

A Study to Establish Correlation between Various Stages of HIV and Clinical and Radiological Findings of Multi Drug Resistance Tuberculosis

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Abstract

Tuberculosis (TB) and HIV together is one of the important causes of morbidity and mortality. With the emergence of multi drug resistance (MDR) this problem increases by many folds. We conducted a study with aim to establish a correlation with severity of HIV (CD4 Counts) with clinical & radiological findings of MDR TB. We conducted a cross sectional study enrolling all MDR TB cases admitted in one year duration among which HIV MDRTB coinfecting cases were taken in to consideration. HIV was staged in four stages on the basis of CD4 counts. Among total 534 cases, 44 (8.2%) patients were found to have coinfecting with HIV-MDRTB. Stage 4 has maximum radiological involvement in chest radiograph and also, patients in this stage show more severe symptoms related to both the disease. It is concluded that HIV MDRTB coinfection should be classified by the clinicians on the basis of CD4 counts for the better understanding of the future course of coinfections.

Keywords: HIV, Tuberculosis, Multi drug resistance TB, coinfection, CD4 counts.

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Introduction

Tuberculosis (TB) is a global public health problem causing illness among millions each year [1]. Globally in 2019, there were an estimated 10 million new TB cases, and 8.6% were living with HIV [5]. Both the disease together becomes a global threat for the increased mortality due to infections. The care and control of tuberculosis are threatened by

the emergence and amplification of multi-drug resistant tuberculosis (MDR-TB) [1].

Drug resistant TB is already a major challenge in developing countries. Multidrug-resistant tuberculosis (MDR-TB) in HIV infected individuals is a serious threat to global efforts to combat tuberculosis [2]. This

was considered as a major public health problem by WHO in 2013 [2]. Worldwide, an estimate says that around 5 lakh new cases of MDR TB. Of them, about 39% (186772) were notified, and 32% (156071) enrolled for treatment in 2018 [3]. The gap in diagnosis of MDR-TB and HIV and treatment of MDR-TB and HIV increases the likelihood of transmission of TB plus MDR-TB [4]

India is the 3rd highest HIV burden country in the world, with an adult prevalence of 0.22 percent [4]. According to the 2019 report, HIV co-infection or co-morbidity with TB in India was nearly 71,000 out of a total 2.64 million cases, amounting to a TB HIV co-Infection rate of 3.4 per cent. Also, mortality among HIV-TB coinfection is 9500 [5].

HIV per se does not predispose to development of MDR-TB. However, several factors during co-treatment of HIV-TB like poor drug absorption, pill burden, toxicities leading to poor compliance, drug interaction leading to sub therapeutic drug levels etc are the reasons for resistance to major anti tubercular drugs and anti-retroviral drugs both [1,2].

A Drug-resistant tuberculosis (DR-TB) case defined when one or more than one anti-tubercular drugs are showing resistant in mycobacteria. There are many forms of DR-TB few important one as per PMDT guidelines are following: mono drug resistant TB (mono DR TB), polydrug resistant TB (poly DR TB), rifampicin resistant TB (RR

TB), multidrug resistant TB (MDR TB), and extensively drug resistant TB (XDR TB) [1].

Till date the data for both HIV and coinfection with multidrug resistant tuberculosis (MDR-TB) is limited. Also, there is no consolidated data on the correlation of CD4 counts and prevalence of HIV-TB coinfection. The aim of this study is to establish a correlation with severity of HIV (CD4 Counts) with clinical & radiological findings of MDR TB.

Materials and Methods

After receiving approval from the ethical committee, a retrospective cross-sectional observational study was carried out at a tertiary care centre for tuberculosis patient BHOPAL from November 2020 to November 2021.

Data was collated on the basis of self-reported information on age, gender, residential address, socioeconomic status, symptoms at presentation and their duration and treatment history of TB, if any and treatment history of HIV was collected by trained investigators who was working in Anti Retrovirus Therapy (ART) center. Chest x ray evaluated by radiologist professionals on different parameters stated above.

