Role of Environmental factors in Transmission of Tuberculosis

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Abstract
Tuberculosis (TB) is an airborne communicable disease plaguing human populations since antiquity. TB continues to be a major public health problem globally and India has one of the largest numbers of TB cases in the world. The risk of progression from exposure to tuberculosis bacilli to the development of active disease is a two-stage process governed by both exogenous and endogenous risk factors. Exogenous factors play a key role in accelerating the progression from exposure to infection, whereas endogenous factors lead in progression from infection to active TB disease. Socioeconomic factors are also shown to increase the susceptibility to infection. Along with emerging variants such as indoor air pollution and tobacco smoke, it plays a significant role at both the individual and population level. Environmental conditions playing a role in disease development were humidity and number of people living in the house. Overcrowded housing and poor ventilation increase both the likelihood of exposure to Mycobacterium tuberculosis (MTB) and progression to disease. The aim of this study was to explore the environmental factors affecting TB risk, including humidity and number of people living in the same house.

Keywords: Tuberculosis, home condition, humidity, Overcrowding

1. Introduction
Tuberculosis (TB), an infection caused by Mycobacterium tuberculosis (MTB), is a pandemic, and the Centers for Disease Control and Prevention state that one-third of the world's population is infected with the bacteria. Globally, TB remains the second leading cause of death from an infectious disease. TB affects mostly adults in the economically productive age groups; around two-thirds of cases are estimated to occur among people aged 15–59 years and also more common among men than women.

In the majority of those infected, however, the infection remains latent, meaning that it does not progress to an active disease. Many factors affect whether TB become an active infection that can then result in more than 2 million deaths a year. Poor housing quality, overcrowding and dampness is associated with poverty, and increased susceptibility to disease.

Throughout the first three quarters of the 20th century, the incidence of TB declined in industrialized countries. Part of this decline may have been due to isolation of infectious TB patients in sanatoria, mainly due to chemotherapy and the pasteurization of milk, but it is generally thought that improved housing and habitat, decreased crowding, better hygiene and sanitation, use of clean water, and better nutrition all contributed to decreased TB
notification\textsuperscript{16, 17}. Since the mid1980s, however, this decreasing trend has slowed down and has even reversed in some countries\textsuperscript{1,4,13}. The resurgence of the disease in the 1980s and increase in TB case rates in developing countries was attributed to a group of factors, including the epidemic of human immunodeficiency virus (HIV) infection, diminished Public health efforts to control TB, rising poverty, homelessness, overcrowded conditions, poorly organized TB control programs with low case finding and cure rates and immigration from countries with a high prevalence of TB\textsuperscript{18,19}.

Socioeconomic factors have long been associated with TB\textsuperscript{15,16}, and they still play a role in conjunction with the HIV epidemic\textsuperscript{20}. In parallel, recent advances in the field of molecular biology and genetics have provided some evidence of the role of genetics in susceptibility to TB at the individual level, introducing a new dimension to understanding the immunologic correlates of protection against TB\textsuperscript{21}. This paper reviews the contribution of environmental factors to the spread of TB infection and disease in populations.

2. Exposure to infection

Development of TB is a two-stage process in which a susceptible person exposed to an infectious TB case first becomes infected and may later develop the disease, depending on various factors. Therefore, the risk factors for infection are quite different from those for the development of disease after infection (Fig. 1)\textsuperscript{22}.

The first step is, to come into contact with an infectious TB case. Risk factors for TB identified in other parts of the world include intensive immigration from high prevalence to low prevalence countries, contact with a TB patient, poor socio-demographic factors, tobacco smoking, alcohol abuse, HIV infection and institutionalization\textsuperscript{23-25}. The role of these and other locally prevalent risk factors threaten TB control. Among persons exposed to an infectious TB case, the risk of getting infected is determined primarily by the combined action of three factors:

1) The infectivity of the case is a function of the frequency of coughing, the density of bacilli in the sputum and the microbial “virulence”\textsuperscript{26,27}.

2) The degree of exposure of the susceptible person to that case\textsuperscript{28}, and

3) The degree of susceptibility of that person to infection\textsuperscript{18}.

