

# Diagnosis of Human Immunodeficiency Virus in Tuberculosis Patients

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## ABSTRACT

**Background:** The risk of developing Tuberculosis (TB) is more than 40 times greater in people living with human immunodeficiency virus (HIV) than among those who remained safe from this infection. The burden of these infectious diseases is huge in many underdeveloped countries. Tuberculosis and AIDS have complex health and social determinants with large impacts on quality of life. TB and HIV have been closely linked since the emergence of AIDS. Worldwide, Mycobacterium tuberculosis is the most common opportunistic bacterium affecting HIV-seropositive individuals. The GeneXpert assay represents a major breakthrough in diagnostics for tuberculosis. The immunochromatography technique and PCR play important roles for HIV diagnosis. The rapid screening assays can be used close to the point of care by operators with minimal technical expertise, enabling correct diagnostic approach towards confirmation of tuberculosis by Gene Xpert.

**Objective:** To evaluate presence of human immunodeficiency virus in tuberculosis patients and to compare the results of polymerase chain reaction with two screening tests (enzyme-linked immunosorbent assay and Immunochromatography).

**Study Design:** Comparative analytical study

**Place and Duration of Study:** Department of Pathology, Liaquat University Hospital Jamshoro/Hyderabad from 1<sup>st</sup> January 2017 to 31<sup>st</sup> December 2017.

**Methodology:** Three hundred and thirty diagnosed patients of tuberculosis were included. Their demographic data was recorded and analyzed. Presence of human immunodeficiency virus (HIV) in these subjects was ruled out by two screening parameters immunochromatography (ICT) and enzyme linked immunosorbent assay (ELISA). Diagnosis of tuberculosis was confirmed by Gene Xpert. Polymerase chain reaction (PCR) was used as the confirmatory diagnostic tool to validate the comparative results of screening tests.

**Results:** Higher prevalence of TB infection observed in male subjects. The prevalence of Human Immunodeficiency Virus infection in Tuberculosis patients was 1.8%. Both the ICT and PCR tests were 100% sensitive and 99% specific, proving to be important tools for diagnosis of HIV. Among different age groups, 20-29 years of female subjects were found to be more affected. Co infection was more prevalent in patients with a history of blood transfusion and patients having multiple sex partners.

**Conclusion:** The increasing prevalence of HIV/TB co infection should be under continuous surveillance by the researchers and health care professionals of HIV and TB endemic countries.

**Keywords:** Human immunodeficiency virus, Tuberculosis, Polymerase chain reaction, Enzyme-linked immunosorbent assay, Immunochromatography

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## INTRODUCTION

Pakistan is ranked as the fifth highly affected country by tuberculosis in the world.<sup>1</sup> Annually 5-15% of HIV infected individuals possess risk of developing active tuberculosis.<sup>2</sup> The risk is more than 40 times greater in people living with HIV than among those who do not have HIV infection.<sup>3</sup> Tuberculosis and the human immunodeficiency virus infection are currently the two leading infectious causes of death worldwide, responsible for almost four million deaths annually.<sup>4</sup> Human immunodeficiency virus has not only contributed towards an increase in the number of cases of tuberculosis but has also been one of the major factors behind the increased mortality seen among coinfecting patients.<sup>5</sup> Among several risk factors for TB including HIV/AIDS, silicosis, malnutrition, alcoholism and smoking, diabetes mellitus has received recent recognition.<sup>6</sup>

The prevalence of TB-HIV co-infection widely varies, the prevalence of HIV among TB patients range from 3.8 to

72.3%, whereas the prevalence of TB among HIV-positive patients range from 2.9 to 64.5%.<sup>7</sup> Diagnosis of TB is based on clinical impression and relevant investigations including a chest radiograph, sputum examination for Acid Fast Bacilli, sputum culture for Mycobacterium tuberculosis and biopsy when deemed necessary by the physician.<sup>8</sup> In HIV-infection associated with tuberculosis disease, atypical clinical and X-ray characteristics and low mycobacterial concentrations delay diagnosis of TB.<sup>9</sup>

The Gene Xpert MTB assay represents a major breakthrough in diagnostics for tuberculosis.<sup>10</sup> This testing platform uses molecular beacon technology combined with polymerase chain reaction in a self-contained modular system.<sup>11</sup> Early diagnosis and treatment is essential to combat the dual epidemic of tuberculosis and HIV.<sup>12</sup>

## MATERIALS AND METHODS

This study was carried out in Pathology Department, Liaquat University of Health Sciences

Jamshoro/Hyderabad. Suspected cases of tuberculosis were referred through OPD for diagnosis of tuberculosis by Gene Xpert. Total 330 cases of both genders were included randomly aged above 15 years. Presence of HIV in these subjects was ruled out by two screening parameters ICT and ELISA. In order to validate the comparative results of these screening tests, PCR was used as the confirmatory diagnostic tool. Computation of demographic data was accomplished at the time of sample collection (sputum and blood). Sputum sample was collected according to WHO (2005) criteria, in small plastic container with tight lid in polythene bags. The blood samples were taken in gel tubes for immunochromatography, ELISA and PCR tests. The data was entered and analyzed through SPSS-20.

## RESULTS

There were 172 (52.1%) males and 158 (47.9%) were females. Seventy four (22.4%) patients belonged to age group of under 20 years, 74 (22.4%) belonged to 20-29 years, 66 (20%) to 30-39 years, 56 (17%) belonged to 40-49 years and 60 (18.2%) were from age group of 50 years and above with mean age was  $33.2 \pm 15.28$  years. One hundred and seventy six (53.3%) patients belonged to urban areas and 154 (46.7%) belonged to rural areas. One hundred and forty six (44.2%) patients had no sex partners, 165 (50%) had single sex partner. Only 19 (5.8%) had multiple sex partners (Table 1). Prevalence of HIV in TB patients, 6 (1.8%) were positive by using ultra-rapid device and PCR 1 male and 5 females. Five (1.5%) was positive by using ELISA method, 1 male and 4 females (Table 2).

