ORIGINAL ARTICLE

Effect of smoking on treatment outcomes among newly diagnosed Tuberculosis patients in Shimla.

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Abstract

Introduction: World Health Organization in 2015 had adopted "End TB Strategy" aimed at ending the global TB epidemic by 2035. Tobacco smoking has been reported to be associated with many aspects of TB disease, including increased vulnerability to being infected, recurrence with TB and related mortality. **Aims & Objectives**: To determine effect of smoking on treatment outcomes of tuberculosis patients at the end of six months of standardized tuberculosis treatment. **Material & Methods**: A prospective cohort study was carried out among newly diagnosed tuberculosis patients of Shimla city of India. Data related to smoking status was collected using the standard questionnaire which was used for collection of data regarding tobacco use in Global Adult Tobacco Survey (GATS). Details of the participant's final treatment outcomes after end of standardized treatment of 6 months was collected from the treatment records of the patients available in the office of district TB center. **Results**: 72 TB patients were included as study subjects. The prevalence of smoking came out to be 37.5% (95% CI: 26.4-49.7). In our analyses, the risk of unfavorable treatment outcomes was higher among smokers (p value 0.049), Smokeless tobacco users (p value 0.031) and those with history of harmful alcohol use (p value 0.002). **Conclusions**: Smoking and smokeless tobacco cessation programs need to be targeted at Tuberculosis patients.

Keywords

Tuberculosis outcome; Smoking; Cohort study; Alcohol

Introduction

Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). (1) The tobacco epidemic is one of the biggest public health threats of all times world has ever faced, killing more than 7 million people a year. (2) As per the India TB report 2018 the estimated incidence of TB in India was approximately 28,00,000 (211/100,000). (3) According to Global Adult Tobacco Survey-2 (2016-17) prevalence of use of any form of tobacco was 28.6% while prevalence of smoking was found to be 10.7 % among adult Indian population. (4)

World Health Organization in 2015 had adopted "End TB Strategy" aimed at ending the global TB epidemic by 2035. (5) As a signatory to this strategy, Government of India has kept the target of TB elimination by 2025 whereas Himachal Pradesh has set to achieve it before 2023 thereby making Himachal the first TB free State of the country. (6) To improve the treatment outcomes and subsequently reduce the morbidity and mortality due to TB there is urgent need to identify the predictors of poor treatment outcomes. Tobacco smoking has been reported to be associated with many aspects of TB disease, including increased vulnerability to being infected, recurrence with TB and related mortality. (7,8). Both TB and smoking damage the lungs and interact at an immunologic and cellular level. (9) Most of the studies on this subject were observational and there are limited number of Randomized Clinical Trials (RCT) on association of smoking with Tuberculosis treatment outcomes. (10)

Aims & Objectives

To determine impact of smoking on treatment outcomes of newly diagnosed tuberculosis patients at the end of six months of standardized tuberculosis treatment.

Material & Methods

Study Type: This study was a prospective cohort study. **Study Population:** Newly diagnosed adult (≥ 18 years) tuberculosis patients who gave consent to participate in the study and registered at the various treatment providing Directly Observed Treatment Short course (DOTS) centers. **Study Area:** Shimla city which is the capital of Himachal Pradesh, a northern state of India. **Study Duration**: - Study was carried out for one year from 1st July 2017 through 30th June 2018. **Sample Size and inclusion criteria:** All consecutive patients registered in various DOTS centers of study area during the study period were included in the study. **Exclusion criteria**: Multi/Xtreme drug resistant, previously treated, patients on immunosuppressive therapy and pregnant patients were excluded from the study.

Data collection: There is one Tuberculosis Unit and two Designated Microscopy Centers (DMCs) in Shimla city from where we had recruited study subjects. Data was collected through a structured interview schedule conducted at respective DOTS centers. Data related to smoking status was collected using the standard questionnaire which was used for collection of data regarding tobacco use in Global Adult Tobacco Survey (GATS). (11) Interview schedules also contained self-reported information on age, alcohol use, socioeconomic indicators, human immunodeficiency virus (HIV) status, diabetic status, housing conditions, overcrowding and other relevant information related to study. Socioeconomic status of participants was determined according to modified BG prasad scale for 2017. Excessive alcohol use included binge drinking, heavy drinking, any alcohol use by people under the age 21 minimum legal drinking age, and any alcohol use by pregnant women.(12) At the time of study enrolment, patients were informed in detail about the objectives, possible benefits and harms of participating in the study and after the patients provided written informed consent, face-to-face interviews of eligible patients was conducted and interview schedule was completed according to study tool. All consecutive eligible patients will be recruited and information collected from them according to same procedure as described above. Details of the participant's final treatment outcomes after end of standardized treatment of 6 months was collected from the treatment records of the patients available in the office of district TB center. Treatment outcome were classified either as favorable (cured or treatment completed) or unfavorable outcome (failure, lost to follow up or died).

