# Determinants of Tuberculosis Treatment Success and Death in Nepal: Evidence from e-TB Surveillance Data

Research Report Prepared by Dr. Sharad Kumar Sharma Undersecretary (Statistics)



Government of Nepal

Office of the Prime Minister and Council of Ministers

## Result Management Division

Statistics Section 2078 Ashoj

# Determinants of Tuberculosis Treatment Success and Death in Nepal: Evidence from e-TB Surveillance Data

## Abstract

## Background

Tuberculosis remains a major cause of ill health around the globe, mainly in developing countries including Nepal. National Tuberculosis Center has been collecting and analyzing tuberculosis case finding and treatment outcome information at the aggregate level but factors associated with treatment success and death using individual-level data is not well explored.

## Objective

To examine individual socio-demographic and clinical as well as geographic determinants of TB treatment success and death.

## Method

Tuberculosis case finding and treatment outcome data reported in electronic tuberculosis register during 2013-2018 was used for the analysis. Cross-tabulation and binary logistic regression analysis were carried out to examine the relationship.

## Result

A total of 66,625 tuberculosis patient information were reported in the electronic register, but treatment outcome information were available only for 28,960 patients. Overall, 87.5% of the patient had successful TB treatment, 5.3% patient died and remaining were treatment failure, lost to follow up and not evaluated. Patient with younger age, female, non-dalit and Muslim, living in Karnali and Province2, extra-pulmonary and pulmonary clinically diagnosed, treated with category1 drug, and without HIV infection were associated with the increased odds of tuberculosis treatment success. While, older age, male, Dalit, living in Gandaki and Sudurpaschim Province, with pulmonary bacteriologically confirmed, treated with category2 drug, and tuberculosis patient with HIV infection had increased odds of death.

## Conclusion

Tuberculosis patient with above characteristics should be considered as high-risk group and efforts should be intensified for early identification and management including targeted interventions among these groups.

Key words: Death, Determinants, Nepal, Treatment Success, Tuberculosis

## INTRODUCTION

Tuberculosis (TB) is a major cause of ill health and is one of the top ten causes of death globally. It is estimated that about 10 million people infected with TB and 1.2 million people died due to TB in 2019 around the globe.<sup>1</sup>

Estimated incidence of TB in Nepal is 245 (per 100000 population).<sup>2</sup> According to the estimate, about 69000 people develop TB every year.<sup>3</sup> However, in 2019, only about 32,043 TB patients were notified and more than a half (54%) of the expected TB patient were missed.<sup>4</sup> National Tuberculosis Program (NTP) should be able to find these missing TB patients and provide appropriate care so as to meet the Sustainable Development Goal (SDG) of reducing TB incidence to 20 (per 100000 population) in 2030.<sup>5</sup> For this, NTP should have a clear understanding of the factors associated with tuberculosis case finding, treatment success and death.

World Health Organization (WHO) suggests that HIV infection, malnutrition, smoking, diabetes, alcohol abuse and indoor pollution are the population level risk factors of TB and these risk factors are affected by the individual socio-economic status and other distant determinants including health system and factors beyond health system.<sup>6</sup> Patient age, gender, education, marital status, employment status, patient type, treatment category, sputum examination result, HIV status, use of tobacco and alcohol, place of residence, type of treatment, are common variables used to examine determinants of TB treatment outcome in previous studies.<sup>7-13</sup> Integrated Health Information Management System (IHIMS) is the main source of data to monitor NTP progress; however, this system can monitor only few aggregated NTP indicators. To capture detail individual disaggregated information, NTP has developed web-based e-TB register as a tool for recording, analyzing and reporting TB patient details, treatment history and outcome.<sup>14</sup>

During the period between 2013 -2018 some 66625 patient's record have been entered in online eTB register, however, detail analysis has not yet conducted. TB information entered in the eTB register has potential to examine the association of TB treatment success and death with individual socio-demographic, household, geographical and clinical characteristics, but this is

not yet explored. Objective of this paper is to provide comprehensive evidence for NTP by looking at the national level cohort of TB patient registered in eTB data and investigate factors associated with success of TB treatment as well as death among TB patient.

## **METHODS**

This paper is based on the retrospective analysis of case finding and treatment outcome of TB patients reported in eTB register during 2013 to 2018. The eTB register is a web-based application to record information of paper based TB treatment register in electronic form. Main function of the eTB register is to capture the case base information. NTP initiated eTB register in 2016, and at the time of roll out, district TB focal persons entered the case base information of TB patients registered in NTP. eTB system has been disrupted currently after transition of Ministry of Health and Population to federal system. However, NTP has committed to rollout the eTB system at all local level governments (LLG) during the fiscal year 2019/20.<sup>4</sup> A total of 66625 TB patients information were entered in the eTB register. However, sputum conversion and treatment outcome information was not complete for all the TB patient. Treatment outcome information was available only for 28960 TB patients, which were used for analysis.

Among the potential determinants for TB treatment success and death suggested by WHO and other previous studies,<sup>7-13</sup> age, gender, ethnicity, place of residence, TB type, registration type, treatment category and HIV status were the only variables available for analysis in eTB data. These variables were included as the explanatory variables in this analysis. Association of these explanatory variables with outcome variables, TB treatment outcome (measured by treatment success) and death among TB patients were examined.

#### Operational definition of key outcome and explanatory variables

National Tuberculosis Programme Nepal-General Manual, third edition, 2012, National Tuberculosis Management Guideline, 2019<sup>15</sup> and Tuberculosis Management Basic Training Manual, 2020<sup>16</sup> were used to define the TB treatment outcome, TB registration type, TB type, TB treatment category and other explanatory variables. The operational definition of key outcome and explanatory variables are as follows.

