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An Overview on Tuberculosis and Worldwide Steps to Combat TB Including Awareness Programme in India

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Authors' contributions

This work was carried out in collaboration with all authors. Author BV designed the study, developed the research conception and took the initiatives of this review, organizing relevant data, prepare to write and drafted the manuscript. Authors BV, PC, and PI revised the review paper and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.*

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Review Article

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ABSTRACT

Objectives of current review is to collate history of Tuberculosis (TB), overview of the current literature on epidemiology, world health organisations (WHO) recent strategic plan to overcome and eliminate TB from the root, and to determine current knowledge gaps for control of TB. This study is a review, a descriptive approach of state-of-science for better treatment strategies for TB. The article finds that to reach to end TB goal, WHO, we have to follow the guideline of who about TB control, along with that the Indian government also maintained awareness program**.** Current findings on TB suggest that with the development of science and technology, researches being conducted to minimise the drug resistance tuberculosis, as well as WHO sets new strategy to fight against TB, which could potentially change the casual outlook of the people towards their health habits, health issues, and will help them in future to tackle from this deadly killer disease.

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Keywords: Tuberculosis; deadly killer disease; epidemiology; world health organization; awareness programme in India.

KEY HIGHLIGHTS

- A brief overlook on TB history including past, present and future challenges to combat TB
- TB epidemiology, diagnosis, treatment, and current scenario with various national and international schemes for supporting to the TB patients and their better livelihood
- Year wise themes of world TB day
- Risk of Developing TB over a Lifetime and WHO's and SDG's End TB strategies
- Worldwide drugs treatment of TB
- Awareness Program in India to eliminate TB

1. INTRODUCTION

Tuberculosis (TB) is an endemic infectious disease in many developing nations and it has resurged in the developed world associated with the HIV/AIDS epidemic [1] and in order to fully address the global TB burden, there is need to know through knowledge about its history, epidemiology, diagnosis, current drug treatment, and novel drug delivery strategies for the effective management of TB. The main thrust of this paper is a review of the present and through report on TB.

1.1 History

In Indian continent TB is oldest communicable, fatal contagious disease that is deeply rooted among Indian population. TB has a history of being together with mankind for very long and was first discovered by Hippocrates in 400 BC [2]. History has evidence that many emperors died and many empire demolished due to this fatal disease in India [3-5] .The first written documents describing TB, dating back to 3300 and 2300 years ago, were found in India and in China respectively [6].

1.2 Epidemiology

TB is a granulomatous airborne infection disease caused by bacterium mycobacterium tuberculosis (M.TB), considered among the leading causes of mortality in India, which transmitted by means of invisible droplet nuclei containing the organisms that have left the reservoir during breathing, sneezing or coughing, of which this organism may remain airborne up to 6 hours, disease [7,8]. TB disease commonly affects the lungs; referred to as pulmonary TB, and extrapulmonary TB is the TB affecting the organ other than lungs, including the larynx, the lymph node, the pleura, the brain, the kidney, or bones and joints [9,10]. Miliary TB, common in infants and children younger than 5 years of age, occurs when tubercle bacilli enter the bloodstream and disseminate to all parts of the body. TB meningitis is the TB in the tissue surroundings the brain or spinal cord [11].

1.3 Discovery

According to Dr. Richard Morton pulmonary TB was associated with 'tubercles' due to the variety of its symptoms [2]. In the Ancient Greece TB was well known and called Phtisis. The extreme anemic pallor of people affected by TB was at the origin of the new term "white plague", coined during the 18th century [6]. By the end of 1839, TB was defined and accepted as one single disease and was termed as TB by a German physician, J.L. Schonlein [2]. Dr. Koch on March 24, 1882, identified, described the bacillus M.TB, after that World Health Organization (WHO) and the International Union declared the first world TB day in 1982 [10,12-15].

