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Chapter 3

Determinants of Survival of Patients with Tuberculosis in Developing Countries

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Additional information is available at the end of the chapter

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Abstract

Tuberculosis (TB), a major disease of public health importance, continues to cause significant morbidity and mortality to populations around the world. In 2016, it accounted for 1.7 million deaths worldwide. While the mortality rate among patients undergoing TB treatment has been declining over the years, TB death rates remains high in developing countries. This chapter discusses the epidemiology of TB mortality, the pathogenesis of TB highlighting susceptibility to mortality, and the interaction of factors which determine an individual's risk to death on account of TB. Furthermore, the chapter proposes the need for a strategic research agenda on reduction of TB burden, focusing on the factors that enable or impede political will towards translating knowledge into effective action.

Keywords: tuberculosis, survival, determinants, patients, developing, countries

1. Introduction

Tuberculosis (TB) remains a disease of public health importance affecting vulnerable populations. TB is the leading cause of death from a single infectious agent worldwide. The burden of the disease is enormous with an estimated 10.4 million new cases and 1.7 million TB deaths reported in 2016. Furthermore, more than one-fifths of reported deaths occurred among those who were HIV-infected [1]. While TB-mortality rate among HIV-negative people was 17 per 100,000 population, it was 5 per 100,000 among people living with HIV. In addition, 12% of incident cases of TB occurred among HIV-positive people while one in ten of new TB cases occurred among children in the same year [1]. According to WHO, the 30 countries most affected by TB include Angola, Bangladesh, Brazil, Cambodia, China, Congo, Central African Republic, DPR Korea, DR Congo, Ethiopia, India, Indonesia, Kenya, Lesotho, Liberia,

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Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, Russian Federation, Sierra Leone, South Africa, Thailand, UR Tanzania, Viet Nam, Zambia, and Zimbabwe [1].

TB mortality burden is continues to pose challenges to socioeconomic development in developing countries as South East Asia, Western Pacific, and African regions accounted for more than 90% of TB-deaths in 2016 [1].

Analysis of cohorts of patients on tuberculosis treatment enables public health programmes to describe the survival of patients and factors associated with mortality experience among patients. While treatment outcomes vary among different cohorts of TB patients, patients with drug resistance TB and those with coexisting debilitating conditions experience worst outcomes. Furthermore, survival of TB patients depends on several medical, demographic and socio-economic factors. This chapter focuses on the epidemiology of TB mortality, and the determinants of survival of TB patients – the factors which represent the most important opportunities for prevention of TB-related deaths in developing countries.

2. Epidemiology of TB mortality

Mycobacterium tuberculosis—the causative organism of TB, is the leading cause of death from a single infectious agent after Human Immunodeficiency Virus (HIV). About 45,000 TB-related deaths occurred in Europe in 2011 and its estimated mortality rate was 5.0 per 100,000 population [2]. While 330 TB-related deaths and an estimated TB-mortality rate of 0.5 per 100,000 population were reported in the United Kingdom, TB-death rates were 0.4, 1.0, 8.9, 15.0, and 16.0 per 100,000 population in Germany, France, Belarus, Russia, and Ukraine respectively [3]. In the United States, more than 50,000 TB-related deaths were reported from 1990 to 2006, accounting for 0.13% of the total number of deaths in the country [4]. While TB was reported as the underlying cause of death in about 40% of the 39,694,210 total deaths that occurred, it was reported as one of the contributing causes of death in more than 60% of the total deaths [1]. The overall mean annual mortality rate was 1.16 per 100,000 person-years during this period [1]. Similarly, 7% of the 301 persons with TB reported to Connecticut TB Control Program from 2007 to 2009 died on account of the disease [5]. Furthermore, 11% of the 40, 125 patients with culture-confirmed TB died on account the disease in California from 1994 to 2008 [3]. In 2014, more than 5% of the 9406 patients with TB in the US died due to the disease [6].

Although TB is a major public health problem worldwide, its mortality in developing countries is alarming. An estimated 2.5 million TB deaths were reported in China from 1990 to 2015 and 2% of these deaths occurred in 2015 [7]. Furthermore, TB-mortality rates were 32 and 44 per 100,000 population in 2016 in India and Pakistan, respectively [1]. While 16% of those who had TB died of the disease in Zimbabwe was in 2013 [8], TB-related mortality rates were estimated at 29, 56, 83, 104, and 222 per 100,000 population in Ethiopia, Ghana, Swaziland, Nigeria, and South Africa respectively in 2016 [1]. In addition, the estimated TB-related mortality rate in in Africa was 72 per 100,000 population while it was 3.4 per 100,000 population in European region and 2.3 per 100,000 population in the WHO Region of the Americas in 2016 [1].

