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Original Article

Pharmacology Section

Clinical Epidemiology of Multidrug Resistant Tuberculosis in a Nodal Drug Resistant-TB Centre in Southern Odisha: A Cross-sectional Study

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ABSTRACT

Introduction: Multidrug-Resistant Tuberculosis (MDR-TB) is a significant public health problem. The number of MDR-TB cases is very high in India and the management is inadequate due to resource constraints. The assessment of MDR-TB burden has to be reliable for programmatic management of MDR-TB under the Revised National Tuberculosis Control Program (RNTCP) of India.

Aim: To find the clinico-demographic profile and pattern of MDR-TB among the tuberculosis patients reporting to a nodal tuberculosis centre in Southern Odisha, India.

Materials and Methods: The patient record based cross-sectional study was carried out on a convenience sample of 125 sputum positive MDR-TB cases admitted to the Directly Observed Treatment Short-course (DOTS) plus centre of the Nodal Tuberculosis Centre at Berhampur, Odisha, India, during the period from April 2017 to March 2018. A predesigned case record form was used to collect data on the socio-demographic profile, addictions, co-morbidity, Human Immunodeficiency Virus (HIV) status, Bacille Calmette-Guerin (BCG) immunisation status, pattern of drug resistance, history of anti-TB treatment, presenting symptoms at admission, adverse drug reactions observed during the treatment for MDR-TB. The data was analysed using GraphPad Prism trial version 7.0. Descriptive statistics were used to present the final data.

Results: Highest number of study participants (95, 76%) were within 18-45 years age group and 90 (72%) of the patients were males. Rural habitation (90, 72%), engagement in labour works (65, 52%), low socio-economic status (75, 60%) were the common socio-economic characteristics. Resistance to rifampicin was the commonest variety 101 (80.8%) and 80 (64%) were newly diagnosed cases of tuberculosis. The commonest presenting symptom was cough in 97 (77.6%) patients and gastrointestinal upset was the commonest adverse drug reaction encountered during therapy.

Conclusion: The MDR-TB affects the population in their most productive age. Rifampicin resistant TB was the predominant variety observed in the study population. The MDR-TB can be successfully treated with maximally effective and complete drug regimes.

Keywords: Demography, Isoniazid resistance, *Mycobacterium tuberculosis*, Rifampicin resistance

INTRODUCTION

Tuberculosis remains the world's most deadly infectious disease. It is among the ten important causes of morbidity worldwide and is the leading cause of death from a single infectious agent [1]. About 85% tuberculosis cases can be successfully treated with a six-month drug regimen. *Mycobacterium tuberculosis* develops resistance to antitubercular therapy drugs. The MDR-TB as an entity is resistant to atleast isoniazid and rifampicin which are the two most powerful anti-tuberculars [1]. Treatment options for MDR-TB are limited. The drugs are expensive, used for longer duration, not easily available, causes multiple adverse effects, thus, making the treatment a challenge. Extensively Drug-Resistant-TB (XDR-TB) is a type of severe MDR-TB with additional resistance to other anti-TB drugs. This has reported in 117 countries worldwide [1]. The latest data reported to World Health Organisation (WHO) have shown that globally, the success rate for treatment of MDR-TB is 57%, making it a major public health concern in many countries. In 2019, MDR was detected in 3.3% of newly diagnosed cases and 18% of pretreated cases [1].

India has the maximum number of TB cases in the world and bears about one-fourth of the TB burden worldwide [2]. Annually, there are about 130,000 incident MDR-TB cases in India [2]. According to the 1st National Drug Resistance Survey, the rate of MDR among the new patients of TB was 2.84% and in previously treated cases it was 11.60% [3]. Detection of MDR-TB is progressively increasing with an increased access to drug sensitivity testing under the RNTCP [4]. In spite of this there are challenges in the detection, completion of treatment and cure of MDR-TB in India [5].

There is a rising trend in the MDR-TB and it varies across geographies. The RNTCP services were established in India in 2006, Programmatic Management of Drug Resistant TB (PMDT) services started in 2007. The complete geographic coverage under this program was achieved in 2013 [6]. The programmatic management in context of RNTCP in India requires the assessment of MDR-TB burden in a reliable and continuous manner. Scientific studies in India have focused on smear positive tuberculosis and have mostly excluded smear negative and extrapulmonary TB cases. Further, such surveys are discrete and have geographical limitations. Thus, a comprehensive analysis of the clinical epidemiology of MDR-TB is essential. Hence, this study was carried out to find the clinico demographic profile and pattern of MDR-TB among the tuberculosis patients reporting to a nodal tuberculosis centre in Southern Odisha.

