ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research

Available Online at www.jbpr.in

CODEN: - JBPRAU (Source: - American Chemical Society)

Index Copernicus Value: 72.80

PubMed (National Library of Medicine): ID: (101671502)

Volume 7, Issue 2: March-April: 2018, 68-75

Research Article

PREVALENCE OF MYCOBACTERIUM TUBERCULOSIS AMONG SMOKERS

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Received 24 March 2018; Accepted 21 April. 2018

ABSTRACT

The convergence of these two important health hazards is likely severely affecting India's TB control programs. This study was carried out to determine the prevalence of smoking in newly diagnosed pulmonary TB patients and the impact of smoking on disease outcomes in a tertiary care hospital. All patients newly diagnosed with pulmonary TB as per the Revised National Tuberculosis Program of India (RNTCP) 2013 criteria were enrolled in the study. On the basis of their self-reported smoking status, the participants were classified as never smokers, current smokers, and ex-smokers. Patients were started on anti-TB treatment and were followed for 2 years. Among the 2350 subjects (1,758 males and 592 females), 1,593 patients (67.78%) were never smokers. Current and ex-smokers numbered 757 (32.21%), of which 751 (31.95%) were males and 6 (0.26%) were females. Smoking was associated with more extensive lung disease, lung cavitation, and positive sputum smear and culture results at baseline. In both current smokers and ex-smokers, sputum smears and cultures were significantly more likely to remain positive after 2 months of treatment. Ex-smokers and current smokers had significantly high rates of defaults, treatment failures, and relapses. The prevalence of smoking is very high in TB patients. Tobacco smoking is associated with a considerably increased risk of advanced and more severe disease in the form of lung cavitations, positive sputum smear and culture results, and slower smear and culture conversion after initiation of treatment.

Key words: Smoking, Tuberculosis, mycobacterium tuberculosis.

1. INTRODUCTION:

Prevalence of tuberculosis in these regions. About 17% of smoking population lives in India.[2,3] At least one-third of the smokers belong to middle age group, and as per surveys, it is in this age group pulmonary tuberculosis is most prevalent. Males are affected two-four times more than females.[4] Tobacco smoking and Tuberculosis are the two major health problems, especially in developing countries. As per estimates, deaths from tobacco consumption will be around 8.4 million in 2020, almost double to that estimated in 1990.[1] These mortality figures are not only contributed by pulmonary diseases like lung cancer and chronic obstructive pulmonary disease but cardiovascular diseases like stroke and coronary heart disease are also attributable. The data of World Health Organization (WHO) show that Indonesia becomes the 3rd biggest country of smoker rate after China and India, followed by Russia and United States[1]. Whereas, according to the total population, Indonesia is in the 4th position after China, India, and United States. It is different with smokers in United States which tend to decrease the smokers in Indonesia indeed have increased in the recent 9 years. Growth of smokers in Indonesia in the period of 2000-2008 was 0.9% every year. There are many diseases which are connected with smoking such as arthritic, impotence, infertility, Alzheimer, TB, and so on [2, 3]. The lung is an organ that suffers the most due to smoking habit. The relationship between smoking and TB was firstly reported at the beginning of the 20nd century. Even though the exact mechanism has been known yet, there have been many researches discussing the relationship between smoking and TB[4].

