MEDDOCS
Open Access Publisher

Review on Non-Communicable Disease among TB Patient

Kedir Mehadi Ahmed; Abdurezak Mohamed*

College of Health and Medical Science, School of Medical Laboratory, Department of tropical & Infectious Diseases, Haramaya university.

*Corresponding Author(s): Abdurezak Mohamed

College of Health and Medical Science, School of Medical Laboratory, Department of tropical & Infectious Diseases, Haramaya university.

Email: abdurezak244341@gmail.com

Abstract

Globally, the incidence of Tuberculosis (TB) is declining very slowly, and the Non-Communicable Disease (NCD) burden for many countries is steadily increasing. But, tuberculosis is a leading cause of mortality in low- and middle-income countries. TB multi-morbidity, TB and at least one non-communicable diseases is common, but studies are rare. Several NCDs, such as diabetes mellitus, cardiovascular diseases, cancer, and chronic respiratory disease were associated with TB and prevalence of self-reported TB increased linearly with increasing numbers of NCDs. Among those with TB, the most prevalent combinations of NCDs were cardiovascular disease (angina) and depression, followed by diabetes and arthritis. The objective of this seminar is to review published study of non-communicable disease including it is type, magnitude and mechanism of interaction among TB patient. Urgent research to understand, prevent and manage NCDs in people with TB is important.

Introduction

Tuberculosis (TB) is the leading cause of deaths from a single infectious disease globally [1]. People from low- and middle-income countries are at a high risk of developing TB [2,3], with over 95% of TB cases and deaths occurring in LMICs [4]. As a long-term infectious disease, TB may lead to the breakdown of immune surveillance [5], increasing one's susceptibility to other conditions such as Non-Communicable Diseases (NCDs) [6,7] (cancer, diabetes, respiratory and cardiovascular diseases), which together contribute to two thirds of the global mortality [8]. The global burden of Non-Communicable Diseases (NCDs), in particular, accounts for two-thirds of mortality worldwide.

The co-occurrence of two or more chronic diseases in one individual at one point of his/her life is typically referred to as multi-morbidity [9,10]. Multi-morbidity is becoming a primary concern in our global healthcare system, especially for LMICs where there is a need to consider economic restraints when planning levels of care [11]. There is evidence that multi-morbidity may occur in 1 out of 4 adults across LMICs [12], and that its prevalence may be increasing due to increasing life expectancy in these settings [13].

In countries where TB is endemic [4], a concerning rapid increase in NCDs has been reported, especially in sub-Saharan Africa [3] and in South Asian regions [14], and particularly for those NCDs associated with TB. First, most research considering TB multi-morbidity presence of TB alongside one or more chronic conditions has included small-scale studies [15], been restricted to a single country [16-18], or only considered one comorbid chronic condition [19,20]. Therefore, given the aforementioned knowledge gap, the aim of this seminar was to re-

view non-communicable disease among TB patient including their interaction mechanism, types and way of prevention and control strategy [21].

Presence of a NCD may indicate the need to actively screen for TB, especially in high-burden countries, which can help improve early and increase TB case detection. Similarly, diagnosis of TB should alert clinicians to actively screen for common non-communicable comorbidities, which may otherwise go undiagnosed, especially in low- and middle income countries where services for NCDs are vastly underdeveloped. Finally, preventive therapy for TB may be warranted in individuals with some of these comorbidities.

Review on non-communicable disease among TB patient

Some preliminary research has suggested that TB multi-morbidity is associated with increased use of healthcare services [22,23], increased symptom complexity [24], high premature mortality risk [25,26], increased disabilities [27,10], poor quality of life [27-29] frequent hospitalization [30,31], and high healthcare expenses [6]. Despite the negative consequences associated with TB multi-morbidity, TB services tend to be single focus programs that rarely screen for NCDs, and NCD care itself is also limited and rarely provided, especially in LMICs. Some studies have reported NCD screening in tuberculosis patients; however, they focused mainly on diabetes [5-7].