Severity of symptoms were decided with the help of VAS score and scored from 0 to 10. CD4 counts along with other investigation was done and classified as following.

Table 1: Patients were classified according to WHO immunological classification of CD4 counts

HIV associated immunodeficiency	CD4 counts
None/not significant/stage 1	>500/mm ³
Mild/stage 2	350-499/mm ³
Advanced /stage 3	200-349/mm ³
Severe /stage 4	<200/mm ³

Chest radiography was done to look for extent of the disease, thorax was divided into various zones. The X ray involvement was evaluated by seeing 3 different parameters i.e bilateral involvement, more than 1 zone involvement, presence of cavitory lesion. Each of these finding was scored as 1, total score was calculated in the end. Symptoms like fever, cough, anorexia, weight loss was evaluated. Finally, Chest Xray findings and symptoms were co related independently with CD4 Count of the patient.

Patients who are already a Known case of HIV and patients who are already a Known case of DRTB with at least rifampicin resistant in any of the microbiological sample were included in this study. On the other hand, if patient has any other immunosuppressive states like Diabetes Mellitus, transplant recipient patient, patient who are immunosuppressive therapy, cancer patient taking chemotherapy or radiotherapy were excluded from the study. Also, non-cooperative patients were not taken into consideration.

Results were expressed in percentages; qualitative data were presented in form of tables and graphs. Chi square test were applied wherever needed.

Results

After applying inclusion and exclusion criteria, data from 534 MDR TB patients was collected. Patients were classified according to WHO immunological classification of CD4 counts.

Among total 534 MDR TB patients enrolled 44 (8.2 %) were found to have HIV co-infection (figure 1). Among them 28 were male infected with HIV-TB coinfection. Patients between 40–60-year age group are more commonly infected with both the disease 20 (45.45%) cases among co-infection were found in between 40-60 years of age (figure 3) with greater male predominance. 10 (22.72%) were in stage 1, 8 (18.18%) were in stage 2, 14 (31.81%) were in stage 3 and 12 (27.27%) were in stage 4 disease as per CD4 count. Total radiological score in stage 1 was 8, in stage 2 it was 15, in stage 3 it was 30 and in stage 4 the score was 36. 19 (43.18%) patients were found to have stage 4 disease with extensive radiological involvement (figure 4). Also, HIV-MDR TB Coinfection was found in 31 (70.45%) patients who had prior history of TB (figure 5) that means coinfection is more common among patients with previous history of TB as compared to patients with no prior history of TB. 31 (70.45%) patients were having more severe symptoms at presentation specially in stage 4 disease (figure 6).

