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Editorial

Why "STOP TB" Is Incomplete Without "QUIT SMOKING"

India bears a fifth of the world's burden of tuberculosis (TB). Despite a highly successful directly observed treatment, short-course (DOTS) programme, TB still remains a formidable disease. In the year 2008, 1.98 million incident cases were reported and there were an estimated 11.1 million prevalent cases. Tuberculosis accounts for 17.6% of deaths from communicable disease and for 3.5% of all causes of mortality in India.[1] The prevalence of smoking in India has been estimated to be anywhere between 14.6% to 43.0%, a significant percentage of smokers reporting respiratory symptoms.[2,3] A sizeable proportion of Indians smoke *bidis,* a tobacco delivery system akin to cigarettes that comprises 0.2g to 0.3g of tobacco rolled in the leaf of the *temburni* plant,[4] and data on the risks of *bidis* in particular are limited. The convergence of the epidemics of smoking and TB, and their association, if causal, represents a modifiable risk factor, and a useful preventive adjunct to curative chemotherapy in further reducing the incidence of TB in India.

Smoking impairs lung defences in several ways. Structurally, the mucosal defense barrier is abrogated, mucociliary clearance is impeded and pathogen adherence affected. The inflammatory changes and mucosal hyperaemia also impair defences against pathogens.[5] Functionally, cigarette smoke is associated with depressed immune function, both cellular and humoral. In the context of the susceptibility to TB, smoking is known to significantly affect macrophage function and depress CD4+ cells and cause a significant increase in CD8+ cell counts.[6,7]

Several studies have analysed the association between smoking and TB. The meta-analyses by Bates *et al*,[8] Lin *et al*,[9] and Slama *et al*[10] were the most comprehensive recent analyses on this association. These analyses looked at the risk for acquiring infection, risk of disease and mortality. While the evidence on risk of infection and mortality do suggest that these are increased among smokers (relative risk[RR] for infection with 95% confidence interval [CI] ranging from 1.45 to 2.11 and for mortality 1.14 to 3.49 across these analyses), the consensus is that the data are limited and insufficient to comment upon. The risk of active TB among smokers was significantly higher with the association being found to be strong, and a RR with 95% CI ranging from 1.97 to 3.37, suggesting that smokers seem to have atleast twice the risk of developing the disease. This association remained strong even in the pooled analysis of studies that adjusted for confounding variables including alcohol use, socio-economic status and gender. Second-hand smoke also appeared to increase the risk of TB, although the data was limited.

The largest Indian study from Tamil Nadu[4] on the association of smoking and mortality from TB was a case-controlled study of the causes of death among 27000 urban and 16000 rural men (aged 25-69 years) with 20000 and 15000 controls, respectively. The study relied on a verbal autopsy for the accurate cause of death. It was found that the RR of death from TB was 4.5 (95% CI 4.0-5.0); 11.44% of all deaths from medical causes were attributed to the disease. Of these, 79% of these patients were smokers, and the authors concluded that 61% of these deaths would have been averted had these patients with TB suffered mortality rates from TB that were comparable to their non-smoking counterparts. The study also found a statistically significant correlation between the amount of tobacco smoked and the risk of the disease. A prospective study of 81,443 men from Mumbai[11] conducted between 1991 and 2003 concluded that 32% of TB deaths could be attributed to *bidi* smoking. The adjusted mortality risk due to TB among *bidi* smokers was 2.60 (95% CI: 2.02 to 3.33) when compared to never-smokers, while the RR of TB (self-reported) among *bidi* smokers was 5.23 (95% CI: 4.01-6.82) when compared to never-smokers.[11] A more recent study[12] from south India conducted among men aged 35-64 years compared 949 cases treated for new pulmonary TB with 1963 controls. A RR of 2.7 [95% CI 2.2 to 3.3, P<0.00001) was found for incident TB among ever-smokers compared with never-smokers. While consumption of alcohol was also found to be associated with TB, the effects of smoking after adjustment for alcohol consumption were stronger than those of alcohol consumption after adjustment for smoking.[12]

Biomass fuels, widely used for cooking, are a significant source of indoor exposure to smoke, especially among women in India, and have been associated with various respiratory diseases, including chronic obstructive pulmonary disease and lung cancer.[13] A study comparing 255 cases of TB and 1275 controls from south India found an unadjusted odds ratio (OR) for the disease among those exposed to biomass fuels using univariate analysis to be 2.9 (95% CI 1.8 to 4.7) and using multivariate analysis to be 1.7 (95% CI 1.0 to 2.9), 36% of cases being attributable to biomass fuel usage. The meta-analysis by Lin *et al*[9] also came to similar conclusions, but asserted that further studies were needed to clarify this association.

The causal association of passive smoking exposure and TB needs further validation using biochemical markers such as cotine to quantify

exposure, and a dose-response risk calculation using similar biochemical means are potential areas of future research.[10]

A recent study from Taiwan[14] consisting of a cohort of 486,341 adults participating in standard medical screening programmes since 1994 and followed till 2007 did provide encouraging results. It concluded that smokers had almost a nine-fold increased mortality due to TB. However, when they quit smoking, the risk was reduced by 65% to a level that was comparable to never-smokers.

There is a significant quantum of well-designed studies and pooled analyses that irrefutably prove the causal association between smoking and the risk of developing TB disease. The increased risk of being infected with TB among smokers, although proven to be higher than non-smokers, needs further validation. In a country where atleast 40% of the population is latently infected,[1] it would be worthwhile conducting further studies to explore this association. The increased risk of mortality due to TB among smokers also needs to be validated by more robust studies. The associations of passive tobacco smoke exposure or biomass fuels with TB are particularly relevant in India, and the limited data do suggest a causal association.

The implications of this are two-fold. First, physicians need to spell out the risk of TB to smokers while counselling them regarding the dangers of smoking and encouraging them to quit. In a country where TB still carries a social stigma, the fear of acquiring it may serve as a negative reinforcement to quit. Secondly, a history of smoking should be sought from every TB suspect, as a positive history should strengthen the index of suspicion. A clinical trial is underway in Pakistan to study the use of the window of opportunity during screening for TB to encourage smoking cessation,[15] and similar trials need to be performed to evaluate various such strategies. The knowledge of the causal relationship between smoking and TB would also cause realisation that smoking predisposed the individual to the disease, and therefore, encourage cessation of smoking.

To conclude, the holistic approach to reducing the TB burden in India would be served well by adopting primary preventive measures such as encouraging smoking cessation, reducing the use of biomass fuels and integrating these into the existing secondary and tertiary care measures.

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