Several studies have shown that sputum-smear-positive pulmonary tuberculosis (PTB) cases are more likely than sputum smear- negative TB cases to infect their contacts\textsuperscript{27}. Household studies showed that the risk of becoming infected increased with the intimacy of contact with a TB case\textsuperscript{28}.

3. Risk of exposure

In patients disease can develop at varying times through reactivation of a previously acquired (latent) infection or exogenous infections\textsuperscript{12,17,26}. The progression time from infection to disease ranges from a few weeks to a lifetime\textsuperscript{17}. It is generally estimated that about 10 persons are infected, on average, with tubercle bacilli during one year by one smear-positive case of the PTB. In 2013, an estimated 9.0 million people developed TB and 1.5 million died
from the disease, 360 000 of whom were HIV-positive. Efforts to combat it must be accelerated if 2015 global targets, set within the context of the Millennium Development Goals (MDGs), are to be met \(^3,26,35\). Epidemiological studies clearly show that the incidence of infection and disease is higher among contacts of smear positive index cases than smear negative cases \(^35,36,37\). The risk of disease after infection are a consequence of human interaction with the environment (Fig.1) \(^22\). Environmental factors may have an impact on the incidence of TB in a given population as a result of their effect on both the risk of infection and the risk of disease once a person is infected \(^14,39\).

![Fig-1](source)

**4. Establishment of infection in host**

The World Health Organization (WHO) has estimated that one-third of the total world population is latently infected with MTB and 5%–10% of the infected individuals will develop active TB disease during their life time \(^2,10\). Population-based studies have shown that some individuals are more at risk of acquiring infection and developing active disease than others. The infection and development of TB are dependent on exposure but exposure on its own may not lead to TB \(^10\). One such issue is how MTB is able to evade innate immune defence mechanisms. MTB can maintain intracellular growth inside the phagosome by inhibiting phagolysosome formation. Recognition of pathogen recognition receptors (PRRs) and the consequent innate immune response in killing MTB is well reported, but the reasons why it fails to restrict MTB growth and infection are not well understood \(^10,11,11b\). Further studies are thus needed to elucidate why some people develop active TB upon infection while others do not.
5. Socio-economic factors and lifestyle

TB is a social disease with medical implications. It has always occurred disproportionately among disadvantaged populations such as the homeless, malnourished, and overcrowded\textsuperscript{25,41}. People with lower socioeconomic status (SES) have a higher likelihood of being exposed to crowded, less ventilated places and have limited safe cooking, practicing facilities\textsuperscript{32,42}. Other factors include drug and alcohol abuse, stress, air pollution, malnutrition, AIDS, Diabetes\textsuperscript{6,18,32,35,43,44}.

The association between environmental factors and TB infection has long been recognized\textsuperscript{30}. While the nature and extent of community-based transmission of TB is still being explored, household contact is accepted as an important risk factor and a focus of detection\textsuperscript{44, 45, 46} and intervention\textsuperscript{25, 28}.

TB has been called a disease of poverty in part because the living conditions of the poor tend to include high population density, cramped conditions, and poor ventilation\textsuperscript{25, 47}. These conditions are often complicated by poor access to health care, a higher burden of HIV, lower nutrition and immunity, and multi-generational family units.

The extent and persistence of contact with an infected person are the main environmental factors for the transmission of TB. An association has been confirmed between overnight cough frequency and increased transmission among household contacts\textsuperscript{25,48}, where droplet nuclei (due to coughing) can stay in the air for a long time\textsuperscript{30,47,48}.

A number of studies have shown that crowding is a risk factor for infection and for increased risk of disease after infection\textsuperscript{49}. The studies of Clark (2002) and Lienhardt et al (2003) suggested that TB incidence was higher in communities with a higher average housing density\textsuperscript{30,50}. In a study it was found that an increase of 0.1 persons per room (PPR) increased the risk of two or more cases of TB in a community by 40\%\textsuperscript{31,51,52}. (PPR is calculated by dividing the number of persons living in a dwelling by the number of rooms)\textsuperscript{47}.

TB transmission has long been known to be associated with poor ventilation and poorly ventilated living conditions are important factors for TB transmission\textsuperscript{40,45}. Factors that may inhibit increased ventilation in a house are the outdoor temperature, noise, comfort, and energy costs, the condition of windows or doors, or cultural and personal habits. TB bacteria hang around in the room if there is no fresh air. Therefore, TB transmission occurs with greater prevalence in poorly ventilated and crowded spaces\textsuperscript{26,31,54}.

