Original Research Paper

Volume - 7 | Issue - 5 | May - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Medicine

A descriptive analysis of MDR-tuberculosis patients started on CAT-IV regimen over a period of seven years in a tertiary care centre.

Sunny George

MD, FRCP, FCCP, DNB, DTCD, MNAMS, FIMSA, Associate Professor & Nodal officer, DOTS Plus site committee, Department of Pulmonary Medicine, Government Medical College, Kozhikode, Kerala, South India

ABSTRACT Multidrug resistant tuberculosis (MDR-TB) is on the rise and is supposed to retard the annual decline of incidence of TB which is currently at the rate of 1.5% which is as against the expected decline rate of 4- 5% by 2020.Hence a clear knowledge about the various aspects of MDR-TB is essential in properly managing these cases and thereby curtailing the spread of the bacilli in the community. India, China and the Russian Federation accounts for 45% of the combined total of 580 000 cases reported in 2015.This study is a humble endeavor in this regard in 680 cases of MDR TB patients attending the DOTs plus site of Government Medical College, Kozhikode to analyse the clinical profile and possible risk factors contributing to the occurrence of MDR-TB (INH & Rifampicin resistance) cases resulting in persistent sputum positivity and active spread of the disease in the community.

KEYWORDS : MDR-TB (multi drug resistant tuberculosis), DOTs plus (Directly observed treatment short course plus), risk factors, CAT-IV regime.

INTRODUCTION

India ranked first in terms of *estimated* total numbers of prevalent MDR-TB cases in 2007. WHO estimates, based on surveys conducted in over 110 settings in the last decade, revealed that nearly half a million cases are multi-drug resistant, and 130,000 of them lethal. In 2010, an estimated 3.4 percent of new TB cases globally were MDR TB and an estimated 20 percent of retreatment TB cases were MDR TB1. MDR-TB is on the rise in some countries, yet only some 3% of cases are being treated according to standards set by the World Health Organization (WHO).

Hence the preventive strategies should be in place & has to be primarily based on risk factor identification leading to its emergence which may have considerable variations according to the prevailing problems in each country. It might have a substantial role in immune modulation of the vulnerable patients and there are factors which are often overlooked. In this study we have tried to pick up possible common risk factors that might have contributed to the development of multidrug resistance in patients started on CAT-IV regime under RNTCP

Materials & Methods

The Department of Pulmonary Medicine, Medical College, Calicut has been functioning as a DOTs centre as well as designated microscopy centre for the last eight years & this centre has later been recognized as a DOTs Plus site for North Kerala with approximately half the population of the state being covered by this centre. Line listed patients from seven districts attend this health care facility for DOTs Plus regime from February 2009 onwards.

All diagnosed MDR-TB patients referred to our site were clinically evaluated and the following data collected using structured questionnaire that included detailed drug history, recording the outcomes of previous DOTs regime was specifically looked in to. Due credit was given to addictions, co-morbidities & low body weight. Physical examination & radiological extent of the disease according to the ATS guidelines at the time of starting the weight based regime was noted. The data collected was systematically analyzed at the end of June 2016, by which time 680 patients were enrolled to this regime.

Table.1 Drug dosage as per weight band

No	Drugs	16-25 Kg	26-45 Kg	46-70 Kg
1.	Kanamycin	500 mg	500 mg	750 mg
2.	Levofloxacin	250mg	750 mg	1 g
3.	Ethionamide	375 mg	500 mg	750 mg
4.	Ethambutol	400 mg	800 mg	1.2 g
5.	Pyrazinamide	500 mg	1.25 g	1.5 g
6.	cycloserine	250 mg	500 mg	750 mg
	Pyridoxine	50 mg	100 mg	100 mg
	Na PAS	5 g	10 g	12 g
	Capreomycin	500 mg	750 mg	1 g

CAT-IV regimen was available as per the weight band-to which each patient belong. All the patients were followed up as per the DOTs Plus strategy & this observational study was intended to be an operational research to find out the clinical profile of MDR-TB patients and to recognize any possible risk associations for the same so that future cohort analysis in a well planned manner could be taken up to establish the same. CAT–IV regime comprises of an initial intensive phase of six to nine months of 6 drugs including Kanamycin and a continuation phase of 18 months of 4 drugs, making a total duration of 24- 27 months as per weight band (Table.1).

