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Factors of Multidrug Resistance Tuberculosis

Dr. Vikas Kumar[1], Dr. Mrs. Vaishali V. Raje[2*]
[1]Department of Community Medicine, Krishna Institute of Medical Sciences Deemed To Be University, Karad-415110, Maharashtra
*[*2]Professor, Department of Community Medicine, Krishna Institute of Medical Sciences Deemed To Be University, Karad-415110, Maharashtra*
Corresponding Author: vaishalidr1703@gmail.com

ABSTRACT

The tuberculosis study subjects were diagnosed on the basis of sputum microscopic examination. Tuberculosis is a chronic, communicable and infectious disease mainly caused by Mycobacterium tuberculosis. This case-control study was carried out among 104 MDR-TB cases and 104 drug sensitive tuberculosis cases as controls. Among cases and controls 66(63.5%) male and 38(36.5%) female tuberculosis patients were on treatment for tuberculosis under district tuberculosis centre Satara. Most of the study participants from both cases and controls group were from rural area. The male predominance was seen in both drug resistant and drug sensitive tuberculosis. Majority of study subject from cases (70.2%) and controls (68.3%) belonged to age group 19 to 40 years of age. So it was concluded that the primary infection that the patients have got is due to multidrug resistance tuberculosis contact. Among medical condition asthma found to be significantly associated with multidrug resistance tuberculosis.

Keywords: Multidrug, Tuberculosis, Treatment, MDR, Mycobacterium

Correspondence:
Vaishali V. Raje
Professor, Department of Community Medicine
Krishna Institute of Medical Sciences Deemed to be University
Karad, Maharashtra
E-mail Address: vaishalidr1703@gmail.com

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INTRODUCTION

Tuberculosis is one of the major public health challenges facing the world today. Tuberculosis is a chronic, communicable and infectious disease mainly caused by Mycobacterium tuberculosis. As mentioned in Rigveda, Tuberculosis is an ancient disease to mankind which existed in India since the earliest days around 1500 BC. It is said that the moon god was the first to become the victim of the disease, hence it is also known as Rajayakshma, king's disease. A decline of 55% after successful Directly Observed Treatment Short Course strategy, however in sputum positive cases mortality has decreased from 29% to 4%. High mortality rate is due to failure to diagnose, inadequate treatment or delayed treatment[1,2]. Inappropriate or incorrect use of antimicrobial drugs Using ineffective drug formulations (eg. Single drug treatment), Treatment interruption (not completing the prescribed complete treatment), Getting infection transmitted from a MDR TB case (especially in crowded settings such as hospitals, slums or prisons). Further mismanagement of these TB cases from healthcare givers and ongoing person to person transmission become the reason for emergence and spread of MDR-TB[3]. Thus the present study was aimed to explore an association of MDR-TB with various host & program induced risk factors among the registered Tuberculosis cases under RNTCP in the district Satara.

AIM AND OBJECTIVES

Aim

To assesses risk factors for MDR Tuberculosis among the Tuberculosis patients under the programme.

Objectives

To study presence of host related risk factors in MDR-TB cases and non MDR-Tuberculosis cases. To study programme related variable present in MDR-TB cases and non MDR-Tuberculosis.

REVIEW OF LITERATURE

Tuberculosis is a chronic infectious disease caused by a bacterial microorganism, the tubercle bacillus or Mycobacterium Tuberculosis. It is a potentially fatal contagious disease that can affect almost any part of the body but mainly involve the lungs primarily resulting in pulmonary tuberculosis. Tuberculosis is defined as two step process. The first step is acquisition of infection and the second is developing to disease. The definition of tuberculosis depends on the stage of infection and it can be divided into two forms; latent infection and active tuberculosis. Infected individuals are not ill and not infectious but may develop to active tuberculosis. Infectious individuals can transmit infection and require TB treatment for cure[4].

