RESEARCH ARTICLE

Performance of GeneXpert in the Diagnosis of Tuberculosis in a Decentralized Area: Example of Hopital De La Paix, in Ziguinchor, Southern Senegal from 2016 to 2018

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Abstract

Introduction: The Xpert MTB/RIF test is one of the innovative responses to the challenges of early diagnosis of tuberculosis and rifampicin resistance. Three years after the arrival of GeneXpert at La Paix hospital, we carried out this study in order to assess its contribution to the diagnostic process.

Methods: This cross-sectional, descriptive and analytical study focused on suspected tuberculosis patients whose pathological products were analyzed at the unit of microbiology of La Paix hospital of Ziguinchor, Senegal from January 2016 to December 2018.

Results: Data from 2137 patients were analyzed. The sex ratio (M/F) was 1.3 and the mean age 41 ± 19 years. GeneXpert performed better in sputum (33.05%) and gastric fluid (25.54%). In 24.30% of cases, the GeneXpert was positive and the smear negative. In 14.86% of cases, the GeneXpert was negative and the smear positive. These cases refer probably to nontuberculous mycobacteria. Therate of resistance to Rifampicin was 3.1%. Male sex and age under 55 were significantly associated with high rates of GeneXpert positivity.

Conclusions: The benefit of GeneXpert was evident in the diagnosis of clinical forms of tuberculosis and in the diagnosis of rifampicin resistance.

Keywords

GeneXpert, Tuberculosis, Ziguinchor, Senegal, Rifampicin resistance

Introduction

Tuberculosis remains a global public health problem. It is the leading cause of death from mono infection and is among the top ten deadliest diseases in the world. According to the World Health Organization (WHO), around 10 million people developed active tuberculosis in 2018 and 1.7 million died from it [1]. The problem of tuberculosis has become more urgent due to the co-infection with HIV/AIDS. In fact, 9% of people with tuberculosis in the world are also infected by HIV [1,2].

Furthermore, the diagnosis and management of tuberculosis remain difficult and complex due to the heterogeneity of the forms of the disease and the growing emergence of strains resistant to first-line anti-tuberculosis molecules. In 2017, more than 500,000 cases of tuberculosis were resistant to Rifampicin; 82% of these strains had additional resistance to isoniazid [1]. The Xpert MTB/RIF test is one of the innovative responses to the challenges of early diagnosis of tuberculosis and real-time detection of rifampicin resistance mutations [3,4]. Thus, the WHO has recommended it as a first-line diagnostic test in countries which have it [1,2]. It is in this vein that Senegal has equipped its various health regions with GeneXpert devices. Three years after setting up GeneXpert at Hopital de la Paix, in Ziguinchor,

we carried out this study with the aim of evaluating its contribution to the diagnosis of tuberculosis in a decentralized environment where culture is not routinely available.

Methods

We carried out a cross-sectional, descriptive and analytical study over a period of 3 years from January 1st, 2016 to December 31st, 2018, covering all the pathological samples of patients suspected having pulmonary and/or extra-pulmonary tuberculosis, coming from the National Tuberculosis Control Program (TCP) services in the various health districts of Ziguinchor and analyzed in the mycobacteriology laboratory of Hopital de la Paix. An Xpert MTB/RIF test was performed on all of these pathological samples. Tuberculosis was suspected based on epidemiological (a history of tuberculosis contagion, history of tuberculosis, HIV status) and clinical (chronic symptoms, signs of tuberculosis impregnation).

Sociodemographic variables were also analyzed. Data entry was done with Epi data software and analysis by Stata software version 11.3. The percentages were compared with the chi^2 test. A value of $p < 0.05$ was considered to be the threshold of significance.

Results

In total, the data of 2,137 patients were analyzed, the majority of which, meaning 864 cases (40.43%) during the year 2016. The male gender was predominant with 1,225 cases (57.32%) for a sex-ratio (M/F) of 1.3. The mean age was 41 ± 19 years (range 1 to 95 years) and the age group of 31 to 45 years was the most represented with 27.52% or 588 cases (Table 1). The HIV serology positivity rate was 7.6% in our series. Fever, weight loss and cough were the reasons for running the Xpert MTB/RIF test in 99.35%, 98.89% and 81.64% of cases respectively. The samples examined were mostly sputum (73.14%) followed by tubing fluid (8.63%) and pleural fluid (8.35%).