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2.1. Global trends in TB mortality

Tuberculosis, often referred to as "consumption," "phthisis," or the "white plague," accounted for the highest number of deaths in Europe and America during the eighteenth and nineteenth centuries. While 70–90% of urban populations of Europe and North America were infected with TB in the late nineteenth century, four-fifths of people infected with TB died of it [9]. Through the knowledge made available by the work of Villemin, Koch, von Pirquet, TB mortality began to decline in the early and mid-nineteenth century [10–12]. TB Decline in TB mortality in these parts of the world was associated with improvement in socio-economic conditions of the populations.

In the United Kingdom, the rapid decline in TB mortality was cited as one of the most important health gains of the twentieth century [13]. Using all certified causes of death (both underlying cause and elsewhere on certificates), TB-mortality in the Oxford region declined from 39.7 deaths per million population in 1979 to 9.0 in 2008. In England, TB-mortality rates fell from 18.5 per million population in 1995 to 12.2 in 2008 [13].

TB mortality has been dropping rapidly since 1900 in developed countries, especially after the development of new anti-tuberculosis drugs. In the United States, 74,842 TB-related deaths were reported in 1933 [14]. This had declined by 22.9% by 1942 and a further decline was reported in the following decade such that only 25,080 TB-related deaths were reported in 1952 [12]. Furthermore, TB-mortality rates were 59.6, 43.1, and 16.1 per 100, 000 population in 1933, 1942, and 1952 respectively in the United States [12]. While 644 TB-deaths were reported in 2006, the estimated number of TB-related deaths was 610 in 2016 [1]. In essence, TB-mortality declined in the US from 59.6 per 100, 000 in 1933 to 0.19 per 100, 000 in 2016 [1, 12].

Due to poor vital registration systems, records on TB-mortality trends in developing countries are limited. A significant increase in TB mortality was recorded from 1990 and 2000 worldwide. However, the increase was more obvious in developing countries (**Figure 1**). In 2004, TB-mortality rate in Bangladesh was 51 per 100,000 population, while it was 81 per 100,000 in 2014 [8, 15]. Similarly, TB-death rates in Nigeria and South Africa in 2004 were 82 and 135

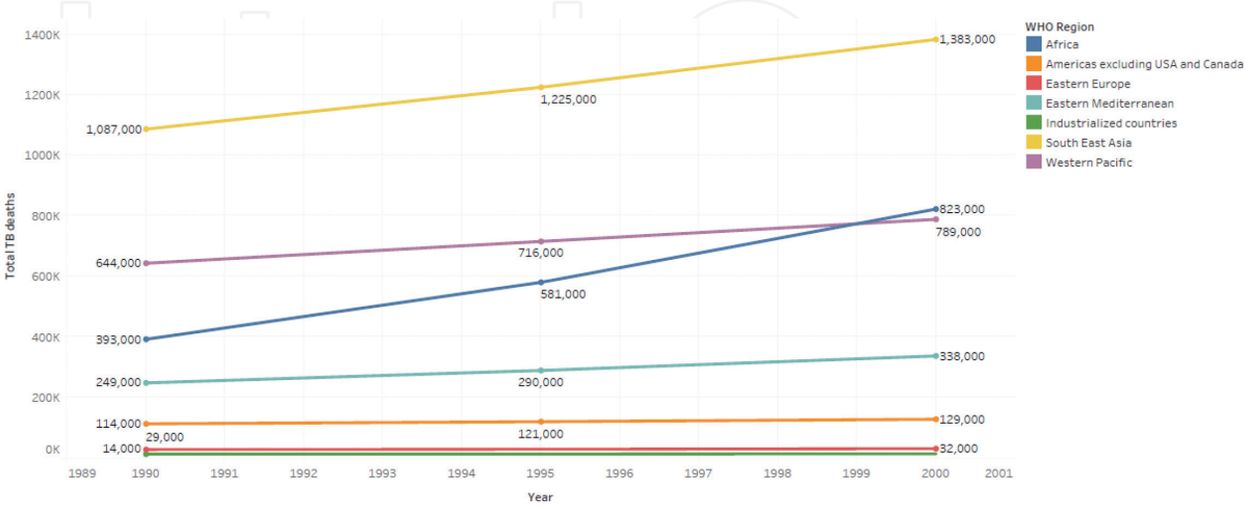


Figure 1. Global trends in TB mortality from 1990 to 2000. Data source: Global tuberculosis report 2013. WHO/HTM/TB/2013.11. Geneva: WHO; 2013.

