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Clinical profile of patients with HIV-positive suspected pulmonary tuberculosis

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Abstract
Globally, an estimated 10.0 million (range, 9.0-11.1 million) people fell ill with TB in 2018, a number that has been relatively stable in recent years. The burden of disease varies enormously among countries, from fewer than five to more than 500 new cases per 100 000 population per year, with the global average being around 130. 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. Considering the chief complaints at presentation, majority of patients (96%) had cough, followed by fever in 40% cases, shortness of breath in 22%, hemoptysis in 6% and weight loss in 6%.
Keywords: HIV-positive suspected pulmonary tuberculosis, CBNAAT, CD4 counts

Introduction

Tuberculosis (TB) is the leading cause of death from a single infectious disease agent worldwide and the leading cause of death among persons living with human immunodeficiency virus (HIV) infection, accounting for approximately 40% of deaths in this population. The United Nations' (UN) Sustainable Development Goals and the World Health Organization's (WHO's) End TB Strategy have defined ambitious targets for 2020-2035, including a 35% reduction in the absolute number of TB deaths and a 20% reduction in TB incidence by 2020, compared with 2015. Since 2000, WHO has produced annual TB estimates for all countries[1].

Globally, an estimated 10.0 million (range, 9.0-11.1 million) people fell ill with TB in 2018, a number that has been relatively stable in recent years. The burden of disease varies enormously among countries, from fewer than five to more than 500 new cases per 100 000 population per year, with the global average being around 130. There were an estimated 1.2million (range, 1.1-1.3 million) TB deaths among HIV-negative people in 2018 (a 27% reduction from 1.7 million in 2000) and an additional 251,000 deaths (range, 223,000-281,000) among HIV positive people (a 60% reduction from 620,000 in 2000). TB affects people of both sexes in all age groups but the highest burden is among men (aged ≥15 years), who accounted for 57% of all TB cases in 2018. By comparison, women accounted for 32% and children (aged <15 years) for 11% [2].

Tuberculosis (TB) disappeared from the global public health agenda in the 1960s and 1970s. The improved socioeconomic conditions and the discovery of anti-TB medications had led to its decline during this period. Nonetheless, with the onset of the HIV pandemic in the 1980s, along with increases in drug resistance, TB re-emerged in the early 1990s and was declared a 'global health emergency' by the World Health Organization (WHO) in 1993[3].

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During 1990-2015, an estimated 7-9 million new cases of TB were reported every year. Around 1.5-2 million individuals died from TB annually during this period, with the count reaching a peak in 2004. In the sub-Saharan Africa, the number of TB patients doubled or tripled in some countries due to the HIV epidemic. TB became the leading cause of mortality in the region, with HIV/AIDS as the commonest underlying factor[4].

In response to the increasingly alarming TB situation, the WHO launched the DOTS strategy, which aimed to use early diagnosis and cure of the infectious cases as the best prevention for TB transmission. The aim was to detect at least 70% of infectious cases, and cure at least 85% of them by the year 2000. The DOTS strategy relied on smear-microscopy for TB detection, and a standardized short course drug regimen for TB treatment[5].

Member States adopted the recommended DOTS Strategy for TB control in 1995. In 2003, the Expanded Framework for DOTS Strategy that incorporated response to TB/HIV co-infection and multi-drug resistant TB was launched. This was followed by the launch of the Stop TB Strategy in 2006. In May 2014, the sixty-seventh World Health Assembly adopted a post-2015 TB prevention, care and control strategy known as the End TB Strategy. It aims to end the global TB epidemic by 2035. In 2015, the United Nations (UN) Sustainable Development Goals (SDGs), which are fully aligned with the WHO End TB Strategy, were adopted. The SDGs have set the target of ending the TB epidemic by 2030. The End TB Strategy was introduced in supporting countries to achieve the indicated goal and targets. It provides a holistic, multisectoral response to overcome issues and challenges, and to end the epidemic in the context of the UN SDGs for 2030[6].

Methodology

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.

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. Extra pulmonary tuberculosis.

