

Full Length Research Paper

Utility of GeneXpert in diagnosis of tuberculosis among HIV infected adults attended OMACU Centre, Omdurman, Sudan, 2022

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Tuberculosis (TB) and human immunodeficiency virus/acquired immune deficiency syndrome constitute the main burden of infectious diseases in resource-limited countries. Rapid tuberculosis diagnostic testing with GeneXpert in all HIV-positive inpatients in high-burden settings might be more appropriate than conventional methods. This study aims to assess the utility of GeneXpert in the diagnosis of TB in HIV-infected adults. An observational prospective and retrospective study was conducted in Omdurman ART clinic (OMACU) among adult patients with HIV/AIDS registered and on regular follow-up who underwent both AFB smear microscopy and GeneXpert testing for TB. Data was collected by the researcher and analyzed using SPSS V 28 software. The study included 190 patients with HIV infection who underwent sputum AFB and GeneXpert testing for TB. The mean age was 38±10, with 58% males, 89.5% living inside Khartoum, and the age at diagnosis was 36±10 years. On presentation, fatigue was the most common presenting symptom (94%), along with weight loss (92%), fever (70%), night sweating (52%), and cough (41%). The detection rate of sputum AFB testing was 14%, while GeneXpert was 60%, with GeneXpert detecting all the cases detected by sputum AFB. Multivariate logistic regression testing revealed that clinical staging, contact history, vaccination status, and cough affect the detection of TB.

Key words: GeneXpert, tuberculosis, HIV, Sudan.

INTRODUCTION

Tuberculosis (TB) is one of the most widespread and serious infectious disease affecting humans. Today, there are more TB cases than ever before in history due to factors such as poverty, inequity, conflict, suboptimal health services in many countries, and the impact of the

HIV/AIDS pandemic. Approximately 95% of TB cases and 98% of TB-related deaths occur in tropical countries (Maynard-Smith et al., 2014).

TB is the most common life-threatening opportunistic infection and a leading cause of death among people

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living with HIV (PLHIV). Individuals who are HIV-positive and have latent TB infection have a 10% annual and 50% lifetime risk of developing active TB disease (Habte et al., 2016).

TB is the primary reason for hospital admissions and in-hospital deaths among individuals with HIV (Ford et al., 2016). Autopsy studies in people living with HIV have shown that nearly 50% of TB-related deaths were undiagnosed at the time of autopsy (Gupta et al., 2015).

Diagnosing tuberculosis in HIV-positive patients who are hospitalized can be challenging. These patients often have severe immunosuppression, disseminated or extrapulmonary TB, non-specific clinical symptoms, and produce specimens with low bacterial load (Swaminathan et al., 2010). Additionally, a significant proportion (31-63%) of hospitalized patients are unable to produce sputum for diagnostic testing (Lawn et al., 2017; Huerga et al., 2017; Gupta-Wright et al., 2018).

GeneXpert represents a revolutionary approach to TB and drug resistance diagnosis. It simplifies molecular testing by integrating and automating the three essential processes of real-time PCR-based molecular testing, which includes specimen preparation, amplification, and detection. Furthermore, GeneXpert can detect both live and dead bacteria (Pinyopornpanish et al., 2015).

Despite the early initiation of highly active antiretroviral therapy (HAART), TB continues to be a significant cause of illness and death among individuals with HIV infection in Sub-Saharan Africa (Ejeta et al., 2018). Sudan reports low TB notification rates and high treatment failure rates (Hassanain et al., 2018). Therefore, this study aims to evaluate the effectiveness of GeneXpert in diagnosing TB in HIV-infected adults.

MATERIALS AND METHODS

Study design

This study is an observational, prospective, and retrospective hospital-based study.

Study duration

The study was conducted from March to October 2022.

Study area

The study was conducted at the Omdurman ART Clinic (OMACU), the largest ART center in Sudan. OMACU is composed of 3 floors and has 4 doctors. It was established by the Sudan National AIDS Control Program (SNAP) in 2002 as an HIV/AIDS clinical management and VCT center. Since then, the center has provided care for over 4530 patients with HIV/AIDS. OMACU strictly follows the WHO guidelines for the clinical management of HIV/AIDS patients.

It is a family-centered clinic that includes an adult clinic, family planning clinic, PMTCT clinic, pediatrics clinic, HIV/AIDS clinic, adolescent clinic, TB/HIV co-infection clinic, STIs clinic, and Post Exposure Prophylaxis (PEP) clinic.