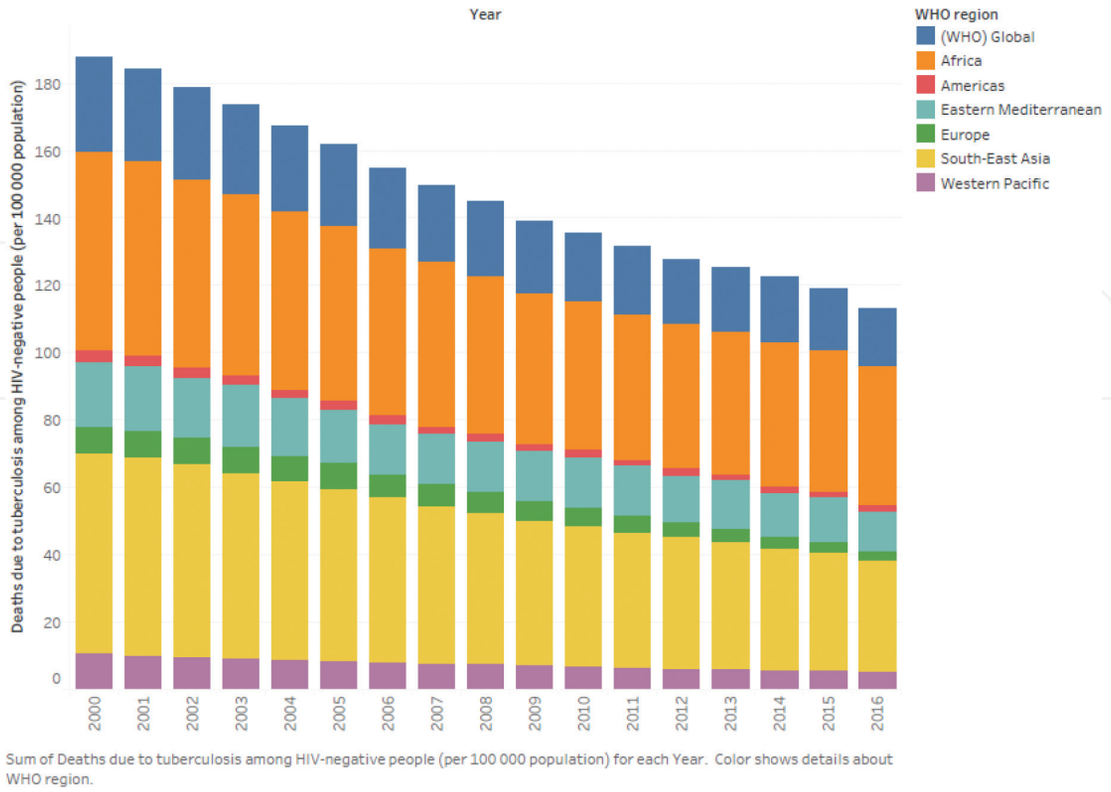


Figure 2. Global trends in TB mortality from 2000 to 2016. Data source: WHO. Global Health Observatory data repository. Tuberculosis [Internet]. Geneva: WHO; 2017 Dec 1 [cited 2018 Feb 12]. Available from: http://apps.who.int/gho/data/node.main.1315?lang=en.

per 100,000 population respectively. By 2014, the mortality rates had increased to 170 per 100,000 in Nigeria while it decreased to 24 per 100,000 in South Africa [7, 14]. Furthermore, TB mortality rates declined significantly between 2000 and 2016 (**Figure 2**).

3. Pathogenesis of TB infection

Tuberculosis (TB) is an old disease of mankind from time immemorial. An evidence of TB spine was found in Egyptian mummies of several thousand years BC, while Babylonian and Chinese writings also referred to the disease [16]. TB is an infection caused by the rod-shaped, non-spore-forming bacterium called *Mycobacterium tuberculosis*, a member of a group called M. tuberculosis complex (MTBC). Other members of this complex include *M. bovis, M. microti, M. africanum, M. caprae, M. canetti* and *M. pinnipedii.* MTBC members are closely related genetically. The genome of *M. bovis* differs from that of M. tuberculosis by less than 0.05% [17]. While *M. bovis* primarily affects cattle, it can also TB disease in other mammals include man [18].

TB infection leads to a complex interaction with the immune system of the human host. This interaction is often moderated by a number of factors with influence survival of TB patients.

