

ORIGINAL ARTICLE

Factors Associated with Treatment Outcomes in Patients with Pulmonary Tuberculosis

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ABSTRACT

Background and Aim: Tuberculosis (TB) is one of the major sources of health problems in developing countries. An effective strategy for tuberculosis treatment can be evaluated with key indicators known as TB control program with their treatment outcomes. Hence, the purpose of this study was to evaluate the factors associated with the treatment outcome of pulmonary tuberculosis in patients.

Methods: This cross-sectional study was carried out on 129 Tuberculosis patients in the department of Pulmonology, Gulab Devi Hospital Lahore from November 2020 to April 2021. Demographic details, clinical examination, and treatment outcomes were evaluated. All the data were extracted from the hospital medical records. Successful treatment outcomes predictors were assessed using bivariate and multivariate regression. SPSS version 20 was used for data analysis.

Results: Of the total 129 tuberculosis patients, 59 (46%) were male and 70 (54%) were females. The overall mean age was 26.54±5.62 years. The overall prevalence of successful treatment rate was 113 (87.6%). Out of 113, the prevalence of cured and complete treatment patients was 57 (50.4%) and 56 (49.6%) respectively. Based on logistic regression models, various parameters with their respective adjustment odds ratio (AOR) were as follows; age 21-40 years (AOR= 2.67, 95% CI=1.32-6.12, p-value=0.003), treatment category (AOR=4.62, 95% CI=1.12-16.74, p-value=0.027), and smear-positive pulmonary tuberculosis (AOR=3.47; 95% CI=1.76-6.69, p-value<0.001) were significantly related with treatment outcomes.

Conclusion: Our study reported that the overall prevalence of successful treatment was 87.6%. Though, the rate of overall successful treatment was found satisfactory, but, to meet international standard strategy for tuberculosis, still, improvement needs to be achieved. Age, treatment category, and tuberculosis types were significantly correlated with treatment outcomes.

Keywords: Pulmonary Tuberculosis; Treatment Outcomes; TB Smears

INTRODUCTION

Tuberculosis (TB) continues to be the leading cause of death as a single infectious disease despite the effective diagnosis and treatment tools availability. One-third of the world's population is infected by TB caused by bacillus *Mycobacterium tuberculosis* [1]. About 10million population suffered and 1.3 million died of tuberculosis in 2017 [2]. Globally, TB accounts for 80% of cases in developing countries being high burdens TB countries with higher rates of mortality [3]. Tuberculosis (TB) is one of the major sources of health problems in developing countries. An effective strategy for tuberculosis treatment can be evaluated with key indicators known as TB control program with their treatment outcomes. TB is a contagious disease instigated by the *Mycobacterium tuberculosis* bacteria that normally affects the lungs [3]. Most bacterial contagions do not result in tuberculosis, and asymptomatic infections account for 90-95% [4]. In people with weakened immune systems, tuberculosis can cause infection [5]. Latent TB usually has no symptoms but causes mortality in half of the infected population among 10% latent infections [6]. Sputum coughing, fever, night sweats, chest pain, and weight loss pulmonary active symptoms [7].

TB is spread through an infected person with active pulmonary disease droplets released through coughing, sneezing, and then inhaled by another person [8]. It can also be transmitted by contaminated milk and meat. Tuberculosis treatment aims to cure patients, prevent TB deaths, and prevent the spread of *Mycobacterium tuberculosis* from infected people to the host community