Types of NCDs among TB patient

A several NCDs such as: Cardiovascular (angina, arthritis), chronic respiratory disease (asthma), diabetes, depression, edentulism, hearing problem, schizophrenia, and visual impairment were assessed in the WHS [1]. Additionally, there is evidence of an increased prevalence of mental health problems in those diagnosed with TB. This rapid increase of NCDs may be because of an ageing population, rapid urbanization, changes in environmental factors and lifestyle changes. People living with chronic communicable diseases such as tuberculosis (TB) is most likely to develop comorbidity with NCDs' with the increase of chronic communicable and NCDs, primary health care services are confronted with a huge challenge [32,33].

Diabetes mellitus among TB patient

Diabetes *is a chronic (long-lasting) disease that affects how the body turns food into energy.* Tuberculosis (TB) is a serious health threat, especially for people living with diabetes. Two TB-related conditions exist: latent TB infection and TB infection. People with latent TB infection are not sick because the body is able to fight the bacteria to stop them from growing. People with TB disease are sick and have active TB because the body cannot stop the bacteria from growing. People living with diabetes who are also infected with TB are more likely to develop TB disease and become sick with TB. Someone with untreated latent TB infection and diabetes is **more** likely to develop TB disease than someone without diabetes. Without proper treatment, diabetes and TB can increase health complications. The prevalence of DM among TB cases was 9.9% which is more than two folds higher than the occurrence of DM in the general population of Eritrea [34].

DM may increase susceptibility for pulmonary TB via multiple mechanisms. Those directly related to hyperglycemia and cellular insulinopenia and the indirect effect on macrophages and lymphocytes function, leading to diminished ability to contain the TB. DM is known to affect chemo taxis, phagocytosis,

activation and antigen presentation by phagocytes in response to TB. Chemo taxis of monocytes is impaired, and this defect does not improve with insulin. It is known that DM is a moderate to strong risk factor for the development of active TB [22].

Cardiovascular diseases among Tb patient

The burden of Cardiovascular Disease and tuberculosis (CVD) is enormous worldwide. CVD rates are rapidly increasing in low- and middle-income countries. Public health programs have been challenged with the overlapping tuberculosis and CVD epidemics. Monocyte/macrophages, lymphocytes and cytokines involved in cellular mediated immune responses against *Mycobacterium tuberculosis* are also main drivers of atherogenesis, suggesting a potential pathogenic role of tuberculosis in CVD via mechanisms that have been described for other pathogens that establish chronic infection and latency. Tuberculosis (TB) is a dominant cause of mortality from a single infectious disease agent. It is a global health issue that has been tagged as a public health emergency for decades. The disease process, which is caused by *Mycobacterium Tuberculosis* (MTB), affects the respiratory system as well as many other organ systems in the body, such as the lymphatic system, Central Nervous System (CNS), gastrointestinal system, and Cardiovascular System (CVS) [23].

Generally, cardiovascular diseases are the leading cause of death worldwide, with most of the mortality in low and middle-income countries. Also, the high mortality rate of TB is skewed to these regions, making the mortality of TB with CVS involvement exceptionally high [21]. The multisystem involvement of TB impacts the cardiovascular system in various forms. While pericarditis caused by TB is quite common, other complications like myocarditis, coronary artery disease, and otitis are rarer, necessitating a high index of suspicion and holistic management [24].

Cancer among Tb patient

Lung cancer has been recognized as one of the greatest common cancers, causing the annual mortality rate of about 1.2 million people in the world. Lung cancer is the most prevalent cancer in men and the third-most common cancer among women (after breast and digestive cancers). Recent evidences have shown the inflammatory process as one of the potential factors of cancer. Tuberculosis (TB), pneumonia, and chronic bronchitis are among the most important inflammation-inducing factors in the lungs, among which TB has a more profound role in the emergence of cancer. TB is one of the important mortality factors throughout the world, and 205,000 death cases are reported annually due to this disease. Chronic inflammation and fibrosis due to TB can induce genetic mutation and alternations. Parenchyma tissue of lung is involved in both diseases of TB and lung cancer, and continuous cough in lung cancer, morphological vascular variations, lymphocytosis processes, and generation of immune system mediators such as interleukins, are all among the factors leading to the hypothesis regarding the role of TB in lung cancer.