A study conducted by shweta Mangal et al. on the involvement of private practitioners showed majority of them (74.35%) were taking random samples for sputum examination. About 70% of the practitioners were referring the suspected TB patients to other centers, mostly government 86%[5]. Another study conducted by Datta et al. in 2010 of the total 260 randomly selected private practitioners in Hooghly district of West Bengal. It was observed that only 11% were following the guidelines of RNTCP were as majority (68%) of them were
prescribing chest X-ray which were against the standard diagnostic test-sputum examination for the diagnosis of tuberculosis[6]. In another study conducted in Pune, it was found that use of sputum microscopy for TB diagnosis was 63% only.[7]

A Study conducted by Nella Harshini et al,[8] on demographical and clinical factors associated among HIV/ Tuberculosis co-infected patients at Government District General Hospital Khammam, Telangana. It was observed that a total 107 HIV patients were found to be positive for Tuberculosis by CBNAAT. Rifampicin resistance was detected in 10 patients (9.34%) and about 54(50.4%) were under pre-antiretroviral therapy and 46 (42.9%) were under antiretroviral therapy and others were 7(6.5%). About 45 (42.05%) patients with HIV/TB co-infection showed CD4 count 500 cells/mm3.

Multiple evidences recommend that tuberculosis can transmitted from infectious persons to the others persons through the air. An untreated individual with active Tuberculosis infection can infect 10-15 other people per year. It was also reported in recent studies that people with prolonged, frequent, or intense contact with Tuberculosis cases are at particular high risk of being infected[9,10]. Thus, Tuberculosis control can be reached by breaking the chain of transmission by identifying and treating infectious disease, preventing severe infections by BCG vaccination.[9-14]

Raazi J, (2017) et al[15] conducted a cross-sectional study to determine the risk factors of tuberculosis among registered tuberculosis patients at the urban tuberculosis unit of Allahabad during the year 2015. In this study total 54 MDR tuberculosis cases and 1016 drug sensitive tuberculosis cases were studied. Majority MDR tuberculosis cases belonged to age group 26-45 years (59.26%) whereas drug sensitive cases were more in age group 45 years (46.75%).

P. Mukherjee , et al (2015)[16] conducted a retrospective record based study to find out the socio demographic and clinical profile of MDR patients in Kolkata from 1st January to 31st December 2013. A total 172 MDR-TB patients were included. Out of 172 MDR tuberculosis cases majority (30.23%), were between age group 21-30 years, followed by 31-40 years (25.58%) with mean age 32.52 ± 13.05 years and range was from 14 to 85 years. Mean age of male patients was 34.97±12.84 years and in female 28.59 ±12.50 years. Male were predominant (61.62%) than female 66(38.37%) and most of the patients (59.9%) were underweight (BMI - 18.5).

Gosavi SV, et al (2015)[17] conducted a hospital based, retrospective cases series study on MDR–TB at Dr. Vasantrao Pawar Medical College Hospital & Research Center, Nasik (Maharashtra) from Jan 2012 to March 2014. Out of 353 MDR tuberculosis cases, majority 49% were between age group 25 to 44 years, female were predominant 52% than male 47.3%. Among all MDR cases, majority of cases had a history of previous treatment (99.4%).

Sachin R.Atre,(2014) et al[18] was found that that among all MDR tuberculosis cases male were 57.5% and female were 42.4%, age group 15 to 24 years was the most affected in both MDR-TB (35.8%) followed by age group 25 to 34 years (27.35%). Among all MDR-TB cases more than half (58.5%) were married, having secondary education (57.5%) and illiterates 18.9%. Majority of MDR cases were unemployed (53.8%), and (82%) had low monthly income group. Habits like Smoking and alcohol was reported in 17.92% and 15% of MDR TB cases. Among MDR tuberculosis cases under nutrition was 70.75% and Glycosylated Haemoglobin were 68.9%.