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2. SMOKING

Tobacco was introduced in Indonesia by Netherland about 2 centuries ago and the using of tobacco by Indonesian was when the local elite of Indonesia tried to copy the habit of Dutch people that was then followed by lower class people. They replaced it by chewing betel, and this became the habit of Indonesian people. The word of rokok (cigarettes) derived from Dutch language roken. Smoking is the activity of smoking cigarettes (tobacco). The danger of smoking has been widely discussed and recognized. Research conducted by scientists has provided evidences of the dangers of smoking and that there is a decline in the lung functions of smokers and the people surrounding. World Health Organization has estimated that in 2020, the diseases caused by smoking will lead to the death of about 8.4 million people in the world and half of them are from Asia. It is estimated that in 2013, around 80% of the diseases caused by smoking will exist in countries with low and middle income [5,7]tobacco by smoking is more dangerous than any other ways and active smokers give rise to a variety of disease than nonsmokers. However, substantially passive smokers also contribute to cause various diseases. Approximately 1.1 billion people are smoking worldwide, more than 80% are in low and middle income countries.[8] China has the largest production and consumption of tobacco in the world. In many countries, about 49% men and 8% women over 15 years old are smoking, it is in contrast to 37% men and 21% women who come from high income countries. More than 60% smokers live in only 10 countries, namely China, India, Indonesia, Russia, the United States, Japan, Brazil, Bangladesh, Germany and Turkey.[9]The consumption of per adult per day (number of cigarettes smoked per day are divided by the population of smokers and non-smokers) has declined by more than 50% in the last 2-3 decades in America, Canada, France and other high income countries. In contrast, smoking prevalence in men has increased sharply in countries with low and middle incomes as China and Indonesia.[10] Marked improvement has occurred in young males. The differences between women and men are associated with differences in tobacco use, in terms of use prevalence, the use of shorter duration or use frequency that is lower in women.[11]

3. TUBERCULOSIS:

Disease caused by the infection of *Mycobacterium tuberculosis* complex and becomes an important public health problem in Indonesia. *M. tuberculosis* has rod-shaped, 5µ length and 3µ width, do not form spores and belongs to aerobic bacteria.[12] Mycobacteria can be given staining like other bacteria, for instance using the Gram staining. But once stained by Gram staining, the colour cannot be removed with acid. Therefore, the mycobacteria is called Acid Bacillus (AFB).[13] In the cell wall of mycobacteria, fat is associated with arabinogalactan and peptidoglycan underneath.[14] This structure reduces the permeability of cell walls, thereby reducing the effectiveness of antibiotics.[15]Lipoarabinomannan of other molecules in the cell wall of mycobacteria play a role in the interaction between host and pathogen, causing *M. Tuberculosis* can survive within macrophages[16]**.** In 1992, WHO declared TB as a global emergency. Currently, tuberculosis mainly attacks productive age people and increases mortality, especially in developing countries. In 2010, it was reported the incidences of tuberculosis in the world were at 8.8 million (from 8.5 to 9.2 million), 1.1 million (0.9-1.2 million) deaths due to HIV-negative TB plus 0.35 million (0.32 to 0.39 million) TB sufferers with HIV-positive. In 2009, it was reported 2.4 million new cases (3.3 million women), 133 cases/100.000 population with HIV sufferers equal to 1.1 million people.[17] Deaths due to TB infection were 1.7 million people (380,000 women), including 380,000 HIV sufferers, in accordance with 4700 deaths per year and became the third leading cause of death in women aged 15-44 years old.[18] Eighty percent of active TB cases were found in 22 developing countries, most of them were in Asia (with 55% cases in the world) and Africa (30%). Approximately 5% of the global burden of TB cases are now resistant to several drugs. In Russia, it was reported that TB cases resistant to drug accounted for over a fifth of all new TB cases in 2008. In 2008, as many as 1.4 million people living with HIV had active TB.[19] HIV positive people more likely to become infected tend to be resistant to drugs and increase the mortality rates. India ranks the first of TB patients in the world (1.6 to 2.4 million). It accounts for about one fifth of the total number of cases in the world with a mortality rate of 17.6%

