



Research Article

MDR-TB- Clinical Profile of MDR-TB Cases at DR-TB Centre

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Abstract

The present study was carried at NKPSIMS, RC & LMH on patients admitted in one year from Dec 2012 to Nov 2013 after confirmation of being a Multidrug resistant tuberculosis (MDR-TB) case (i.e. resistant to Rifampicin or to both Isoniazid & Rifampicin). 96 patients (69 males & 27 females) were registered, admitted and treated for MDR-TB/ XDR-TB and were thoroughly reviewed regarding age, sex, residence, socio-economic status, symptomatology, duration of illness, prior regularity or irregularity in respect of treatment received, prior receipt of number of anti-TB regimens and comorbid illnesses and adverse drug reactions. Males outnumbered the females, residents of Nagpur district (urban and rural areas) were found to be more than other districts of Vidarbha region.

One patient of Extra Pulmonary MDR-TB was registered and initiated on CAT- IV regimen and there was one confirmed case of XDR-TB who was admitted and investigated for auxiliary investigations and initiated on CAT-V regimen.

This study reflects the case of "NKPS Nagpur Model" a PPP model which delivers to TB & MDR-TB patients and nutritional supplements as well. The unique feature of this model is that Public sector role is to provide human resources and free investigations with free drug delivery and the private sector provides specialist care to DR-TB patients along with infrastructure support. This approach has become known as the "NKPS Nagpur Model".

Early diagnosis, registration and initiation of Anti MDR-TB and XDR-TB regimens can prevent the dissemination and transmission of the deadly and dreadful resistant bacilli.

Keywords: Multi Drug Resistant TB, Extremely Drug Resistant TB, Extended framework of DOTS package, DOTS Plus regimens (Cat 4 and Cat 5), Public Private Partner-ship NKPS Nagpur Model.

Introduction

Tuberculosis is an important public health problem throughout the world and about one third of the population of the world is infected by Mycobacterium TB. Tuberculosis continues to be an important public problem in India. WHO estimates that largest number of new TB cases are from Asia. In Asia, India is also high burden country along with China.¹

In India, almost 40% population is infected with Tubercle bacilli; every 5th New patient worldwide is living in this sub continent. With an estimated 2 million new cases of TB and 5 lakh TB related deaths in India annually², India accounts for one fifth of global TB burden³. Recently MDR-TB & XDR-TB have emerged as the greatest threat to mankind worldwide. MDR-TB is defined as a case whose sputum is culture positive for MTB and is resistant in vitro to Isoniazid & Rifampicin with

other anti-tubercular drugs based on C-DST results from an RTCP certified laboratory⁴. XDR-TB is defined as a case whose mycobacterium isolate is resistant to at least Isoniazid & Rifampicin and Fluoroquinolones & Second Line Injectable anti TB Drugs.

The increasing incidence of resistance of MTB strains to the most effective First Line anti TB drugs is a major factor contributing to the current epidemics. Emergence and spread of MDR-TB strains is a phenomenon thereby playing a great role to destabilize global tuberculosis control. Host genetic factors also contribute to development of MDR-TB. It is also to be stressed that MDR-TB is man- made phenomenon, as poor treatment, poor drugs and poor adherence leads to the development of MDR-TB.

Data from the several studies conducted in India suggest that the rate of MDR-TB is 2 to 3 % in New TB cases and 17.2% in previously treated TB cases⁵; thereby a large absolute number of cases are emerging annually⁶. Prevalence of DR-TB mirrors the functional status and efficacy of Tuberculosis control programmes. To address the issue of MDR-TB, the RNTCP has initiated the DOTS Plus strategy for appropriate management of MDR-TB patients with a view of preventing the propagation and dissemination of MDR-TB. Literally, Programmatic Management of Drug Resistant TB (PMDT) services refer to DOTS programme that adds components for MDR-TB diagnosis, management and comprehensive health care. Provision of DOTS-Plus Strategy for MDR-TB patients is a supplementary service under the expanded framework of the DOTS package⁷. India launched its first programmatic services for MDR-TB patients in Gujarat in 2007⁸. Experiences from RNTCP and elsewhere showed that partnership between Government, private, corporate and NGO health care sectors can increase TB detection rates and improve patient adherence.

NKPSIMS is a classic Public Private Mix (PPM) model which delivers clinical services to TB & DR-TB patients and nutritional supplementation as well. The unique feature of this model is that the Public

Sector role is to provide human resources and free investigation with free drug facility and private sector provides specialist care to DR-TB patients along with infrastructure support. This approach is known as "NKPS Nagpur Model". This study was planned with the objective to assess treatment response under PMDT services of RNTCP in detail and to study clinical, radiological and bacteriological profile of diagnosed MDR-TB patients.