Table 1: Demographic information of the patients

Variable	No.	%
Gender		
Male	172	52.1
Female	158	47.9
Age (years)		
<20	74	22.4
20-29	74	22.4
30-39	66	20.0
40-49	56	17.0
> 50	60	18.2
Location		
Urban	176	53.3
Rural	154	46.7
Sex partner		
None	146	44.2
Single	165	50.0
Multiple	19	5.8

Table 2: Prevalence of HIV in TB Patients

Test	Overall (n=330)	Male (n=172)	Female (n=158)
ICT	6 (1.8%)	1 (0.6%)	5 (3.2%)
ELISA	5 (1.5%)	1 (0.6%)	4 (2.5%)
PCR	6 (1.8%)	1 (0.6%)	5 (3.2%)

## DISCUSSION

The emergence of HIV has paved the way for the resurgence of Mycobacterium tuberculosis infection. HIV is the most powerful risk factor for the progression of Mycobacterium tuberculosis infection to tuberculosis

disease.<sup>13</sup> The challenge of the tuberculosis and human immunodeficiency virus co-epidemic has been recognized by World Health Organization (WHO), and collaborative activities were launched in 2004 to manage the TB/HIV co-infection.<sup>14</sup>

We included 330 confirmed cases of tuberculosis in this study with random selection of gender. The data analysis showed among these, 52.1 % were male. This reflects that in our community set up, there is enhanced exposure of men to contract TB as compared to women, keeping up with the WHO avowal that males are more prone to contracting the disease in comparison to females.<sup>15</sup> As TB is an airborne infection, the reason behind male predominance could be high occupational exposure of males as they are the earning members and needs to go out more frequently and meet different people.<sup>16</sup> In addition, men usually have habit of smoking, gutka and manpuri chewing that probably decrease their immunity, thereby making them more prone to fall a victim of these deadly infections.

In the current study, majority of the patients exhibited HIV/TB co infection fall in the age ranges of 20-29 years. A study of Cape Town also observed almost same pattern in their young adults of 20-24 years of age having highest prevalence of HIV/TB co infection.<sup>17</sup>

Previous data proposed the fact that young age of 12-24 years comprises the highest risk factor for acquiring the disease as they have broad span of social contacts as compared to children and older individuals. This fact and our results were supported in a study reflecting WHO global TB surveillance data and documented highest number of TB cases in 20-24 year of patients.<sup>18</sup>

Regarding association of HIV prevalence with TB infected patients; most of our co infected patients were from rural regions. This finding implies that HIV is generally the disease of poor and rural population. HIV, TB, and malaria has been collectively labelled as the 'infectious diseases of poverty' (IDoPs), as the rural regions of Africa, Latin America and Asia are potentially affected by these , additionally geographic overlap has intensified the levels of HIV/TB co infection. The meager health conditions, social and bad economic conditions of rural inhabitants create vulnerable environment which expedite the transmission of pathogens, ultimately resulting in long term disease states which further result in exacerbation of poor socioeconomic status.<sup>19</sup>

As sexual contact has been implicated as the most important risk factor for HIV infection, similar attribute have been observed in our study with high prevalence of HIV/TB co infection in subjects having history of multiple sex partners. The prevalence of HIV was predominant in female population of this study. This female preponderance with increased rate of HIV infection might be associated with multiple partners that might be due to unreported sexual assault cases in rural areas. In accordance with our observation, a study recognizing the risk factors for HIV/TB co infection studied 50 TB patients with confirmed HIV, and reported heterosexuality as the probable route of HIV spread.<sup>20</sup> Another study confirmed multiple heterosexual sex partners as a concrete risk factor for HIV infection in both males and females.<sup>21</sup>

The importance of early detection for any disease is globally accepted, and for this rapid and correct detection within 30 min strategy is required. ICT method using Ultra rapid test device for HIV detection showed promising results and performed with basic laboratory support and expert personnel. This technique gives test results within 30 min, which is in line with the recommendations of WHO for same day test result and initiation of treatment.<sup>22</sup>The performance features of ICT and ELISA proved to be efficient screening tools with the PCR as a validation and confirmatory parameter.

In this study the prevalence of HIV in TB patients came out to be 1.8% by ultra-rapid test and PCR while it was 1.5% by ELISA. We observed a quite increased percentage of HIV in TB patients as compared to previous studies of 1997, 2012 and 2007, done in province of Sindh including Karachi. Collectively the HIV/TB coinfection in these studies was 0.34% only.<sup>23</sup>Hence, our observation shows increase in the prevalence of HIV in TB patients, which clearly depicts the picture of poor management strategies for TB and HIV infections individually and for TB/HIV co infection in our country.

In 2016, study from China reported the HIV prevalence of 13.66% in TB patients, and for this high rate they identified risk factors like unprotected sex, intravenous drug users, professional sex workers, use of contaminated needles, diseases like hepatitis, herpes and tuberculosis.<sup>24</sup>

In spite of the fact that Pakistan is having lesser number of HIV cases, still great concern regarding HIV/TB co infection epidemic is present due to certain risk factors prevailing in the community, like IV drug abuse, unsafe sexual activities, malnutrition related compromised immunity, unsafe blood transfusion practices, inadequate health facilities and low socioeconomic condition of people.

## CONCLUSION

The increasing prevalence of HIV/TB co infection should be under continuous surveillance by the researchers and health care professionals of HIV and TB endemic countries. Individuals having risk factors should be screened regularly to prevent spread of the co infection in the community.

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