[9]. Tuberculosis medical assessment involves exposure history, infections, and risk factors such as patient's physical examination, treatment plan medical information, HIV infection, sputum sample microbiological tests, and chest abnormalities detected through chest X-rays [10]. Tuberculosis treatment can be difficult for patients because it necessitates multiple drugs usage for at least half a year [10]. The typical treatment of TB comprises a 2-months intensive phase involving four drugs to quickly exterminate *Mycobacterium tuberculosis* [12]; and a 4-month continuation phase involving two drugs (isoniazid, rifampicin) to eradicate the remaining bacilli and avoid relapse [13]. World health organization targeted a global rate of 85% for successful treatment outcomes as treatment completed, cured, treatment failed, lost to follow-up, treatment success, cured plus completed treatment, and not evaluated [14]. Factors related to socio-demographic and economic, HIV, nutrition, and tuberculosis management and treatment strategies such as DOTS influenced the treatment outcomes [15, 16]. Limited research has been carried out on the factors associated with tuberculosis's poor treatment outcomes. Tuberculosis control strategy of both national and international programs could effectively implement interventions and manage tuberculosis with efficient protection interventions. Therefore, the present study aims were to assess the factors associated with treatment outcomes in patients of pulmonary tuberculosis.

MATERIALS AND METHODS

This cross-sectional study was carried out on 129 Tuberculosis patients in the department of Pulmonology, Gulab Devi Hospital Lahore from November 2020 to April 2021. Demographic details, clinical examination, and treatment outcomes were evaluated. All the data were extracted from the hospital medical records. Successful treatment outcomes predictors were assessed using bivariate and multivariate regression. Tuberculosis suspected patient’s sputum sample was composed in 5 ml sterile bottle within 15 ml another sterile bottle for infectious sample leakage prevention as per standard protocol. The laboratory technician labeled the sample and further processed it for necessary laboratory tests. Tuberculosis was diagnosed and monitored by fluorescence microscopy and staining with microscopic smears. Table-1 demonstrates the clinical cases and treatment outcomes standard definition as per the world health organization. The combination of complete treatment and cure was defined as treatment success while the loss to follow-up, mortality, and failed treatment was referred to as poor treatment.

The principal investor double-checked the collected data for completeness. Statistical Package for Social Sciences (SPSS) version 20 was used to enter data, clear it, and perform descriptive analyses. At the 95 percent confidence level, a binary logistic regression model was used to examine the relationship between treatment outcome and potential determinate variables. A p-value of less than 0.05 was deemed statistically significant.

Table-1 WHO Treatment outcomes standard definition

Treatment Outcomes	Standard Definition
Cured	Positive sputum-smears with negative bacteriology after treatment
Treatment Completed	Treatment completed but did not met cure criteria
Treatment Failure	A smears positive patients remains positive
Death	Patients mortality during study period for any reasons
Successful Treatment Outcomes	Completely cured patients
Unsuccessful Treat. Outcomes	Failure in treatment
Smears positive Pulmonary TB	Microscopic based two positive AFB sputum
Smears Negative Pulmonary TB	Symptoms suggestive TB but two negative sputum
Extra-pulmonary tuberculosis	Lymph nodes, genitourinary tract, abdomen, skin, the meninges, joints and bones, and others

RESULTS

Of the total 129 tuberculosis patients, 59 (46%) were male and 70 (54%) were females. The overall mean age was 26.54±5.62 years. The overall prevalence of successful treatment rate was 113 (87.6%). Out of 113, the prevalence of cured and complete treatment patients was 57 (50.4%) and 56 (49.6%) respectively. Based on logistic regression models, various parameters with their respective adjustment odds ratio (AOR) were as follows; age 21-40 years (AOR= 2.67, 95% CI=1.32-6.12, p-value=0.003), treatment category (AOR=4.62, 95% CI=1.12-16.74, p-value=0.027), and smear-positive pulmonary tuberculosis (AOR=3.47; 95% CI=1.76-6.69, p-value<0.001) were significantly related with treatment outcomes. Age and gender distribution are shown in Figures1 and 2 respectively. Of the total 129 TB patients, the prevalence of smear-positive, smear-negative, and Extra Pulmonary Tuberculosis (EPTB) were 63 (48.8%), 21 (16.3%), and 45 (34.9%) respectively as shown in Figure-3. The trend of TB patients’ treatment outcomes is shown inTable-2 while Table-3 shows the successful treatment outcomes predictor factors in enrolled tuberculosis patients.

