Tuberculosis: the current status in India

Vikas Deep Mishra[1], Jai Krisna Mishra[2]

[1]Assistant Professor, Dept. of Tuberculosis & Chest Disease, Heritage Institute of Medical Sciences, Varanasi, [2]Professor & Head, Dept. of Tuberculosis & Respiratory Disease, Institute of Medical Sciences, Banaras Hindu University, Varanasi

***Corresponding Author:**
Email: jkmishra.imsbhu@gmail.com, vikasdmishra@gmail.com

Abstract

Pulmonary tuberculosis is endemic globally and is responsible for considerable morbidity and mortality. India is classified among the 22 high burden countries by WHO. According to WHO global TB report 2015 incidence of TB in India in 2014 was 2.2 million (including patients with HIV/TB) while, prevalence was 2.5 million (includes patients with HIV/TB). Mortality (excluding patients wit HIV/TB) was 0.2 million and case detection for all forms of TB was approximately 74%. With the emerging threat of Drug-Resistant TB, We need to improve our surveillance and treatment facility to eliminate TB by 2050.

Key words: Pulmonary tuberculosis, HIV/ TB

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-2738.2016.00010.8

Introduction

History of tuberculosis is probably as old as mankind. There have been references to this ancient disease in the *Vedas*, and it was called "Rajyakshama" [meaning "wasting disease"]. Hippocrates [460-377 BC] called the disease "pthsis", a Greek word which meant "to consume"[1,2]. The word "consumption" has been used to describe tuberculosis in English literature. Although as early as 1689, it was established by Dr. Richard Morton that the pulmonary form of disease was associated with "tubercles", the name tuberculosis was given by J.L. Schönlein in 1839.[3] In 1882, the bacillus causing Tuberculosis, *Mycobacterium tuberculosis* was discovered by Robert Koch[4]. Tuberculosis is caused by a group of closely related bacterial species termed *Mycobacterium tuberculosis* complex. Today the principle cause of human tuberculosis is *Mycobacterium tuberculosis*. Other members include *M. bovis*, *M. microti* and *M. africanum. M. microti* is not known to cause TB in humans; and infection with *M. africanum* is very rare. Human become infected by *M.bovis*, usually via milk and milk products or meat from an infected animal[5,6]. It is estimated that in the pre-antibiotic era, *M.bovis* was responsible for about 6% of tuberculosis death in humans[7,8],

Tuberculosis is the second greatest killer due to a single infectious agent (first being HIV/AIDS) in the world[9]. Even though tubercle bacilli was identified almost 130 years ago, a definitive understanding of patho-genesis of the disease is still deficient[10,11]. Individual with deficient immune system e.g. with HIV infection, are at increased risk of disease. Since the immune system in healthy people walls of the causative bacteria, TB infection in healthy people is often asymptomatic. This bacterium lives and multiplies in the macrophages, thus avoiding the natural defence system in patients' serum. Tuberculosis can result in two outcomes: (a) asymptomatic latent tuberculosis infection (LTBI) or (b) Tuberculosis disease. Without treatment the death rate is high. Studies from the pre chemotherapy era found that about 70% of people with sputum smear-positive pulmonary tuberculosis died within 10 years, and that this figure was 20% among culture positive(but smear-negative) case of pulmonary tuberculosis[12].

Global Scenario

According to WHO Global report 2015, in 2014, there were approximately 9.6 million incident case of TB (range 9.1 million- 10.0 million) globally. This is equivalent to 133 case per 100000 population. The absolute number of incident cases is falling slowly at an average rate of 1.5% per year 2000-2014 and 2.1% between 2013-2014. The cumulative reduction in the TB incidence rate 2000-2014 was 18%. Most of the estimated number of cases in 2014 occurred in Asia (WHO Regions of South-East Asia and the Western Pacific)(58%) and the Africa Region (28%).

The 22 High Burden Countries (HBC) viz. Afghanistan, Bangladesh, Brazil, Cambodia, China, DR Congo, Ethiopia, India, Indonesia, Philippines, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, South Africa, Thailand, Russian Federation, Uganda, UR Tanzania, Vietnam, and Zimbabwe accounted for 83% of all estimated incident cases worldwide. India, Indonesia, China alone accounted for a combined total of 43% of global cases in 2014.[13]

Directly observed treatment-short course (DOTS) is an internationally recognized strategy for delivering the basics of TB case finding and cure[14]. Between

2000-2014 TB treatment alone saved an estimated 35 million lives among HIV-negative people. Among HIV positive people, TB treatment supported by ART saved an additional 8.4 million lives.

