



An Epidemiological Study on Causes of Multi-Drug Resistant Tuberculosis (MDR-TB) in DISTRICT Hamirpur, Himachal Pradesh, India

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Abstract

Various components of MDR TB have been derived from the previous literature review and then examined in District Hamirpur through primary and secondary study. The present research summarizes, concludes and makes some useful recommendations on the basis of the results, review of previous literature and findings. This research is divided into three parts. The first part includes summary and conclusions based on the findings of the present study and review of previous researches. The second part presents some recommendations and suggestions to the management of MDR-TB for future strategies and policy making. The third part identifies the areas for further research.

Keywords: MDR-TB; Epidemiological study; Causes; RNTCP

Introduction

Tuberculosis (TB) is as old as the mankind. TB is the most common cause of death due to a single infectious agent worldwide in adults. In 1993, the World Health Organization (WHO) took an unprecedented step and declared TB to be a global emergency. According to the recent estimates, one third of the human population is infected with *Mycobacterium tuberculosis* worldwide. TB is principally a disease of poverty, with 95% of cases and 98% of deaths occurring in developing countries. Of these, more than half the cases occur in five South East Asian countries. In 1997, nearly 1.87 million people died of TB and the global case fatality rate was 23%. This figure exceeded 50% in some of the African countries where Human Immunodeficiency Virus (HIV) is highly prevalent. It is estimated that between 2002 and 2020, approximately 1000 million people will be newly infected, over 150 million people will get sick, and 36 million will die of TB if proper control measures are not instituted. According to WHO reports, one third of the world's population is infected with TB. In 2016, 10.4 million people around the world became sick with TB disease. There were 1.7 million TB-related deaths worldwide. TB is a leading killer of people who are HIV infected. Tuberculosis mostly affects adults in their most productive years. However, all age groups are at risk. Over 95% of cases and deaths are in developing countries. People who are infected with HIV are 20 to 30 times more likely to develop active TB. The risk of active TB is also greater in persons suffering from other conditions that impair the immune system. One million children (0-14 years of age) fell ill with TB, and 250,000 children (including children with HIV associated TB) died from the disease in 2016. Tobacco uses greatly increases the risk of TB disease and death. Eight percent of TB cases worldwide are attributable to smoking [1,2].

Classification Based on Drug Resistance

Cases are classified in categories based on Drug Susceptibility Testing (DST) of clinical isolates confirmed to be *M. tuberculosis*:

- Monoresistance: Resistance to one first-line anti-TB drug only.
- Polydrug resistance: Resistance to more than one first-line anti-TB drug (other than both isoniazid and rifampicin).
- Multidrug resistance: Resistance to at least both isoniazid and rifampicin.
- Extensive drug resistance: Resistance to any Fluoroquinolone and to at least one of three second-line injectable drugs (Capreomycin, Kanamycin and Amikacin), in addition to multidrug

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resistance [3].

- Rifampicin resistance: Resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether monoresistance, multidrug resistance, polydrug resistance or extensive drug resistance. These categories are not all mutually exclusive. When enumerating Rifampicin-Resistant TB (RR-TB), for instance, Multidrug-Resistant TB (MDR-TB) and Extensively Drug-Resistant TB (XDR-TB) are also included. While it has been the practice until now to limit the definitions of monoresistance and polydrug resistance to first-line drugs only, future drug regimens may make it important to classify patients by their strain resistance patterns to fluoroquinolones, second-line injectable agents and any other anti-TB drug for which reliable DST becomes available [4].

TB Control Strategy in India

The National Tuberculosis Program of India (NTP) was initiated in 1962 for TB control with a network of more than 446 District TB Centers, 330 TB clinics and more than 47,600 TB beds. Despite the NTP being in existence since 1962, no appreciable change in the epidemiological situation of TB in the country could be observed. In view of this, in 1992, Gol, with WHO and SIDA reviewed the TB situation and the performance of the NTP. The Government decided to give a new thrust to TB control activities by jeopardized the NTP, with assistance from international agencies. In 1993, the Revised National TB Control Program was piloted in a population of 2.4 million in five states. This was later expanded to cover 13 million people by 1995, and 20 million by 1996.

In 1997, the RNTCP was launched as a national program. The RNTCP formulated, adopted the internationally recommended Directly Observed Treatment Short-course (DOTS) strategy, as the most systematic and cost-effective approach to jeopardize the TB control program in India.

The objectives of the RNTCP were to achieve at least 85% rate among the new smear-positive cases initiated on treatment, and thereafter a case detection rate of at least 70% of such cases. The RNTCP was built on the infrastructure and systems built through the NTP. Major additions to the RNTCP, over and above the structures established under the NTP, was the establishment of a sub-district supervisory unit, known as a TB Unit, with dedicated RNTCP supervisors posted, and decentralization of both diagnostic and treatment services, with treatment given under the support of DOT providers. The entire country was covered by the end of 2005. DOTS strategy has proved to be an effective tool in controlling TB on a mass scale and practiced in over 200 countries. The target under MDG for tuberculosis is to halt and begin reversal of incidence of tuberculosis, malaria and other major diseases by 2015. The indicators were to reduce the prevalence and death rates by 50% between 1990 and 2015.

In India National AIDS Control Program (NACP) and RNTCP have developed "National framework of joint TB/HIV Collaborative activities" in 2007. Programmatic management of Drug Resistant (DR) TB services began in 2007 and national coverage has been achieved in March 2013 [5-7].

Potential Causes of Drug Resistance

Various factors have been implicated in the causation of MDR-TB

Genetic factors: Though there is some evidence to postulate host

genetic predisposition as the basis for the development of MDR-TB, it has not been conclusive. In a recent study from India, patients with HLA-DRB and DRB were found to have two-fold increased risk of developing MDR-TB. Park et al. found that susceptibility to MDR-TB in Korean patients was strongly associated with HLA DRB1-DQB1 haplotypes. The exact role of these factors is not known. It is likely that these loci or the alleles linked with them play a permissive role in conferring increasing susceptibility to the development of MDR-TB.

Factors related to previous ant tuberculosis treatment:

Incomplete and inadequate treatment: TB patients in India get treated with DOTS regimens not only through the Revised National Tuberculosis Control Program (RNTCP), but also receive treatment from private medical practitioners. Irregular, incomplete, inadequate treatment is one of the means of acquiring drug resistant organisms.

Lack of laboratory diagnostic facilities: good laboratory support is not available in developing nations. These are the areas where MDR-TB is a major health hazard. For patients jeopardized as treatment failure the WHO re-treatment regimen consists of three drugs (isoniazid, rifampicin, and ethambutol) for a period of eight months, supplemented by pyrazinamide during the first three months and streptomycin during the first two months. If mycobacterial culture and *in vitro* sensitivity testing are not routinely performed, it is not possible to establish whether these patients are excreting multidrug-resistant bacilli. If this WHO re-treatment regimen is administered to treatment failure patients who actually have MDR-TB.