#### **TB treatment outcome:**

- **Cured:** A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear-negative in the last month of treatment and on at least one previous occasion.
- **Treatment completed:** A TB patient who completed treatment without evidence of failure but with no record to show that sputum smear result in the last month of treatment and on at least one previous occasion were negative, either because test were not done or because result are unavailable.
- **Treatment failed:** A TB patient whose sputum smear was positive at month 5 or later during treatment. Also applies to smear negative patient and Extra Pulmonary (EP) TB patient who become smear positive at 2 months.
- **Died:** A TB patient who dies for any reason before starting or during the course of treatment.
- Lost to follow-up: A TB patient who did not start treatment or whose treatment was interrupted for two consecutive months or more.
- Not evaluated: A TB patient whose treatment outcome was not assigned. This includes cases that were transferred out to another treatment center as well as cases for whom the treatment outcome is unknown to the reporting unit.
- **Treatment success:** Treatment success was defined as the sum of cured and completed treatment.
- **Treatment not successful:** Treatment not successful was defined as all other treatment outcome, including treatment failed, died, loss to follow up and not evaluated.

## **Tuberculosis type:**

- **Pulmonary bacteriological confirmed (PBC):** It is one form of Pulmonary TB cases whose sputum specimen was positive by smear microscopy, culture or WHO-recommended rapid diagnostics-WRD such as Xpert MTB/RIF.
- **Pulmonary clinically diagnosed (PCD):** It was the Pulmoanry TB cases who does not fulfill the criteria for bacteriological confirmation but had been diagnosed with active TB by a health worker based on strong clinical evidence and has decided to give the patient a full course of TB treatment.

• Extra-pulmonary (EP): It was any bacteriologically confirmed or clinically diagnosed TB involving organs other than the lungs, such as, pleura, lymph nodes, abdomen, genitourinary tract, skin, joins, bones etc.

## **Registration type:**

- New: TB patient who have never been treated for TB or have taken anti-TB drug for less than one months
- **Re-treatment:** Previously treated patients who have received one month or more of anti-TB drugs in the past.
- **Transfer-in:** TB patients taking TB medication from a health facility and transferred to the other facility for continuation of TB treatment.

## **Tuberculosis treatment category:**

- **Category 1 (Cat 1):** This treatment category was for newly diagnosed sputum positive PTB, sputum negative PTB with extensive parenchymal involvement, and severe form of EPTB treated with of Fist line Anti-TB drugs \*(FLD).
- Category 2 (Cat 2): This treatment category was for treatment of previously treated patients (failure case, relapse case and return after interruption) treated with FLD. It is to be noted that this regimen has been revised now and Cat 2 is no longer used.
- **Category 3 (Cat 3):** This treatment category was for sputum negative PTB within minimal involvement (other than those in Category 1) and less severe form of EPTB, who are treated with FLD.

\*Note: All the above mentioned category 1, 2 and 3 are used for the treatment for Rifampicin sensitive TB and separate categories and regimens were used for the treatment of MDR/RR TB Rest of the variables included in the analysis are self-explanatory.

## Statistical analysis:

Stata15 was used for data analysis.<sup>17</sup> Frequency and percentage were used to summarize the socio-demographic characteristics of TB patient and their clinical profile, and treatment outcome. The relationship between the outcome variables (TB treatment success and death among TB patients) and explanatory variables (socio-demographic and clinical characteristics of TB cases) were examined using cross-tabulation. Multiple binary logistic regression analysis was used to examine the association between explanatory and outcome variables. The adjusted odds

ratio (aOR) and corresponding 95% confidence interval (CI) and p-values were reported for each explanatory variables. P-value of less than 0.05 was considered statistically significant.

## **Ethical consideration:**

Secondary data with personal information and patient identifier removed was used for this paper. All cases included were anonymized and thus written consent from individual patient were not sought. The e-TB data was owned by NTCC, which gave permission to use the data for this paper.

#### **RESULTS**

A total of 66625 cases were entered in the eTB database from FY 2013/14 to FY2018/19. About 37665 cases with unknown treatment outcome were excluded from analysis. Thus, the analysis was based on 28960 TB cases. The mean age of the patients was  $39.9 \pm 19.6$  years. About twothird (64%) of the patients were male, about one-third (33%) were Janjatis, slightly more than a quarter were Brahmin/Kshetri (28%), and about 15% were Dalit and Madhesi. More than a quarter TB cases were from Lumbini Province (27%), more than a half (55%) were pulmonary TB cases, new patients constituted 88% and more than 9 in 10 (91%) cases were in Cat1 treatment. About one percent were HIV positive, about a half (47%) were HIV negative confirmed and HIV status was not known among more than a half of the TB cases (52%). During the assessment period, 3% TB cases were lost to follow up and 3% were not evaluated (Table 1). Trend of the outcome of the treatment among the TB cases entered in the eTB register are presented in Figure 1 and Figure 2. While treatment success rate remained constant at around 87% and loss to follow-up remained constant at around 3% (Figure 1), after FY 2014/15, there has been gradual increase in percentage of death due to TB (from 4.3% in FY 2014/15 to 9.6% in FY2018/19), and treatment failure (from 0.6% in FY 2014/15 to 1.1% in FY2018/19) (Figure 2). Overall, treatment success was 87.5% and 5% patient died among those with TB. Other patients with un-successful treatment include loss to follow up (3%), not evaluated (3%) and treatment failed (1%).

