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Original Research Article

Clinico-radiological manifestations of multidrug resistant tuberculosis (MDR-TB) in HIV/AIDS patients and its co - relation with treatment outcome in Southern Odisha

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Abstract: Multidrug resistance tuberculosis (MDR-TB) is one of the infections among the human immunodeficiency virus (HIV) seropositive cases. Varied clinical and radiological manifestations and treatment outcomes are being observed according to the immune status of the HIV serpositive MDR-TB patients. In this retrospective study, the data of the diagnosed cases of MDR-TB patients with HIV seropositivity who were registered in DR TB centre of Southern Odisha, over a period of three years. The detailed basal demographic characteristics, clinical, radiological, laboratory investigation findings, the treatment outcomes were noted and analysed statistically. In this setup, Maximum patients were (61.54%) within the age range of 26-35yrs with male preponderance. (M: F = 12:1). 88.89% of them were from rural areas and all were Hindus. The major clinical presentations were anaemia (100%), fever (84.61%), persistent cough (92.31%) weight loss (46.15%), and decreased appetite (38.46%). The radiological findings were cavitary lesions (53.84%) and infiltrations (46.15%) Among this study sample, only 23.08% of patients were declared to be cured, 46.15% died following successful treatment. 23.08% patients were declared to be default and 7.69% were lost to follow up within the study period. In the present study, MDR –TB patients co-infected with HIV were commonly observed among adult males. The treatment outcomes were poor probably due to non-adherence to multiple drug regimens under RNTCP and ANTI-HIV drugs.
Keywords: MDR-TB, HIV co-infection, Cavitary lesion, DOTS Plus, Treatment outcomes

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) is caused by Mycobacterium tuberculosis showing resistant to rifampicin and isoniazid, the two main first line antimicrobials with or without other first line drugs [1] MDR – TB has emerged as a global epidemic. In 2015, there were 4, 80,000 new cases of multidrug-resistant Tuberculosis (MDR-TB) detected globally. AS per drug surveillance data in 2015, 3.9% of new and 21% of previously treated cases was estimated to have rifampicin or Multidrug-resistant tuberculosis (MDR/RR- TB). [2]. In India the prevalence of MDR-TB has been estimated to be very low which accounts for 3% of new cases and 12-17% of in retreatment cases [3]. However MDR TB with HIV/AIDS remains less common. The Global HIV epidemic infection has caused explosive increase in TB incidence and contributing to the rising incidence of MDR-TB.

The HIV - TB co-infection has been described as the 'cursed duet' [4]. Usually the patients in advanced stage of HIV have TB or other opportunistic infections which is the major contributor of increase mortality. MDR – TB has been associated with inadequate treatment, poor patient compliance to drug intake, defective implementation of RNTCP guidelines, hospital infection control program or HIV co-infection [5]. The prevalence of Hospital acquired infection outbreaks of MDR-TB are less in developed countries with improved treatment and hospital infection control program. [6,7] However such outbreaks are more in developing countries like India with limited resources [8,9]. The management of MDR TB with DOTS Plus regimen has been implemented in DR TB Centre of Southern Odisha since November 2012. Despite the growing incidence of MDR TB in HIV/AIDS patients,

there is paucity of data in this regard. High death rate is found in MDR –TB with HIV even in those remaining on HAART and WHO recommended DOTS plus strategy. HIV positivity among MDR-TB patients varies in districts of Odisha. Among high prevalence districts. HIV seropositivity in MDR –TB patients is high in Ganjam district of South Odisha.

With this background, the present study was carried out to assess the 1) clinico - radiological profile, 2) the pattern of drug resistance to both first line and second line anti-tubercular drugs and their correlation with the treatment outcomes in HIV patients Co-infected with MDR -TB attending in DR- TB centre of South Odisha.

MATERIAL AND METHODS

It was a retrospective record based study of MDR-TB with HIV/AIDS patients, who were admitted in DR - TB centre of South Odisha between the periods of November 2012 to December 2015. The study protocol was approved by Institutional Ethics Committee. The study population included HIV infected patients (seropositive) of either sex in all age groups registered in antiretroviral clinic (ART center) who were diagnosed to have active MDR-TB as well as MDR- TB patients registered in DR- TB centre of South Odisha were later screened and diagnosed as HIV/ AIDS cases. The patients having no record of baseline characteristics and laboratory findings were excluded from this study. In this zone of Odisha the patients are being referred from different districts for drug sensitivity testing. Two diagnostic technologies are being used in this centre: Catridge Based Nucleic Acid Amplification Testing (CBNAAT), Line probes Assay (LPA) as per PMDT guidelines. [10] The HIV infection was documented by commercially available third generation Enzyme Linked Immunoabsorbent Assay (ELISA) kits to detect antibodies to HIV-1 and HIV – 2 as per WHO strategy.