The effectiveness of a DOTS program with first-line therapy fell short of the 85% target set by WHO. First-line therapy may not be sufficient in settings with a high degree of resistance to antibiotics.

Multidrug-Resistant TB (MDR-TB) Global scenario: Anti-TB medicines have been used for decades and strains that are resistant to 1 or more of the medicines have been documented in every country surveyed. Drug resistance emerges when anti-TB medicines are used inappropriately, through incorrect prescription by health care providers, poor quality drugs and patients stopping treatment prematurely [8]. Multidrug-Resistant Tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to isoniazid and rifampicin, the 2 most powerful, first-line anti-TB drugs. MDR-TB is treatable and curable by using second-line drugs. However, second-line treatment options are limited and require extensive chemotherapy (up to 2 years of treatment) with medicines that are expensive and toxic. In some cases, more severe drug resistance can develop. Extensively Drug-Resistant TB (XDR-TB) is a more serious form of MDR-TB caused by bacteria that do not respond to the most effective second-line anti-TB drugs, often leaving patients without any further treatment options [9,10].

Aim

Multidrug-Resistant Tuberculosis: A review Study in District Hamirpur, Himachal Pradesh.

Objectives

The present study was taken up with the following objectives:

- To study the emergence of MDR-TB amongst the tuberculosis patients
- To find out the factors contributing MDR-TB
- To correlate MDR-TB with demographic variables of the sample.

Methodology

Study area

Hamirpur is one of the twelve districts of the state of Himachal Pradesh, India. The headquarters of the district is in the Hamirpur town. The district occupies an area of 1,118 square jeopardize or 432 square miles. It is the smallest district of Himachal Pradesh. It is the most educated district of Himachal and has the highest density of roads amongst all districts in India. The district comprises four subdivisions: Hamirpur, Barsar, Nadaun and Bhoranj. Hamirpur district divided in to 10 tehsils. 1. Hamirpur Sadar 2. Nadaun 3. Sujanpur 4. Badsar 5. Touni Devi 6. Bhoranj 7. Dhatwal (Bijhari) 8. Galore 9. Kangoo 10. Bhota. According to the 2011 census, Hamirpur district has a population of 454,768, The district has a population density of 407 inhabitants per square jeopardize (1,050/sq mi) Hamirpur has a sex ratio of 1095 females for every 1000 males, and a literacy rate of 100%.

National TB Control Program was started in 1962 and later on converted to Revised National TB Control Program. In HP RNTCP started from district Hamirpur as pilot project in 1995, whole of the state was covered by 2002. Programmatic Management of Drug Resistant Tuberculosis (PMDT) program for treatment of Multi Drug Resistant (MDR) TB started in 2011 in HP. While the Central government is targeting to eliminate Tuberculosis (TB) by 2025, Himachal Pradesh Government has set the target for 2023 so that it becomes the first TB-free state in the country. In Himachal, around 15,000 new cases of TB are registered every year, whereas around 9,000 TB patients seek treatment from the private sector. Revised National Tuberculosis Control Program has been implemented in Himachal Pradesh in phased manner. Hamirpur was the first district

to take up the activity in 1995, followed by Kangra at Dharamshala and Mandi in 1998.

Study period

The period of the study was from January 2018 to April 2018.

Research design

Descriptive approach of research was adopted to accomplish the objectives of the study. The purpose of descriptive research design is to assess, observe and describe various aspects of the study.

List of variables used

Demographic variables: The demographic variables in this study are Age, gender, educational qualification, socioeconomic status, type of family, area of living (rural/urban), marital status, socio economic background, type of housing, ventilation and other hygiene factors and income.

Study variables: the study variables in the present study are Addiction, contact/exposure with other TB patients, after how much time hospital visited, regularity of treatment, other kinds of medicines used, any other disease along with TB, kind of TB, Resistance pattern, HIV positivity, side effects of treatment, symptoms persisted even after treatment, treatment, precautions taken and health care provider services [11].

Tools used

Mathematical and statistical tools:

Patients' characteristics at treatment initiation will be summarized using averages, percentages, frequencies applied to structured questionnaire/schedules.