MATERIALS AND METHODS

Type of study: This case-control study was carried out for the assessment of host related risk factors and Programme related influencing factors for Multidrug Resistance among Tuberculosis patients enrolled for DOTS under Revised National Tuberculosis Control programme during the period of 2016 to 2018 at various sub- district levels. This study was carried out under District tuberculosis Center, Satara. District tuberculosis center is located in the campus of District hospital, Satara, which is 52 kilometers from Krishna Institute of Medical Sciences, Karad. The population covered by District tuberculosis center in 2016 was 3,12,2696. To this population, under Revised National Tuberculosis control Programme, District Tuberculosis Centre catered their services through 10 Tuberculosis Units, 56 Designated Microscopic center, 400 DOT Centers, 3 Tertiary Care Centers, 2 sub-district hospital, 14 Rural Hospitals, 71 PHC's and 2 medical college. Total 2475 suspected cases of tuberculosis were reported during the period of November 2016 to October 2017 and for all these cases, CBNAAT was carried out. Out of 2475 suspected cases, confirmed Drug sensitive tuberculosis cases were 2348, while confirmed Multidrug resistant tuberculosis cases were 120, and Extensively drug resistant tuberculosis were 7 in number. The sample size of 97 each cases and controls were calculated based on the Risk factor glycosylated (HbA1c) haemoglobin for Multidrug resistance tuberculosis. There for after applying exclusion and inclusion criteria total 104 cases and 104 controls were included in the study.

OBSERVATIONS AND RESULTS

In the Present study total 208 Tuberculosis patients were studied. In this case-control study 104 cases and similar number i.e 104 controls were studies. Cases were those who had shown resistance to Isoniazid, Rifampicin or both and controls were those tuberculosis cases who were on treatment and sensitive to Isoniazid and Rifampicin according to gene expert. Among cases and controls 66(63.5%) male and 38(36.5%) female tuberculosis patients who were on treatment were studies. The controls were matched to the cases with their age + 5years and sex.

Table 1: Matching of cases and controls according to age and sex

Age group	Male Cases		Controls		Total(%) 104		Female Cases		controls		Total(%) 104	
16-20 years	02 (40.0)	(3.0)	02 (60.0)	(4.5)	5	(3.8)	5 (45.5)	(13.2)	6 (54.5)	(15.8)	11 (14.5)	
21-25 years	11 (64.7)	(16.7)	6 (35.3)	(9.1)	17 (12.9)		9 (56.2)	(23.7)	7 (43.8)	(18.4)	16 (21.1)	
26-30 years	11 (47.8)	(16.7)	12 (52.2)	(18.2)	23	(17.4)	7 (50.0)	(18.4)	7 (50.0)	(18.4)	14 (18.4)	
31-35 years	9 37.5	(13.6)	15 (62.5)	(22.7)	24 (18.2)		7 (58.3)	(18.4)	5 (41.7)	(13.2)	12 (15.8)	
36-40 years	12 (70.6)	(18.2)	5 (29.4)	(7.6)	17 (12.9)		3 (27.3)	(7.9)	8 (72.7)	(21.1)	11 (14.5)	

41-45 years	6 (40.0)	(9.1)	09 (13.6) (60.0)		15	(11.4)	3 (75.0)	(7.9)	1 (25.0)	(2.6)	4	(5.3)
46-50 years	4 (44.4)	(6.1)	5 (55.6)	(7.6)	9	(6.8)	00 (0.0)	(0.0)	1 (100.0)	(2.6)	1	(1.3)
51-55 years	6 (50.0)	(9.1)	6 (50.0)	(9.1)	12	(9.1)	2 (66.7)	(5.3)	1 (33.3)	(2.6)	3	(3.9)
56-60 years	2 (50.0)	(3.0)	2 (50.0)	(3.0)	4	(3.0)	2 (66.7)	(5.3)	1 (33.3)	(2.6)	3	(3.9)
61-65 years	2 (40.0)	(3.0)	3 (60.0)	(4.5)	5	(3.8)	00 (0.0)	(0.0)	1 (100.0)	(2.6)	1 (100.0)	(1.3)
66-70 years	1 (100.0)	(1.5)	0 (0.0)	(0.0)	1	(0.8)	00 (0.0)	(0.0)	00 (0.0)	(0.0)	00 (0.0)	(0.0)
Total	66 (100.0) (50.0)		66 (100.0) (50.0)		132 (100.0)		38 (100) (50.0)		38(100.0) (50.0)		76 (100.0)	

Table 1 shows the matching of cases and controls according to age and sex. However it shows that there is an variation in number among cases and controls, though it has been taken as 1:1. This variation is due to age matched within the range of 5 years and sex.