1.4 Transmission and Pathogenesis

Transmission and progression driven by social factors such as poor living conditions and poor nutrition [16], spread through inhalation of airborne M.TB cells, multiply in macrophages and within the large cystic tubercles, formed liquefied tissue surrounded by infected macrophage [12], also tubercle bacilli spread via lymphatic system and bloodstream to many different organs [17]. After the inhalation, establishes primary infection, may cure if human have a strong immune system [12]. The major sources of infection are human and bovin, of which human beings with M. bovis almost occurs by inhalation of aerosols and consumption of milk containing bacillus [13]. There are complex factors including factors that determine the strength and infectivity of the source, the integrity

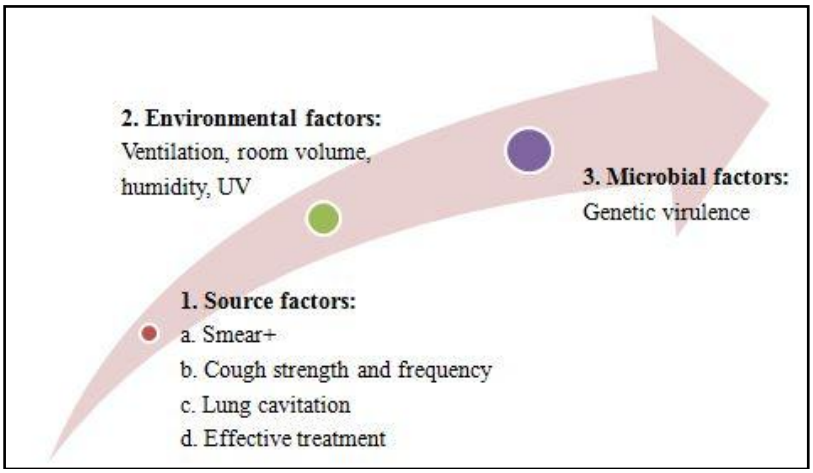

Fig. 1. Source of TB infection, adapted from source [18]

of the host defence of the exposed individuals, intrinsic properties of the bacillus itself, including viability, vulnerability or resistance to environmental stressors, genetic mutations, drug resistance, and virulence for a particular host [18]. As can be seen in Fig 1, the sources of transmission of M.TB are environmental factor, microbial factor other such as through coughing.

1.5 Microbiology of Mycobacterium Tuberculosis

Mycobacterium genus covers more than 140 species, these species are divided into three major sets, M.tuberculosis complex, M. leprae, and mycobacteria other than tuberculosis (MOTT) [19]. The M.tuberculosis complex of organisms, which can cause human disease, consists of M Tuberculosis, *M. africanum*, M. bovis, M. microti, and M. canetti. M. bovis was responsible for about 6% of all human tuberculosis deaths in Europe before the introduction of milk pasteurisation; subsequent attenuation of a laboratory strain of M. bovis led to the development of BCG vaccine in 1921 [13]. M. tuberculosis is an intracellular pathogen, aerobic, non-motile, non-encapsulated, non-spore forming, acid fast bacilli [9], grows most successfully in tissues with high oxygen content. The lipid rich cell wall of mycobacteria plays an essential role in growing the bacteria, made up of two segments, upper and lower, with core a mycoyl arabinogalactan-peptidoglycan complex. The upper segment made up of free lipids, some with longer fatty acids complementing the shorter alpha chain and vice versa, where proteins, phosphatidyl inositol mannosidase, the phthiocerol containing lipids, lipomannan, and lipoarabinomannan also can be found. Furthermore, the cell envelope of M. tuberculosis also contains an additional layer beyond peptidoglycan that rich in unusual lipids, glycolipids, and polysaccharides. M. tuberculosis is able to parasite human mononuclear phagocytes. M. tuberculosis will spend most of its life cycle in macrophages. M. tuberculosis has the ability to multiply inside the macrophage phagosome [19].

