Journal of Communicable Diseases
Volume 54, Issue 4 - 2022, Pg. No. 62-68
Peer Reviewed & Open Access Journal

Research Article

Predictors for Mortality in Multidrug Resistant Pulmonary Tuberculosis Patients in a South Indian Region

T Smitha[1], O Prabhakar[2]

[1]Department of Pharmacy Practice, Jayamukhi College of Pharmacy, Narsampet, Warangal Rural, Telangana, India.
[2]Assistant Professor, Department of Pharmacology, GITAM Institute of Pharmacy, GITAM University, Gandhi Nagar, Rushikonda, Visakhapatnam, Andhra Pradesh, India.
DOI: https://doi.org/10.24321/0019.5138.2022104

I N F O

Corresponding Author:
O Prabhakar, Department of Pharmacology, GITAM Institute of Pharmacy, GITAM University, Gandhi Nagar, Rushikonda, Visakhapatnam, Andhra Pradesh, India.
E-mail Id:
porsu@gitam.edu
Orcid Id:
https://orcid.org/0000-0002-9523-4963
How to cite this article:
T Smitha, O Prabhakar. Predictors for Mortality in Multidrug Resistant Pulmonary Tuberculosis Patients in a South Indian Region. J Commun Dis. 2022;54(4):62-68.

Date of Submission: 2022-10-31
Date of Acceptance: 2022-11-19

A B S T R A C T

Background: Although various factors depicting the mortality in multi drug resistant tuberculosis available there exist no concise data on the factors contributing to mortality globally. The predictors for mortality in multi drug resistant tuberculosis patients vary from localities.

Objectives: The study aimed to find the factors contributing to mortality in multi drug resistant tuberculosis in Warangal district of Telangana.

Materials and Methods: The prospective study determining the predictors of mortality in multidrug resistant pulmonary tuberculosis patients had a sample size of 296. The follow-up of the patients was conducted for twenty four months to determine the treatment outcome. Patients' mortality was noted from the hospital case sheets, relatives and healthcare facilitators' viz., National tuberculosis elimination program supervisors, Auxiliary Nursing Midwifery in case of death at home. Patients' demography was denoted in number and percentage. Predictors for mortality determined using binary logistic regression analysis. The predictor variables significant with $p<0.2$ in univariate analysis were considered for binary logistic regression analysis. The dependent variable was the occurrence of event - mortality and the independent variables chosen from the available literature.

Results: The predictors for mortality identified as low body weight of 16-30kg (p=0.002; aOR=10.43); comorbids (p=0.002; aOR=3.21); severe radiological manifestations at admission to hospital (p=0.001; aOR=6.98) and incompliance to treatment (p=0.0001; aOR=5.06) in the present study.

Conclusion: The factors identified for mortality in multidrug resistant tuberculosis patients are malleable and modifiable with timely follow-up of the patients. The results imply strengthening the anti-TB program with a multidisciplinary approach for a systematic follow-up of the patients and favorable treatment responses.

Keywords: Multidrug Resistant Tuberculosis, Mortality, Predictors, Radiological Manifestations, Treatment Adherence

Introduction

Death by Tuberculosis ranks at the top among other communicable diseases. Globally, the successful treatment outcome in 2019 was 56% for multidrug resistant tuberculosis and 39% for extensively drug resistant tuberculosis. Emergence of drug resistant tuberculosis is a major concern and a threat to public health. Resistance to rifampicin is rifampicin resistance and to both first line drugs isoniazid and rifampicin considered multidrug resistant tuberculosis. These require second line antitubercular drugs to treat for nine to twenty months. Around 10 million fell ill with this infection in 2018 and an estimated 390,000 cases with new diagnosis of multi drug resistant pulmonary tuberculosis noticed. Incidence of rifampicin resistance was noticed in a half million of initial diagnosis of tuberculosis and prevalence in 3.4% to 18% in new and recurrent TB cases in 2018. Similarly, 1.2 million deaths by TB in non-human immunodeficiency and 251,000 in human immunodeficiency reported globally in the same year.[1]