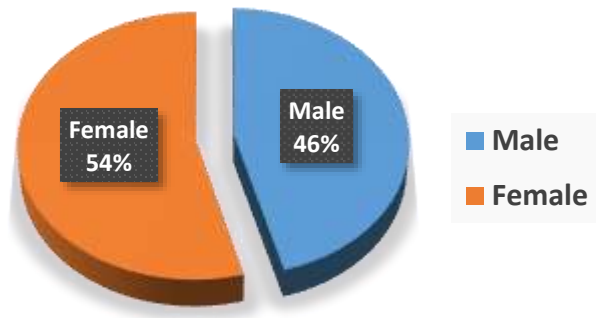


Figure-1 Gender Distribution (n=129)

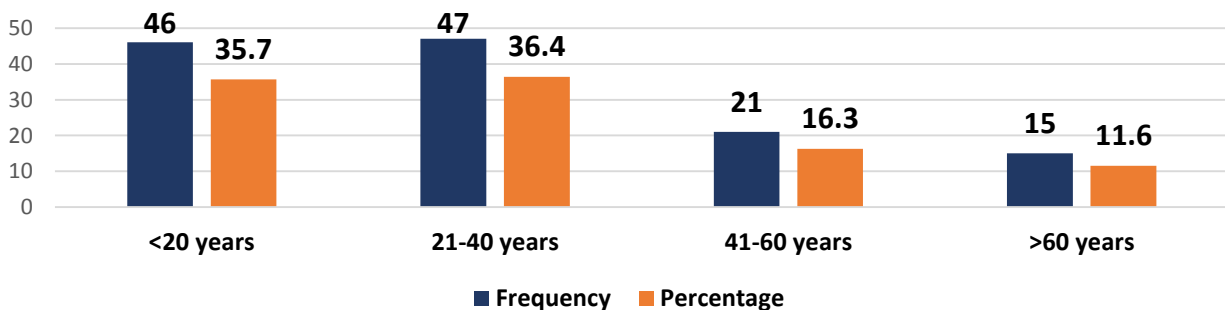


Figure-2- Age wise distribution (n=129)

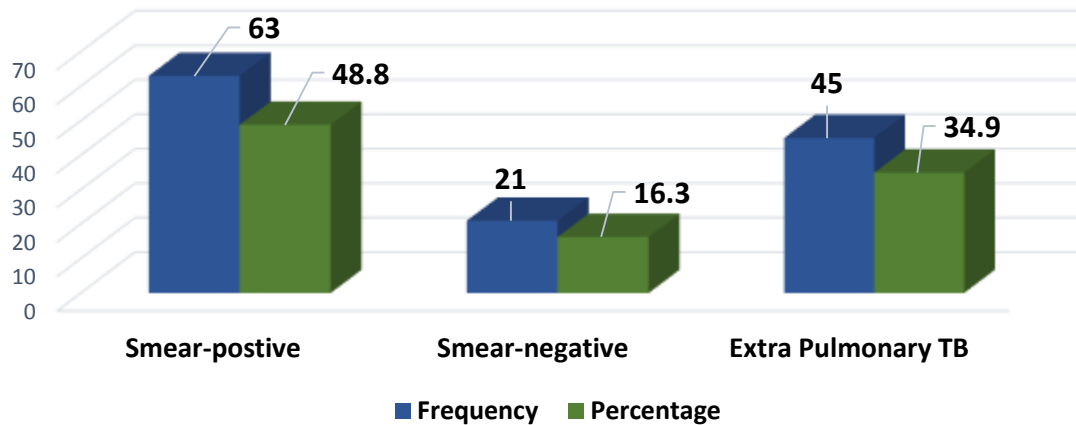


Figure-3 Prevalence of smear-positive, negative and EPTB (n=129)