3.1. Transmission

TB is transmitted from a person with active TB disease to an uninfected person through the air by droplet nuclei—particles measuring 1–5 μm in diameter containing MTBC [19]. These droplet nuclei are produced when persons with pulmonary or laryngeal TB cough, sneeze, speak, or sing. Iatrogenic transmission of TB may also occur during aerosol treatments, sputum induction, bronchoscopy, or during tissue or secretion processing in hospitals or laboratories. Droplet nuclei can remain airborne for long periods of time after expectoration. The transmission of TB depends on a number of factors including the number of tubercle bacilli present in droplets, its virulence and exposure to ultraviolet light, the extent of ventilation, and the immune status of exposed persons. After inhalation of an infectious droplet nucleus, it settles in the respiratory tract and reaches a respiratory bronchiole or alveolus where the tubercle bacilli may establish an infection depending on the bacterial virulence and the inherent mycobactericidal capacity of the alveolar macrophage. With the activation of the host defenses, phagocytosis by alveolar macrophages often initiates a cascade of events resulting in either a successful control of the infection, which is usually followed by latent tuberculosis. The invading mycobacterium may overwhelm host defense mechanisms followed by progression to active disease, known as primary progressive tuberculosis [19]. Within the alveolar macrophage, the tubercle bacillus continues growing slowly and dividing almost every 25–32 h for 2–12 weeks such that they reach 10^3–10^4 thereby eliciting a cellular immune response which is often detected by a positive reaction to a tuberculin test. For an immunocompetent person, the formation of granulomas around the invading mycobacterium occurs at this time.

Prior to the development of cellular immunity, tubercle bacilli may be disseminated via the lymphatics to the hilar lymph nodes and the bloodstream. When these bacilli reach more distant sites, they may give rise to extra pulmonary TB infection of the brain meninges, larynx, lymph nodes, spine, and kidney.

3.2. Pathophysiology

Granulomas formed by accumulation of T lymphocytes and microphages limit mycobacterial replication and spread [20]. Although the environment provided by granuloma formation destroys macrophages and produces early solid necrosis at the center of the lesion, tubercle bacilli often adapt to enhance their survival [20]. The formation of caseous necrosis, a soft-cheese structure with low oxygen levels, low pH, and limited nutrients in the following 2–3 weeks creates a condition that limits further mycobacterial growth. Latent tuberculosis is established at this stage. While tuberculous lesions undergo fibrosis and calcification thereby controlling the infection, the tubercle bacilli within the lesions may begin to multiply rapidly if the immune system of the individual deteriorates [21].

For an immunocompromised person, granuloma formation also occurs following infection with MTBC. However, the granulomas formed are unable to contain the infection. Hence, this progresses to primary progressive tuberculosis [21]. The necrotic tissue of the granuloma liquefies and the fibrous wall breaks down. Furthermore, the semiliquid necrotic matter may drain

into surrounding structures including the bronchi, and nearby blood vessels leaving an empty, air-filled cavity at the middle of the initial lesion. In addition, discharge of the necrotic material into a vessel may lead to extra pulmonary TB and mortality from TB may be related to this.

4. Factors associated with survival among TB patients in developing countries

The management of patients suspected of TB disease involves clinical assessment and treatment (**Figure 3**). Of the treatment outcomes, Cured and Completed treatment are considered as successful outcomes while the remaining ones are often referred to as poor treatment outcomes [1, 22].

Although deaths on account of TB disease occur worldwide, developing countries account for more than 90% of TB mortality in recent times. Hence, the focus of this section will be on developing countries. Several factors influence susceptibility of TB infection, its severity as well as mortality.

Factors associated with survival among TB patients in developing countries can be discussed using a framework proposed by the Commission on Social Determinants of Health (CSDH) established by WHO (**Figure 4**) [23].

Factors associated with survival among patients with TB disease can be classified into patient and community/social factors. In the context of the CSDH framework, most of the patient factors can be described in terms of the health system while community/social factors are related to the structural determinants of health and health inequities. Patient characteristics include age, sex, alcohol use, cigarette smoking, previous history of TB treatment, HIV co-infection, and comorbid conditions, TB diagnostic methods, and treatment regimens. On the other hand, structural determinants of health associated with TB survival include the presence of education, employment, access to health care and protection from catastrophic expenditure associated with TB morbidity.

4.1. Age

Aging affects the immune system at multiple levels including reduced production of B and T cells and diminished function of mature lymphocytes in secondary lymphoid tissues. Furthermore, aging causes a profound alteration in the composition and quality of the mature lymphocyte pool and alters the patterns of gene expression in mature B and T cells. Compared to young people, elderly individuals respond to immune challenge in a less efficient manner [24].