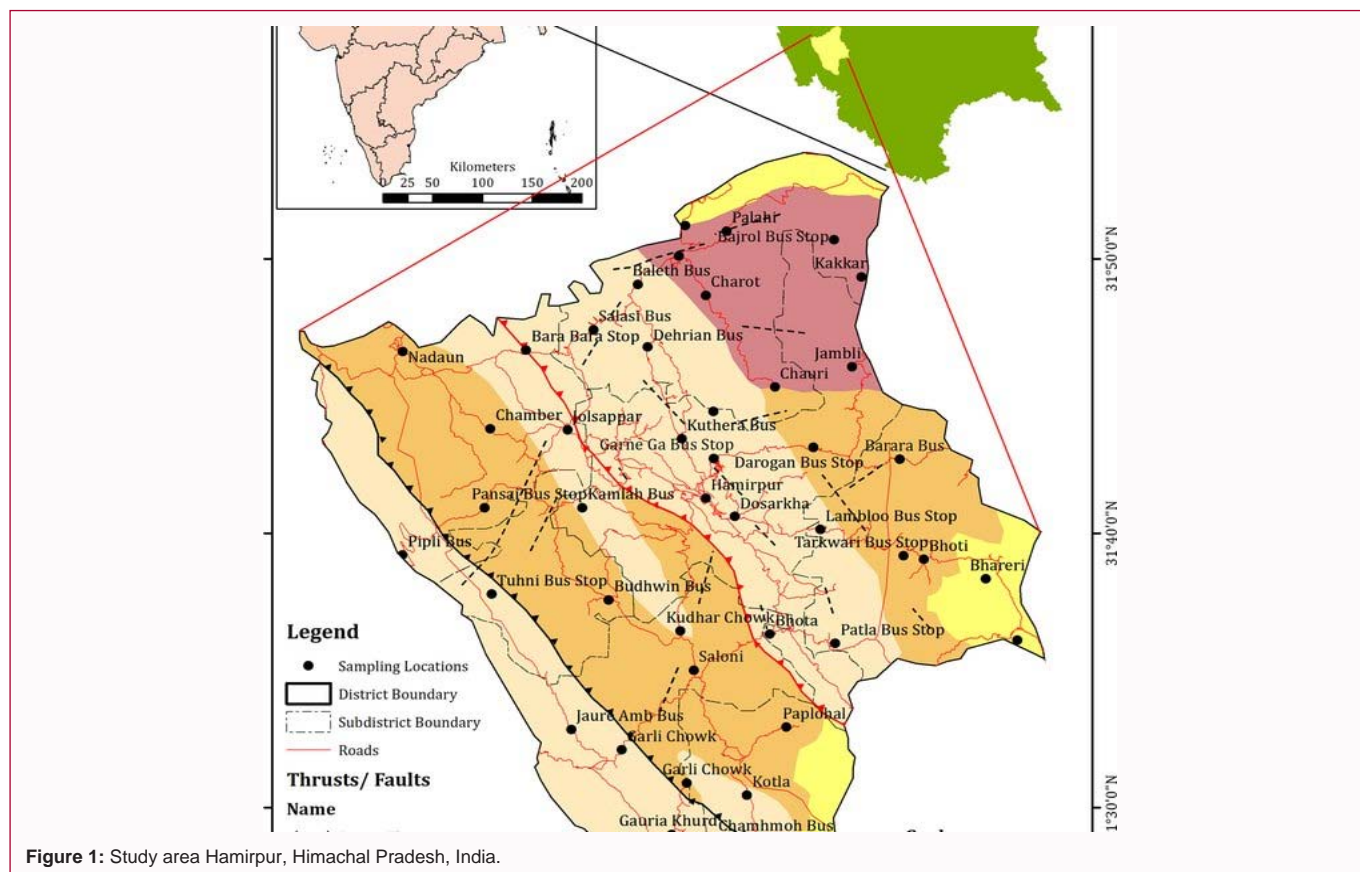


Figure 1: Study area Hamirpur, Himachal Pradesh, India.

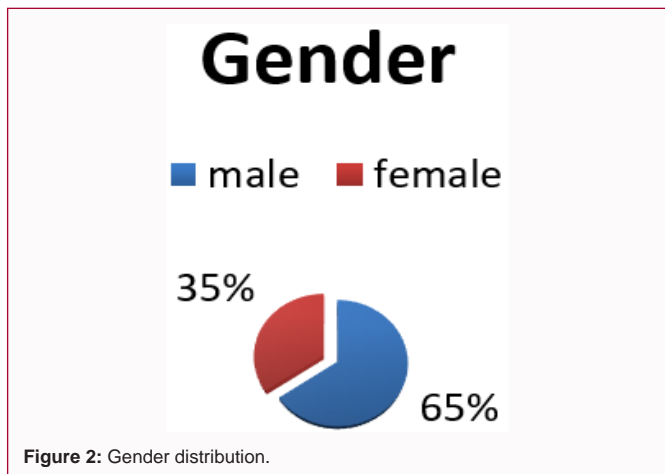


Figure 2: Gender distribution.

Population

The population used for the present study was tuberculosis cases diagnosed from 2011 to 2018 in RH, District Hamirpur, Himachal Pradesh; which was 2277 (Table 1).

Sample size

There were a total of 93 MDR cases out of 2277 TB patients in District Hamirpur, Himachal Pradesh from the year 2011 to 2018; out of which 13 died; therefore only 80 MDR TB cases consisted of sample size (Table 2).

Research methodology provides an empirical and logical basis for data collection, data analysis and thereafter to make logical conclusion and suggestions for the accomplishment of the objectives of the present study. Primary as well as secondary data was collected for the purpose of the study. Personal interviews were taken from the Dist. Project Officer and other health officials and documents, brochures, etc. were collected from the ZH Hamirpur.

Secondary Data

The secondary data has been collected from various sources like journals, brochures, magazines, books, annual reports, office records, published and unpublished documents, state library, Panjab University library and the libraries of the neighboring universities, web-sites of WHO, RNTCP, Government of Himachal Pradesh and other websites.

Primary Data

The primary data has been collected through pilot survey, personal interviews, questionnaires/schedules filled up by 93 mDR TB patients and personal observations.

Design of the Questionnaire/Schedule

A questionnaire is a formalized set of questions for extracting information from the target respondents. A structured questionnaire was developed by dividing the questionnaire into two sections:

Section A: To collect the demographic information of the respondents.

Section B: To extract information about the factors contributing to MDR-TB from the MDR-TB patients.

The questionnaire was prepared through a long process in the following steps:

Construction of the Preliminary Form

The list of important variables of factors contributing to MDR-TB were sorted out on the basis of the research gaps identified in the review of previous literature, studies and interviews with the patients and TB Project Officers, doctors and experts. These variables were then constructed in the form of statements. Thus, a questionnaire was prepared [12,13].

Pilot study: this questionnaire was presented to the 10 MDR-TB patients in Hamirpur who were requested to add comments and other statements if necessary. Thus, the questionnaire/schedule was pre-tested and was refined for use in the final study. The table below gives the details of the employees selected for the purpose of pilot survey:

Direct Personal Interviews: The first-hand information has also been collected through personal interviews of the patients.

Observation method

In order to have an insight into certain practices like attitude of the employees, working conditions and hidden information the observation method has also been applied.

Informal discussions

In order to know the ground realities in a better way, personal visits to various projects were made and interviews and informal discussions were carried out.

Personal observations

Personal observations were used to study and to observe closely hidden, unrevealed and unexplored aspects related to the objectives of the study [14].

Results

Analysis and Interpretation of Data

The collected data is analyzed and interpreted with the help of following methods:

- A. Mathematical Methods
- B. Statistical Methods
- C. Diagrammatic and Graphic Methods.

Multidrug-Resistant Tuberculosis (MDR-TB)

MDR-TB is defined as resistance to isoniazid and rifampicin, with or without resistance to other First-Line Drugs (FLD). XDR-TB

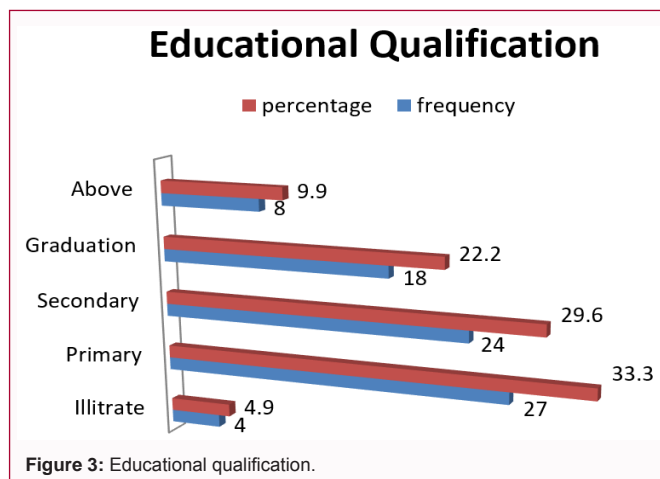


Figure 3: Educational qualification.