MATERIALS AND METHODS

The patient record based cross-sectional study was carried out in the Nodal Tuberculosis Centre at Berhampur, Odisha, India. Being the only Nodal Tuberculosis Centre in Southern Odisha, the study sample is representative of the entire population of the southern part of the state. The study was carried out during the period from April 2017 to March 2018. This study was approved by the Institutional Ethics Committee of MKCG Medical College, Berhampur (Approval No. 609). Since it is a patient record based study waiver of informed consent was permitted by the Institutional Ethics Committee.

Inclusion criteria: Sputum positive patients of either gender, more than 18 years of age and with confirmed drug resistance tuberculosis, admission duration of more than seven days in the DOTS plus centre in the Nodal Tuberculosis Centre at Berhampur, Odisha, India, were included. For including study participants, convenience sampling technique was adopted. Being the only Nodal Tuberculosis Centre in Southern Odisha, the study sample is representative of the entire population of the southern part of the state.

Exclusion criteria: Patient of age less than 18 years, admitted for less than seven days, patients with poor general conditions and those with pregnancy and lactation were excluded. During the screening process out of 136 patients records 11 were excluded as per the exclusion criteria.

Sample size calculation: Assuming a prevalence of MDR-TB to be 9% from available literature [3] at a confidence level of 95% (two sided) at an absolute precision of 5% the sample size was calculated to be 125 using nMasters software developed by Department of Biostatistics, CMC Vellore, India.

Study Procedure

The MDR-TB diagnosis was based on the reports obtained from the Intermediate Testing Laboratory at SCB, Medical College, Cuttack, Odisha, India. Data was collected in a predesigned case record form. The first part of the case record form recorded information on the socio-demographic profile of the cases like age, gender, habitation, level of education, family size, socio-economic status etc., the second part of the case record form collected data on the addictions, co-morbidity, HIV status, BCG immunisation status, contact with confirmed TB case, health seeking behaviour etc. The third part of the case record form included data on the pattern of drug resistance, history of anti-TB treatment, presenting symptoms at admission, adverse drug reactions observed during the MDR-TB treatment. All the data were collected by the investigators with the assistance of paramedics posted in the in-patients department of the DOTS plus centre. In TB cases with confirmed resistance to isoniazid (H) or rifampicin (R) or both isoniazid and rifampicin or any fluroquinolines like ofloxacin, levofloxacin, moxifloxacin or second-line injectable drugs like kanamycin, amikacin or capreomycin were labelled as XDR-TB. This was confirmed from the MDR to TB test reports obtained from the RNTCP quality assured Intermediate Reference Laboratory (IRL), Cuttack, Odisha, India. Suspected MDR-TB with sputum culture positive and with resistance in-vitro to atleast isoniazid and rifampicin were considered as a case of confirmed MDR-TB (the drug sensitivity test result being from an RNTCP accredited IRL) [7].

Patients were categorised according to RNTCP criteria for initiation of MDR-TB treatment i.e., Category (CAT) I failure, CAT II positive at diagnosis, CAT II failure, and any follow-up sputum positive [6].

STATISTICAL ANALYSIS

Data was analysed for the prevalence in each category. GraphPad Prism trial version 7.0 software was used to analyse the data. Descriptive statistics was used to represent results.

RESULTS

The present study was carried out on 125 confirmed cases of MDR-TB. Most subjects (95, 76%) belonged to 18-45 years of age. A total of 90 (72%) of the patients were males and belonged to the rural habitation (90, 72%). Total 65 (52%) patients were engaged in labour works and 75 (60%) were having a low socio-economic status. Overcrowding was common in the habitation of the study participants and was present in 60 (48%) of the patients. All the patients were addicted to some kind of substances, alcohol being the predominant was seen in 70 (56%) of participants. Diabetes mellitus was the commonest co-morbidity present in 67 (53.6%) of the patients. Ten (8%) were positive for HIV. Ninety (72%) of the subjects sought medical advice from a government healthcare facility as the 1st point of contact for their current illness. About 81% of the patients were immunised as evidenced from the presence of a BCG scar. Majority (115, 92%) had a contact history with a confirmed case of tuberculosis. Very few patients (10, 8%) had adopted safe sputum disposal practices [Table/Fig-1].

