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Review Article

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Tuberculosis the Lernaean Hydra of 21st Century - A Post Covid Update on the Indian Scenario

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Abstract: Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. Tuberculosis usually affects the lungs, but it can also affect other parts of the body, such as the brain, kidneys, and spine. In most cases, tuberculosis is preventable. However, tuberculosis patients can die if not treated properly. According to the World Health Organization (WHO), tuberculosis (TB) is a worldwide pandemic. It is the primary cause of mortality among HIV-infected individuals. Poor adherence to Tuberculosis treatment can lead to prolonged infection and poor treatment outcomes. Prevention plays a very important role in the fight against TB. Directly Observed Treatment aims to improve adherence to TB treatment by observing patients while they take TB medications. India's DOTS (directly observed treatment short course) program is the world's fastest-growing and biggest in terms of patients beginning on treatment, as well as the second-largest in terms of population coverage. Its purpose is to reduce TB mortality and morbidity while also reducing infection transmission until TB is no longer a serious public health concern in India. Multidrug-resistant tuberculosis (MDR-TB) is caused by organisms that are resistant to at least two of the most potent tuberculosis drugs, isoniazid and rifampicin. Multidrug-resistant tuberculosis (MDR-TB) is an increasing danger to tuberculosis eradication, and it is the outcome of a failing tuberculosis control program. Community-based programs can improve patient outcomes by allowing patients to receive treatment at home and addressing socioeconomic barriers to adherence to treatment. This article discusses about Tuberculosis and the ways to manage tuberculosis.

Keywords: Tuberculosis, DOTS, HIV-Infected individuals, MDR-TB, TB control

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1. INTRODUCTION

Tuberculosis (TB) is one of the humanity's oldest diseases, dating back over 17,000 years based on molecular evidence. Despite modern diagnostic and treatment approaches, people continue to suffer from tuberculosis, and it remains one of the top ten deadly infectious illnesses in the world, second only to HIV. TB is a worldwide pandemic, according to the World Health Organization (WHO)[1]. Tuberculosis (TB) is a disease caused by the bacteria *Mycobacterium tuberculosis.* The rampant presence of TB across the globe painfully surfaced only during the 17th and 18th-century industrial eras. Because it primarily affects the lungs, pulmonary illness is the most prevalent manifestation. The respiratory system, the gastrointestinal (GI) system, the lymphoreticular system, the skin, the central nervous system, the musculoskeletal system, the reproductive system, and the liver are also typically impacted organ systems. India accounted for 38% of the world's total HIV-negative cases of tuberculosis and 34% of the combined cases in 2020. [2.] Worldwide, in 2020, adult men accounted for 55% of all TB cases, while women accounted for 33% and children 11%. Despite modern diagnostic and therapeutic approaches for tuberculosis, millions of people continue to suffer and die from this illness. TB is one of the world's top three infectious diseases of the world. The higher prevalence of TB in men has been observed consistently across national surveys as well. Certain groups of people are placed at a higher risk of acquiring TB infection.[3] There has been a concentrated global campaign to eliminate TB during the last few decades. Global tuberculosis incidence is expected to be dropping by 16% per year, considerably short of the 4–5% necessary to meet WHO's End TB Strategy objectives. Global Burden of Diseases, Injuries, and Risk Factors data for tuberculosis (1990–2016) show that if current trends in incidence continue, few countries are likely to meet the UN Sustainable Development Goals' target to end the epidemic by 2030[4]. In 2019, an estimated 10.0 million people had active tuberculosis disease worldwide, with 1.4 million people dying from the disease.[5] Tuberculosis is a global concern, and incidence rates are rising not just in impoverished countries but increasingly in developed ones like the United States. In tandem with the rise of TB in the United States, the number and proportion of cases caused by Mycobacterium tuberculosis strains resistant to various first-line medicines has increased alarmingly[6]. Tuberculosis primarily affects people in their prime years of work. All age groups, however, are at danger. Developing nations account for almost 95% of cases and fatalities[7]. The risk of infection and disease progression are two distinct elements, and a thorough knowledge of these factors is critical for developing effective TB control methods. Exogenous variables, such as the infectiousness of the source case, proximity to contact, and social and behavioral risk factors such as smoking, drinking, and indoor air pollution, are the primary determinants of infection risk following TB exposure.[8] ·The most susceptible to Tuberculosis are the HIV-positive and other immune-compromised people, under-nourished people, intravenous substance abusers, alcoholics, and those living in unhygienic, crowded living conditions (like densely populated urban slums, prison).[9] TB infection presents atypically in children and often goes unnoticed. [10] Obvious signs and symptoms surface only when the disease has advanced to later stages, thus escaping detection during tuberculosis control programs. Furthermore, children tend to spread the infection much faster than adults. They are not only vulnerable but also dangerous. [11.] Poverty and vulnerability to TB infection have a clear correlation. The poor often do not seek medical services immediately either due to ignorance or denial or may lack access to medical services; both of which make them vulnerable to TB. [12] Multidrug-resistant tuberculosis (MDR-TB) is another increasing danger to tuberculosis eradication, and it is the outcome of a failing tuberculosis control program. Extensively drug-resistant tuberculosis (XDR-TB) is resistant not only to isoniazid and rifampicin but also to any fluoroquinolone and any of the three injectable second-line aminoglycosides. For LTBI and active TB illness, as well as drug-sensitive and drug-resistant TB disease, diagnostic and treatment options differ. [30]. Even though public health approaches to TB have saved tens of millions of lives, little moderate progress has been made in controlling (let alone eliminating) tuberculosis. More research and better treatment options should be made available for tuberculosis so that we have TB Free India. This article aims to review Tuberculosis and the challenges faced to control tuberculosis.