According to the report of the World Health Organization, India accounts for 26% of incidence and ranks first among 30 other high tuberculosis burden countries. India's noticed 28% of resistance to single anti-tuberculosis drug and 6.19% resistance to more than one anti-tubercular drug in its first survey of drug resistance in Tuberculosis (TB) patients.[2] Mortality by TB in India also recorded high with 38% of global deaths. Globally, mortality by TB was doubled in 2020 compared to HIV where COVID-19 had a great impact on the survival of patients diagnosed with TB.[3] Poor treatment outcomes of mortality and loss-to-follow-up with the treatment remain a major challenge in accomplishing the set goal of ZERO TB by 2035.[4] The unsuccessful treatment outcomes signify inefficient organization of anti-TB programme. The determinants denoting the factors for mortality and timely intervention reduce the unfavorable outcomes of treatment.[5] Left untreated it was estimated for an incidence of 98% of deaths by TB in developing countries like India and within a span of twenty years mortality among 35 million people ensured as per the statistics of the World Health Organization.[6] Therefore, an effective investigation into the risk factors for mortality in MDRPTB patients is a prerequisite.

The indicators related to patient and or anti-TB programme contribute to the high mortality.[7] The risk factors predicting the unfavorable outcomes based on patients' related factors include demography, social habits, comorbidities, clinical complications and awareness about the infection among patients.[8] Studies reported the patients at greater risk for DRTB with a past history of TB. Prolonged treatment and the associated adverse drug reactions, toxicities,[9] delay in the diagnosis of infection,[10] lack of self-support and care, clinical presentation of infection,[11] anemia[12] identified as the risk factors for poor outcomes of the anti-TB treatment. Programmatic management of drug resistant tuberculosis involved in early screening, diagnosis, treatment, monitoring of patients and in special needs striving to prevent the emergence of resistant tuberculosis. Implemented globally observed varied mortality rate across countries and settings among resistant tuberculosis patients.[13]

Factors determining the mortality help to design timely interventions and premature deaths. However, the factors attributing to mortality are undetermined in Warangal district of Telangana state. These considerations envisaged finding the predictors contributing to mortality in multi drug resistant tuberculosis in Warangal district of Telangana

Materials and Methods

Prior approval from Institutional Review Board (IRB number (JCP/IRB/2019/12)) of Jayamukhi College of Pharmacy obtained for the conduction of study. The study was conducted in Government chest and tuberculosis hospital, Warangal with District Nodal center for Multidrug resistant tuberculosis patients. This prospective study was conducted from February 2018 to December, 2020 in MDRPTB patients.

The sample size was calculated based on the favorable outcome of MDRPTB reported as 74% in India.[14] A proportion of 95% confidence interval and precision of 0.05 was considered for calculating sample size 296. The identified factors contributing to mortality from the previous literature included in the study. The response variable was the time of death. The explanatory variables include gender, locality, co-existing clinical conditions in MDRPTB, treatment duration, prescribed regimen, resistance pattern, weight band, recurrence, radiological grading at admission and adherence to treatment in the present study. The follow-up of the patients was conducted through regular contact and their visit to the hospital for health check-ups and monitoring therapy. Informed consent was obtained from the patients before initiating the study and followed-up till the completion of treatment duration. The follow-up of the individual patient was conducted for twenty four months to determine the treatment outcome.

Definition of Independent Predictor Variables

The confirmation of anti-TB drug resistance was based on cartridge based nucleic acid amplification test and first line and second-line probe assay techniques and used to describe the resistance pattern in the patients. Gender was categorized as male and female; locality as rural and urban. Presence or absence of comorbidities in MDRPTB, shorter and prolonged treatment duration, regimen prescribed as per WHO guidelines. Patients classified in 16-30kg, 31-45kg or 46-70kg weight band for

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2022104

dosing the mediations in the regimen. Adherence to anti-tubercular medication verified using the treatment chart and responses from the patients during the treatment tenure. Patients' mortality was noted from the hospital case sheets, relatives and healthcare facilitators' viz., NTEP supervisors, Auxiliary Nursing Midwifery in case of death at home. Recurrence of MDRPTB was identified by the thorough verification of the medical history, usage of anti-TB regimen among patients. Reinfection and relapse considered in recurrence of MDRPTB. Radiological grading identified by the manifestations obtained on the chest X-ray at admission. Involvement of single lung lobe with few interstitial infiltrations, no pleural involvement and absence of cavities categorized as mild. The findings of involvement of unilateral lung, with more interstitial infiltrations, pleural involvement and presence of cavitation's identified as moderate. The illustrations of bilateral lung lobes, alveolar infiltrations, pleural involvement and presence of cavitations indicated as severe grading of lung.