The 9.6 million incident TB cases in 2014 included 1.1 million-1.3 million (11-13%) among PLHIV. The proportion of TB cases co-infected with HIV was highest in countries in the African region. Overall 32% of TB cases were estimated to be co-infected with HIV in this region, which accounted for 74% of TB cases among PLHIV worldwide.

According to WHO Global report 2015 the best estimate is that there were 480000 (range-360000-600000) new cases of MDR-TB worldwide in 2014. Globally, the mortality rate (excluding death among HIV positive people) fall 47% between 1990-2015, narrowly missing the target of a 50% reduction.

Indian Scenario

In India, TB has been mentioned in the *Vedas* and the old Ayurvedic scriptures. Early period of TB control in India was marked with non-availability of any chemotherapeutic agents, absence of diagnostic X-ray facility and lack of any TB control program. In India, the first open air sanatorium for treatment and isolation of TB patient was established in 1906 in Tiluania, near Ajmer city of Rajasthan and, the first TB dispensary was established in Bombay (now Mumbai) in 1917.[15] Chest radiography was started for detecting tuberculous consolidation in 1925 and mass miniature radiography (MMR) in 1945. In 1948, with support from WHO and UNICEF, a BCG vaccine production centre was set up in Guindy, Madras (now Chennai). India started a mass BCG vaccination campaign to control TB in 1951. This was the first nationwide campaign against TB[16].

Post-independence, in 1961, District Tuberculosis Program was prepared by the Indian Government and Anantpur District in Andhra Pradesh was the first model District TB Centre (DTC). The aim was to integrate TB control measures with the existing Government Health Services to reduce the TB problem in the community, as economically as possible[17]. Using this District TB Centre Model, in 1962, the Indian Government launched The National TB Control Program (NTCP). In 1956, under the auspices of Indian Council of Medical Research (ICMR), Chennai State Government, The WHO and The British Medical Research Council (BMRC). The Government of India established the Tuberculosis Research Centre (TRC) in Chennai (now National Institute for Research in Tuberculosis). This centre provided information on the mass domiciliary application of chemotherapy in the treatment of Pulmonary Tuberculosis. In 1959, National Tuberculosis Institute was established in Bangalore to frame out a practicable TB program that could be applied in all parts of country by training medical and para-medical workers.

Current WHO-assisted ongoing TB control program in India

In 1992, Government of India, WHO and The Swedish International Development Agency (SIDA) reviewed the NTCP and concluded that it had many short comings[18]. In 1993, WHO declared TB to be a Gobal emergency and devised the DOTS strategy. World Bank agreed to provide credit assistance for the NTCP, to adopt the DOTS strategy. Presently, other bilateral and multilateral agencies viz. Danish International agency (DANIDA), Department for International Development (DFID), US Agency for International Development (USAID), Global Fund To Fight HIV/AIIDS, Tuberculosis and Malaria (GFATM), Global Drug Facility (GDF) and WHO are providing invaluable support to the program. GFATM is the single largest source for external funding for TB control[19]. To give a new boost and to revitalize the NTCP, with assistance from the above mentioned International agencies, in 1997, the Revised National Tuberculosis Control Program (RNTCP) was launched[20].

To monitor RNTCP effectively, a web based monitoring application called NIKSHAY has been developed by National Informatics Centre (NIC). This is used by health functionaries at various levels across the country in association with Central TB Division (CTD), Ministry of Health & Family Welfare[21].

TB and HIV

HIV-positive people infected with TB are 20 to 40 times more likely to develop active TB than HIV-negative people living in the same country[22]. TB is the commonest HIV associated opportunistic disease in the world[23]. It accelerates HIV disease progression, increasing infectivity and reducing HIV treatment efficacy[24,25].

In India, there are about 21.17 lakh (17.11-26.49 lakh) people living with HIV and AIDS (PLHIV) at the end of 2015, while the estimated new HIV infection was around 86 thousand (56-129 thousand)[26]. The interaction between HIV and TB in person co-infected with HIV and TB is bidirectional and synergistic. The level of immuno-suppression determines clinical presentation of the resulting disease[27,28]. Pulmonary involvement occurs in about 75% of all HIV/TB infected patients[29,30]. HIV and TB co-infection also results in more rapid development of MDR-TB.[31,32]

A National Policy to co-ordinate common activities for HIV-AIDS and TB has been formulated by the National AIDS Control Organization and The Central TB Division. TB and TB/HIV interventions are reciprocally included in the National Policies of both the program[33]. Among the 2.2 million TB cases reported under the national program in 2015, approximately 5% (4.5%-5.4%) were HIV positive[34]. Implementation of the revised "national framework of

joint TB/HIV collaborative activities" began in early 2008, and interventions now cover the entire country. An "intensified TB/HIV package" was initiated in 2008 and the entire country has been covered by it in June 2012[35].