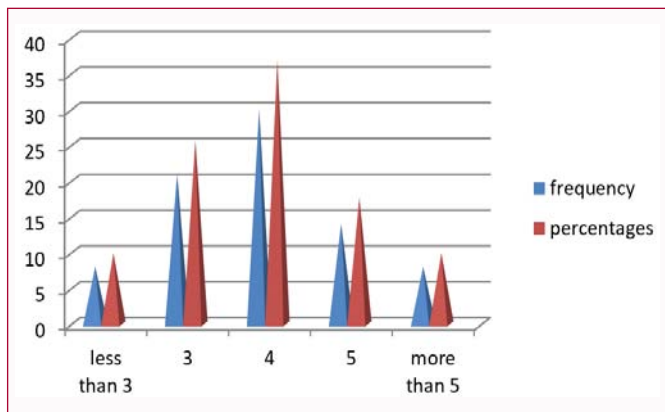


Figure 4: Number of family members who do not have the disease.

is defined as resistance to at least isoniazid and rifampicin, and to any fluoroquinolone, and to any of the three second-line Injectable (Amikacin, Capreomycin and Kanamycin).

Multidrug-Resistant Tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to isoniazid and rifampicin, the 2 most powerful, first-line anti-TB drugs. MDR-TB is treatable and curable by using second-line drugs. However, second-line treatment options are limited and require extensive chemotherapy (up to 2 years of treatment) with medicines that are expensive and toxic. In some cases, more severe drug resistance can develop. Extensively Drug-Resistant TB (XDR-TB) is a more serious form of MDR-TB caused by bacteria that do not respond to the most effective second-line anti-TB drugs, often leaving patients without any further treatment options. In 2016, MDR-TB remains a public health crisis and a health security threat. WHO estimates that there were 600,000 new cases with resistance to rifampicin-the most effective first-line drug-of which 490,000 had MDR-TB. The MDR-TB burden largely falls on 3 countries-India, China and the Russian Federation-which together account for nearly half of the global cases. About 6.2% of MDR-TB cases had XDR-TB in 2016.

Among the socio demographic factors, only age of respondents and number of rooms in the household were significantly associated with the occurrence of MDR-TB. Study participants whose age was ≤ 30 years were seven times more likely to have MDR-TB compared to those whose age was >30 years.

Total MDR TB cases in Hamirpur district till 2018 were 94. Out of which 25 are still on treatment. In the year 2011, all of 04 patients were cured; whereas in the year 2012, out of 03 MDR TB patients 01 was cured and 01 was died. In the year 2013, out of 16 MDR-TB patients 14 were cured; in 2014 out of 15 MDR-TB patients 9 were

Table 2: Sample size.

Year	Total MDR Patient Put on Treatment	Died	Total Sample Size
2011	04		04
2012	03	01	02
2013	16		16
2014	15	04	11
2015	21	01	20
2016	22	06	16
2017	10	01	09
2018	03		03
Total	94	13	81

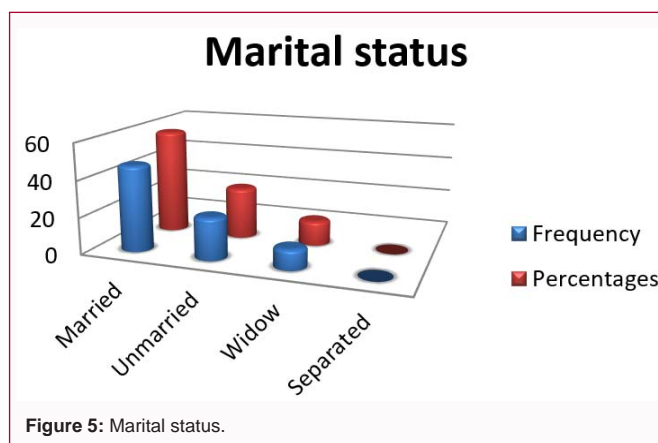


Figure 5: Marital status.

cured, 4 died and 2 patients were switched to XDR (CAT V); in 2015 out of 21, 14 were cured, 1 died and 5 were switched to XDR (CAT V); in 2016, out of a total of 22 patients 15 are still on treatment, 6 died and 1 switched over to XDR; in 2017, out of a total number of 10 patients 8 are still on treatment, 1 died and 1 switched to XDR (CAT V) and in the year 2018, out of till date reported 2 patients 2 are on treatment only. There are 6 cases of defaulters also during the whole period of 8 years.

Most of the patients were in the group of 46 to 55 of age. Comparison between Gender and Marital Status, it can be seen that losing partner for a female might be a factor for the low nutrition and lack of care which decreases immunity. Chronic addiction of any kinds leads to TB, damaging the lungs n heart. If the addiction is not quit then drug resistance can be easily found. The patients do not consume tobacco and same percentage of patients does not consumed alcohol. Only 38.3% patients consume tobacco as well

Table 1: Total cases registered under RNTCP.

Year	New Smear +VE	New Smear -VE	Extra pulmonary (EP)	Relapse I	Failure (F)	Treatment After Default (TAD)	Others	Total
2011	313	70	232	114	9	8	25	771
2012	315	81	190	117	14	10	25	752
2013	324	101	180	115	7	6	28	761
2014	312	84	169	113	9	8	23	718
2015	324	97	205	117	5	7	25	780
2016	363	104	131	109	16	3	40	766
2017	326	68	196	120	13	4	24	751
Total	2277	605	1303	805	73	46	190	5299

Sample: All the MDR/XDR TB cases of the above said cohort

Table 3: Total MDR TB cases (Registered) in Hamirpur District: (2011-2018).

Year	Total MDR patients put on treatment	Still on treatment	Cured	Died	Default	Switched to XDR (CAT V)
2011	04		04			
2012	03		01	01	01	
2013	16		14		02	
2014	15		09	04		02
2015	21		14	01	01	04+01
2016	22	15		06	01	
2017	10	08		01	01	
2018	03	02				
Total	94	25	42	13	06	07

*Source: Data collected from RH Hamirpur (HP)

Table 4: Total cases registered under RNTCP in Hamirpur District.

