Smoking Prolongs the Infectivity of Patients with Tuberculosis

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Abstract
We sought to establish if smokers on anti-tuberculosis treatment are more likely to have a prolonged period of infectivity, compared to non-smoking tuberculosis patients, in a low tuberculosis prevalence country. We conducted a cross-sectional, retrospective study in Ireland that recruited 53 microbiologically confirmed cases of pulmonary tuberculosis (PTB). The age-sex adjusted odds ratios (AOR) suggest that the infectivity status of PTB on treatment was four times more likely to be prolonged beyond 6-8 weeks, if the cases had a smoking history (AOR: 4.42; 95% CI: 1.23; 15.9). Smoking was associated with delayed sputum smear conversion in PTB patients on treatment.

Introduction
Tobacco use and tuberculosis disease (TB) are global public health challenges. Recent evidence suggests that active smoking is a risk factor for progression from latent tuberculosis infection to reactivation and TB mortality, especially in resource-poor settings. Evidence also suggests that following the onset of tuberculosis treatment, it takes approximately six to eight weeks before a tuberculosis patients sputum is bacillus-free, depending on the patients biological and immunological response to mycobacterium tuberculosis. There are many factors influencing such a response directly or indirectly. Factors influencing delayed sputum smear conversion have been studied. However, the effect of active smoking on tuberculosis patients infectivity status in response to anti-tuberculosis treatment has not been evaluated in a low tuberculosis incidence country such as Ireland. The aim of this study was to investigate whether smokers currently on anti-tuberculosis treatment are more likely to have a prolonged infectivity compared to non-smoking tuberculosis patients.

Methods
A cross-sectional, retrospective study was conducted at St James Hospital - a tertiary care referral hospital in Dublin. Following ethical approval, we looked at all 160 cases of pulmonary tuberculosis (PTB) patients who attended our service between April 2007 and April 2008. Based on the following inclusion/exclusion criteria, we studied a group of 53 patients who shared similar characteristics; although they were not, strictly speaking, a cohort. Inpatients and outpatients were included who had sputum AFB-stain-smear and culture positive adult active PTB currently on anti-tubercular treatment (ATT). We excluded extra-PTB as they are least infectious and are sputum smear and culture negative. We conducted the study radio graphically diagnosed PTB cases with negative or no sputum smear or culture completed, and cases with cavitory lesions and extensive lung involvement or cases associated with immune-compromised conditions, including: diabetes, hepatitis, cancer, and HIV/AIDS.

We excluded PTB with no or incomplete sputum smear or culture results, and Multiple Drug Resistant or Extreme Drug Resistant cases - because drug resistant TB strains do not respond to the usual first line drugs and the sputum conversion to negative in such cases is usually delayed. We also excluded patients whose charts lacked smoking data. A pro forma with detailed individual information on demographics, socioeconomic and clinical characteristics was set up using patients' charts. Patients microbiology data was recorded related to both sputum smear and culture positivity and time (weeks) taken by the sputum smear and culture to turn negative after treatment. Three consecutive sputum smear results were recorded. Two sputum culture results were assessed because Acid Fast Bacillus (AFB) sputum smear positivity alone is not a reliable measure of a patients infectivity and response to treatment. Treatment history (completed, continuing, defaulted) was assessed, including the date of onset of treatment.

Both bivariate and multivariate logistic regression analyses were performed using SPSS, (14.0) and SAS (9.1 version, Cary NC.) softwares, respectively available at Trinity Colleges computer centre. Pearson's Chi2 test for proportions was performed comparing smokers with non-smokers (who have not smoked for the past six months and/or who have never smoked) across several co-variates. Multivariable logistic regression analyses were performed to adjust for several co-variates (age, sex, nationality, employment status) for the exposure-outcome association studied: infectivity status (outcome of interest) vis-à-vis smoking status (exposure of interest) of the tuberculosis cases. Hosmer Lemeshow tests were applied to test the goodness-of-fit models.