Statistical Analysis

Patients' demography was denoted in number and percentage. Predictors for mortality determined using binary logistic regression analysis. The predictor variables significant ($p<0.2$) in univariate analysis were considered for binary logistic regression analysis. The subcategories of the predictors coded as follows: Occurrence of the event - mortality 1, censor 0; Gender - female as 0, male as 1. The other predictor variables in normal values coded as 0 and abnormal as 1 for regression analysis. The data was analyzed using Statistical Package for Social Sciences version 25.0.

Results

Demography

The study conducted to find the predictors with a follow-up of individual patients between 2018 and 2020 in Warangal District. Majority were male (n=207). Patients attended more from rural localities (n=235) in the present study. As per the age categories the distribution of patients was as follows: below 20 years (n=21); 21-30 years (n=57); 31-40 years (n=71); 41-50 years (n=75); 51-60 years (n=45) and above 60 years (n=27). Most of the patients belong to the age between 21 to 50 years. Drug resistance to one anti-TB drug was more in the patients. The drug resistance pattern to anti-TB drugs observed resistance to rifampicin resistance in major (n=217) followed by fluoroquinolones and second line injectable (n=79). Majority patients categorized in low body weight bands of 16-30kg and 31-45kg (n=227). Few patients reported comorbid conditions (n=77) and diabetes was prominent. The treatment duration varied based on regimen as 9 months on shorter regimen (n=147) for treating rifampicin resistance and 20 months for pre-extensive drug resistance (n=99) and conventional therapy (n=50).

The shorter and conventional regimens include injectable and pre-extensive drug resistance with all oral anti-TB medications. The radiographs were categorized as mild (n=62); moderate (n=107) and severe (n=127). The severe manifestations include pleural involvement, cavitations, extensive infiltrations, alveolar infiltrations, hyperinflation, pleural effusion and bilateral lung involvement. Follow-up of the patients noticed few (n=38) to derelict the treatment. Patients neglected the treatment by the completion of intensive phase and or when free from the signs and symptoms of the infection. The event of mortality observed in n=69 MDRPTB patients during the study period. There were no significant differences in the distribution of patients in the variables with recurrence and duration of treatment. The details of demography and clinical findings were given in Table 1.

Predictors of Mortality in MDRPTB Patients

The Univariate analysis considered the factors with a significance of $p<0.2$ and identified the variables treatment months, comorbid, weight band, radiograph and adherence to treatment. Univariate analysis of the predictors was given in Table 2. The factors identified in univariate analysis chosen into binary logistic regression analysis with the significance $p<0.05$. The model fitness was determined by omnibus test ($p=0.0001$) and Hosmer and Lemeshow test ($p=0.828$). The improvement in analyzing the predictors determined by classification table noticed 89.9%. The accuracy of the model was 89.9% with a specificity of 99.6% and sensitivity of 58%.

Binary logistic regression identified weight band 16-30kg, severe manifestations of radiograph, non-adherence to medication and comorbid conditions along with MDRPTB as the significant predictors. Binary logistic regression analysis predicting the independent variables for mortality was given in Table 2. Patients with comorbid in MDRPTB had 2.43- fold risk compared to MDRPTB (a OR=2.43, 95% CI=1-5.89). MDRPTB patients in the low body weight range of 16-30kgs had 8.05 fold increased risk than the patients in other weight bands of 31-45kg and 46-70kg (a OR= 8.05, CI= 1.46-44.23). Similarly, radiograph with severe manifestations associated with a 13.69 fold increased risk compared to mild and moderate chest X-ray findings (a OR=13.69, CI=2.50-74.91). Patients non-compliant to treatment was associated with an increased risk to mortality of 309.25 fold, compared to the patients adherent to treatment (a OR=309.25, CI=36.12- 2647.3).