and 3.5% of the total deaths. The next is China (1.1 to 1.5 million), South Africa (0.4 to 0.59 million), Nigeria (0.37 to 0.55 million) and Indonesia (0.35 to 0.52 million). In the United States, it was reported a significant decrease, in 1945 it was reported 73/100.000 population, in 1993 was 9.0/ 100,000 population and in 2009 there was 3.8/100,000 population.[20] In Nigeria. Diagnosis can be established based on clinical symptoms, physical examination, bacteriological examination that have important meaning in establishing the diagnosis. Material for this bacteriological examination can be derived from the phlegm, pleural fluid, cerebrospinal fluid, bronchial washings, gastric washings, broncho alveolar lavage/ BAL, urine, faces and biopsy tissue (including fine needle biopsy/ BJH).[21] Radiological examination with standard examination of chest X-ray of PA (posteroanterior) and other radiology examinations are lateral photos, top-lordotic, oblique or CT-Scan. Other supporting examinations are such as pleural fluid analysis, tissue histopathological and blood examination. Clinical symptoms of TB can be divided into 2 groups, namely local symptoms and systemic symptoms. If the infected organ is the lung, the local symptom is respiratory symptom (Local symptoms in according to organs involved). Respiratory symptoms are such as cough ± 2 weeks, coughing up blood, shortness of breath and chest pain.[22] These respiratory symptoms are highly various, ranging from no symptoms until the symptoms quite severe depending on lesion area. Sometimes patients are diagnosed during medical check up. If the bronchus is not involved in the disease process, the patients may not suffer cough symptoms. The first cough occurs due to bronchial irritation, and the next coughs are needed to get rid of phlegm out. The systemic symptoms caused by TB infection are fever, malaise, night sweats, anorexia and weight loss.[23]On pulmonary tuberculosis, the acquired abnormalities depend on the area of lung structural abnormalities. At the beginning (early) development of disease, in general it is not (or difficult) found abnormalities. Pulmonary abnormalities are generally located in the superior lobe area, especially apex and posterior segments (S1 and S2), as well as inferior lobe apex area (S6).[24] On physical examination, it can be found, among others, bronchial breath sounds, amforik, decreased breath sounds, wet rhonchi, withdrawal signs of lung, diaphragm and mediastinum. At TB pleurisy, physical examination abnormalities depend on the amount of fluid in the pleural cavity.[25]

4. RELATIONSHIP BETWEEN SMOKING AND TUBERCULOSIS:

In 1918 the relationship between smoking and TB were first reported.[26] The exact mechanism that correlates smoking with TB is not fully understood, but there are a lot of evidences of declining respiratory tract defense that affect susceptibility to TB infection in smokers. Trachea, bronchi and bronchioles that form the respiratory tract that supply air to the lungs provide the first line of defense by preventing TB germs to reach the alveoli. Smoking is proven to interfere with mucociliary clearance. In pulmonary alveolar macrophages constituting a primary defense, there is a function decline in phagocytosis and kill germs in individuals who smoke, as reported in diabetes.[27] Smoking has been found to be associated with decreased levels of proinflammatory cytokines that are released. These cytokines are essential for early responses of local defense to bacterial infection including TB.[28]

It was found that smoking was significantly related to TB germ conversion time elongation in patients who were on anti-TB drug therapy. Other studies showed increased rates of recurrence of TB patients who smoked.[29,30] Control case study in 111 patients of BTA positive with 333 controls performed in India on September 2004 to August 2005, it was found the increased incidence of TB infection in smokers equal to 3.8 times compared to non smokers and was associated with the number of smoking, body mass index and social economy status. Many of them are based on infection or mortality rates. These studies have various limitations such as control case designs or crosssectional sample size that is small, and lack in socio-economic data, alcohol, HIV infection and other influential factors. In Hongkong, smoking and TB are two common conditions. Smoking prevalence is much higher in men than in women. More than 20% adult males are active smokers and TB incidence equal to 100 per 100,000 population per year and more common in men aged above 65 years old. Smoking is associated

