attending TB/directly observed treatment short course clinic were invited to participate and enrolled at the time of presentation to the clinic.

Methods

Presumptive pulmonary TB cases submitted two sputum specimens: on-the-spot (S-S) within an hour interval. Sputum smears, appropriately labeled were made on clean grease free slides (2 cm × 1 cm) and stained smears were read at X1000 magnification and graded according to the WHO/IUATLD system.

Xpert MTB/RIF assay: Sputum specimens were processed directly from Xpert MTB/Rif test according to manufacturer's protocol. Sample reagent (SR) which contains NaOH and Isopropanol was added in 2:1 ratio to unprocessed sputum in 15 ml falcon tube and the tube was manually agitated twice during a 15 minute incubation period at room temperature. Then 2 ml of the inactivated sample was transferred to the test cartridge by a sterile disposable pipette (provided with kits). Cartridge was loaded into the Genexpert instrument and an automatic process completed the remaining assay steps. Interpretation of data from MTB/RIF test was software based [9]. Ethical approval for the study was obtained from the ethical committee of the hospital. All patients consented to participate in the study.

Results

A total of 1500 sputum specimens were run in the Xpert MTB/RIF assay. MTB was detected by Xpert in 389 (25.9%) specimens while MTB was not detected in 1,111 (74.1%) specimens **(Table 1)**.

Conventional analysis using microscopy (Ziehl- Neelsen technique) detected acid fast bacilli (AFB) in 237 (15.8%) specimens whereas no AFB was detected in 1263 (84.2%) specimens i.e., smear negative. In comparism, Xpert MTB/RIF detected all the smear positive cases of microscopy and an additional 153(12.0% 0 positive cases from the 1263 smear negative cases as presented in **Table 2.**

Rifampicin resistance among MTB detected cases was observed by Xpert in 12 (3.1%) out of 389 MTB cases **(Table 3).** The socio-demographic characteristics of these pulmonary tuberculosis patients is presented in **Table 4.** The PTB patients were mostly males (66.1%) in the age group 25-34 years (37.8%) and traders (52.4%).

Discussion

A highly sensitive and specific tuberculosis diagnostic test would contribute immensely to achieve the 90% reduction in tuberculosis incidence by 2035 as established by the End-TB strategy [13].

In this study, we offered Xpert MTB/RIF test to all presumptive pulmonary tuberculosis cases as is done in other countries [14,15]. Xpert MTB/RIF test detected 389 (25.9%) pulmonary tuberculosis cases out of 1500 presumptive pulmonary TB cases. It had been emphasized [10]. that Xpert can be used as an initial diagnostic test for tuberculosis detection and rifampicin resistance in patients suspected of having tuberculosis, MDR-TB or HIV associated tuberculosis.

Xpert may also be valuable as an add-on test following microscopy for patients who have previously been found to be smear negative [16]. We compared the performance of smear microscopy with Xpert MTB/RIF assay in MTB detection. Smear microscopy detected 237 (15.8%) MTB cases whereas Xpert MTB/RIF test correctly detected all 237 positive cases of smear microscopy in addition to 152 (12.0%) positive cases among

Table 1 Detection of MTB in sputum specimens using Xpert MTB/RIF assay.

No. sputum Specimens	MTB detected (%)	MTB not detected (%)
1500	389 (25.9)	1111 (74.1)

Table 2 Comparative detection of MTB using microscopy Vs. Xpert MTB/RIF.

No of specimen examined	Microscopy		Xpert MTB/RIF	
	AFB+ (%)	AFB- (%)	MTB detected (%)	MTB detected (%)
1500	237 -15.8	1263 -84.2	389 -25.9	1111 -74.1

Table 3 Rifampicin resistance among MTB detected cases.

	MTB detected (n=389)			
No of samples	MTB not detected (%)	RIF resistance detected (%)	RIF not detected (%)	RIF Resistance indeterminate (%)
1500	1111 (74.1)	12 (3.1)	374 (96.1)	3 (0.8)

Table 4 Rifampicin resistance among MTB detected cases. Socio-demographic characteristics of PTB patients.

Characteristics	PTB+(%) n=389
Gender	
Males	257 (66.1)
Females	132 (33.9)
Age group(Years)	
15-24	54 (13.9)
25-34	147 (37.8)
35-44	99 (25.4)
45-54	47 (12.1)
55-64	29 (7.5)
65 and above	13 (3.3)
Occupation	
Trading/business people	204 (52.4)
Unemployed	124 (31.9)
Civil servants	21 (5.4)
Students	40 (10.3)
Marital status	
single	103 (26.5)
Married	225 (57.8)
Divorced/widowed	61 (15.7)
Level of Education	
No formal	188 (48.3)
Primary	120 (30.8)
Secondary	48 (12.3)
Tertiary	33 (8.5)

1263 suspects with smear negative results. Thus, Xpert MTB/RIF outperformed smear microscopy and established a diagnosis in a significant proportion of presumptive pulmonary tuberculosis cases with smear negative tuberculosis. This is compatible with a study [3]. Where by ZN microscopy 77% MTB detection was observed while 82.5% detection was seen with Xpert MTB/RIF. Other workers [8,17] have reported that the smear microscopy detected only 9.3% (21/227) of cases whereas Xpert MTB/RIF detected 16.7% (38/227) of cases. In agreement, they noted that Xpert MTB/RIF diagnosed more patients than smear microscopy.