Materials and Methods

This was a retrospective study of one year duration from December 2012 to November 2013. Total 96 MDR-TB patients were admitted at DR-TB Centre, NKPSIMS & LMH, Nagpur. Patients having culture report resistant to Rifampicin/INH & Rifampicin both by Line Probe Assay from IRL, Nagpur were admitted and critically analysed for pretreatment evaluation and initiation of treatment. It was ensured that all necessary pre treatment investigations, Psychiatric evaluation and counselling had been undertaken. After well formed decisions, Cat IV & Cat V regimens were started and adverse reactions of the drugs if experienced were monitored.

Results

In the present study, all the patients were from Nagpur Division of Vidarbha Region i.e. Bhandara, Gadchiroli, Gondia, Wardha, Nagpur Rural, Nagpur Corporation, Chandrapur from 21/12/2012 to 30/09/2013 (three quarters). The present study was carried out at NKPSIMS, RC, & LMH, Digdohills, Nagpur from December 2012 to November 2013.

Table 1: Age and Gender wise distribution

Demographic/Age Group	Male	Female	Total Patients enrolled
Below 14	0	0	0
15-24	9	7	16
25-34	24	9	33
35-44	14	6	20
45-54	15	4	19
55-64	5	1	6
65 & above	2	0	2
Total	69	27	96

Table 2: District wise distribution of cases

District	No. of cases	Percentage(%)
Nagpur Corporation	25	26.04
Nagpur Rural	21	21.87
Wardha	13	13.54
Bhandara	14	14.58
Gondia	4	4.16
Chandrapur	12	12.5
Gadchiroli	7	7.29
Total	96	100

Table 3:Demographic parameters

Criteria	Male	Female	Total
Literacy			
Literate	55	15	70
Illiterate	14	12	26
Total	69	27	96
Residence			
Urban	33	20	53
Rural	34	9	43
Socio-economic Status			
Upper	0	0	0
Middle	26	10	36
Lower	43	17	60

Table 4: Weight Band

Band	Male	Female	Total
<16 Kg	0	0	0
16-25 Kg	1	1	2
26-45Kg	55	21	76
46-70 Kg	12	5	17
>70 Kg	1	0	1

Table 5: Body Mass Index

BMI	Male	Female	Total
<18.5	61	25	86
18.5-24.9	7	2	9
>25	1	0	1

Table 6: Symptomatology

Symptoms	No. Of patients
Cough with / without expectoration	90
Breathlessness	35
Haemoptysis	17
Fever	86
Loss of weight	66

Table 7: Duration of Symptoms

Duration of Symptoms	No. of Cases
< 1 year	30
1-3 Years	40
3-5 Years	18
>5Years	8

Table 8: Previous Treatment History

District	Private	Government	Both	Total
Nagpur Corporation	2	16	7	24
Nagpur Rural	0	18	3	21
Wardha	0	10	3	13
Bhandara	0	12	2	14
Gondia	0	3	1	4
Chandrapur	0	9	3	12
Gadchiroli	0	7	0	7

Table 9: Previous Regimens of Patients on Cat IV

Previous Regimen	No. of Cases
Private	2
Cat I	2
Cat II Relapse	44
Cat II Failure	20
Cat II Default	27
Non Dots	1

Table 10: Interval between last treatment & diagnosis

Interval	No. of Cases
< 6 months	55
6 months to 1 Year	19
1 to 3 Years	15
3 to 5 Years	5
>5 Years	2

Table 11: No. Of regimens received

No. of prior regimen	Regular	Irregular	Total
1	6	2	8
2	26	9	35
3-4	30	15	45
5 or more	5	3	8

Table 12: Addictions

Addiction	No. of Patients
Smoking	30
Alcohol	23
Tobacco Chewing	18
Non Addict	25

Table 13: Associated Co-morbid Conditions

Diseases	No. of Patients
Diabetes Mellitus	8
Renal Disease	0
Hypertension	0
Retroviral Disease	7
Potts spine	1

Table 14: Radiological Presentation

CXR (Chest X-ray) Extent	No. of Patients
Bilateral Lesion	57
Unilateral Lesion	
< Half Lung Field	15
Half Lung Field	23
Cavitary Lesion	60
Non Cavitary lesion	35

Table 15: MDR- TB patients subtype

Resistance Pattern	No. of patients	%
Rifampicin Resistant	31	32.29
INH + Rifampicin	65	67.71
Total	96	100

Table 16: Adverse Drug Reactions

Adverse Drug Reactions	No. of patients	%
Gastro-Intestinal Disturbance	9	9.37
Joint Pain	5	5.20
Psychiatric Disturbance	3	3.12
Hearing Loss/Tinnitus	6	6.25
Non Adverse Reaction	73	76.04