Year	New Smear +VE	New Smear -VE	Extra pulmonary (EP)	Relapse (R)	Failure (F)	Treatment After Default (TAD)	Others	Total
1996	223	311	82	60	0	0	16	692
1997	224	329	78	58	0	0	33	722
1998	305	284	107	70	12	8	12	798
1999	345	223	164	122	110	17	18	899
2000	352	238	158	129	9	11	20	917
2001	387	232	150	103	5	9	24	910
2002	319	218	140	130	6	12	17	842
2003	336	208	150	97	11	9	28	839
2004	290	168	144	108	15	11	36	772
2005	276	146	159	88	9	10	26	714
2006	298	120	169	95	11	4	32	729
2007	283	209	158	86	5	13	31	785
2008	300	193	193	86	13	8	47	840
2009	319	130	200	97	13	4	30	793
2010	377	130	215	128	11	16	29	906
2011	313	70	232	114	9	8	25	771
2012	315	81	190	117	14	10	25	752
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2017	326	68	196	120	13	4	24	751

*EP: Extrapulmonary; R: Relapse; F: Failure; TAD: Treatment after Default

*Source: Data collected from RH Hamirpur (HP)

as alcohol. Out of these 33.3% patients have quit tobacco during the treatment while 38.3% patients have quit alcohol during the treatment. Before the treatment 30.9% of total patients smoked more than 10 a day and 7.4% smoked more than 15 times a day. Only 8.6% respondents smoked less than 5 times a day. Out of these tobacco users 34.6% smoked and only 3.7% chewed the tobacco. Among the alcohol takers maximum patients (28.4%) were taking alcohol less than 3 times a week. Only 4.9% respondents were taking it on daily basis. After the disease was detected and treatment started only 2.5% patients continued the same quantity whereas 38.3% patients quit alcohol. The respondents did not agree to take any other kind of substance. All the respondents agreed that symptoms subsided during the secondary treatment. All the respondents agreed that they are getting their sputum checked up regularly and that their sputum

is found negative after the second treatment. The sputum is checked after the one month, then 2 months, then after 3 months and then at the end of the treatment. MDR TB causes morbidity if not treated in time. Therefore, it is very important to manage the disease and known risk factors while managing it, like exposure with other patients, HIV Infections, timely treatment, feedback from the patient and smoking and alcohol abuse etc. to ensure improvement in public health.

Various components of MDR-TB have been derived from the previous literature review and then examined in District Hamirpur through primary and secondary study. The present research summarizes, concludes and makes some useful recommendations on the basis of the results, review of previous literature and findings. This research is divided into three parts. The first part includes summary and conclusions based on the findings of the present study

Table 5: Age group.

S. No.	Age group	Frequency Total= 81	Percentage
I.	Less than 16	0	0
II.	16-25	14	17.3
III.	26-35	17	21
IV.	36-45	16	19.8
V.	46-55	25	30.9
VI.	Above 55	9	11.1

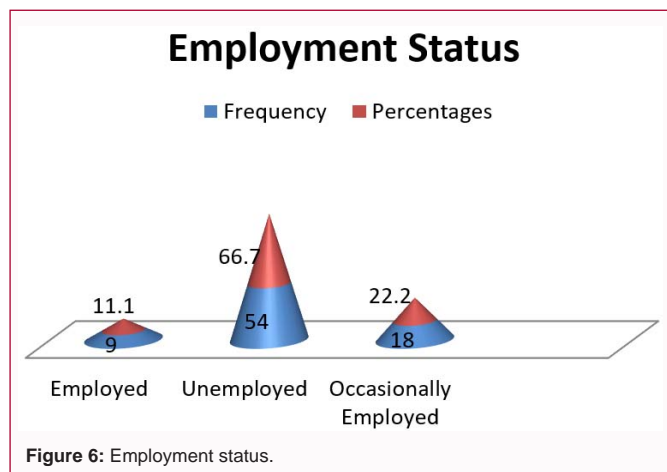


Figure 6: Employment status.

and review of previous researches. The second part presents some recommendations and suggestions to the management of MDR TB for future strategies and policy making. The third part identifies the areas for further research.

MDR-TB causes morbidity if not treated in time. Therefore, it is very important to manage the disease and known risk factors while managing it, like exposure with other patients, HIV infections, timely treatment, feedback from the patient and smoking and alcohol abuse etc. to ensure improvement in public health.

To identify whether Demographic Factors relate with the failure of primary treatment, various socio demographic variables were taken up for the study. It can be seen from the study that though, the disease was found among all the age groups, yet during the middle age it is more apparent. The disease was found from 16 to above 60 years of age. There was no correlation between the gender and the MDR-TB. More of the males were trapped by the disease. One half of the females as compared to males were the victims of MDR-TB. Most of the Patients with MDR-TB have not completed less than secondary education. Here, education seems to be playing a role. More of the married patients are resistant to TB than unmarried ones. A small percentage of widowed respondents are also suffering from the disease. Marital status does not seem to correlate with the resistant pattern of the disease. Very large people have lost their jobs after the disease. They may be suffering from the side effects, as almost all the patients were complaining drowsiness, loss of weight and fatigue. It is also a communicable disease therefore; people do not hire a person with TB and that too if they come to know that the person is resistant to the disease. Socioeconomic background seems to be having a connection between the adherences of the disease as all the patients are from rural areas. Similarly, ventilation and other hygiene factors plays a role in it like, separate toilet facilities, dampness in the house, no sunlight, no cross ventilation and proper nutrition. Half of the patients used

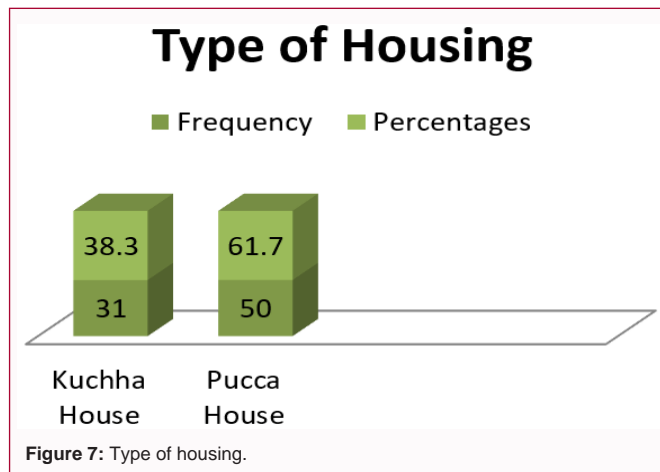


Figure 7: Type of housing.

to smoke or drink alcohol, so as such not much correlation is found in the study; still more work should be done in this regard. Exposure with other TB patients seems to be correlated with the presence of disease. Therefore, contact with the children in the family should be strictly banned and the utensils, clothes, towels, handkerchiefs of the patient should not be used by the children. Coughing should be done by covering the mouth with the handkerchief or a clean cloth which should not be touched by anybody else in the house and the clothes should be kept very clean and should be washed daily. The room should be kept very clean and airy. Windows should be opened and free flow of air should not be restricted in the house. Patient's room must be cleaned daily. Patient's food should be very nutritional with high quantity of proteins in the diet. Fruits and vegetables should be necessarily eaten. Eggs, paneer, milk should be taken. A plain spit box should be kept handy in the room or vicinity of the patient. The patient should spit in it only. Some sand or ash should be put in the spit box to restrict infection. The box should be cleaned properly daily after every use. The patient should abide by everything the health provider asks to do. Periodic check should be done and the sputum checkup should also be done regularly. The medicines should be taken regularly without fail (Table 3, 4).