#### Factors associated with treatment success and death

The result from multiple logistic regression analysis on the factors associated with TB treatment success and death due to TB are presented in Table 2. Among the explanatory variables included in the analysis, age, gender, ethnicity, province of residence, TB type, TB category and HIV

status were statistically significantly associated with both TB treatment success and death among TB patient. Registration type was not found to be associated with TB treatment success. The logistic regression result further indicates that patient who were older than 15 years had lower odds of having successful TB treatment and higher odds of death due to TB compared to the patient with age under 15 years. In other words, TB patients of age 15-64 year had 2 times higher odds and patient of age 65 or more years had 8 times higher odds of death due to TB compared to those who were of age below 15 years.

TB treatment success and death among TB patient also varied by gender. Male were significantly less likely to have successful TB treatment (aOR, 0.81) and more likely to die (aOR, 1.20) compared to female.

With regard to ethnicity, Janjati, Madhesi and Brahmin/Kshetri had higher odds to Dalit, whereas Muslim had lower odds of successful TB treatment compared to Dalit (aOR of Janjati, 1.46; aOR of Madhesi, 1.18 aOR of Brahmin/Kshetri, 1.44 and aOR of Muslim, 0.84). Similarly, Janjati and Brahmin/Kshetri had lower odds of death due to TB compared to Dalit (aOR of Janjati, 0.74; aOR of Brahmin/Kshetri, 0.74).

Significant geographical variation in success of TB treatment and death was also observed. While TB patient living in Province2 and Karnali were significantly more likely to have a successful TB treatment compared to those living in Province1 (aOR of Province2, 1.37; aOR of Karnali, 1.40). TB patients living in Gandaki and Sudurpascim province were significantly more likely to die due to TB compared to those living in Province1 (aOR of Gandaki, 1.30; aOR of Sudurpaschim, 1.35). Likewise TB patient living in Bagmati were less likely to die due to TB compared to those living in Province1 (aOR of Bagmati, 0.75).

TB type, TB category and HIV status were also significant predictors of successful TB treatment and death among TB patient. Pulmonary TB patients who were clinically diagnosed (PCD) and extra-pulmonary (EP) TB patient had higher odds of successful TB treatment (aOR of PCD, 1.18; aOR of EP, 1.25) and EP TB patient had lower odds of death due to TB (aOR of EP, 0.86) compared to Pulmonary Bacteriologically Confirmed (BCB) patients. Finally, TB patient who

were HIV positive were significantly less likely to complete TB treatment (aOR, 0.91) and more likely to die due to TB (aOR, 1.14) compared to those who were not HIV positive.

#### DISCUSSION

In this paper, the factors related to success of TB treatment and death among TB patient in Nepal was examined using the NTP surveillance data collected and entered in the eTB register during FY2013/14 - FY2018/19. Among 28960 TB patient with treatment outcome information available, almost nine in ten (87.5%) TB patient had a successful TB treatment outcome and 5% TB patient died.

The treatment success rate, cure rate and default rate remained similar over the analysis period; however, there has been some increase in treatment failure and death rate. The TB treatment success and death among TB patient as well as TB type and HIV positive percentage observed in this analysis is similar to that shown in the most recent NTP annual report published in 2020.<sup>4</sup> The TB treatment success rate observed in this analysis as well as overall treatment success rate shown in national NTP annual report is more than the global TB treatment success target of 85% or more.<sup>8</sup> However, the reported treatment success rate of all form of TB is in declining trend in Nepal (from 91% in FY2015/16 to 89% in FY 2019/20).<sup>4</sup> One of the reasons for this decline could be due to the impact of COVID-19 pandemic. The other potential reasons for this lower level of TB treatment success could be due to delay in receiving care as a result of stigma, lack of true knowledge on TB sign and symptoms, inadequate community involvement in TB care, lack of treatment supervised and forget to administer daily DOT. Additional reasons could be; delayed diagnosis, faulty diagnosis, increasing co-morbidities with more deaths among elderly resulting in negative outcome, daily DOT mechanism till in place as policy at most place, insufficient patient support and rehabilitation, poor support, stigma and discrimination at community level.

The analysis also indicated that observed percentage of death among TB patient is 5%, which is in line with the global target of less than 6% case fatality rate (CFR) to achieve the 2025 global milestone for reductions in TB death.<sup>18</sup> NTP annual report FY2018/19 also shows that reported death rate due to TB remained 3% over the past three years.<sup>4</sup> Thus, the challenge for NTP is to

increase TB treatment success rate and maintain death rate due to TB at this level or to decrease further. For this, NTP has to identify the important social determinants of TB treatment success and death in Nepal.

Patient age has also been identified as an important determinant of treatment success and death in other countries.<sup>6,19</sup> Previous studies indicated that people with lower literacy levels and with family history of TB were at increased risk of acquiring TB,<sup>20</sup> and patients who were less than 35 years old were more likely to have successful treatment outcomes compared to older.<sup>7</sup> Our analysis also showed that the treatment success decreased and death among TB patient increased with age. Higher loss to follow up, severe TB morbidity along with other co-morbidities, higher family responsibility, limited family support leading to non-compliance to TB medication could be the reasons behind the lower treatment success and higher death among older patient.<sup>10-16,21</sup> Similar result was observed in other studies conducted in Brazil, Nigeria, and other resource limited settings.<sup>22-24</sup>

We found that male were less likely to have successful TB treatment and more likely to die. This is a common global phenomenon and similar finding was reported in other countries such as Malaysia, <sup>25</sup> Mozambique, <sup>26</sup> and Ethiopia.<sup>27</sup> Reasons for the low treatment success and high death due to TB among male is not quite clear, however it is speculated that male are more likely than female to be exposed to the diseases or have better access to health service. In addition, higher rates of death among men may also be related to smoking. STEPS Survey 2019 indicates that prevalence of any tobacco use was significantly higher among men (48%) than among women (12%). Men also have high co-morbidities like diabetes, HIV and COPE, which are all co-morbidities for TB and are higher in men accordingly.<sup>28</sup> It is also likely that women might have under-reported their disease and have less access to health service because of socio-economic constraints.<sup>10</sup>