Demographic variables	N (%)
Age (in years)	
18-45 years	95 (76%)
>45 years	30 (24%)
Gender	
Male	90 (72%)
Female	35 (28%)
Habitation	
Urban	35 (28%)
Rural	90 (72%)
Education	
Literate	113 (90.4%)
Illiterate	12 (9.6%)
Occupation	
White collar	60 (48%)
Labour class	65 (52%)
Family size	
Less than equal to 4	92 (73.6%)
More than 4	33 (26.4%)
Socio-economic status	
High	5 (4%)
Middle	45 (36%)
Low	75 (60%)
Addictions	
Smoker	30 (24%)
Alcoholic	70 (56%)
Other	25 (20%)
Co-morbidity	
Diabetes mellitus	67 (53.6%)
Hypertension	30 (24%)
Other	28 (22.4%)
1st Point Of Contact (POC)	
Govt. healthcare facility	90 (72%)
Private healthcare facility	20 (16%)
DOTS Centre	10 (8%)
Others	5 (4%)
Presence of overcrowding	60 (48%)
Co-existing HIV infection	10 (8%)
BCG Immunisation status (BCG Scar)	101 (80.8%)
Contact with confirmed TB cases	115 (92%)
Adoption of safe sputum disposal practices	10 (8%)

[Table/Fig-1]: Demographic characteristics of the MDR-TB cases (N=125).

A total of 101 (80.8%) patients were resistant to rifampicin followed by 20 (16%), 10 (8%), 4 (3.2%) being resistant to isoniazid, both rifampicin and isoniazid and fluroquinolone or a second line injectable drug, respectively [Table/Fig-2]. About 80 (64%) were newly diagnosed cases of tuberculosis. Relapse, defaulters, failure of anti-tubercular therapy constituted 20 (16%), 15 (12%) and 10 (8%) cases respectively [Table/Fig-3]. The commonest presenting symptom was cough in 97 (77.6%) patients followed by fever, generalised weakness (110, 88%), and weight loss (90, 72%) in that order [Table/Fig-4]. Gastrointestinal upset, fatigue, headache, vertigo were the common adverse drug reactions encountered during the anti-tubercular therapy for MDR-TB constituting 49 (39.2%), 35 (28%), 30 (24%), 20 (16%) of the cases, respectively [Table/Fig-5].

Resistance pattern	N (%)
Resistance to Rifampicin	101 (80.8%)
Resistance to Isoniazid	20 (16%)
Resistance to both Rifampicin and Isoniazid	10 (8%)
Resistance to any of the fluroquinolone like ofloxacin, levofloxacin or moxifloxacin and to second-line injectable drugs like kanamycin, amikacin or capreomycin	4 (3.2%)

[Table/Fig-2]: Resistance pattern to anti-tubercular drugs in MDR-TB patients.

Anti-tubercular treatment category	N (%)
New	80 (64%)
Relapse	20 (16%)
Defaulter	15 (12%)
Failure of ATT	10 (8%)

[Table/Fig-3]: History of anti-tubercular treatment category in MDR-TB patients.

Symptoms	N (%)
Cough	97 (77.6%)
Generalised weakness	110 (88%)
Weight loss	90 (72%)
Fever	85 (68%)
Chest pain	70 (56%)
Anorexia	60 (48%)
Breathlessness	20 (16%)

[Table/Fig-4]: Presenting symptoms at time of admission to DOTS plus centre.

Adverse drug reactions	N (%)
Gastrointestinal symptoms	49 (39.2%)
Fatigue	35 (28%)
Headache	30 (24%)
Vertigo	20 (16%)
Drowsiness	18 (14.4%)
Loss of appetite	12 (9.6%)
Ringing of ears	12 (9.6%)
Skin lesions	10 (8%)
Psychiatry	10 (8%)
Joint pain	10 (8%)
Oral ulcers	10 (8%)
Vision problems	10 (8%)
Thyroid	2 (1.6%)
Convulsions	2 (1.6%)

[Table/Fig-5]: Adverse drug reactions experienced by patients during MDR-TB patients.