Old age increases the likelihood of death from TB. Evidence for this has been reported in previous studies. While several age cut-points have been used in studies to show vulnerability, TB infection in people over the age of 60 years is associated with increased mortality. A retrospective study among adult patients with clinically and/or bacteriologically diagnosed TB in Argentina reported increased mortality among people who were older than 50 years [22]. A similar study conducted in South Africa reported that patients who were 60 years or

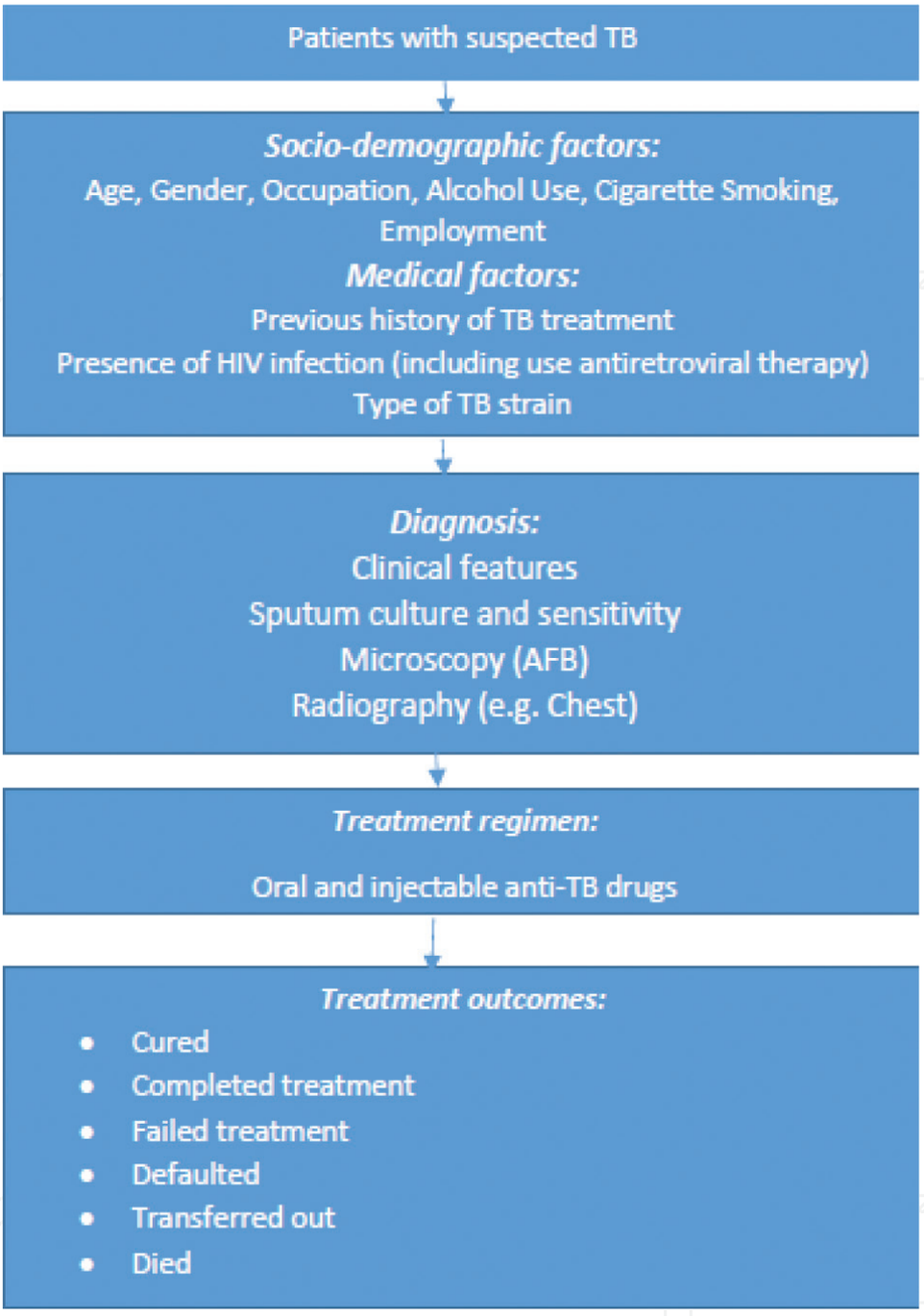


Figure 3. Clinical assessment and treatment of TB patients.

older were twice more likely to die from TB than the younger ones [25]. In addition, patients aged 65 years and above were two times more likely to die from TB than other patients in a study in Zimbabwe [26].

4.2. Sex

Infectious diseases including TB generally affect males more than females. Studies have shown that interactions between sex hormones and the immune system render males more

