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Review Article

Association between Tobacco and Tuberculosis: A short narrative review

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ABSTRACT

Background & Objectives: Tobacco use increases the risk of contracting tuberculosis (TB), and blights the response to treatment of the disease. Although Links between Tobacco and TB have long been suspected, still many Indian patients continue to use tobacco. Our goal is to couple reviews of older and new research to provide definitive evidence of this dangerous connection so as to put an end to the TB epidemic.

Materials and Methods: Search of studies with English language abstract published between 2000 to June 2020 was undertaken in Google Scholar and PubMed. Search included the use of keywords “tobacco” with “tuberculosis,” “cessation,” or “Tuberculosis Control Programme”. Reference lists of the articles were examined for other relevant titles that included effective estimates of tobacco exposure in relation to tuberculosis outcomes.

Results: Available evidence shows a strong association between tobacco and tuberculosis. People who use tobacco unknowingly put themselves at high risk of getting this disease. Reduction in the prevalence of tobacco use is urgent to bring about collateral benefits in the control of the TB problem.

Interpretation & Conclusion: It is high time that TB control programs must begin to address tobacco control. Within the healthcare system opportunities must be created to provide encouragement for the TB patients so that it is easier for them to overcome this addiction.

Key Messages: There urgent need for research in the field of tobacco and tuberculosis so as to reduce the burden of tuberculosis in India.

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1. Introduction

Worldwide Tuberculosis is the second largest cause of death from an infectious disease. One-third of the world’s population is infected with Mycobacterium (M.) tuberculosis.¹ All human beings are not equally sensitive to this infection. Ten to fifteen percent of those infected will develop active TB sometime in their life.² In 2018 approximately 10 million people fell ill and 1.5 million died from TB worldwide.³ About 20% among these were from India alone and this disease continues to be the largest public health problem in our country. The major drivers of the

TB epidemic involve the emergence of drug resistant, TB bacteria and the coexistence of Human Immunodeficiency Virus (HIV).⁴ There is sufficient consensus that high prevalence of tobacco use is a risk factor for TB and approximately 20% of TB cases are associated with tobacco consumption, but it is disappointing that only recently tobacco and tuberculosis relationships started to receive attention. Health care workers who have been focusing on TB since ages have rarely considered the impact of tobacco cessation on these patients. According to World Health Organization (WHO) it is estimated that the risk of both Mycobacterium tuberculosis infection and active tuberculosis is double among people who smoke. Active and passive smoking are independent risk factors for TB

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infection, increased progression to pulmonary TB resulting in high mortality rates. TB affects 70% of people in their most productive years of life i.e 15-54 years and 50% of these cases occur before 34 years of age. TB patients using tobacco regularly are less amenable with TB treatment because smoking prompts coughing and other symptoms consistent with tuberculosis, due to which delayed diagnosis of tuberculosis among smokers as compared to non-smokers have been observed. If TB patients were not smoking, one in every five deaths could be prevented.⁵ As reported by Gajalakshmi in 2003, the risk of death from TB in India for every smoker is around 5% with homogenous incidence across rural and urban areas.⁶ Many TB patients use Smokeless Tobacco (SLT) products instead of smoking. SLT products are linked to cancer but many studies have shown that the use of SLT increases the risk of death from respiratory diseases and TB. On this, it makes it necessary for the perception that smokeless tobacco use is less harmful for patients with TB needs to be corrected. Many patients who were advised to quit smoking, alternatively engaged in the use of SLT as a form of harm reduction. However, researchers prove that the use of tobacco in any form is equally harmful for TB patients. Therefore, tobacco use puts enormous burdens on countries like India who are already ailing economies and contribute to existing impoverishment. Despite having substantial evidence about the impact of tobacco control measures, particularly tobacco cessation, on TB outcomes, the integration of TB and tobacco control still remains far-off. This white paper discusses the role of tobacco in increasing cases of TB making this connection deadly to the entire nation. With widespread awareness and strong data of the association between the two, control in reaching the ambitious goal of ending the TB epidemic by 2030 can be achieved.

1.1. Mechanism of the effect of Tobacco on TB infection

Tobacco use weakens the lung defence mechanism and makes patients susceptible to infection, which involves the decrease in activity of Natural Killer (NK) cells as well as mucociliary clearance. Furthermore, tobacco may have an irreversible inhibitory effect on nitric oxide synthase – the enzyme needed by alveolar macrophages to form nitric oxide to inhibit the multiplication of *M. tuberculosis*.⁷ In lower respiratory tract, tobacco increases the availability of iron which binds with nitric oxide to stimulate toxic radicals that can interfere with macrophages,⁸ disrupts the function of macrophages (CD4+ and CD8+ T-cells) and production of cytokines (TNF- α and IL-12) which are key defenders against TB.⁹ Study done by Murya et al. in 2002, reported that tobacco contains oxidants which are responsible for an increase in oxidative stress in the lungs of smokers.¹⁰ Thus, antioxidant levels are reduced in the serum of smokers. In aged smokers there's decrease in the antioxidant defences of the alveolar macrophages. This imbalance of oxidant and

antioxidant levels may result in tissue damage in the lungs of smokers.