Table-2 TB patient's treatment outcomes trends

Treatment Outcomes	Frequency (n)	Percentage (%)
Cured	57	50.4
Completed	56	49.6
Total Successful	113	87.6
Mortality cases	1	0.7
Unsuccessful	16	12.4
Defaulted	8	6.2
Transfer out	2	1.6
Unrecorded	6	4.7

Table-3 Successful treatment outcomes predictor factors

Parameters	TB cases (%)	Successful outcomes (%)	COR (95%CI)	P-value	AOR (95%CI)	P-value
Gender						
Male	59(46)	50(84.7)	0.09(0.46-1.31) 0.9	0.40	0.89(0.49-1.59) 0.9	0.79
Female	70(54)	63(90)				
Age (years)						
<20	46(35.7)	40(87.0)	3.2(1.6-6.9)	0.001	3.5(1.6-7.79)	0.002
21-40	47(36.4)	41(87.2)	2.8(1.4-5.71)	0.005	2.67 (1.3-6.12)	0.010
41-60	21(16.3)	18(85.7)	2.89(1.1-6.89)	0.015	2.79(1.1-7.41)	0.033
>61	15(11.6)	13(86.7)	0.9		0.9	
TB types						
Smear-positive	63(48.8)	57(90.5)	2.78(1.6-5.23)	0.00	3.47(1.76-6.69)	<0.001
Smear-negative	21(16.3)	18(85.7)	1.1(0.6-2.2)	0.812	1.2(0.6-2.50)	0.72
EPTB	45(34.9)	38(84.4)	0.9		0.9	
Patient Category						
New	117(90.7)	109(93.2)	0.61(0.06-4.61)	0.61	0.6(0.06-4.6)	0.51
Relapse	5(3.9)	3(60)	0.2(0.01-2.5)	0.22	0.21(0.01-2.5)	0.22
Others	7(5.4)	4(57)	0.9		0.9	
Treatment Category						
CAT-I	123(95.3)	110(89.4)	0.2(0.05-0.71)	0.01	4.62(1.76-6.69)	0.03
CAT-II	6(4.7)	3(50)	0.9		0.9	

DISCUSSION

The current study was conducted for the evaluation of treatment outcomes and identifying predictors of various treatment outcomes in TB patients. We discovered that the overall TB treatment success rate (i.e. having a cured or treatment completed outcome) at the end of the treatment was 87.6%, which is comparable to other low resources countries like Ethiopia (85.6%) [17], India (89-91 %) [18], Uzbekistan (88%) [19], Nigeria (89.4%) [20], Thailand (86.5–88.5%) [21], and higher than war-torn countries such as Somalia (81.8%) [22]. Also, the success rate of TB treatment outcomes was higher compared to preceding

Pakistani studies [23-24] however, still lower than the target set by the End Tuberculosis Strategy. Age, tuberculosis types, clinical factors, and demographic details were significantly related to TB patients' treatment outcomes. Improved TB diagnosis and treatment have been critical in reducing and forestalling millions of TB mortality each year. Yet, treatment programs for TB in Asian countries like Pakistan face a number of challenges that make them less effective than expected, and as a result, these factors become unsuccessful treatment outcomes. The successful and unsuccessful outcomes as well as the tuberculosis treatment outcomes were evaluated, which is critical to the national TB control strategy successful implementation.

According to the study's findings, the majority of TB patients were either cured or completed treatment; thus, the rate of successful treatment outcome in the study areas was 87.6%. Despite the fact that the majority of patients responded to the treatment, the rate of treatment success was lower than the national rate of 89.7% [25].

Our study found that patients under the age of 60 were nearly three times more likely to have a successful treatment outcome than patients over the age of 61. These findings matched with Ethiopia-based previous research [26]. This could be because a higher risk of mortality among old age patients or poor treatment outcomes might be caused by older patients more susceptible to chronic comorbidities such as hypertension, cancer, and cardiovascular disease. Other reasons for poor outcomes might be poor treatment adherence, the difficulty in visiting early at health facilities, and poor socioeconomic status in older patients. These findings emphasize the close follow-up facilitation for older patients in order to improve their treatment outcomes.