Working definitions: - Current smokers were defined as those who smoke daily or non-daily basis at the time of interview whereas past smoker as those who had ever smoked in their lifetime either daily or less than daily basis, but not smoking at the time of interview. Ever smoker is defined as either current or past smoker. Treatment outcomes were defined as per recent RNTCP guidelines.

1. Favorable Outcomes: -
   a) Cured: Microbiological confirmed TB patients at the beginning of treatment who was smear or culture negative at the end of the complete treatment
   b) Treatment completed: A TB patient who completed treatment without evidence of failure or clinical deterioration but with no record to show that smear or culture results of biological specimen in the last month of treatment was negative, either because test was not done or because result is unavailable.
2. Unfavorable outcomes: -

a) Failure: A TB patient whose biological specimen is positive by smear or culture at the end of treatment.
b) Lost to follow up: A TB patient whose treatment was interrupted for one consecutive month or more
c) Died: A patient who has died during the course of anti TB treatment.

Ethical Approval, Consent: Study was carried out after taking due permission from Institutional Ethics Committee of Indira Gandhi Medical College Shimla and after taking informed consent from participants.

Data analysis: Data was analyzed using Epi Info software version 7.2.2. Frequencies and percentages were used for description of variables. Pearson Chi-square and Fischer Exact test was used for univariate association analysis. A two-sided p value of < 0.05 was considered as statistically significant.

Results

During the study period 735 patients from all over the state of Himachal Pradesh were registered in two Designated Microscopy Centers (DMCs) of the study area. Out of these, 129 patients were residents of Shimla city. Fifty-seven patients were excluded from the study according to exclusion criteria. So finally, 72 patients were included as study subjects. (Figure 1)

Mean age (SD) of 72 study participants was 32.4 (14.2) years ranging from 18 to 80 years. Prevalence of current smoking came out to be 9.7% (95% CI: 4.0-19.0%). 27.8 % of patients were past smokers whereas majority (62.5%) were non-smokers. We have combined current and past smokers as single category as Ever Smoker. Then the prevalence of smoking came out to be 37.5% (95% CI: 26.4-49.7). Among Smokers median age of starting smoking was 19 years, ranging from minimum of 10 years to maximum of 43 years. Median value of smoking index came out to be 80 (Range 1.7-1020). Cigarette Smoking was found to be most common (55.6%) tobacco product used followed by Bidi smoking which was found in 37 % of participants. There were a greater number of smokers in males as compared to females. Smokers had fewer years of education, lower unemployment as compared to non-smokers. None of the study participants had tested positive for both Diabetes and Human Immunodeficiency Virus (HIV). Majority (88.9%) of the participants had no associated co-morbid condition (hypertension, epilepsy, Hepatitis B etc.) and 31 i.e. 43.1 % of participants were undernourished (BMI < 18.5). Smokeless tobacco use and harmful use of alcohol were more frequently reported by smokers than non-smokers. (Table 1)

Of these 72 participants, 3 (4.2%) had unfavorable outcome – 2 lost to follow up and 1 failed treatment. The univariate analysis for the risk of unfavorable treatment outcomes was higher among smokers (p value 0.049), Smokeless tobacco users (p value 0.031) and those with history of harmful alcohol use (p value: 0.002). Other baseline sociodemographic and clinical characteristics did not have significant effect on treatment outcomes in our study group. (Table 2)