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2022104

Table 1.Demographic Description of Patients for Survival Analysis in MDRPTB Patients

Category	Subcategory	n (%)	X^2	p-value
Gender	Male	207 (69.93)	47.04	0.0001
	Female	089 (30.06)		
Locality	Rural	230 (77.71)	90.86	0.0001
	Urban	066 (22.29)		
Resistance	One drug	211 (71.28)	53.63	0.0001
	Two drugs	85 (28.72)		
Weight band	16-30	16 (5.41)	222.21	0.0001
	31-45	218 (73.64)		
	46-70	62 (20.94)		
Comorbids	Present	80 (27.03)	62.48	0.0001
	Absent	216 (72.97)		
Reoccurrence	Yes	143 (48.31)	0.33	0.56
	No	153 (51.68)		
Treatment months	Shorter	147 (49.66)	0.01	0.907
	Prolonged	149 (50.33)		
Treatment adherence	Persistent	226 (76.35)	82.26	0.0001
	Interrupted	70 (23.64)		
Radiograph	Mild	67 (22.63)	17.48	0.0001
	Moderate	104 (35.13)		
	Severe	125 (42.22)		
Treatment regimen	Pre-XDR BDQ	96 (32.43)	99.93	0.0001
	Shorter	131 (44.25)		
	Conventional	51 (17.22)		
	Mixed	18 (6.08)		
Mortality	No	227 (76.68)	84.33	0.0001
	Yes	69 (23.31)		

Table 2.Predicting Survival Probabilities in MDRPTB Patients

Clinical parameter	Subcategory	Crude Odds ratio	Confidence interval		Sig.	Adjusted Odds ratio	Confidence interval		Sig.
			LL	UL			LL	UL	
Gender	Male	0.89	0.50	1.60	0.70				
Comorbids	Yes	1.77	0.99	3.16	0.05	3.21	1.55	6.63	0.002
Treatment months	9 months	0.47	0.27	0.82	0.008	0.41	0.17	0.96	0.04
Locality	Rural	0.93	0.49	1.77	0.83				
Resistance to TB treating drugs	>1 drug	1.21	0.68	2.18	0.50				
Weight band	16-30	11.25	3.20	39.47	0.0001	10.43	2.42	44.84	0.002
	31-45	2.06	0.92	4.61	0.07	1.65	0.66	4.12	0.28
Reoccurrence	Yes	1.53	0.89	2.64	0.12	0.64	0.28	1.49	0.31

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2022104

Radiograph	Moderate	2.86	0.91	8.97	0.07	2.00	0.58	6.91	0.27
	Severe	10.15	3.47	29.67	0.0001	6.98	2.15	22.58	0.001
Treatment regimen	Shorter	0.63	0.33	1.21	0.17				
	Conventional	1.93	0.93	4.00	0.07				
Adherence to treatment	No	6.19	3.41	11.24	0.0001	5.06	2.57	9.97	0.0001

Note: LL - Lower Limit; UL- Upper Limit

Discussion

Conceptualization of predictors for mortality provided an assessment on the prevailing risk factors in multidrug resistant tuberculosis patients. The present study illustrated the predictors for mortality in Warangal region of Telangana.

The core plan of National Strategic Plan- NSP (2017-2025) is to End TB by 2025 by improving the health care services in screening, diagnosis and treatment. Early diagnosis, treatment of active TB patients and achieving sustainable development by 2025 is a primary concern of NSP. Effective TB Preventive Treatment (TPT) and its programmatic management is a strategy in preventing drug resistant tuberculosis. The present study noticed priority to engage the community and implementation of information and communication technology to motivate the patients adherent to treatment.[15] Programmatic Management of Drug Resistant Tuberculosis (PMDT) addressed access to special health care in the patients with comorbidities and to ensure the awareness of the drug resistant tuberculosis infection. PMDT assured guidance and patient centric mentoring needs to be addressed satisfactorily.[16]

The factors such as non-compliance to treatment, severe involvement of lung infection, co-existing clinical conditions and low weight band of 16-30kg were identified as the predictors for mortality. Radiological manifestations are more sensible in the diagnosis of TB than signs and symptoms.[17] Severe lung manifestations, cavitation in radiograph considered as the predictors for unsuccessful outcome of the anti-TB therapy[18] confirmed in the current investigation. Studies reported 3+ bacillary loads in cavitary presentations reduce the favorable outcome.[19] Increased bacillary count, bilateral cavitations reduce the influx of drugs into the cavitation and increase the chances of relapse, resistance, reinfection thereby leading to failure of anti-TB treatment.[20]

