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Research Article

Outcome Analysis of Shorter Regimen of Rifampicin Resistant Tuberculosis

Tarun Tiwari, Rajveer N Kuldeep*, Ramakant Dixit, Neeraj Gupta, Srishankar Bairy

Department of Tuberculosis & Respiratory Diseases, Jawahar Lal Nehru Medical College, Ajmer, Rajasthan, India.

Abstract

Introduction: Globally, about half a million new cases of rifampicin-resistant TB (RR-TB) were found in 2019. Out of them, 78% had confirmed multidrug-resistant tuberculosis (MDR-TB). In the year 2020, a total of 18,05,670 TB cases were notified. Out of these, 49,679 were diagnosed as MDR/RR TB patients. Management of drug-resistant TB requires a longer duration of treatment with second-line anti-TB drugs that cause more side effects. WHO introduces the shorter regimen for RR-TB with a total duration of 9-11 months consisting of 4 to 6 months of intensive phase and 5 months of continuation phase.

Aim and material & method: This is an observational study conducted on 129 patients of rifampicin-resistant tuberculosis admitted at the PMDT site at the Department of Respiratory Medicine from July 2018 to October 2020 to assess treatment outcomes of shorter regimens in RR-TB. Approval from the ethical committee was obtained.

Result and conclusion: A favorable outcome was observed in 52.7% of patients; however, 51.12% of patients experienced at least one side effect. Treatment outcome was not affected in patients with HIV and a past history of anti-TB drugs. Diabetic patients were more likely to have treatment failure than non-diabetic patients. (*p-value* <0.005).

Keywords: Tuberculosis, Rifampicin-resistance, Shorter regimen.

Introduction

In the year 2020, a total of 18,05,670 TB cases were notified. Out of them, 49,679 were confirmed MDR/RR TB patients. The results of drug-resistant tuberculosis management have not been optimal.[1] This is due to challenges in implementing the treatment regimens, as they are very long, often poorly tolerated, and difficult to monitor.

WHO introduced the shorter regimen for MDR/RR-TB patients in May 2016 with a total duration of 9 to 11 months, which consists of 4 to 6 months of intensive phase with Mfx^{h} Km/Am Eto Cfz Z H^{h} E and 5 months of continuation phase with Mfx^{h} Cfz Z E.[2]

In the shorter regimen, the intensive phase must be given for at least 4 months, which can be extended up to 6 months in case of delayed sputum conversion. If sputum conversion is not achieved at the end of the 6^{th} month of treatment, the patient will be observed as a "treatment failure" and switch to the appropriate treatment regimen accordingly.

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This is a hospital-based observational study conducted on 129 patients of rifampicin-resistant tuberculosis admitted at PMDT site at our centre from July 2018 to October 2020, to assess the treatment outcome of a shorter regimen in RR-TB.

Material and Method

It is a hospital-based observational study to assess the treatment outcome of a shorter regimen in RR-TB. Approval from the ethical committee was obtained.

All diagnosed patients of rifampicin resistance at our center. From July 2018 to October 2020 at the PMDT site were included in this study (a total 129 Shorter regimen patients

Address for correspondence: Rajveer N Kuldeep,
Department of Tuberculosis & Respiratory Diseases, Jawahar Lal Nehru Medical College, Ajmer, Rajasthan, India.
E-mail: dr.rajveerking@gmail.com

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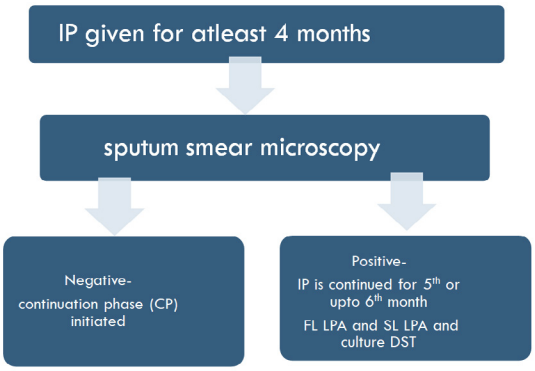

Figure 1: Follow up of shorter regimen

were enrolled during this time period). A detailled clinical evaluation was done apart from periodic sputum examination, culture and radiological assessment. Inclusion and exclusion criteria for the shorter regimen were as per NTEP, Govt. of India. Treatment regimen, duration, follow up, extension of treatment etc were adopted as per national guidelines (Figure 1). Detailled clinical, bacteriological and radiological assessment was done during the course of treatment. Adverse drug reactions were also noted.

