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Multidrug resistant tuberculosis in the isles

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Abstract

Background: Despite implementation of DOTS and tremendous effort by government Tuberculosis (TB) continues to be a major public health problem worldwide with multi drug resistant tuberculosis becoming a major area of concern.

Aims and objectives: To evaluate the incidence of MDR-TB in the islands and describe the basic demographic correlates of new cases of MDR -TB.

Methodology: Retrospective data mining on new cases of multi-drug resistant tuberculosis from state Tuberculosis control society under Revised National Tuberculosis Control Programme from January 2012 to December 2018.

Results: Total number of MDR -TB cases from 2012 TO 2018 was 275 which included 172 males and 103 females. Incidence of multi drug resistant Tuberculosis varied from 2.09 to 15.19 per lakh population.

Conclusion: The numbers of cases have increased from 2012 to 2018. Rapid diagnosis, treatment and surveillance are a must to fight the battle of MDR -TB.

Keywords: Multi drug resistant tuberculosis, Andaman, India, drug resistant tuberculosis

Introduction

Tuberculosis (TB) still continues to remain a gigantic public health problem worldwide. Despite implementation of Stop TB strategy, tuberculosis that is resistant to first-line drugs is becoming a rising concern worldwide and poses to be new barrier, challenging the control of multidrug-resistant TB (MDR-TB). MDR-TB is a man-made problem resulting from poor management and low quality of ant tuberculosis drugs [1].

Multi-drug-resistant tuberculosis (MDR-TB) is a type of tuberculosis (TB) infection which is caused by bacteria which are resistant to treatment with at least two of the most common first-line anti-TB medications (drugs), isoniazid and rifampin [2]. MDR-TB incurs a huge socioeconomic burden on developing countries due to its prolonged, expensive and toxic treatment [3, 4]. India accounts for most number of multidrug-resistant tuberculosis (MDR-TB) cases in the world, contributing to one-fourth of the global load [5]. As per WHO global TB report 2018, in India people who fell ill with drug resistant TB in 2017 was 135000 as compared to China which had 73000 drug resistant TB [6].

Multidrug-resistant TB (MDR-TB) causation is multifactorial. It can be the result of various reasons like inappropriate or incorrect use of antimicrobial drugs, or use of ineffective formulations of drugs, improper management, poor supply and quality of drugs, bad storage conditions, wrong and premature interruption of drugs and airborne transmission of bacteria at public and crowded spaces [7, 8]. The three countries which account for major MDR burden are India, China and the Russian Federation. They together bear nearly half of the global cases [6, 9]. In India incidence of MDR TB is about 1-3% in new cases and 12-17% in retreatment cases [10, 11, 12, 13].

In the absence of surveillance network and lack of consistent prevalence studies, have made it difficult to assess the true extent of MDR-TB in India. We therefore sought to measure the extent of MDR tuberculosis in Andaman and Nicobar Islands. Hence present study was undertaken to evaluate the following objectives:

1. To evaluate the incidence of MDR-TB in the islands
2. Describe the basic demographic correlates of new cases of MDR -TB.

Materials and Methods

In this retrospective data mining, the researchers collected data on new cases of multi-drug

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resistant tuberculosis from state Tuberculosis control society under Revised National Tuberculosis Control Programme from January 2012 to December 2018. There are 09 TU functioning in Andaman & Nicobar Islands - three each in South Andaman District, North & Middle Andaman District, & Nicobar District. MDR TB is diagnosed only in Port Blair TU; situated in South Andaman District. The summative data contained information on demographic characteristics of all MDR-TB cases during the course of treatment of each patient.

We analyzed data of all new Multi drug resistant Tuberculosis cases.

Ethical Clearance was obtained from the Institutional Ethics Committee. The data was cleaned & entered in MS-Excel spread sheet and analyzed using IBM SPSS 20.0 software (Chicago). Data was presented using frequencies and percentages.

Operational definitions of outcomes for MDR-TB patients treated using second-line treatment are as follows-Case of multidrug-resistant TB (MDR-TB) - TB that is resistant to two first-line drugs: isoniazid and rifampicin. For most patients diagnosed with MDR-TB, WHO recommends treatment for 20 months with a regimen that includes second-line anti-TB drugs.