The study has provided pertinent information about factors associated with MDR-TB which can support activities being implemented to decrease the burden of TB in Ethiopia for planners and decision makers. Patients' age, history of previous treatment, and living in a house with only one room, were strong predictors for MDR-TB; while HIV infection had an association but of weaker statistical significance.

Among the sociodemographic factors, only age of respondents and number of rooms in the household were significantly associated with the occurrence of MDR-TB. Study participants whose age was ≤ 30 years were seven times more likely to have MDR-TB compared to those whose age was >30 years.

Total MDR-TB cases in Hamirpur district till 2018 were 94. Out of which 25 are still on treatment. In the year 2011, all of 04 patients were cured; whereas in the year 2012, out of 03 MDR-TB patients 01 was cured and 01 was died. In the year 2013, out of 16 MDR-TB patients 14 were cured; in 2014 out of 15 MDR-TB patients 9 were cured, 4 died and 2 patients were switched to XDR (CAT V); in 2015 out of 21, 14 were cured, 1 died and 5 were switched to XDR (CAT V); in 2016, out of a total of 22 patients 15 are still on treatment, 6 died and 1 switched over to XDR; in 2017, out of a total number of 10

Table 6: Addiction factors.

Sr. No.	Factors	Addiction Factors										
		Tobacco					Alcohol				Any Other	
1	Tobacco consumption	Yes 31 (38.3%)		No 50 (61.7%)			Yes 31 (38.3%)		No 50 (61.7%)		Yes 0 (0)	No 81 (100%)
2	How many times (Tobacco-per day) (Alcohol-Per week)	0-5 7 (8.6)	6-9 0 (0)	10-15 19 (23.5)	>15 6 (7.4)	NA 49 (60.5)	0-3 23 (28.4)	4-6 4 (4.9)	6-7 4 (4.9)	NA 50 (61.7)	NA	
3	Intake during treatment	Same 1 (1.2)	Less 4 (4.9)	Quit 27 (33.3)	NA 49 (60.5)		Same 2 (2.5)	Less 0 (0)	Quit 31 (38.3)	NA 48 (59.3)	NA	
4	Kind of tobacco intake	Smoking 28 (34.6)		Chewing 3 (3.7)		NA 50 (61.7)						

patients 8 are still on treatment, 1 died and 1 switched to XDR (CAT V) and in the year 2018, out of till date reported 2 patients 2 are on treatment only. There are 6 cases of defaulters also during the whole period of 8 years.

Sociodemographic profile of MDR-TB patients in DISTT. HAMIRPUR (H.P.)

Age: The study depicted that there was no patient under the age of 16. From age 16 to 25 there were 14 (17.3%) MDR TB patients while from age 26 to 35 there were 17 (21%) patients, from 36 to 45 of age there were 16 (19.8%) patients, from 46 to 55 of age there were 25 (30.9%) patients and above 56 of age there 9 (11.1%) patients. Most of the patients were in the group of 46 to 55 of age (Figure 1 and Table 5).

Gender: Among the total population of 81 patients 53 (65.4%) males had MDR-TB and 28 (34.6%) females had MDR TB. Males were more opt to the disease (Figure 2).

Analyzing the educational qualifications, it was found that the least number of patients 4 (4.9%) were illiterate, 27 (33.3%) of the respondents were holding Primary education; which was the maximum number, 24 (29.6%) were secondary passed, 18 (22.2%) were graduate and only 8 (9.9%) were holding a degree above graduation (Figure 3).

Number of family members does not seem to have any connection with the disease; as the patients who were unmarried or having less than 3 members in the family were the least that is 8 (9.9%). Families having 3 members have 21 (25.7%) patients and 30 (37%) patients hail from families with 4 members; 14 (17.7%) patients are from families with 5 members and 8 (9.9%) respondents are from families with more than 5 members. These days maximum families have 4 members normally (Figure 4).

Marital status: Maximum patients 47 (58%) are married, 23 (28.4%) of the patients are unmarried while 11 (13.6%) have lost their spouse. In Table 3, 4, a cross tabulation analysis between Gender and Marital Status, it can be seen that losing partner for a female might be a factor for the low nutrition and lack of care which decreases immunity. This can be seen among the females; 39.2% females were suffering from the disease while no male who lost his partner is suffering it. Whereas more of the married males are suffering from the disease that is 69.8% while only 35.7% females are suffering from the disease. Among the unmarried, percentage is almost the same, though little higher in males (Figure 5).

Employment status after treatment: The employment status after the detection and treatment is 54 (66.7%) are unemployed and depend on the family members only. Only 9 (11.1%) are employed

even after detection and treatment. 18 (22.2%) are occasionally employed (Figure 6).

It is very interesting to know that the socioeconomic background all of the respondents 81 (100%) was rural.

Living area factors: 49 (60.5%) houses have toilet attached to the patient’s room. Only 1 patient agreed to the open defecation and the rest of the 80 (98.8%) patients have a toilet in their house. 74 (91.4%) patients have their own separate room in the house, only 7 (8.6%) do not have a separate room for their own. 41 (50.6%) of the patients agreed that they have cross ventilation in the house, but only 41 (50.6%) have 2 windows in their room. 38 (46.9%) patients have only one window in their room which does not guarantee proper cross ventilation facilities. Even 2 (2.5%) of the patients have no windows in their room. 5 (6.2%) patients agreed to have dampness in their house while 76 (93.8%) of the respondents did not have dampness their house, according to them. 66 (81.5%) of the patients agreed to have sunlight in the house while 15 (18.5%) agreed not to have proper sunlight in the house. However, dampness is one of the criteria that enhance the chances of TB (Figure 7).

Income per month: Income of more than 50% patients 55 (67.9%) is less than Rs. 10,000 whereas Rs 10,000-20,000 group of income contained 24 (29.6%) patients and only 2 patients have income more than Rs. 20,000 incomes under Rs. 20,000-40,000 slabs. No patient is having more than Rs. 40,000 income (Figure 8).