Study population

The study included adult patients with HIV/AIDS who were registered and on regular follow-up at the HIV center in Omdurman and who had tuberculosis (TB) during the study period. The following criteria were used for inclusion.

Inclusion criteria

HIV-infected adults (aged 18 years and above) underwent both AFB smear microscopy and GeneXpert testing for TB

Exclusion criteria

These criteria typically excluded pregnant women, individuals with severe comorbidities other than HIV and tuberculosis, those previously treated for tuberculosis, non-HIV-positive participants, individuals with drug-resistant TB strains, those unable to provide consent or comply with study procedures, and participants with severe immunodeficiency unrelated to HIV. Patients who refused to participate in the study

Sampling

Sample size

The minimum required sample size was estimated using the following equation:

$$n = N/(1+N*d^2)$$

where n = sample size; d = tolerated margin of error (e.g., we want to know the real proportion within 5%); N = total study population is 1000 sample size = 200.

Sampling technique

A random sampling technique was applied to select a representative study sample.

Data collection tool and methods

Data was collected from the patients and their records by the principal investigator using a data collection sheet that covered demographic, clinical, and investigation data, including GeneXpert results.

Data management

The data was cleaned and entered into Microsoft Excel data sheet and analyzed using SPSS version 28 software. Categorical data was represented in the form of frequencies and proportions, while continuous data was represented as mean and standard deviation.

The chi-square test was used as a test of significance for qualitative data, and the ANOVA test was used as a test of significance for quantitative data. Logistic regression analysis was used to assess associations. Microsoft Excel and Word were used to create various types of graphs, such as bar diagrams. A P-value (Probability that the result is true) of <0.05 was considered statistically significant, assuming all the rules of statistical tests and the level of confidence. The data was presented after analysis in the form of univariable tables, cross-tabulation (bivariable tables),

Table 1. Demographic characteristics of HIV infected adults with TB coinfection in Omdurman ART clinic (OMACU) 2022.

| Variable | Frequency/Mean±SD | Percentage |
|------------------|-------------------|------------|
| Age | 38± 10 | - |
| Gender | - | - |
| Male | 111 | 58 |
| Female | 79 | 42 |
| Residence | - | - |
| Inside Khartoum | 170 | 89.5 |
| Outside Khartoum | 20 | 10.5 |
| Age at diagnosis | 36± 10 | - |

Table 2. Presenting symptoms of HIV infected adults with TB coinfection in Omdurman ART clinic (OMACU) 2022.

| Variable | Frequency | Percentage |
|----------------|-----------|------------|
| Fever | 132 | 70 |
| Weight loss | 174 | 92 |
| Cough | 78 | 41 |
| Night sweating | 98 | 52 |
| Fatigue | 178 | 94 |

Table 3. Physical examination of HIV infected adults with TB coinfection in Omdurman ART clinic (OMACU) 2022.

| Variable | Frequency | Percentage |
|-------------------------|-----------|------------|
| Fever | 124 | 65 |
| Positive chest findings | 36 | 19 |

figures, and narrative illustrations.

Ethical considerations

Written ethical clearance and approval for conducting this research were obtained from the Sudan Medical Specialization Board Ethical Committee (EDC). Written permission was obtained from the administrative authority of Omdurman ART Clinic (OMACU). Written consent was obtained individually from all participants. The study data/information was used for research purposes only, and privacy issues were taken into account. Participation in the study was voluntary, and participants had the right to withdraw at any stage.

RESULTS

The study included 190 patients with HIV infection who underwent sputum AFB and GeneXpert testing for TB. The mean age was 38±10, with 58% males, and 89.5% living inside Khartoum. The age at diagnosis was 36±10 years (Table 1).

In more than half (57%) of the patients, the duration of HIV infection since diagnosis was less than 6 months.

The majority of patients (73%) used regimen 1K, and the duration of treatment was less than 6 months in 58% of patients.

Regarding the clinical stage of the disease, 28% were in stage 1, 22% in stage 2, 40% in stage 3, and 10% in stage 4. The history of contact was positive in 19% of patients and the majority (67%) were vaccinated.

On presentation, fatigue was the most common symptom, reported by 94% of patients, followed by weight loss (92%), fever (70%), night sweating (52%), and cough (41%) (Table 2). Examination revealed fever in 65% of patients and positive chest findings in 19% (Table 3). Chest X-ray (CXR) revealed consolidation in 26% of cases, hilar shadow in 15%, cavity in 5%, pleural effusion in 6%, abscess in 2%, and collapse and miliary dissemination each in 1% (Table 4).