The detailed history, baseline demographic characteristics, clinical findings, radiological observations, routine laboratory investigation findings related to tests for assessing renal function, liver function, thyroid function, blood sugar (fasting and post prandial) and other routine haematological test parameters recorded in the register were extracted. Following all these investigations the confirmed cases of MDR-TB with HIV cases were being enrolled for initiation of DOTS Plus regimen and offered drugs free of cost form our health centre in accordance with the RNTCP guidelines of Ministry of Health and Family Welfare, Government of India as well as Highly Active Retroviral Therapy (HAART) for HIV as per NACO guidelines.[11] The patients were being followed up at 3,4,5,6,7, 9,10, 11,12, 15, 18, 21 and 24 moths of initiation of DOTS Plus regimen to test for sputum conversion. The treatment outcomes for each patient were being noted at the end of 2 years. All these recorded baseline characteristics and follow up observations were noted in a predesigned case record form.

For all data obtained, the frequencies, percentages and means were calculated. For the purpose of assessment of treatment outcomes, the patient who had completed treatment but had less than 12 months post treatment follow up were excluded from analysis. However all death, default and failure cases were included for analysis. All analyses were done using IBM SPSS - 20 Software.

RESULT AND DISCUSSION:

DR-TB centre of Southern Odisha caters eight southern districts of Odisha covering a huge population of 1.4 Crores approximately. Out of that 285 MDR-TB patients were registered within our study period. 13 patients among them met inclusion criteria i.e they had MDR-TB with HIV co-infection whose outcomes were analysed during our study period. The descriptive statistics of baseline demographic characteristics of the diseased cases revealed that maximum patients (61.54%) were in the age group of 16-35 years, the mean age being 32.54± 1.98 years (Table-1). In this study male patients outnumbered females, the male female ratio being 12:1. All patients had history of previous treatment with ATT. The mean body weight of the enrolled patients was 40.46± 2.76kg. Among all cases, 2 (15.38%) were within weight band of 16-25 kg. Majority 7 (53.85%) were within 26-45 kg., the rest 4 cases (30.77 %) belonged to 46-70 kg weight band. In this study population, 88.89% (n=8) belonged to rural area and they were within 16-35 yrs age group. All the patients were of Hindu religion. (Table-1).

Table-1: Demographic characteristics of HIV-infected MDR TB Patients

Profile	Number of cases(n=13)	Percentage
Age(years)		
16-25	1	7.69
26-35	8	61.54
	4	30.77
36-45	0	0
>45		
Gender		
Male	12	92.31
Female	1	7.69
Locality		
Rural	11	84.61
Urban	2	15.48
Religion		
Hindu	13	100
Other than Hindu	0	
Body weight(kg)		
16- 25	2	15.38
26-45	7	53.85
46-70	4	30.77

Table 2: The radiological and laboratory findings of MDR-TB with HIV co- infected patients.

Characteristics	No of patients (16-35 years)	No of patients (>35 years)
Radiological findings-		
Site of lesion : unilateral	2	0
Bilateral	7	4
Type of lesion: Infiltration	6	0
Cavitary lesion	4	3
Laboratory findings-		
FBS>100mg%	2	1
PPBS > 140mg%	4	1
Hb- < 11.0gm%	7	3
Hb >11.0gm%	2	1
Serum SGOT (>35IU/L)	1	2
Serum SGPT(>45IU/L)	1	1
Ser. alkaline phosphatase (>128IU/L)	1	0
Serum bilirubin (total)		
>1mg%	5	2
<1mg%		
Serum bilirubin (direct)	3	2
< 0.4mg%		
Serum urea (>40mg/dl)	0	0
serum creatinine(1.1mg/dl)	5	3

