ISSN 2382-1019

Role of Environmental factors in Transmission of Tuberculosis

Kanchan Srivastava, Surya Kant, Ajay Verma,
Department of Respiratory Medicine, KGMU, UP, Lucknow.

Correspondence: Dr Surya Kant: skantpulmed@gmail.com
Received: 25/8/2015; Revised: 21/10/2015; Accepted: 10/11/2015

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[1]. Globally, TB remains the second leading cause of death from an infectious disease[2,3]. TB affects mostly adults in the economically productive age groups; around two-thirds of cases are estimated to occur among people aged 15–59years and also more common among men than women.[4]

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[1,5-10]. Poor housing quality, overcrowding and dampness is associated with poverty, and increased susceptibility to disease[11,13,14].

Throughout the first three quarters of the 20th century, the incidence of TB declined in industrialized countries[15]. 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

ISSN 2382-1019

notification[16, 17]. Since the mid1980s, however, this decreasing trend has slowed down and has even reversed in some countries[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[18,19].

Socioeconomic factors have long been associated with TB[15,16], and they still play a role in conjunction with the HIV epidemic[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 TB21. 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)[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[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"[26,27].
2) The degree of exposure of the susceptible person to that case[28], and
3) The degree of susceptibility of that person to infection[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[27]. Household studies showed that the risk of becoming infected increased with the intimacy of contact with a TB case[28].

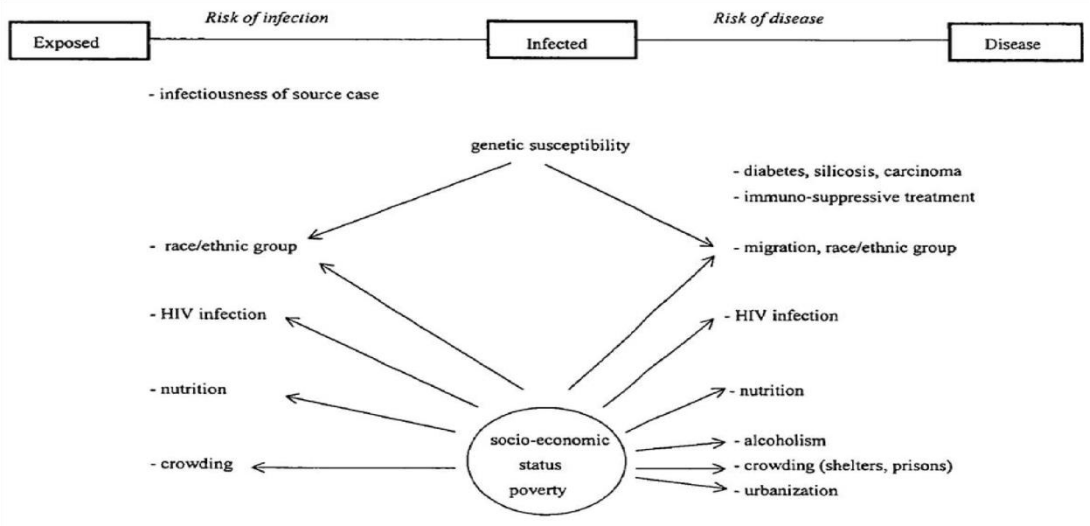
3. Risk of exposure

In patients disease can develop at varying times through reactivation of a previously acquired (latent) infection or exogenousinfections[12,17,26]**.** The progression time from infection to disease ranges from a few weeks to a lifetime[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

ISSN 2382-1019

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: Lienhardt, C. 2001 [40]

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.

ISSN 2382-1019

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[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[32, 42]. Other factors include drug and alcohol abuse, stress, air pollution, malnutrition, AIDS, Diabetes[6,18,32,35,43,44].

The association between environmental factors and TB infection has long been recognized[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[44, 45,46] and intervention[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[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 householdcontacts[25,48], where droplet nuclei (due to coughing) can stay in the air for a long time[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[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[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%[31,51,52]. (PPR is calculated by dividing the number of persons living in a dwelling by the number of rooms)[47].