The detection rate of sputum AFB testing was 14%, while GeneXpert had a detection rate of 60%. GeneXpert detected all the cases detected by sputum AFB (Table 5).

Multivariate logistic regression testing revealed that clinical staging, contact history, vaccination status, and the presence of cough affect the detection of TB.

Table 4. Radiological findings of HIV infected adults with TB coinfection in Omdurman ART clinic (OMACU) 2022.

| Variable | Frequency | Percentage |
|------------------|-----------|------------|
| Consolidation | 50 | 26 |
| Hilar shadow | 28 | 15 |
| Cavity | 10 | 5 |
| Pleural effusion | 12 | 6 |
| Collapse | 2 | 1 |
| Miliary | 2 | 1 |
| Abscess | 4 | 2 |

Table 5. Sputum AFB vs. Gene expert results in HIV infected adults with TB coinfection in Omdurman ART clinic (OMACU) 2022.

| AFB microscopy | GeneXpert | | Total (%) | p-value |
|----------------|--------------|--------------|-----------|---------|
| | Negative (%) | Positive (%) | | |
| Negative | 76 (46) | 88 (54) | 164 (86) | 0.001 |
| Positive | 0 | 26 (100) | 26 (14) | |
| Total | 76 (40) | 114 (60) | 190 | |

GeneXpert showed an increased detection rate with advanced stage (p-value 0.02), while sputum AFB microscopy did not (p-value 0.7). Significantly, GeneXpert showed good detection in cases with negative or unknown contact history, vaccinated cases, and patients with no cough during presentation compared with sputum AFB microscopy (Table 6).

DISCUSSION

Tuberculosis (TB) is the most common life-threatening opportunistic infection and a leading cause of death among people living with HIV (PLHIV). Diagnosing tuberculosis in HIV-positive inpatients presents challenges. These patients are typically severely immunosuppressed, may have disseminated or extrapulmonary tuberculosis, and often produce specimens with low bacterial count (paucibacillary specimens) (Swaminathan et al., 2010). Therefore, the GeneXpert test was introduced to improve TB detection. This study aims to assess the usefulness of GeneXpert in diagnosing TB in HIV-infected adults in Sudan.

The study included 190 patients with HIV infection who underwent sputum acid-fast bacilli (AFB) and GeneXpert testing for TB. The mean age was 38 ± 10 , with 58% males, and 89.5% residing in Khartoum. The median age of HIV infection diagnosis was found to be 36 years, with slightly more males than females (55% vs. 45%) according to a recent study on demographic and HIV-specific characteristics (Sharma et al., 2015).

Common presenting symptoms included fatigue, weight loss, fever, night sweats, and cough. Physical examination

revealed fever and a few positive chest findings. Imaging tests (chest X-ray) revealed consolidation, hilar shadow, cavity, pleural effusion, abscess, collapse, and miliary dissemination. Takhar et al. (2018) found that cough followed by low-grade fever, anorexia, and weight loss were the most common presenting symptoms, with 50% of patients being febrile during examination. This finding aligns with broader literature demonstrating GeneXpert's superiority in TB detection, particularly in populations with high HIV prevalence. Previous studies have shown comparable or slightly higher detection rates with GeneXpert, ranging from 47.7 to 66.7% in HIV-infected patients across different epidemiological settings. These studies highlight GeneXpert's consistent performance and its crucial role in overcoming the limitations of smear microscopy, which often fails to detect TB in individuals with compromised immune systems.

The detection rate of sputum AFB testing was 14%, while GeneXpert had a detection rate of 60%. A study by Sorsa and Kaso (2021) on patients with TB-HIV coinfection found that the AFB smear detection rate was 32.5%, while the GeneXpert detection rate was 47.7%. The GeneXpert test had almost twice the detection rate compared to smear microscopy (Sorsa and Kaso, 2021). TB often presents in HIV-infected patients in stages 3 and 4 (Takhar et al., 2018), giving GeneXpert an advantage over AFB microscopy as it detects more cases with microscopy (Weinberg and Kovarik, 2010). Saeed et al., 2017 reported 100% advanced stages sensitivity of GeneXpert in diagnosing TB in HIV-infected patients (Saeed et al., 2020). In this study, GeneXpert successfully detected all the cases identified by AFB microscopy. Additionally, the reported detection rate in smear-negative

Table 6. Factors associated with detection rate of TB in HIV infected adults with TB coinfection in Omdurman ART clinic (OMACU) 2022.