The size of the Mycobacterium is less than 5μ and the generation time of this bacterium is 18-24 hours[18], which is extremely slow compared with other bacteria (Escherichia coli divides every 20 minutes). This slow replication rate and ability to persist in a latent state result in the need for the long durations of drug therapy for the prevention TB infection. M. tuberculosis can remain dormant for a few years without the symptoms [12,13,20,21]

1.5.1 Types of TB

1. Childhood-type TB,
2. Adult-type TB.

1.6 Risk of Developing TB Over a Lifetime

Person's with latent TB infection is not infectious, however, about 10% of healthy individuals with latent TB infection, active TB may eventually develop over their lifetime [22], highest risk of progressing to active TB disease is in the first two years after initial infection, left untreated, a person will infect on average 10 to 15 persons a year. The most effective approach to TB control is the identification and cure of these infectious cases. Proper treatment of infectious cases makes them very quickly non-infectious so that they can no longer spread TB to others. Because effective treatment breaks the cycle of transmission, cure is the best prevention.

Patients with active pulmonary TB may be asymptomatic, have mild or progressive dry cough or present with multiple symptoms, including fever, fatigue, weight loss, night sweats, and a cough that produces the bloody sputum. If TB is detected early and treated fully, people with the disease quickly becomes non-infectious and eventually cure [23]. Multi drug resistance (MDR) are the TB where M. TB strain are resistant to all recommended therapies for people with latent infection who are not known contacts for a person with active MDR-TB disease. The priority population for testing and preventive therapy for latent infection is household contact of TB patients who are likely to be infected by their household members. However, in settings where the incidence of new is high, infections also frequently occurs outside the home [24,25].

1.7 Diagnosis [26-31]

Following are the sign and symptoms of pulmonary tuberculosis

- Persistent cough for more than two weeks
- Sputum production which may or may not be blood stained.
- Weight loss
- Chest pain
- Shortness of breath
- Intermittent fever
- Loss of appetite, fatigue and malaise
- History of contact with a smear positive PTB cases

1.7.1 Laboratory diagnosis

To understand the actual tuberculosis burden situation, the burden sometimes needs to be determined in terms of incidence per capita rather than by use of absolute number to enable comparisons with other regions [32]. Diagnosis of childhood tuberculosis is a challenge due to the pauci-bacillary nature of infection and the difficulty in obtaining appropriate sample [33]. The difference between diagnosing of TB infection and active TB disease is fully depends on the screening of tests [11] and it is included in Table 1.

Table 1. Difference between tuberculosis infection and tuberculosis active disease on the basis of diagnosing test

Characteristics	Tuberculosis infection	Tuberculosis Disease
Symptoms	None	Cough present, weight loss, fever, night sweat
Tuberculin skin test	Positive	Usually positive
Interferon gamma immune assay (IGRA)	Positive	Usually positive
Sputum bacteriology	Negative	Usually positive
Chest radiography	Normal	Usually abnormal
Infectiousness	No	Often infectious (before treatment)
Case of Tuberculosis	No	Yes
Preferred Treatment	Preventive treatment	Tuberculosis treatment

Adapted from source [73]

2. CURRENT SCENARIO OF TB

About 1/3rd of the world's population is infected with TB. Every year ~3 million people die from tuberculosis, mostly in developing countries where it kills 1 in 5 adults. India accounts for one quarter of the global TB burden. Primarily it affects the lungs, although it can affect other organs and systems. WHO reported that 10 million people fell ill with TB and there were 1.5 million TB deaths (including 251000 among people with HIV) in 2018, making it the top infectious killer worldwide [11,34-38]. The eight countries which contribute to 60 % of global epidemic burden of TB is depicted in Fig. 2.