TB transmission has long been known to be associated with poor ventilation and poorly ventilated living conditions are important factors for TB transmission[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[26,31,54].

Although dampness and mould could be considered proxies for inadequate ventilation[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[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)[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[8]. Nearly 61% of TB deaths are attributable

ISSN 2382-1019

to smoking[75]. The risk of the prevalence of TB infection is more among the current or ex-smokers than non-smokers[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[81,82]. A higher incidence of TB transmission to children has been associated with exposure to environmental tobacco smoke[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[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[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[62,66,67,68,69]. CorPulmonale (heart disease, secondary to chronic Lung Disease)[60,85,86] has been found to be prevalent and to develop earlier than average in non-smoking women, who cook with biomass[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**.**[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[23,92]. Early tuberculin skin test surveys have shown that infection with MTB increases with age and then declines in older adults[23]**.** 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[92]. It also may reflect a genuine sex difference in susceptibility to TB infection related to a different predisposition to responsiveness to delayed-type

ISSN 2382-1019

hypersensitivity[92]. 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[23,92].

10. HIV infection

HIV infection has emerged as the most important risk factor for the development of TB in persons infected with MTB[94]. Because of the immunosuppresion caused by HIV infection, persons with latent TB as well as newly infected persons may progress rapidly to clinical disease[95]. The estimated risks of clinical disease in HIV-infected persons are between 6 and 26 times the risk in non-HIV-infected persons[95,96]. Structural and environmental factors have been found to make a significant contribution to the spread of HIV infection in developed and developing countries[19]. The relation between economic underdevelopment, poverty, and acquired immunodeficiency syndrome (AIDS) is apparent cross-nationally[96]. Conversely, AIDS exacerbates poverty in countries hit hard by the epidemic, contributing to a cycle of underdevelopment and AIDS-related mortality[19]. 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[97,98]. For these reasons, factors that increase HIV infection will clearly contribute to increase in TB incidence[98].

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[99] 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[100,101]. 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[101].

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[21]. Genetic studies have shown a possible association of the *HLA-DR2* allele with susceptibility to TB[21]. Mutations in the interleukin-12 receptor genes have been found to be associated with impaired immune defence against mycobacteria in humans[29,99].

ISSN 2382-1019

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[105]. For example, that most infections in Europeans are in the lungs, while Asians and Africans get most TB infections in other organs[104]. 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[99,106].

13. Migration

The risk of TB in ethnic minorities has been reported to be higher than in the general population[98,106]. 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[98,109]. 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[106,107]. 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[106.] 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[111,106].

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[18].
- 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[4,102].
- 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[35].
- 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.

ISSN 2382-1019

- Genetic factors might play a role in susceptibility to TB but socioeconomic factors are more responsible in transmission of TB[104].
- The weakened/low immune system will make it harder to fight off infections as easily[102].

Ethical Considerations

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

Acknowledgements

The study was generously supported by DST New Delhi for providing financial support through the project WOS-LS-24/2008.

Conflict of interest: none

References

1. CDC (2010) Reported Tuberculosis in the United States, Atlanta, GA: U.S. Department of Health and Human Services.
2. Dye C, Williams BG. (2010) The population dynamics and control of tuberculosis. *Science,* 328, 856– 861.
3. World Health Organization. 2014.
4. World Health Organization. 2011.
5. Donald PR. (2004) Childhood tuberculosis: the hidden epidemic. *Int J Tuberc Lung Dis*, 8, 627-632.
6. Lönnroth K, Jaramillo E, Williams BG, Dye C, *et al.* (2009). Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Social Sci. and Med,* 68, 2240–2246.
7. Maher D. (2009) The natural history of *M.tb* infection in adults. In: Schaaf HS, Zumla A, editors. *Tuberculosis: A Comprehensive Clinical Reference.* Elsevier Health Sciences, 129–132.
8. Kant S, Maurya AK, Kushwaha RAS, Nag VL. (2010).Multi Drug resistant tuberculosis; an iatrogenic problem. Biosciences Trends, 4, 48-53.
9. Lönnroth K, Williams BG, Cegielski P, Dye CA (2010). Consistent log-linear relationship between tuberculosis incidence and body mass index. *Int J of Epid,* 39, 149–155.
10. World Health Organization. (2010). Equity, Social Determinants and Public Health Programs. Geneva

10b. Moller M, de Wit E, Hoal EG. (2010). Past, present and future directions in human genetic susceptibility to tuberculosis. *FEMS Immunol Med Microbiol,* 58, 3–26.