Results

This hospital-based observational study was conducted on 129 cases of RR TB patients admitted for a specified duration at our center. Out of them, a majority (83.70%) were males, with only 21 (16.3%) females with a mean age of 38.81 ± 14.44 years. In this study, 27.9% of patients belonged to 21 to 30 years of age group, followed by 20.9% of patients belonging to 51-60 years of age group. The majority of patients, 126 (97.7%) had pulmonary TB, while three patients had extra-pulmonary TB.

Cough (95.3%) and fever (82.2%) were the most common symptoms. The least common symptom was hemoptysis, observed only in 4.7% of patients (Figure 2).

An important factor in the development of drug-resistant tuberculosis is a history of irregular or incomplete anti-TB

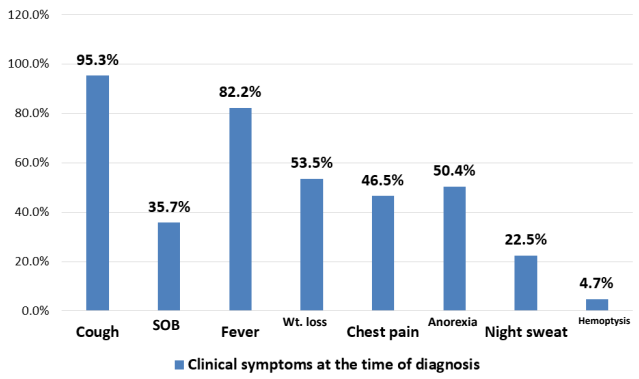

Figure 2: Clinical symptoms at the time of diagnosis

drug intake. In the present study majority of patients, 119 (92.2%), had a previous treatment history of tuberculosis. In comparison, only ten patients out of 129 (7.8%) were newly diagnosed with TB and carried resistant strains.

After starting a shorter regimen, 38.8% turned negative -in 2nd month, 22.5% turned sputum negative in the 3rd month. However, 18 patients (14%) failed to convert to sputum negative and were regarded as treatment failure. Sputum smear report of 28 patients (21.7%) was not available (Figure 3).

Clinically, on treatment completion, 59.8% of patients in our study showed complete clinical improvement, also 2.7% of patients showed partial clinical improvement. However, 20.5% of patients experienced no improvement in symptoms as well as 17% complained of exacerbation of symptoms after starting a shorter regimen (Figure 4).

Out of 129 patients, favorable outcome was seen in a total of 68 (52.7%) patients in the form of treatment completion (31%) and cure (21.7%) (Figure 5). Treatment change was done in 13.2%. Lost to follow-up during treatment was found in 11 patients (8.5%). Treatment failure was observed in 14% of patients. 14 patients (10.9%) died during treatment, while 1 (0.8%) patient was transferred out to other centres for treatment.

On follow-up Chest x-rays of RR patients after treatment completion, 118 out of 129 (91.5%) showed regression of lesions. However, in 11 patients (8.5%), progression of findings was observed.

During the course of a shorter regimen, 17 patients of RR TB developed additional resistance to drugs. Out of these 1 (5.8%) developed additional isoniazid resistance, 10 (58.8%) developed additional flouroquinolone resistance, 3 (17.6%) developed additional resistance to second-line injectables, and 3 (17.6%) developed additional resistance to more than one type of drugs. Routine LPA to 1st and 2nd line drug revealed additional resistance, therefore, it is essential to go for FL & SL LPA for all those cases diagnosed as RRTB.

In this study, we also assessed factors that may contribute to failure of treatment, such as low body mass index was found in 53.3% of patients with a mean BMI being 18.43 ± 3.23 kg/m^2. HIV co-infection was found in 5 (3.9%) patients. 19.4% (25) were found to have diabetes mellitus, while 80.6% (104) patients were non-diabetic.

