

High bacillary load among suspected of having pulmonary tuberculosis diagnosed by Genexpert at the hospital central of the armies in Brazzaville, Republic of Congo

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Abstract

Introduction: This study investigated the molecular diagnosis of low bacillary load pulmonary tuberculosis by GeneXpert among individuals suspected of having pulmonary tuberculosis at the Hospital Central of the Armies Pierre Mobengo in Brazzaville, Republic of Congo.

Objective: To demonstrate the importance of the GeneXpert MTB7RIF technique in the detection of high bacillary load among individuals suspected of having pulmonary tuberculosis.

Methodology: Ninety patients aged between 15 and 82 years, suspected of having pulmonary TB and consenting, were recruited when they came for their sputum examination at the medical biology laboratory of the Hôpital Central des Armées between July and November 2019. Three different tests were performed in each patient, including: (1) sputum BAARs microscopy, (2) *Mycobacterium tuberculosis* detection, and (3) rifampicin resistance detection by GeneXpert.

Results: Of a total of 90 patients, 28 patients were pulmonary TB detected by GeneXpert and 11 pulmonary TB patients were detected by microscopy. Of the 90 patients, 4 patients were resistant to rifampicin and 86 patients were not resistant. Concerning TB/HIV co-infection, 8 of the 20 HIV-infected patients were co-infected.

Conclusion: GeneXpert significantly improves the detection of tuberculosis, especially in patients with paucibacillary disease, TB/HIV co-infection and offers a more reliable detection of rifampicin.

Keywords: Molecular Epidemiology, *Mycobacterium Tuberculosis*, Pulmonary Tuberculosis

Introduction

Tuberculosis is still a major public health problem in sub-Saharan Africa. Pulmonary involvement is the most frequent localization and represents the usual source of transmission, and it is caused mainly by *Mycobacterium tuberculosis* [1].

In countries with a high prevalence of tuberculosis, microscopy-negative tuberculosis should be suspected in the presence of suggestive clinical and radiological signs. If the immediate evolution with anti-tuberculosis drugs was considered favor-

able, an atypical mycobacteria infection cannot be excluded in the absence of culture. Bacteriological diagnosis is difficult because of the pauci-bacillary form and the difficulty of collecting sputum. Currently, LED fluorescence is undoubtedly the most plausible alternative to ZN staining. Many African countries use fluorescence microscopy, which is not the case in the Republic of Congo.

In 2018, the incidence of tuberculosis in the country was 277 per 100,000 inhabitants, mortality is 63 per 100,000 inhabitants, TB/

HIV incidence is 99 per 100,000 inhabitants, TB/HIV mortality is 43 per 100,000 inhabitants, incidence (TBMR/RR) is 12 per 100,000 inhabitants [2].

The presence of BAAR on direct examination does not mean that it is *Mycobacterium tuberculosis*. Indeed, it may be another *Mycobacterium* (mycobacteriosis). But it is the clinical context, the data of the anatomopathological examination and especially the results of the culture that will decide. Molecular examination by Genexpert is the examination of choice for the detection of *Mycobacterium tuberculosis* at the Hospital Central of the Armies in Brazzaville, because up to now mycobacterial culture is not implemented in Brazzaville in the Republic of Congo.

Individuals with a positive molecular diagnosis of sputum are particularly contagious. By decreasing the bacillary density, treatment reduces the risk of contagiousness. The aim was to study the diagnostic aspects of pulmonary tuberculosis with a high bacillary load at the Hôpital Central des Armées.

Methodology

This study was conducted at the Hospital Central of the Armies in the city of Brazzaville in the medical biology laboratory. It is a cross-sectional and descriptive study conducted between July 12 and November 15, 2019. The study population consisted of patients suspected of pulmonary tuberculosis coming for consultation to the Hospital Central of the Armies. Patients were classified into new and old cases.

All criteria for inclusion in the study were explained to the study subjects and their legal representative. All patients, who had their examination report requested, who gave their informed consent, were included in the study. A standardized data collection form was used to collect information from patients regarding their socio-demographic, clinical, risk factor, and biological data.

