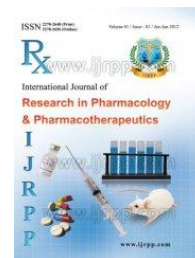




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Research Article

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An overview on the national burden of tuberculosis and its current status Keerthy J*, Hrishi V, Sagarika B.H, Lakshmi I, Prasanth Kumar S, Dr. K. Sattanathan and Dr. R. Sambathkumar

J.K.K.Nattraja College of Pharmacy, Kumarapalayam, Erode, Tamil Nadu, India-638 183

*Correspondence Author: Keerthy J

Email Id: ktyvirgo23@gmail.com

ABSTRACT

Tuberculosis (TB) still remain a major challenging global health problem. India is one the high TB burden country, adding to 26 per cent of the worldwide TB burden. During the 20th century, TB became treatable and the therapeutic success of short-course chemotherapy was a break through. In the early 1980s, human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) pandemic resulted in a resurgence of TB globally with more complications and challenges like occurrence of multidrug-resistant and extensively drug-resistant TB (M/XDR-TB). Atypical clinical presentation still poses a challenge. While treatment of TB and HIV-TB co-infection has become simpler, efforts are on to shorten the treatment duration. However, drug toxicities, adverse drug reactions and drug-drug interactions still possess a significant challenge. Hurdles like the lack of adequate coverage, low economy and weak health services limit access to high-quality tuberculosis care in some of the countries. Further, many public and private health-care providers remain delinked from national tuberculosis control efforts. In addition, tuberculosis is a disease of the poor and the absence of universal health coverage aggravates the economic burden of TB on the poor. Even though the advancements in tuberculosis control over the past two decades are strong, relatively high effort is needed to wipe out the pandemic. A pursuit for novel biomarkers for predicting a durable cure, relapse, discovery/repurposing of newer anti-TB drugs, development of newer vaccines continues to attain the goal of eliminating TB altogether by 2050. The present review focuses on the global and Indian tuberculosis situation. It emphasizes the epidemiological situation in India and the burden of disease in the nation over time.

Keywords: Tuberculosis (TB), Drug resistance, Multi drug resistance TB.

INTRODUCTION

Tuberculosis (TB) is a major global health problem. It causes ill-health among millions of people each year and ranks alongside the human immunodeficiency virus (HIV) as a leading cause of death worldwide. In 2014, there were an estimated 9.6 million new TB cases: 5.4 million among men, 3.2 million among women and 1.0 million among children. There were also 1.5 million TB deaths (1.1 million among HIV-

negative people and 0.4 million among HIV-positive people), of which approximately 890 000 were men, 480 000 were women and 140 000 were children. The number of TB deaths is unacceptably high: with a timely diagnosis and correct treatment, almost all people with TB can be cured.¹ Tuberculosis remains one of the major public health concerns in the South- East Asia Region of WHO. The Region accounts for 38% of the global burden of tuberculosis (TB) in terms of incidence.

It is estimated that about 3.4 million new cases of TB occur each year and about 440 000 people died of this disease in 2013, most of these in five countries, namely, Bangladesh, India, Indonesia, Myanmar and Thailand, which are among the 22 high-TB-burden countries in the world. Levels of multidrug-resistance are lower than 2.2% among new cases and 16% among retreatment cases; however, this translates into nearly 89 000 estimated multi-drug-resistant TB (MDR-TB) cases among all TB cases notified in 2013. In 2013, 43% of TB patients knew their HIV status and HIV-positive TB patients were 6.1%. While 88% of HIV-positive TB patients were on cotrimoxazole preventive therapy, 81% were on antiretroviral therapy². Though India is the second-most populous country in the world, one fourth of the global incident TB cases occur in India annually. At 2012, out of the estimated global annual incidence of 8.6 million TB cases, 2.3 million were estimated to have occurred in India. India's TB control program is on track as far as reduction in disease burden is concerned. There is a 42 % reduction in TB mortality rate by 2012 as compared to 1990 level. Similarly, there is a 51 % reduction in TB prevalence rate by 2012 as compared to 1990 level.³

A brief overlook on tuberculosis

Tuberculosis (TB) is caused by bacteria (*Mycobacterium tuberculosis*) that most often affect the lungs. Tuberculosis is curable and preventable. TB is spread from person to person through the air. When people with lung TB cough, sneeze or spit, they propel the TB germs into the air. A person needs to inhale only a few of these germs to become infected. About one-third of the world's population has latent TB, which means people have been infected with TB bacteria but are not (yet) ill with the disease and cannot transmit the disease. People infected with TB bacteria have a 10% lifetime risk of falling ill with TB. However, persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a much higher risk of falling ill. When a person develops an active TB disease, the symptoms (cough, fever, night sweats, weight loss etc.) may be mild for many months. This can lead to delays in seeking care, and results in transmission of the bacteria to others. People with active TB can infect 10-15 other people through close contact over the course of a year.

Without proper treatment, 45% of HIV-negative people with TB on average and nearly all HIV-positive people with TB will die.