Table 1 shows the Association of different factors with treatment failure after shorter regimen. Patients with diabetes had higher treatment failure as compared to others (20.7%) (*p-value* <0.005)

In this study, we observed a reasonable correlation between clinical symptoms and radiological findings. In patients who showed complete improvement 67 /112 or partial improvement 3/112 showed only regression in lesions on chest x-ray. While amongst 23 patients who did not find any relief in symptoms 16 showed regression of findings on chest x-ray, while 7 showed progression of lesions. Even amongst

Table 1: Association of different factors with treatment outcome of shorter regimen in RR TB patients

Factors		*Treatment success*	*Treatment failure*	*p-value*
Age (years)		37.65 ± 14.28	38.33 ± 3.57	0.84
Gender	Male	60 (81.1%)	14 (18.9%)	0.26
	Female	8 (66.7%)	4 (33.3%)	
BMI	Underweight	39 (81.2%)	9 (18.8%)	0.59
	Normal	27 (75.0%)	9 (25.0%)	
	Overweight	2 (100.0%)	0	
HIV status	Non-reactive	65 (79.3%)	17 (20.7%)	1.0
	Reactive	3 (75.0%)	1 (25.0%)	
DM status	Non diabetic	63 (60.5%)	5 (4.8%)	0.001
	Diabetic	5 (20.0%)	13 (52.0%)	
History of ATT regimen	Newly diagnosed	5 (83.3%)	1 (16.7%)	1.0
	Previously treated	63 (78.8%)	17 (21.2%)	
Type of TB	Extra pulmonary	1	0	1.0
	Pulmonary	67	18 (21.2%)	
Chest x-ray finding during diagnosis	Lesion +nt	64	18 (22.0%)	0.57
	Lesion –nt	4	0	

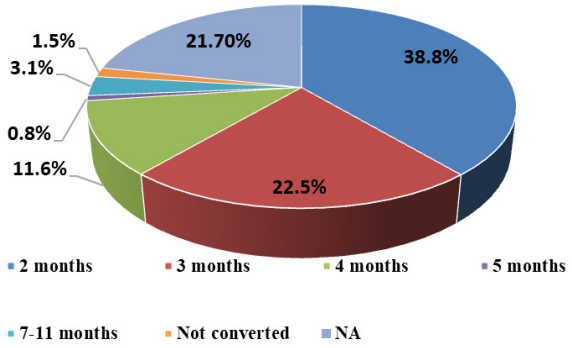

Figure 3: Timing of sputum conversion in study subjects (n = 129)

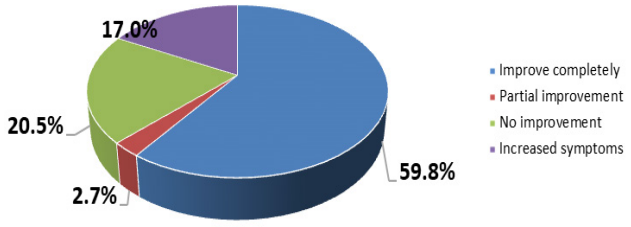

Figure 4: Clinical outcome of shorter regimen in RR TB patients (n = 129)

19 patients whose clinical symptoms aggravated after being put on treatment, majority, i.e., 16 showed regression in chest x-ray findings.

Discussion

The present study was an observational study to evaluate treatment outcomes of shorter regimens in RR TB patients enrolled at a PMDT site in a tertiary care hospital in central Rajasthan.

In this study, a total 129 patients with RR TB were included. Out of them, 126 (97.7%) patients had pulmonary TB, while 3 (2.3%) patients had extra-pulmonary TB. Amongst the extra-pulmonary TB patients, two had cold abscesses (nodal TB), while one had both cold abscesses and pleural tuberculosis. Of these three extra-pulmonary TB patients, one patient completed their treatment, the other had treatment failure and the third was identified as lost to follow-up. According to study done by Desai & Joshi[3] out of a total of 1743 drug-resistant TB patients, 4.4% were extra pulmonary DRTB cases. Extra-pulmonary sites involved were lymph nodes 51.3%, spine 19.7%, pleural effusion 11.9%, bones 7.9%, disseminated extra-pulmonary disease 6.6% and central nervous system 2.6%.