Table 2: Distribution of study subjects according to distance of Dots provider from the house of study participants

Particulars	Cases		Total(%) 104	χ^2& p value	Controls		Total(%) 104	χ^2& p value
	Male (%) 66 (63.5)	Female (%) 38 (36.5)			Male (%) 66 (63.5)	Female (%) 38 (36.5)		
Distance from Dots Provider								
<2500mts	53 (80.3) (64.6)	29 (76.3) (35.4)	82(78.8)	0.230**	45 (68.2) (64.3)	25 (65.8) (35.7)	70(67.3)	0.063**
>2500mts	13 (19.7) (59.1)	09 (23.7) (40.9)	22(21.2)	0.632**	21 (31.8) (61.8)	13 (34.2) (38.2)	34(32.7)	0.802**

**Fischer's exact test

Table no. 2 shows, the maximum number (78.8%) cases and (67.3%) controls were living at a distance of less than 500 meters to 2500 meters from DOTS provider place whereas (21.2%) cases and (32.7%) controls, lived at the distance of more than 2.5 kilometers from the DOTS provider. It was observed that proportionately higher number of male multidrug resistant (80.3%) as well as sensitive drug (68.2%) tuberculosis cases were residing within 2.5 kilometers range DOTS provider place whereas high proportion of female tuberculosis cases (21.2%) multidrug resistant tuberculosis cases and 32.7% drugs sensitive tuberculosis patients were staying at far distance from dots provider place i.e. more than 2.5 kilometers which makes the patients to have poor compliance towards the treatment.

Table 3: Distribution of cases and controls according to consistency in Tuberculosis treatment

Treatment phases	Cases		Total(%) 104	χ^2&p value	Controls		Total(%) 104	χ^2& p value
	Male (%) 66(63.5)	Female (%) 38 (36.5)			Male (%) 66(63.5)	Female (%) 38 (36.5)		
Intensive phase (IP)								
Consistent	52 (78.8) (62.7)	31 (81.6) (37.3)	83(79.8)	0.117	62 (93.9) (66.7)	31 (81.6) (33.3)	93 (89.4)	0.093**
Irregular	14 (21.2) (66.7)	07 (18.4) (33.3)	21(20.2)	0.733	04 (6.1) (36.4)	07 (18.4) (63.6)	11 (10.6)	
Continuous phase (CP)								
Consistent	55 (83.3) (60.4)	36 (94.7) (39.6)	91(87.5)	0.126**	54 (81.8) (64.3)	30 (78.9) (35.7)	84(80.8)	0.128
Irregular	11 (16.7) (84.6)	02 (5.3) (15.4)	13(12.5)		12 (18.2) (60.0)	08 (21.1) (40.0)	20(19.2)	0.721

Table 3 describes the consistency of patients to treatment in intensive as well as continuation phase. In the intensive

phase it was found that Majority of the cases (79.8%) as well as controls (89.4%) were consistent to treatment. However it was observed that among the cases more proportion of male patients (21.2%) were irregular with intensive phase treatment were as among the controls female patients were found predominately (18.4%) irregular with intensive phase therapy. With respect to continuous phase it was found that 87.5% of cases and 80.8% controls were more consistent with the Continuation phase. It was noted that, 12.5% of the cases and 19.2 % of the controls had irregular treatment in continuation phase. Male MDR Tuberculosis cases (16.7%) and female drug sensitive Tuberculosis cases (21.1%) were irregular with the treatment during continuation phase.