People at risk

Tuberculosis mostly affects adults in their most productive years. However, all age groups are at risk. Over 95% of cases and deaths are in developing countries. People who are infected with HIV are 20 to 30 times more likely to develop active TB (see TB and HIV section). The risk of active TB is also greater in persons suffering from other conditions that impair the immune system. One million children (0-14 years) fell ill with TB, and 140 000 children died from the disease in 2014. Tobacco use greatly increases the risk of TB disease and death. More than 20% of TB cases worldwide are attributable to smoking.

Global impact of TB

TB occurs in every part of the world. In 2014, the largest number of new TB cases occurred in the South-East Asia and Western Pacific Regions, accounting for 58% of new cases globally. However, Africa carried the most severe burden, with 281 cases per 100 000 population in 2014 (compared with a global average of 133). In 2014, about 80% of reported TB cases occurred in 22 countries. The 6 countries that stand out as having the largest number of incident cases in 2014 were India, Indonesia, Nigeria, Pakistan, People's Republic of China and South Africa. Some countries are experiencing a major decline in cases, while in others the numbers are dropping very slowly. Brazil and China, for example, are among the 22 countries with a sustained decline in TB cases over the past 20 years.

Treatment

TB is a treatable and curable disease. Active, drug-susceptible TB disease is treated with a standard 6 month course of 4 antimicrobial drugs that are provided with information, supervision and support to the patient by a health worker or trained volunteer. Without such support, treatment adherence can be difficult and the disease can spread. The vast majority of TB cases can be cured when medicines are provided and taken properly. Between 2000 and 2014, an estimated 43 million lives were saved through TB diagnosis and treatment.

TB and HIV

At least one-third of people living with HIV worldwide in 2014 were infected with TB bacteria. People living with HIV are 20 to 30 times more likely to develop active TB disease than people without HIV. HIV and TB form a lethal combination, each speeding the other's progress. In 2014 about 0.4 million people died of HIV-associated TB. Approximately one third of deaths among HIV-positive people were due to TB in 2014. In 2014 there were an estimated 1.2 million new cases of TB amongst people who were HIV-positive, 74% of whom were living in Africa. WHO recommends a 12-component approach of collaborative TB-HIV activities, including actions for prevention and treatment of infection and disease, to reduce deaths.

Multidrug-resistant TB

Standard anti-TB drugs have been used for decades, and resistance to the medicines is widespread. Disease strains that are resistant to a single anti-TB drug have been documented in every country surveyed. Multidrug-resistant tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the 2 most powerful, first-line (or standard) anti-TB drugs. A primary cause of MDR-TB is inappropriate treatment. Disease caused by resistant bacteria fails to respond to conventional, first-line treatment. MDR-TB is treatable and curable by using second-line drugs. However second-line treatment options are limited and recommended medicines may not be always available. The extensive chemotherapy required (up to 2 years of treatment) is more costly and can produce severe adverse drug reactions in patients. In some cases, more severe drug resistance can develop. Extensively drug-resistant TB, XDR-TB, is a form of multi-drug resistant tuberculosis that responds to even fewer available medicines, including the most effective second-line anti-TB drugs. About 480 000 people developed MDR-TB in the world in 2014. More than half of these cases were in India, the People's Republic of China and the Russian Federation. It is estimated that about 9.7% of MDR-TB cases had XDR-TB.⁴

EPIDEMIOLOGY OF TUBERCULOSIS

Global burden

Globally in 2014, there were an estimated 9.6 million incident cases of TB: 5.4 million among men, 3.2 million among women and 1.0 million among children. In 2014, there were an estimated 1.2 million new HIV positive TB cases (12% of all TB cases) worldwide. Almost three-quarters of these cases were in the African Region.

Globally in 2014, there were an estimated 1.5 million deaths from TB: 1.1 million deaths among people who were HIV negative and 390 000 deaths among people who were HIV positive. TB ranks alongside HIV (1.2 million deaths in 2014, including the 390 000 TB deaths among HIV-positive people) as a leading cause of death worldwide. The South-East Asia and Western Pacific Regions collectively accounted for 58% of the world's TB cases in 2014. The African Region had 28% of the world's cases, but the most severe burden relative to population (281 incident cases per 100 000 population on average, more than double the global average of 133). India, Indonesia and China had the largest numbers of cases (23%, 10% and 10% of the global total, respectively). The TB incidence rate has fallen at an average rate of 1.5% per year since 2000. Globally, the TB mortality rate in 2015 was 47% lower than in 1990: the target of a 50% reduction was almost met. The target was achieved in four WHO Regions (the exceptions were the African and European regions), and in 11 HBCs. globally, the TB prevalence rate in 2015 was 42% lower than in 1990. The target of a 50% reduction was met in three WHO regions and in nine high burden countries (HBCs); and has accounted for an estimated one quarter (26%) of all TB cases worldwide.