In the present study, 3.9% of patients were HIV co-infected. According to a study done by Sultana *et al.*[4] and meta-analysis done by Mesfin *et al.* suggested that HIV-infected patients are more likely to develop MDR-TB in their lives. In a study done by Baluku *et al.*[5], the prevalence of RR was found to be three times more in TB/HIV-coinfected patients as compared to TB patients without HIV co-infection (32.4 *vs.* 11.5%).

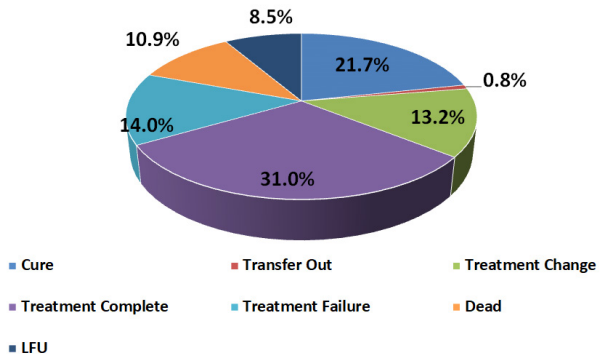

Figure 5: Outcome of shorter regimen in RR TB patients (n = 129)

In this study, 80.6% patients were non-diabetic, 19.3% had been diagnosed with diabetes mellitus. Treatment failure was found to be significantly higher in diabetic patients (52%) as compared to non-diabetic (20.7%) (*p-value* =0.001).

According to a study done by Huangfu *et al.*,[6] tuberculosis patients with diabetes mellitus were identified with a higher risk of mortality, poor treatment outcome, higher relapse rate and increased risk of developing primary MDR TB as compared to tuberculosis patients without diabetes mellitus. Observations made by Gautam *et al.*[7] also had similar conclusions. Therefore, screening for diabetes among TB patients is recommended. Also, preventive and curative strategies, along with optimal care, should be provided for both TB and diabetes. In this study, most of the patients presented with cough (95.3%), followed by fever (82.2%), weight loss (53.5%) and loss of appetite (50.2%) and chest pain (46.5%). Only 4.7% of patients presented with hemoptysis. According to R. Loddenkemper *et al.*[8], the constitutional symptoms of pulmonary TB, i.e., chronic cough, sputum, fever, night sweats, decreased appetite, loss of weight and hemoptysis, were observed in their study. K Zaman[9] stated that symptoms of TB depend on site of bacterial growth. Patients with pulmonary tuberculosis may present with chronic cough, chest pain, hemoptysis, weakness or fatigue, weight loss, fever, and night sweats. In this study, 92.2% RR TB patients had a previous history of treatment, while only 7.8% of patients were newly diagnosed TB cases who carried drug-resistant strains. The prevalence of MDR-TB/RR-TB in India was estimated at 2.5% in newly diagnosed patients and 16% in previously treated patients.[10] Seung *et al.*[11] found that the prevalence of MDR-TB was 3.8% in newly diagnosed patients and 20% in previously treated patients in their study. They also found that MDR TB is highly prevalent in Eastern Europe and Central Asian countries.

Ragonnet *et al.*[12] conducted a study on the development of drug resistance in previously treated cases of tuberculosis. They suggested that lack of proper diagnosis of MDR TB in newly diagnosed cases significantly increases the prevalence of MDR/RR-TB in previously treated cases. These results emphasize the requirement of a methodological approach to the prevention and treatment of RR-TB.

A study by Faustini *et al.*[13] stated that previously treated cases have 10.23 times more risk of developing MDR-TB than newly diagnosed cases. They concluded that a previous history of anti-tubercular treatment was the most common risk factor for developing MDR-TB in European countries.

In India, 1.56 million TB cases were diagnosed in 2020[14] (both drug-sensitive and drug-resistant). Out of them, 89% were newly diagnosed cases and 11% were previously treated cases. (Rajasthan: 86% new, 14% previously treated).