Cure is defined as a patient who has completed treatment with no evidence of failure and three or more consecutive negative cultures taken at least 30 days apart after the intensive phase.

Treatment completed - As recommended by the national policy without evidence of failure but no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase

Failure - is defined as when treatment is terminated or if there is a need for a permanent regimen change of at least two anti-TB drugs because of lack of conversion by the end of the intensive phase, bacteriological reversion in the continuation phase after conversion to negative, evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, or adverse drug reactions

Died - A patient who dies for any reason during the course of treatment.

Lost to follow-up (Defaulter) - A patient whose treatment was interrupted for 2 consecutive months or more.

Extensive drug resistance (XDR) refers to: resistance to any fluoroquinolone and to at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance^[14].

Results

Total number of MDR -TB cases from 2012 TO 2018 was 275 which included 172 males and 103 females. In 2012 total MDR cases diagnosed were 8 which included 5males (62.50%) and 3 females (37.50%). In 2013 there were 21 cases consisting of 14 males (66.70%) and 7 females (33.30%), 2014 had 39 cases with 29 males (74.40%) and 10 females (25.60%), in 2015 total cases registered were 46 which included 31 males (67.40%) and 15 females (32.60%), in 2016 total number of cases were 52, 26

males(50.0%) and 26 females (50.0%), in 2017 total MDR cases diagnosed were 49, 29 males (59.20%) and 20 females (40.80%) and in 2018 there were 60 cases which included 38 males (63.30%) and 22 females (36.70%). (Table 1) (Figure 1)

Incidence of multi drug resistant Tuberculosis per lakh population in 2012 was 2.09, in 2013 it was 5.46, in 2014 incidence was 10.08, in 2015 it was 11.83, in 2016 it was 13.30, in 2017 it was 12.47 and in 2018 incidence was 15.19. (Table 2) Treatment outcomes from 2012 to 2016 (first 2 quarters) total cured cases are 63, transfer out 10, deaths 36, failure 2, defaulter 12, still on treatment 3, treatment completed 10 and XDR cases were 4. In 2012 there were 8 cured cases, 2 deaths, 1 defaulter and completed treatment 1. In 2013 cured cases were 6, deaths 9, defaulter 1, completed treatment 3 and 2 cases of XDR. In 2014, MDR cases which got cured were 16, deaths 6, defaulter 6, still on treatment 2, completed treatment 6 and 2 cases of XDR. In 2015, cured cases were 26, transfer out 5, deaths 11, failure 1, defaulter 2, still on treatment 1. Outcomes for first two quarters of 2016 consisted of 11 cured, 5 transfer out, 8 deaths, 1 failure, 2 defaulter. (Table 3)

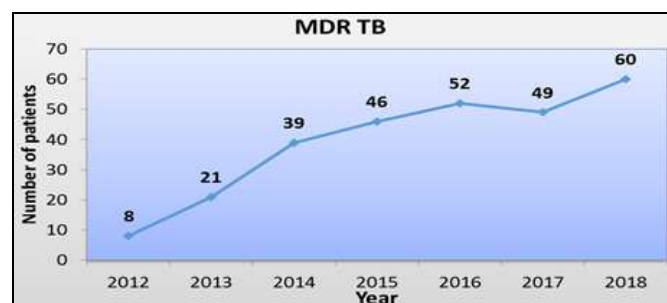


Fig 1: Trend of MDR- TB

Table 1: Year- wise MDR- TB Cases (2012-2018)

MDR TB					
Year	Male		Female		Total
	n	%	n	%	
2012	5	62.5%	3	37.5%	8
2013	14	66.7%	7	33.3%	21
2014	29	74.4%	10	25.6%	39
2015	31	67.4%	15	32.6%	46
2016	26	50.0%	26	50.0%	52
2017	29	59.2%	20	40.8%	49
2018	38	63.3%	22	36.7%	60

Total males cases- 172 Total Female cases -103

Table 2: Year-wise Incidence of MDR TB

Year	No of cases	Population	Incidence Per Lac
2012	8	382725	2.09
2013	21	384837	5.46
2014	39	386919	10.08
2015	46	388970	11.83
2016	52	390990	13.30
2017	49	392981	12.47
2018	60	394942	15.19

