Review Article

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HIV & smoking in India

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There are approximately 2.5 million people living with HIV/AIDS (PLWHA) in India - the young being particularly vulnerable. The prevalence of smoking has increased in India especially among rural, lower socio-economic and illiterate men. Studies have shown that HIV-infected smokers may be at additional risk for several infectious and non-infectious complications, including malignancies and cardiovascular events. Smoking alters immunological mechanisms and suppresses host defenses in the alveolar environment. HIV-infected smokers have also been found to have a poorer response to antiretroviral therapy and a higher risk of death. HIV-infected individuals who smoke could be at a greater risk for developing TB and subsequently suffer higher morbidity and mortality than those who do not smoke. Currently available smoking cessation interventions like physician's advice, nicotine replacement therapy and pharmacological agents like bupropion and varenicline have had varying degrees of success. Smoking cessation intervention in the HIV-infected population might be more complex because of associated psychosocial problems like drug addiction, alcoholism, depression, *etc*. More research including clinical trials testing the efficacy of smoking cessation interventions in HIV-infected persons is required in India. In addition to public health measures like banning smoking in public places and raising tobacco tax, comprehensive guidelines for health workers can help address this problem. Counselling on smoking cessation should be one of the main components of primary care, especially in the management of HIV-infected persons. This review highlights the importance of smoking cessation among HIV-infected persons in India.

Key words HIV - India - smoking cessation - tobacco - tuberculosis

Introduction

Tobacco consumption is currently the single leading preventable cause of death[1]; over 500 million people may die due to tobacco by 2030[2]. Cigarette smoking is associated with a ten-fold increase in the risk of dying from chronic obstructive lung disease[3]. About 90 per cent of all deaths from chronic obstructive pulmonary diseases (COPD) are attributable to cigarette smoking[3]. Environmental tobacco smoke is a leading asthma trigger[4]. Cigarette smoking increases the risk for cancers of the lip, oral cavity, pharynx, oesophagus, pancreas, larynx, lung, uterine cervix, urinary bladder, and kidney[5]. Cigarette smokers are 2-4 times more likely to develop coronary heart disease than non smokers and cigarette smoking approximately doubles a person's risk for stroke[6]. Smoking cessation has received little attention in HIV-infected persons. Yet smoking contributes significantly to the pulmonary complications of HIV (COPD, pneumonia)[7].

Smoking prevalence in India

Of the estimated 1.1 billion smokers worldwide, about 182 million (16.6%) are in India and by 2020 it is predicted that tobacco will account for 13 per cent of all deaths[8]. The National Family Health Survey (NFHS) is a large scale multi-round survey conducted in a representative sample of households throughout India. According to NFHS-3 conducted in 2005-06, which collected data on tobacco use directly by asking respondents to report on their own tobacco use, the percentage of women and men aged 15-49 yr who smoked cigarettes or *bidis*, in India was 1.4 and 32.7 per cent respectively[9]. *Bidis* are thin, often flavoured and are made of tobacco wrapped in a tendu (or temburini; *Diospyros melonoxylon*) leaf. Bidis have higher concentrations of nicotine, tar, and carbon monoxide than conventional cigarettes[10]. Prevalence of cigarette/*bidi* smoking in different States was variable with a low of 14 per cent of men in Goa to a high of 74 per cent in Mizoram. Four in 10 male smokers reported that they smoked 10 or more cigarettes/*bidis* in the previous 24 h. Two per cent of rural women smoke cigarettes or *bidis*, while less than 1 per cent of urban women smoke. The lower prevalence of smoking rates in women in India compared to men is presumed to be due to social and cultural factors. In NFHS-2 done in 1998-99, the smoking prevalences in males and females were 29.3 and 2.3 per cent respectively[11]. Comparing NFHS-2 and NFHS-3, we found that the prevalence of smoking among males (both rural and urban) has increased. Further, the rates among illiterates, rural and lower socio-economic groups were consistently higher in both the surveys (Table I). The same groups were also more vulnerable to HIV, suggesting that smoking is likely to be an important co-morbidity among HIV-infected individuals in India.

A multicentric study in four districts (Bangalore, Chandigarh, Delhi and Kanpur) showed that the prevalence of smoking was 15.6 per cent (male 28.5%, female 2.1%), that significant respiratory morbidity was associated with smoking and that quit rates were low (10%)[12]. In a study of smoking habits among medical students, 46 per cent of the medical students smoked (all were male and no female smoked)[13]. In recruits enrolled for military training (in the age group 17 to 23 yr), 43 per cent were smokers[15]. In the Global Youth Tobacco Survey (GYTS) reported from the northern region of India[14], among school going children aged 13 to 15 yr, the prevalence of ever used tobacco was 2.9 to 8.5 per cent in boys and 1.5 to 9.8 per cent in girls although the majority of them reported desire to quit. In the GYTS conducted in Tamil Nadu, 10 per cent of the students had ever used tobacco and a significantly higher percentages of current tobacco users (one in three students) compared to never tobacco users thought smoking or chewing tobacco made a boy or girl more attractive[15]. These rates of tobacco use in the school going age group is a cause for alarm. In most studies from India, prevalence of smoking in the female population was generally very low. However, in a study in Bihar, smoking prevalence in females was reported to be 23.4 per cent[17].