In our study, 76.8% sputum conversion rate was achieved in RR TB patients on a shorter regimen. A study by K J M Aung *et al.*,[15] observed a 93% sputum conversion rate. Also, a study by Andrew J Nunn *et al.*[16] showed favorable bacteriological outcomes in 84.9% of cases on shorter regimens. In TB India Report 2020, 58.9% of patients reported sputum conversion at the end of 4th month. This difference in sputum conversion varied due to adherence to the treatment and scheduled follow-up.

Clinically at the end of a treatment regimen, 59.8% of patients in our study showed complete clinical improvement, and 2.7% of patients showed partial clinical improvement. However, 20.5% of patients showed no improvement in symptoms and 17% complained of exacerbation of symptoms after starting a shorter regimen.

The "Treatment failure" is defined as a patient whose treatment regimen needs to be terminated or permanently changed to a new regimen option or treatment strategy due to lack of microbiological conversion at the end of treatment or adverse drug reactions (ADR) or evidence of additional acquired resistance for drugs in the regimen. The "cure" is defined as a microbiologically confirmed MDR/RR TB patient who completed treatment as recommended by the national policy with evidence of bacteriological response and no evidence of treatment failure and was culture negative at the end of treatment and on at least one previous occasion.[17]

In our study 21.7% of patients achieved a cure, while 31% of patients achieved treatment completion but did not fulfill the criteria of a cure. About 13.2% of patients underwent treatment change. Lost to follow-up during treatment was found in 11 patients (8.5%). Treatment failure was observed in 14% of patients. 14 patients (10.9%) died during treatment while 1 (0.8%) patient was transferred out to other centers for treatment.

A variable success rate with shorter regimens has been observed in previous studies. A study by C Kuaban *et al.*,[18] in Cameroon found that 89.33% of patients successfully completed treatment. They preferred the use of gatifloxacin as a fluoroquinolone and put patients on 12-month treatment. The longer duration of treatment was probably associated with better results.

A meta-analysis by Faiz Ahmad Khan *et al.*,[19] and a study by S. H. Harouna *et al.*,[20] in Niger, both found the treatment

success rate was 83% with the 9-month regimen. In another study by Andrew J Nunn *et al.* (STREAM trial),[21] Valerie Schwoebel *et al.*,[22] and Syed Abidi *et al.*,[23] found treatment success in 78.8, 79.3 and 80.0%, respectively in patients with shorter regimen group. The slight variation in the treatment success rate is probably due to different geographical regions and socioeconomic statuses; however, the results of our study are more or less similar to that of national and international data.

A study by Le T. N. Anh *et al.*,[24] in Vietnam found 5.3% of patients were treatment failure. In another study at West Bengal, India by Prasanta Kumar Das *et al.*,[25] found 4.9% treatment failure and study by Andrew J Nunn *et al.* (STREAM trial)[16] found 7.75% of patients were treatment failure. In our study, we observed a higher rate of treatment failure, i.e., 14%, which may be due to differences in socioeconomic status, sample size, etc. A study by Alberto Piubello *et al.*,[26] in Nigeria found 9.2% of patients were treatment failure and a study by Valerie Schwoebel *et al.* (2019)[22] in nine African countries found 9.6% probability of both failure and relapse, this high failure rate may be due to underdeveloped African countries and poor health facilities.

In the present study out of 129 patients on the shorter regimen, 14 (10.9%) patients were declared "Died" during treatment. In India TB Report 2020[19] there were 11% of patients declared as "Died," which is consistent to our study. Studies by Alberto Puibrllo *et al.,*[26] in Niger and by Valerie Schwoebel *et al.*[22] in nine African countries found 9.2% of patients and 8.6% were declared "died" during treatment, respectively. Studies by C Kuaban *et al.*,[18] in Cameroon and in a meta-analysis by Faiz Ahmad Khan *et al.*,[19] found 6.6% and 6% deaths, respectively. In one another study by Andrew J Nunn *et al.* (STREAM trial),[16] found 7.34% of patients "died" during treatment.

