Tobacco use and body mass index: Do they have synergistic effect on mortality due to tuberculosis?


SUMMARY
A population-based cohort study was done in the city of Mumbai, in which 148 173 persons aged 35 years and above were recruited between 1991 and 1997. Information on sociodemographic variables, viz. age, education, religion, mother tongue and tobacco use was taken and the weight and height of each participant was measured at baseline. Exposure variables were body mass index (BMI) and tobacco use. BMI was categorized as extremely thin (<16.0), very thin (16.0–<17.0), thin (17.0–<18.5), normal (18.5–<25.0), overweight (25.0–<30.0) and obese (≥30.0). Tobacco use was classified as never used tobacco, used smokeless tobacco only, and those who smoked tobacco. The follow-up was done after a mean period of 5.5 years after the baseline survey during 1997–2003. Data of participants were censored either at the time of migration or death. Causes of deaths were ascertained with the municipal corporation death registers. The outcome variable was death due to tuberculosis (TB). Never tobacco users and overweight were considered as the reference group. Multivariate Cox proportional hazards regression model was used to calculate association between exposure variables and outcome. Taking gender as the effect modifier, gender stratified adjusted hazard ratio (HRs) and 95% confidence intervals (CIs) were estimated for the joint effect of BMI and tobacco use on death due to TB. To quantify the interaction between the two exposure variables, expected HRs for multiplicative model were calculated by multiplying individual HRs for the various categories of tobacco use across BMI and for the additive model by adding individual HRs and then subtracting 1 from the total. Observed HRs higher than the calculated expected HRs indicated synergistic interaction, in contrast it was indicated as antagonistic interaction if it is lower. Population attributable risk for various exposures was also reported.

Among men, in a particular BMI category, the adjusted HR was highest among smokers followed by smokeless tobacco users and never tobacco users. In the extremely thin BMI category, HR among smokers, smokeless tobacco users and never tobacco users were 36.22 (CI 19.41–67.61), 25.50 (CI 13.55–48.00) and 25.40 (CI 13.02–49.54), respectively. Further, in a particular tobacco use category the adjusted HR increases as BMI decreases. Among smokers, HR for extremely thin, very thin, thin and normal were 36.22 (CI 19.41–67.61), 13.59 (CI 6.93–26.65), 8.67 (CI 4.51–16.70) and 2.89 (CI 1.54–5.42), respectively. TB mortality was found to be associated with self-reported TB at baseline but no association with diabetes was reported. It was found that tobacco use and BMI had a synergistic effect in men but antagonistic effect among women—the observed HR in men was 36.22 (CI 19.41–67.61) which is more than the expected HR 23.37, whereas in women the observed HR was 19.39 (CI 6.79–55.35), which is less than the expected HR 30.32.

Among men with a BMI <18.5 kg/m², deaths due to TB were 9%, 22% and 27% in never smokers, smokeless tobacco user and smoker, respectively. Among women with a BMI <18.5 kg/m², deaths due to TB were 12% and 37% among never smokers and smokeless tobacco users, respectively.

COMMENT
There are many studies from India and globally reporting the individual effect of tobacco use and BMI mortality due to TB but there are few studies showing the combined effect of both. This study reports the interactive effect of tobacco use and BMI on mortality due to TB. The strength of this study is that it is a large, prospective cohort study and the period of follow-up is adequate to observe the joint effect of BMI and smoking. Confounders particularly history of previous exposure to TB and diabetes mellitus were adjusted along with other sociodemographic factors. However, there are a few issues which require closer scrutiny. The authors have included only persons ≥35 years of age. Also the ascertainment of outcome is based on municipal records, the reliability of which can be questioned but there was no other means by which this data could be obtained. Confounding variables such as HIV status and malignancy, which are important particularly in the older age group, were not adjusted. Worldwide, about one-third of HIV-infected individuals are coinfected with TB. This can have a remarkable effect on progression of TB and HIV can also lead to under-nutrition and increase the mortality due to TB. Among the risk factors there should have been a group of former tobacco users, as clubbing of this group with never users or tobacco users will lead to a misclassification bias. In this study, exposure measurement was done only at baseline. It is possible that the exposure status may change over time. This study could have been designed as a nested case–control to answer this particular research question.