India and HIV

The adult HIV prevalence in India in 2007 is approximately 0.36 per cent, amounting to between 2 and 3.1 million infected people[18]. The prevalence is lower among adult females (0.29%) than males (0.43%). Prevalence is also high in the 15-49 yr age group (88.7% of all infections), indicating that AIDS still threatens those in the prime of their working life. While adult HIV prevalence among the general population is relatively low, high-risk groups, inevitably, show higher numbers. Among injecting drug users (IDUs), it is as high as 8.7 per cent, while it is 5.7 and 5.4 per cent among men who have sex with men (MSM) and female sex workers (FSWs), respectively. While recent

Table I. Prevalence of smoking in various groups according to survey data from National Family Health Survey 2 and 3 (NFHS 2 and NFHS-3)

	NFHS 2 1998 to 1999	NFHS 3 2005 to 2006
Overall smoking prevalence	Male 29.3% Female 2.3%	Male 32.7% Female 1.4%
Lower socio-economic status	Higher	Higher
Illiterate population (no education)	Higher	Higher
Rural	Male 32.5% Female 3.0 %	Male 35% Female 1.8%
Urban	Male 21.4% Female 0.8%	Male 28.7% Female 0.5%

Source: Refs 8, 10

estimates have lowered the prevalence rates of HIV, in absolute numbers, India's AIDS figures are still substantial.

Smoking and HIV

HIV-infected smokers have additional risks, adding to the general bad health consequences of smoking. HIV-infected individuals have a very high burden of bacterial infections with bacterial pneumonia being common[19]. Smoking may alter immunologic mechanisms and suppress host defenses in the alveolar environment and thereby contribute to bacterial pneumonia. HIV-infected smokers were found to have a significant decrease in the percentage and absolute number of CD4+ and CD8+ T cells in the broncoalveolar lavage fluid[20]. A decrease in CD4/CD8 cell ratios was also observed. In addition, production of both interleukin-1β (IL-1β) and tumour necrosis factor-α (TNF α) was suppressed with cigarette smoking. Smoking decreases lung macrophage function in HIV-infected individuals[21]. Smoking also decreases alveolar macrophage accessory cell function and secretion of the proinflammatory cytokines IL-1 and IL-6. These observations show that cigarette smoking in HIV-infected persons is associated with suppression in localized lung defenses and might help understand the frequent occurrence of pulmonary complications in this population. Tobacco use increases the risk of pulmonary diseases, particularly *Pnemocystis jirovecci* and community acquired pneumonias, two respiratory infections with high prevalence and morbidity risks, even in the era of highly active anti retroviral therapy (HAART)[22]. HIV-infected individuals are at increased risk for the development of respiratory symptoms such as cough, sputum production, wheezing and dyspnoea even prior to the onset of AIDS-related pulmonary complications[23]. Sinusitis and bacterial respiratory infections have a significant relationship with smoking in HIV-infected individuals[24]. Lung cancer is presently recognized as an important cause of death in patients with HIV infection who smoke[25], occurs at a younger age and responds poorly to therapy[26]. Lung cancer in HIV infected women is strongly associated with tobacco use, being twice as common and several fold above what is expected when matched for age and race[27].

Smoking has been associated with a host of other complications including an increased incidence of periodontal disease[28], oral candidiasis[29], oral hairy leukoplakia[30] and diverse oral lesions[30]. Cigarette smoking may increase the risk of contracting AIDS-related spontaneous pneumothorax[32]. The incidence of genital warts and HPV related cervical disease in HIV-infected women has also been linked to cigarette smoking[33]. Smoking seems to pose significant risks to pregnant HIV-infected women[34]. There have been several studies linking smoking to HIV disease progression. Sherman reported a fall in CD4+T lymphocytes in heavy smokers[35] while Nieman *et al*[36] observed that HIV disease progression was faster in smokers. Feldman *et al* [37] showed that among women on HAART, smokers had a poorer virological and immunological response, greater risk of virological rebound and more frequent immunological failure as well as death than non smokers and concluded that some of the benefits provided by HAART were negated by cigarette smoking. A systematic review of studies indicated that smoking might be independently associated with acquiring HIV infection, that is increased risk of HIV seroconversion but not to progression to AIDS[38]. Crothers *et al*[7] found that among veterans on HAART, smokers had increased respiratory symptoms, COPD, bacterial pneumonia and decreased quality of life along with significantly increased mortality. Smoking induces an increase in cardiac risk especially in individuals with hypertension and elevated serum lipids. Some anti-retroviral drugs (*e.g*., protease inhibitors, efavirenz) also cause lipid abnormalities and hence the possibility of multiple cardiac risks leading to accelerated atherosclerosis needs to be considered. In HIV-infected populations, in addition to smoking, excessive alcohol consumption and illicit drug use often co-exist[39]. In addition to these factors, cigarette smoking has been observed to be an important and significant marker of inferior adherence to antiretroviral medication[40].