Discussion

Proportions of participants with favorable treatment outcome (Treatment Success) came out to be 95.8%. The results were concordant with the global priority indicators and targets for monitoring the implementation of the End TB Strategy (2015-2035) which have set the target of achieving 90% treatment success rate. (5) Various recent studies in India have reported treatment success rates of 83.4 %, 85.5% and 93.2% respectively. (13,14) There is a high prevalence (37.5%) of smoking among patients with tuberculosis in our study. Prevalence of smoking among people older than 15 years is 20.2% (15) Globally and 10.7 % in India. (4) However, the prevalence of smoking among people with tuberculosis is often well above 20%. In a study conducted in Georgia, 59.9% of the tuberculosis patients were either current smokers or individuals who had ceased smoking no more than two months earlier. (16) According to some recent studies done in various part of India prevalence of smoking in TB patients vary from 23% to 33%. (14,17)

In our study tobacco smoking was found to be significantly associated with unfavorable treatment outcomes. Previous studies have shown that smoking is associated with increased risk of tuberculosis mortality, (18) tuberculosis treatment failure, (9) and relapse after treatment completion. (8) Smoking induces coughing and other symptoms consistent with tuberculosis, there may be longer delays in the diagnosis of tuberculosis among smokers than among non-smokers and they are presenting with more advanced disease at the time of diagnosis. Biological mechanisms related to smoking that impair host defenses and increase the

risk of M. tuberculosis infection probably contribute to the relatively poor results of tuberculosis treatment among smokers. (16)

Harmful use of alcohol was found to be significantly associated with unfavorable treatment outcomes of Tuberculosis in the present study. A systematic review to assess the association between alcohol use, alcohol use disorders and Tuberculosis (TB) found that heavy alcohol use strongly influences both the incidence and the outcome of the disease and was found to be linked to altered pharmacokinetics of medicines used in treatment of TB, higher rate of re-infection, higher rate of treatment defaults and development of drug-resistant forms of TB.(19) Regarding the course of the disease, there is sufficient evidence indicating that heavy alcohol consumption disrupts medication intake regimens and negatively affects help-seeking and treatment processes, leading to worse treatment outcomes compared to abstinence. (20)

We have also found significant association between use of smokeless tobacco and adverse treatment outcomes in our study. Pramil N. Singh et al did a study in Cambodia to find out role of Betel quid use in relation to different infectious disease outcomes and they found an association between the intensity of betel quid use and tuberculosis (OR 1.50, 95% CI 0.96–2.36). (21) Betel quid use could potentially increase the risk of developing infectious disease by providing an oral route of entry for pathogens through the constant injury to the oral mucosa. Additionally, several studies have demonstrated that the submucosal fibrosis, oral leucoplakia, and oral erythroplakia that are commonly associated with betel quid, can impair a wide range of immune function parameters which include but are not limited to: CD3 cells (T lymphocytes), CD4 cells (helper/inducer T lymphocytes), B lymphocytes, macrophages, (22) and natural killer cells. (23) Thus, under such a level of constant immunosuppression, it is biologically plausible that users experience an increased risk of opportunistic infections and further hamper their treatment outcomes

Conclusion

There is high prevalence of tobacco smoking and cigarette was most common tobacco product smoked among study participants. Risk factors associated with unfavorable treatment outcome from our study came out to be Smoking, harmful use of alcohol and smokeless tobacco use.

Recommendation

Smoking and smokeless tobacco cessation programs need to be targeted at Tuberculosis patients. International Union against TB and Lung Disease (The Union) has developed an intervention “ABC for TB” that guides the health care provider to ask about smoking habit, give brief advice on smoking cessation and provide cessation support. (24, 25) Such type of interventions should be included in RNTCP in order to achieve goal of ending TB from India by 2025.

Limitation of the study

Primary exposure variable – self-reported smoking status – was subject to potential misclassification. It is possible that our participants could have underreported their tobacco use.

Authors Contribution

All authors have contributed in design, data collection, analysis and report writing of the study.

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Tables

TABLE 1 COMPARISON OF SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS AMONG SMOKERS AND NON- SMOKERS

Characteristics	Overall n (%)	Non-Smokers n (%)	Smoker n (%)
Gender			
Male	38 (52.8)	15 (39.5)	23 (60.5)
Female	34 (47.2)	30 (88.2)	4 (11.8)
Age (Years)			
< 60	67 (93.1)	43 (64.2)	24 (35.8)
≥ 60	5 (6.9)	2 (40.0)	3 (60.0)
Education (Years)			
≤ 10	27 (37.5)	10 (37.0)	17 (63.0)
>10	45 (62.5)	35 (77.8)	10 (22.2)
Occupation			
Employed	38 (52.8)	17 (44.7)	21 (55.3)
Unemployed	34 (47.2)	28 (82.4)	6 (17.6)
Religion			
Hindu	66 (91.7)	41 (62.1)	25 (37.9)
Others	6 (8.3)	4 (66.7)	2 (33.3)