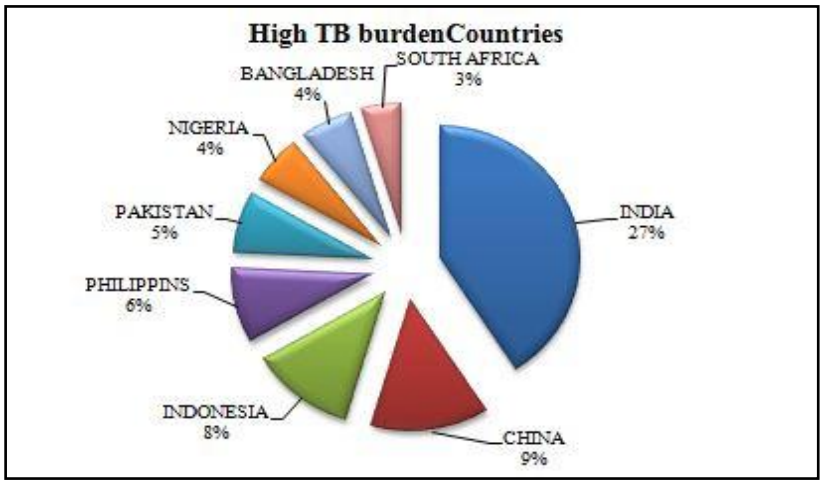

Fig. 2. Current scenario of high TB burden countries [73]

It is most ordinary opportunistic infection in Acquired-Immuno Deficiency Syndrome and is a very old scourge [39]. Amita Gupta et al mentioned that pregnant women, children < 15 years old and, HIV-infected persons contribute approximately 20% of the global TB burden [40]. TB treatment is challenging, requiring accurate and early diagnosis, drug-resistance screening and the administration of effective treatment regimens for at least 6 months through directly observed therapy (DOT) and follow-up support [41,42].

2.1 World Health Organization's (WHO) Target

In 2014 WHO launched the End TB strategy within the framework of the United Nations (UN) Sustainable Development Goals (SDGs), include the core anti TB interventions (diagnosis, treatment and preventions), under Pillar I, and several socioeconomic and health interventions, (Health, economy, finance, interior and justice) under pillar II. Intensified research activities and innovation are covered by pillar III [43]. In the agenda UN, 2018, meeting on TB, "United to End TB: An Urgent Global Response to a Global Epidemic", with the targets of reducing TB deaths and cases by 95% and 90% respectively between 2015 and 2035. India which contributes to one quarter of the global burden of TB has set in motion the National Strategic Plan (NSP) for TB elimination 2017-2025. As it can be seen in the Table 2, the year wise themes of world TB day which emphasis on what should be our action in future to be combat TB, for an example the theme of world TB day 2019 according to is "It's time for action it's time to end TB [44-50].

Table 2. Yearly themes of world tb day

Year	Theme of world TB day
24th March 2021	**The clock is Ticking**
24th March 2020	**It's Time to end TB**
24th March 2019	**"It's TIME" –** put the accent on the urgency to act on the commitment made by global leaders to: • Scale up access to prevention and treatment • Build accountability • Ensure sufficient and sustainable financing including for research • Promote an end TB stigma and discrimination and • Promote an equitable, rights-based and people centered TB response.
24th March 2018	**"Wanted: Leaders for a TB–free world"** It is focuses on building commitment to end TB, not only at the political level with hands of State Ministers of health, but at all levels from Mayors, Governors, Parliamentarians and with TB, Civil society advocates, health workers, doctors or nurses, NGOs and other partners. All can be leaders of efforts to end TB in their own work or terrain

Year	Theme of world TB day
24th March 2017	**"Unite to end tuberculosis: Leave no one behind"** 2017 is the second year of two-year "unite to end TB" campaign for world TB day. This year WHO will place special focus on uniting efforts to "Leave no one behind", including actions to address stigma, discrimination, marginalization and overcome barriers to access care.
22th March 2016	**"Unite to end tuberculosis"**
17th March 2015	**"Gear up to end TB"**
19th March 2014	**"Reach the 3 million":** TB is curable, but current efforts to find, treat and cure everyone who get ill with the disease are not sufficient of the 9 million people a year

Adapted from source [48]

3. WORLDWIDE TREATMENT OF TUBERCULOSIS

One of the challenges in treatment of latent and active TB is the lengthy duration of treatment regimens [51]. India is one of the first countries to invest in TB control after independence and the national TB programme is in place since 1962, which led to the establishment of district TB Centres (DTC) and TB Clinics across the country [52]. Sometimes, experts do talk about failures or shortcomings of NTP (National Tuberculosis Programme) and RNTCP (Revised National Tuberculosis Control Programme). It is important to review the strategies and evaluate the programme. In the recently developed NSP, all inputs have been taken from various stakeholders [53]. RNTCP is being implemented in-line with NSP [48], Action Plan (TAP) for the tribal patients [54], developed comprehensive guidelines for diagnosis and treatment of pulmonary tuberculosis and to monitor RNTCP effectively a web enabled and case based monitoring application called NIKSHAY has been developed by National Informatics Centre (NIC) [55].