The SARS-CoV-2 pandemic was a significant factor affecting the study results, as it hampered the chain of timely medicine supply, patient visits and follow-up. It was also a contributing factor in the 8.5% of cases that were lost to follow-up. COVID-19 also affected the number of study subjects.

A large drop of 18% decrease in newly diagnosed patients was observed between 2019 and 2020 from 7.1 million in 2019 to 5.8 million in 2020. Although the number of subjects limited our study, we observed better compliance and tolerance for shorter regimens in RR-TB patients.[27]

In our study, although 66 (51.12%) patients experienced at least one adverse drug reaction, most of them were mild and manageable. The most common ADR reported was GI symptoms. About 19 (14.72%) patients experienced symptoms like nausea, vomiting, abdominal pain, diarrhea, gastritis etc. An almost similar number of cases, i.e., 18 (13.95%) developed rashes, while 6 (4.65%) patients experienced both GI symptoms and rashes. Peripheral neuropathy was experienced by nine patients (6.98%), 8 (6.20%) suffered from hepatotoxicity. Ototoxicity in the form of hearing disturbances and tinnitus was seen in 4 (3.10%) patients, while two patients (1.15%) experienced symptoms of psychosis.

In a study by S. H. Harouna *et al.*,[20] at Niger found that 50% of children/adolescents and 68% of adults experienced at least one adverse reaction. The most common adverse drug reaction was vomiting (40%), followed by ototoxicity (20%) and other adverse reactions, such as gastritis (4%), depression (3%), arthralgia (5%), skin rash (2%), peripheral neuropathy (3%), optic neuritis (3%), nephrotoxicity (2%) and hepatotoxicity (5%) were also recorded only in adults.

In one another study by Andrew J Nunn *et al.* (STREAM trial)[16] found that an adverse event occurred in 48.2% in the shorter regimen group. From the above discussion, we concluded that approximately half of the cases observed at least one adverse effect in a shorter regimen.

Conclusion

The older TB regimens associated with more side effects and increased mortality as compaired to the new regimen that raises the questions against the relevance of the older TB regimen. There is improved survival and fewer side effects are noted with new treatments such as bedaquiline. Currently, short-term models containing multiple drugs at high doses reported fewer side effects, setting an example of an excellent treatment regimen. The increased drug side effects we found with formal monitoring may perhaps present a more complete picture of shorter regimen toxicity and has implications for a fixed short regimen. It also confirms concerns about injectable-containing regimens as a WHO-endorsed treatment option.

Although the number of subjects limited our study, we observed better compliance and tolerance for shorter regimens in RR-TB patients.

References

1. India TB Report 2020. Ministry of Health and Family Welfare, Government of India. Available from: [www.tbcindia.gov.in/showfile.php?lid=3538]
2. Prasad R, Gupta N, Banka A. Shorter & cheaper regimen to treat multidrug-resistant tuberculosis: A new hope. Indian J Med Res. 2017;146(3):301-303.
3. Desai U, Joshi JM. Extrapulmonary drug-resistant tuberculosis at a drug-resistant tuberculosis center, Mumbai: Our experience - Hope in the midst of despair! Lung India. 2019;36(1):3-7.
4. Sultana ZZ, Hoque FU, Beyene J, et al. HIV infection and multidrug resistant tuberculosis: a systematic review and meta-analysis. BMC Infect Dis. 2021;21(1):51.
5. Baluku JB, Mugabe P, Mulwana R, et al. High Prevalence of Rifampicin Resistance Associated with Rural Residence and Very Low Bacillary Load among TB/HIV-Coinfected Patients at the National Tuberculosis Treatment Center in Uganda. Biomed Res Int. 2020;2020:2508283.
6. Huangfu P, Ugarte-Gil C, Golub J, et al. The effects of diabetes on tuberculosis treatment outcomes: an updated