Ethnicity has been well recognized as an important social determinant of TB and TB treatment outcome in global literature.<sup>6</sup> However, ethnic disparity on TB treatment outcome and death is not well examined in Nepalese context. We found that, both the TB treatment success and death among TB patient varied across the ethnicity. Dalit and Muslim were relatively less likely to

have successful TB treatment. Janjati, Madhesi and Brahmin had higher odds of TB treatment success than Dalits. Muslim had even lower odds of TB treatment success than Dalits. Likewise, Janjati and Brahmin had lower odds of death due to TB than Dalit. Muslim had higher odds of death due to TB than Dalit, although it was not significant. A study conducted in Brazil also showed similar result of ethnic-racial disparity in TB incidence and treatment follow-up. The burden of TB was higher among indigenous and black people compared to other categories.<sup>29</sup> This ethnic variation in the TB indicators was explained by poor living condition, lower income and limited access to health services among black and indigenous population. In addition, indigenous homes are small and crowded, with little natural light and ventilation, contributing to enabling environment and preservation and spread of the TB bacillus.<sup>30</sup>

Historically, Dalits have been facing social, economic and political discriminated in Nepal. A study conducted in Nepal to examine health care access for Dalit found that they lacked access to health care, health information about disease and medicine. They also face financial barrier as well as discrimination and lack of social capital in comparison to non-Dalit.<sup>31</sup> Similarly, further analysis of Nepal Demographic and Health Survey data collected in 2006 and 2011 indicated that Dalit, Muslim and Terai/Madhesi group had consistently low level of modern maternal and child health and other social indicators.<sup>32,33</sup> This could be due to their preference to traditional health care practice, including visiting faith healers, as they are available immediately in time of ill health. Lack of knowledge on health care service as well as low decision making power due to traditional belief were other possible reasons for preventing Muslim and Dalits from utilizing modern health care services.<sup>34</sup> It is also evident that extreme poverty, unemployment and low income coupled with high prevalence of malnutrition-contribute to high TB burden in the ethnic minority population which further aggravated by higher stigma and discrimination in this group. Low level of education is closely associated with the poor socio-economic condition that further increase their vulnerability to TB infection and other disease related to poverty.<sup>29</sup> Thus, to reduce the ethnic inequality in notification and treatment of TB, it is crucial to involve multisector government bodies in design, implementation and development of control strategies and to encourage social development initiative to improve the general living condition and health of the area specific segments of the population including stigma reduction where TB is an important public health problem.<sup>29</sup>

We also found that both TB treatment success and death varied across geographical region. While Province2 and Karnali Province had higher odds of treatment success than Province1, Gandaki and Sudurpaschim Province had higher odds of death due to TB and Bagmati Province had lower odds of death among TB patient compared to Province1. This variation of treatment success and death across Provinces could be due to differences in ability of clinical diagnosis, access to TB care, and effectiveness of provincial surveillance system.<sup>35</sup> However, true reasons behind the provincial variation in TB treatment success and death need to be explored further. A study conducted in Uganda suggests that lack of motivated and dedicated TB focal persons, lack of funding to implement TB activities and poor implementation of community-based DOTS are common barriers found in the districts with low rate of treatment success.<sup>36</sup> The facilitators of the high treatment success districts include practice of using data to make decisions and designing interventions, continuous quality improvement, capacity building and prioritization of better management of people with TB.<sup>36</sup> These factors should be taken into consideration while implementing intervention to make active and passive TB case finding more effective in Nepal. Type of tuberculosis, registration category, category of treatment regimen and HIV status among TB patient are immediate determinants of Tuberculosis treatment success and death. We found significant association of TB type with treatment success and death. Clinically diagnosed pulmonary (PCD) TB patient as well as extra-pulmonary (EP) TB patients had higher odds of treatment success compared to bacteriologically confirmed pulmonary (PBC). Similarly, the EP TB patient had lower odds of death. This result contradicts with the result found in Nigeria in which, no difference of TB treatment success was found between PTB and EPTB patients.<sup>7</sup> Other studies conducted in Ethiopia and Malaysia showed that smear negative and EP TB patient had higher odds of unsuccessful TB treatment.<sup>25, 37</sup> Reason of this contradictory result in association of TB type and treatment outcome in Nepal and other countries is not clear and therefore need further exploration. The reason could be over-diagnosis of EPTB where the treatment was given and completed and in fact, it might not have been TB. Poor utilization of Xpert testing before 2018 and minimal utilization of X-ray probably led to over diagnosis and when we do not know that signs and symptoms are just not significant enough for diagnosing TB. However, a study conducted in Korea indicated that smear positive pulmonary TB was independently associated with high mortality. Having advanced disease among pulmonary positive TB patient was given reason for higher mortality among such patients.<sup>38</sup>

We also found that TB treatment success and death varied across the TB treatment category. Patient in category II treatment were less likely to have successful TB treatment and more likely to die. This is because Cat II was initiated without checking for Rif resistance due to limited testing capacity at that time, resulting in adding single drug (streptomycin) is already failing regimen in population where drug resistance was nearly 15%,<sup>39</sup> hence leading to poor treatment outcomes. This was later revised and Cat II with streptomycin has been phased out. With regard to the association of TB registration type with treatment outcome and death, we found no significant difference across the TB registration categories for TB treatment outcome. However, transfer- in patients were significantly less likely to die compared to other categories of TB patients.