Although dampness and mould could be considered proxies for inadequate ventilation\textsuperscript{56}, dampness and mould have not been directly linked with the acquisition of TB infection. However, they have been implicated in increased susceptibility to respiratory infection, asthma and allergies\textsuperscript{56,57}.

6. Smoking and lifestyle

The association between smoking and TB disease is supported by a substantial body of epidemiological evidence gathered over the past 50 years, which shows that smoking is a risk factor for TB infection and for the development of pulmonary tuberculosis (PTB)\textsuperscript{8,24,58,76}. Smoking increases the chances of MTB infection, the risk of progression from infection to disease, and the risk of death among TB patients\textsuperscript{8}. Nearly 61\% of TB deaths are attributable
to smoking\textsuperscript{75}. The risk of the prevalence of TB infection is more among the current or ex-smokers\textsuperscript{8,72,73,77-79}. Among children living with a patient with active PTB; incidents of passive smoking can accelerate the acquisition of active TB in those children\textsuperscript{81,82}. A higher incidence of TB transmission to children has been associated with exposure to environmental tobacco smoke\textsuperscript{69,85,88}.

7. Air pollutants

While organized societies have taken important steps to reduce and control emissions, the quality of the air we breathe today remains a critical concern. Air Pollution and Community Health transforms the major epidemiological works of the past 40 years into a coherent picture of the effects of air pollution on respiration, hospitalization, and mortality. Health impacts depend on the pollutant type, its concentration, and length of exposure, other coexisting pollutants and individual susceptibility\textsuperscript{59,60}. The term “Traditional fuels” refers principally to biomass fuels used mainly for household energy, and any material derived from living or recently living material, including animal dung, twigs, grass, agriculture residues crop wastes, wood, and charcoal. More than half of the world’s population uses biomass as a major source of energy for cooking, baking, and heating\textsuperscript{63-65}. This occurs predominantly in rural areas of lesser developed countries where biomass are burned indoors. Because homes are poorly ventilated and this fuel source is inefficient, requiring fires to be kept going for many hours a day, women and their infant children are exposed to years of daily smoke\textsuperscript{62,66,67,68,69}. CorPulmonale (heart disease, secondary to chronic Lung Disease)\textsuperscript{60,85,86} has been found to be prevalent and to develop earlier than average in non-smoking women, who cook with biomass\textsuperscript{81,86}.

8. Occupational Factors

Occupational exposure is also an important factor that should be taken into consideration. Inadequate air change rates, negative air flow and recirculation of air have been identified as an occupational hazard in hospitals with respect to TB transmission. Studies in hospitals and health care facilities have shown that poor ventilation design or construction have contributed to the transmission of infection. Certain occupations, such as mining, are also at an increased risk of TB\textsuperscript{12,91}.

9. Age and sex

Age and sex variations in the prevalence of TB infection and disease have been reported worldwide, in both developed and developing countries\textsuperscript{23,92}. Early tuberculin skin test surveys have shown that infection with MTB increases with age and then declines in older adults\textsuperscript{53}. The prevalence of tuberculin sensitivity is usually similar in males and females until adolescence, after which prevalence is higher among males. This difference after adolescence may reflect greater exposure among adult males because of differentiated social roles and economic activities\textsuperscript{92}. It also may reflect a genuine sex difference in susceptibility to TB infection related to a different predisposition to responsiveness to delayed-type
hypersensitivity. It is probable that, in addition to genuine age and sex differences in susceptibility, socioeconomic and cultural factors may play a role in determining age and sex differences in rates of infection, progression to disease, and treatment outcome.

10. HIV infection
HIV infection has emerged as the most important risk factor for the development of TB in persons infected with MTB. Because of the immunosuppression caused by HIV infection, persons with latent TB as well as newly infected persons may progress rapidly to clinical disease. The estimated risks of clinical disease in HIV-infected persons are between 6 and 26 times the risk in non-HIV-infected persons. Structural and environmental factors have been found to make a significant contribution to the spread of HIV infection in developed and developing countries. The relation between economic underdevelopment, poverty, and acquired immunodeficiency syndrome (AIDS) is apparent cross-nationally. Conversely, AIDS exacerbates poverty in countries hit hard by the epidemic, contributing to a cycle of underdevelopment and AIDS-related mortality. Urbanization has largely increased in many resource-poor countries over the past 30 years and has dramatically enhanced HIV infection to spread into densely populated areas. For these reasons, factors that increase HIV infection will clearly contribute to increase in TB incidence.