Weight below normal was considered as an anticipator for poor treatment outcome and all-cause mortality for MDRTB patients.[21] Low body mass index represents malnutrition with severe clinical presentation, mostly positive sputum. Malnutrition in TB reduces the antibodies, immune responses and is vulnerable to other infections.[22] TB bacilli catabolize energy sources utilizing carbohydrates, lipids and assimilate amino acids from host.[23] The YY peptide hormone increases in TB infection limiting food intake and reducing appetite.[24] Delayed improvement in BMI characterized by comorbidities, psychological illness, noncompliance to treatment and poor response to treatment in MDRPTB patients. Studies suggest a delayed increase in BMI, a potential biomarker in predicting the treatment outcome.[25] Improvement in weight was the useful predictor for determining the response to treatment. A five percent gain in weight from the baseline by third month after the initiation of treatment resulted in favorable outcome of the patients.[26] Being an easy measure of weight should be evaluated every month.

Current study noticed very few patients with comorbid and found it as a predictor for mortality. Diabetic patients predominate in this investigation. Anemia was prevalent in 90% of MDRPTB patients but not considered as a risk factor for mortality. Type 2 diabetes, anemia was noteworthy among the patients similar to one another study.[27] The combination of metabolic disorders, hyperglycemia and bacterial genetics impair the functions of phagocytosis, chemotaxis and inflammatory mediators.[28] This results in unfavorable treatment outcomes and at risk of failure in therapy, relapse and has an association in development of MDRPTB, mortality.[29] Comorbidities in MDRPTB considered a challenge in the management of the patient. Such conditions are in need of prompt follow-up for the beneficial treatment outcomes.

Non-compliance to the MDRPTB treatment identified as the predictor for mortality in this study. Adherence to treatment was minimal during the continuation phase of treatment in few patients. The same evidenced as the factor contributing to the poor outcomes in previous studies and at risk for reinfection, relapse and mortality.[30] Demography, economical status, medical support, severity of the infection and patient factors influence the adherence to treatment.[31] Direct observation of treatment and by the family remain a pillar for treatment support in MDRPTB patients. Information and communication technology enabled monitoring the adherence to treatment was acceptable by the patients through the audible and visual intimations proved to improve the compliance to treatment.[32]

These findings have been a major challenge for beneficial

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2022104

outcomes and require a reinforcement of improved social assistance for psychological support, patient counseling, rehabilitation of persons addicted to alcohol in the anti-TB program. National strategic plan set goal of End TB by 2025 can be achieved through effective communication between the health care providers, patients and their family members. Close monitoring of patients and implementation of interventions in need helps to improve the adherence to treatment and improve the success rate of anti-TB programs. The findings reflect an improvement in the quality of healthcare services, pharmaceutical TB care.

Conclusion

The burden of mortality in multi drug resistance tuberculosis patients evidenced low body weight of 16-30kg, non-compliance to treatment, comorbid and intensified lung manifestations at admission. The identified predictors for mortality were modifiable and malleable on prompt follow-up of the patients. The results imply strengthening the anti-TB program with a multidisciplinary approach for a systematic follow-up of the patients and favorable treatment responses.

Acknowledgement

We sincerely thank Dr. Sravan Kumar, Superintendent of Govt. Chest and TB hospital, Warangal, Telangana, India for permitting to utilize the hospital facilities. It's my privilege to thank Dr. S. Vasudeva Murthy, Principal, Jayamukhi College of Pharmacy for his support, motivation and critical analysis of the research work. We are also grateful to the participants in accomplishing the research.