In our analysis, HIV status was significantly associated with both the TB treatment success and death. TB patient who were HIV positive were 0.91 times less likely to have successful TB treatment and 1.14 times more likely to experience death. This could be mainly because of compromised immune system among HIV infected people. However, drug burden among HIV infected patient taking ART has been shown to affect adherence to treatment.<sup>7</sup> Similar finding of poor treatment outcome among HIV infected TB patient was reported by other studies.<sup>25, 37, 40</sup> This study has several limitations. First, the data used in analysis of this study did not include complete list of TB patient in the district. This include only the TB patient, which were entered in the eTB register and treatment outcome result were available. This was a retrospective study based on data extracted from clinical record and excluded non-clinical cases such as the death of TB patient occurred in the community. The data also lacked the information of TB patient and provider perspectives, as they were not interviewed. Second limitation of this study is that it included only the variables available in eTB data. Therefore, certain important social and clinical determinants of TB treatment success and death were missing. For example, socio-economic status of TB patient (education, employment, income etc.), existing co-morbidity (diabetes, malnutrition), TB patient risk behavior (smoking, alcohol and drug use) were not available in the data set. Further studies should look at these important variables for comprehensive analysis to examine determinants of TB treatment success and death. Inclusion of these variables in NTP surveillance will enhance the documentation and identification of risk factors for TB and implementing interventions to prevent TB transmission in community in the future. Third

limitation of this study is that treatment outcome of 57% of the patient entered in eTB register were unknown and we could not use these cases in the analysis, this may have contributed to over or under estimation of our result.

#### CONCLUSION

We found that various individual, social, geographical and clinical variables were associated with TB treatment success and death. The factors increasing the odds of TB treatment success include younger age, female, non-Dalit and Muslim ethnicity, Karnali Province and Province1, being an extra-pulmonary and pulmonary clinically diagnosed TB case, getting category1 TB drug and HIV status negative case. Similarly, the factors increasing the odds of death include, older age, male, Dalit ethnicity, occupant of Gandaki and Sudurpaschim Province, being pulmonary bacteriologically confirmed case, getting category2 drug and being HIV positive. These TB cases should be considered as high-risk group and pay more attention during management and treatment and targeted interventions should be carried out. Various policy recommendations for improving Tuberculosis program management are given.

#### Recommendations

- To improve treatment success and reduce death among older population, program should focus on early diagnosis of TB among these population, develop effective adherence support mechanic like community based DOTS approach with focused monitoring and management of TB among older population. In addition, in consultation with geriatric specialists, develop comorbidity management policy and implement interventions for effective management of TB among old age population among older population.
- Develop guideline on TB-HIV collaborative activities to effectively deliver integrated TB-HIV service and effectively implement mandatory provision of HIV testing among TB patients to improve treatment success and reduce death among HIV infected TB patients. Strengthen similar approach for TB-Diabetes program.
- As TB treatment success and death varies across provinces, deeper knowledge about need and condition of people in different places should be gained before designing implementing program interventions for management and care for TB patients. Effective counseling on TB medication and treatment adherence should be provided through trained service providers in local language.

- Designing messages in local languages, mobilization of TB service providers who are from local community, speak local language and know local cultural norms can be some strategies to improve TB treatment outcome among people living in hard to reach areas.
- Dalit, Muslim, and other minority groups face some physical, financial, stigma and information related barriers to access TB related information and care. Therefore, government should implement targeted interventions to empower them socially and economically. This will improve access to health information and service to these minority groups. Local level providers should be trained to communicate effectively and respectful manner among ethnic minority groups.
- Regular monitoring and supportive supervision of TB diagnosis and treatment center, wide spread health education through various media, contact tracing of bacteriologically positive TB patient and targeted TB screening among high risk groups are other cost effective interventions recommended to improve case notification and treatment outcome in Nepal.
- Additional study should be conducted by using comprehensive framework to include all social determinant of TB to identify root cause of low treatment success and high death due to TB.

## ACKNOWLEDGEMENT

The authors wish to acknowledge the NTCC team specially Pushpa Raj Joshi for his generous support while preparing data and literature review. We are also thankful to previous NTCC directors, all the staffs working in DOTS centers, DR hostels, DR centers and sub-centers, TB lab network, TB focal persons, Global Fund, Save the Children and all Sub-recipients for directly and indirectly supporting to develop and manage the e-TB data.

#### REFERENCES

- World Health Organization. 2020. Global Tuberculosis Report 2019. Geneva, Switzerland: WHO. CCBY-NC-SA3.01G0. <u>https://www.who.int/publications/i/item/1789240013131</u>.
- National Tuberculosis Control Center. 2020. National Tuberculosis Prevalence Survey 2018-19. Thimi, Bhaktapur, Nepal: NTCC. <u>http://nepalntp.gov.np/wp</u> content/uploads/2021/03/ntps-report-bodypages.pdf.
- National Tuberculosis Control Center. 2020. National Tuberculosis Prevalence Survey 2018-19 Brief. Thimi, Bhaktapur, Nepal: NTCC. <u>http://nepalntp.gov.np/wp-</u> <u>content/uploads/2020/03/nepal-national-tb-prevalence-survey-brief-March-24-2020.pdf</u>.
- National Tuberculosis Control Center. 2020. National Tuberculosis Profile FY2076/77. Thimi, Bhaktapur, Nepal: NTCC. <u>http://nepalntp.gov.np/wp-</u> content/uploads/2021/04/factsheet\_final.pdf.
- National Planning Commission. 2017. Sustainable Development Goals Status and Road Map: 2016-2030. Singhadurbar, Kathmandu, Nepal: NPC. <u>http://sdg.npc.gov.np/resource/2659/</u>.
- World Health Organization. 2010. Equity, Social Determinants and Public Health Program. Geneva, Switzerland: WHO. <u>https://apps.who.int/iris/bitstream/handle/10665/44289/</u> 9789241563970/eng.pdf?sequence=1&isAllowed=y.
- Umeokonkwo CD, Okedo-Alex IN, Azuogu BN, Utulu R, Adeke AS, Disu YO. Trend and determinants of tuberculosis treatment outcome in a tertiary hospital in Southeast Nigeria. *Journal of Infection and Public Health.* 2020, 13:1029-1033.
- Diefenboch-Elstob T, Plummer D, Dowi R, Wamagi S, Gula B, Siwaeya K, Pelowa D, Siba P, Warner J. The social determinants of tuberculosis treatment adherence in a remote region of Papua New Guinea. *BMC Public Health*. 2017, 17:70. Doi10.1186/s12889-016-3935-7.
- 9. European Center for Disease Prevention and Control. 2018. Social Determinants and Risk Factors in Tuberculosis Surveillance in the EU/EEA. Stockholm: ECDC. <u>https://www.ecdc.europa.eu/en/publications-data/social-determinants-and-risk-factors-tuberculosis-surveillance-eueea</u>.
- Tola A, Minshore KM, Ayele Y, Mekuria AN. Tuberculosis treatment outcome and associate factors among TB patients attending public hospital in Harar town, Eastern Ethiopia: a fiveyear retrospective study. *Tuberculosis Research and Treatment*. 2019, Article ID 1503219. https:// doi.org/10.1155/2019/1503219.