Estimates of TB Burden 2014:

	Number (Thousands)	Rate (Per 1,00,000 Population)
Mortality (excludes HIV+TB)	220 (150-350)	17 (12-27)
Mortality (HIV+TB only)	31 (25-38)	2.4 (2-2.9)
Prevalence (includes HIV +TB)	2500 (1700-3500)	195 (131-271)
Incidence (includes HIV+TB)	2200 (2000-2300)	167 (156-179)
Incidence (HIV+TB only)	110 (96-120)	8.3 (7.4-9.3)
Case detection, all forms (%)	74 (70-80)	------

Estimates of MDR-TB Burden 2014 :

	New	Retreatment
Percent of TB cases with MDR-TB	2.2 (1.9-2.6)	15 (11-19)
MDR-TB cases among notified pulmonary TB cases	24000 (21000 -29000)	47000 (35000-59000)

TB Case Notification 2014 :

	New	Relapse
Pulmonary, bacteriologically confirmed	754268	124679
Pulmonary, clinically diagnosed	343032	112066
Extra-pulmonary	275502	------

- **Total new and relapse - 1609547**
- Previously treated, excluding relapses - 74368
- **Total case notified - 1683915**

Among 1609547 new and relapse cases: 95709 (6%) cases aged under 15 years; male: female ratio: 1.9.

TB/HIV 2014:

	No.	%
TB patients with known HIV status	1034712	61
HIV-positive TB patients	44171	4
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	41066	93
HIV-positive TB patients on anti-retroviral therapy (ART)	39800	90
HIV-positive people screened for TB	1114394	---
HIV-positive people provided with IPT	------	---

Current Challenges

Relapse: Effective treatment takes at least six months to kill all the TB bacteria. During course of treatment many patients start to feel better within a few weeks of anti-tuberculosis therapy so they tend to skip doses of medication, due to this reason the TB bacteria will grow again and individual shows the symptom of active TB. This is also the cause of Drug Resistant TB.

Drug Resistant Tuberculosis: *M. tuberculosis* strain that are resistant to isoniazid and rifampicin are termed as multi drug resistant TB (MDR-TB) strain. Extensive drug resistant TB (XDR-TB) is the form in which the mycobacterium is resistant to isoniazid and rifampicin as well as to any fluoroquinolone plus any second-line injectable drug[36]. Both MDR-TB and XDR-TB are the emerging threats to the success of anti-TB programs. Latest emerging threat is the extremely drug resistant TB (XXDR-TB), sometimes also referred to as totally drug resistant TB, which is defined as mycobacterial strains resistant to all the first and second line anti-TB drugs[37]. This makes it almost but not totally impossible to treat. Drug resistance can be primary i.e. among new cases or acquired i.e. among previously treated cases[38]. The emergence of drug resistance in TB patients is mostly a result of deficient or deteriorating TB control programs. In India, according to WHO Global TB report 2015, MDR-TB cases among notified pulmonary TB cases was 24000 (21000-29000) among new cases and 47000 (35000-59000) among retreatment cases.

Conclusion

As can be seen from above discussion we have come a long way in our fight against tuberculosis but we still have to go a long way to make this planet free

from tuberculosis. WHO with its "STOP TB STRATEGY" has given a vision to eliminate TB as a public health problem by 2050[39]. We need to further strengthen our surveillance programs to accurately estimate the burden of TB. There should be rationale use first and second line anti-TB drugs. These should not be available as over the counter drugs. In India and other developing countries Government should encourage efforts for local manufacturing of anti-TB drugs, thus resulting in more efficient monitoring of their manufacturing and quality control standards. Many studies have shown that there is circulation of counterfeit and sub-standard medicines in developing countries[40,41].

Working association between physician, private sector, religious bodies and other NGOs should be strengthened for better dissemination of awareness about diagnosis, management and control of disease. Existing laboratories need to be strengthened with routine training/refresher courses for the involved personnels. The link, between primary health centres and DOTS centers should be strengthened, and special attention should be given to areas like utilizing human resources of related public health programs. The use of homeopathy and other alternative modes for treating TB and HIV should be discouraged.[42]