Table 3: Year-wise Treatment outcome of MDR TB

Year	Cured	Transfer Out	Death	Failure	Defaulter	Still on treatment	Treatment completed	XDR	Total
2012	4	0	2	0	1	0	1	0	8
2013	6	0	9	0	1	0	3	2	21
2014	16	0	6	0	6	2	6	2	38
2015	26	5	11	1	2	1	0	0	46
2016*	11	5	8	1	2	0	0	0	27
Total	63	10	36	2	12	3	10	4	140

*: Data available for only first two quarters

Discussion

The cost effective measure for prevention of drug resistant tuberculosis is to treat the drug susceptible tuberculosis by proper implementation and rationale use of good quality DOTS. All follow up smear positive cases that are suspected to be drug resistant should be screened by culture or rapid molecular biological testing. At present CB-NAAT molecular biological method is being used for rapid diagnosis of MDR-TB cases [15].

The major problem with MDR-TB is that it requires treatment for a longer period [16]. According to WHO new cases of MDR/RR-TB estimated in 2017 was 558000 of which only 160 684 were detected and notified and 139114 (87%) were enrolled for treatment [17]. As per the Global TB report incidence of MDR-TB in India in 2017 was 135000 [18]. As per our study total number of MDR cases in Andaman and Nicobar Islands in 2018 was 60 and in 2017 it was 49. Incidence per lakh population in 2018 was 15.19 and in 2017 were 12.47

Globally in 2016, there were an estimated 600 000 new cases of MDR/RR-TB, 240 000 deaths of MDR cases and most of these deaths occurred in Asia. Anti TB drug resistance surveillance data reported 4.1% new and 19% of previously treated cases in the world to have multi drug resistant Tuberculosis and approximately 6.2% of MDR-TB cases emerged as extensively drug-resistant TB (XDR-TB) [19].

While in 2016 incidence of MDR cases in India increased to 147000 [5], comparatively in Andaman and Nicobar Islands total number of cases were 52 and incidence was 13.30 per lakh. In 2015 globally there were an estimated 580,000 MDR-TB/RR-TB cases out of which only 132,120 (23%) were detected, and even smaller number 124,990 (20%) were started on treatment, and only about 52% of them were successfully treated [20].

In India in the year 2015, prevalence of MDR-TB among new and previously treated patients was 2.5% and 16%, respectively. Out of 130,000 cases of MDR-TB, only 79,000 cases were notified out of which only 28876 (36%) were diagnosed, only 26988 (34%) were started on treatment, and treatment success rate was only 46% which is issue of grave concern [20]. In Andaman and Nicobar Islands total number of cases in 2015 was 46 and incidence was 11.83 per lakh.

In 2014 the level of drug resistance in world among new cases remained low. It was estimated that 3.3% of new cases and 20% of previously treated cases developed MDR. Out of 480,000 people estimated to have developed MDR-TB only about a quarter of this ie.123000 was detected and reported and 190,000 people died due to MDR-TB across the globe [21, 9].

Estimated MDRTB cases in India in 2014 was 71000, notified were 25748 and cases enrolled on treatment were 24073 [9]. In Andaman and Nicobar Islands total number of cases in 2014 was 39 and incidence was 10.08 per lakh.

In the year 2013 worldwide about 3.5% of new and 20.5% of previously treated TB cases was expected to have had MDR-TB. Out of estimated 300000 MDR TB cases only 136000 were detected, diagnosed and notified and only 97000 were started on treatment. Advancement in detection could be facilitated because of new and rapid diagnostic techniques [22].

In India in 2013, incident cases were 62,000 cases [22]. In Andaman and Nicobar Islands total number of cases in 2013 was 21 and incidence was 5.46 per lakh.

Globally in 2012 about 3.6% were newly diagnosed TB cases and 20% of previously treated for TB developed MDR-TB. Incident cases estimated in 2012 were 450000 and deaths estimated were 170000. Out of which 94 000 were detected and 77000 were started on second line treatment. It was observed that at least one case of extensively drug-resistant TB (XDRTB) was reported by 92 countries by the end of 2012 [23].

And in 2012 India accounted for 64,000 cases of MDR-TB [24]. In Andaman and Nicobar Islands total number of cases in 2012 was 8 and incidence was 2.09 per lakh.