DISCUSSION

The present study was carried out on 125 confirmed cases of MDR-TB. Most patients (95, 76%) were between 18 and 45 years of age. In a study done by Kulkarni GS et al., in Southern India, they have shown that the maximum number of MDR-TB case occurred during the economically productive age (15-55 years) [8]. In this study, also majority were males. In our study, majority were males and belonged to the rural habitation and were in labour class with a low socio-economic status. This explains the direct and indirect cost incurred in the cure of MDR-TB. In a study done by Liang L et al., in China, they have observed that financial burden, lack of knowledge, adverse effects, lack of coordination of services, unsatisfactory supervision contribute to the emergence of MDR-TB [9]. Addiction to alcohol was common where as diabetes mellitus was the commonest co-morbidity. Most of the patients preferred a government healthcare facility as the 1st point of contact for their current illness. This may be due to the resource poor setting prevalent. Overcrowding was common in the habitation and this may be due to the low socio-economic status of the study participants. Close contact with confirmed cases, especially in overcrowded habitations often lead to the emergence of new MDR-TB [10].

In the present study, there were few cases positive for HIV. In some studies, they have reported the prevalence of HIV to be nil among MDR-TB cases [11]. This may be due to geographical variations. The risk factors for acquisition of MDR-TB infection include the co-infection with HIV, overcrowded habitations, tobacco smoking, co-existing opportunistic infections, and non compliance to treatment under national programs for tuberculosis, like DOTS program [12-15].

A majority of the patients were immunised for tuberculosis as evidenced from the presence of a BCG scar. This may be due to the wide vaccination coverage. Majority had a contact history with a confirmed case of tuberculosis and few patients had adopted safe sputum disposal practices. This may be due to lack of sensitisation, low socio-economic and educational background.

Resistance to rifampicin was commonest followed by isoniazid resistance, combined rifampicin and isoniazid resistance and resistance to fluroquinolone or second line injectable drug. In a research work conducted in Varanasi, in India, out of 54% TB isolates were MDR [16]. In a study done in Delhi, 353 TB cases were subjected to drug sensitivity testing, it was observed that 239 (68%) were MDR-TB. The same study found out that resistance to three or more drugs including rifampicin and isoniazid (86.1%) was greater than that of resistance to rifampicin and isoniazid only (13.8%) [17].

In another study done in Odisha, the prevalence of MDR-TB among new sputum positive pulmonary TB patients was 0.85%. The prevalence of MDR-TB observed among 44 previously treated cases were 4.54%. Prevalence of mono resistance to streptomycin, isoniazid, rifampicin and ethambutol in new cases were 3.41%, 2.56%, 0 and 0.85%, respectively. While mono resistance to streptomycin, isoniazid, rifampicin and ethambutol in previously treated cases were 2.27%, 13.6%, 2.27% and 0, respectively and one showed resistance to both streptomycin and isoniazid in previously treated as well as in new case [18]. In another study done in Mayurbhanj district of Odisha, resistance to any anti-tubercular drug was observed to be 2.18% among new cases and 7.14% among previously treated patients, while MDR-TB was found to be 0% in new as well as in previously treated cases. The study reports an unchanged low level of MDR-TB prevalence among new cases in the district over a decade. Such a low level of resistance may be due to good adherence to the basic DOTS plus strategy and limited use of TB drugs outside the ongoing program [19]. The difference in the clinico-demographic profiles in different studies may be due to geographical and socio-cultural variations.

Transmission of MDR-TB can be stopped by timely identification and use of proper treatment regimens. Improper treatment practices lead to drug resistance. Areas with higher rates of MDR-TB are those with a poor TB control. The variability in resistance pattern may be due to the different treatment patterns and geographical factors.

This study observed that, most of the MDR-TB occurred in newly diagnosed cases of tuberculosis followed by its occurrence in relapse, defaulters, failure of anti-tubercular therapy. In a study done by Kulkarni GS et al., in North India it was observed that most of the MDR were diagnosed in the beginning of CAT II treatment. These were patients who have already taken anti-TB treatment before [8]. Prasad SV et al., have observed that every three patients among 10 retreatment patients develop MDR-TB [20].

The prevalence of MDR-TB was higher among CAT II failure cases. Hence, all sputum-positive patients at the diagnosis of CAT II should be screened for MDR-TB. Furthermore, any sputum-positive patient, either at the start of treatment or during follow-up, should be suspected for MDR-TB. According to Burugina Nagaraja S et al., [21] treatment outcome of a patient who fails first line ATT and not given MDR regimen is poor [21]. Kulkarni GS et al., have recommend that MDR regimen should be given to DR TB other than MDR-TB [8].

