REVIEW ARTICLE

Tuberculosis Elimination: Implications and Challenges

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ABSTRACT

Background: Tuberculosis elimination remains a significant global health challenge, despite the efforts made by governments and international organizations to control and eliminate the disease. The study objectives were to explore the global TB control efforts and highlight the possible challenges and implications in the way to TB elimination. Recommendations to add momentum to current health care efforts were also outlined**.**

Methods: Relevant works of literature were retrieved from different journals and web pages. The electronic databases were searched using the key.

Results: A review of the progress made over the past years in the control of TB has shown that the goal of TB elimination has not yet been achieved. The high burden of TB, limited access to TB diagnosis and treatment, drug-resistant TB, weak health systems particularly in low- and middle-income countries, socioeconomic factors, and lack of political commitment and resources are among the major challenges that have hindered the successful elimination of tuberculosis.

Conclusions: a sustained and coordinated effort from governments, private sector, international organizations, and other stakeholders, including increased funding, political commitment, and a focus on addressing the root causes of TB transmission and disease burden are required to address these challenges.

Keywords: Control, Challenges, Elimination, Tuberculosis

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INTRODUCTION

Tuberculosis (TB) is a major global public health problem, affecting millions of people around the world each year. According to the World Health Organization (WHO), TB is the 13th leading cause of death and the second leading infectious killer after COVID-19 worldwide and in 2023, an estimated 10.6 million people fell ill with TB and 1.6 million died from the disease.[1] TB is particularly prevalent in low- and middle-income countries, where factors such as poverty, malnutrition, crowded living conditions, and weak healthcare systems contribute to its spread. It is also a persistent health threat in high-income countries, especially among most vulnerable segments of the population and those with weakened immune systems, such as people living with HIV/AIDS.[2]

Control and elimination of TB are both important goals in public health, but they have different aims and strategies. Control of TB aims to reduce the incidence and prevalence in a population through a range of measures such as early diagnosis, effective treatment, contact tracing, infection control, and public awareness campaigns. On the other hand, TB elimination aims to reduce the incidence of TB to very low levels, till completely eradicate it from a population. It requires more ambitious goals and strategies, such as active case-finding specifically for latent TB, targeted testing and treatment, vaccination, and improved living conditions. TB elimination programs are usually implemented in countries with low TB incidence and better resources.[3] Indeed, significant progress has been made towards TB control in recent years, however, eliminating TB remains a complex and challenging task, with several implications and challenges.

The objectives of the current review were to explore the global TB control efforts and highlight the possible challenges and implications in the way to TB elimination. Recommendations to add momentum to current health care efforts were also outlined.

METHODOLOGY

Relevant literature was retrieved from different journals and web pages. The Science Direct, Embase, UpToDate, PubMed, Scopus, and Web of Science (ISI) databases were searched using keywords. The search terms of tuberculosis elimination, control, eradication, challenges, implications, treatment, diagnostics and vaccines were used. Relevant articles were identified, then screened and selected based on title and abstract from the year 1997 up to 2022

RESULTS & DISCUSSION

While there have been significant advancements in the prevention and control of infectious diseases worldwide, TB remains a major global health threat.[4] TB eradication represents the ultimate goal in the fight against TB, and involves the complete elimination of the disease from the human population. Elimination is a step further than TB control, with the aim to reducing the incidence of TB to less than one case per million people per year.[5] Achieving this aim requires sustained efforts to control the disease, as well as innovative approaches to identifying and treating the most vulnerable populations.