11. Shaw M. (2004). Housing and Public Health. *Annual Review of Public Health,* 25, 397-418.

11b. Mathema, B, Kurepina, N, Fallows, D *et al*, (2008).Lessons frommolecular epidemiology and comparative genomics. *Seminars in Respiratory and Critical Care Medicine,* 29, 467–480.

12. Singh M, Mynak ML, Kumar L *et al.* (2005). Prevalence and risk factors for transmission of infection among children in household contact with adults having pulmonary tuberculosis. *Arch of Disease in Childhood,* 90, 624-28.
13. Radhakrishna S, Frieden T.R, Subramani R, *et al.* (2007), Additional risk of developing TB for household members with a TB case at home at intake: a 15-year study. *Int. J of Tuber and Lung Dis.*, 11, 282–288.
14. Matyssek R.T, Clarke N, Cudlin P, Mikkelsen TN, *et al.* (2013).Conclusions and perspectives. In: Matyssek R, Clarke N, Cudlin P, (eds). Climate Change, Air Pollution and Global Challenges: Understanding and Perspectives from Forest Research. *Develop in Environmental Science.* 13, 591-607
15. Dubos R, Dubos J. (1987)The white plague: tuberculosis, man and society. New Brunswick, NJ: Rutgers University Press,

ISSN 2382-1019

16. Bloom B, Murray CJL. (1992) Tuberculosis: commentary on a re emergent killer. *Science* 257, 1055-64.
17. Smith PG. (1994) Epidemiology of tuberculosis. In: Bloom B, ed. Tuberculosis, pathogenesis, protection and control. Washington DC: American Society for Microbiology,
18. Schmidt CW (2008). Linking TB and the environment: an overlooked mitigation strategy.
19. TahaM, DeribewA, Sahilu F, Assegid L (2011). Risk Factors of Active Tuberculosis in People Living with HIV/AIDS in Southwest Ethiopia: A Case Control Study, *Ethiop J Health Sci*. 21, 131–139.
20. Snider DE, Roper WL. (1992). The new tuberculosis. *N Engl J Med*, 326:703-5.
21. Salazar -Vergara RM, Sia IG, Tupasi TE *et al.* (2003). Tuberculosis infection and disease in children living in households of Filipino patients with tuberculosis: A preliminary report. *Int J Tuberc Lung Dis*. 7, 494-500.
22. Comstock GW. (1995). Frost revisited: the modern epidemiology of tuberculosis. *Am J Epidemiology*, 101, 363-82
23. Crampin AC, Glynn JR, Floyd S, &Ngwira BM, *et al*. (2004).Tuberculosis and gender: exploring the patterns in a case control study in Malawi. *Int. J. Tuberc. Lung Dis.* 8, 194–203
24. Bothamley GH. (2005).Smoking and tuberculosis: a chance or causal association? *Thorax*, 60, 527528.
25. Haider BA, Akhtar S. Hatcher J. (2013).Daily contact with a patient and poor housing affordability as determinants of pulmonary tuberculosis in urban Pakistan. *Int.J.of. Mycobacteriology*, 2, 38-43.
26. Shaw JB, Wynn-Williams N. (1954). Infectivity of pulmonary tuberculosis in relation to sputum status. *Am Rev of Tuberculosis*. 69, 24–732