The commonest presenting symptom was cough fever, generalised weakness, weight loss in that order. These were similar to that of pulmonary tuberculosis in general. Chest radiography often raises suspicion of disease but cough is the common presentation. The classic clinical features of pulmonary TB include chronic cough, sputum production, appetite loss, weight loss, fever, night sweats, and haemoptysis [22].

Gastrointestinal upset, fatigue, headache, vertigo were the common adverse drug reactions encountered during the anti-tubercular therapy for MDR-TB. Adverse drug reactions are more common with second-line anti-TB drugs than the first-line drugs. Side-effects are inevitable in the normal course of treatment, and it is a challenge for the clinician to diagnose and manage them. Mismanagement of adverse drug reactions is a major cause for non adherence MDR-TB treatment [23]. Yang TW et al., in their study done in Korea have observed atleast one side-effect in 95 (37.1%) cases. Consequently, this resulted in the dropping of one or more drugs from the regimen of 17.2% patients. In the study, the commonly encountered adverse effects were gastrointestinal disturbance (18.4%), psychiatric disorder (5.5%), arthralgia (4.7%), hepatitis (3.9%), peripheral neuropathy (3.1%), hypothyroidism (2.3%), epileptic seizures (2%), dermatological effects (2%), ototoxicity (1.6%), and nephrotoxicity (1.2%). But, the success rate of MDR-TB treatment was 85.9% [24].

Drug susceptibility testing is the mainstay of diagnosis and treatment of MDR-TB. WHO recommends that, for the programmatic management of drug-resistant tuberculosis, rapid testing and detection cases needs to be expanded. They have set the target of one laboratory for every five million people for the drug susceptibility testing. Many of the countries with high TB and MDR-TB burden have not yet achieved this goal [25].

Limitation(s)

The major limitation of the present study is its small sample size. Since, the study is hospital based it is prone to selection bias and is not representative of the general population at large. Further large scale studies are essential to have an organised database on MDR-TB.

CONCLUSION(S)

The MDR-TB affects the population in the most productive age group. Rifampicin resistant TB is the predominant variety. The MDR-TB is difficult to treat. The emergence and spread of MDR-TB can be prevented by achieving high adherence to treatment with first-line anti-TB drugs. Accurate, reliable and timely drug susceptibility testing, ensuring direct observation of the complete treatment course and the use of maximally effective drug regimens are essential for successful treatment of MDR-TB.

REFERENCES

[1] Tuberculosis. https://www.who.int/news-room/q-a-detail/tuberculosis-multidrug-resistant-tuberculosis(mdrtb)#:~:text=Multidrug%2Dresistant%20TB%20(MDR%2D,person%2Dto%2Dperson%20transmission. [Last assessed on 21-12-2021].

[2] Kim DH, Kim HJ, Park SK, Kong SJ, Kim YS, Kim TH, et al. Treatment outcomes and survival based on drug resistance patterns in multidrug-resistant tuberculosis. Am J Respir Crit Care Med. 2010;182:113-19.

[3] Report of the First National Antituberculosis Drug Resistance Survey India (2014-16). New Delhi: Central TB Division, Ministry of Health and Family Welfare, Government of India; 2018. Available from: https://tbcindia.gov.in/showfile.php?lid=3315.

[4] Singh N, Gupta D. Revised national tuberculosis control programme (RNTCP) in India; current status and challenges. Lung India [Clinical Review] 2005;22:107-11.

[5] Chaudhuri A. Recent changes in technical and operational guidelines for tuberculosis control programme in India-2016: A paradigm shift in tuberculosis control. J Assoc Chest Physicians. 2017;5:01-09.

[6] Guidelines on Programmatic Management of Drug Resistant TB in India. New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare, NirmanBhavan; 2012.

[7] Grover GS, Takkar J. Recent Advances in Multi-Drug-Resistant Tuberculosis and RNTCP. Indian J Community Med. 2008;33(4):219-23. Doi: 10.4103/0970-0218.43238. PMID: 19876493; PMCID: PMC2763697.

[8] Kulkarni GS, Palwe SD, Patil NP, Telkhade AJ, Kadukar J. Prevalence of multidrug-resistant tuberculosis at a regional drug-resistant tuberculosis center of Maharashtra. Indian J Respir Care. 2020;9:30-34.

[9] 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):632-38. Doi: 10.1136/thoraxjnl-2011-200018. Epub 2012 Mar 8. PMID: 22403070.

