Mycobacterium tuberculosis AND ITS RESILIENCE

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ABSTRACT

Drug resistant pathogens today are emerging and spreading more rapidly than in previous decades. These organisms are widespread but also occur increasingly in the community, affecting developed and developing countries, and rapidly spreading through international travel. The increase in microorganisms that have developed resistance to currently available antimicrobial agents has become a major cause for concern worldwide. Some of these strains are multi drug resistant/ total drug resistant and the agents available to treat infections caused by them are few and dwindling. Over recent years there have been a number of responses by national, international and professional bodies to this situation, many aimed at curbing this unprecedented growth in resistance, but there is an increasing recognition that a major problem in the management of infections caused by such organisms is the paucity of new drugs, the problem of resistance to antimicrobials was complex and that multiple solutions would be required. Treatment of infections caused by resistant microbes is increasingly hampered either by the prohibitive cost of existing ‘new generation’ agents or by a total lack of effective antimicrobial agents.

KEYWORDS: Tuberculosis, Drug resistance, diagnostics, Vaccine.

Tuberculosis (TB) is a global problem that we can't afford to keep ignoring. Several potent drugs have been available for the treatment of TB from the past 70 years. However, poor management of TB continues to take a heavy count of human lives. The disease has become prevalent in countries like Africa, India, China and Russia. In India nearly 500,000 people die every year due to this dreadful disease.[14] In the early times, in the absence of any cure, infected patients faced slow and painful death. Many patients died unattended in infirmaries.

There are about 10 million new TB cases added every year worldwide. About 2 million people succumb to this life threatening disease. Some of the main factors which have contributed to this death causing disease are the absence of basic sanitary facilities and the emigration of people from rural to urban areas. About 2 billion people are carrying M. tuberculosis (MTB) in the dormant form worldwide. Out of this, only 10% will develop active form of the disease during their life time. The development of the disease takes place whenever the immunity goes down due to various factors like old age, HIV/AIDS, Diabetes mellitus. It becomes difficult to understand how the bacteria survive for months and years without multiplying or showing any signs of the disease. However the bacteria remain noninfectious during its dormant form but this form continues to be an unlimited pool of infection. Several diagnostic tests have been available to detect latent infection. The antiquated tuberculin test for latent TB is not authentic as it gives false positive results.[2,3] TB killed almost twice as many people as malaria—and it is the leading cause of death among people living with HIV/AIDS. The latest anti-TB drug resistance surveillance data show that 4.1% of new and 19% of previously treated TB cases in the world is estimated to have rifampicin- or multidrug-resistant tuberculosis (MDR/RR-TB). In 2016, an estimated 600 000 new cases of MDR/RR-TB emerged globally. MDR/RR-TB caused 240 000 deaths in 2016. Most cases and deaths occurred in Asia. About 6.2% of MDR-TB cases have additional drug-resistance, extensively drug-resistant TB (XDR-TB).[4,5,6] This is all the more tragic because these deaths are preventable. For a long time the world thought that we had defeated TB, but just because TB doesn't make headlines don’t mean it has gone away. The fact is that TB is getting worse, as complacency, lack of adequate tools and funding fuel the disease and the spread of drug resistance (DR).[7,8] DR-TB is the wake-up call; it is an airborne epidemic of increasingly untreatable disease. DR-TB develops when TB patients take low-quality drugs, do not finish their full course of treatment, or pass...
DR- TB from one person to another. Mismanagement of the anti tubercular drugs may lead to the development of drug resistance. The time duration for treatment is 6-9 months and symptoms of disease usually disappear after 2-3 months of the treatment. Hence patient may discontinue the medication which is major cause for the drug resistance development. Sometimes it also occurs in the patients who delay the regular administration of the drugs or do not take all the four prescribed drugs. Patients may also develop TB again after the treatment in the past. DR-TB is communicable through air from one person to another. DR-TB occurs in many forms such as multi-drug resistant tuberculosis (MDR-TB), extensively drug resistant tuberculosis (XDR) and totally drug resistant tuberculosis (TDR-TB).[18, 9]

MDR-TB is resistant to the two most commonly used first-line TB drugs, and requires long, complex and expensive treatment. Several injectable drugs like streptomycin, amikacin, kanamycin and oral fluoroquinolones can also be given as an alternate therapy. Apart from these, the duration of the treatment may extend up to 18-24 months instead of 6-9 months. The faulty treatment regimen and unreliable diagnostic tests are also the major factors which may lead to the development of resistance. Only 1- 3% of the cases are on proper treatment but still have poor outcomes.[8] XDR-TB is resistant to first- and second-line drugs, severely limiting treatment options. It is mainly widespread in the countries like Africa, Asia and Soviet Union having majority of cases of HIV/AIDS. XDR-TB has the highest mortality and morbidity rates if co-infected with HIV/AIDS. TDR-TB is the worst form of TB. It is a condition in which the patients become resistant to all the first and second line drugs ultimately leading to death.[10,11]