There are three different regimens and each regimen is recommended for defined group [56]

- Directly Observed Therapy Short-course (DOTS) has been one of the major strategies to combat the epidemic of TB globally. In DOTS the patients are given the drugs under observation by the health workers. This direct supervision by health worker ensures patient adherence to the treatment.
- Long course chemotherapy (LCC), which is for 12 months.
- Retreatment regimen

3.1 Vaccination as Part of Treatment

Immunisation with the BCG vaccine is known to protect children from severe and disseminated forms of disease, decrease infection by 30%, and potentially offer some protection to adult populations [57]. A 2018 phase 2b study of a novel vaccine candidate known as M72/AS01E (GlaxoSmithKline, London, UK) was found to provide more than 50% protection from progression to active tuberculosis among adults with tuberculosis infection and could be a candidate to advance into larger studies [58]. Agger EM (2016) has reviewed and discussed the BCG vaccine, developed by an attenuation of the virulent M. bovis, further two different TB vaccination strategies are being pursued; replacing the current BCG with an improved BCG or an attenuated M.TB, or alternatively boosting BCG-immunity either shortly after BCG administration in infants or more predominantly as a booster in adolescence when there is an increase in TB incidence. Currently, there are sixteen novel vaccines in clinical development, of which the majority are BCG booster vaccines [59].

3.2 Drugs for the Treatment of TB

For the treatment of TB first line oral anti-TB drugs, injectable anti-TB drugs, newer second line anti-TB drugs, oral second line anti-TB drugs and drugs with unclear function [39,60-63] are summarises in Table 3.

Now a days, researches focus on employing non-antibiotic drugs for the eradication of TB infection. Vitamin C, A, D singly as well as in combination with first line drugs are also used, which show that trace elementals play an important role in the success of anti-TB drugs [62].

Table 3. Classification of anti-tb drugs

First Line Oral anti-TB drugs	Injectable anti-TB drugs	Newer second line anti-TB drugs	Oral second line anti-TB drugs	Drugs with unclear function in the treatment of drug resistant TB
Isoniazid	Sterptomycin	Levofloxacin	Thioacetazone	Clofazimine
Pyrazinamide	Kanamycin	Ceprofloxacin	P-amino salicylic acid	Linezolide
Ethambutol	Amikacin	Oflaxacin	Ethionamid	Thioacetazone
Rifampicin	Capreomycin	Moxifloxacin	Cycloserine	Clarithromycin
Sterptomycin	Vincomycin	Gatifloxacin		

Adapted from source [39, 60, 61, 62, 63]

Table 4. The dosage regimen for adults

Patient Body Weight (Kg)	Initial phase			Continuation phase		
	2 months			4 months		6 months
	Daily HRZE 75mg+150mg+400mg+275mg	or Daily HRZ 75mg+150mg+400mg	or 3 times per week HRZ 150mg+150mg+500mg	Daily HR 75mg+150mg	or 3 times per week HR 150mg+150mg	Daily EH 400mg+150mg
30-39	2	2	2	2	2	1.5
40-54	3	3	3	3	3	2
55-70	4	4	4	4	4	3
71 and more	5	5	5	5	5	3

Adapted from source [56]