11. Malnutrition and Low Immunity
Malnutrition and TB are both problems of considerable magnitude in the majority of underdeveloped regions of the world. It is important to consider, how these two problems tend to interact with each other. The term consumption has been virtually synonymous with TB throughout the history and so is the link between TB and malnutrition. Before the advent of antituberculosis chemotherapy, a diet rich in calories, proteins, fats, minerals, and vitamins was generally considered to be an important factor in the treatment of TB. Malnutrition profoundly affects cell-mediated immunity (CMI), and CMI is the principal host defence against TB. This secondary immunodeficiency increases the host’s susceptibility to infection and hence increases the risk for developing TB. Vitamins and minerals can play important role in the treatment of TB. The supplementation with vitamin A and zinc improved the effectiveness of the antituberculosis drugs in the first two months.

12. Implication of genetic factors
Various lines of evidence indicate that genetic factors determine in part the differences in host susceptibility to infection with mycobacteria and those that might contribute to the pattern of clinical disease. The most convincing evidence comes from twin studies: because twins theoretically share the same environment, higher concordance rates for monozygous than for dizygous twins suggest that genetic factors are important in susceptibility to TB. Genetic studies have shown a possible association of the HLA-DR2 allele with susceptibility to TB. Mutations in the interleukin-12 receptor genes have been found to be associated with impaired immune defence against mycobacteria in humans.
Ethnicity may explain some of the differentials in morbidity and mortality due to TB, which could affect the outcome of planned trials for new TB drugs. For example, that most infections in Europeans are in the lungs, while Asians and Africans get most TB infections in other organs. It is therefore reasonable to assume that allowing for ethnicity will improve diagnosis tests, monitoring treatment and drug development. To assess and better understand the role genetic factors play in susceptibility to TB, future studies must account for confounding effects of socio-economic and socio-environmental factors.

13. Migration

The risk of TB in ethnic minorities has been reported to be higher than in the general population. TB particularly affects vulnerable populations; migrants are a key affected population. Migration as a social determinant of health increases TB-related morbidity and mortality for migrants and their communities along all migration pathways. In low and middle TB-burden countries, TB among foreign-born populations is often high, due to existing infection or reactivation of latent TB. Migrant and mobile populations from and within high TB-burden countries face a range of risk factors. Undocumented migrants face challenges such as fear of deportation that limit their access to diagnostic and treatment services. A DNA fingerprint analysis of TB patients detected that 84 percent of the TB cases among foreign-born persons resulted from reactivation of infections acquired abroad. However, several studies have found that the increase in TB case rates in the last decade was attributable mainly to socioeconomic factors rather than immigration.

14. Conclusion

- In populations that already suffer high rates of TB, crowded housing and poor ventilation increase the risk of transmission and progression of disease among those who share living space.
- Interventions against TB should include public awareness campaigns followed by policy actions to reduce the risk of infection from smoking, hazardous lifestyles and living conditions.
- Future research will need to allow the inclusion of genetical factors and ethnic
- In endemic countries, diagnosis and treatment of smear-positive cases remains the key to TB control by reducing transmission from infectious cases. In addition to passive case-finding practices, early diagnosis of smear-positive cases can be improved through untargeted case-finding strategies in endemic countries.
- A more coordinated approach involving the National Health and Private Health is necessary for early diagnosis and treatment of TB cases (45% in countries like India) accessing health care through the private sector.
- Both innate and adaptive immune responses are important and have pivotal roles in host defence against mycobacteria.
- Malnutrition and indoor air pollution are recognized risk factors which are confounded with the socioeconomic status of a setting, increased awareness activities should be considered.
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- Genetic factors might play a role in susceptibility to TB but socioeconomic factors are more responsible in transmission of TB.
- The weakened/low immune system will make it harder to fight off infections as easily.

Ethical Considerations

The study was ethically approved by the institutional ethics committee of King George’s Medical University (KGMU), Lucknow, U.P, India.

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