Source of Funding: None

Conflict of Interest: None

References

1. WHO. Global Tuberculosis Report. Geneva, Switzerland World Health Organization. 2019.
2. Directorate of Health Services, Ministry of Health & Family Welfare, Government of India CTD. National Anti-TB Drug Resistance Survey.pdf. 2018.
3. WHO. Global tuberculosis report. Geneva World Health Organization; 2021. License: CC BY-NC-SA 3.0 IGO. 2021.
4. Chuang CU, Van Weezennbeek C, Mori T, Enaeso DA. Challenges to the global control of tuberculosis. Respirology. 2013;18:596-604. [PubMed] [Google Scholar]
5. Glaziou P, Falzon D, Floyd K, Raviglione M. Global epidemiology of tuberculosis. Semin Respir Crit Care Med. 2013;34(1):3-16. [PubMed] [Google Scholar]
6. World Health Organization. Global tuberculosis control surveillance, planning, financing: WHO report. World Health Organization. 2008. Available from: https://apps.who.int/iris/handle/10665/43831.
7. Bei C, Fu M, Zhang Y, Xie H, Yin K, Liu Y, Zhang L, Xie B, Li F, Huang H, Liu Y, Yang L, Zhou J. Mortality and associated factors of patients with extensive drug-resistant tuberculosis an emerging public health crisis in China. BMC Infect Dis. 2018;18(1):261. [PubMed] [Google Scholar]
8. World Health Organization. Global Tuberculosis Report. Geneva World Health Organization. Contract No. WHO/HTM/TB. 2016.
9. Schnippel K, Berhanu RH, Black A, Firnhaber C, Maitisa N, Evans D, Sinanovic E. Severe adverse events during second-line tuberculosis treatment in the context of high HIV Co-infection in South Africa a retrospective cohort study. BMC Infect Dis. 2016;16(1):593. [PubMed] [Google Scholar]
10. Tefera KT, Mesfin N, Reta MM, Sisay MM, Tamirat KS, Akalu TY. Treatment delay and associated factors among adults with drug resistant tuberculosis at treatment initiating centers in the Amhara regional state, Ethiopia. BMC Infect Dis. 2019;19(1):489. [PubMed] [Google Scholar]
11. Kassa GM, Tadesse A, Gelaw YA, Alemayehu TT, Tsegaye AT, Tamirat KS, Akalu TY. Predictors of mortality among multidrug-resistant tuberculosis patients in central Ethiopia a retrospective follow-up study. Epidemiol Infect. 2020;148:e258. [PubMed] [Google Scholar]
12. Tola H, Holakouie-Naieni K, Mansournia MA, Yaseri M, Gamtesa DF, Tesfaye E, Mahamed Z, Sisay MM. National treatment outcome and predictors of death and treatment failure in multidrug-resistant tuberculosis in Ethiopia a 10-year retrospective cohort study. BMJ Open. 2021;11(8):e040862. [PubMed] [Google Scholar]
13. Samuels JP, Sood A, Campbell JR, Ahmad Khan F, Johnston JC. Comorbidities and treatment outcomes in multidrug resistant tuberculosis a systematic review and meta-analysis. Sci Rep. 2018;8(1):4980. [PubMed] [Google Scholar]
14. Singh A, Prasad R, Kushwaha RAS, Srivastava R, Giridhar BH, Balasubramanian V, Jain A. Treatment outcome of multidrug-resistant tuberculosis with modified DOTS-plus strategy. A 2 years' experience. Lung India. 2019;36(5):384-92. [PubMed] [Google Scholar]
15. Central TB Division. National Strategic Plan for Tuberculosis Elimination. Dir Gen Heal Serv Minist Heal Fam Welf. 2017:110-08.
16. Guidelines for Programmatic Management of Drug resistant Tuberculosis in India. Central TB Elimination Program. Directorate of Health Services, Ministry of Health & Family Welfare, Government of India CTD. 2021.
17. Liu CH, Li L, Chen Z, Wang Q, Hu YL, Zhu B, Woo PC. Characteristics and treatment outcomes of patients