Chronic respiratory among Tb patient

Chronic Obstructive Pulmonary Disease (COPD) and tuberculosis (TB) are two important causes of mortality and morbidity in our country and are among top 10 causes of death. The interrelationship between TB and COPD is very complex. A substantial number of TB patients develop post-tubercular airway disease or TB-associated COPD. This is the most commonly reported relationship. However, many different associations

have also been published. COPD patients are also at high risk of developing pulmonary TB [1]. COPD is a common comorbidity in patients with TB, second only to diabetes [1], History of TB negatively impacts the long-term course of COPD with early mortality and increased frequency of exacerbations [1], COPD also alters the clinical presentation of TB and is a risk factor for increased morbidity and mortality from TB [40]. Smoking, TB, and COPD all damages the lungs. Smoking suppresses the innate and adaptive immune response with decreased levels of pro-inflammatory cytokines and circulating immunoglobulin and reduces the activity of alveolar macrophages, dendritic cells, and natural killer cells. This complex interrelationship of smoking, COPD, and TB with increased expression of proteolytic enzymes, cytokines, and interleukins results in the structural damage seen in both COPD and TB [33].

Magnitude

Despite this, evidence on NCD multi-morbidity in people with TB remains scarce, with numerous gaps and limitations in the literature. The prevalence of one or more of these NCDs was 68.8% in people with TB, and 34.4% in people without TB. Among those with TB, the strongest correlations in terms of the pairs of NCDs were observed for depression and schizophrenia, followed by cardiovascular disease such as arthritis and angina. The most prevalent pairs of concurring NCDs among people with TB were angina and depression (15.3%), followed by arthritis and asthma (14.6%), asthma and angina (10.7%), and depression and arthritis (9.7%). people with TB could be attributable to NCDs including depression, angina, schizophrenia, asthma, arthritis and diabetes. NCDs were three times higher in TB patient than NCDs in participants without TB. Moreover, in people with TB, just over 55% of total were in patients with 2 or more NCDs, 24% in patients with one NCD and 21% in patients with no NCD according to one study [1]. This epidemiological shift adds to the existing infectious disease load, creating a double burden of communicable diseases and NCDs in the populations [25].

Interacting mechanism

Strong association between active TB disease and NCDs that exercise a toll on the immune system. Factors associated with TB-NCD multi-morbidity may include older age, gender and lower socio-economic status. Moreover, TB-NCD multi-morbidity has been found to have negative effects on physical and mental health and quality of life. However, most NCDs, like most infectious diseases, are more common in the lower socioeconomic groups. This is certainly true in high-income countries, but also to a growing extent also in middle- and low-income countries. Therefore, the double burden of communicable diseases and NCDs is most pronounced among the poor, and this is further underscored by the causal links between them. There is a growing body of evidence describing the links between Tuberculosis (TB) and a number of NCDs and their risk factors, such as DM, smoking- and alcohol-related conditions, COPD, mental illness and malnutrition, are responsible for a significant proportion of TB cases [18].

Risk factor

The relationship between TB and chronic physical conditions may be bidirectional. Several health conditions, such as diabetes [35-37] and chronic lung diseases including chronic obstructive pulmonary disease and silicosis [6], have been previously reported as important risk factors for TB. TB comorbidity with

Non-Communicable Diseases (NCDs) and other Communicable Diseases (CDs) is highly prevalent in TB endemic regions of the world. The determinants of multi-morbidity include socioeconomic factors (unemployment, deprivation level, and economic restrains), low accessibility to healthcare [38], and health risk behaviors (low physical activity, poor diet) [38,39].

In addition, factors associated with increased risk of TB have been widely reported, including malnutrition, diabetes [16], poverty, overcrowding [40], alcoholism, smoking [6], Human Immunodeficiency Virus (HIV) and chronic pulmonary disease [5]. All these determinants are very evident and alarming in LMICs [41]. Current reports show a growing evidence of links between communicable diseases and NCDs, or risk factors thereof such as tobacco use, physical inactivity, unhealthy diet, the harmful use of alcohol, and cardio-metabolic risk factors such as high blood pressure, overweight/obesity, and dyslipidemia [2,3,16].