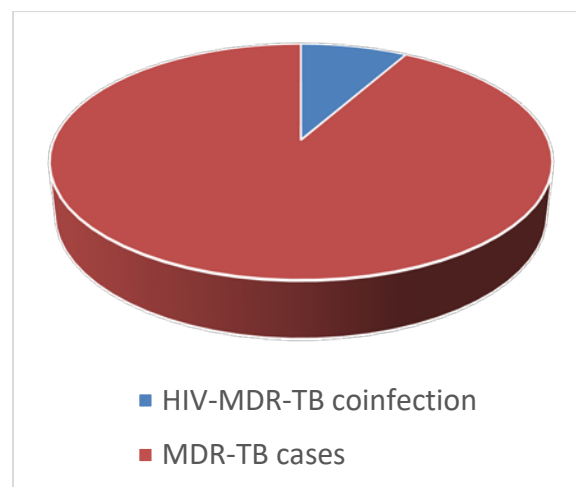


Figure 1: HIV-MDR TB coinfection prevalence among 534 patients

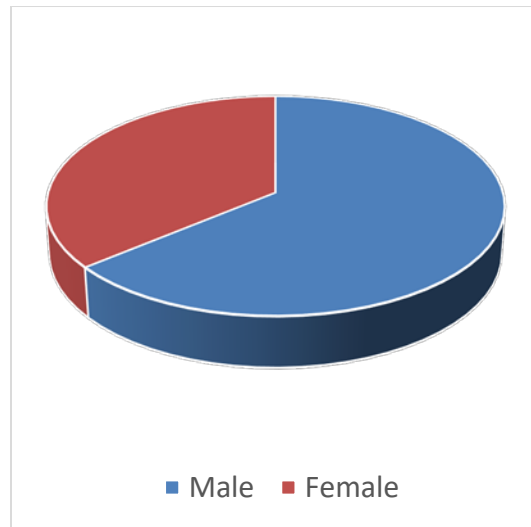


Figure 2: Gender distribution among coinfecting cases

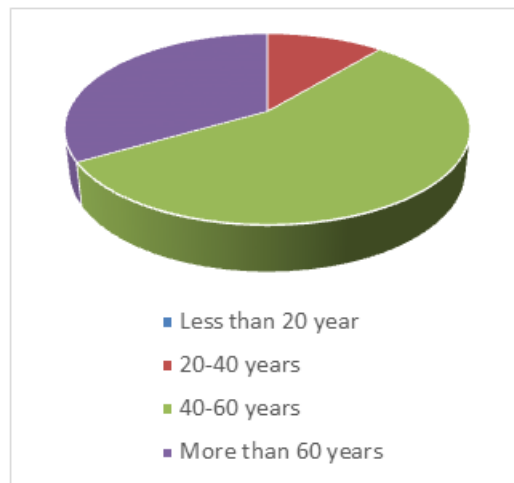


Figure 3: Maximum number of patients were found in 40–60-year age groups

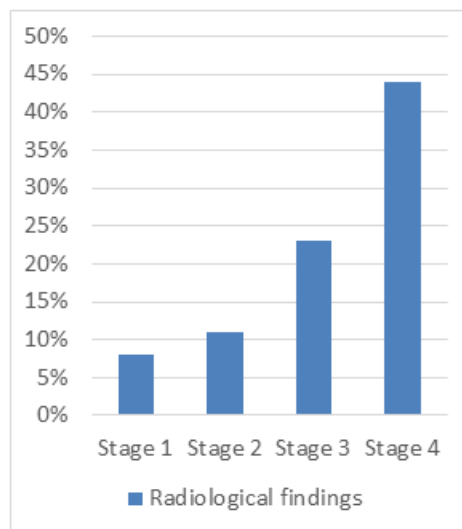


Figure 4: Lung parenchymal involvement in chest radiography

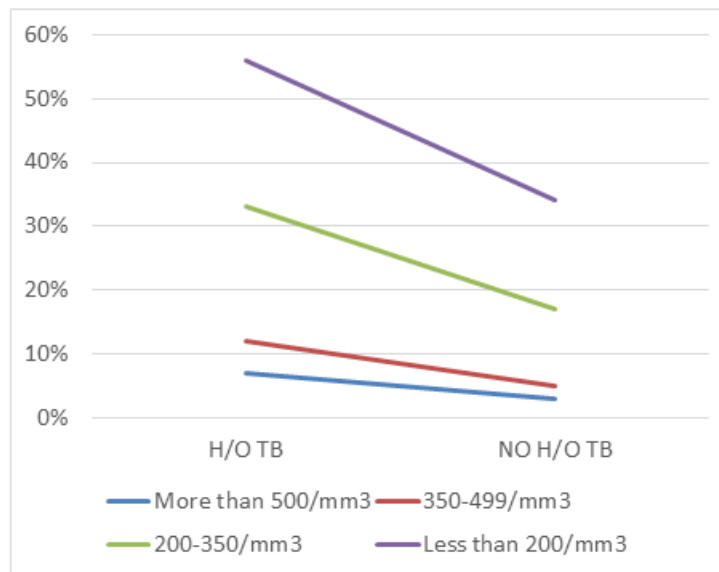


Figure 5: HIV-MDR TB cases were least among patients with no previous history of TB.