with MDR and XDR tuberculosis in a TB referral hospital in Beijing a 13-year experience. PLoS One. 2011;6(4):e19399. [PubMed] [Google Scholar]
18. Soeroto AY, Pratiwi C, Santoso P, Lestari BW. Factors affecting outcome of longer regimen multidrug-resistant tuberculosis treatment in West Java Indonesia. A retrospective cohort study. PLoS One. 2021;16(2):e0246284. [PubMed] [Google Scholar]
19. Wen Y, Zhang Z, Li X, Xia D, Ma J, Dong Y, Zhang X. Treatment outcomes and factors affecting unsuccessful outcome among new pulmonary smear positive and negative tuberculosis patients in Anqing, China. A retrospective study. BMC Infect Dis. 2018;18(1):104. [PubMed] [Google Scholar]
20. Pizzol D, Di Gennaro F, Chhaganlal KD, Fabrizio C, Monno L, Putoto G, Saracino A. Prevalence of diabetes mellitus in newly diagnosed pulmonary tuberculosis in Beira, Mozambique. Afr Health Sci. 2017;17(3):773-9. [PubMed] [Google Scholar]
21. Van Deun A, Maug AK, Salim MA, Das PK, Sarker MR, Daru P, Rieder HL. Short, highly effective, and inexpensive standardized treatment of multidrug-resistant tuberculosis. Am J Respir Crit Care Med. 2010;182(5):684–92. [PubMed] [Google Scholar]
22. Scrimshaw NS, SanGiovanni JP. Synergism of nutrition, infection, and immunity an overview. Am J Clin Nutr. 1997;66:464S-77S. [PubMed] [Google Scholar]
23. Warner DF. Mycobacterium tuberculosis metabolism. Cold Spring Harb Perspect Med. 2014;5(4):a021121-a021121.
24. Chang SW, Pan WS, Lozano Beltran D, Oleyda Baldelomar L, Solano MA, Tuero I, Friedland JS, Torrico F, Gilman RH. Gut Hormones, Appetite suppression and cachexia in patients with pulmonary TB. PLoS One. 2013;8(1):e54564. [PubMed] [Google Scholar]
25. Diallo A, Diallo BD, Camara LM, Kounoudji LAN, Bah B, N'Zabintawali F, Carlos-Bolumbu M, Diallo MH, Sow OY. Different profiles of body mass index variation among patients with multidrug-resistant tuberculosis. A retrospective cohort study. BMC Infect Dis. 2020;20(1):315. [PubMed] [Google Scholar]
26. Parmar MM, Sachdeva KS, Dewan PK, Rade K, Nair SA, Pant R, Khaparde SD. Unacceptable treatment outcomes and associated factors among India's initial cohorts of multidrug-resistant tuberculosis (MDR-TB) patients under the revised national TB control programme. Evidence leading to policy enhancement. PLoS One. 2018;13(4):e0193903. [PubMed] [Google Scholar]
27. Dash M, Behera BP. Socioepidemiological status and clinical outcome of MDR TB patients in a tertiary medical college in Southern Odisha. J Family Med Prim Care. 2022;11(4):1275-81. [PubMed] [Google Scholar]
28. Nijland HM, Ruslami R, Stalenhoef JE, Nelwan EJ, Alisjahbana B, Nelwan RH, van der Ven AJ, Danusantoso H, Aarnoutse RE, van Crevel R. Exposure to rifampicin is strongly reduced in patients with tuberculosis and type 2 diabetes. Clin Infect Dis. 2006;43(7):848-54. [PubMed] [Google Scholar]
29. Lönnroth K, Roglic G, Harries AD. Improving tuberculosis prevention and care through addressing the global diabetes epidemic From evidence to policy and practice. Lancet Diabetes Endocrinol. 2014;2(9):730-9. [PubMed] [Google Scholar]
30. Gashu KD, Gelaye KA, Lester R, Tilahun B. Effect of a phone reminder system on patient-centered tuberculosis treatment adherence among adults in northwest Ethiopia. A randomised controlled trial. BMJ Health Care Inform. 2021;28(1):e100268. [PubMed] [Google Scholar]
31. World Health Organization. Adherence to long-term therapies evidence for action. World Health Organization, 2003. Available from: https://apps.who.int/iris/handle/10665/42682 [Google Scholar]
32. Thomas BE, Kumar JV, Periyasamy M, Khandewale AS, Hephzibah Mercy J, Raj EM, Kokila S, Walgude AS, Gaurkhede GR, Kumbhar JD, Ovung S, Paul M, Rajkumar BS, Subbaraman R. Acceptability of the medication event reminder monitor for promoting adherence to multidrug-resistant tuberculosis therapy in two Indian cities. Qualitative study of patients and health care providers. J Med Internet Res. 2021;23(6):e23294. [PubMed] [Google Scholar]

ISSN: 0019-5138
DOI: https://doi.org/10.24321/0019.5138.2022104