

# To Study the Prevalence of HIV Seropositivity in Drug Resistant- Tuberculosis Patients.

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## ABSTRACT

**Background:** Drug resistance is a threat to TB control program worldwide. Patient infected with multiple drug resistant strains are less likely to become cured. Multidrug – resistant and extensively drug -resistant tuberculosis continues to emerge in high HIV prevalence settings, and their mortality in HIV co-infected patients remain high. **Methods:** This retrospective study was carried out at DR-TB centre, Amritsar. This study included drug resistant TB cases registered over the period of 2012 to 2018 at DR-TB centre, Amritsar. **Results:** A total of 1163 patients of Drug resistant tuberculosis were registered during the period of 7 years , among these 1027, 39 and 97 patients were of MDR, XDR and isoniazid mono-resistance respectively. The prevalence of HIV seropositivity was 2.7%, 2.9% and 2.6% in total drug resistant cases, MDR and XDR cases respectively. No case of isoniazid mono-resistance was found positive for HIV. And only one case with primary MDR tuberculosis was HIV positive. **Conclusion:** In this high drug-resistant TB settings, previous TB treatment failure was strong risk factor for both MDR and XDR-TB in HIV seropositive patients. And HIV seropositivity was more prevalent in MDR-TB cases.

**Keywords:** Human Immunodeficiency Virus, Drug-Resistant Tuberculosis, Multi-drug resistant Tuberculosis.

## INTRODUCTION

The Human Immunodeficiency Virus (HIV) pandemic is one of the greatest challenges facing tuberculosis (TB) control. Immune suppression increases the risk of reactivation of latent TB infection and rapid progression to active TB disease.<sup>[1]</sup> TB diagnosis is more difficult in people living with HIV infection and initiation of HIV treatment can paradoxically worsen TB by restoring immune function.<sup>[2]</sup> TB is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS. In 2016, there were an estimated 1.3 million TB deaths among HIV negative people (down from 1.7 million in 2000) and an additional 374000 deaths among HIV-positive people.<sup>[3]</sup> MDR-TB can be a result of failure of drug sensitive TB treatment with development of resistance (acquired MDR-TB) or direct transmission of an MDR strain (primary MDR). A history of prior TB treatment remains the

most important risk factor for MDR-TB.<sup>[4]</sup> Given the dynamic interplay between HIV and TB, it is not surprising that MDR-TB has complicated the picture. HIV and MDR-TB are an even deadlier combination. More than 50% of HIV-infected MDR-TB patients in Peru died within two months of diagnosis.<sup>[5]</sup> A study in the UK estimated that MDR-TB patients who are immune-compromised are nine times more likely to die than those not immune-compromised.<sup>[6]</sup> In addition to increasing the TB burden in general, HIV infection may also contributing to increases in MDR-TB prevalence among patients with TB and has been associated with acquired rifamycin resistance. A better understanding of the association between HIV infection and anti-TB drug resistance is, therefore, critical to the future of HIV treatment and the care and control of the global MDR-TB epidemic.

## MATERIALS AND METHODS

This retrospective study was carried out at Drug resistance Tuberculosis Centre (DR-TB), Amritsar. It included all the registered cases of DR-TB from RNTCP certified laboratories from 8 Districts of Punjab which are under DR-TB center, Amritsar over the period of 2012 to 2018. Study included

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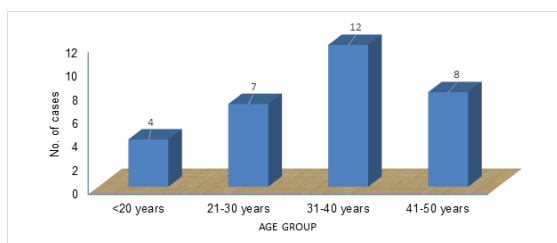
diagnosed DR-TB patients through Carriage based nucleic acid amplification technique (CBNAAT) and Line probe assay (LPA). The approval of institutional thesis and ethics committee was taken before the start of study.