As per the sub national drug resistant surveys which was carried in India among 3 states of India by well-qualified and accredited laboratories it was concluded that approximately 3% of new TB cases and 12 to 17% of previously treated cases have MDR-TB [25].

A cross-sectional study was carried out in a tertiary care centre of south-west coastal Karnataka observed 6.3% of MDR cases [26]. In comparison as per the WHO data 2011 and TB India data 2013, MDR cases among the notified PTB cases ranged from 3.6 to 6.2% which consisted of newly diagnosed cases in the range of 1.5 to 2.7% and retreatment cases to 17% [27]. Study done in Gujarat by Ramachandran *et al.*, found 2.4% of MDR-TB was present in the newly diagnosed cases and presence of 17.4% of MDR-TB in previously treated cases and about presence of 3.8% of the XDR cases. [13] While in Kerala MDR was reported in 2% of newly diagnosed cases [28]. While in Kashmir Dutta *et al.* reported primary drug resistance of 5.4% and a secondary drug resistance of 36.5% among the study population [29] where as in a study done in Mangalore observed 4% of prevalence of MDR-TB [30].

Global median prevalence of primary and acquired MDR-TB reported by WHO was 2.9% and 15.3% respectively [31]. In India prevalence of MDR-TB found to be 1–3% in new cases and approximately 12% in re-treatment cases [32]. Study done in other states of India eg. In Gujarat, prevalence of MDR-TB was found to be 2.4% in new cases and roughly 17.4% in previously treated cases [13]. Study done at a referral tuberculosis hospital in Amargad, Gujrat prevalence of MDR-TB has been observed to be higher among previously treated patients [33]. As per WHO global tuberculosis reports about 4.1% of new TB cases are reported to be MDR [5].

Studies done among countries outside India like in Brazil incidence of MDR-TB ranged between 1-8% among new cases and 3–13% among previously treated TB patients [34, 35, 36]. The researchers have observed in the present study that males are affected more than females from 2012 to 2018. Almost similar finding was seen in a study done in northern India [37] and in Gorakhpur [38] and study done in China [39]. Eight year surveillance study in France observed majority of MDR cases were males [40]. This could be because males have more exposure to people outside as compared to females which could be either occupational or their lifestyle like having more of social activity exposing themselves to drug resistant cases. Drug-resistant Tuberculosis (DR-TB) is a major public health concern in global TB control among several developing countries. It requires an uninterrupted Surveillance for MDR-TB which should be based on routine drug susceptibility testing of TB patients which also include systematic collection and analysis of data to monitor trend in drug resistance [41].

It has been observed from the present study conducted in Andaman and Nicobar Islands that though the numbers of cases are less compared to other states in India and world. However it is a state of alarm seeing the increasing number of cases every year with hardly 4 Lakh population in whole of Andaman and Nicobar Islands. To combat drug resistance tuberculosis in the islands urgent efforts are required in few priority areas which include prevention of drug resistance through high quality treatment of drug susceptible Tuberculosis by proper implementation of DOTS, maximizing early case detection and treatment and enhancing contact tracing. In these islands one of the important requirement is expansion of rapid testing centres for MDR-TB in other islands also as presently MDR-TB is tested and diagnosed only in Port Blair TU, provision for immediate access to treatment for MDR cases, check compliance of both service provider and patients by regular follow up until the patient is completely cured, proper care of such patients, prevent transmission of MDR-TB through strengthening of infection control activities especially in facilities where MDR cases are treated, ensure correct use, dosage, administration and length of antimicrobial drugs, facilitate uninterrupted supply of good quality drugs and above all increase political commitment with financing and collaboration among health and social organizations will help in reducing the burden of MDR-TB in these islands.

Conclusion

According to our study MDR –TB is on a rise in Andaman and Nicobar Islands. The numbers of cases have increased from 2012 to 2018. Year wise incidence of MDR –TB has increased from 2.09 per lakh population in 2012 to 15.19 per lakh population in 2018. Males are affected more than females as per the study. There is an urgent need to increase community awareness about danger of MDR-TB. Primary aim to prevent drug resistance TB is to prevent its emergence itself. Emphasis should be laid on proper implementation on DOTS and completion of treatment to prevent drug resistant cases in the community. Rapid diagnosis, treatment and surveillance are a must to fight the battle of MDR –TB.

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