Rifampicin resistance is a precursor to the development of multi-drug resistant tuberculosis (MDR-TB) and a reliable predictor of multi-drug resistance in settings where the prevalence of rifampicin resistant MTB is high [16]. In our study, among 389 (25.9%) MTB cases, rifampicin resistance was detected in 12 (3.1%) patients. This is similar to a study where rifampicin resistance was detected in 16 (6.5%) out of 245 patients. Other studies [18] had reported similar but higher rates of rifampicin resistance. Since we excluded PTB patients already on tuberculosis medicine, all the 12 rifampicin resistant cases were primarily infected (MDR-TB cases). This is worrisome as MDR-TB spread on the community could be on-going. Thus, WHO recommends that if Xpert detects rifampicin resistance in patients considered at risk of MDR-TB, an appropriate MDR-TB regimen should be initiated while additional sputum specimens are obtained for culture and drug sensitivity testing [19].

Socio-demographic characteristics of these PTB patients revealed that they were mostly young males in the age group 25-34 years, employed as traders/business people and married. It had been documented [20] that traders amongst occupational groups were populations at risk of tuberculosis in Abia state.

Conclusion

Xpert MTB/RIF test is an accurate method for rapid diagnosis of PTB. It outperformed microscopy and detected MTB in smear negative cases. It could adequately serve as initial diagnostic test for PTB detection and rifampicin resistance in Anambra state and Nigeria.

References

1 Walis RS, Pai M, Menzies D, Doherty TM, Walzi G, et al. (2010) Biomarkers and diagnostics for tuberculosis: progress, needs, and translation into practice. Lancet 375: 1920-1937.

2 McNerney R, Daley P (2011) Towards a point-of-care test for active tuberculosis: obstacles and opportunities. Nat Rev Micriobiol 9: 204-213.

3 Darwish M, Magda AEW, Hazem A (2013) Diagnostic assessment of Xpert MTB/RIF in sample of Mycobacterium tuberculosis. Egyptian patients. Afr J Microbiol Res 7: 5107-5113.

4 World Health Organization (2011) Global Tuberculosis Control, Switzerland.

5 Ozkutu KN, Surucuoqls S (2014) Evaluation of the Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary tuberculosis in intermediate-prevalence setting. Microbiol Bul 48: 223-232.

6 Cresswell J, Codlin AJ, Andre E (2014). Results from early programmatic implementation of Xpert MTB/RIF testing in nine countries. BMC Infect Dis 14: 2.

7 VanRie A, Page-Ship L, Scott L, Sanne I, Stevens W (2010) Xpert MTB/RIF for point-of-care diagnosis of tuberculosis in high HIV burden, resource-limited countries; Hype or hope. Expert Rev Mol Diagn 10: 937-946.

8 Dereje AG, Yoseph CM, Adugua NG, Gizachew TA, Melaku TD, et al. (2015) Xpert MTB/RIF assay for diagnosis of pulmonary tuberculosis in sputum specimens in Remote healthcare facilities. BMC Microbiology 15: 220.

9 Boehme CC, Nabeta P, Hillemann D (2010) Rapid molecular detection of tuberculosis and rifampicin resistance. N Engl J Med 363: 1005-1015.

10 Steingart KR, Schiller I, Horne DJ (2014) Xpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Databases Syst Rev 1 CD009593 Pub 3.

11 Banada PP, Sivasubramani SK, Blakemore R, Boehme C, Perkins MD, et al. (2010) Containment of bioaerosol infection risk by the Xpert MTB/RIF assay and its applicability to point-of-care settings. J Clinic Microbiol 48: 3551-3557.

12 Federal Ministry of Health/NTBLCP (2012) National Tuberculosis and Leprosy Control Programme Annual Report. Abuja, Nigeria.

13 Uplekar M, Diana W, Knut L (2015) WHO New End -TB Strategy. Lancet 385: 1799-1801.

14 Raizadan N, Sachdeva KS, Srenivas A (2014) Flexibility of decentralized development of Xpert MTB/RIF test at lower level of health system in India. PLOS one 9: e89301.

15 Theron G, Zijenah L, Chanda D (2014) Feasibility, accuracy, clinical effect of point-of-care Xpert MTB/RIF testing for tuberculosis in primary care settings in Africa: a multicentre randomized controlled trial. Lancet 383: 424-435.

16 Stangart KR, Sohn H, Schiller I (2013) Xpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane database Syst Rev 1 CD 009593 Pub 2.

17 Chang K, Lu W, Wang J, Zang K, Jia S, et al. (2012) Rapid and effective diagnosis of tuberculosis and rifampicin resistance with Xpert MTB/RIF assay: A meta analysis. J Infect 64: 580-588.

18 Mustapha G, Jumoke O, Nwadike P, Emeka E, Akang G, et al. (2015) Assessment of Gene-Xpert MTB/RIF programme implementation and the challenges for enhanced tuberculosis diagnosis in Nigeria. SAARC J Tuberc Lung Dis HIV/AIDS, p: 2.

19 World Health Organization (2013) Multidrug resistant tuberculosis (MDR-TB) update. Switzerland.

20 Nwachukwu MC, Orji A, Kanu I, Okereke H (2009) Epidermiology of pulmonary tuberculosis in some parts of Abia state, Federal Republic of Nigeria. Asian J Epidemiol 2: 13-19.