6 (9) Km Z E Lfx Eto Cs / 18 E Lfx Eto Cs,

(Km:Kanamycin, Z: Pyrazinamide, E: Ethambutol Lfx: Levofloxacin,Eto: Ethonamide,Cs:Cycloserine)

Observations & results

There were a total of 680 cases attending the tertiary care setting of Calicut medical College, DOTs Plus site during these 7 years. There was more or less a constant flow of patients to the site except during 2013 & 2014 when a surge was noted owing to too many back log cases being enrolled as there was a technical standstill at the intermediate reference laboratory (IRL) for a short while due to engineering works and the IRL getting temporarily shut down.Fig.1

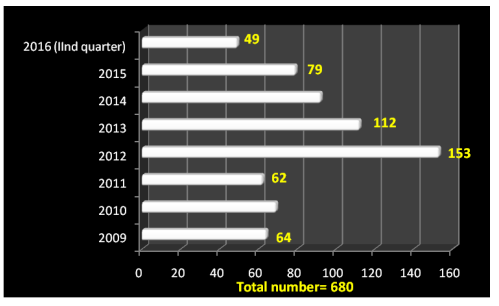

Fig.1 Distribution of MDR TB cases over 7 years

There were 534 males (78.5%) and 146 females (21.5%) as shown in fig.2.

The gender preponderance for males noted may be due to the fact that males may be more at risk owing to their increased mobility within the community & thereby augmented chance of contact from those who are infected. It may be also due to increased non

adherence to proper treatment resulting from other priorities like job related issues.

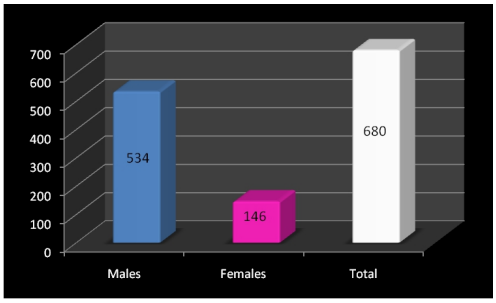

Fig.2 Gender preponderance

The male to female ratio of occurrence is hence 3.7:1

Weight	Patients (n=534)	% (n = 680)
<25 Kg	5	0.74%
26- 45 Kg	288	42.4%
45-60 Kg	379	55.1%
>70Kg	8	1.2%

Table.2 Weight band profile

When BMI was calculated it was seen that a majority of patients belonged to the <20 category which comes to about 76.9 % (523/680) of total cases Tab.2. Mean height of all the patients taken together was 161 cm which points obviously towards the possibility of significant underweight states that may be associated with significant immune compromise in these patients. Lack of proper glycaemic control in diabetic patients is a well known reason for weight loss. Hence a low body weight may be a confounding factor in both tuberculosis as well as in diabetes mellitus as well.

Age (yrs)	Males (n=534)	Females (n=146)	Total (n = 680)
20 -40	224	61	289
41- 60	278	48	330
>60	41	14	61

Table.3 Age & Gender of MDR TB patients

91% cases belonged to the age group of 20-60 years which is the economically productive group having large economic health impact to the family and society.