- Tanue EA, Nsagha DS, Njamen TN, Assob NJC. Tuberculosis treatment outcome and its associated factors among people living with HIV and AIDS in Fako Division of Cameroon. *Plos ONE*. 2019, 14(7):e0218800. <u>https://doi=org/10.1371/journal.pone.0218800</u>.
- Hargreaves JR, Boccia D, Evans CA, Adato M, Petticrew M, Porter JDH. The social determinants of Tuberculosis: from evidence to action. *American Journal of Public Health*. 2011, 10(4). doi:10.2105/ajph.2010.199505.
- Amante TD, Ahemed TA. Risk factors for unsuccessful treatment outcome (failure, default and death) in public health institutions, Eastern Ethiopia. *Pan American Medical Journal*. 2015, 20:247. doi: 10.11604/pamj.2015.20.247.3345.
- National Tuberculosis Control Center. 2019. Epidemiological Review of Tuberculosis Surveillance in Nepal. Thimi, Bhaktapur, Nepal: NTCC. <u>http://nepalntp.gov.np/wpcontent/uploads/2021/04/EPI-Report-27-May-2020.pdf</u>.
- 15. National Tuberculosis Control Center (NTCC). 2019. National Tuberculosis Management Guideline. Thimi, Bhaktapur, Nepal: NTCC. <u>http://nepalntp.gov.np/wp-</u> <u>content/uploads/2019/10/National-Tuberculosis-Management-Guidelines-2019\_Nepal.pdf</u>.
- National Tuberculosis Control Center. 2020. Tuberculosis Management Basic Training Manual. Thimi, Bhaktapur, Nepal: NTCC.
- 17. StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.
- World Health Organization. 2018. Global Tuberculosis Report 2017. Geneva, Switzerland: WHO. <u>https://www.who.int/publications/i/item/9789240013131</u>.
- Duarte R, Lonnroth K, Carvalho C, Lima F, Carvalho ACC, Munoz-Torrico M, Centis R. Tuberculosis social determinants and comorbidities (including HIV). *Pulmonol*. 2018, 24(2):115-119.
- 20. Bhatta S, Pant N. Epidemiological profile and determinants of tuberculosis in urban Nepalese population. *Nepalese Medical Journal*. 2019, 2(2): 250-254. doi: 10.3126/nmj.v2i2.25946.
- World Health Organization. 2010. Treatment of Tuberculosis Guidelines 4<sup>th</sup> Edition. Geneva, Switzerland: WHO. <u>https://www.who.int/tb/publications/2010/9789241547833/en/</u>.
- 22. Maruza M, Albuquerque MFPM, Coimbra I, Moura LV, Montarroyos UR et al. Risk factors for default from tuberculosis treatment in HIV infected individuals in the state of lpernambuco, Brazil: a perspective cohort study. *BMC Infect dis.* 2011, 11:351. <u>http://dx.doi.org/10.1186/1471-2334-11-351</u>.