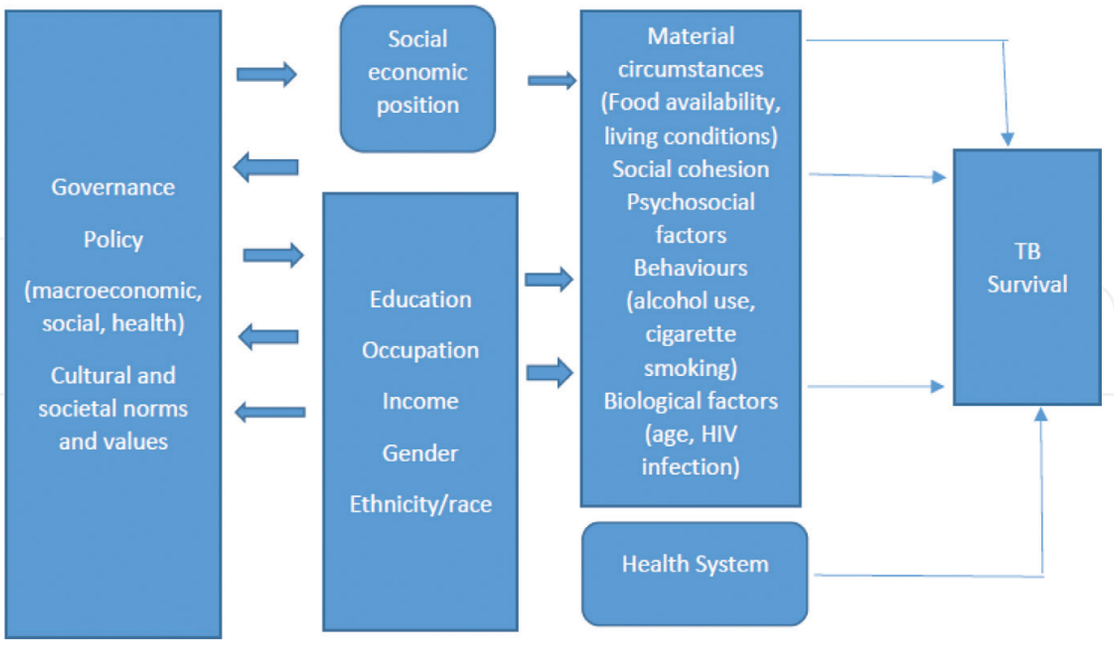


Figure 4. Conceptual framework for the social determinants of health and health inequities [23].

susceptible to infection and disease, with differences in genetic make-up likely playing a role [27, 28].

A recent study in Brazil aimed at examining sex bias in ten major pathogens also reported the characteristic male bias of a male-to-female ratio of almost 2:1 [2]. While tuberculoid leprosy is slightly more common in females (0.85:1), the study reported a ratio of almost 3:1 for the severe lepromatous form. Host immune response to leprosy has been compared to that in tuberculosis and lepromatous leprosy was considered as being analogous to active tuberculosis. Furthermore, tuberculoid leprosy may be seen as analogous to latent TB or cured or TB [29]. Since both diseases are caused by the same pathogen—Mycobacterium, the male bias observed supports the hypothesis that physiological differences may be responsible for the observed differential susceptibility to TB. This physiological hypothesis (PH) has also been found to be relevant in TB disease as a driver of sex differences in disease susceptibility [1, 2]. TB mortality is also in keeping with differential susceptibility between males and females as more than 65% of adult TB deaths in 2016 occurred among males [1]. This is also similar to the twentieth century in New York which showed a male-to-female TB mortality ratio of approximately 2:1 [30].

A consistent finding in literature shows that males are more likely to die from tuberculosis than females. A study in Ethiopia, showed that males are twice more likely to have poor treatment outcome (including death) following TB treatment [31]. In addition, a systematic review and meta-analysis consisting of multidrug resistant-TB (MDR-TB) data from 31 treatment programmes from 21 countries showed that males are less likely to have a successful outcome after treatment [32]. Although there was no association between sex and survival among patients in a study in South Africa, male patients were more likely to have unfavorable TB treatment outcomes [33].

4.3. Education

Educational status is an important factor which moderates health care seeking behavior and adherence to prescribed medications. The level of educational achievement may protect against acquiring TB infection through promotion of healthy habits. In addition, education been recognized as a marker of economic status. Hence, low level education may be associated with lack of access to resources, overcrowding and poor hygienic conditions which may also contribute to increased mortality. In a study in Peru, MDR-TB patients who attended formal school for 6 or less years had about threefold increase in TB mortality risk [34]. Similarly, attendance or completion of primary school level was associated with TB treatment failure [35]. While educational status may be a significant factor influencing survival in most health conditions, only a few studies reported it as a determinant of survival among patients with TB in developing countries [32, 34].

4.4. Occupation

Occupations which compromise structural and/or functional integrity of the lungs predispose individuals to the transmission of TB as well as to higher risk of mortality on account of the disease. While exposures to dust inside the mines damage the structure and function of the lungs (e.g., silicosis), associated social conditions outside the mines (e.g., crowding) drive HIV and TB epidemics. This makes mining a strong predictor of TB mortality. Studies in Southern Africa have reported the strong association between mining and TB mortality [36, 37].