Table 17: Response of Cat-IV at the end of 6 months

Response	No. of Patients	%
Culture Conversion	64	66.66
Culture Non conversion	20	20.83
Death	6	6.25
Defaulted	6	6.25
Total	96	100

Table 18: Final Outcome

Response	No. of Patients	%
Cured	38	39.58
Treatment Completed	7	7.29
Death	19	19.79
Failure	7	7.29
Default	19	19.79
Switched to Cat- V	6	6.25

In present study most of the patients were from Nagpur Urban area (26.04 %) and the least were from Gondia District (4.16 %). Most of the patients were between 25 to 34 age groups (34.37 %) and the least in 65 and above age group (2.08 %). Gender wise 69 patients were male (71.87 %) and 27 patients were female (28.18 %). Present analysis indicated that 61 male patients (63.54 %) and 25 female patients (26.04 %) had BMI less than 18.5 (under weight) where as 1 male patients (1.04 %) and 0 female patient (0 %) had BMI more than 25

(over weight) and 7 male patients (7.29 %) and 2 female patient (2.08 %) had normal weight (BMI 18.5-24.9). I 65 patients (67.1 %) had Resistance to both INH and Rifampicin where as 31 patients (32.9 %) had Resistance to Rifampicin only. In present study, 49 patients (51.04 %) were from the category of Smear positive at diagnosis Retreatment case, where as 47 cases (48.95 %) were from the category of "any follow up Smear Positive.

70 cases (72.91%) were literate as they were able to read and write and 26 cases (27.08%) were illiterate. 53 patients (55.20%) were urban dwellers while 43 (44.79%) patients were residents of rural areas.60 patients (62.5 %) were from lower socio-economic strata and 36 patients (37.5 %) from middle socio-economic group; there was none from Upper Strata.(Table 3)

55 out of 69 males (79.71 %) and 21 out of 37 female patients (56.75 %) belonged to 26 to 45 kg Weight Band. 61 males (63.54%) and 25 females patients (26.04 %) had BMI less than 18.5 where as 7 males(7.29 %) and 2 females (2.09 %) had BMI in the range of 18.5 to 24.9 and one patient (1.04 %) had BMI more than 25 (Table 4& 5).

90 patients (93.75 %) had cough with or without expectoration. 35 patients (36.45 %) had breathlessness, 86 patients (89.58 %) had haemoptysis, 86 patients (89.58 %) fever , and 66 patients (68.75 %) had weight loss. 30 patients (31.25 %) had less than 1 year duration of symptoms while 40 patients (41.66 %) had 1 to 3 years duration of symptoms. 18 patients (18.75 %) had 3 to 5 years duration of symptoms and 8 patients (8.33 %) had more than 5 years of illness. (Table 6 & 7)

2 patients had received Anti TB treatment from private doctors (2.08%), 75 patients (78.12%) from Govt. Facility and 19 patients (19.79%) from both. At the time of diagnosis ,2patients(2.08%) were under Cat 1, 44 patients (45.83%) under Cat 2 Relapse, 20 patients (20.83%) under Cat 2 failure and 27 patients (28.12 %) Cat 2 defaulter, 2 patients under AKT from private doctor and 1 patient (1.04 %) under Non DOTS AKT. (Table 9)

67 patients (69.79 %) were regular and 29 patients (30.20 %) were irregular in consuming AKT before starting Cat 4 regimen. 8 patients (8.33 %) had received AKT once, 35 patients (36.45%) twice, 45 patients (46.87%) 3 or 4 times and 8 patients (8.33 %) had received AKT 5 times or more before Cat 4 regimen. (Table 11)

71 patients (73.95 %) were found to be addicted to either Tobacco Chewing, Alcohol, or Smoking and 25 patients (26.04 %) had no addiction. (Table 12)

8 patients (8.33 %) had associated Diabetes Mellitus, 7 patients (7.29 %) had Retroviral Disease and 1 patient (1.04 %) had Extra Pulmonary MDR-TB. (Table 13)

57 patients (59.35 %) had bilateral lesions and 38 patients (39.58 %) unilateral of which 15 (15.62 %) had less than half lung field and 23 (23.95%) more than half lung field affected. Quantitatively 60 patients (62.5%) had cavitary lesion, and 36 patients (37.5 %) had non cavitary lesion. (Table 14) 65 patients (67.70 %) had resistance to both INH & Rifampicin where as 31 patients (32.29 %) had resistance to Rifampicin only. (Table 15)

23 patients (%) experienced 1 or more adverse reaction during and post initiation of treatment, out of them 9 patients (9.37 %) complained of Gastrointestinal Disturbance, 5 patients (5.20 %) had joint pain, 3 patients (3.12 %) had Psychiatric Disturbance and 6 patients (6.25%) had hearing loss. (Table 16)

Outcomes: In the present study, at the end of Intensive Phase of Six months, 64 patients (66.66 %) were culture converted, 20 patients (20.83%) were not culture converted, 6 patients defaulted (6.25 %), and 6 patients (6.25 %) died.