- 23. Alobu I, Oshi SN, Oshi DC, Ukwaja, KN. Risk factors of treatment default and death among tuberculosis patients in a resource-limited setting. *Asian Pac J Trop Med.* 2014, 9:e111910. http://dx.doi.org/10.1016/s1995-7645 (14)60172-3.
- 24. Oshi DC, Oshi SN, Alobu I, Ukwaja KN. Profile and treatment outcome of tuberculosis in elderly in Southern Nigeria, 2011-2012. *PloS ONE*. 2014, 9:e111910. <u>http://dx.doi.org/10.1371/Journal.pono.0111910</u>.
- 25. Tok PSK, Liew SM, Wong LP, Razali A, Loganathan T, Chinna K, Ismali N, Kadir NA. Determinants of unsuccessful treatment outcome and mortality among tuberculosis patient in Malaysia: a registry-based cohort study. *PLoS ONE*. 2020, 15(4):e0231986. <u>https://doi.org/10.1371/Journal.pono.0231986</u>.
- 26. Pizzol D, Veronese N, Marotta C, Gennaro FD, Moiane J, Chhaganlal K et al. Predictors of therapy failure in newly diagnosed pulmonary tuberculosis cases in Beira, Mozambique. *BMC Res Notes*. Dec 2018, 11(1):99. <u>https://doi.org/10.1186/s13104-018-3209</u> PMD: 29402317.
- 27. Tafess K, Beyen TK, Abera A, Tasew G, Mekit S. et al. Treatment outcome of tuberculosis at Asella teaching hospital, Ethiopia: ten years retrospective aggregated data. *Front Med.* Feb 2018, 5:38.
- 28. Dhimal M, Bista, B, Bhattarai S, Dixit LP, Hyder MKA, Agrawal N, Raini M, Jha AK, 2019. Non-communicable disease risk factors: STEPS survey Nepal 2019. Ramshahpath, Kathmandu, Nepal: NHRC. <u>https://www.who.int/docs/default-source/nepaldocuments/ncds/ncd-steps-survey-2019-compressed.pdf?sfvrsn=807bc4c6\_2</u>.
- 29. Viana PVDS, Goncalves MJF, Basta PC. Ethnic and racial inequalities in notified case of tuberculosis in Brazil. *PLoS ONE*. 2016, 11(5):e0154658. Doi.10.1371/journal.pone.154658.
- 30. Basta PC, Coimbra JrCEA, Welch JR, Alves LCC, Santos RV, Camacho LAB. Tuberculosis among the xavante Indians of Brazilian Amazon: an epidemiological and ethnographic assessment. *Ann Hum Bio*. 2010, 37:643-657. Doi.10.3109/03014460903524451, PMD: 20113213.
- Samata Foundation. 2012. Health is Wealth: Health Care Access for Dalit Communities in Saptari, Nepal. https://sipa.columbia.edu.
- 32. Pandey J, Dhakal MR, Karki S, Poudel P, Pradhan MS. 2013. Maternal and child health in Nepal: The Effects of Caste Ethnicity and Regional Identity: Further Analysis of the 2011

Demographic and Health Survey, Calverton, Maryland, USA: Nepal Ministry of Health and Population, New Era, and ICF International.

- 33. Bennett L, Dahal DR, Govindasamy P. 2008. Caste, Ethnic and Regional Identity in Nepal: Further analysis of the 2006 Nepal Demographic and Health Survey. Calverton, Maryland, USA: Macro International Inc. <u>https://dhsprogram.com/Pubs/Pdf/FA.58/FA58.pdf</u>.
- 34. Pandey S, Bissell P, Teijlingen EV, Simkhada P. Perceived barriers to accessing female community health volunteers (FCHV) service among ethnic minority women in Nepal: a qualitative study. *PLoS One.* 2019, 14(6):e0217070. <u>https://doi.org/10.1371/Journal.pone.</u> 0217070.
- 35. Osei E, Oppong S, Adanfo D, Doepe BA, Owusu A, Kupour AG, Der J. Reflecting on tuberculosis case notification and treatment outcomes in the Volta region of Ghana: a retrospective pool analysis of a multicenter cohort from 2013 to 2017. *Global Health Research and Policy*. 2019, 4:37. https://doi.org/10.1186/s41256-019-0128-9.
- 36. Izudi J, Tamwesigire I.K, Bajunirwe F. Explaining the successes and failures of tuberculosis treatment programs; a tale of two regions in rural eastern Uganda. *BMC Health Service Research*. 2019, 19:979, <u>https://doi.org/10.1186/s12913-019-4834-2</u>.
- Biruk M, Yimam B, Abrha H, Biruk S, Amide FZ. Treatment outcomes of tuberculosis and associated factors in Ethiopian university hospital. *Advanced Public Health*. 2016, Article ID 8504629. <u>http://dx.doi.org/10.1156/2016/8504629</u>.
- 38. Mok J, An D, Kim S, Lee M, Kim C, Son H. Treatment outcome and factors affecting treatment outcome of new patients with tuberculosis in Busan, South Korea: a retrospective study of citywide registry, 2014-15. *BMC Infect Dis.* Dec 2018, 13;18(1):655. doi: 10.1186/s12879-018-3574-y.
- Nepal Anti Tuberculosis Association (NATA)/German Nepal Tuberculosis Project (GENETUP). 2012. Surveillance on Anti Tuberculosis Drug Resistance among TB Patients in Nepal 2011/12. Kathmandu, Nepal: GENETUP.
- 40. Heunis JC, Kigozi, NG, Chikobvu P, Botha S, Rensburg HCJDV. Risk factors for mortality in TB patient: a 10-year electronic record review in South African Provinces. *BMC Public Health.* 2017, 17:38. doi.10.1186/s12889-016-3972-2.

# LEGENDS

Table 1. Socio-demographic and clinical characteristics of treatment success and death ofTuberculosis patients

TB treatment							
	was successful		TB patient died				
Socio-demographic & Clinical	(%)		(%)				
Characteristics	No	Yes	Total	No	Yes	Total	Number (%)
Age Group							
below 15 year	6.8	93.2	100	98.3	1.7	100	1,928 (6.7)
15-64 year	11.5	88.5	100	96.1	3.9	100	22,797 (78.7)
65+ year	20.2	79.8	100	85.6	14.4	100	4,235 (14.6)
Sex							
Female	10.6	89.4	100	95.8	4.2	100	10,374 (35.8)
Male	13.5	86.5	100	94.1	5.9	100	18,586 (64.2)
Ethnicity							
Dalit	14.9	85.1	100	93.8	6.2	100	4,401 (15.2)
Janjati	11.6	88.4	100	95.4	4.6	100	9,491 (32.8)
Madhesi	12.3	87.7	100	94.4	5.6	100	4,250 (14.7)
Muslim	16.2	83.8	100	92.3	7.7	100	1,017 (3.5)
Brahman/Chhetri	11.6	88.4	100	95.1	4.9	100	8,149 (28.1)
Others	13.8	86.2	100	93.3	6.7	100	839 (2.9)
Unknown	13.3	86.7	100	93.8	6.2	100	813 (2.8)
Province							
Province1	12.7	87.3	100	95.3	4.8	100	1,606 (5.5)
Province2	11.1	89.9	100	95.1	4.9	100	5,796 (20.0)
Bagmati	13.9	86.1	100	96.6	3.4	100	5,150 (17.8)
Gandaki	12.8	87.2	100	93.4	6.7	100	3,220 (11.1)
Lumbini	12.4	87.6	100	93.7	6.3	100	8,055 (27.8)
Karnali	8.5	91.5	100	96.3	3.7	100	1,917 (6.6)
Sudurpaschim	14.9	85.1	100	93.8	6.1	100	3,216 (11.1)
Tuberculosis Type							