Another significant finding was that patients with smear-positive pulmonary tuberculosis were more prevalent to have a successful treatment outcome compared to other types of TB patients. This finding matched with previous research [27]. Smear-positive pulmonary tuberculosis patients may be easily diagnosed, receive prompt treatment, and be closely monitored by health professionals could be the reasons for successful outcomes. World health organization standards were followed for TB patients' treatment in the current study. Category I and II were the treatment categories whereas our study findings revealed that CAT-I patients were more prevalent in successful treatment outcomes compared to CAT-II.

The Tuberculosis smear-positive patients are potentially risky for others which may cause TB transmission to society. Tuberculosis progress could be minimized with its early detection, diagnosis, and treatment. The fatality rate was 0.7% lower than previously reported [28]. In contrast, the mortality rate in Pakistan might raise due to the lack of access to health facilities, poverty, lack of early diagnosis, and malnutrition in our community. The tuberculosis patient's mortality rate and unsuccessful treatment outcomes can be effectively mitigated with a better understanding of associated factors. According to the current study, the unsuccessful TB treatment risk increases with aging among new TB patients (whether smear-positive or smear-negative) over the age of 45. Other reports [29, 30] back this up. Older TB patients' unsuccessful treatment was primarily due to higher default and mortality rates [31]. According to Lefebvre et al., the most important determinant of death among TB patients is advancing age [32]. Additionally, older TB patients' atypical clinical manifestations, as well as other age-related diseases, can affect TB diagnosis, prominent to increased death in older patients [33]. As a result, specific strategies are required to address TB patients regarding TB management over the age of 45 in this study area.

CONCLUSION

Our study reported that the overall prevalence of successful treatment was 87.6%. Though, the rate of

overall successful treatment was found satisfactory, but, to meet international standard strategy for tuberculosis, still, improvement needs to be achieved. Age, treatment category, and tuberculosis types were significantly correlated with treatment outcomes.

