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Study of Profile of Multi-Drug Resistant Tuberculosis in HIV Positive Patients

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Abstract:
Background*: TB is the most common opportunistic infection in HIV patients. HIV patients are at increased risk for developing drug-resistant tuberculosis as the disease advances and CD4+ T cells decrease. TB is the major cause of morbidity and mortality in patients with HIV infection.*
Materials and Methods: *This is hospital based prospective observational study including all the consecutive MDR-TB patients co-infected with HIV presented to Government Hospital for Chest and Communicable Diseases.*
Results*: Out of 38 patients 71% were male, 11% were females. Majority of the patient were in the age group of 30-50 years of age. 68.45 were smokers. 92% patients had a previous history of tuberculosis and ATT usage, with 71% using irregular treatment. 71% patients were diagnosed as HIV positive prior to MDR-TB detection among which 74% were using ART irregularly. 73.7% patients had a low CD4+ T cells <500 cells/mm^3.*
Conclusion: *Male sex, smoking, previous history of TB and irregular use of ATT and ART, low CD4+ T cells were observed to be the major risk factors for developing MDR-TB in HIV positive patients.*
Key Word*: HIV, MDR-TB, co-infection, low CD4+ T cells.*

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I. Introduction

Tuberculosis and Human immunodeficiency virus (HIV) infection are the two major public health issues in many developing countries including India. TB is also the most common opportunistic infection in HIV infected persons in India (1,2). Multidrug-resistant tuberculosis (MDR-TB) has become a major public health problem worldwide and considered to be an obstacle for effective global TB control TB is the leading cause of morbidity and mortality in People Living with HIV (PLHIV). People living with HIV are 15-22 times more likely to develop TB than persons without. TB is the most common presenting illness among people living with HIV, including among those taking antiretroviral treatment, and it is the major cause of HIV-related deaths (3).

Worldwide 10 million people have been detected with TB during the year 2019, of which two-thirds of people are from 8 countries, India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa. About half million people have developed MDR/RR TB in 2019, of which about half the cases were from China, India and Russian Federation. 3.5 million people living with HIV have been detected with TB and started treatment in 2019 (4).

Incidence of TB in India in 2019 was 2.6 million, with 436000 deaths. Incidence of TB in HIV-positive people was 71000 in 2019 with 9500 deaths. MDR/RR TB incidence was 124000 in 2019 (4).

II. Material And Methods

Study design: Hospital-based prospective observational study**.**
Study setting: Government Hospital for chest and communicable diseases, a teaching hospital of Andhra medical college, Visakhapatnam, Andhra Pradesh, also a Nodal DR-TB center for Visakhapatnam District.
Study period: 2 years from June 2018 to May 2020
Patient selection: All consecutive patients admitted to the hospital co-infected with MDR-TB and HIV during the study period were enrolled in the study according to the inclusion and exclusion criteria.
Study sample: 38 patients were recruited in the study following the inclusion and exclusion criteria.

Inclusion criteria

1. Patients age more than 18 years
2. Patients willing to participate in the study
3. Patients detected with MDR/RR TB
4. Patients with HIV positive status (on ART or newly detected)

Exclusion criteria

1. Patients less than 18 years of age
2. Patients not willing to participate in the study

All the patients detected with DR-TB (MDR and XDR TB), presenting to the Government hospital for chest and communicable diseases, during the study period were enrolled in the study. Demographic data, comorbidities, smoking and biomass smoke exposure, past history of tuberculosis and treatment history, HIV status and treatment history, and CD4 count was recorded and analysed.

III. Result

Out of 38 patients diagnosed as DR-TB with HIV, 27 (71%) were males, 11 (29%) were females. 3 patients were aged less than 20 years, 8 patients were between 20-30 years of age, 12 patients were having age between 31-40 years, 11 patients were in the age group of 41-50 years and 4 patients were above 50 years. Among males 22 were smokers with mean smoking pack years of 25, and 5 were never smokers. Among females 4 patients were chutta smokers with habit of reverse smoking. 10 patients among males and all the female patients had exposure to biomass fuel smoke.