Prevention and control strategies

The rise of NCDs is important for TB control for a variety of reasons. First, many NCDs are risk factors for TB, especially for progression from infection to disease due to negative impact on host defense mechanisms against Mycobacterium tuberculosis. Secondly, NCDs may complicate treatment and management of TB, due to clinical challenges (among people with DM) as well as behavioral challenges (among people with alcohol use disorders). Thirdly, TB can trigger or aggravate NCDs. For instance, TB, like other infections, can worsen glucose control and trigger DM, and a history of TB, although not a classical risk factor for COPD, is one of the leading causes of lung sequelae and bronchiectasis, and has been identified as an independent risk factor for COPD in a recent review [31]. The absence of investigation of NCD co- and multi-morbidity amongst patients with TB may impact negatively on the success of TB control programs [40]. In addition, TB, and especially MDR-TB, may aggravate the social and financial stress contributing to substance abuse and mental illness. However, the link between TB and NCDs also creates opportunities for improved diagnosis and management of both [8].

Population attributable TB risk estimates for diabetes, malnutrition, smoking, excessive alcohol use, and HIV infection are high. Kaplan et al, The Lancet 2009, Decision-making based on data and evidence (vital statistics, surveillance and outbreak investigations, laboratory science), A focus on populations rather than individual, A goal of social justice and equity, An emphasis on prevention rather than curative care.

Globally, TB incidence is declining, but at a slow pace. Additional efforts are needed to speed up the decline. Improved diagnosis and treatment of all forms of TB will be required, backed by poverty alleviation and general socioeconomic development, for long-term TB control and elimination. However, there is also a need to address a set of major TB risk factors and comorbidities.

Conclusion

TB is more common among people with the NCDs reviewed here than among the general population. Low- and Middle-Income Countries (LMICs) are experiencing an increasing double burden of communicable and Non-Communicable Diseases (NCDs), with limited capacity of the health system to address non-communicable diseases in addition to endemic communicable diseases such as Tuberculosis (TB) Current reports show a growing evidence of links between communicable diseases and

NCDs are tobacco use, physical inactivity, unhealthy diet, the harmful use of alcohol, and cardio-metabolic risk factors such as high blood pressure, overweight/obesity, and dyslipidemia. The secondary objective of the study was to investigate factors associated with tuberculosis, TB-diabetes and TB-hypertension co-morbidities, and to assess the feasibility of integrating screening for non-communicable diseases and their risk factors into routine tuberculosis care.

The growing burden of NCD has important implications for TB epidemiology, TB case management and TB treatment outcomes. Several NCD put people at increased risk for *M. tuberculosis* infection and weaken immune responses which increases risk for TB. Some of them can make detection more difficult, affect TB drug effectiveness, worsen the general conditions of the patient, worsen treatment adherence, and increase the risk of treatment failure, TB recurrence and death. At the same time, these diseases and conditions are preventable and treatable. TB programs and clinicians treating TB must work more closely with those in general health services providing prevention and care for NCDs, within the context of primary care and the general health system. Ultimately, the many opportunities for improved collaboration, which will strengthen control efforts in both communicable and non-communicable disease control, will need to be exploited to provide the best care and have a greater impact on both TB and NCD control.

References

1. Stubbs B, Siddiqi K, Elsey H, Siddiqi N, Romano E, et al. Tuberculosis and Non-Communicable Disease Multimorbidity: An Analysis of theWorld Health Survey in 48 Low- and Middle-Income Countries. Int. J. Environ. Res. Public Health. 2021.

2. Falzon D, Mirzayev F, Wares F, Baena IG, Zignol M, et al. Multidrugresistant tuberculosis around the world: What progress has been made? Eur. Respir. J. 2015; 45: 150-160.

3. Roche S, de Vries E. Multimorbidity in a large district hospital: A descriptive cross-sectional study. S. Afr. Med J. 2017; 107: 1110-1115.

4. World Health Organization. Tuberculosis. Available online: https://www.who.int/news-room/fact-sheets/detail/tuberculosi (accessed on 20 May 2020).