Of 1399 sputum collected, the Ziehl-Neelsen's direct microscopy came back positive in 33.6% of cases. All of our patients (2,137 patients) had received an Xpert MTB/RIF test. Of the 627 samples that returned positive (29.34%), 563 were of pulmonary origin, with a positivity rate of 33.05% on sputum (Table 2). The performance of GeneXpert was variable depending on the nature of the samples with higher sensitivity in sputum (33.05%) and in gastric tubing fluid (25.54%).

Considering the samples on which both the GeneXpert and the microscopy were carried out, the GeneXpert was negative and the smear positive in 14.86% of cases. Among the AFB samples negative by microscopy, 226/930 or 24.30% were positive with the Xpert MTB/RIF test. Rifampicin resistance was detected in 20 cases, meaning 3.1% (Table 3). Of the 6 cases of rifampicin resistance detected with GeneXpert, 5 were culture-confirmed MDR-TB.

Table 1: Socio-demographic characteristics of patients followed for tuberculosis at the peace hospital in Ziguinchor, Senegal from 2016 to 2018 (n = 2,137).

Characteristics	Effectifs	%
Year of the test		
2016	864	40.43
2017	615	28.77
2018	658	30.80
Sex		
Male	1225	57.32
Female	912	42.68
Age range		
0-14	188	8.88
15-29	498	23.30
31-45	588	27.52
46-60	512	23.96
> 60	341	16.42

Table 2: Results of GeneXpert and microscopy of patients followed for tuberculosis at the peace hospital of Ziguinchor, Senegal from 2016 to 2018.

Variables	Effectifs	%
Microscopy (n = 1399)		
Negative	929	66.4
Positive	470	33.6
GeneXpert (n = 2 137)		
Négative	1510	70.65
Positive	627	29.34
Rifampicin resistance (n = 2 137)		
No	2114	99.06
Yes	20	0.93

Table 3: Performance of GeneXpert according to the type of pathological product of patients followed for tuberculosis at the peace hospital in Ziguinchor, Senegal from 2016 to 2018 (n = 2,137).

Samples	Effectifs	Positive case	%
Sputum	1561	516	33.05
Liquide de tubage gastrique	184	47	25.54
Gastric tubing fluid	178	26	14.60
Peritoneal fluid	109	7	06.42
Ganglion specimens	56	28	50.00
Spinal fluid	46	3	06.52
Pericardial fluid	03	0	00.00
Total	2137	627	29.34

In the analytical study, the sensitivity of GeneXpert was greater in males (32% vs. 25%, p = 0.006). The positivity rate for the Xpert MTB/RIF assay was 28.7% vs. 17.7% by microscopy alone. The sensitivity of GeneXpert did not show any difference according to the HIV status. In addition, the sensitivity of GeneXpert

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Table 4: Sensitivity of GeneXpert according to sex, age, HIV serological status and microscopy result of patients followed for tuberculosis at the peace hospital of Ziguinchor, Senegal from 2016 to 2018 (n = 2,137).

Variables	GeneXpert n (%)		p-value
	Positive	Négative	
Sex			
Male	397 (32)	852 (68)	0.006
Female	230 (25)	695 (75)	
HIV status			
Positive	48 (29)	119 (71)	0.308
Négative	579 (29)	1428 (71)	
Age range			
< 55 ans	518 (32.68)	1067 (67.32)	0.0000
≥ 55 ans	109 (19.22)	458 (80.78)	
Microscopy (AFP)			
Positive	400 (85.14)	70 (14.86)	0.0000
Négative	227 (24.32)	702 (75.68)	

was significantly greater in patients under 55-year-old compared to patients over 55-year-old (p = 0.000) (Table 4).

Discussion

Of the 2,137 Xpert MTB/RIF test results analyzed; male represented 57.32% and the mean age was 41 ± 19 years (range 1 to 95 years). This male predominance has been found in several studies in Africa. It was 75% in Dakar [5]; 60.6% in Madagascar with an average age of 40.19 years [6]; 60.3% in Marrakech [7]; in Conakry 63.7% with an average age of 30.1 years [8]. This predominance of tuberculosis in young adults is linked to the fact that this range of the population is the most active in our context and therefore more exposed to the disease.