1.2. Prevalence of smoking in tuberculosis patients

As tobacco has a strong negative impact on the clinical manifestations, treatment outcomes and progression, it is important to evaluate the pattern of tobacco smoking, history of previous quit attempts, and attitude towards quitting in tuberculosis patients. In India 14% of TB cases and 32% of TB deaths were attributable to smoking. Navya et al. 2019 reported that 435,000 deaths were caused by TB due to tobacco use in 2016.¹¹ Tobacco smoking increases the risk of dying of TB and causes a significant risk of tuberculosis recurrence despite treatment. Another study conducted in Dakshina Kannada district between January and June 2017 reported a total of 413 adult patients with TB registered under Revised National tuberculosis Control Programme (RNTCP), Out of the total patients, tobacco use was documented in 322 (78%). Among them 86 (21%) patients were current tobacco users. Of these 86 tobacco users, the one who used Smokeless tobacco were 21 (5%) and those who smoked were 39 (10%). Mathematical modelling based study has estimated that between 2010 and 2050, smoking could raise 18 million TB cases worldwide.¹² These findings explain the importance of tobacco cessation interventions in smokers with tuberculosis.

1.3. Tobacco control intervention implemented into tuberculosis control programs

Since 1992, the Government of India (GOI) put forth many national programmes to control TB together with WHO and Swedish International Development Agency (SIDA). The program primarily focused on identification of TB patients through diagnosis and treatment of TB patients, but still faces setbacks in the success of the program. This is majorly due to insufficient funding, traditional diagnosis methods through X-ray, unmonitored programs, moth-eaten treatment protocol, managing medication by low cost, inadequate funding, neglected cases and treatment investigations.¹³ Pathetic situation of program implementation able to identify 30% of TB cases and successfully treated only 30% from the identified case. After various modifications, up gradation in the program with revised strategies by increasing the funds against TB from World bank, adopting advanced techniques and advancement in treatment regimen to lowering the TB cases.

In this phase of implementing the program, the GOI launched updated and adopted new strategies in TB control through Revised National TB Control Programme (RNTCP), 2016. And started implementation of Nation Strategic plan for TB elimination through “Detect, Treat, Prevent and Build” (DTPB). For detection of TB patients

by segregating to sensitive and resistant TB cases with high sensitive diagnostic test method functioning in more than 196 (TB lab) and 2500 (molecular diagnostic labs) of centres nationwide.¹⁴ Improved treatment for TB such as free drugs for daily course and short-course regimen, specified drugs for resistant TB patients, nutritional support and monitoring and follow-up treatment. Treatment associated with HIV's/ alcohol creating health care facilities with advanced bacteriological screening labs with testing set-up of Cartridge Based Nucleic Acid Amplification (CBNAAT), Line Probe Assay (LPA), Liquid culture, airborne infection control and addressing social determinants of TB. Supporting welfare of TB patients through a patient support system to improve the nutritional status and private health care providers with online incentives support of Rs.6750/- through TB reporting software "Nikshay". And in enabling the program by empowering institutions/ centers with full-scale enhanced capacities of resources and infrastructure and organizing partnership activities of program needs.¹⁴

Additionally, RNTCP collaboratively developed the framework program of TB with Diabetes (NPCDCS), Tobacco use (NTCP) and Alcohol consumption, as this will increase health risk of TB patients. Through these collaborative programs, the TB patients screened and facilitated special attention by promoting them to bidirectional screening and treatment for tobacco and TB cases. The identified TB-tobacco user's advice in brief for routine cessation program through NTCP for 5A's (Ask, Advice, Assess, Assist and Arrange) and 5R's (Relevance, Risks, Rewards, Roadblocks and Repetition) research based counselling.¹⁵ Patients of TB cum tobacco instructed to follow-up for the regular visit cessation center, healthcare provider and recommended for national helpline/ quitline links. Even though the integrated measures of TB-tobacco taken for the control of two global epidemics results with a shortfall in coordination of two programs.

1.4. Effective strategies to control two global epidemics

Vast information of integration of TB and tobacco exist in the record level only about the policy, planning, training, practice and monitoring.¹⁶ WHO actively proposes guidance and attractive programs for global robustness, but the outcome seems underdeveloped.¹⁷ In certainty, there is poor integration between TB and tobacco programs.¹⁸ The fact needs to be revealed, for that requires a sufficient period of time to get an update about the program report or literature. From national and international researchers' lots of recommendation, suggestion and guidance are listed for the betterment of program outcome¹⁹

Few were listed below;

1. Gap analysis to create sufficient evidence in capturing information in the region-wise as a part of TB and

tobacco control program.