TB is one of the most common causes of morbidity and mortality in India, especially in the productive age group. Despite the Revised National Tuberculosis Control Programme (RNTCP) being operational for around 20 years, there has been little decline in mortality due to TB. India has more new cases annually than any other country. According to the WHO global report 2010, prevalence of TB in India was estimated to be 249 per 100 000 population and mortality due to TB was 23 per 100 000 population. WHO has reported that though there is an increase in and improved diagnostic and treatment services this is annulled by an increase in the prevalence of risk factors such as HIV infection, diabetes, tobacco, malnutrition, silicosis, malignancy, environmental factors such as indoor air pollution, ventilation, crowding and socioeconomic factors such as urbanization, migration and poverty. These risk factors lead to progression of latent TB to active TB. It also leads to an increase in the incidence of TB though there is a reduction in disease transmission.

Tobacco use is one of the major contributors of mortality due to TB. Tobacco use also leads to a decrease in BMI and has a positive interaction with BMI in causing death due to TB.

In India tobacco is used as a smokeless form and smoking. There are more smokeless tobacco users in comparison to cigarette smokers. Smoking contributes to around 149 000 male TB deaths per year in India. Although, all forms of tobacco use can have
serious health consequences. Nearly 50% of Indian adults have different types of chronic energy deficiency, and have a BMI <18.5 kg/m². A similar study done in Lucknow, Uttar Pradesh has shown that there was a positive association between pack-years, BMI and socioeconomic class. In a study it was reported that there is a positive association between tobacco smoking and pulmonary (bacillary) TB. This association also shows a strong dose–response relationship. Since the magnitude of tobacco use and lower BMI is higher in India, clustering of these two effects in India is inevitable. This leads to a higher risk of deaths due to TB. The prevalence of tobacco use is also increasing. So, strategies for control of TB should be synergized with tobacco control efforts and should focus on the nutritional status of the patients to have a positive impact on reducing mortality due to TB.

REFERENCES

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Heavy consumption of alcohol: A risk factor for cancer deaths?


SUMMARY
According to the International Agency for Research on Cancer, alcohol is a group 1 carcinogen, i.e. there is sufficient evidence of carcinogenicity in humans. However, results obtained from various epidemiological studies are inconsistent and demonstrate male–female differences. The exact dose–response relationship has not yet been reported by meta-analysis at the time of this study. Hence, this meta-analysis was done to elucidate the association of alcohol drinking with all cancer mortality, and the corresponding dose–response relationship.

A PubMed search was done to identify eligible studies published in English up to April 2012. Case–control, case–cohort and cohort studies which focused on the association of drinking alcohol with all cancer mortality, and which presented the odds ratio, risk ratio or hazard ratio estimates with the corresponding 95% confidence intervals (CI), were included. Other studies which provided sufficient data to calculate non-occasional drinking as the reference category, were also included. If multiple papers were published from the same population, the most informative one (often the most recent) was included. Studies reporting the estimates of only a specific kind of alcoholic beverage were excluded.

Finally, 18 eligible papers were included in the meta-analysis, 17 with an association for ≥3 categories of alcohol, and one with an association of drinking versus non-drinking. All of these were cohort studies. The duration of follow-up ranged from 4.6 to 19 years across studies. The number at risk ranged from 1620 to 490 000 persons in four studies, and 107 385 to 82 716 472 person-years in 14 studies. Two investigators independently extracted data with concealment of journals, authors, supporting funds and organizations. Two reviewers independently did quality assessment of the selected studies, using a set of questions modified from previous studies. On a scale of 0 to 10, the quality scores ranged from 3.5 to 8.5, with a median of 6.5 for methodological assessment. A total of 48 178 deaths from all cancers were observed among all these cohort studies.

Alcohol consumption reported across studies in various units were converted to grams of alcohol, and alcohol drinkers were grouped into three, viz. light, moderate and heavy drinkers defined as an ethanol intake of ≤12.5 g/day (≤1 drink/day), 12.6–49.9 g/day (2–3 drinks/day) and ≥50 g/day (≥4 drinks/day), respectively. To evaluate heterogeneity, Cochrane Q test and I² statistics were calculated. Random effects model was used when a notable heterogeneity (p of Q test ≤0.1 and/or I² index ≤50%) was present. Subgroup analysis and cumulative meta-analysis were done. Publication bias was assessed by Egger linear regression and Begg rank correlation. Begg funnel plot was also drawn. Flexible restricted cubic splines method was used in the dose–response analysis.

As compared with non-/occasional drinkers, the pooled relative risks (RRs) were 1.05 (95% CI 1.00–1.10; p for heterogeneity=0.008) for any, 0.91 (95% CI 0.89–0.94; p for heterogeneity=0.449) for light, 1.02 (95% CI 0.99–1.06; p for heterogeneity=0.105) for moderate, and 1.31 (95% CI 1.23–1.39; p for heterogeneity=0.442).