Global efforts to eliminate TB: There has been a global commitment to eliminate TB, with various organizations, governments, and stakeholders working towards this goal. In 1993, WHO declared TB a global health emergency[6] due to the increasing number of cases of tuberculosis and advocated for urgent action to address it. Since then, there have been significant global efforts to control and eventually eliminate TB as a public health threat. These efforts included the implementation of The Directly Observed Treatment, Short-course (DOTS) strategy in 1995, which is a comprehensive public health approach to control the global TB epidemic. It aimed to ensure that all people with TB had access to diagnosis, treatment, and follow-up care, with a particular focus on those who were most likely to transmit the disease. The DOTS strategy has been highly successful in reducing the global burden of TB and has served as a model for other public health interventions.[7] However, despite the success of DOTS in many countries, there have been challenges to its implementation and effectiveness. These challenges included the lack of trained health workers to deliver DOTS, inadequate funding for TB control programs, poor patient adherence to treatment, and the emergence of drug-resistant TB. In 2001, a global initiative called The Stop TB Partnership was launched. It aimed to accelerate the fight against TB by bringing together governments, civil society, and international organizations. The partnership focuses on improving TB prevention, diagnosis, and treatment, as well as promoting research and innovation in TB control. One of the key achievements is the Global Plan to Stop TB, which was launched in 2006 to address the DOTS challenges. This Plan set an ambitious target for reducing the global burden of TB by 2015, and emphasized the importance of scaling up existing interventions, promoting innovation, research in TB control, increasing funding and resources for TB control efforts. Indeed, the strategy had led to significant progress in reducing TB incidence and mortality in many countries, but challenges remained, particularly in the areas of drug-resistant TB and TB/HIV co-infection. Overall, the Stop TB Partnership represented a renewed commitment to fighting the global TB epidemic, and it continued to be a critical platform for global TB advocacy and coordination.[8] In addition, there have been efforts to increase funding for TB. The Global Fund to Fight AIDS, Tuberculosis, and Malaria in 2002 has invested over $11 billion in TB programs, and worked closely with other global health partnerships, such as the Stop TB Partnership

and the WHO, to coordinate efforts and ensure a comprehensive and integrated approach to fight TB.[9]In 2015, the WHO updated the Stop TB Strategy and built on the lessons learned with a new global strategy called the End TB Strategy, which aimed to reduce tuberculosis deaths by 90% and reduce the incidence of the disease by 80% by 2030. The strategy had three main pillars focused on integrated patient-centered care and prevention, bold policies and supportive systems, and intensified research and innovation. The strategy also recognized the importance of addressing the social determinants of TB, such as poverty and inequality. Simultaneously, the United Nations (UN) set out 17 Sustainable Development Goals in 2015, which included a goal to "Ensure healthy lives and promote well-being for all at all ages". This goal included specific targets to end TB epidemic by 2023 also. Recognizing the urgent action to end TB by 2030, the UN advocated to a coordinated, multi-sectoral approach that involved not only the health sector but also other sectors such as education, housing, and social protection.[10]

The UN's commitment to tackling TB is also reflected in the political declaration from the 2018 High-Level Meeting on TB, which calls for increased funding and resources for TB control efforts, as well as a focus on addressing social and economic factors that contribute to TB. The meeting was seen as a significant step forward in the global fight against TB and provided a framework for continued progress in the years to come.[11]

TB challenges: Despite the global efforts, there are several challenges that need to be addressed in order to achieve the goal of tuberculosis elimination.

Infectiousness of TB: Tuberculosis is a highly contagious infection which can be spread through the air when an infected person coughs, sneezes, or talks. The bacteria can survive in the air for several hours, especially in enclosed spaces with poor ventilation. However, not everyone who is exposed to the bacteria will develop active TB disease but there are categories in the pathogenesis of the disease.[12] TB has been described as "hiding in plain sight" because it can be difficult to detect and diagnose, especially in its early stages. The symptoms of tuberculosis can be non-specific and can be easily confused with those of other respiratory illnesses, making it challenging to diagnose. During this time, the infected person can unknowingly spread the bacteria to others, increasing the risk of transmission in the community. Additionally, some people with tuberculosis may not show any symptoms at all, which can make it even more difficult to detect the disease. This is known as latent infection, where the bacteria lay dormant in the body, controlled by white blood cells within a granuloma, for many years with no symptoms. It is estimated that approximately one-third of the world's population has latent TB infection[11] that can serve as a reservoir of infection in the population. However, the risk of progression to active TB disease from latent infection is generally estimated to be around 5-10% over the course of a person's lifetime. Indeed, it can be higher in certain populations such as those with weakened immune systems, people living in areas with high TB prevalence and close contacts of people with active TB disease. According to WHO, contact of an active case are at 10-60 times higher risk of developing the disease and people with active TB can infect up to 5-15 other people through close contact over the course of a year.[1] Consequently, identifying and treating the hidden pool of latently infected individuals is a core challenge of TB elimination.[13] A range of tools and strategies have been developed to address the challenge of detecting, diagnosing and active case-finding. However, there is still a need for further research and development of more accurate and accessible diagnostic tools, especially in low- and middle-income countries where access to healthcare and laboratory services may be limited.