27. Loudon RG, Spohn SK. (1969). Cough frequency and infectivity in patients with pulmonary tuberculosis. *Am Rev Respir Dis.* 99, 109.
28. Narain R, Nair SS, Rao GR, *et al*. (1966). Distribution of tuberculous infection and disease among households in a rural community. *Bull World Health Organ*, 34, 6
29. Newport MJ, Huxley CMP, Huston S, *et al.* (1996). A mutation in the IFNy receptor gene and susceptibility to mycobacterial infection. *N Engl J Med*, 26, 1941-9.
30.Clark M, Riben P, Nowgesic E. (2002).The association of housing density, isolation and tuberculosis in Canadian First Nations communities. *Int J Epidemiology*. 31, 940-43
31. Beggs CB, Noakes CJ, Sleigh PA *et al.* (2003).The transmission of tuberculosis in confined spaces: An analytical review of alternative epidemiological models. *Int J Tuberc Lung Dis* 7, 1015-26.
32. Kant, S. (2004).Health hazards of smoking; An Overview Preceding National Conference of Indian Association for Bronchology: 57-62.
33. Wanyeki I, Olson S, Brassard P *et al.* (2006). Dwellings, crowding, and tuberculosis in Montreal. *Soc Sci Med.* 63, 501-11
34. Le TG,Ngo L,Mehta S,Do VD.*et al.* (2012).Effects of short-term exposure to air pollution on hospital admissions of young children for acute lower respiratory infections in Ho Chi Minh City, Vietnam. *Res Rep Health Eff Inst*.169, 73-83.
35. Satyanarayana, S, Nair SA, Chadha SS, Shivashankar R. *et al.* (2011). From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. *PLoS ONE.*, 6, 241-60.
36. Hernández-Garduño E, Cook V, Elwood R. K *et al.* (2004).Transmission of tuberculosis from smear negative patients: a molecular epidemiology study. *Thorax*, 59, 286–290.
37. Dharmadhikari A. S, Nardell E. (2009).Transmission of *Mycobacterium tuberculosis*. In: Schaaf HS, Zumla A, editors. Tuberculosis:A Comprehensive Clinical Reference. Elsevier *Health Sciences*. 8–17.
38. Vynnycky E, Fine PE. (1997). The natural history of tuberculosis: the implications of age-dependent risks of disease and the role of reinfection. *Epidemiology Infect*, 119, 183-201.
39. Braga Alfesio LF, Saldiva, Paulo HN, Menezes, *et al.* (2001).Health Effects of Air Pollution on Children and Adolescents in Sao Paulo, Brazil. *Paediatric Pulmonology*. 31, 106-113.
40. Lienhardt, C. (2001). From Exposure to Disease: The Role of Environmental Factors in Susceptibility to and Development of Tuberculosis. *Epidemiologic Reviews.* 23, 288-301
41. Lopez De Fede A,Stewart JE,Harris MJ,Mayfield-Smith K. (2008). Tuberculosis in socioeconomically deprived neighbourhoods: missed opportunities for prevention. *Int J Tuberc Lung Dis.*12, 1425-30.