PREVENTION AND INTERVENTION

Prevention plays a very important role in the fight against TB. It has been judiciously strategized to target two crucial spreading points - prevention of new cases from acquiring the bacteria and limiting LTBI cases from progressing into a full-blown active Tb. BCG vaccination to prevent new infections among children is undertaken. A single dose is administered at birth. It has proved to be efficacious in children below 5 years of age. [13-14]Currently, there is no anti-TB vaccine for adolescents and adults. Thus, the potential for the development of a vaccine for adolescents and adults is being explored. Furthermore, vaccines that are equally effective against drug-sensitive and drug-resistant bacteria are also being developed [15]. LTBI control - efforts are also being made to prevent cases of LTBI from turning into active TB cases. This requires easy access to care, which is often lacking in the poorer developing countries.

Current management of TB

Anti-tubercular drug therapy varies based on the stage of the disease and drug sensitivity of TB, for each has its virulence and pathogenicity.

LTBI

WHO recommends a regimen of 6-9 months of Isoniazid, 3 months of rifampicin plus isoniazid, or 3-4 months of rifampicin alone, along with regular follow-up and counseling of the patient. [16]

Active drug-sensitive TB cases

Drug therapy is meted out in two phases- first, an intensive two- months phase with rifampicin, isoniazid, pyrazinamide, and ethambutol, followed by a 4 months continuation phase with isoniazid and rifampicin. [17,18] Patients also experience mild to severe levels of toxicity due to the prolonged use of such potent medications, resulting in patients dropping out of the therapy, which then leads to the development of drug resistance.

DOTS program

To ensure patient compliance, the directly observed therapy (DOTS) program has been undertaken, in which each dose of the anti-TB medication is directly dispensed and supervised by

the appointed health worker. DOTS is widely used and valuable in many countries. Technological advancements are also being incorporated with mobile phone reminders and video DOTS [9].

Newer drugs

Bedaquiline has been approved by the US FDA and the European Commission in 2014.[20] Delamanid (a nitroimidazole-oxazole compound) has also been approved for MDR-TB. [21] The two anti -TB drugs are known to act on M. tuberculosis in a new way and are known to have a sterilizing property which would result in the much-needed shorter treatment durations. [20-22] They have also not displayed cross-resistance with other anti-TB drugs that are presently in use [12].