Table 5. RNTCP daily treatment regimen

Category	Type of Patient	Regimen	
		Initial phase	Continuation phase
I (RED)	New smear positive Seriously ill smear negative PTB Seriously ill extrapulmonary TB	2HRZE	4RH
II (BLUE)	Previously treated sputum smear positive: -relapse -treatment after interruption; -Treatment failure	2HRZES/1HRZE	5RHE
III (GREEN)	New smear negative PTB (older than category I) and less severe form of extrapulmonary TB	2HRZE	4RH

Adapted from source [56]

Table 6. Nikshay poshan yojana in Every State In India

Sr. No.	State	Economic assistance	Nutritional support	Psycho-social support
1	Arunachal Pradesh	-	TB patients receive food support and are counselled on treatment adherence.	
2	Assam	-	MDR-TB patients receive wheat, rice, green gram, pulses, chickpeas, jaggery, soy bean and peanuts every months for 6 months	Cured TB patients become champions for treatment completion and are invited to speak about their challenges and experiences to motivate TB patients to adhere to treatment
3	Bihar	-	TB patients receive monthly ration pack for a period of 6 months. Ration pack includes rice, wheat and a variety of pulses. The food based support is complemented by monthly checkups to track improvements in the patients weight	
4	Chhattisgarh	MDR-TB patients receive a benefits package of Rs. 50,000 per family per annual income under state insurance scheme to cover	Chhattisgarh provides monthly food baskets containing milk powder, ground nut and soy bean oil. At the time of distribution of first basket patients are counselled on treatment adherence	Patients receive counselling for the side effects managements, treatment adherence and microbiological and clinical

Sr. No.	State	Economic assistance	Nutritional support	Psycho-social support
		the cost of in patients care. The benefit package includes pre-treatment evaluation covering all costs of hospitalization, clinical and laboratory tests follow up evaluation and medicines for side effects managements.	and the importance of nutrition.	examinations. Cured TB patients called as ***'Axshya Saathis'*** share their stories at time of food disbursement to motivate current patients to adhere to treatment.
5	Delhi	Cash benefits given to patients for treatment and diagnostic service required. Patients received educational training, livelihood training in-kind support such as treatment incentives and blankets	Monthly ration in the form of dry ration or consisting of wheat flour, rice green gram, soy beans and groundnuts. MDR-TB patients receive additional supplements of protein powder with milk, biscuit, and pulses,	Patient are counselled on how best to use the monetary assistance towards their recovery and betterment
6	Goa	Patients receive Rs. 600 incentives as a financial assistance till full DOTS completion. DR-TB patients receive financial assistance till full treatment completion	-	-
7	Gujarat	TB patients below poverty line receive Rs. 500 per month on a quarterly basis through DBT or RTGS. Beneficiaries includes nomadic tribes, Scheduled caste (SC), Scheduled tribes (ST), and socially as well as educationally backward classes	District TB office provides raw food materials to TB patients with special focus on drug resistant TB patients (DR-TB)	-
8	Himachal Pradesh		DR-TB patients receive a packaged 'Nutrimix' (food supplement) containing roasted wheat, sugar, soy bean, black gram, refined oil, whole milk powder, and groundnut, for the entire duration of treatment. Ten packets of Nutrimix 100gm each are distributed to patients every month.	
9	Jharkhand	TB patients belonging to	TB patients admitted in missionary hospitals in	