5. Bates M, Marais BJ, Zumla A. Tuberculosis comorbidity with communicable and non-communicable diseases. Cold Spring Harb. Perspect. Med. 2015; 5: a017889.

6. Marais BJ, Lönnroth K, Lawn SD, Migliori GB, Mwaba P, et al. Tuberculosis comorbidity with communicable and non- communicable diseases: Integrating health services and control efforts. Lancet Infect. Dis. 201; 13: 436-448.

7. Peltzer K. Tuberculosis non-communicable disease comorbidity and multimorbidity in public primary care patients in South Africa. Afr. J. Prim. Health Care Fam. Med. 2018; 10: e1-e6.

8. Beaglehole R, Bonita R, Alleyne G, Horton R, Li L, et al. UN high-level meeting on non- communicable diseases: Addressing four questions. Lancet. 2011; 378: 449-455.

9. Foguet-Boreu Q, Violán C, Rodríguez-Blanco T, Roso-Llorach A, Pons-Vigués M, et al. Impact of multimorbidity: Acute morbidity, area of residency and use of health services across the life span in a region of south Europe. BMC Fam. Pract. 2014; 15: 55.

10. Lange-Maia BS, A Karvonen-Gutierrez C, Kazlauskaite R, Strotmeyer ES, Karavolos K, et al. Impact of Chronic Medical Condition Development on Longitudinal Physical Function from Mid- to Early Late-Life: The Study of Women's Health Across the Nation. Journals Gerontol. Ser. A Boil. Sci. Med Sci. 2019; 75: 1411-1417.

11. Stubbs B, Vancampfort D, Veronese N, Kahl KG, Mitchell AJ, et al. Depression and physical health multi-morbidity: Primary data and country-wide meta-analysis of population data from 190,593 people across 43 low- and middle-income countries. Psychol. Med. 2017; 47: 2107-2117.

12. France EF, Wyke S, Gunn JM, Mair FS, McLean G, et al. Multimorbidity in primary care: A systematic review of prospective cohort studies. Br. J. Gen. Pract. 2012; 62: e297-e307.

13. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: Prevalence and trend over the last 20 years. Eur. J. Gen. Pract. 2008; 14 (Suppl. S1): 28-32.

14. Siegel KR, Patel SA, Ali MK. Non-communicable diseases in South Asia: Contemporary perspectives. Br. Med Bull. 2014; 111: 31-44.

15. Valenzuela-Jiménez H, Manrique-Hernández EF, Idrovo AJ. Association of tuberculosis with multimorbidity and social networks. J. Bras. de Pneumol. 2017, 43, 51-53. Int. J. Environ. Res. Public Health. 2021; 18: 2439.

16. White LV, Edwards T, Lee N, Castro MC, Saludar NR, et al. Patterns and predictors of co-morbidities in Tuberculosis: A cross-sectional study in the Philippines. Sci. Rep. 2020; 10: 41.

17. Reis-Santos B, Gomes T, Macedo LR, Horta BL, Riley LW, et al. Prevalence and patterns of multimorbidity among tuberculosis patients in Brazil: A cross-sectional study. Int. J. Equity Health. 2013; 12: 1-8.

18. Adejumo OA, Olusola-Faleye B, Adepoju VA, Gidado M, O Onoh M, et al. The pattern of comorbidity and its prevalence among drug-resistant tuberculosis patients at treatment initiation in Lagos, Nigeria. Trans. R. Soc. Trop. Med. Hyg. 2020; 114: 415-423.

19. Schepisi MS, Navarra A, Gomez MNA, Dudnyk A, Dyrhol-Riise AM, et al. Burden and Characteristics of the Comorbidity Tuberculosis-Diabetes in Europe: TBnet Prevalence Survey and Case-Control Study. Open Forum Infect. Dis. 2018; 6: ofy337.

20. Song ATW, Schout D, Novaes HMD, Goldbaum M. Clinical and epidemiological features of AIDS/tuberculosis comorbidity. Rev. Hosp. Clin. 2013; 58: 207-214.

21. Negin J, Abimbola S, Marais BJ. Tuberculosis among older adults-time to take notice. Int. J. Infect. Dis. 2015; 32: 135-137.