[10] Metanat AM, Sharifi-Mood B, Shahreki S, Dawoudi SH. Prevalence of multidrug-resistant and extensively drug-resistant tuberculosis in patients with pulmonary tuberculosis in Zahedan, Southeastern Iran. Iranian Red Crescent Medical Journal. 2012;14(1):53-55.

[11] Mehari K, Sehaye T, Asmelash, Hailekiros H, Wubayehu T, Godefay H, et al. Prevalence and factors associated with multidrug-resistant tuberculosis (MDR-TB) among presumptive MDR-TB patients inTigrayregion, Northern Ethiopia. Canadian Journal of Infectious Diseases and Medical Microbiology. 2019;2019:2923549, 8 pages https://doi.org/10.1155/2019/2923549.

[12] Mekonnen F, Tessema B, Moges F, Gelaw A, Eshetie S, Kumera G. Multidrug resistant tuberculosis: Prevalence and risk factors in districts of Metema and WestArmachiho, Northwest Ethiopia. BMC Infectious Disease. 2015;15(1):461.

[13] Vashakidze L, Salakaia A, Shubladze N. Prevalence and risk factors for drug resistance among hospitalized tuberculosis patients in Georgia. International Journal of Tuberculosis and Lung Disease. 2009;13(9):1148-53.

[14] Abdella K, Abdissa K, Kebede W, Abebe G. Drug resistance patterns of Mycobacterium tuberculosis complex and associated factors among retreatment cases around Jimma, Southwest Ethiopia. BMC Public Health. 2015;15(1):599-605.

[15] Berhan A, Berhan Y, Yizengaw D. A meta-analysis of drug resistant tuberculosis in Sub-Saharan Africa: How strongly associated with previous treatment and HIV co-infection? Ethiopian Journal of Health Sciences. 2013;23(3):271-82.

[16] Maurya AK, Singh AK, Kumar M, Umrao J, Kant S, Nag VL, et al. Patterns and trends of multidrug-resistance tuberculosis. Indian J Med Microbiol. 2013;31:40-46.

[17] Singh N, Sidiq Z, Bhalla M, Myneedu VP, Sarin R. Multi-drug resistant tuberculosis among category I treatment failures-A retrospective study. Indian J Tuberc. 2014;61:148-51.

[18] Das D, Satapathy P, Murmu B. First line Anti-TB drug resistance in an urban area of Odisha, India. JCDR. 2016;10(11):DC04-06.

[19] Satapathy P, Mallick BC, Das D. First line drug resistance study in pulmonary tuberculosis patients from Mayurbhanj district of Odisha, India. Int J Health Sci Res. 2018;8(5):287-91.

[20] Kandi S, Prasad SV, Sagar Reddy PN, Reddy VC, Laxmi R, Kopuu D, et al. Prevalence of multidrug resistance among retreatment pulmonary tuberculosis cases in a tertiary care hospital, Hyderabad, India. Lung India. 2013;30:277-79.

[21] Nagaraja SB, Satyanarayana S, Chadha SS, Kalemane S, Jaju J, Achanta S, et al. How do patients who fail first-line TB treatment but who are not placed on an MDR-TB regimen fare in South India? PLoS One. 2011;6(10):e25698. Doi: 10.1371/journal.pone.0025698. Epub 2011 Oct 11. PMID: 22022433; PMCID: PMC3191158.

[22] Lawn SD, Zumla AI. Tuberculosis. Lancet. 2011;378(9785):57-72. Doi: 10.1016/S0140-6736(10)62173-3. Epub 2011 Mar 21. PMID: 21420161.

[23] Seung KJ, Keshavjee S, Rich ML. Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis. Cold Spring HarbPerspect Med. 2015;5(9):a017863. Doi: 10.1101/cshperspect.a017863. PMID: 25918181; PMCID: PMC4561400.

[24] Yang TW, Park HO, Jang HN, Yang JH, Kim SH, Moon SH, et al. Side effects associated with the treatment of multidrug-resistant tuberculosis at a tuberculosis referral hospital in South Korea: A retrospective study. Medicine (Baltimore). 2017;96(28):e7482. Doi: 10.1097/MD.0000000000007482. PMID: 28700490; PMCID: PMC5515762.

[25] WHO, Global Tuberculosis Control: Surveillance, Planning, Financing, World Health Organisation, Geneva, Switzerland, 2010. https://apps.who.int/iris/bitstream/handle/10665/144567/9241563141_eng.pdf?sequence=1[last assessed on 15-06-21].

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