REFERENCES

1. E. A. Tanue, D. S. Nsagha, T. N. Njamen, and N. J. C. Assob, "Tuberculosis treatment outcome and its associated factors among people living with HIV and AIDS in Fako Division of Cameroon," *PLoS One*, vol. 14, no. 7, pp. 1–14, 2019.
2. P. Narasimhan, J. Wood, C. R. Macintyre, and D. Mathai, "Risk factors for tuberculosis," *Pulmonary Medicine*, vol. 2013, Article ID 828939, 11 pages, 2013. [5] G. Aryee, E. Kwarteng, R. Essuman et al., "Estimating the incidence of tuberculosis cases reported at a tertiary hospital in Ghana: a time series model approach," *BMC Public Health*, vol. 18, no. 1, p. 1292, 2018.
3. B. Z. Katala, P. M. Mbelele, N. A. Lema et al., "Whole genome sequencing of mycobacterium tuberculosis isolates and clinical outcomes of patients treated for multidrug-resistant tuberculosis in Tanzania," *BMC Genomics*, vol. 21, no. 1, p. 174, 2020.
4. A. Zumla, E. Petersen, T. Nyirenda, and J. Chakaya, "Tackling the tuberculosis epidemic in sub-Saharan Africa - unique opportunities arising from the second European Developing Countries Clinical Trials Partnership (EDCTP) programme 2015-2024," *International Journal of Infectious Diseases*, vol. 32, pp. 46–49, 2015.
5. K. Floyd, P. Glaziou, R. M. G. J. Houben, T. Sumner, R. G. White, and M. Raviglione, "Global tuberculosis targets and milestones set for 2016-2035: definition and rationale," *The International Journal of Tuberculosis and Lung Disease*, vol. 22, no. 7, pp. 723–730, 2018.
6. A. Tola, K.M. Minshore, Y. Ayele, and A.N. Mekuria, "Tuberculosis treatment outcomes and associated factors among TB patients attending public hospitals in Harar town, Eastern Ethiopia: a five-year retrospective study," *Tuberculosis Research and Treatment*, vol. 2019, Article ID 1503219, 11 pages, 2019.
7. G. Abebe, Z. Bensa, and W. Kebede, "Treatment outcomes and associated factors in tuberculosis patients at Jimma University Medical Center: a 5-year retrospective study," *International Journal of Mycobacteriology*, vol. 8, no. 1, pp. 35–41, 2019.
8. G. Aliyu, S. S. el-Kamary, A. Abimiku, W. Blattner, and M. Charurat, "Demography and the dual epidemics of tuberculosis and HIV: analysis of cross-sectional data from sub-Saharan Africa," *PLoS One*, vol. 13, no. 9, p. e0191387, 2018.
9. A. K. Tetteh, E. Agyarko, J. Otchere, L. Bimi, and I. Ayi, "An evaluation of treatment outcomes in a cohort of clients on the DOTS strategy, 2012–2016," *Tuberculosis Research and Treatment*, vol. 2018, 7 pages, 2018.
10. S. A. Ohene, S. Fordah, and P. dela Boni, "Childhood tuberculosis and treatment outcomes in Accra: a retrospective analysis," *BMC Infectious Diseases*, vol. 19, no. 1, p. 749, 2019.
11. R. P. Frimpong-Mansoh, B. N. Calys-Tagoe, E. T. Coffie, and K. O. Antwi-Agyei, "Evaluation of the tuberculosis surveillance system in the Ashaiman Municipality of the Greater Accra Region," *Pan African Medical Journal Conference Proceedings*, vol. 1, 2018.
12. Gao J, Ma Y, Du J, Zhu G, Tan S, Fu Y, et al. Later emergence of acquired drug resistance and its effect on treatment outcome in patients treated with standard short-course chemotherapy for tuberculosis. *BMC Pulm Med*. 2016;16(1):26.