Data depicted in Table-2 reveals that on radiological examination, the bilateral cavitation and bilateral infiltration was observed in 4 (44.44%) and 6 (66.66%) patients within 16-35 years age group respectively. 3 cases (75%) had bilateral cavitation in > 35 yrs of age group. **(Table-2).** In this study population, the major clinical presentations were anaemia (100%), fever (84.61%), persistent cough (92.31%) weight loss (46.15%), and decreased appetite (38.46%). All of them were found to have anaemia i. e blood haemoglobin

level below the normal range of 11-15.5 gm%. Among the patients of age range 16-35 years, only 2 cases had high blood FBS (> 100mg%) and 4 cases had post - prandial Blood sugar more than 140mg%. High blood FBS and post prandial blood sugar were found in 1 patient each in > 35 years age group. In young group patients, only 1 case had high SGOT (normal range- < 35 IU/L) and SGPT (< 45IU/L) level at the time of hospitalisation. In elder age cases 2 patients had high and 1 had high SGPT level in serum. The total and direct bilirubin in serum was high (Normal range: total- 0.1-1.0 mg%, direct- 0.1-0.4 mg %) in 5 and 3 cases among young patients. But among elders only 2 cases had high total and direct bilirubin in serum. 5 young age group patients and 3 of elder age group had high serum creatinine (normal: 0.6-1.1mg/dl). All patients had serum urea level in normal range (15-40mg/dl).

Table 3: Treatment outcomes in MDR-TB patients with HIV co-infection

Treatment Outcomes	Number of cases	percentage
Cured	3	23.08
Default	3	23.08
Death	6	46.15
Lost to Follow Up	1	7.69
Total	13	100

LPA or line probe test was the only available culture medium in our setup. After the installation of newer diagnostic technology Catridge Based Nucleic Acid Amplification Test (CBNAAT). Both LPA and CBNAAT were used in some patients for the culture of sputum in the later part. Eleven [11] patients had sputum negativity within the 3rd month of initiation of therapy. 2 patients had positive sputum culture on first visit (3rd month). Only 3 patients completed treatment and were declared as cured bearing the criteria fixed by the PMDT Guidelines. 1 patient was declared as lost to follow up. 3 patients were declared as default. The proportion of death was 46.15% (n=6) in this study group **(Table-3)**. In our study, Thirteen (13) patients out of 285 MDR TB cases were seropositive whose outcomes were known. In the study of Datta *et al.;* and Poulomi *et al.;* the seropositive case prevalence was 1.9% and 2.9% respectively but in our setup it is higher (4.56%) [12, 13]. The present study showed that younger age group; particularly males were more affected with MDR TB and HIV co-infection. Our observations corroborate with Poulomi *et al.;* 2015 [13]. Most of them were from rural areas. Radiologically bilateral lesion was more common in all age groups. Such observation was also reported in other Indian studies [14, 15]. Death was highest in this study group. Among all registered patients, 76.92% showed resistance to both first line drugs, INH and rifampicin. Only 23.08% of them were resistant to rifampicin alone. Simultaneously with DOTS Plus regimen, all patients were on HAART regimen (NACO guideline) consisting of stavudine/ zidovudine with lamivudine and a NNRTI like nevirapine or efavirenz. Medication adherence to all the drugs included in DOTS Plus and HAART regimen was poor in 76.92% of patients. It could be due to intolerance to adverse effects of drugs or non-willingness to take the drugs psychologically. Various adverse drug reactions were also observed in all patients. In this setup, poor medication adherence and adverse drug reaction could be attributed to poor treatment outcomes like death and default. Other Indian studies have reported that the patients on HAART in resource poor setting have increased mortality commonly due to TB or other opportunistic infections and poor medication adherence [16-19]. In our setting the initial improvement, fear for social stigma, lack of awareness of disease and susceptibility to new opportunistic infections could also be other contributing factors for poor outcome. Our observations made in this study do not reflect the outcomes of MDR TB in HIV patients in the state as a whole.

CONCLUSION:

From this study it can be concluded that there is poor treatment outcome (unfavourable) in spite of active treatment. It indicates there is urgent need of implementation of patient retrieval and counselling services in our locality. Early diagnosis of drug resistant TB and HIV co infection are required from all the re-treatment cases. Quality DOTS services and rational use of second line ATT drugs can prevent emergence of MDR TB in HIV cases which pose a major public health problem. Further long term prospective studies are required to identify the breech in the programme implementation strategy and predictors of poor treatment outcome.

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