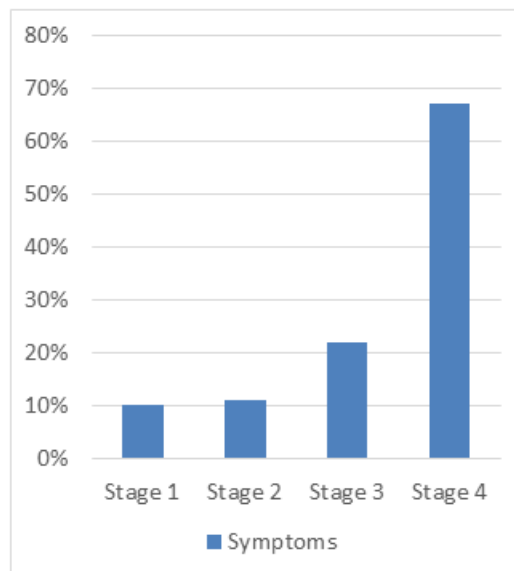


Figure 6: Severity of symptoms were more found in stage 4 cases

Table 2: Distribution of various parameters with staging of disease on the basis of CD4 counts.

Stage on the basis of CD4 counts	Radiological score (total score = sum of all three radiological finding)	Symptoms severity score (Total of VAS scale from 0-10)	Prior history of TB (n= no of patients having prior history)
Stage 1 = 10 (22.72%)	8	50	3
Stage 2 = 8 (18.18%)	15	67	4
Stage 3 = 14 (31.81%)	30	78	6
Stage 4 = 12 (27.27%)	36	92	5

The relation between radiological involvement and CD4 count was found to be statistically significant (P value- 0.009). Also, relation between severe symptoms and CD4 counts were also found to be statistically significant (P value- 0.004), However, relation between prior history of TB is statistically related with CD4 counts (P value- 0.212) (table 2).

Discussion

Current study mainly focusses to classify patients with HIV- TB coinfection on the basis of CD4 counts or staging of HIV. As in current situation as per guidelines for antiretroviral therapy almost all the patients undergo CD4 monitoring. This classification can help the clinicians to predicts high risk patients who may develop MDR-TB in later course of the disease.

In our study the prevalence of HIV is 8.2% which is in concordance with many studies done globally. The prevalence of HIV in MDR TB varies from 5-16% in various studies [6-8]. In our study male is more commonly infected with both these infections and also, age above 40 years is more common in case of coinfection. This finding is also in concordance with Bloom *et al* [9] who also finds that older age group and male gender are more predispose for coinfection. This finding indicate that older males are commonly avoid their disease and reluctant to seek medical care early in the course.

We divide patient on the basis of CD4 counts maximum patients were in stage 3. This finding is in consistent with Alexander *et al* [10] who also found that maximum numbers of patients were in later stages but Pontali *et al* [11] suggest that early stages are more commonly found. This discrepancy may be because of different population enrolled in different study.

In our study we observe that the higher the stage more chances of getting an abnormal

chest radiograph. Stage 4 has maximum radiological score compared to lower stage. This finding suggests that in stage 4 host defense become too weak to keep the infection confined to one zone. Cavitory disease shows that stage 4 also has more chances of high bacterial load and higher chances of transmission of MDR-TB [12].

In our study we find that patients with lesser CD4 counts are more prone to develop severe symptoms related to both the infections. This finding is in concordance with Méndez *et al* [13] who also finds that constitutional symptoms in HIV are more common in higher stages. [14]

Prior history of TB and anti tubercular treatment also an important risk factor in the development of HIV-MDR TB co infection. Although relation is not statistically significant but data clearly shows that prior exposure increases the likelihood of MDR TB in HIV patients.

In our study the sample size is small also, this is a cross sectional study hence no follow up done during this period. We didn't took HIV DNA into consideration in this study. A larger multicenter study is needed to overcome these issues in future.

Conclusion

The presentation of MDR TB in HIV is different from Non-HIV patient. These patients are at risk of having HIV-MDR-TB coinfection as they are immunosuppressed. Early diagnosis & treatment are essential to improve outcome. Patients with prior history of TB are at increased risk of reactivation, reinfection. Radiological finding and symptomatology could be used as screening tool.

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