

Comorbidity burden of Tuberculosis: Implications for Sri Lanka

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Abstract-

Introduction and aims:

Rising trends of comorbidities associated with tuberculosis (TB) have been observed in recent literature. This review explores these global trends and the implications of these for Sri Lanka.

Methods

Literature search was done in PubMed and Embase databases using subject headings and keywords. Articles and content of grey-literature were screened for the relevance and quality. Selected articles were included in a narrative review of the findings.

Results:

The evidence for the rising TB-comorbidity burden was synthesized under 6 domains: TB comorbidity burden in general, TB-diabetes, TB-HIV, TB-malnutrition, TB-mental disorders and TB-other non-communicable conditions. The relevant statistics, pathophysiological basis and the implications were discussed.

Conclusions and Recommendations:

Person-centered care model is recommended as comorbidity-burden of TB is rising. Additional strategies must be integrated in Sri Lanka in addressing the burdens of TB and comorbidities. More research must be promoted.

Index Terms- Tuberculosis, Co morbidities, Non- Communicable Diseases, Diabetes Mellitus, Mental Health Disorders

I. INTRODUCTION

Tuberculosis (TB) is regarded as the global leading cause of death among the infectious diseases(1). It is caused by the organism *Mycobacterium tuberculosis*. It is reported than only in 2017 it has been attributed as the cause of 1.3 million deaths. To make the situation worse, in the same year an additional 10 million cases were newly reported (1). While a relatively adequate attention is given on the burden of TB around the world, even some developing settings like Sri Lanka have managed to keep the TB burden as “low” within their regions(2). However, a new facet related to TB has been highlighted in recent global literature, which

of importance to all settings including those which are well-controlling TB in the form its comorbidity-burden. This means that the patients with TB are found to be associated with numerous disease conditions with a higher prevalence compared to those without TB. Similarly, the burden of TB is found to be associated with numerous disease conditions with a higher prevalence compared to those without TB. Similarly, the burden of TB is found to be relatively higher among people with many such conditions.

This research was done to explore the published literature and novel insights on the TB-comorbidity burden and to synthesize implications in relation to the Sri Lankan healthcare system.

II. METHODS

A comprehensive literature search was done in PubMed and Embase databases. The related subject headings (MeSH in PubMed and Emtree in Embase) as well as related keywords were used in the search strategy. In addition, related grey literature was searched in reputed websites. The articles and content were screened by the investigator for the eligibility (relevance and quality). The selected articles were included in a narrative review of the findings under 6 domains: TB comorbidity burden in general, TB-diabetes, TB-HIV, TB-malnutrition, TB-mental disorders and TB-other non-communicable conditions.

III. RESULTS

TB-comorbidity burden

Even the World Health Organization has highlighted the comorbidity burden of TB. It has emphasized the importance of detecting these comorbidities due to several reasons. One is that the co-management of the conditions can be done smoothly. Secondly the high prevalence of these comorbidities could be worsening

the TB burden. On the other hand, the proper control of these conditions would help in reducing the TB burden(3). It can be argued that in the same line, the proper management of TB could enable reducing the burden of these other conditions as well.

A significant comorbidity burden has been observed in relation to many disease groups throughout the world. Comorbidities of TB have been well observed in relation to “HIV, diabetes, smoking, alcoholism, chronic lung diseases, cancer, immunosuppressive treatment, malnutrition” according to the Marais et al (2013)(4). Owing to these associations, they highlighted the importance of integrated management of TB in relation to both the communicable and non-communicable diseases among the national programmes(4).

TB and Diabetes

Ill effects of TB-diabetes comorbidity have been observed even in relatively developed regions like the Europe as well as in developing regions. The prevalence of diabetes among the people with TB has been documented as in the range of 44% to 28.5% with an overall figure of 10.7%(5). The magnitude of this burden has been found to vary among people among certain demographic groups. The Asians are categorized as within the high-risk group for this burden along with the Pacific Islanders and Hispanic diabetics. It has been also documented that the prevalence of TB among these groups have increased from 4.6% to 9.6% between 1998 to 2011(6). In Ethiopia, the prevalence of diabetes has been documented as higher than among the people with TB, compared to the national estimates(7).

It has been mentioned that while TB can impair the glycaemic control among the people with diabetes, the clinical profile of TB could be negatively affected by diabetes. It is also mentioned that the risk of getting TB is 2-3 times higher among the people with diabetes compared to those who without(3). Tesket *et al* (2017) have documented that the risk of mortality from TB is nearly two times among the diabetics compared to those without diabetes(8). In addition other worse outcomes like; slower conversion of bacteria, reduced cure rate, more relapses and increased drug resistances have been observed due to diabetes-TB comorbidity(8). Of the chest images of people with

TB, it has been reported that the cavities are seen more when the person is affected with diabetes(5).

Mechanism which lead to this increased TB burden among diabetes is describes as related to the effects on cytokines, reactive oxygen species and antioxidants. All these are expected to increase the vulnerability of a person for infectious agents(8). Other suggested reasons include; deficiencies of micronutrients, microangiopathies of lungs as well as renal implications (e.g. renal insufficiencies) which are associated with diabetes(7).