4.5. Smoking

Smoking is one of the most important risk factors associated with incidence, morbidity, recurrence and mortality from TB. Smoking has been associated with a fourfold increase in TB mortality risk [38].

4.6. Previous history of TB treatment

Previous TB treatment has been associated with TB mortality. A prospective study among smear positive TB patients with Iranian nationality who had successful TB treatment showed that those who had previous history of TB treatment were almost three times more likely to die [39]. Similarly, patients with a previous history of TB treatment were almost seven times more likely to die than treatment-naive patients in another study in Iran [40]. This may be related to development of resistance following treatment default, failure, or loss to follow up.

4.7. Type of TB strain

Multidrug-resistant tuberculosis (MDR-TB), a form of TB disease resistant to both isoniazid and rifampicin is a global problem. Increasing incidence of this type of TB is a reflection of the health care system of a country. It arises as a result of weak TB treatment programmes coupled with poor adherence to anti-TB therapy. While the extent and burden of the disease

varies among countries, it often overwhelms the capacity of the health system in many high burden resource-poor countries.

Studies have consistently shown that MDR-TB is a strong predictor of TB mortality. In 2016, it was responsible for a large percentage of TB mortality worldwide [1]. MDR-TB was associated with almost eightfold increase in mortality risk in a retrospective study in Peru [32]. Other studies have also shown similar findings. Furthermore, MDR-TB associated hazard ratio (HR) estimates in TB mortality increase in previous studies were in the range of 7.8–8.5 [41, 42].

Extensively drug-resistant tuberculosis (XDR-TB), a variant of MDR-TB resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin) in addition to isoniazid and rifampin. XDR-TB has also been associated with high death rates while on treatment.

There are multiple causes for the increased risk of multidrug-resistant TB strains. MDR-TB infection often occur with other co-morbid conditions including HIV infection, diabetes, renal disease, and Substance Use Disorders [43]. In addition, MDR-TB has been associated with high rates of treatment failure and relapse which increases TB mortality. With high toxicity of anti-tuberculosis drugs used in the treatment of MDR-TB and the extended duration of use, an increase in toxicity profile of patients and consequent adverse effects may be related to increased mortality experienced among MDR-TB patients.

4.8. HIV co-infection

Studies have shown that HIV/TB co-infection is associated with increased TB mortality risk before, during, or after TB treatment. In most cases, deaths are usually caused by complications of HIV infection rather than TB disease itself. However, a synergistic interaction occurs between TB and HIV infection which speeds up the progression of illness and increasing mortality risk. HIV infection enhances the reactivation and progression of latent *Mycobacterium tuberculosis* to active TB disease, and the active TB disease accelerates HIV disease progression in infected patients. Furthermore, HIV infection alters the clinical presentation of TB and complicates TB treatment follow-up [44].

In Malawi, HIV positive patients were 2.5 times more likely to die from TB infection in a prospective cohort study among TB patients [45]. Another study in Malawi also reported almost fourfold increase in TB mortality among HIV/TB co-infected patients compared to HIV seronegative TB patients [46]. Furthermore, HIV co-infection was associated with almost sixfold increase in TB mortality in a study in Ethiopia [35].

Among patients who were HIV/TB co-infected, being on antiretroviral therapy (ART), initiation of cotrimoxazole prophylactic therapy (CPT), being ambulatory, and having high CD4 counts were factors associated with survival in several studies. Patients who were on ART were 0.35 times less likely to die from TB compared to those who were not on ART [47].

While MDR-TB infection is associated with increased mortality risk for both HIV-seropositive and seronegative patients, HIV/MDR-TB co-infection increases the risk of death. A study in Thailand reported that patients who were HIV positive patients infected with MDR-TB

were twice more likely to die compared to HIV seropositive patients who had non-MDR-TB co-infection [48]. Similarly, HIV/TB co-infected patients who delayed initiation of ART 6 or months or more after TB diagnosis were 2.6 times more likely to die compared with those who initiated ART in less than 6 months following TB diagnosis [47].

4.9. Extra pulmonary TB

Although extra pulmonary TB is not as common as pulmonary disease, its occurrence has consistently been shown in literature as a predictor of TB mortality. Patients with extra pulmonary TB including TB meningitis, TB pericarditis, TB peritonitis, bilateral or extensive pleural effusion due to TB, Potts disease, TB of the genitourinary tract, and TB of the intestine were twice more likely to die on account of the disease than patients with pulmonary disease in a study in Brazil [49]. Furthermore, patients who had extra pulmonary TB were three times more likely to die than those who had pulmonary TB [50]. Similarly, miliary TB has also been associated with poor outcomes [51].