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Results
Of the total 53 PTB cases, 28 were smokers, and 25 were non-smokers. Twenty-three of the 28 smokers were currently smoking i.e. who smoked cigarettes daily for the past thirty days; and five were former (or -ex) smokers (i.e. who have stopped smoking for the past thirty days). Of the 28 in the smokers group, 18 (64%) had less than twenty cigarettes per day (light smokers), while ten (19%) smoked twenty or more cigarettes per day (heavy smokers). Seventy-nine percent (22/28) of smokers had a prolonged infectivity status (>6 weeks sputum positivity) compared to 48% (10/21) of the non-smokers (p=0.02*) (Table 1 and Figure 1). Thirty-five cases were e25 years of age, Irish (n=23) and unemployed (n=26).

The age-sex adjusted odds ratios (AOR) suggest that the infectivity status of PTB patients currently on ATT were four times more likely to be prolonged beyond 6-8 weeks if they had a smoking history compared to those with no smoking history (AOR: 4.42; 95% CI: 1.23; 15.9). On further adjustment a similar upward trend persisted in sputum smear results alone is not a reliable measure of a patient's infectivity and response to treatment. Hosmer Lemeshow tests were applied to test the goodness-of-fit models.

Figure 1: Smoking prolongs infectivity status of PTB Patients

*Statistically significant

Smoking Prolongs the Infectivity of Patients with Tuberculosis
This study showed that smoking is potentially associated with a prolongation of the infectivity status in active PTB patients currently on ATT. The consequences of a prolonged infectious interval include an increased public health risk of spreading the epidemic, and prolonged isolation of the TB patient. We have demonstrated that smoking is such a negative factor in a low TB prevalence country (Ireland TB case rate ~11/100,000 pop/yr) with evidence that demonstrates the negative effects of smoking on TB patients - such as prolongation of clinical disease and mortality. Recently this issue of smoking prolongation was addressed in higher incidence / prevalence countries (Spain and Kuwait). TB rates of 30 and 24/100,000, respectively.6 Our estimates of infectivity prolongation are conservative, compared to the Spanish study; and the Kuwaiti study found the effect in expatriate workers only, who would have come from higher incidence countries.7,8 Although Ireland experienced a large immigrant population in recent years, who tend to smoke greater than the general Irish population,9,10 our study showed a similar upward trend when nationality was accounted for; especially in Irish subjects (p=0.036* table1) but this was underpowered when all nationalities were considered.

Unemployment is an independent risk factor for smoking in the general population and a similar trend was initially observed (p=0.03* Table1). But on further adjustments the present study shows that nationality and unemployment were not independent risk factors for the association studied. However, it is worth considering whether Irish nationals are indeed more susceptible to a prolonged infectivity status if they have PTB and smoke at the same time. The Global TB Control Programs have yet to embrace smoking cessation as an important strategy. However, the STOP TB Partnership and WHO’s Stop TB Strategy is a step in the right direction - WHO has developed a policy paper on the integration of TB Control Programs have yet to embrace smoking cessation as an important strategy. However, the STOP TB Partnership and WHO's TB Strategy is a step in the right direction - WHO has developed a policy paper on the integration of TB control and tobacco control activities into primary care services using the Practical Approach to Lung Health (PAL) framework.11-14

The study findings lend further support to the negative health effects of tobacco use, as shown by other studies. Archavi et al have presented data that links smoking to increased susceptibility to infection in general, although the biological basis by which tobacco smoking may increase the risk of developing active TB is poorly understood. This aspect of host immune impairment is not well researched, but it shares some of the mechanisms that link infection and smoking generally. Nicotine might interfere with TB immunity potentially by decreasing the TNF— response to infection. A mechanism linking vagal stimulation, nicotine, and impaired TB responses in smokers exists, as suggested recently by Dheda et al , yet no mechanistic evidence for increase TB susceptibility has been published yet.

This cross-sectional study has limitations. Due to missing information about some of the variables, Table 1 shows that 53 cases were selected as our final sample, yet our final number fell, (i.e. n=47-2, Table 1) but this did not have a substantial effect on the overall study results. Because of a low prevalence of tuberculosis in Ireland, the study was underpowered for sub-group analyses. A larger sample size with a longer follow-up in a high TB prevalence setting could address this potential statistical issue. No causal inferences are plausible and recall bias is a possibility. In conclusion, PTB patients currently on ATT might recover faster if they are also advised to quit smoking earlier. Further basic and epidemiological research that studies the causal link between smoking and reactivation tuberculosis should be undertaken, especially in low prevalence countries, if the goal of TB elimination in such countries is to be achieved.

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