2. Updating records of both tobacco and TB by capturing valid information through surveys/ databases revealed in common platforms such as PubMed, WHO, Clinical trial, EU tobacco control database, tobacco control laws database, etc.
3. Drafting a bi-directional screening mechanism where tobacco users are screened for TB symptoms and vice versa (screening TB patients using tobacco) which should be followed with appropriate referral mechanisms.
4. Establish continuous care and support among TB patients (in TB clinics) who wish to quit tobacco and help them by providing a supportive environment where healthcare workers keep a check on their smoking habits and are recorded on routine. TB reporting forms followed by counselling them on quitting tobacco and ensuring healthcare facilities are strictly smoke-free. Cured patients must be instructed/warned to not use tobacco again as it may lead to re-infection and disease
5. Training of the TB and tobacco control core experts by WHO, EU, US, etc. for gap analysis in activities and monitoring to carry out smooth accomplishment of tasks.
6. Focus in developing tobacco-TB experts nationwide for team performance by engaging them with a proper strategic action plan.
7. Increasing surveillance on cessation care facility/ centre based approach by periodically inspection at various departments belongs to the program.
8. Creating awareness towards the TB-tobacco associated health outcome via. SMS, mail/ web-based popup, advertisement, social/ scientific interface like Radio, Television, Twitter, LinkedIn, ResearchGate, announcement in Public gathering areas, etc.

2. Materials and Methods

Literature search on this review in Google Scholar and PubMed were performed from 2000 to June 2020. Search terms included: tobacco with tuberculosis, cessation, and Tuberculosis Control Programme. Studies that included the investigation of the relationship between SLT, smoking, TB, death due to TB were focus of our interest. Reference lists of the articles were obtained for other relevant and similar titles which included effective estimates of tobacco exposure in relation to tuberculosis outcomes. Studies in English were only taken into consideration. Results were obtained by descriptive and narrative synthesis of findings which highlights the association between TB and Tobacco.

3. Results and Discussion

Data on the prevalence of tobacco has been clearly associated with the problem of tuberculosis. Due to very little research in this particular area, people put themselves at the risk of developing this disease. As per the literature above, it was noticed that there exists a high number of the population consuming tobacco in any form have TB. The prevalence increases day by day because coughing—a general symptom of TB is often disassociated with that occurring from smoking. Hence, in the initial phase when the person who is a smoker has excessive coughing, it is considered as a consequence of it which delays the diagnosis of TB by making it even more threatening to an extent that the risk of death increases. Continuous consumption of tobacco changes the mechanism of lung functioning thereby weakening the immune system and changing the respiratory function. A study by Kark et al. found that tobacco users are 1.44 times more likely to develop respiratory infection as compared to nontobacco users.²⁰ This includes both active and passive types of smoking. Global TB report by WHO in 2007 clearly stated that smoking is one of the major risk factors for TB. Many studies support the idea that the morbidity of TB in smokers is 1.6 – 2.5 times than that of non-smokers. It has also been proved that tobacco abuse from a young age i.e less than 16 years is a key factor of active tuberculosis.²¹

As described above, the two epidemics “tobacco and Tuberculosis” require many policies and effective strategies to slow down their pace. Understanding the dreadful effects of smoking on TB outcomes is essential to control TB on the whole. A strong need to educate the population on these two concepts is critically important. And as tobacco hinders the treatment of TB to a great extent leading to drug resistance, this problem also needs to be addressed. The evidence on this is also vast. Quite a lot of studies focus on recurrence of tobacco which is found to be significantly higher among tobacco users. Chuang et al. confirms by his study that smokers have a higher rate of failure in treatment of tuberculosis and thus tobacco users require a longer treatment plan.²² If tobacco consumption is carried on for longer period of time, it can lead to devastating effect on the entire population by spreading of TB which is contagious. This never ending bond between the two might lead to a condition which will be both expensive and difficult to treat.

4. Conclusion

Tobacco on the whole can increase the incidence and mortality of TB in clear manner. The recurrence rate of TB is higher among tobacco users as compared to non-tobacco users. Thus, it can be concluded that there is an urgent need to highlight the relationship between tobacco use and tuberculosis which has been misunderstood since ages. Policies that reduce the use of tobacco are likely to reduce the prevalence of tuberculosis. Thus, such healthcare

systems must be initiated so as to encourage TB patients to quit tobacco with keenness. Combined these efforts could translate into major gains in population health. There is a need to expand the evidence base on morbidity especially in lower income countries. If such plans are initiated in countries, beating TB by 2030 wouldn't be impossible.

5. Source of Funding

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6. Conflict of Interest

The authors declare no conflict of interest.

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