ISSN 2382-1019

42. Grady JO, Maeurer M, Atun R, Abubakar I *et al*. (2011). Tuberculosis in prisons: anatomy of global neglect. *European Respiratory Journal*.38, 752–754.
43. Muniyandi M, Ramachandran R, Gopi PG, *et al*. (2007). The prevalence of TB in different economic strata: a community survey from South India. *Int J of Tuber and Lung Dis*. 11, 1042–1045.
44. Dehghani M, Anushiravani A, Hashemi H, Shamsedini N. (2014). Survey on air pollution and cardiopulmonary mortality in Shiraz from 2011 to 2012: an analytical-descriptive study. *Int J. Prev Med.*5, 734-40.
45. World Health Organ. (19974). Tuberculosis in a rural population of South India: a five-year epidemiological study. *Bull.* 51, 473-88
46. Tornee S, Kaewkungwal J. Fungladda W. *et al.* (2005).The association between environmental factors and tuberculosis infection among household contacts. *Southeast Asian J Trop. Med. Pub. Health.* 36, 221-224
47. Claessens NJ, Gausi FF, Meijnen S *et al.* (2002).High frequency of tuberculosis in households of index TB patients. *Int J Tuberc Lung Dis*. 6, 266-269.
48. Fitzgerald J.M, Fanning A, Hoepnner V, *et al.* (2003).The molecular epidemiology of tuberculosis in western Canada. *Int J Tuberc Lung Dis.* 7, 132-138.
49. Guwatudde D, Zalwango S, Kamya R *et al.* (2003). Burden of tuberculosis in Kampala, Uganda. *Bulletin of the World Health Organization*. 81, 99-805.
50. Lienhardt C, Sillah J, Fielding K, *et al*. (2003).Risk factors for tuberculosis infection in children in contact with infectious tuberculosis cases in the Gambia, West Africa. *Paediatrics*, 111, 608- 614.
51. Kass EH. (1971). Infectious diseases and social change. *J Infect Dis* 123, 110-14.
52. Dhingra VK, Rajpal S, Aggarwal N, Taneja DK. (2004). Tuberculosis trend among household contacts of TB patients. *Ind. J Community Medicine.*29, 1–3.
53. McPhendran FM & Opie EL (1935) .The spread of Tuberculosis in families. *Am. J of Epidemiology*.22, 565–643.
54. Iseman MD. (2000).A clinician's guide to tuberculosis. Lippincott Williams and Wilkins, Philadelphia
55. Fitzgerald JM, Wang L, & Elwood RK. (2000). Tuberculosis: Control of the disease among aboriginal people in Canada. *CMAJ*, 162, 351-355.
56. Dye C, & Williams BG. (2010).The population dynamics and control of tuberculosis. *Science*, 328, 856–861.
57. Dales R, Zwanenburg H, Burnett R, *et al*. (1991).Respiratory health effects of home dampness and molds among Canadian children. *Am J Epidemiology*. 134, 196-203.
58. Lipfert FW. (1994), Air Pollution and Community Health: A Critical Review and Data Sourcebook
59. Kampa, M. and Castanas E. (2008). Human health effects of air pollution. *Environ. Health*. 151, 362367.
60. Shah AS, Langrish JP, Nair H, McAllister DA, *et al.* (2004). Global association of air pollution and heart failure: a systematic review and meta-analysis. *Lancet.* 21; 382, 1039-48
61. Schell LM, Gallo MV. Denham. Ravenscroft J. (2006). Effects of pollution on human growth and development: an introduction. *J. Physiol. Anthropol*., 25, 103.
62. Zanobetti A, Canner MJ, Stone PH, Schwartz J, Sher D, *et al.* (2004). Ambient pollution and blood pressure in cardiac rehabilitation patients. *Circulation*, 110, 2184-9.
63. Miller KA *et al.* (2007).Long- term exposure to air pollution and incidence of cardiovascular events in women. *N Engl J Med.*, 356**,** 447–458
64. Brook RD. (2008).Cardiovascular effects of air pollution. *Clin Sci (Lond)*, **115,** 175–187.
65. Hoek, G, Raaschou-Nielsen O (2014).Impact of fine particles in ambient air on lung cancer. *Chin J Cancer.* 33, 197-203.
66. Bruce N, Perez-Padilla R, &Albalak R. (2000). Indoor air pollution in developing countries: a major environmental and public health challenge. *Bull WHO*, 78, 1078–1092.
67. Ezzati, M &Kammen, DM. (2002). The health impacts of exposure to indoor air pollution from solid fuels in developing countries: knowledge, gaps, and data needs. *Environ Health Perspect.* 110, 1057– 1068.
68. Chauhan AJ, Johnston SL. (2003) Air pollution and infection in respiratory illness. *Br Med Bull.* 68, 95–112.