Particular attention was paid to the respect of ethical rules by following the Nuremberg code (1947) and the Helsinki declaration, amended in 2000. All inclusion procedures were subject to the prior free and informed consent of the individuals participating in the study. The participants were informed orally about the purpose of the study, the use of their biological material and the use of the data collected. The consent of their parent or legal

representative. All samples were coded to protect the identity of the individuals participating in the study.

The Director General of the Hospital Central of the Armies gave his written authorization before starting the study and exploiting all data. This study is an integral part of the laboratory work that is routinely done in the medical biology laboratory. We collected the data while respecting the anonymity of the patients, as well as the confidentiality of their information after approval.

According to the diagnostic strategy used at the Hospital Central of the Armies, the patient was given two (02) unbreakable sterilized spittoons to collect the sputum. The proper conditions for collection were indicated to the patients. Briefly, two to five milliliters of sputum are required. Sputum was collected the next day and the day after that in the morning after waking up in a sitting position after rinsing the mouth twice with water and before brushing the teeth. It was explained to the patient that he should cough to spit and not spit saliva or nasopharyngeal mucus and press the spittoon under his lower lip to avoid contaminating the outside of the container.

Molecular Analysis of Samples

Sputum was analyzed for the Xpert/MTB/RIF test. Socio-demographic variables (Age - Sex - Social status - Occupation - Marital status), clinical variables (Cough- Type of cough- Quality of cough-Fever), risk factors (Alcohol-Prison-Tobacco-Drugs-Diabetes-Antituberculosis) and biological variables (TB status by microscopy - TB status by Xpert MTB/RIF - Rifampicin resistance - HIV status) were studied. Microsoft Excel 2016 was used for data entry and graphing and Epi info version 7.2 for database processing. Frequency was used to determine the different variables among the patients in our study. Comparison between groups was performed using the Chi2 test or the Fisher test, when the expected values in a cell were <5.

Results

Socio-Demographic Characteristics

The mean age was 38.9 ± 12.7 . The median was 38 years, the maximum age was 81 years, and the minimum was 15 years. The age range <25 years was represented by 12 individuals or 13.33% and 78 had an age range >25 years, or 86.67%.

Clinical Characteristics

Table 1: Distribution of individuals according to clinical characteristics

Variables	Frequency	Percentage	IC. 95%
Cough			
Yes	76	84.44%	75.28-91.23
No	14	15.56%	8.77-24.72
Type of cough			
Chronic	37	48.68%	37.04-60.43
Acute	39	51.32%	39.57-62.96
Duration of cough			
<2 weeks	30	39.47%	28.44-51.35
>2 weeks	46	60.53%	48.65-71.56

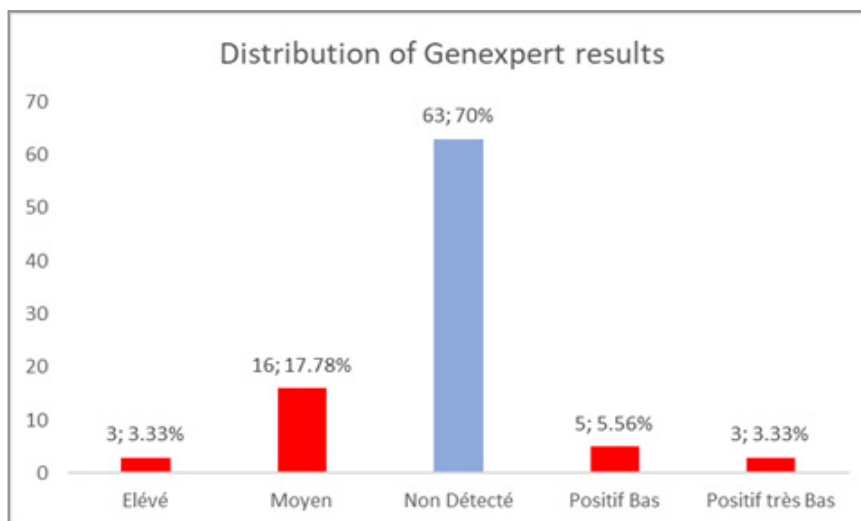
The table I shows that there were more individuals with cough (84.44%), acute cough was the majority (39/87), duration of cough > 2 weeks had a percentage of 60.53%.