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Results

Table 1: Age distribution of patients

Distribution of study subjects based on age		
Age Group	**Frequency**	**Percent**
20-30 yrs	5	10
30-40 yrs	15	30
40-50 yrs	17	34
50-60 yrs	11	22
60-70 yrs	2	4
Total	50	100

Out of 50 patients, the majority was in the 40-50 years age group which constituted 34%, followed by 30% in the 30-40 years, 22% in the 50-60 years, 10% in the 20-30 years and 4% in the 60-70 years age group.

Table 2: Distribution based on chest X-ray

Distribution of study subjects based on results of chest x-ray		
Chest-X-ray	**Frequency**	**Percent**
Abnormal	18	36
Normal	32	64
Total	50	100

In our study, 32% had abnormal chest x-ray findings and the rest 64% had normal chest x-ray.

Table 3: Distribution based on CD4 counts

Distribution of study subjects based on CD4 Counts		
CD4 count	**Frequency**	**Percent**
<200	13	26
>200	37	74
Total	50	100

In our study, among 50 cases, 26% had CD4 counts below 200, while 74% had CD4 counts above 200.

Table 4: Clinical profile of patients

Clinical Profile of the patients		
Patient Profile	**Frequency**	**Percent**
Prior h/o pulmonary Koch		
No	48	96
Yes	2	4

Chief Complaints		
Cough	48	96
Fever	20	40
SOB	11	22
Hemoptysis	3	6
Weight loss	3	6
CBNAAT		
Normal	37	74
P-low	6	12

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P-medium	5	10
P-high	2	4
Rifampicin Resistance		
Detected	1	2
Not detected	12	24
NA	37	74
Chest -X-ray		
Abnormal	18	36
Normal	32	64

Considering the chief complaints at presentation, majority of patients (96%) had cough, followed by fever in 40% cases, shortness of breath in 22%, hemoptysis in 6% and weight loss in 6%.

Discussion

One of the main reasons for high mortality in tuberculosis patients is the lack of proper diagnosis at the correct time. With HIV and TB co-infection, this is particularly important because the detection rates are very low. Especially in high HIV prevalent areas, there is an immediate need to implement the latest diagnostic modalities for the detection of tuberculosis[7].Conventional sputum microscopy has decreased sensitivity in PLHIV patients due to scanty sputum production and lack of caseous necrosis leading to a decreased number of bacilli in sputum. The role of CBNAAT with a potential to diagnose tuberculosis and rifampicin resistance within 2 hours is promising. The Xpert MTB/RIF assay is a rapid molecular assay which can be used with minimal hands-on technical time, enabling diagnosis of TB and also a simultaneous assessment of rifampicin resistance in less than 2 hrs. It uses real-time PCR (rt-PCR) technology to diagnose TB and also to detect rifampicin resistance using unprocessed specimens, regardless of the smear status. This assay is conducted in a simple and fully automated cartridge-based system. Rifampicin resistance is particularly amenable to rapid molecular detection since >95% of the rifampicin-resistant strains contain mutations located in the 81 bp core region of RNA polymerase rpoB gene, which encodes the active site of the enzyme in the bacteria. Mutations which occur in this 81bp core region of rpoB gene are highly suggestive of rifampicin resistance. The susceptible isolates will have the same wild-type nucleotide sequence most of the time. The basis for the detection of rifampicin resistance is the difference between the first cycle threshold (early CT) and the last cycle threshold (late CT) M. tuberculosis-specific beacon (ΔCT)[8].

Among 50 patients with PTB-HIV co-infection, the mean age of patients was 43 years. The age group of the patients varied from 20 to 70 years. Most of the patients (34%) were from the age group of 40 to 50 years, followed by the age group of 30 to 40 years which was about 30%. In the study by Patel *et al*. [9], 34% were below 30 years of age, 64% were in the age group of 31-50 years and only 2% were above 50 years of age. In a study by Christopher *et al*. [10]in Nigeria, 32% of the patients were below 30 years of age, 56% were in the age group of 31-50, 8% were 51-65 years and 4% above 65 years.

Conclusion

Majority of patients (96%) had cough, followed by fever in 40% cases, shortness of breath in 22%, hemoptysis in 6% and weight loss in 6%.

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