Smoking on Treatment Outcomes Among Tuberculosis Patients

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Abstract: *Background:* Smoking is a risk factor not only for the development of cancer and coronary heart disease but also for tuberculosis (TB). The aim of this study was to determine the prevalence of smoking in patients with TB, identify demographic and clinical characteristics associated with smoking and to evaluate TB treatment outcomes in the smokers. *Method:* A retrospective cohort study of patients with TB was conducted at Khyber Teaching Hospital, Peshawar, Pakistan. All patients with pulmonary and extrapulmonary TB and those coinfected with HIV, hepatitis or diabetes mellitus were included in the study. The patients were categorized into smokers and nonsmokers. Treatment outcomes were evaluated by smear testing at the end of the treatment. *Results:* Of 472 enrolled subjects, 68 (14.4%) were smokers. The prevalence of smoking among male and female patients with TB was 11.8% and 2.5%, respectively. Univariate analysis indicated that the gender, age group and marital status of patients with TB were associated with smoking. The results indicated that patient gender ($P = 0.05$), age: 15 to 24 years ($P = 0.05$) and age >55 years ($P = 0.004$) were risk factors associated with smoking among TB patients. Of the 68 smokers with TB, the treatment outcomes among 54 patients (79.4%) were unsuccessful. The treatment outcomes was statistically significantly associated with smoking (odds ratio: 2.58, $P = 0.004$). *Conclusions:* Findings from the current study proved smoking to be one of the main factors associated with the occurrence of TB and significantly reducing the outcomes of TB therapy.

Key Indexing Terms: Tuberculosis treatment outcomes; Tuberculosis smoking prevalence; Pulmonary Tuberculosis; Extrapulmonary Tuberculosis. **[Am J Med Sci 2015;349(6):505–509.]**

Tuberculosis (TB) is one of the leading causes of morbidity and mortality throughout the world. In 2011, 8.7 million new cases of TB were diagnosed, and 1.4 million TB deaths were reported.[1] The burden of TB is highest in Asia, Africa, India and China, with these regions accounting for almost 40% of TB cases worldwide. About 60% of TB cases are in Southeast Asia and Western Pacific Regions.[2] The current estimated incidence rates of TB in Pakistan are 231 per 100,000, and the TB-related mortality burden is 62,000.[3] In the last 4 years, Pakistan has moved up from 8th position in the top 22 high-TB burden countries and is now ranked 5th.[3] Studies have indicated that smoking is a risk factor not only in the development of cancer and coronary heart disease but also in TB.[4,5] Independent of other risk factors, such as intravenous drug use, alcohol consumption and socioeconomic conditions, studies found that exposure to tobacco smoke increased the risk of developing TB.[5,6] Deaths associated with tobacco and TB, both of which represent major sources of mortality and morbidity, are projected to increase to 8.4 million by 2020.[7]

The traditional approach to TB control has focused on smear-sensitive diagnosis and direct observational therapy (DOT), as recommended by the World Health Organization. However, DOT has achieved only a modest decline in TB rates.[8] In 2010, the World Health Organization proposed that greater emphasis should be placed on preventing risk factors for TB.[9] Tobacco smoke is known to be directly associated with the development of TB. According to one study, highlighting smoking as a risk factor for TB may have a greater impact on smoking cessation rates than advertising its role as a risk factor in cancer and cardiovascular disease.[10] Despite growing evidence of the association of TB with tobacco smoking, the prevalence of TB among smokers in Pakistanis is not well documented.

Therefore, this study aimed to determine the prevalence of TB among smokers, identify risk factors for TB patients associated with smoking and to evaluate TB treatment outcomes among smoking and nonsmoking patients with TB in Peshawar city of Pakistan.

METHODS

Study Design

The current retrospective cohort study conducted at respiratory ward Khyber Teaching Hospital, Peshawar, Khyber Pakhtunkhwa, Pakistan. The city of Peshawar is the provincial and district capital, with an estimated population of 4,650,000. The main aim of this study was to estimate the prevalence of smoking among TB patients. In addition, through this cohort design the association of smoking with TB and its treatment outcomes was also assessed. The duration specified for data extraction from the medical records was from November 2009 to December 2010.

Study Area and Study Sample

All patients of both genders who were diagnosed with TB and treated at Khyber Teaching Hospital in Peshawar, Pakistan were included in the study. All patients suffering from pulmonary and extrapulmonary TB, including those with or without HIV coinfection, hepatitis and diabetes mellitus, were included in the study, in addition to those with lymph node-, intestinal-, fallopian tube-, bone- and pleura extrapulmonary type TB. Patients younger than 15 years and female pregnant patients were excluded. The selected cohort of TB patients was categorized into smokers and nonsmokers. An enrolled TB patient was defined as a smoker if he/she had smoked during the last year.[11] The prevalence of smokers was estimated by dividing the number of patients with TB who smoked by the total number of patients with TB. A patient with TB was defined as cured if he/she was smear negative 1 month before the

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completion of the treatment. Treatment outcomes were evaluated by smear testing at the end of the treatment, and the results (ie, positive or negative) were assessed with respect to the patient's smoking status. Ethical approval from local authorities was obtained before conducting the study.

Data Collection

All eligible TB cases were identified by reviewing the TB registration book at the study site. In the absence of electronic data, the patient paper-based records were used as the data source. A self-developed, validated detailed data collection form was used to record the patients' demographic and clinical data. A panel of experts assisted in improving and validating the final version of the data collection form.