with increased susceptibility to influenza and TB. From the studies using experimental mouse animal with rats receiving exposure to M. TB aerosolly, it was found that the interferon ³(IFN³) production by T cells would decrease with a decrease in transcription factors that regulate the expression of IFN³ in mice exposed to cigarette. This study provided the first demonstration that exposure to cigarette smoke directly inhibited T cell responses to M. TB and influenza virus on animal physiology so that it increased the susceptibility to both pathogens [31,32] Smokers have a extremely high mortality rates from tuberculosis, as many as nine times greater than those who have never smoked, but once they stop, the risk is substantially reduced and similar to those who never smoked. Quitting smoking has benefits for smokers far beyond reducing the risk of TB, but a good tobacco control can affect the mortality rate of TB and reduce the burden public health and by quitting smoking can reduce nearly one third of deaths from TB. TB risk can be reduced by nearly two-thirds if someone quitting smoking becomes strong evidence of the important role of smoking in TB control, such as smoking was responsible for more than one-third of TB deaths in Taiwan (37.7%). Controlling tobacco succeeded in reducing smoking in form of affecting mortality rates of TB and reducing nearly a third (30.7%) of the public health burden that had long interfered the residents of Taiwan. This is a big health impact on enhancing the public 's health, especially when applied to countries such as China, India that have the prevalence of smoking and the higher incidence of TB. Quitting smoking has been shown to reduce the incidence of TB, so it is needed an increase in knowledge and research on the benefits of quitting smoking to reduce mortality rates. With two thirds of Chinese men smoking and about three million cases of TB, thus, the good prevention and treatment guidelines need to carry out. Smoking substantially exacerbates the risk of death in those with a history of TB infection.[33]

5. MATERIALS AND METHODS:

Prevalence were determined by a predefined procedure and protocols, here represent an example of study design.

1. Source of data:

Data were from the inpatient and outpatient departments of pulmonary medicine and internal medicine and the DOTS center (TB unit) at a tertiary care hospital in the Belgaum district of Karnataka in India.

2. Population:

All newly diagnosed pulmonary TB patients registered for treatment in the above hospital were included.

3. Study design: This was a prospective study.

4. Inclusion criteria: These were as follows:

(1) Both male and female patients newly diagnosed with pulmonary TB per the RNTCP. (Revised National Tuberculosis Program of India) 2013 criteria and

(2) Age ＞15 years.

5. Exclusion criteria: Patients were excluded from the study if they had any of the following conditions:

(1) Pregnancy,
(2) HIV infection,
(3) Connective tissue disorders,
(4) Chronic renal failure,
(5) Chronic liver disease,
(6) Malignancies with long-term steroid or cytotoxic drug therapy,
(7) Chronic alcoholism,
(8) Previous treatment for TB, and
(9) Unclear smoking status.

Procedures all patients newly diagnosed with pulmonary TB per the RNTCP 2013 criteria were enrolled in the study. Initial baseline details of the patients such as age, sex, sputum smear/culture for Mycobacterium tuberculosis status, chest radiography findings, and other relevant details pertaining to TB were recorded.[34] Patients were started on anti-TB treatment. After informed consent was obtained, all patients completed standardized interviewer-administered questionnaires administered by trained resident doctors or nurses. Four questions pertained to smoking:

(1) Self-reported current smoking status (current cigarette/bidi smoker? Yes/No),
(2) Self-reported previous smoking status (previous cigarette/bidi smoker? Yes/No),
(3) Number of cigarettes/bidis smoked per day, and

(4) Age at which the participant started or quit smoking.

An ever-smoker was defined as one who had smoked the equivalent of at least one cigarette per day for a period of 1 year. An ex-smoker was defined as an ever-smoker who had stopped smoking for at least 1 year before the current TB episode, and a current smoker was defined as an ever-smoker who was still smoking or had stopped smoking for less than 1 year. Patients who did not fulfill the criterion of an ever-smoker were classified as never smokers. Relapse was defined as recurrence of TB after successful completion of treatment, either proven by isolation of *Mycobacterium tuberculosis*, or in the absence of bacteriological confirmation, recurrence diagnosed on clinical, radiological, or histological grounds. Participants were followed for 2 years after the initiation of treatment as per RNTCP guidelines for treatment outcome.[35]