Factors relating to the disease, MDR TB

Chronic addiction of any kinds leads to TB, damaging the lungs n heart. If the addiction is not quit then drug resistance can be easily found. From Table 4, 5 it can be seen that 50 (61.7%) of the

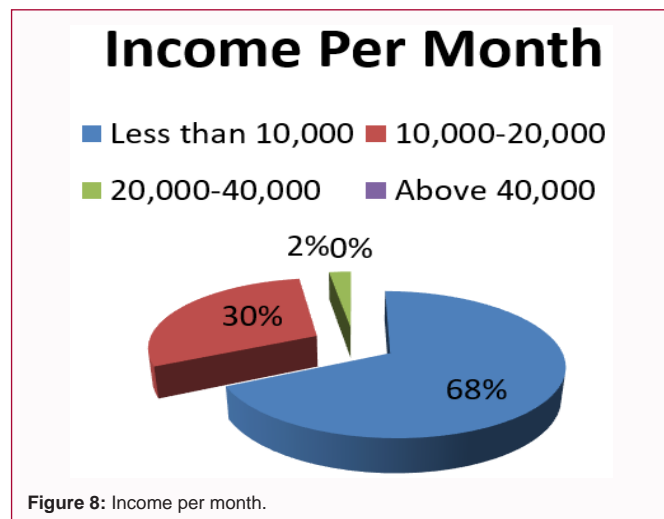


Figure 8: Income per month.

patients do not consume tobacco and same percentage of patients do not consumed alcohol that is 50 (61.7%). Only 31 (38.3%) patients consume tobacco as well as alcohol. Out of these 27 (33.3%) patients have quit tobacco during the treatment while 31 (38.3%) patients have quit alcohol during the treatment. Before the treatment 30.9% of total patients smoked more than 10 a day and 7.4% smoked more than 15 times a day. Only 8.6% respondents smoked less than 5 times a day. Out of these tobacco users 34.6% smoked and only 3.7% chewed the tobacco. Among the alcohol takers maximum patients (28.4%) were taking alcohol less than 3 times a week. Only 4.9% respondents were taking it on daily basis. After the disease was detected and treatment started only 2.5% patients continued the same quantity whereas 38.3% patients quit alcohol. The respondents did not agree to take any other kind of substance (Table 6).

Contact with other patients: Only 9.9% of the respondents were exposed to other TB patients. Out of these, 4.9% caught the disease by being exposed to the spouse and 4.9% were infected by other family members. 90.1% were not exposed to any TB patient before. Outcome of the TB patient they were exposed to was that 6.2% were survived and are now healthy while 1.2 % could not survive and are dead.

The disease: 97.5% of the respondents visited hospital within 2 months of appearance of the symptoms and 2.5% respondents agreed to visit hospital after 2 months. 96.3% of the patients agreed to take medicines regularly while only 3.7% of the patients left medicines. The main cause to leave the medicines and treatment is due to negative side effects of the drugs (2.5%) and due to depressive state of mind (3.7%). Poor monetary condition is not one of the factors because the treatment is free of cost from the government hospitals. The missed dose was though, resumed within 15 days. 6.2% of the patients are using other kinds of therapy too for the general symptoms. 6.2% of the patients used Homeopathic medicines for this purpose.

Other diseases with MDR TB: 12.3% of the patients suffered with diabetes and 3.7% of the patients are suffering from other kinds of diseases.

Side Effects of the Treatment: As it was secondary treatment, very few patients felt any kind of side effects of the drugs except drowsiness, gastro upsets and skin problems. 32.1% of the patients are feeling Gastrointestinal symptoms, 9.9% of the patients are facing Psychiatric problems, 7.4% of the patients are feeling ringing in the ear, and 1.2% feeling even deafness and 1.2% are suffering from Thyroid enlargement. An enormous 81.5% are feeling Drowsiness during the treatment, 9.9% are having skin problems and 7.4% are feeling many other kinds of side effects too. Only 2.5% of the patients complained about having persistent fever even after treatment.

Secondary treatment: All the respondents agreed that symptoms subsided during the secondary treatment. All the respondents agreed that they are getting their sputum checked up regularly and that their sputum is found negative after the second treatment. The sputum is checked after the one month, then 2 months, then after 3 months and then at the end of the treatment.

Precautions taken by the patient: 93.8% of the patients agreed that they do not spit in the bathroom or wash basin where other members of the family use it. Only 6.2% of the patients agreed to use bathroom or wash basins to spit. 98.8% of the patients are using plain spit box for this purpose but no one used ash or sand in the spit box as a precaution. Everybody agreed to cover their mouth while coughing. All of the patients are using separate utensils for food and water. Only

17.3% of the patients agreed that they are keeping their children away from them as a precaution, however 82.7% of the patients are not taking any precautions while dealing with their children. 3.7% of the patients agreed that neighbor/family member was also diagnosed TB during their treatment.

Kind of TB: 98.8% of the patients are having pulmonary TB while all the 100% of the patients are having H & R resistant TB.

Discussion

Among the sociodemographic factors, only age of respondents and number of rooms in the household were significantly associated with the occurrence of MDR-TB. Study participants whose age was ≤ 30 years were seven times more likely to have MDR-TB compared to those whose age was >30 years.

Total MDR TB cases in Hamirpur district till 2018 were 94. Out of which 25 are still on treatment. In the year 2011, all of 04 patients were cured; whereas in the year 2012, out of 03 MDR-TB patients 01 was cured and 01 was died. In the year 2013, out of 16 MDR-TB patients 14 were cured; in 2014 out of 15 MDR-TB patients 9 were cured, 4 died and 2 patients were switched to XDR (CAT V); in 2015 out of 21, 14 were cured, 1 died and 5 were switched to XDR (CAT V); in 2016, out of a total of 22 patients 15 are still on treatment, 6 died and 1 switched over to XDR; in 2017, out of a total number of 10 patients 8 are still on treatment, 1 died and 1 switched to XDR (CAT V) and in the year 2018, out of till date reported 2 patients 2 are on treatment only. There are 6 cases of defaulters also during the whole period of 8 years.

Most of the patients were in the group of 46 to 55 of age. Comparison between Gender and Marital Status, it can be seen that losing partner for a female might be a factor for the low nutrition and lack of care which decreases immunity. Chronic addiction of any kinds leads to TB, damaging the lungs & heart. If the addiction is not quit then drug resistance can be easily found. The patients do not consume tobacco and same percentage of patients does not consumed alcohol. Only 38.3% patients consume tobacco as well as alcohol. Out of these 33.3% patients have quit tobacco during the treatment while 38.3% patients have quit alcohol during the treatment. Before the treatment 30.9% of total patients smoked more than 10 a day and 7.4% smoked more than 15 times a day. Only 8.6% respondents smoked less than 5 times a day. Out of these tobacco users 34.6% smoked and only 3.7% chewed the tobacco. Among the alcohol takers maximum patients (28.4%) were taking alcohol less than 3 times a week. Only 4.9% respondents were taking it on daily basis. After the disease was detected and treatment started only 2.5% patients continued the same quantity whereas 38.3% patients quit alcohol. The respondents did not agree to take any other kind of substance. All the respondents agreed that symptoms subsided during the secondary treatment. All the respondents agreed that they are getting their sputum checked up regularly and that their sputum is found negative after the second treatment. The sputum is checked after the one month, then 2 months, then after 3 months and then at the end of the treatment. MDR-TB causes morbidity if not treated in time. Therefore, it is very important to manage the disease and known risk factors while managing it, like exposure with other patients, HIV Infections, timely treatment, feedback from the patient and smoking and alcohol abuse etc. to ensure improvement in public health.