Statistical Analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS version 20.0). Categorical data are presented as numbers and percentage, and continuous data are represented as the mean SD. A χ^2 test and Fischer's exact test were used to detect significance between the variables. Significant patient variables were analyzed using a univariate analysis. A multivariate analysis (binary logistic regression) was applied to patient factors that were associated with smoking. Odds ratios (ORs) were used to interpret the effect of variables within a group. A P-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 472 patients with TB who visited Khyber Teaching Hospital for TB treatment fulfilled the inclusion criteria. Sixty-eight of the patients were smokers, giving a prevalence of 14.4%. The prevalence of smoking among male patients with TB was 82.35%, and the prevalence of smoking among female patients with TB was 17.65% (Figure 1).

Of the 472 patients with TB, 56 smokers (11.9%) were men and 12 (2.5%) were women. Patient gender had a significant association with smoking status ($P < 0.001$). Of the 56 patients who smoked, 52 (92.8%) had diabetes and 6 (10.7) had HIV. The type of TB was significantly associated with the smoking status of the patient ($P = 0.05$) (Table 1).

The patient variables associated with smoking were further analyzed using a univariate analysis. Male gender (OR, 5.6; 95% confidence interval [CI], 2.96–10.94; $P < 0.001$), age: 15 to 24 years (OR, 1.64; 95% CI, 1.03–2.61; $P = 0.03$), age >55 years (OR, 0.51; 95% CI, 0.32–0.81; $P = 0.005$) and marital status (OR, 2.8; 95% CI, 1.59–5.23; $P = 0.001$) had a significant association with the smoking status of patients with TB (Table 2).

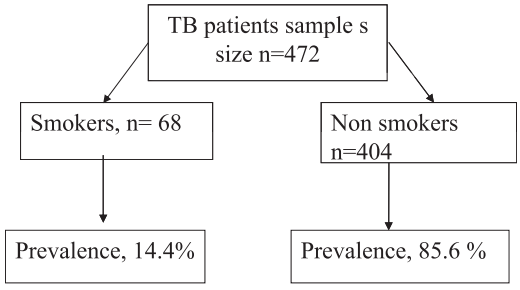

FIGURE 1. Prevalence of smoking among patients with TB.

Multivariate analysis (multiple logistic regression) was applied to patient factors that showed a significant association with smoking. Patient gender (OR, 1.45; 95% CI, 0.98–2.13; $P = 0.05$), age: 15 to 24 years (OR, 1.65; 95% CI, 0.99–2.77; $P = 0.05$) and age >55 years (OR, 0.48; 95% CI, 0.27–0.77; $P = 0.004$) were associated with smoking among patients with TB (Table 3).

Association of Treatment Outcome With Patient Smoking Status

The treatment outcomes were evaluated by smear testing at the end of the treatment, and the results (ie, positive or negative) were compared with the smoking status of the patient. Of the 68 patients with TB who smoked, 54 (79.4%) had an unsuccessful treatment outcome, and 14 (20.6%) had a successful treatment outcome. The smoking status of the patient had a statistically significant association with the treatment outcome (OR, 2.58; $P = 0.004$) (Table 4).

DISCUSSION

A national health survey of Pakistan reported that the prevalence of smoking among patients with TB was 15.2%.[12] The same survey reported that the prevalence of smoking was 28.6% among men and 3.4% among women. This study found a smoking prevalence of 14.4% among a study population of patients with TB. The prevalence of smoking in men was 82.35% compared with 17.65% in women. However, as this study was conducted in a single center in Khyber Pakhtunkhwa province of Pakistan, the findings are not representative of the overall scenario in Pakistan.

Studies with different study designs conducted around the world have reported an association between tobacco smoking and TB. Although the exact mechanism underling the role of tobacco in TB is not known, it is thought that the nicotine in tobacco smoke may interfere with the immune response of the host to *Mycobacterium tuberculosis*.[13] A case-control study in India reported an association between tobacco smoke and the development of pulmonary TB and stated that tobacco smoke was a potential risk factor for the development of TB.[14] Tachfouti et al[15] reported a similar finding in a study of the association of smoking among patients with TB. In their study, the TB treatment failure rate was higher in smokers compared with that in nonsmokers (9.1% versus 4.5%, $P < 0.01$). Studies conducted in South Africa and China/Hong Kong reported a higher OR of TB mortality among smokers.[16,17] Data from Canada suggested that smokers were less adherent than nonsmokers to TB medication and that they had a higher risk than nonsmokers for TB default.[18] In an extension to previous research, this study further investigated the influence of tobacco smoke on TB. The authors found a highly significant association among smoking and patient gender (OR, 5.6; $P < 0.001$). Previous studies indicated that the influence of age and gender on the risk of TB was largely due to smoking.[19,20] The authors also detected a significant association ($P = 0.005$) between smoking and the type of TB (pulmonary and extrapulmonary TB), with an overwhelming number of smokers being diagnosed with pulmonary TB. However, in the univariate analysis, the influence of smoking on the type of TB (pulmonary and extrapulmonary TB) was not statistically significant. A multicenter study with a larger sample size may provide different results.

In a study of treatment outcomes among patients with TB, Fahrettin et al[21] reported that treatment outcomes were successful in 91.7% of patients. They also identified multiple patient factors that affected TB treatment outcomes. Studies of