TB is a social disease: Tuberculosis is often referred to as a social disease because its prevalence and impact are strongly linked to social and economic factors. TB disproportionately affects marginalized and vulnerable populations, such as people living in poverty, migrants, refugees, and those who are malnourished or have weakened immune systems. Social determinants such as gender, education, and employment status can also influence an individual's risk of TB infection. women may be at higher risk due to gender inequalities that limit their access to healthcare and increase their exposure to TB in the home. Similarly, people who are unemployed or working in jobs with poor working conditions may be more vulnerable due to factors such as stress, poor nutrition, and exposure to environmental risk factors. Furthermore, Stigma and discrimination against people with TB can be a significant barrier to achieving TB elimination.[14] In some communities, there may be misconceptions about the causes of TB or how it is transmitted, leading to fear and avoidance of individuals with the disease. This can prevent people from seeking diagnosis and treatment, which can lead to ongoing transmission of the disease. While highest prevalence is in low- and middle-income countries, where poverty, malnutrition, overcrowding, and poor access to healthcare are common, certain populations in high-income countries, may have a higher risk of TB, such as individuals with weakened immune systems or those living in overcrowded or institutional settings.[2]

TB morbidity and mortality: The global efforts to combat TB have been ongoing for many years, and progress has been made in reducing the incidence and mortality rates associated with the disease. According to world TB report 2022, between 2015 and 2020, the cumulative reduction in TB incidence was 11%, which is over halfway towards the End TB Strategy milestone of 20% reduction during the same period. However, there was a big global drop in the number of people newly diagnosed with TB and reported. It was estimated that 18% global drop from 7.2million in 2019 to 5.8 million in 2020.[15] Ad-

ditionally, close to one in two TB-affected households face costs higher than 20% of their household income, according to latest national TB patient cost survey data. The world did not reach the milestone of 0% TB patients and their households facing catastrophic costs as a result of TB disease by 2020.For mortality from TB, there was also significant global reduction in TB deaths between 2000 and 2019, but the TB deaths increased in 2020 due to the emerged COVID-19 pandemic. The cumulative reduction of TB deaths between 2015 and 2020 was 9%, which is less than quarter of the way to the milestone of a 35% reduction set out in the End TB Strategy. The WHO has warned that the COVID-19 pandemic could set back progress on TB by several years. Forecasts for TB deaths and cases in 2021 and 2022 were concerning, with estimates suggesting that the number of TB deaths and cases have increased during this period.

COVID19 pandemic: The pandemic has had a significant impact on TB programs, including disruptions to TB services, delays in diagnosis and treatment, and diversion of resources away from TB control efforts. Many people with TB symptoms have been reluctant to seek care at health facilities due to fear of contracting COVID-19. Additionally, some health facilities have been closed or operating at reduced capacity due to pandemic-related restrictions. Resources have been diverted from TB services to addressing the COVID-19 pandemic. As a result, decline in global spending on essential TB services from $ 6.0 in 2019 to 5.4 billion in 2021, which is less than half of the target set by UN high level meeting on TB.[16] While increased funding is important to address the challenges posed by the COVID-19 pandemic on TB programs. The need for action has become even more pressing in the context of the ongoing conflicts and crises around the world, including War in Ukraine, the global energy crisis, and the global food security outbreak. These events can worsen the factors that contribute to the spread of tuberculosis.