Conclusion

MDR-TB causes morbidity if not treated in time. Therefore, it is

very important to manage the disease and known risk factors while managing it, like exposure with other patients, HIV Infections, timely treatment, feedback from the patient and smoking and alcohol abuse etc. to ensure improvement in public health.

To identify whether Demographic Factors relate with the failure of primary treatment, various sociodemographic variables were taken up for the study. It can be seen from the study that though, the disease was found among all the age groups, yet during the middle age it is more apparent. The disease was found from 16 to above 60 years of age. There was no correlation between the gender and the MDR-TB. More of the males were trapped by the disease. One half of the females as compared to males were the victims of MDR-TB. Most of the Patients with MDR-TB have not completed less than secondary education. Here, education seems to be playing a role. More of the married patients are resistant to TB than unmarried ones. A small percentage of widowed respondents are also suffering from the disease. Marital status does not seem to correlate with the resistant pattern of the disease. Very large people have lost their jobs after the disease. They may be suffering from the side effects, as almost all the patients were complaining drowsiness, loss of weight and fatigue. It is also a communicable disease therefore; people do not hire a person with TB and that too if they come to know that the person is resistant to the disease. Socioeconomic background seems to be having a connection between the adherences of the disease as all the patients are from rural areas. Similarly, ventilation and other hygiene factors plays a role in it like, separate toilet facilities, dampness in the house, no sunlight, no cross ventilation and proper nutrition.

Areas for Further Research

Despite such a high percentage of MDR-TB and the level of morbidity, no study has been taken to assess its risk factors. What were the causes that the previous treatment failed the correlation between various factors and the MDR-TB and treatment failure factors? Correlation between addiction of any kind and the disease should also be researched. There are so many fields of further research in this regard.

Limitations of the Study

There were so many limitations to the study. One was the geographical location of Himachal Pradesh where it is so difficult to travel and fill the schedules. Another limitation was to translate the questionnaire into the local dialect so that the respondents could understand it properly. Thirdly, the respondents do not want to reveal much about the disease they are fighting as it is a social stigma in Himachal Pradesh. Last but not the least, time and cost constraints were also there

To know the extent to which a study is reliable, it is important to state the limitations under which it was conducted. The main limitations of the present study were:

- The study is accomplished with the help of primary data which is collected.
- The study is also based on the secondary data and hence, with its obvious limitations.
- Majority of the respondents were initially hesitant and unwilling to disclose some information about their disease.

Recommendations

The pattern of primary treatment, identification of drug resistance

and the lapses should be guarded carefully, only this can be used to the development of secondary treatment of MDR-TB. The patients should be taught cleanliness in the house as well as their own room and body. Proper and healthy nutrition is also very important during primary treatment. Any kind of addiction should also be identified and counselled.

The pattern of primary treatment, identification of drug resistance and the lapses should be guarded carefully, only this can be used to the development of secondary treatment of MDR-TB. The patients should be taught cleanliness in the house as well as their own room and body. Proper and healthy nutrition is also very important during primary treatment. Any kind of addiction should also be identified and counselled.

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References

1. Mohan A, Sharma SK. Epidemiology. In: Sharma SK, Mohan A, editors. Tuberculosis. New Delhi: Jaypee Brothers Medical Publishers; 2001. p. 14-29.
2. Rao S. An uncontrolled trial of pefloxacin in the retreatment of patients with pulmonary tuberculosis. *Tuberc Lung Dis.* 1995;76(3):219-22.
3. Singla R, Gupta S, Gupta R, Arora VK. Efficacy and safety of sparflaxacin in combination with kanamycin and ethionamide in multidrug-resistant pulmonary tuberculosis patients: Preliminary results. *Int J Tuberc Lung Dis.* 2001;5(6):559-63.
4. Subhash HS, Ashwin I, Jesudason MV, Abharam OC, John G, Cherian AM, et al. Clinical characteristics and treatment response among patients with multidrug-resistant tuberculosis: A retrospective study. *Indian J Chest Dis Allied Sci.* 2003;45(2):97-103.
5. Flament-Saillour M, Robert J, Jarlier V, Grosset J. Outcome of multi-drug-resistant tuberculosis in France: A nationwide case-control study. *Am J Respir Crit Care Med.* 1999;160(2):587-93.
6. Tahaoglu K, Torun T, Sevim T, Atac G, Kir A, Karasulu L, et al. The treatment of multidrug-resistant tuberculosis in Turkey. *N Engl J Med.* 2001;345(3):170-4.
7. Blumberg HM, Burman WJ, Chaisson RE, Daley CL, Etkind SC, Friedman LN, et al. American Thoracic Society/Centers for Disease Control and Prevention/ Infectious Diseases Society of America: Treatment of tuberculosis. *Am J Respir Crit Care Med.* 2003;167(4):603-62.
8. Schluger NW. The impact of drug resistance on global tuberculosis epidemic. *Int J Tuberc Lung Dis.* 2000;4(2 Suppl 1):S71-5.
9. Borisov SE, Dheda K, Enwerem M, Leyet RR, D'Ambrosio L, Centis R, et al. Effectiveness and safety of bedaquiline-containing regimens in the treatment of MDR- and XDR-TB: A multicentre study. *Eur Respir J.* 2017;49(5):1700387.
10. Zignol M, Hosseini MS, Wright A, Weezenbeek CLV, Nunn P, Watt CJ. Global incidence of multidrug-resistant tuberculosis. *J Infect Dis.* 2006;194(4):479-85.
11. Gandhi NR, Moll A, Sturm AW, Pawinski R, Govender T, Lalloo U, et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet.* 2006;368(9547):1575-80.
12. Liang L, Wu Q, Gao L, Hao Y, Liu C, Xie Y, et al. Factors contributing to the high prevalence of multidrug-resistant tuberculosis: A study from China. *Thorax.* 2012;67(7):632-8.
13. Casal M, Vaquero M, Rinder H, Tortoli E, Grosset J, Rüscher-Gerdes S, et al.

A Case-control study for multidrug-resistant Tuberculosis: Risk factors in four European Countries. *Microb Drug Resist.* 2005;11(1):62-7.

14. Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City--turning the tide. *N Engl J Med.* 1995;333(4):229-33.