TB and HIV

The co-infection between the TB and HIV has been described as the leading infectious disease burden in many resource-poor settings(9). It is documented that in AIDS settings, Tb is the leading single cause of death. TB is attributed to 26% of AIDS deaths while 99% of these occur in developing settings(10). The agents responsible for these two disease conditions do “potentiate” each other according to the available literature leading to a diminished and deteriorated immune system. Thus in relation to HIV, the progression to AIDS is accelerated whereas for TB, “susceptibility to primary infection, reinfection as well as risk of reactivation” is increased(9). As documented by Pawlowski and others (2012) the latent-Tb reactivation risk is increased by 20 times with HIV(10).

TB and Malnutrition

Patients wit TB are found to be with reductions in both lean body mass and fat mass. The parameters like “arm muscle area”, “mid arm circumference”, “skin fold thickness” as well as “serum albumin” levels are found to be lower in patients with TB(11). These associations are augmented through the evidence available on vitamin D receptors, immunity status and infections of the respiratory system of malnourished children(12). Also the processes among the TB patients like; reduced appetite, malabsorption of nutrients and alterations of metabolism are suggested as responsible for this association(13).

TB and Mental disorders

In a recent scoping review done by Resnsburg et al (2020), associations of mental disorders with TB were

explored(14). The review identified four comorbidities of TB- alcohol use, depression, anxiety and general mental health. Both men (especially for alcohol use) and women (for worse mental health outcomes) were observed to be affected by these associations. These associations were augmented in relation to advantaged age and history of mental illnesses(14). The review emphasized the utility of its findings especially for the lower income countries.

TB and other Non Communicable Diseases

Yakar et al (2017) have documented the negative impact of TB on the progression of Chronic Obstructive Pulmonary Disease(15). They concluded that the even though the mortality remained the same, when there was a history of TB, the diagnosis and deaths were found to be 5 years earlier(15). In some settings, the TB-COPD comorbidity becomes only second to that of TB-diabetes. In Indian literature, 32.4% of the patients with COPD were found to be with a history of TB (16). The impact of prevalent risk conditions like smoking and alcoholism are also being described with worsening the TB burden(4, 16). As an example, risk of getting TB is documented as 3-5 times higher among smokers. Similarly, worse clinical course (e.g. high degree of dissemination, extensiveness of involvement of lung and less closure of lung cavities) is also observed among the smokers(16).

IV. DISCUSSION

TB is described to be associated with multiple infectious as well as non-communicable conditions. These non-communicable conditions include not only physical elements but extend across the mental well-being as well. Based on the findings, important implications were synthesized in relation to the novel recommendations and for the way forward of Sri Lanka.

Novel strategies

Considering these facts, a customized approach is recommended in the recent literature for TB management. This is based on the fact that holistic care is needed in optimizing the well-being of the clients.(14) TB is associated with many comorbidities and hence the clinical profile is influenced by each of

these conditions in addition to the socio-demographic characteristics of the patient. Since the effects of TB-comorbidity burden extends into the psychological domains as well, addressing of both the physical as well as mental wellbeing components are needed. This optimal care package is termed as “person-centred TB care”. In a review by Resnsburg et al (2020), it was identified that just one study has been done up to the time of that review on such a model(14). This highlights the paucity of evidence on the person-centred model throughout the world. Countries need to expand the evidence generations in relation to individualized care for TB and explore the best service delivery model for each setting.

Implications for Sri Lanka

Sri Lankan health achievements are well appreciated in comparison to those countries with similar economic statuses. Prior to the ongoing Covid-19 pandemic, Sri Lanka had been able to control the communicable diseases except for few conditions like dengue and leptospirosis. Even for TB, within the South East Asian region, Sri Lanka is regarded as a low prevalence country with an estimated prevalence rate (of all types of TB) being 103 per 100,000 people(2). It is utmost essential that Sri Lanka continue to maintain the low burden of TB in the coming years.

However, Sri Lanka is undergoing a demographic and an epidemiological transition as a result of which the non-communicable disease burden is on the rise. Disease conditions like diabetes and chronic respiratory diseases are being shown among the main non-communicable conditions. In addition, the risk factors associated with these conditions are also becoming more prevalent. The findings of the current review suggest that the burden of TB is expected to increase with these conditions. Hence the burden of comorbidity must be given complete emphasis by the policy planners in the longer run. This becomes essential in identifying these comorbidities early in minimising the healthcare costs associated with these, as otherwise once the complications are developed the cost becomes increased. On the other hand, for ensuring the holistic care for the clients of the healthcare system, it becomes essential in screening the people with any of these conditions for the other.

In order to achieve these, the clinical guidelines of management of TB as well as of these other conditions must be revisited. Periodic screenings for these comorbidities must be incorporated into these guidelines. These must be conveyed throughout all levels of healthcare even to the level of general practitioners whom play an essential role in the achievement of universal health coverage. More research must be encouraged in eliciting the local findings in relation to what have been documented in global literature. This is vital as the global literature suggest variations of these comorbidities across different regions and demographic groups. By applying these measures Sri Lanka will be able to retain the low burden of TB as well as would be able to lower the burdens of associated comorbidities.

V. CONCLUSIONS AND RECOMMENDATIONS

Comorbidity-burden of TB is rising with the increase of the prevalence of comorbid conditions and their risk factors. Person-centred care model is recommended to be introduced in managing this burden. By integrating the strategies suggested, Sri Lanka would be able to retain the current low TB-burden as well as the burden of the comorbid conditions. More research must be promoted on TB-comorbidity burden.

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