#### **Inclusion criteria:**

1. Rifampicin resistant tuberculosis cases
2. Multidrug resistant tuberculosis cases
3. Isoniazid mono-resistant tuberculosis cases
4. Extensively drug resistant tuberculosis cases

## RESULTS

A total of 1163 patients of DR-TB were registered over the period of 7 years, among these 1027, 39, 97 patients were of MDR, XDR, Isoniazid mono-resistance respectively. Among these 31 (2.7%) patients were HIV seropositive. The prevalence of HIV sero-positivity was 31 (2.7%), 30(2.9%), 1(2.6%) in total drug resistance cases, MDR and XDR cases respectively. No case of isoniazid mono-resistance was found positive for HIV. Only one case with primary MDR-TB was HIV seropositive. HIV sero-positivity was more common in males (74%) than in females (26%). 12 (38%) patients were 31-40 year old, 8 (25%) were 41-50 year old, 7 (22%) were 21-30 year old and 4 (13%) were less than 20 year old. And 3 (0.1%) were in pediatric age group. Majority of HIV seropositive patients (96%) were having previous history of anti-TB treatment. And majority of patients were of rifampicin resistance (80.6%), followed by rifampicin-isoniazid (3.2%) resistance pattern. Only one case of XDR-TB was HIV seropositive.



	No. of cases of drug resistant TB	No. of HIV positive cases	%age
Total cases	1163	31	2.7%
MDR-TB	1027	30	2.9%
XDR-TB	39	1	2.6%
H-mono-resistance	97	0	0

## DISCUSSION

Tuberculosis is the commonest opportunistic disease in HIV positive persons in India. Many studies have been available regarding HIV seropositivity and DR-TB. There is paucity of data regarding HIV as a risk factor for drug resistant tuberculosis. Reliable data

on HIV infection prevalence among patients with TB are limited, especially in many countries where the HIV infection epidemic is more generalized.<sup>[7,8]</sup> There has been conflicting evidence about whether HIV is an independent risk factor for primary or acquired DR-TB. In our study most of the HIV positive DR-TB cases were males of 31-40 year old age group, with only 3 patients in pediatric age group. This may be due to the high risk behavior of intravenous drug abuse in males. Intravenous drug use is a risk factor for HIV infection and non-adherence to treatment, the latter promoting development of drug resistance. In contrast to other studies, in our study majority of patients (96%) were having previous history of anti-TB treatment. Other studies support the fact that HIV seropositivity is associated with primary drug resistance than acquired drug resistance. Drug malabsorption in HIV infected patients, especially rifampin and ethambutol, can lead to drug resistance and has been shown to cause treatment failure.<sup>[9]</sup> Drug resistant strains may be less virulent and preferentially lead to disease progression in immuno compromised patients, as opposed to immune-competent individuals.<sup>[10]</sup> In our study HIV seropositivity was more prevalent in patients with MDR-TB. However, the association between HIV infection and MDR-TB could be confounded by other factors. First, an observed association could be confounded by time window. HIV-negative patients are likely to reactivate a latent infection from decades ago, whereas HIV infected patients, in whom disease progresses rapidly, are likely to reactivate an infection acquired more recently following community or institutional transmission. With increasing prevalence of drug resistance globally, a higher percentage of recent infections are likely to be multi-drug resistant, resulting in higher rates of MDR-TB in HIV-positive individuals. Second, the association between HIV infection and MDR-TB may be confounded by shared risk factors such as injection drug use, imprisonment, socioeconomic status, alcohol use and hospitalization. People living with HIV may also be more likely to be exposed to MDR-TB patients, due to either to increased hospitalizations in settings with poor infection control or association with peers who may have MDR-TB, including in prison settings.<sup>[11]</sup> The high case fatality rates of MDR and XDR-TB in HIV co-infected patients could have devastating and demoralizing effects on health care workers and communities. Concomitant MDR-TB and antiretroviral treatment requires adherence to 6 to 10 daily medications for more than one year, and is characterized by high levels of toxicity and drug-drug interactions, leading to increased complexity of patient management. In addition, gaining a better understanding of how HIV infection affects the epidemiology of drug resistant TB will be critical.

## CONCLUSION

In this high drug-resistant TB settings, previous TB treatment failure was strong risk factor for both MDR and XDR-TB in HIV seropositive patients. And HIV seropositivity was more prevalent in MDR-TB cases. Unlike other studies, In our study HIV seropositivity was associated with acquired drug resistance than with primary drug resistance as majority of cases in our study were having previous history of anti-TB drug intake.

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