22. Lehnert T, Heider D, Leicht H, Heinrich S, Corrieri S, et al. Review: Health Care Utilization and Costs of Elderly Persons with Multiple Chronic Conditions. Med Care Res. Rev. 2011; 68: 387-420.

23. Machado VDSS, Valadares ALR, Costa-Paiva LH, Osis MJ, Sousa MH, et al. Aging, obesity, and multi-morbidity in women 50 years or older: A population-based study. Menopause. 2013; 20: 818-824.

24. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. Lancet. 2012; 380: 37-43.

25. Jani BD, Hanlon P, Nicholl BI, Mc Queenie R, Gallacher KI, et al. Relationship between multimorbidity, demographic factors and mortality: Findings from the UK Biobank cohort. BMC Med. 2019; 17: 1-13.

26. Gallo JJ, Hwang S, Joo JH, Bogner HR, Morales KH, et al. Multimorbidity, Depression, and Mortality in Primary Care: Randomized Clinical Trial of an Evidence-Based Depression Care Management Program on Mortality Risk. J. Gen. Intern. Med. 2016; 31: 380-386.

27. Fortin M, Stewart M, Poitras ME, Almirall J, Maddocks H. A Systematic Review of Prevalence Studies on Multimorbidity: Toward a More Uniform Methodology. Ann. Fam. Med. 2012; 10: 142-151.

28. Fortin M, Lapointe L, Hudon C, Vanasse A, Ntetu AL, et al. Multimorbidity and quality of life in primary care: A systematic review. Heal. Qual. Life Outcomes. 2004; 2: 51.

29. Williams JS, Egede LE. The Association between Multi-morbidity and Quality of Life, Health Status and Functional Disability. Am. J. Med Sci. 2016; 352: 45-52.

30. Alaba O, Chola L. The social determinants of multimorbidity in South Africa. Int. J. Equity Health. 2013,; 12: 63.

31. Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, et al. Causes and consequences of comorbidity: A Review. J. Clin. Epidemiol. 2001; 54: 661-674.

32. Koyanagi A, Vancampfort D, Carvalho AF, De Vvlder JE, Haro JM, et al. Depression comorbid with tuberculosis and its impact on health status: Cross-sectional analysis of community-based data from 48 low0- and middle-income countries. BMC Med. 2017; 15: 209.

33. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015; 386: 743-800.

34. World Health Organization. Diabetes country profiles. 2019. Available from: http://origin.who.int/diabetes/country-profiles/ eri_en. pdf. Accessed August 7, 2019.

35. A Baker M, Harries AD, Jeon CY, E Hart J, Kapur A, et al. The impact of diabetes on tuberculosis treatment outcomes: A systematic review. BMC Med. 2011; 9: 81.

36. Jeon, C.Y, Murray, M.B. Diabetes mellitus increases the risk of active tuberculosis: A systematic review of 13 observational studies. PLoS Med. 2008; 5: e152.

37. Stevenson CR, Forouhi NG, Roglic G, Williams BG, A Lauer J, et al. Diabetes and tuberculosis: The impact of the diabetes epidemic on tuberculosis incidence. BMC Public Health. 2007; 7: 234.

38. Vancampfort D, Koyanagi A, Ward P, Rosenbaum S, Schuch FB, et al. Chronic physical conditions, multimorbidity and physical activity across 46 low- and middle-income countries. Int. J. Behav. Nutr. Phys. Act. 2017; 14: 6.

39. Melaku YA, Temesgen AM, Deribew A, Tessema GA, Deribe K, et al. The impact of dietary risk factors on the burden of non-communicable diseases in Ethiopia: Findings from the Global Burden of Disease study 2013. Int. J. Behav. Nutr. Phys. Act. 2016; 13: 122.

40. Hargreaves JR, Boccia D, Evans CA, Adato M, Petticrew M, et al. The social determinants of tuberculosis: From evidence to action. Am. J. Public Health. 2011; 101: 654-662.

41. Thrush, A, Hyder, A. The neglected burden of caregiving in low- and middle-income countries. Disabil. Health J. 2014; 7: 262-272.