ISSN 2382-1019

69. Cohen AR., Ostro B, Pandey KD, Krzyzanowski M. Kunzli N. *et al.* (2005).The global burden of disease due to outdoor air pollution. *J. Toxicol. Environ. Health*, 68, 1301
70. Boman. BC, Forsberg AB, Jarvholm BG. (2003).Adverse health effects from ambient air pollution in relation to residential wood combustion in modern society. *Scand J Work Environ Health*.29, 251–260.
71. Parikh J, Biswas, H and Karmakar, S. *(*2003).Cooking with Biofuels: Risk Factors Affecting Health Impact on Rural Women. *Economic and Political Weekly*. 38, 26, 2681-2692.
72. Gajalakshmi V, Peto R, Kanaka TS (2003). Smoking and mortality from tuberculosis and other diseases in India: retrospective study of 43 000 adult male deaths and 35000 controls. *The Lancet*, 362, 507–515.
73. Gajalakshmi V, Peto R. (2009). Smoking, drinking and incident tuberculosis in rural India: population-based case-control study. *Int. J. of epidemiology*. Access published June 4, 1-8
74. Mishra VK, Retherford RD, Smith KR. (1999).Biomass cooking fuels and prevalence of tuberculosis in India. *Int. J. of Infec Dis.* 3, 119–129.
75. Mishra P, Srivastava R. Krishnan A. S, *et al,* (2012). Indoor Air Pollution-related Acute Lower Respiratory Infections and Low Birth weight: A Systematic Review. *J Trop Pediatric*. 58, 457-466.
76. Beelen R, Hoek G, Fischer P, *et al.* (2008). Long- term effects of traffic-related air pollution on mortality in a Dutch cohort (NLCS-AIR study).*Environ Health Perspect*.116, 196-202.
77. Pai M, Mohan A, Dheda K, *et al.* (*2007).* Lethal interaction: the colliding epidemics of tobacco and tuberculosis. *Exp. Rev of Anti-Infective Therapy.* 5, 385–391.
78. Slama K, Chiang CY, Enarson DA. *et al.* (2007).Tobacco and tuberculosis: a qualitative systematic review and meta-analysis. *Int J of Tuber and Lung Dis.*11, 1049–1061.
79. Pai M. (2010). Spectrum of latent tuberculosis existing tests cannot resolve the underlying phenotypes, *Nature Reviews Microbiology*. 83,242.
80. Pandey M, Neupane R, Gautam A, *et al*.(1989).Domestic smoke pollution and acute respiratory infections in a rural community of the hill region of Nepal. *Environ Int*.15, 337–340.
81. Mishra, P, Srivastava, R. Krishnan, A. Sreenivaas, V. *et al,* (2012).Indoor Air Pollution-related Acute Lower Respiratory Infections and Low Birth weight: A Systematic Review. *J Trop Pediatric*.58, 457466.
82. den Boon S, van Lill S.W, Borgdorff MW, Verver S. (2005). Association between smoking and tuberculosis infection: a population survey in a high tuberculosis incidence area. *Thorax,* 60, 555-557
83. McIntyre EA, Gehring U, Mölter A, Fuertes E, Klümper C, *et al.* (2014), Air pollution and respiratory infections during early childhood: an analysis of 10 European birth cohorts within the ESCAPE Project. *Environ Health Perspect*, 122, 107-13.
84. Raaschou-Nielsen O, Andersen ZJ, Beelen R, Samoli E, *et al.* (2013).Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE).*Lancet Oncol*.14, 813-22.
85. Brunekreef B, Beelen R, Hoek G, Schouten L, *et al*. (2009). Effects of long-term exposure to traffic-related air pollution on respiratory and cardiovascular mortality in the Netherlands: the NLCS-AIR study. *Res Rep Health Eff Inst.* 139, 5-71
86. Kunzli N., Tager IB. (2005). Air pollution: from lung to heart, Swiss Med Wkly. 135, 697
87. Wen CP, Chan TC, Chan HT, Tsai MK, *et al,* (2010).The reduction of tuberculosis risks of smoking cessation. *BMC Infect. Dis*. 10, article 156
88. Cesaroni G, Forastiere F, Stafoggia M, *et al.*(2014).Long term exposure to ambient air pollution and incidence of acute coronary events: prospective cohort study and meta-analysis in 11 European cohorts from the ESCAPE Project. *BM*, 21, 348, 7412.
89. Edelson PJ, Phypers M. (2011).TB transmission on public transportation: a review of published studies and recommendations for contact tracing. *Travel Med Infect Dis*. 9, 27-31.
90. Mohr OM Askar S, Schink T, Eckmanns G, *et al,* (2012). Evidence for airborne infectious disease transmission in Public ground transport- A literature review. *Euro surveillance,* 17, 35
91. Patil PJ, Vithal G, Thakare S, Patil P. (2014). Comparative study of lung function test of policemen in traffic control with those in general duty. *Natl J Physiol Pharma Pharmacol*. 3, 162-166
92. Hudelson P. (1996). Gender differentials in tuberculosis: the role of socioeconomic and cultural factors. *Tuber Lung Dis.* 77, 391-400.