Among all the patients 24 (63.2%) had a history of type 2 diabetes mellitus, 17 among males and 7 among females. 35 (92%) patients had a history of Tuberculosis in the past, of these 10 (28.6%) patients have completed optimal treatment period (COTP) and were declared cured, 15 (42.8%) patients were defaulters, and 10 (28.6%) patients were lost to follow-up.

27 (71%) patients were using Anti-Retroviral Therapy (ART) prior to the MDR-TB detection, of which 20 patients were not using ART regularly. 11 (29%) patients were diagnosed as HIV positive at the time of anti-tubercular treatment initiation for MDR-TB. 10 patients had CD4 more than 500 cells/mm^3, 10 patients had CD4 count between 200-500 cells/mm^3, and 18 patients had CD4 count below 200 cells/mm^3.

Out of 38 patients 10 patients were detected with resistance to only Isoniazid and were treated with H-mono/poly drug resistance TB regimen. 14 patients detected with only Rifampicin resistance, and 14 patients detected with MDR-TB and were given conventional MDR-TB regimen.

IV. Discussion

HIV is the strongest of all known risk factors for the development of TB and is known to affect Th-1 cell mediated immune responses that are the central immune defence against Mycobacterium tuberculosis. HIV infected patients are at increased risk for progressive disease following primary TB infection, as well as reactivation of Latent TB infection (LTBI). HIV infection also increases the risk of subsequent episodes of TB from exogenous re-infection and it also increases the chance of relapse. The annual risk of reactivation of TB among those co-infected with HIV and TB is estimated to be 5-8%, with a cumulative lifetime risk of 50-60%, which is very high compared to the cumulative lifetime risk of 5-10% in HIV-seronegative adult patients (5).

In this study majority of the patients were males, predominantly between 30-50 years of age. Smoking is observed in 68.4% patients which is a risk factor for the development of TB. 92.1% patients had history of tuberculosis of which 71.4% patients did not complete their complete course of treatment. Incomplete treatment or irregular treatment is an established risk factor for the development of MDR-TB. 71% patients in this study were having HIV infection prior to the detection of MDR-TB, which is the risk factor for majority of patients in this study. Low CD4 count, less than 500 cells/mm^3 was observed in 73.7% patients, another risk factor for the new infection or reactivation of TB due to immunocompromised status.

The presentation of TB in HIV infected persons is often atypical and poses a considerable challenge for diagnosis. In HIV infected persons, TB can occur and with any CD4+ count. As the immunosuppression increases the likelihood of development of TB increases, presentation becomes more atypical, even in pulmonary tuberculosis (6). Evidence shows that TB bacilli is seldom identified in sputum smears in PLHIV patients infected with TB (7), requiring nucleic acid amplification tests, gene-probed tests and mycobacterial culture to aid in diagnosis. Cartridge bases nucleic acid amplification test (CBNAAT) have high sensitivity for diagnosis of both smear positive and smear negative pulmonary TB cases with high rates of detection of TB as well as rifampicin resistance simultaneously (8), helping in early detection of drug resistant TB bacilli.

The use of ART in HIV-infected patients with TB improves the survival of both susceptible and drug-resistant diseases. However, patients with HIV infected DR TB without the benefit of ART may experience

mortality rates of more than 90 percent. When both treatments are started simultaneously, the likelihood of adverse effects could compromise the treatment of HIV or DR TB. It is necessary to initiate second-line anti-TB drugs first, followed by ART as soon as second-line anti-TB drugs are tolerated. This should generally be within the first two weeks of the initiation of treatment with DR TB. The undue delay in initiating ART, on the other hand, could result in a significant risk of HIV-related death among patients with DR TB (9).

Treatment of MDR-TB in those with HIV infection, especially those receiving HAART, greatly complicates patient treatment and management overall. Overlapping toxicities and interactions between anti-TB and antiretroviral drugs complicate treatment leading to non-adherence of both ATT and ART, which results in development of drug-resistant tuberculosis and increased morbidity and mortality.

V. Conclusion

In this study the male sex, previous history of tuberculosis, non-compliance and non-adherence to ATT and ART treatment have shown to be the risk factors to develop MDR-TB in people living with HIV.

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