systematic review and meta-analysis. Int J Tuberc Lung Dis. 2019;23(7):783-796.
7. Gautam S, Shrestha N, Mahato S, et al. Diabetes among tuberculosis patients and its impact on tuberculosis treatment in South Asia: a systematic review and meta-analysis. Sci Rep. 2021;11(1):2113.
8. Loddenkemper R, Lipman M, Zumla A. Clinical Aspects of Adult Tuberculosis. Cold Spring Harb Perspect Med. 2015;6(1):a017848.
9. Zaman K. Tuberculosis: a global health problem. J Health Popul Nutr. 2010; 28(2): 111-113.
10. Prasad R, Gupta N, Banka A. Multidrug-resistant tuberculosis/ rifampicin-resistant tuberculosis: Principles of management. Lung India. 2018;35(1):78-81.
11. Seung KJ, Keshavjee S, Rich ML. Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis. Cold Spring Harb Perspect Med. 2015;5(9):a017863.
12. Wejse C, Ragonnet R, McBryde ES, Trauer JM. Modelling tuberculosis control priorities: more of the same will not do. Lancet Glob Health. 2019;7(10):e1319.
13. Faustini A, Hall AJ, Perucci CA. Risk factors for multidrug resistant tuberculosis in Europe: a systematic review. Thorax. 2006;61(2):158-163.
14. India TB Report 2020. Ministry of Health and Family Welfare, Government of India. Available from: [www.tbcindia.gov.in/ showfile.php?lid=3538]
15. Aung KJ, Van Deun A, Declercq E, et al. Successful '9-month Bangladesh regimen' for multidrug-resistant tuberculosis among over 500 consecutive patients. Int J Tuberc Lung Dis. 2014;18(10):1180-1187.
16. Nunn AJ, Phillips PPJ, Meredith SK, et al. A Trial of a Shorter Regimen for Rifampin-Resistant Tuberculosis. N Engl J Med. 2019;380(13):1201-1213.
17. Guidelines on Programmatic Management of Drug-Resistant Tuberculosis in India. Ministry of Health and Family Welfare, Government of India; 2019.
18. Kuaban C, Noeske J, Rieder HL, et al. High effectiveness of a 12-month regimen for MDR-TB patients in Cameroon. Int J Tuberc Lung Dis. 2015;19(5):517-524.
19. Ahmad Khan F, Salim MAH, du Cros P, et al. Effectiveness and safety of standardised shorter regimens for multidrug-resistant tuberculosis: individual patient data and aggregate data meta-analyses. Eur Respir J. 2017;50(1):1700061.
20. Harouna SH, Ortuno-Gutierrez N, Souleymane MB, et al. Short-course treatment outcomes and adverse events in adults and children-adolescents with MDR-TB in Niger. Int J Tuberc Lung Dis. 2019;23(5):625-630.
21. Nunn AJ, Phillips PPJ, Meredith SK, et al. A Trial of a Shorter Regimen for Rifampin-Resistant Tuberculosis. N Engl J Med. 2019;380(13):1201-1213.
22. Schwœbel V, Trébucq A, Kashongwe Z, et al. Outcomes of a nine-month regimen for rifampicin-resistant tuberculosis up to 24 months after treatment completion in nine African countries. EClinicalMedicine. 2020;20:100268.
23. Abidi S, Achar J, Assao Neino MM, et al. Standardised shorter regimens versus individualised longer regimens for rifampin- or multidrug-resistant tuberculosis. Eur Respir J. 2020;55(3):1901467.
24. Anh LTN, M V Kumar A, Ramaswamy G, et al. High Levels of Treatment Success and Zero Relapse in Multidrug-Resistant Tuberculosis Patients Receiving a Levofloxacin-Based Shorter Treatment Regimen in Vietnam. Trop Med Infect Dis. 2020;5(1):43.
25. Das PK, Ganguly SB. Effectiveness of the shorter MDR regimen in the management of tuberculosis: Shortfall in the outcome of disease- a multidimensional approach and evaluation for a better alternative. Biomed Biotechnol Res J. 2020;4(2):143-147.
26. Piubello A, Souleymane MB, Hassane-Harouna S, et al. Management of multidrug-resistant tuberculosis with shorter treatment regimen in Niger: Nationwide programmatic achievements. Respir Med. 2020;161:105844.
27. Trajman A, Felker I, Alves LC, et al. The COVID-19 and TB syndemic: the way forward. Int J Tuberc Lung Dis. 2022;26(8):710-719.