Socio economic status			
Upper & Middle Class	54 (75.0)	34 (63.0)	20 (37.0)
Lower Class	13 (25.0)	7 (53.9)	6 (46.1)
Overcrowding			
Present	34 (47.2)	20 (58.8)	14 (41.2)
Absent	37 (52.8)	24 (64.9)	13 (35.1)
Co- Morbid Condition*			
Present	8 (11.1)	5 (62.5)	3 (37.5)
Absent	64 (88.9)	40 (62.5)	24 (37.5)
Body Mass Index			
Normal	33 (45.8)	22 (66.7)	11 (33.3)
Underweight & Obesity	39 (54.2)	23 (59.0)	16 (41.0)
Site of TB			
Pulmonary	39 (54.2)	22 (56.4)	17 (43.6)
Extrapulmonary	33 (45.8)	23 (69.7)	10 (33.3)
Smokeless Tobacco use			
Ever User	8 (11.1)	2 (25)	6 (75)
Never User	64 (88.9)	43 (67.2)	21 (32.8)
Passive Smoking			
Present	16 (22.2)	7 (43.8)	9 (56.2)
Absent	56 (77.8)	38 (67.9)	18 (32.1)
Biomass Fuel Use			
Yes	12 (16.7)	8 (66.7)	4 (33.3)
No	60 (83.3)	37 (61.7)	23 (38.3)
Harmful Alcohol Use			
Yes	10 (13.9)	2 (20.0)	8 (80.0)
No	62 (86.1)	43 (69.4)	19 (30.7)
* Any Chronic conditions such as hypertension, epilepsy, Hepatitis B etc			

TABLE 2 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC CHARACTERISTICS AND RISK OF POOR TUBERCULOSIS TREATMENT OUTCOMES

Characteristics	Favourable Outcome n (%)	Unfavourable Outcome n (%)	p Value
Gender			
Female	34 (100)	0 (0)	0.242
Male	35 (92.1)	3 (7.9)	
Age (Years)			
< 60	64 (95.5)	3 (4.5)	1.000
≥ 60	5 (100)	0 (0)	
Education (Years)			
>10	44 (97.8)	1 (2.2)	0.552
≤ 10	25 (92.6)	2 (7.4)	
Occupation			
Employed	36 (94.7)	2 (5.3)	1.000
Unemployed	33 (97.1)	1 (2.9)	
Religion			
Hindu	63 (95.5)	3 (4.5)	1.000
Others	6 (100)	0 (0)	
Socio economic status			
Upper & Middle Class	53 (98.2)	1 (1.8)	0.094
Lower class	11 (84.6)	2 (15.4)	
Overcrowding			
Absent	37 (100)	0 (0)	0.105
Present	31 (91.2)	3 (8.8)	

Co- Morbid Condition			
Absent	61 (95.3)	3 (4.7)	1.000
Present	8 (100.0)	0 (0.0)	
Body Mass Index			
Normal	33 (100.0)	0 (0.0)	0.245
Underweight & Overweight	36 (92.3)	3 (7.8)	
Site of TB			
Pulmonary	36 (92.3)	3 (7.7)	0.245
Extrapulmonary	33 (100.0)	0 (0.0)	
Smoking Status			
Never-Smoker	45 (100.0)	0 (0.0)	0.049
Smoker	24 (88.9)	3 (11.1)	
Smokeless Tobacco use			
Absent	63 (98.4)	1 (1.6)	0.031
Present	6 (75.0)	2 (25.0)	
Passive Smoking			
Absent	54 (96.4)	2 (3.6)	0.535
Present	15 (93.8)	1 (6.2)	
Biomass Fuel Use			
No	58 (96.7)	2 (3.3)	0.426
Yes	11 (91.7)	1 (8.3)	
Harmful Alcohol Use			
No	62 (100.0)	0 (0.0)	0.002
Yes	7 (70.0)	3 (30.0)	

Figures

FIGURE 1 FLOWCHART OF PARTICIPANTS DURING THE COURSE OF THE STUDY