FINAL outcome: In present study at the end of completion of RNTCP endorsed treatment, 38 patients (39.58 %) were found to be cured, 7 patients (7.29%) had been noticed to have completed Treatment, 19 patients (19.79 %) defaulted, 7 patients (7.29 %) were categorized as Treatment Failure, 6 patients (6.25 %) were switched to Cat V, as categorized as XDR-TB and 19 patients (19.79 %) died.

Discussion

The emergence of MDR-TB is a global problem threatening to destabilize the best efforts of TB control and has been attributed to factors such as non adherence to treatment, inappropriate treatment regimens, drug malabsorption, poor drug quality and poor health infrastructure for effective delivery of treatment.^{10,11} WHO and its partner countries launched DOTS- plus initiative to develop a global policy to provide technical assistance to DOTS programme and to enable access to second line drugs under rational use for the management of MDR-TB in poor economical settings¹². Worldwide, in 13 different studies, it was observed that cure rates were ranging from 38% to 100% highlighting the outcome of MDR-TB treatment¹³.

The mean age group of the patients enrolled in our study was ----- which is similar to study by Sharma et al (2011)¹⁴ where the mean age was 33.5. This shows that MDR-TB affects relatively younger age group individuals, which is the productive age group both socially and economically. The average BMI of the patient was 17 which showed that most of the MDR-TB patients fall in the malnourished category. This suggests that low body mass index is risk factor for MDR-TB. The male to female ratio in our study was more in favour of males 71.86% which is comparable with study by Joseph et al in 2011 which has 66% males. Majority (55.20%) of the patients were from urban areas as compared to study of Joseph et al (2011)¹⁵ in which 69% patients belonged to urban areas.

In this study, 23% of MDR-TB patients had initial resistance and 77% had secondary resistance in contrast with study by Datta et al (2009)¹⁶ which had initial and secondary resistance in 36.5% and 63.4% patients respectively. Most of the patients had been previously treated under CAT-II relapse 52.02%, CAT-II failure 22.91 % and CAT-II defaulter 31.25%. These patients need close follow up for early diagnosis of MDR-TB as compared to study of Sharma et al (2011)¹⁴ in which respective figures were 73%, 7% and 20%.

In present study bilateral involvement on Chest X-ray PA view was found in 51.31% cases as

compared to study of Singla et al(2009)¹⁸ 84%, while cavitatory lesion was noted in 61.45% cases which is high as compared to 43% in study by Singla et al. The most common symptom found in present study was cough in 93.75 % patients. Overall 17% patients experienced adverse reactions and treatment was modified in 7.29% of cases and Kanamycin has to be stopped in 6.25% of cases due to profound hearing loss. The default rate of 6.25% was significantly less as compared to 17.4 % in study by Singla et al¹⁸. There were 6.25% deaths as compared to 11.1% deaths in the study by Singla et al¹⁸.

Tuberculosis had been declared by WHO as " Public Health Emergency " in the year 1990. It usually affects the people in the reproductive age group, so it creates an important financial and social burden on the country. MDR-TB is spreading with a great speed with an all round manner in the Indian Society. The relationship between poverty and MDR-TB has now been well established as it is seen more commonly in the persons of lower socioeconomic class and relatively younger age bread earner group of patients and thereby making a vicious cycle. By and large socioeconomic status of the needs to be improved judiciously. Poor nutrition is directly associated with adverse outcome (death and default) in the management of MDR-TB. Addiction is a major factor associated with poor outcome in PMDT programme which should be dealt judiciously by providing programmes and counselling.

Conclusions

Adherence to the adequate drug regimens should be encouraged highlighting its importance in both curing and preventing the transmission of MDR-TB strain. Early recognition of MDR-TB status and initiation of second line drugs under PMDT services is the need of the hour in preventing the dissemination of drug resistant strain by having a high degree of suspicion of MDR-TB case in persons with a history of prior treatment defaults, and treatment failures. Early sensitisation of private practitioners and DOTS providers should be

facilitated to refer patients for early sputum culture and drugs susceptibility testing at Intermediate Reference Laboratory. Finally highest priority would be to ensure the effective running and implementation of DOTS programme and judicious use of first line drugs in new patients to halt the pace of emergence of MDR-TB. Private sector involvement leads to quality health delivery as seen in the case of "NKPS Nagpur Model". Reorganization of the strength of private sector will have a synergistic effect on the control of DRTB in India. Continuous interaction and mutual trust between the Public and Private sectors are essential prerequisites for the success of the collaboration. At the same time, the standard diagnostic guidelines of the programme need to be followed by all sectors to ensure the quality of RNTCP service delivery.

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