6. STATISTICAL ANALYSIS:

Mean values (±SDs) were calculated for normally distributed numerical outcomes. Mean values (±SD) for demographic characteristics among never smokers, ex-smokers, and current smokers were analyzed by using the Mann Whitney test. The chi-square test was used to compare non-numerical variables. ANOVA was used for numerical variables in the univariable analysis. Logistic regression analysis was used for multivariable analysis of treatment outcome, and Kaplan Meier analysis was used for univariable analysis of relapse with Cox proportional hazards modeling for multivariable analysis. The significance level was kept at a p value≤0.05. The analysis was done after adjustment for cofounding variables like age, duration of smoking, nutritional status (body mass index, or BMI), socioeconomic status, and diabetes.[36]

7. RESULTS:

A total of 2,504 newly diagnosed pulmonary TB patients were registered for treatment in the hospital during the study period. A total of 154 subjects were excluded from the study because they did not meet the inclusion criteria. Among the 2,350 subjects (1,758 males and 592 females), 1,593 patients (67.78%) were never smokers. Current and ex-smokers numbered 757 (32.21%), of which 751 (31.95%) were males and 6 (0.26%) were females (Table 1). The demographic details of the participants are shown in Table 2. When TB severity and treatment outcome were compared between never smokers, ex-smokers, and current smokers, there was a statistically significant difference in the severity of TB between never smokers and ex-smokers and current smokers. Both ex- and current smokers had more subjects with multiple cavities: 13.5% and 17.4% compared with 8.6% in never smokers ($p < 0.05$). About 73.7% of exsmokers and 73.9% of current smokers were culture- or smearpositive for Mycobacterium tuberculosis, whereas 68.9% of never smokers were smear/culture-positive at the time of diagnosis ($p < 0.05$). At the end of 2 months, 10.2% and 12.4% of ex- and current smokers were smear/culture-positive, respectively ($p < 0.05$).[36]

8. DISCUSSION:

The prevalence of smoking in the current study in newly diagnosed pulmonary TB patients was estimated to be 32.21% in the total study population: 31.95% in males and 0.26% in females. Compared with the prevalence in the general population, this prevalence is very high. The prevalence of smoking in this part of the country (South India) is around 25% to 26% and is negligible in women.7,8 In a study by Wang et al., the proportion of cigarette smoking was 54.6% in TB cases, which was significantly higher than that in controls (45.1%) in China.9 Because that study included both pulmonary and extrapulmonary TB cases, our study is unique in that we enrolled subjects with newly diagnosed pulmonary TB only. Also, in the present study, the number of female smokers was very small compared with China, Nepal, and other Western countries.10,11 In India, the prevalence of smoking among women is negligible because tobacco smoking among women is regarded as socially unacceptable.

The effects of smoking on clinical parameters (lung cavitations, positive sputum smear and culture results) and slower smear and culture conversion after initiation of treatment highlight a serious need for prevention of community-level transmission. Even for patients with initially drug-sensitive TB, the treatment completion rates fell substantially below the WHO target of 85% among both current and ex-smokers in this study. The high proportion of smokers who default treatment

also raises concern over the emergence of drug resistance and secondary spread within the community. The emerging results from our study as well as the many studies discussed above have demonstrated that a large number of smoking TB patients, despite successful treatment, run a substantially higher risk for redeveloping active TB compared with the overall TB risk in the general population. The unfavorable outcome in these TB patients with prolonged smoking behavior poses a risk of a prolonged period of contagiousness.[37,38]

9. CONCLUSION:

From the analysis result, the effects of smoking habit on the development of tuberculosis disease are: Smoking and TB remain a significant health problem in both developed countries and developing countries. Cigarette smoke has the effects of both pro-inflammatory and immunosuppressive in the immune system of respiratory tract. Smoking increases the infection risk of Mycobacterium tuberculosis, the risk of disease progression and death in patients with TB. Quitting smoking plays a role in global tuberculosis control and reduces mortality in patients with TB. The prevalence of smoking is very high in TB patients. Tobacco smoking is associated with a considerably increased risk of advanced and more severe disease in the form of lung cavitations, positive sputum smear and culture results, and slower smear and culture conversion after initiation of treatment. Smoking has a profound negative effect on treatment completion, cure, and relapse rates in patients with pulmonary TB.

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