4.10. Co-morbid conditions

Co-morbid conditions including malnutrition, chronic renal disease, chronic liver disease, drug induced immunosuppression, and diabetes mellitus are predictors of mortality among TB patients.

4.10.1. Diabetes

The synergistic interactions between diabetes mellitus and TB are well documented in literature [52]. Diabetes alters host immunity to TB which leads to higher baseline mycobacterial burdens and longer times to achieve culture conversion with treatment. While treatment failure or death was reported in 41% of patients with TB and diabetes in case-control study, these outcomes were only reported in 13% of those with TB alone. Furthermore, seven of the eight patients in the TB and diabetes group died of respiratory failure related to TB [53].

4.10.2. Malnutrition

Malnutrition has been cited as a predictor of mortality among TB patients. Malnourished patients were 27 times more likely to have unfavorable TB outcome and death in a study in South Africa [54].

4.10.3. Chronic renal disease

The presence of end stage renal disease requiring dialysis was associated with sevenfold increase in TB mortality risk in a previous study [55].

4.10.4. Drug-induced immunosuppression

The presence of drug induced immunosuppression was associated with increased TB mortality risk with adjusted odds ratio of 3.2 [51].

4.11. Poor adherence to anti-Koch therapy

Studies have shown that TB patients with poor adherence to medications are more likely to die compared to other patients. A retrospective study involving patients in 48 clinics in Rwanda among patients treated in 48 clinics in Rwanda showed that poor treatment adherence was associated with more than threefold increase in TB mortality [56].

4.12. Neighbourhood and social factors

Neighbourhood factors refer to issues within the society that contribute to TB mortality which are not directly related to a patient's individual condition but a constellation of factors which affect a patient's access to care, treatment enablers, emergency services, and attitudes of the general population to health. These include societal norms and values, policy, and governance issues within and outside the health system (**Figure 4**).

Neighbourhoods play a role in TB morbidity and mortality as good housing may influence air quality and disease transmission. Access to nutritious foods may also be important for immune responses and recovery from TB infection. In addition, Service characteristics of neighbourhoods can create and support employment opportunities which may reinforce socioeconomic disparities in health.

The level of the commitment of health authorities at the local, regional, and national levels towards TB treatment, care and support influences the survival of patients [1]. For instance, the failure of a TB treatment programme to follow up on patients on treatment may contribute to increased mortality. In addition, failure of the health system to screen and test HIV positive patients for TB may also affect their survival.

Social protection is one of the functions of the health system. However, unemployment, low status occupation, low annual income, high cost of travel to the health care facility for TB treatment, poor living conditions, low literacy level, and high out-of-pocket expenditure on TB treatment have been described as factors associated with poor treatment adherence, unfavorable TB treatment outcomes, and death. Furthermore, a strong correlation was reported between TB treatment outcomes and overall health system performance in a study in South Africa where TB treatment centers with higher health system performance rating also had higher percentage of successful treatment outcomes [57].

4.13. Climatic factors and TB seasonality

Studies have shown that seasonal variation in the incidence of TB disease occurs in many developing countries. In India and Hong Kong, TB seasonality was highest among young children. However, seasonality of notified TB cases was more pronounced among males in Mongolia and South Western Cameroon [58]. In Southern Africa, most significant declines in the diagnoses of pulmonary TB occurred in December, followed by April–May. While these may not be unrelated to climatic factors, changes in health-seeking behavior and fluctuations in clinical activities were cited as responsible factors [59]. In China, increased incidence of TB was associated with increased temperature, precipitation, and wind speed [60].

Seasonality of TB disease may be related to differences in TB risk factors at certain seasons. A study in Peru showed the complex interaction of social determinants of TB infection, exposure to infection and increased transmission. Overcrowding, increased indoor time, and poorer ventilation, poorer nutrition, lower immunity, health-seeking behavior, and education interact in a complex way to an increase in TB disease at certain seasons than others. Vitamin D deficiency, more likely to occur in winter, was also associated with TB seasonality [61].

5. Conclusion

The burden of TB and the mortality on account of the disease has been discussed. While differences in mortality between population groups due to society's characteristics have been noted, factors associated with reduced survival among TB patients have been highlighted. Furthermore, it is important to note that changes in social and cultural environments of people are associated with changes in their risks of acquiring TB infection, and the risk of dying from the disease. Although associations between social factors and TB morbidity and mortality are well known, there is paucity of studies regarding the underlying processes linking social determinants and TB treatment outcomes and effective ways to intervene. While TB morbidity and mortality have reduced significantly in many parts of the third world in recent times, limited progress achievement are been recorded in other countries. A crucial obstacle in this regard is often the lack of political will. A strategic research agenda on reduction of TB burden should focus on the factors that enhance or impede political will to translate knowledge into effective action.

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