TB and HIV: The high burden of TB is also exacerbated by other factors, such as the HIV epidemic. People living with HIV are particularly vulnerable to TB infection, and HIV/TB co-infection is a significant public health challenge in many parts of the world. It is not only increasing the risk of TB infection but makes TB more difficult to diagnose and treat. According to WHO, in 2022, people living with HIV accounted for around 6.7% of the total number of people who fell ill with TB worldwide. The co-infection of TB and HIV can be especially deadly, an estimated 187,000 people died from TB and HIV co-infection.[2] Research has indicated that with correct TB treatment, an HIV-positive individual with TB can gain around 20 additional years of life compared to those who do not receive adequate treatment.[17] This highlights the importance of ensuring that individuals with TB and HIV receive comprehensive care that addresses both conditions simultaneously. Coordinated efforts between TB and HIV programs, healthcare providers, and public health agencies are essential to achieve optimal outcomes.

TB and Diabetes Mellitus: Other striking factor that contributed to the burden of TB in developing countries is diabetes mellites. People with diabetes are two to three times more likely to develop TB disease than people without diabetes, and they are also at higher risk of dying during TB treatment. In addition, people with diabetes are more likely to develop multidrug-resistant TB, which is more difficult to treat and can be associated with poorer outcomes.[18] The global prevalence of diabetes is expected to rise in the coming decades, which could further exacerbate the burden of TB. Specifically, the global estimate of diabetes is expected to rise from 463 million people in 2019 to 578 million by 2030 and 700 million by 2045.[19] So, it is important to take proper care of diabetes in patients suffering from diabetes/TB.

TB and Tobacco: Tobacco use, including smoking and vaping, has been identified as a risk factor for TB infection and disease progression. Indeed, tobacco and vaping continue to be public health concerns, and their rates of use can vary depending on various factors, including geographical location and demographic characteristics.[20] It is important to address the challenges posed by the emerging use of tobacco and vaping in TB control. Specifically, prevalence of TB is three times as high among ever-smokers and almost 38% of TB deaths are associated with the use of tobacco.[21] To effectively tackle tobacco and vaping use in relation to TB, healthcare professionals play a crucial role. It is essential to provide training for healthcare professionals, including physicians, on effective smoking cessation strategies. By enhancing their knowledge and skills in communicating the risks associated with tobacco/vaping use, providing support, and delivering appropriate interventions, physicians can make a significant impact on helping patients quit smoking or vaping.[22] Targeting both individual behaviors change through education and healthcare provider support through training, we can work towards reducing the burden of TB associated with tobacco and vaping use.

TB vaccine: Developing an ideal TB vaccine that can prevent or eradicate infection with M. tuberculosis still remained a challenge. The available TB vaccine, Bacille Calmette-Guérin (BCG), was first introduced in 1921 and is primarily used to prevent severe forms of TB, such as tuberculous meningitis and miliary TB, in infants. However, it is not known to provide reliable protection against latent TB or adult TB transmission, which accounts for the majority of TB cases worldwide. BCG's efficacy is also variable, ranging from 0% to 80% in different populations. The reasons behind this variability are not fully understood and continue to be an area of research. One hypothesis that has gained increasing epidemiological support suggests that prior exposure to certain non-tuberculous environmental mycobacteria could have provided partial immunity to the population,

potentially masking the benefits of BCG vaccination.[23,24] In 1982, a WHO Expert Committee concluded that BCG vaccination can prevent tuberculosis in individuals who are not already infected, its impact on reducing the overall risk of infection in the community as a whole is relatively small.[21,25]

It is worth mentioning that there are ongoing efforts to develop new and more effective TB vaccine candidates in clinical trials, including subunit vaccines and recombinant BCG constructs. These vaccines aim to either boost the efficacy of BCG or serve as possible replacements for it. Hence, improving knowledge in the field of immunology, molecular microbiology, cell biology, and biotechnology may have the potential in development of efficient vaccines.[26]