India, Indonesia and China alone accounted for a combined total of 43% of global cases in 2014.¹

Indian scenario

With a population of about 1252 million, India is the largest country in the Region. It is ranked first among the high-burden countries and contributed 24% of the estimated global incident TB cases and about 20% of global TB-related deaths in 2013.⁵

WHO estimated burden of tuberculosis in India, 2012³

TB burden	Number (Millions)	Rate Per 100,000 Persons
Incidence	2.2 (2.0–2.4)	176 (159–193)
Prevalence	2.8 (1.9–3.9)	230 (155–319)
Mortality	0.27 (0.17–0.39)	22 (14–32)
HIV among estimated incident TB patients	0.13 (0.12–0.14)	5.6 (5.4–6.2)
MDR-TB among notified pulmonary TB patients	0.064 (0.049–0.079)	
MDR-TB among notified New pulmonary TB Patients	0.021 (0.018–0.025)	2.2% (1.9–2.6%)
MDR-TB among notified Re-treatment pulmonary TB patients	0.043 (0.033–0.054)	15% (11–19%)

Risk factors

Conventionally several genetic, social, environmental and biological determinants of health have been intuitively recognized by clinicians as risk factors for TB.

Genetic factors

Certain key issues should be considered while evaluating genetic susceptibility to TB disease. Susceptibility to TB does not follow a Mendelian pattern and is polygenic and multifactorial. Presence of two different genomes, (of the TB bacillus and the host) and their interaction can have influence on the disease. Several reports have implicated a long list of genes with risk of developing TB.

HIV infection

HIV infection and AIDS stand out as the most significant among all the risk-factors for TB and has consistently and significantly altered the incidence rate of TB over the last three decades. The impact of HIV/AIDS has been most profound in HIV prevalence sub-Saharan Africa where a dramatic increase in TB notification rates have

been documented concurrent with increasing HIV prevalence. Among persons living with HIV (PLWH) TB can develop at any stage of HIV infection and there is strong evidence suggesting that a declining CD4+ T-lymphocyte count and high viral load are risk factors for disease, while treatment with highly active antiretroviral therapy (HAART) reduces risk.

HIV infection and MDR-TB

Even though several institutional outbreaks of MDR-TB among HIV-infected patients drew attention to the problem two decades ago as per currently available evidence, HIV infection *per se* does not appear to be a risk-factor for MDR-TB.

Diabetes mellitus

The lethal interaction between diabetes mellitus (DM) and TB is being increasingly recognized world over. Epidemiological modelling data suggest that in India, 14.8 per cent of all pulmonary TB cases and 20 per cent of sputum smear-positive cases have DM suggesting that DM substantially contributes to the burden of TB, especially sputum smear-positive pulmonary TB in India. ⁵⁻²¹

Global effects in controlling Tb in 21st century⁵

Year	Important developments
2000	Creation of the Global Alliance for TB Drug Development Establishment of the Green Light Committee Ministerial meeting on TB, Amsterdam, The Netherlands Guidelines for establishing DOTS-Plus projects published
2001	Global DOTS Expansion Plan launched Global Drug Facility launched Formalization of the Stop TB Partnership governance Global Plan to Stop TB 2001–2005
2002	Establishment of the Global Fund to fight AIDS, Tuberculosis and Malaria Financing and strategy for 22 high-burden countries included in WHO Global Tuberculosis Report An Expanded DOTS Framework for Effective TB Control issued
2003	Third edition of the “Guidelines for National Programmes” published Financing and strategy (all countries) included in the in WHO Global Tuberculosis Report
2005	Creation of FIND WHO TB-HIV policy launched
2006	Global Plan to Stop TB 2006–2015 Establishment of UNITAID Launch of the WHO Stop TB Strategy Emergence of XDR-TB
2008	Creation of the TB Vaccine Initiative
2009	WHO policy on TB infection control in health-care facilities, congregate settings and households published Online data collection introduced in the in WHO Global Tuberculosis Report
2010	Updated Global Plan to Stop TB 2011–2015 Fourth edition of the “Guidelines for National Programmes” published
2012	ENGAGE-TB initiative developed by WHO. This initiative aims at integrating community-based activities to control TB in the ongoing work of such NGOs, aligned with national strategies and plans and supported by new operational guidance
2013	Post-2015 TB Strategy In February 2013, participants in a workshop convened by the WHO and the Stop TB Partnership have proposed a set of goals and targets to guide the global fight against TB after 2015.

Source: Ref: 22-23

CONCLUSION

The last 70 years have witnessed an initial euphoria of emergence of drug treatment of TB that raised hopes and even signalled a likely 'elimination' of TB. In spite of political commitment, global and national programmatic strategy to contain and control TB, eventual elimination of TB in near future appears to be a mirage as of now. The widespread occurrence of X/MDR-TB threatens to take us back to the era of untreatable TB. TB has come a long way, from despair and the status of an

incurable malady, through a brief interlude of a curable disease to a scourge that is menacingly threatening the return to dark ages. The fall in the absolute number of TB cases globally observed since 2006 is heartening. With newer and repurposed anti-TB drugs emerging and becoming available for use, the march of the humankind towards the goal of TB elimination, *i.e.*, reducing the annual incidence to less than 1 case/1,000,000 population by 2050 appears to be on course in the right direction.

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