PBC	14	86	100	94.1	5.9	100	15,869 (54.8)
PCD	11.3	88.7	100	94.4	5.6	100	4,857 (16.8)
EP	10.2	89.8	100	96.1	3.9	100	8,234 (28.4)
<b>Registration Type</b>							
New	12	88	100	94.9	5.1	100	25,359 (87.6)
Previously treated	17.4	82.6	100	91.7	8.3	100	2,705 (9.3)
Other	11.1	88.9	100	97.4	2.6	100	117 (0.4)
Transfer-in	10.4	89.6	100	97.2	2.8	100	779 (2.7)
Tuberculosis Category							
Cat I	11.9	88.1	100	95	5	100	26,204 (90.5)
Cat II	18.5	81.5	100	91.4	8.6	100	2,380 (8.2)
Cat III	8.7	91.3	100	98.3	1.7	100	289 (1.0)
Missing	19.5	80.5	100	95.4	4.6	100	87 (0.3)
HIV Status							
No	11.7	88.3	100	94.8	5.2	100	13,659 (47.2)
Yes	20.1	79.9	100	92	8	100	348 (1.2)
Unknown	13	87	100	94.7	5.3	100	14,953 (51.6)
<b>Outcome of Treatment</b>							
Cured							12485 (43.1)
Treatment completed							12861 (44.4)
Treatment failure							348 (1.2)
Died							1531 (5.3)
Loss to follow up							831 (2.9)
Not evaluated							904 (3.1)
Total	12.5	87.5	100	94.7	5.3	100	28,960

Socio-demographic / clinical	TB trea	tment success	Death among TB patients			
characteristics	aOR	CI	aOR	CI		
Age Group						
below 15 year (Ref)	1		1			
15-64 year	0.641***	(0.522 - 0.787)	2.043***	(1.389 - 3.006)		
65+ year	0.328***	(0.264 - 0.407)	8.075***	(5.460 - 11.94)		
Sex						
Female (Ref)	1		1			
Male	0.813***	(0.752 - 0.877)	1.209***	(1.076 - 1.358)		
Ethnicity						
Dalit (Ref)	1		1			
Janjati	1.462***	(1.311 - 1.631)	0.744***	(0.632 - 0.877)		
Madhesi	1.183**	(1.038 - 1.349)	0.899	(0.742 - 1.091)		
Muslim	0.835*	(0.688 - 1.012)	1.243	(0.945 - 1.634)		
Brahman/Chhetri	1.443***	(1.293 - 1.610)	0.744***	(0.632 - 0.876)		
Others	1.119	(0.901 - 1.390)	1.094	(0.806 - 1.486)		
Unknown	1.216*	(0.972 - 1.520)	0.922	(0.669 - 1.272)		
Province						
Province1 (Ref)			1			
Province2	1.363***	(1.140 - 1.630)	0.855	(0.648 - 1.126)		
Bagmati	0.876	(0.740 - 1.038)	0.744**	(0.562 - 0.984)		
Gandaki	1.049	(0.873 - 1.261)	1.303*	(0.988 - 1.718)		
Lumbini	1.105	(0.933 - 1.309)	1.226	(0.945 - 1.591)		
Karnali	1.534***	(1.224 - 1.922)	0.797	(0.564 - 1.128)		
Sudurpaschim	0.848	(0.704 - 1.021)	1.346*	(0.010 - 1.794)		
Tuberculosis Type						
PBC (Ref)	1		1			
PCD	1.180***	(1.065 - 1.307)	1.025	(0.887 - 1.184)		
EP	1.253***	(1.147 - 1.370)	0.865**	(0.755 - 0.992)		

Table 2. Logistic regression result to examine relationship between TB treatment success,

TB related death and socio-demographic / clinic characteristics of TB patient

Observations	28,960		28960	
Constant	10.60***	(8.022 - 14.04)	0.0173***	(0.0108 - 0.0281)
Yes	0.913***	(0.878 - 0.949)	1.135***	(1.072 - 1.202)
No (Ref)	1		1	
HIV Status				
Missing	0.550**	(0.322 - 0.940)	0.951	(0.343 - 2.631)
Cat III	0.728	(0.461 - 1.151)	0.948	(0.362 - 2.483)
Cat II	0.642***	(0.501 - 0.824)	1.472**	(1.024 - 2.115)
Cat I (Ref)	1		1	
Tuberculosis Category				
Transfer In	1.171	(0.924 - 1.484)	0.651*	(0.422 - 1.005)
Other	1.202	(0.668 - 2.163)	0.470	(0.147 - 1.509)
Previously treated case	1.033	(0.812 - 1.315)	1.159	(0.818 - 1.642)
New Case (Ref)	1		1	
Registration Type				

*CI Eform in parentheses, \*\*\* p<0.01, \*\* p<0.05, \* p<0.1* 



Figure 1. Trend of TB treatment success and default rates among TB patients reported in eTB register, FY2013/14-FY2018/19



Figure 2. Trend of treatment failure and death due to TB among TB patients reported in eTB register, FY2013/14-FY2018/19