Drug resistant strains: Tuberculosis is a treatable disease, but the emergence of drug-resistant strains is a major challenge to its successful treatment. The standard treatment for drug-susceptible TB involves a combination of antibiotics, usually isoniazid, rifampicin, ethambutol, and pyrazinamide. Treatment typically lasts for six months and is highly effective, with cure rates of around 85%.[27] However, the emergence of drug-resistant TB strains, particularly multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), has complicated the treatment of the disease. MDR-TB is resistant to at least isoniazid and rifampicin, the two most important first-line drugs, while XDR-TB is resistant to additional second-line drugs, making it even harder to treat. The treatment of drug-resistant TB is much more complex and costlier than that of drug-susceptible TB, and cure rates are lower, often around 50% or less.[28] There are several reasons behind the emergence of resistant strains. Inadequate treatment can occur when patients do not receive the full course of medication prescribed to them, which can result in the survival of TB bacteria that are resistant to the drugs that were used. Similarly, inconsistent use of medication can allow TB bacteria to survive and develop resistance over time. Lastly, the use of substandard or counterfeit drugs. These medications may not contain the active ingredients needed to effectively treat TB, or they may contain incorrect doses or formulations that can contribute to the development of drug resistance.[29] To address the emergence of resistant TB strains, it is important to ensure that patients receive high-quality, consistent treatment that follows recommended guidelines for the duration and dosage of medications. This may require increasing access to diagnostic tools to help identify TB strains and guide appropriate treatment, as well as ensuring that patients have access to high-quality medications that are effective against drug-resistant strains.[30] In addition, efforts to improve infection control practices in healthcare settings can help to prevent the spread of TB and limit the development of resistant strains. This may include strategies such as isolating patients with infectious TB and providing healthcare workers with appropriate protective equipment's.[31] It is crucial to act to contain the threat of drug-resistant TB, as the consequences of inaction could be devastating. Without effective treatment options, TB can cause serious illness, disability, and death. However, there are reasons for optimism as new therapeutic options being developed to treat drug-resistant TB. These include novel antibiotics and combination therapies that have shown promise in clinical trials. In addition, there are efforts underway to develop new diagnostic tools that can identify drug-resistant strains of TB more quickly and accurately, which can help guide appropriate treatment and prevent the spread of resistant strains. There are also initiatives to improve access to existing treatments for drug-resistant TB, such as through the development of more affordable and accessible formulations of existing drugs. This can help to ensure that patients receive the appropriate treatment they need to combat drug-resistant TB, regardless of their financial or geographic circumstances.[2]

Implications of TB elimination: Eliminating TB will have far-reaching implications for individuals, populations, and global health security. First, the elimination of TB can lead to significant improvements in health outcomes for individuals and populations. The incidence and prevalence of the disease can be significantly reduced, resulting in improved quality of life and increased life expectancy for individuals. This can also have important population-level benefits, such as reduced healthcare costs and increased productivity, as individuals are able to lead healthier, more productive lives. Second, TB elimination is important for global health security, as TB is a communicable disease that can spread across borders. By eliminating TB, countries can help prevent the spread of the disease and improve global health security. This is particularly important in the context of emerging infectious diseases, where effective global cooperation is essential to preventing the spread of disease and containing outbreaks. Finally, TB elimination can have important economic benefits, particularly in low- and middle-income countries where TB is a significant economic burden. By reducing the burden of TB, resources can be freed up for other important public health initiatives, leading to improved economic growth and development.[32]

RECOMMENDATIONS

Elimination of TB could operate and articulate in the following parameters:

Public Information, Education and Communication

Creating awareness about TB symptoms, risk factors, and the importance of seeking medical care can help individuals recognize the signs of TB and take prompt action. This is particularly crucial for individuals at higher risk, including those with weakened immune systems, close contacts of TB patients, and

those living in crowded and poorly ventilated environments. By educating these individuals about their susceptibility to TB and encouraging them to seek medical care if they experience relevant symptoms, early detection and appropriate management can be facilitated. In addition to addressing TB-specific awareness, it is important to dispel myths, reduce stigma, and overcome misconceptions associated with the disease. Education and awareness campaigns can play a vital role in challenging societal beliefs and reducing discrimination towards individuals affected by TB. This can encourage individuals to seek timely care without fear of social repercussions.