| Variable | Sputum AFB | | GeneXpert | |
|--------------------|-------------|---------|-------------|---------|
| | OR/Detected | p-value | OR/Detected | p-value |
| Age | 1.04 | 0.09 | 1.05 | 0.06 |
| Gender | 0.3 | 0.09 | 1.8 | 0.08 |
| HIV duration | 0.5 | 0.4 | 0.9 | 0.9 |
| Treatment duration | 5 | 0.08 | 1.9 | 0.3 |
| Clinical staging | 1.07 | 0.7 | 1.5 | 0.02* |
| Stage 1 | 6 (11%) | - | 24 (45%) | - |
| Stage 2 | 4 (10%) | - | 26 (63%) | - |
| Stage 3 | 12 (16%) | - | 50 (66%) | - |
| Stage 4 | 4 (20%) | - | 14 (70%) | - |
| Contact history | 6 | 0.003* | 3.9 | 0.005* |
| Positive | 12 (32%) | - | 28 (76%) | - |
| Negative | 14 (12.5%) | - | 58 (52%) | - |
| Unknown | 0 | - | 28 (68%) | - |
| Vaccination | 0.2 | 0.005* | 2.2 | 0.04* |
| Positive | 8 (6%) | - | 80 (63%) | - |
| Negative | 14 (34%) | - | 26 (63%) | - |
| Unknown | 4 (18%) | - | 8 (36%) | - |
| Cough | 10 | 0.001* | 8 | 0.001* |
| Yes | 22 (28%) | - | 66 (84.6%) | - |
| No | 4 (4%) | - | 48 (43%) | - |

subjects was 54%. Similarly, Cuong et al. (2021) conducted a study to evaluate the performance of GeneXpert in HIV-infected patients with smear-negative pulmonary TB and found a detection rate of 66.7%. As for the clinical stage of the disease, 28% were in stage 1, 22% in stage 2, 40% in stage 3, and 10% in stage 4. Multivariate logistic regression testing revealed that clinical staging, contact history, vaccination status, and the presence of cough affect the detection of TB. The study also explored GeneXpert's performance across different clinical stages of HIV infection. It found a clear association between advanced HIV stages (3 and 4) and increased TB detection rates using GeneXpert. This correlation emphasizes GeneXpert's ability to diagnose TB even in patients with severe immunosuppression, where conventional tests like AFB microscopy often fall short due to reduced bacterial load and atypical clinical presentations. Similar studies have documented higher TB detection rates with GeneXpert in advanced HIV stages, highlighting its critical role in early and accurate TB diagnosis among the most vulnerable populations. GeneXpert demonstrated an increased detection rate with advanced stages (p-value 0.02), while Sputum AFB microscopy did not (p-value 0.7). This aligns with the findings of Sorsa and Kaso (2021) as they reported that advanced clinical stage was associated with higher TB detection with GeneXpert, but not AFB Positive contact history was reported in 19% of cases, and the majority

had received vaccinations. Moreover, GeneXpert's effectiveness in diagnosing TB in smear-negative cases is particularly significant. In the Sudan study, GeneXpert detected TB in 54% of patients whose sputum samples were negative for AFB microscopy. This capability is crucial as smear-negative TB poses a diagnostic challenge due to low bacterial burden, which is common in HIV co-infections. Studies elsewhere have reported similar findings, with GeneXpert demonstrating detection rates ranging from 60 to 80% in smear-negative patients, underscoring its reliability in overcoming the diagnostic limitations of traditional methods. Significantly, in this study, GeneXpert demonstrated good detection in cases with negative or unknown contact history, vaccinated individuals, and patients without cough upon presentation, when compared with sputum AFB microscopy. These findings are highly significant, as recent studies have shown that a large proportion of inpatients are unable to produce sputum for diagnostic testing (Lawn et al., 2017; Huerga et al., 2017; Gupta-Wright et al., 2018).

Conclusion

The study found that HIV-infected adults with TB coinfection typically presented with symptoms such as fatigue, weight loss, fever, night sweats, and cough. GeneXpert exhibited a 60% detection rate for TB cases

compared to 14% with Sputum AFB microscopy. GeneXpert also demonstrated significantly good detection rates in advanced clinical stages, cases with unknown TB contact history, vaccinated individuals, and patients without cough upon presentation.

RECOMMENDATIONS

GeneXpert demonstrated a 4-fold higher detection rate than sputum AFB microscopy, indicating its potential as a replacement for conventional methods in TB diagnosis. It is recommended to incorporate GeneXpert into regular TB testing protocols to expedite treatment for individuals with suspected TB.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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