TB as an obstreperous disease is common in many cases. It usually attacks the lungs, but it can also affect other parts of the body. It is spread through the air when people who have an active TB infection cough or sneeze. Symptoms of TB include a chronic cough with blood-tinged sputum, fever, night sweats, and weight loss. Diagnosis relies on chest X-rays, a tuberculin skin test (TST), and blood tests, as well as microscopic examination and microbiological culture of bodily fluids. Some other tests like CB-NAAT, Line probe Assay (LPA), and BACTEC are also authentic to diagnose the disease.[10,12, 13, 14] TB is very challenging essentially due to several reasons (a) poor detection rate as in India it takes about 4-6 months to detect the resistant strains, (b) co-infection with HIV/AIDS (c) enhanced transmission in overcrowded slums, hospitals and prisons, (d) malnutrition, poverty and poor healthcare system, (e) increasing cases of diabetes (f) foetal malnutrition, (f) poor patient compliance and (g) absence of biomarkers to monitor the success of the treatment and complete eradication of the disease. The above reasons presuppose the need of new drugs for the complete and successful treatment of DR-TB.[13,16]

A person falls ill with TB about every three seconds—the vast majority of whom live in poor countries. According to the World Health Organization (WHO), 95 percent of all TB deaths occur in developing countries, resulting in about 10 million children who are orphaned due to TB deaths of one or both parents. People in the developing world are more likely to contract TB because their immune systems are more likely to be compromised due to HIV/AIDS and it is the leading cause of death for people infected with HIV/AIDS.

This disease offers a glaring example of the health care inequities that exist in the world. Drugs to fight TB have been in existence for 50 years, yet the disease continues to kill almost 4,000 people every day—nearly all of them in developing countries.[14]

Treatment is difficult and requires long courses of multiple antibiotics—typically at least six months for drug-susceptible TB, according to the Centers for Disease Control and Prevention. Social contacts are also screened and treated if necessary. When people fail to complete the drug regimen for TB, the disease becomes resistant to treatment. It often develops into the more deadly MDR-TB.

While progress is being made, much more is needed. Basic TB control is one of the most cost-effective interventions in global health. Appropriate treatment can save a life and stop the spread of disease. It is essential that countries implement the WHO internationally recommended Stop TB strategy, which includes directly observed treatment short course programme (DOTS). But due to outdated tools and methods, DOTS alone is not enough. The remarkable fact is that global control of TB, a disease that kills someone every 20 seconds, depends upon a 125-year-old test, an 85-year-old vaccine and drugs that take six months to cure and haven't changed in four decades. To successfully treat TB and prevent resistance, we need to use current tools better and accelerate the development of new tools for the future. Simple improvements in TB control, such as expanding the use of under-utilized technologies, can have enormous impact. We also need new drugs, vaccines, diagnostics and biomarkers as well as innovations in TB control and case management. Better diagnostics are already available, and new drugs and vaccines are coming. But more commitment and resources are needed. Better prevention and control of TB is the surest way to stop drug resistance. At the same time, we should expand access to M/XDR-TB treatment and diagnostics for those who already have DR-TB.[14, 16]

Some of the most innovative solutions can come from the private sector and through partnerships. An untapped market of two billion people carries the TB bacterium. Approximately one-third of the world’s population harbors a latent TB infection which greatly complicates efforts aimed TB control. The success of TB pathogen is attributed in significant measure to its ability to survive indefinitely in a dormant state within the host as a latent
infection. Therefore priority research goal is to understand the properties of dormant bacteria in order to devise more effective strategies for TB control and to prevent reactivation and clinical control. Since TB requires a comprehensive approach, companies should also explore opportunities to work together and pool complementary technologies to ensure new tools are used most effectively. The major recommendations were as follows:

(i) Rapid and accurate TB diagnosis is critical to TB patient care and halting disease transmission.
(ii) Improved technology and increased efforts are needed to reduce the spread of resistant strains both in the environment and in hospitals.
(iii) Improved hygiene and public awareness programmes.
(iv) Rapid, sensitive and specific biomarkers are urgently needed.
(v) Incentives are required to encourage the quality of life for countless patients.

REFERENCES