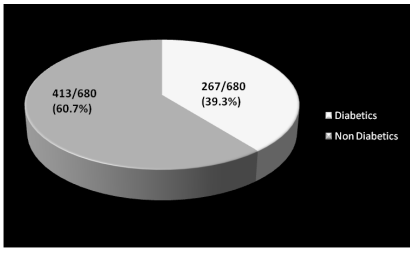

Fig.3 Diabetic status of MDR TB patients

On analyzing the co-morbid illness it was noticed that 39.3% (267 out of 680) cases had diabetes mellitus fig.3.Though most of the patients were known diabetics already on treatment, a large majority of them had uncontrolled diabetes with very high blood sugar values (fig.4). Diabetes mellitus is a well known risk factor for various bacterial as well as fungal infections in the body which is supposed to be an aftermath of macrophage defect as a result of high tissue levels of glucose which hinders proper opsonisation of invading organism leading to their delayed clearance from the body giving them the opportunity to generate mutants and gain resistance to first line medications. Hence uncontrolled diabetes has to be properly addressed in cases of both sensitive as well as drug resistant cases of tuberculosis in ensuring a cure as well as avoiding generation of drug resistant cases owing to the compromise of the host immune responses.

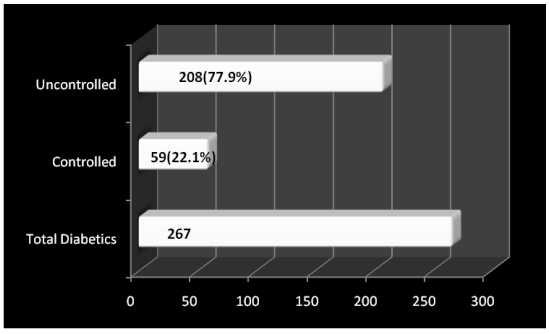

Fig.4 Glycaemic status at initiation of CAT-IV

A large majority of the diabetics had uncontrolled diabetes on diagnosis. It was also noted that there were a large number of failure cases amongst properly treated cases of active tuberculosis among those who developed MDR-TB. This points towards additional risk factors for the development of MDR-TB other than genetic susceptibility or Primary drug resistant states which may be considered as non-modifiable risk factors. Uncontrolled diabetes is seemingly such a modifiable risk factor which often gets overlooked.

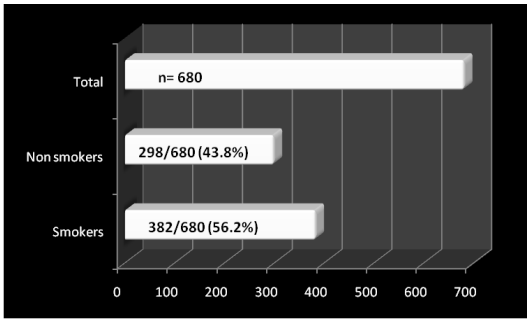

Fig.5 Smoking status of MDR TB patients

There were a total of either 56.2% of current or ex smokers.Fig.5. All females were non smokers. Reported alcohol intake status amongst the male patients was about 26%, but none had any evidence of decompensated alcoholic liver disease. There were 53.4% cases with far advanced radiological disease and 53.1% cases amongst first line failures were diabetics which points towards both as decisive risk factors. Table.4 & 5

Radiological Extent (ATS)	Number of Patients (n=680)	(%)
Minimal Tuberculosis	85	12.5
Moderately Advanced TB	232	34.1
Far Advanced TB	363	53.4

Table.4 Radiological extent of the disease

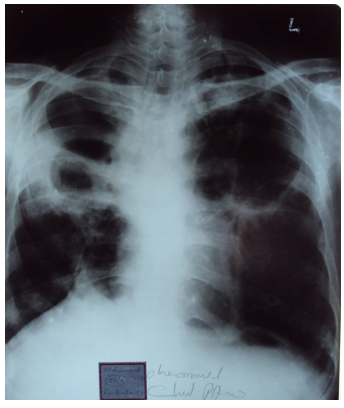

Fig.4 Bilateral upper/ mid zone cavities

Total no of patients	680	%
First line failures	262	38.5

Diabetics among failures	139	53.1
HIV positive cases	13	1.9

Table. 5 Diabetics among failed first line cases

2% of total cases were HIV positive and hence cannot be a major risk factor for developing MDR TB as earlier thought to be 2. The extent of radiological involvement were recorded as per the ATS (American thoracic Society) guidelines which classifies the radiological lesions in to minimal, moderate and far advanced disease according to the extent of involvement of lung parenchyma. The success rate of the regime at the time point of this study showed that 59.4% (313/680-153) cases were either cured or completed treatment. This falls within the range of currently acceptable rate of cure as per available literature.Tab.6

Total Cases	680
Transferred out	11
Death	96
Default & non traceable	76
Stopped due to Adverse effects	2
Switched to XDR regime	29
Continuing treatment	153
Treatment completed	103
Cured	210

Table.6 Status of MDR cases at the time of study.