Moreover, public health educational programs, smoke free policies and targeted messaging can be effective tools in disseminating information about the link between tobacco/vaping and TB.[33] By highlighting the specific risks, health consequences, and available resources for smoking cessation, these campaigns can raise awareness about the detrimental effects of tobacco/vaping on TB susceptibility and outcomes. This, in turn, may motivate individuals to quit or reduce their tobacco/vaping habits, leading to improved respiratory health and potentially lower TB risk.

Lastly, it is crucial to address the underlying social determinants of health that contribute to TB. Poverty, poor living conditions, and inadequate access to healthcare can increase the risk of TB transmission and hinder timely diagnosis and treatment. In summary, raising awareness, dispelling myths, reducing stigma, and addressing social determinants of health, alongside targeted education and messaging, can collectively contribute to early detection, improved health-seeking behavior, and better management of TB.[34]

Strengthening health care system

It is crucial for ensuring that individuals have access to quality healthcare services, regardless of their socio-economic status or geographic location. This is particularly important in the context of TB and other health problems, such as HIV and diabetes, which require integrated and coordinated care.[35] The COVID-19 pandemic has further highlighted the importance of maintaining essential health services, including TB services, and implementing appropriate infection prevention and control measures to protect patients and healthcare workers. Investing in the health system, including trained and skilled healthcare providers, health infrastructure, health financing, health information systems, health policies, and regulations, is also essential to ensure that these services are available and accessible to all. Furthermore, strengthening surveillance and monitoring systems is critical in improving health outcomes.[36] Identifying gaps in the health system and take action to address them, can lead to more effective prevention, diagnosis, and treatment of TB and other health conditions,

Access to new diagnostics in resource limited settings

Increasing access to improved diagnostics is a key strategy for early detection of latent TB infection and prevention of the development of active TB disease. In addition to interferon-gamma release assays and tuberculin skin tests, there are other diagnostic tools that have been developed for TB detection, such as the GeneXpert system and the Lateral Flow Urine Lipoarabinomannan test, which have proven to be effective in early detection of TB and can be used in resource-limited settings. indeed, improving laboratory capacity, strengthening healthcare systems, training of skilled health care workers are also critical components of increasing access to improved diagnostics for early detection of TB.[37]

The development and distribution of a new TB vaccines and new medicines

Investing in the development of new vaccines and medicines is crucial in the fight against tuberculosis. A new vaccine could be more effective than the available BCG vaccine and protect against all forms of TB, including drug-resistant strains.[38] Moreover, current TB drugs are limited in their efficacy and can have severe side effects, and drug-resistant TB strains have emerged due to the misuse of existing medicines. Therefore, investing in the development of new TB medicines that are more effective, easier to administer, and have fewer side effects is critical.[39]

Multisectoral collaboration in addressing TB:

Engaging a wide range of stakeholders, including governments, civil society organizations, the private sector, and affected communities, is essential in ensuring that all voices are heard and all perspectives are considered when addressing complex health issues like TB.[40] Moreover, collaboration and coordination across different sectors, including health, agriculture, and food systems, is critical in addressing the social determinants of TB and other diseases. Poverty, malnutrition, and limited access to healthcare are some of the key factors that contribute to the spread of TB, and addressing these underlying issues requires a multi-sectoral approach.[41] By working together, these stakeholders can leverage their expertise, resources, and networks to accelerate progress towards ending the TB epidemic. This collaborative approach can lead to more effective prevention, diagnosis, and treatment of TB, as well as improved health outcomes for individuals and communities affected by the disease.

CONCLUSION

To overcome these challenges and accelerate progress toward TB elimination, a comprehensive approach is required. This includes strengthening health systems, expanding access to quality diagnosis and treatment services, promoting research and development for new tools and strategies, addressing socioeconomic determinants, and ensuring sustained political commitment and financial resources. Col-

laboration among governments, international organizations, civil society, and affected communities is essential to address the multifaceted nature of the TB epidemic and work towards its eventual elimination.

In Summary, Robert Koch's words from over a century ago still ring true today. The struggle against tuberculosis has indeed caught hold along the whole line, and there has been significant progress in the fight against TB. However, much work remains to be done to achieve the goal of a world free of TB.[42]

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