Sr. No.	State	Economic assistance	Nutritional support	Psycho-social support
		Scheduled caste (SC), Scheduled tribes (TB), and Other Backward Class (OBC) receive monetary support up to Rs. 10,000 via bank transfer	remote tribal areas receive nutritional support for 2-3 months in addition to indoor care. MDR-TB patients in Bokaro district receive supplementary food packages containing rice, pulses, grams and soy bean on a monthly basis.	
10	Kerala	Patients with annual family income below Rs. 1, 00,000 receives Rs. 1,000 per month through the TB pension plan.	Patients with annual family income below Rs. 1, 00,000 receives food baskets comprising of oats, toor dal, soy beans, peanuts, milk powder, and ragi powder every month	Treatment support group (TSGs) encourage patients struggling with treatment adherence through counselling, food kit provision, travel support, and pension assistance among other services
11	Madhya Pradesh		MDR-TB patients receive supplementary nutrition support in the form of dry ration on a monthly basis	
12	Maharashtra	TB patients travelling in Maharashtra State Road transport Corporation (MSRTC) buses can now travel for free by showing an RNTCP issued ID	TB patients in Mumbai receive support in the form of pulses, rice, peanuts, jiggery and wheat for a period of two months as part of a new initiative by Brihanmumbai Municipal Corporation (BMC)	
13	Meghalaya		Meghalaya provides economically weaker TB patients with food baskets which comprises Bengal gram, Horlicks and 2.5 dozen eggs every months	
14	Punjab		Community based organization provides nutrition support and supplementary medicine to drug resistant TB patient. Under Antodaya Ann Yojana, the state also provides nutrition support to drug resistant TB patients at subsidized rates.	
15	Tamil Nadu	Small and Marginal farmer, Inland fisherman, and plantation labourers suffering from TB are given a monthly pension of Rs.1000 for the entire duration of	DR-TB patients receives monthly support in the form of ration such as peanuts, groundnuts, dates, green peas, chick peas, soy milk and protein powder for 6 months. In patients nutrition care includes proteins and vitamins	Sensitization meeting are organized to inform patients about their right and responsibilities and to motivate them to adhere to treatment

Sr. No.	State	Economic assistance	Nutritional support	Psycho-social support
		treatment. Patients receive water filters, water cans, bed sheets and pillows. Livelihood training like tailoring and craft-making is organized for patients to generate income	supplements. Patients also taught food preparations and are counselled on the importance of nutrition	
16	Telengana	Patients receive the financial assistance in the form of vocational training, livestock and payment of school tuitions, among other upon treatment completion	The state provides raw materials like rice, groundnuts, edible oil, jiggery and milk to Below Poverty Line (BPL) and DR-TB patients. Children under 6 years suffering from TB are provided double the ration through ICDS' Anganwadi system	Home based counselling is provided to MDR-TB patients, on social stigma, depression, side-effects management and treatment adherence. Field staff sensitizes households on their entitlements and linkages to applicable social welfare schemes

Adapted from source [48]

In 2006, a more resistant strains of M.TB, XDR-TB emerged which is resistant not only to isoniazid and rifampicin but also to fluoroquinolones and second line aminoglycosides. XDR-TB may be MDR-TB with additional resistance to any fluoroquinolone and at least one of the three second line injectable drugs. Treatment for XDR-TB requires the use of third line anti-TB drugs but these drugs have more side effects than first or second line TB drugs [42,64,65]. Treatment of MDR-TB is expensive, prolonged (18–24 months) and complex (with at least a combination of five drugs that include some injectable drugs), and is associated with a higher incidence of adverse effects [63,66].

3.2.1 Recently approved drug in TB treatment

Bedaquiline, approved by the Food and Drug Administration (FDA), targets both active and dormant bacilli and Delaminid, by the European Medicine Agency, is a metronidazole derivative with bactericidal and sterilising activity. Unlike bedaquiline and Delamanid does not show cross-resistance with other anti-TB drugs [22,67]. Pretomanid is a nitroimidazooxazine drug which inhibits synthesis of mycolic acid. This leads to defective cell wall formation, ultimately causing bacterial cell death. It is active against both replicating and non-replicating M. tuberculosis. Following promising result in a phase III trial, pretomanid was approved by United States Food and Drug Administration in August 2019. This orally active drug has been approved as part of a combination regimen of bedaquiline, pretomanid and linezolid (BPaL regimen) to treat adults with pulmonary extensive drug resistant tuberculosis (TB) or treatment-intolerant or non-responsive multidrug resistant TB. Peripheral neuropathy and increased liver enzymes are some of the reported adverse events associated with pretomanid [68].

3.2.2 Phases of anti-TB treatment

There are two phases of treatment [26,30,56]
1. Initial phases, 2. Continuation phase

Table 4 depicts the dosage regimens for adults and Table 5 shows the RNTCP daily treatment regimen.