13. Gebrezgabihier G, Romha G, Ejeta E, Asebe G, Zemene E, Ameni G. Treatment outcome of tuberculosis patients under directly observed treatment short course and factors affecting outcome in southern Ethiopia: a five-year retrospective study. *PLoS One*. 2016;11(2):e0150560.
14. World Health Organization. Global tuberculosis report 2016. Available online: <http://www.searo.who.int/tb/documents/global-tuberculosis-report-2016/en/>. Accessed 21 Nov 2016.
15. Global Tuberculosis Report 2019. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO.
16. MacNeil A, Glaziou P, Sismanidis C, Maloney S, Floyd K. Global epidemiology of tuberculosis and progress toward achieving global targets-2017. *Morb Mortal Wly Rep*. 2019;68(11):263–6. <https://doi.org/10.15585/mmwr.mm6811a3>.
17. World Health Organization (WHO). Global tuberculosis report 2018. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0. IGO.
18. Khan MT, Malik SI, Ali S, Masood N, Nadeem T, Khan AS, et al. Pyrazinamide resistance and mutations in *pncA* among isolates of mycobacterium tuberculosis from Khyber Pakhtunkhwa, Pakistan. *BMC Infect Dis*. 2019;19: 116. <https://doi.org/10.1186/s12879-019-3764-2>.
19. Ahmad T, Zohaib DM, Zaman Q, Saifullah JMA, Ismail M, Tariq M, et al. Prevalence of tuberculosis infection in general population of district Dir (lower) Pakistan. *Middle-East J Sci Res*. 2015;23(1):14–7. <https://doi.org/10.5829/idosi.mejrs.2015.23.01.91145>.
20. Ahmad T, Jadoon MA, Khattak MN. Prevalence of sputum smear positive pulmonary tuberculosis at Dargai, district Malakand, Pakistan: a four year retrospective study. *Egyptian J Chest Dis Tuberc*. 2016;65(2):461–4. <https://doi.org/10.1016/j.ejcdt.2015.12.004>.
21. Lalokhil MS, Khan A, Adnan M, Khan MI. Prevalence of pulmonary tuberculosis in district Mardan Khyber Pakhtunkhwa, Pakistan. *Microbiology*. 2019;3(1):1–7.
22. Ahmad T, Haroon KM, Khan MM, Ejeta E, Karami M, Ohia C. Treatment outcome of tuberculosis patients under directly observed treatment short course and its determinants in Shangla, Khyber-Pakhtunkhwa, Pakistan: a retrospective study. *Int J Mycobacteriol*. 2017;6:360–4. https://doi.org/10.4103/ijmy.ijmy_69_17.
23. Atif M, Anwar Z, Fatima RK, Malik I, Asghar S, Scahill S. Analysis of tuberculosis treatment outcomes among pulmonary tuberculosis patients in Bahawalpur, Pakistan. *BMC Res Notes*. 2018;11(1):370. <https://doi.org/10.1186/s13104-018-3473-8>.
24. Abbasi S, Tahir M. Effectiveness of directly observed therapy short course (DOTS) in patients with tuberculosis registered at Federal General Hospital, Islamabad. *Int J Infect Dis*. 2018;73:1. <https://doi.org/10.1016/j.ijid.2018.04.4194>.
18. Block Wise Provisional Summary Results of 6th Population & Housing Census-2017.
25. World Health Organization. Treatment of tuberculosis: guidelines for national programmes, third edition. Revision approved by STAG, June 2004. WHO/CDS/TB/2003.313. [Retrieved on 06-02-2019].
26. Centers for Disease Control and Prevention. Treatment of tuberculosis, American thoracic society, CDC, and infection diseases Society of America: treatment of tuberculosis. *Morb Mortal Wkly Rep*. 2003;52:1–77
27. Pai M, Behr MA, Dowdy D, Dheda K, Divangahi M, Boehme CC, et al. Nature reviews disease primers. *Tuberculosis*. 2016;2:16076. <https://doi.org/10.1038/nrdp.2016.76>.
28. Ramya VH, Gayathri G, Gangadharan V. A study of treatment outcomes of pulmonary tuberculosis and extrapulmonary tuberculosis patients in a tertiary care Centre. *Int J Adv Med*. 2017;4(4):1133–7. <https://doi.org/10.18203/2349-3933.ijam20173246>.
29. Akarkar NS, Pradhan SS, Ferreira AM. Treatment outcomes among tuberculosis patients at an urban health Centre, Goa, India- eight year retrospective record based study. *Int J Comm Med Public Health*. 2017;4(3): 831–4. <https://doi.org/10.18203/2394-6040.ijcmph20170767>.
30. Trivedi PR, Khakhkhar TM. Treatment outcome of tuberculosis patients under directly observed treatment short-course and factors affecting the outcome in tertiary care hospital. *Int J Basic Clin Pharmacol*. 2019;8(5):981–6. <https://doi.org/10.18203/2319-2003.ijbcp20191588>.
31. Sakajiki MA, Garba B, Ibrahim Y, Mohammed BA, Abdullahi U, Sada KB, Ibrahim TM. Treatment outcome of tuberculosis at a specialist hospital in North Western Nigeria - a 30 months retrospective study. *Pakistan J Chest Med*. 2018;24(1):04–9.
32. Somsong W, Lawpoolsri S, Kasetjaroen Y, Manosuthi W, Kaewkungwal J. Treatment outcomes for elderly patients in Thailand with pulmonary tuberculosis. *Asian Biomed*. 2018;12(2):75–82. <https://doi.org/10.1515/abm2019-0004>.
33. Ali MK, Karanja S, Karama M. Factors associated with tuberculosis treatment outcomes among tuberculosis patients attending tuberculosis treatment centres in 2016–2017 in Mogadishu, Somalia. *Pan Afr Med J*. 2017;28:197. <https://doi.org/10.11604/pamj.2017.28.197.13439>.