Discussion

WHO has realized that in areas where the prevalence of MDR-TB is high, it represents a special threat to tuberculosis control, and has advocated the policy of DOTS-Plus. Prevalent cases worldwide could be two or three times higher than the number of incident cases. Diabetic patients with MDR-TB are at risk for poor outcomes. Investigators at Bellevue Hospital carried out a case-control study and found that 53 identified patients had verified tuberculosis infection and diabetes3. They selected 105 control cases from non diabetic patients with a discharge diagnosis of tuberculosis during the same time period. They reported that 36% (18 cases) of the patients with diabetes and tuberculosis had multidrug-resistant tuberculosis (MDR-TB) compared to only 10% (10 cases) in the control group ($p < 0.01$). The relative risk of MDR-TB was calculated to be 8.6 (confidence interval, 3.1 to 23.6) in the diabetic group compared to the control group. They sum up noting that there was a significant association between diabetes and MDR-TB and they pointed out that diabetes continues to be a risk factor for tuberculosis and that it was associated with MDR-TB in their patients[3]. It is estimated that India has the largest number of diabetes patients in the world with 41 million in 2007[4]. Prevalence of Diabetes is estimated to be more than 21 per cent by investigators among the urban and rural parts of Kerala. Our study also picked up this risk factor and also this study found that male gender, those with BMI<20, smokers, history of failed ATT and advanced radiological shadows do have a higher risk for developing MDR TB in smear positive cases5,6. Diabetes mellitus is associated with impaired gastrointestinal drug absorption, impaired alveolar macrophage function, reduced tissue concentration of drugs & reduced bactericidal activity[7].

CONCLUSIONS

This study has identified certain risk factors for the development of MDR TB which could be easily overlooked. Hence a clinical scoring system utilising factors like (MUS**I**CF: Males, Uncontrolled diabetes, Smoking status, BM**I<20,**Chest-Xray showing advanced disease, Failed ATT) could be devised and properly validated by further studies to suspect and diagnose this menace as early as possible even from the peripheral health care facilities.

REFERENCES:

1. WHO. 2011a. Global Tuberculosis Control: WHO Report 2011. http://whqlibdoc.who.int/publications/2011/9789241564380_eng.pdf (accessed November 15, 2011).
2. Frieden TR, Sterling T, Pablos-Mendez A, et al. (1993). "The emergence of drug-resistant tuberculosis in New York City". N Engl J Med 328 (8): 521–56.
3. Mona Bashar, MD; Phil Alcabes, PhD; William N. Rom, MD, MPH, Rany Condos MD."Tuberculosis and diabetes: Patients on the Bellevue Chest Service, 1987 to 1997"; Chest. 2001; 120:1514-1519.
4. Mbyana JC, Gan D, Allgot B, Bakker K, Brown JB, Ramachandran A, et al. IDF Diabetes Atlas, 3rd ed. Brussels: Hoorens; 2006.
5. Holmes CB, Hausler H, Nunn P; A review of sex differences in the epidemiology, IJTLD, 1998, 2:96-104.
6. Cegieleski J P,Kohlmeier L et al;Malnutrition and Tuberculosis in a nationally representative cohort of adults in United states 1971-1987,American journal of Tropical Medicine and Hygiene,1995,53:152-157.
7. Kim SJ et al; Incidence of Pulmonary Tuberculosis among diabetics: Tubercle and Lung disease 1995:76:529-533