Table 2: Distribution of individuals according to cough and type of cough and detection of *Mycobacterium tuberculosis*

Variables		GeneXpert results		P-value
		Positive	Negative	
Type of cough	Acute	7 (17,95%)	32 (82,05%)	0,01
	Chronic	17 (45,95%)	20 (54,05%)	
Cough	Yes	52 (68,42%)	24 (31,58%)	0,01
	No	14 (100%)	0 (0%)	

Table II shows us that chronic cough 17 (45.95%) was more important among GeneXpert positive cases. Cough cases 52 (68.42%) were more important among GeneXpert positive cases.

Characteristics of individuals according to molecular results

**Figure 1: Distribution of individuals according to molecular results**

Of the 90 individuals participating in the study, 63 (70%) had no presence of *Mycobacterium tuberculosis*. GeneXpert results were represented by the detection of *Mycobacterium tuberculosis*: 3 high detection cases (3.33%), 16 medium detection cases (17.78%), 5 low detection cases (5.56%) and 3 very low detection cases (3.33%). The prevalence of pulmonary tuberculosis by microscopy was therefore 12.22%.

Discussion

Sputum smear microscopy allows rapid and reliable identification of patients with pulmonary tuberculosis when there are more than 5000 bacilli/ml of sputum. If the sputum contains less than 5000 bacilli/ml, it is very unlikely that the sputum smear will diagnose pulmonary tuberculosis, resulting in low overall sensitivity for pulmonary tuberculosis [3, 4]. Smear-negative pulmonary tuberculosis is less common than smear-positive pulmonary tuberculosis, but it is a transmissible infectious form of tuberculosis [5-7]. The Genexpert catches, therefore, cases where the sputum has less than 5000 bacilli/ml and thus allows with important implications for clinical decision making for individuals considered highly contagious and at high risk of contamination [8].

In our study, the average age was approximately 39 years, and the most affected age group was over 25 years. The Genexpert test detected 30% of the cases with high bacillary load represent-

ed by detection levels ranging from high to very low (Figure 1). Nevertheless, 70% of the individuals did not have *Mycobacterium tuberculosis* strains. Some samples that were found to be paucibacillary and not detectable by microscopy, Xpert allowed a diagnosis with a delayed Ct [9-11]. With this detection a possible presence of RIF resistance would be known, thus early and optimal management will be initiated.

Chronic cough was associated with the presence of *Mycobacterium tuberculosis* ($p=0.01$) (Table I). This has been widely described in several studies of pulmonary tuberculosis [12-14]. The presence of cough on clinical examination is also associated with the presence of *Mycobacterium tuberculosis* ($p=0.01$) (Table II). Cough is a risk factor for pulmonary tuberculosis and chronic cough is significantly related to the detection of *Mycobacterium tuberculosis* [14-15].

Although microscopy-negative pulmonary tuberculosis may not be a primary focus for national tuberculosis control programs due to its lower infectiousness, clinicians recognize its significance as timely initiation of anti-tuberculosis treatment plays a vital role in managing the disease and preventing potential complications. The diagnosis of pulmonary tuberculosis therefore remains a public health problem in our country, especially in immunocompromised subjects [16, 17]. With the introduction of GeneXpert in our TB management system, more and more

efforts are being made to improve firstly the diagnosis of pulmonary TB and secondly to better guide the therapeutic management.

This Genexpert technique detected *Mycobacterium tuberculosis*, the pathogen that confers tuberculosis, in 28 patients or 31.11%. Okonkwo et al. in a similar study found a prevalence of 19.8% of *Mycobacterium tuberculosis* detected [17]. This higher prevalence is certainly due to the fact that our study took place in a hospital setting where there is a high concentration of patients with suspected tuberculosis.

Conclusion

With the introduction of the GeneXpert, we now rely only on clinical, radiological and microscopic data. In view of the prevalence of pulmonary tuberculosis which was 12.22% and 31.11%, respectively by microscopy and GeneXpert. There is therefore a considerable catching up of microscopy negative pulmonary TB cases that were found positive by GeneXpert. The weaker the TB bacilli, the lower the chance of finding BAARs. This allows us to conclude that there is a strong need to provide molecular equipment to referral and base hospitals in the country.

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