4. AN OVERLOOK AT TB AWARENESS PROGRAM IN INDIA

Improving quality of TB care in the private sector is crucial to end TB in highest TB burden. Modelling shows that optimism private sector engagement in India could avert 8 million deaths from TB between 2019 and 2045. In high drug resistance TB burden countries, access to rapid drug susceptibility testing (DST) and second-line drugs is essential to success [44,45,46]. Simulated patient studies among tuberculosis care providers in India, Kenya, China, and South Africa show that a wide spectrum exists in the quality of services offered to people with tuberculosis, with many receiving suboptimal services [69]. An awareness of atypical clinical manifestations of tuberculosis is important, especially in regions where TB continuous to be major public health problem, such as India [70]. Today, India aware people by giving the advertisements on Television, newspapers, hoardings on the public place, posters on the walls, public transport and many other ways about TB. In DOTS there is tagline saying “Pura Course, Pakka Ilaaj” also on the television advertisement by the National Health Mission (NHM) saying “TB Harega Desh Jeetega”. The NHM of India starts ‘Nikshay Poshan Yojana’ under Extended Gram Swaraj Abhiyaan for the nutritional support to TB patients and under this financial incentive of Rs. 500/- per month per each notified TB patient for the complete duration of treatment. The incentives are distributed via DBT (direct benefit transfer). According to this Yojana every state in India is giving financial support for the nutritional support to the TB patients. Table 6 information highlights the Nikshay Poshan Yojana in every state in India [48].

5. CONCLUSION

TB has been called the perfect expression of an imperfect civilisation [16]. TB is now found in every corner of globe and is one of the killer communicable disease caused by M. TB, transmitted by means of invisible droplet nuclei containing the organisms that have left the reservoir during breathing, sneezing or coughing sneezing. Infection and disease caused by M.TB strongly stimulates human moral immunity in humans [71]. In order to fully address the global TB burden, there is need improved diagnostic tests for active TB, seek to address the unmet needs for this patient group [72,73]. RNTCP is an on-going centrally sponsored scheme, being implemented under the umbrella of NHM [48]. First-line anti-TB drugs viz. Pyrazinamide, Isoniazid, Rifampicin, and Ethambutol are given by oral route, and drugs such as Amikacin, Capreomycin, Kanamycin, streptomycin, and

Vincomycin are the injectables, given by IV route. Newer second-line anti-TB drugs viz. Nevofloxacin, Ceprofloxacin, Oflaxacin, Moxifloxacin, Gatifloxacin, oral second-line anti-TB drugs such as Thioacetazone, P-amino salicylic acid, Ethionamid, Cycloserine are used to treat TB. Third-line anti-TB drugs are needed for the treatment of extensively drug resistant TB, however these drugs get more side effects than first- or second-line TB drugs. Multi drug resistant, treatment is costly, takes a long time (18–24 months), and is complicated, as well as having a higher rate of side effect. The NHM of India starts 'Nikshay Poshan Yojana' under Extended Gram Swaraj Abhiyaan for the nutritional and financial support to TB patients [48]. So, to eliminate the TB from its grass root the awareness among the society about this deadly communicable disease, its transmission, prevention, treatment and WHO strategies, as well as governments initiatives and the fact related to this is a current and important need of today's era. As of now various preventive and treatment strategies has been developed, and along with that the various drug delivery system as well as mode of administration has been changed depending on the severity of the disease. One of the major challenges with this disease is its lengthy duration of treatment, so there is a need of the new drug delivery than the conventional, which is able to target the site of infection where mycobacterium resides. Inhalable drug delivery design could potentially solve this problem and many researchers are working on such a platform by preparing microparticulate and nanoparticulate systems to reduce the frequency of dosing and duration of drug treatment by sustaining it as well as to target pulmonary alveoli, the site of infection. There are a lot to do in this field of TB; it would be formulation aspects, new drug synthesis, patient compliance aspects, socioeconomic aspects and many more, to live healthy and respectful life for TB patient.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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