Studies in the United States have shown that smoking rates are higher among HIV-infected than in general population[41]. Niaura *et al*[42] have shown that among HIV-infected persons, more than 70 per cent smoke and among these individuals, 80 per cent did not consider quitting smoking in the near future. To date, no study has attempted to find the smoking prevalence or quit rate among HIV-infected persons in India. A small survey conducted among patients attending the Tuberculosis Research Centre clinic at Government Rajaji Hospital, Madurai, Tamil Nadu showed that history of ever smoking among males (HIV without TB) was 66 per cent whereas among females only one patient (0.4%) gave a history of ever smoking. Among 138 men with HIV and TB, the history of ever smoking was 76 per cent whereas no female gave a history of smoking.

In the same survey, among HIV-negative pulmonary tuberculosis patients, history of ever smoking was 73 per cent; 42 per cent of these patients smoked cigarettes while approximately 18 per cent smoked bidis and 40 per cent reported smoking both. While these pilot data did not demonstrate higher smoking rates among HIV-infected compared to uninfected TB patients, they do suggest that smoking is a significant co-morbidity that would need to be addressed. Because there is a scarcity of data from India, larger studies are required to estimate smoking rates among HIV-infected persons in different geographic areas and among various socio-economic groups.

Smoking and TB

The association between smoking and tuberculosis is well described. A nested case control study at Tuberculosis Research Centre (TRC), Chennai, showed a positive association between tobacco smoking and pulmonary tuberculosis, [crude odds ratio 2.48 (95% C.I 1.42 to 4.37), $P<0.001$], and a strong dose response relationship[43]. In a cross-sectional observational study, TB patients who smoked developed more pulmonary diseases, (adjusted odds ratio 1.5), cavitatory lesions, (adjusted odds ratio 1.9) and were more likely to require hospitalization than those who did not (adjusted odds ratio 1.8). The authors concluded that smoking leads to faster and more severe progression of TB and also noted that cost of TB related treatment was comparatively higher[44]. In another study at TRC, Chennai, smoking was shown to be one of the independent predictors of relapse of pulmonary tuberculosis (adjusted odds ratio 3.1; 95% CI 1.6 to 6.0)[45]. In a retrospective study of 43,000 adult male deaths and 35000 controls performed in both rural and urban areas in Tamil Nadu, India, mortality from tuberculosis was four times as great among smokers as among non smokers[46]. In a large cohort study at Mumbai, the risk of death from tuberculosis (RR 2.30, CI 1.68-3.15) was significantly higher in male smokers than in those who had never used tobacco[47]. A suggested mechanism is that iron loads the broncho-alveolar macrophages secondary to smoking[48] promoting the growth of *Mycobacterium tuberculosis* resulting in severe clinical disease and eventually death. Since tuberculosis is one of the commonest opportunistic infections among HIV-infected patients, the additive risks of smoking are likely to be detrimental and contribute to the high mortality and morbidity observed.

Smoking cessation

The usual strategies adopted for smoking cessation include physician's advice, nicotine replacement therapies and pharmacological agents like bupropion and varenicline. Table II summarizes the various approaches for smoking cessation and their efficacy. Even a brief smoking cessation initiative delivered by a physician is partially effective[56]. Nicotine replacement therapy (NRT) is a common approach. Currently available NRTs are nicotine patches, gums, spray, inhaler, sublingual tablets and lozenges. All the commercially available forms of NRT are effective as part of a strategy to promote