ISSN 2382-1019

93. Wells CD, Nelson LJ. (2004).New international efforts in childhood tuberculosis. Proceedings of the2002 Workshop on Childhood Tuberculosis, Montreal, Canada, *Int J Tuberc Lung Dis* 8, 630-5.
94. Lienhardt C, & Rodrigues LC. (1997). The impact of HIV infection on tuberculosis: tuberculosis risks revisited? *Int J Tuberc Lung Dis*.1, 196-204.
95. Seeley J, Charlotte H, Watts Kippax S. Russell R. *et al*. (2011). Addressing the structural drivers ofHIV: a luxury or necessity for programmes? *J of the Int AIDS Society*.15, 17397
96. Diedrich CR and Flynn J.L. (2011). HIV-1/Mycobacterium tuberculosis Co infection Immunology:How Does HIV-1 Exacerbate Tuberculosis? *Infec & Immu*, 79, 1407–1417
97. KibretKT,YalewAW,BelainehBG,*et al.* (2013). Determinant factors associated with occurrence of tuberculosis among adult people living with HIV after antiretroviral treatment initiation in Addis Ababa, Ethiopia: a case control study. *PLoS One*, 21, 8, 64488.
98. Springett, VH. (1964).Tuberculosis in immigrants. *Lancet*, 1,1091-5.
99. Zink A, Sola C, Reischl U, *et al*., 2003, Characterization of Mycobacterium tuberculosis complex DNAs from Egyptian mummies by Spoligotyping, J *Clin Microbiol*, 41, 359–67.
100. Sinclair D, Abba K, Grobler L, Sudarsanam TD. (2011) Nutritional supplements for people being treated for active tuberculosis.*Cochrane Database Syst Rev.* 9, CD006086.
101. Kant S, Gupta H, Ahluwalia S. (2015) Significance of nutrition in pulmonary tuberculosis.Crit Rev Food Sci Nutr. 55, 955-63. doi: 10.1080/10408398.2012.679500
102. Catherine MS. (2011). Genetic Epidemiology of Tuberculosis Susceptibility: Impact of Study Design PLoS Pathog. 7(1): e1001189.
103. Wilkinson R, Llewelyn M, Toosi Z, et al. (2000). Influence of vitamin D deficiency and vitamin D receptor polymorphisms on tuberculosis among Gujarati Asians in west London. Lancet, 355, 618-21.
104. Giorgio S., Branwen JH, Adebowale AAet al., (2008)Genetic studies of African populations: an overview on disease susceptibility and response to vaccines and therapeutics, Human Gene.123, 557-598
105. World Health Organization. 2003.
106. Narasimhan P. James WJ. MacIntyre CR et al, (2013) Risk Factors for Tuberculosis.Pulmonary Medicine, 1-11, Article ID 828939,
107. Grady JO, Maeurer M, Atun R, et al. (2011). Tuberculosis in prisons: anatomy of global neglect, European Respiratory Journal. 38, 752–754.
108. Ahmad S, (2011) Pathogenesis, Immunology, and Diagnosis of Latent Mycobacterium tuberculosis Infection. Clin. and Developmental Immun. 2011 Article ID 814943, 17 pages