The positivity rate for GeneXpert in our study was 29.34%. This result was higher than the 12.1% reported in Madagascar [9] and lower than the 40.7% and 49% noted in Casablanca, respectively in microscopy negative pulmonary tuberculosis and in the cases of relapse with HIV positive patients [10]. In South Korea the sensitivity of the Xpert MTB/RIF test was 67.7% in the diagnosis of extra-pulmonary tuberculosis compared to culture [11]. With his 128 patients, 40% of whom were HIV positive, Niang reported a sensitivity of 91% for the Xpert MTB/RIF test for microscopy positive/culture positive cases and 60% for microscopy negative/culture positive cases [12]. These differences are believed to be due to the different contexts, the population of study and methods used.

In this study, Mycobacterium tuberculosis was detected by GeneXpert in 227/968 (24.32%) specimens that were microscopically negative. The high sensitivity of the Xpert MTB/RIF test compared to microscopy is well established. Lee in South Korea found that the

sensitivity and specificity of the Xpert MTB/RIF assay of 81.6% and 100% in bronchoalveolar lavage fluid (BAL) was significantly higher than that of microscopy, respectively, of 13.2% and 98.8% [13]. In London, sensitivity was 68% compared to culture, of which 44.7% microscopic positive and 55.3% microscopic negative [14]. In Nepal 79.7% of patients diagnosed with GeneXpert had negative microscopy [15]. Iram S, et al. reported 15% in Pakistan [3]. Based on these results, the WHO has recommended GeneXpert as a first-line diagnostic test in countries that have it, specially in patients infected with HIV [1,2].

In this study; 7.6% of patients were infected with HIV. The GeneXpert positivity rate in this population was 28.7% versus 17.7% by microscopy alone. The benefit of GeneXpert in HIV positive patients is widely described in the literature. Our results only confirm an already established evidence [16,17].

Furthermore, among the 470 microscopically positive cases, Mycobacterium tuberculosis was not detected in 70 (14.86%) of them. Those cases are probably related to non-tuberculosis Mycobacteria. In Mali, a study showed that 11/142 or 8% of chronic tuberculosis cases were from non-tuberculosis mycobacteriosis [18]. The culture not carried out in our study would have enabled us to confirm these cases of non-tuberculosis mycobacteriosis.

Resistance to anti-tuberculosis drugs is currently one of the major challenges in the management of tuberculosis [1]. About 16% of the strains isolated in a study in Brazzaville were resistant to rifampicin [8]. In such a situation, the role of the Xpert MTB/RIF test is unequivocal. In China, a meta-analysis of 18 studies with GeneXpert showed sensitivity and specificity for the detection of resistance to rifampicin at 94.1% and 97.0%, respectively with pulmonary tuberculosis andrespectively 80.4% and 86.1% for extra-pulmonary tuberculosis, [3]. In Nepal, after its introduction in 16 health districts, the Xpert MTB/RIF test detected 21.1% of cases of rifampicin- resistance among suspected cases of resistant tuberculosis [15]. In this study, with GeneXpert, resistance to rifampicin was detected in 3.18%. Compared to our observations, all of these studies attest on the one hand to the emerging nature of resistance to anti-tuberculosis drugs and on the other hand, the major role that the Xpert MTB/RIF tests play in their detection in environments, especially in decentralized settings, where culture is often lacking. However, in our case, six of our cases of resistance to Rifampicin (6/20) benefited from culture and sensitivity tests. The existence of multidrug-resistant strains was confirmed in 83.3% of cases (5/6). Several studies have reported similar results [8,11,15].

Conclusion

GeneXpert has been of great help in the early

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detection of pulmonary and extra-pulmonary tuberculosis but also in the detection of resistance to rifampicin, a problem of growing concern, particularly in a decentralized environment where culture is not available in routine.

State of Current Knowledge on the Subject

- The great difficulty of diagnosing extra pulmonary tuberculosis (and pulmonary tuberculosis in immunocompromised subjects) as well as resistant forms by conventional methods used in developing countries;

- The GeneXpert MTB/RIF® test has proven its performance in the diagnosis of tuberculosis (including resistant forms to rifampicin) in large African cities.

- There is a paucity of data on the performance of GeneXpert MTB/RIF® in decentralized settings.

Contribution of Our Study to Knowledge

This study contributes to improving the availability of data on the performance of GeneXpert MTB/RIF® in the diagnosis of clinical forms of tuberculosis in decentralized settings where culture is not routinely available.

Conflicts of Interest

The authors declare no conflict of interest.

Thanks

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