Table 4: Distribution of study participants according to Phases of treatment

Continuous phase (CP)	Cases		Total(%)	χ^2& p value	Controls		Total (%)	χ^2& p value
	Intensive phase (IP)		104		Intensive phase(IP)			
	Consistent	Irregular			Consistent	Irregular	104	
Consistent	72 (85.7) (79.1)	19 (95.0) (20.9)	91 (87.5)		75 (80.6) (89.3)	9 (81.8) (10.7)	84 (80.8)	
Irregular	12 (14.3) (92.3)	01 (5.0) (7.7)	13 (12.5)	0.454**	18 (19.4) (90.0)	2 (18.2) (10.0)	20 (19.2)	1.000**
Total	84 (100) (80.0)	20 (100) (19.2)	104(100)		93 (100.0) (89.4)	11(100.0) (10.6)	104 (100)	

**Fischer's exact test

Presented in table no. 4, regarding patients compliance to the treatment the information was collected on consistency in taking treatment during intensive as well as continuation phase. Among drugs sensitive tuberculosis cases it was observed that 75 (80.6%) cases were consistent with treatment during intensive as well continuations phase and 18 (19.4%) were consistent to intensive phase but irregular with continuation phase. It was observed that only 2 patients were very much irregular during intensive as well as continuation phase. Similarly among the drug resistant tuberculosis case though they found resistant to Isoniazid and Rifampicin, majority of them were very regular with the treatment during intensive as well continuation phase (72 patients). More number of Multidrug resistant cases were found irregular with intensive phase who had taken continuation phase consistently than the 9 drug sensitive tuberculosis cases.

DISCUSSION

Multidrug resistance tuberculosis (MDR-TB) is emerging as growing threat to tuberculosis control program all over the world. In 2013, in India 62,000 cases of multidrug resistant had been reported. In the presence study out of 208 study subject 104 tuberculosis cases were Multidrug Resistant tuberculosis and similar number 104 tuberculosis cases were drug sensitive tuberculosis. The more proportion of multidrug resistant cases from rural area may be due to poor environmental condition particularly air pollution in rural area which favors easy transmission of multidrug resistant bacilli. This high proportion of male patients in the present study could be due to male gender is commonly exposed to external environment and prone for high risk behavior like smoking and alcohol etc. this may lead to chance of having MDR among male patient. While majority of females working at household level it might be lesser chance to develop multidrug resistant tuberculosis among them. As BMI is known that under nutrition is an important risk factor for development of tuberculosis. Similarly it is a risk factor for development of drug resistant if nutritional status is not improved because under nutrition affects cell-mediated immunity and breaks down functioning of immune system. High proportion of cases habituated to tobacco and alcohol in the present study could be due to lower socio economic status, poor nutritional status, ignorance, poor educational status of the study participants.

CONCLUSION

In the present study the risk for multidrug resistance tuberculosis for example host related risk factors and programme related risk factors were assessed among multidrug resistant tuberculosis and drug sensitive tuberculosis cases in Satara district. In the current study total 104 multidrug resistant tuberculosis cases and 104 drug sensitive cases were studied. Regarding host related risk factors in similar with the reference study it is concluded that tuberculosis infection along with multidrug resistance is found predominantly in middle age grouped patient particularly among married. It states that suffering by multidrug resistance tuberculosis is more with those who has responsibility of their family. Also it is concluded that most commonly affected patients are just literate, rural based farming workers belonged to middle social class.

Regarding habits majority of multidrug resistance male tuberculosis patients were habituated to tobacco and alcohol. It was concluded that migration is most significant risk factor found among multidrug resistance tuberculosis cases as majority of them were migrated out of tuberculosis unit for the sake of earning purpose, where there is uncertainty of adequate nutrition, proper housing, environmental hygiene which might have landed the patients into contracting infection with multidrug resistance bacilli. Similarly history of contact with the patient is high among multidrug resistance cases. So it was concluded that the primary infection that the patients have got is due to multidrug resistance tuberculosis contact. Among medical condition asthma found to be significantly associated with multidrug resistance tuberculosis. However bronchitis, emphysema, pre-diabetic condition, under nutrition, and diabetes mellitus, though they are proportionately higher in number among Multidrug resistant cases than drug sensitive

tuberculosis cases, there was no significant association was found. Therefore it concluded that these medical conditions are host related risk factors for development of drug resistance. The infrastructure to implement Revised National Tuberculosis Control programme at District level must be fulfilled the guidelines of programme to function smooth and efficiently. All the contractual staff are working satisfactory as per the guidelines of Revised National Tuberculosis Control Programme, the distance to cover by DOTS provider is convenient for supervised treatment.

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