Table II. Different approaches and strategies used for smoking cessation

	Strategy	Efficacy (mean, 95% CI)
1.	Physician's advice	10.2% (8.5-12.0)[49]
2.	Nicotine replacement therapy (NRT)	
	Nicotine gum	23.7% (20.6-26.7)[49]
	Nicotine inhaler	22.8% (16.4-29.2)[49]
	Nicotine spray	30.5% (21.8-39.2)[49]
	Nicotine patch	17.7% (16.0-19.5)[49]
	Increasing dose of NRT	Higher patch doses provided a small benefit compared with standard patch (odds ratio 1.21; 95% CI 1.03,1.42)[50]
	Increasing duration of NRT	It may be more beneficial to use NRT for longer periods of time to prevent relapse[51]
	Individually tailored approach	35% decrease in smoking compared to control group[52]
	Combining two NRT	28.6% (21.7-35.4%). Statistically significant benefit when combining the patch with another form of NRT (Odds ratio 1.42; 95% CI 1.14, 1.76)[49]
3.	Pharmacological intervention	
	Bupropion	30.5% (23.2-37.8)[49]
	Clonidine	25.6% (17.7 to 33.6)[49]
	Nortripyline	30.1% (18.1-41.6)[49]
4.	Combining NRT and bupropion SR	Efficacy increased by 13 per cent[53]
5.	Varenicline	44 to 65%[54,55]

Superscript numerals denote Reference numbers

smoking cessation[57]. It has been shown that advice (9%), counselling (12%) and nicotine gum (17%) prescribed by physicians significantly increase the likelihood of cessation at six months[58]. In actual practice setting, the combination of bupropion SR and minimal or moderate counselling was associated with 1-year quit rates of 24 to 33 per cent[59]. In a study done in Delhi comparing the effect of counselling alone with counselling and medication (bupropion), the continuous abstinence rate in the counselling group at 1, 3, 6 and 12 months was 17, 17, 16 and 15 per cent respectively whereas in the medication group the rates were 60, 58, 54 and 53 per cent respectively ($P<0.001$ for all comparisons)[60]. Varenicline is a novel orally administered alpha4beta2 nicotinic acetylcholine (ACh) receptor partial agonist developed specifically for smoking cessation. It has been approved by the US FDA (Chantix trade mark) and the European Commission (Champix (R)) for use as an aid to smoking cessation therapy. Varenicline tartrate demonstrated both short-term and long-term efficacy compared to placebo[61]. Varenicline is well tolerated and appears to attenuate the urge to smoke[62]. Co-administration with food, smoking restriction, and time-of-day dosing did not affect the pharmacokinetics of varenicline[63]. Most smoking cessation trials have been conducted in developed countries and various strategies need to be explored in India, given the differences in educational, cultural and economic factors.

Smoking cessation interventions in an HIV-infected population might be even more complex than in the general population, because of psychosocial differences and special needs. Smoking in HIV is often associated with illicit drug use and emotional stress[64] and depressive symptoms are highly prevalent in HIV infected smokers with high nicotine dependence[65]. Hence, simple advice and minimal interventions are far less likely to work in these smokers who are battling psychiatric illness and/or substance use. Smokers with such co-morbidities might do better with more intensive interventions including repeated counselling, nicotine replacement as well as psychiatric assistance. Attention to psychological factors and involvement of the family in smoking cessation efforts as well as clinical trials to test different strategies need to be undertaken in India.

The US Department of Health and Human Services, Public Health Service, 2000[49] recommends the "5 A" strategy for use by primary care clinicians/health care personnel as an intervention in the primary care setting. Clinicians should *ask* the patient if he or she uses tobacco, *advise* him or her to quit, *assess* willingness to make a quit attempt, *assist* him or her in making a quit attempt, and *arrange* for follow up contacts to prevent relapse. Currently there are no standard guidelines for smoking cessation treatment in India. Recent efforts to ban smoking in public places and increase in tobacco tax are likely to be helpful in reducing the number of smokers or at the very least, the amount smoked by individuals. Experience from Canada suggests that such a ban resulted in high levels of public support and a reduction in smoking prevalence[66]. A multi-pronged strategy is required, and in addition to public measures, individual guidance and assistance is required to help smokers quit. Guidelines for health care workers need to be developed and disseminated as efforts to encourage smoking cessation within the health care setting which are currently negligible.

Conclusion

India is home to a large number of HIV-infected individuals - adult males who are uneducated and from the lower socio-economic strata especially vulnerable group. These groups also have the highest rates of smoking. HIV-infected smokers are at a high risk for bacterial pneumonia, tuberculosis and a host of other infectious and non infectious complications that substantially increase morbidity and possibly mortality. While data on smoking rates among HIV-infected persons in India are lacking, preliminary observations suggest that it is likely to cause significant co-morbidity. Physicians and public health specialists need to pay attention to the growing epidemic of smoking and try innovative approaches to prevent young people from starting as well as to help people quitting smoking. In addition to the ban on smoking in public places and increase in tobacco tax, incorporation of advice regarding the harmful effects of smoking and assistance with smoking cessation should be one of the components of primary care, with special focus on patients with HIV infection.

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