NATIONAL PROGRAM FOR TUBERCULOSIS

Rntcp in India -Revised National Tuberculosis Control Program

Large-scale implementation of the Government of India's Revised National Tuberculosis Control Program (RNTCP) (Referred to as RNTCP 1) began in 1997. The RNTCP was subsequently extended until the whole country was covered in March 2006. RNTCP uses the Directly Observed Treatment Short Course (DOTS) strategy recommended by World Health Organization (WHO) and reaches more than 1 billion people. The RNTCP is responsible for the implementation of the Government of India's 5-year national TB strategic plans. National AIDS Control Organisation (NACO) had collaborated with the RNTCP and had made HIV-TB collaboration effective. Most TB patients registered by the RNTCP were receiving HIV screening and 90% of HIV positive TB patients were receiving antiretroviral treatment. [15]
In 2020, the RNTCP has renamed the National Tuberculosis Elimination Program (NTEP) to highlight the Indian government's goal of eliminating TB in India by 2025.

Complete geographical coverage

Complete geographical coverage for diagnostic and treatment services for multi-drug resistant TB (MDR TB) was achieved in 2013. A total of 93,000 people with MDR TB were diagnosed and had been given treatment for drug-resistant TB by 2015.

EPIDEMIOLOGY, DIAGNOSIS, AND MANAGEMENT OF DRUG-RESISTANT TB

An estimated 5 % of the cases develop MDR- TB. The distribution of MDR – TB is highly skewed towards countries like India and China. [23] India is now facing the emergence of completely drug-resistant strains. [24] For drug-resistant TB three types of tests are available – The phenotypic, The Culture-based, and the Molecular- based test. Culture-based tests, test the bacterial ability to multiply in the presence of anti-TB drugs. Whereas, the molecular-based test can detect the mutation that has made the bacteria resistant to drugs. Newer diagnostic methods are aiming at improving molecular tests, enabling identification of mutations of drug resistance, and also making them less technique sensitive and cost-effective to be used in low socioeconomic countries with limited skilled personnel. Discovering a Biomarker that would identify the risk of active TB is also in the pipeline. [25,26] Treating active drug-resistant TB cases is complex as they have developed resistance to some of the strongest available anti-tuberculosis drugs and as such a traditional standard drug regimen may not work. It becomes crucial to consider which drugs the bacilli is still sensitive to along with due consideration to relevant host characteristics. Thus, for the drugs to be effective, they will need to be modifications in the regimen according to the requirements of the case. There are two regimens currently in use- a shorter drug regimen and the longer 6-9 months regimen. The shorter regimen Includes anti-TB medicines that have not been previously prescribed, or higher doses of currently used anti – TB medicines [27,28] and 're-purposed' drugs (drugs used to manage infections other than TB) such as fluoroquinolones, which are known to be equal to isoniazid ineffectiveness. Linezolid, carbamazepine and refapentine are alternatives. [29]

2. CONCLUSION

Given the grave status of high burden countries such as India and their limited resources, it becomes necessary to ensure rapid transfer of improved technologies as well as existing tools from the developed countries. A more committed and generous approach from the international community would help to eradicate TB sooner. Strengthening the health care infrastructure is crucial for the success of the TB control programs. The absence of which is presently acting as a major impediment in successfully preventing and treatment. National policies and governments need to allocate higher resources in this direction. Many other factors indirectly affect the disease incidence and prevalence, such as unplanned urban development with poor housing facilities, unemployment, and migration to densely populated urban areas. These need to be addressed by government policies. The fight against TB will not be won unless a well-coordinated multispectral approach is undertaken, with international aid and national commitment.

3. AUTHOR CONTRIBUTION

Dr. T.G.Srinivvasan conceptualized and collected empirical data, Dr. Anita formulated the basic framework and layout, Dr. Raghavendra Jayesh and Dr. S Bhuminathan helped in designing and analyzing the data of the manuscript and Dr. K G Sruthi gave her inputs and compiled the data for the manuscript. All the authors read and approved the final version of the manuscript.

4. CONFLICT OF INTEREST

Conflict of interest declared none.

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