References

1. Flick LF. Development of our knowledge of tuberculosis. Philadelphia: Wickersham; 1925.
2. Webb GB. Tuberculosis. New York: Hoeber;1936.
3. News-medical.net [Internet]. History of Tuberculosis. Available: http://www.news-medical.net/health/History-of-Tuberculosis.aspx.
4. Nobleprize.org [Internet].Sweden: The Nobel Prize in Physiology or Medicine 1905: Robert Koch.c2010.Available from: http:/nobleprize.org/noble_ prizes/ medicine/laureates/1905/koch.html.
5. Prasad H, Singhal A, Mishra A, Shah N, Katoch V, Thakral S, et al. Bovine tuberculosis in India: Potential Basis for Zoonosis. Tuberculosis. 2005;85:421-8.
6. Srivastava K, Chauhan DS, Gupta P, Singh HB, Sharma VD, Yadav VS, et.al. Isolation of Mycobacterium bovis and M. tuberculosis from cattel of some farms in north India-possible relevance in human health. Indian J Med Res.2008;128:26-31.
7. Hardie RM, Watson JM. Mycobacterium bovis in England and Wales: Past, Present and future. Epidemiol Infect. 1992;109:23-33.
8. O'Reilly LM, Daborn CJ. The Epidemiology of M. bovis infections in animals and man: A review. Tuber Lung Dis.1995;76:S1-46.
9. Geneva: WHO; 2010. World Health Organization. Fact Sheet No.104: Tuberculosis. Available http:/www.who.int/mediacentre/factsheets/fs104/en/print. html.
10. Cole ST, Brosch R, Parkhill J, Garnier T, Churcher C, Harris D, et.al. Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence. Nature. 1998;393:537-44.
11. Brosch R, Gordon SV, Marmiesse M, Brodin P, Buchrieser C, Eiglmeier K, et.al. A new evolutionary scenario for the Mycobacterium tuberculosis complex. Proc Natl Acad Sci USA. 2002;99:3684-9.
12. Tiemersma EW et al. Natural history of Tuberculosis: Duration and fatality of untreated Pulmonary tuberculosis in HIV-negative patients: A systematic Review. PLoS ONE,2011,6(4):e17601.
13. World Health Organization. Global Tuberculosis Report 2015. Who/htm/tb/2015.22.
14. Geneva: WHO; 2006.World Health Organization. THE GLOBAL PLAN TO STOP TB 2006-2015: PART I Strategic directions. http:/www. searo.who.int/ Link Files/TB_ Day_Kit_The_Global_Plan_to_Stop_TB_2006-2015.pdf.
15. Proceedings of the Tuberculosis Association of India. New Delhi, India: Tuberculosis Association of India;1939.
16. Bangalore, India: 1962. Proceedings of 5th All India BCG Conference.
17. Agarwal SP, Vijay S, Kumar P, Chauhan LS. Tuberculosis Control in India. New Delhi, India: Directorate General of Health Services, Ministry of Health and Family Welfare; 2005. The history of Tuberculosis Control in India: Glimpses through decades; pp. 15-22.
18. World Health Organization. Tuberculosis programme review-India. Geneva: WHO; 1992.
19. Theglobalfund.org [Internet]. The Global Fund to Fight AIDS, Tuberculosis and Malaria. http:/www.theglobalfund.org/en/ commitments disbursements/eng.
20. World Health Organisation. Joint TB Programme Review-India: WHO, SEARO-TB-224.Geneva: WHO;2000.
21. Nikshay.gov.in/AboutNikshay.htm. [Internet].
22. World Health Organisation. Monograph on integrated monitoring of TB/HIV- a case study in Malawi. Geneva: WHO;2009.
23. Lawn SD. Tuberculosis and HIV co-infection. Medicine. 2005;33:112-3.
24. Chaovavanich A, Chottanapand S, Manosuthi W, Sungkanuparph S, Thongyen S. Survival rate and risk factor of mortality among HIV/tuberculosis-coinfected patients with and without antiretroviral therapy. J Acquir Immune Defic Syndr.2006;43:42-6.
25. Dagnra AY, Adjoh K, Tchaptchet Heunda S, Patassi AA, Sadzo D, Hetsu F et. al. Prevalence of HIV/TB co-infection on pulmonary tuberculosis outcome in Togo. Bull Soc Pathol Exot. 2010
26. India HIV estimation 2015. Technical report. Available at. naco.gov.in/ upload/ 2015%20MSLNS/HSS/India%20HIV%20Estimation%20 2015.pdf.
27. Kumarsamy N, Vallabhaneni S, Flanigan TP, Mayer KH, Solomon S. Clinical profile of HIV in India. Indian J Med Res.2005;121:377-94.
28. Sharma SK, Mohan A, Kadhiravan T. HIV-TB co-infection: Epidemiology, diagnosis and management. Indian J Med Res. 2005;121:550-67.
29. Deivanayagam CN, Rajasekaran S, Senthilnathan V, Krishnarajasekhar R, Raja K, Chandrasekar C, et.al. Clinicoradiological spectrum of tuberculosis among HIV sero-positive a Tambaram study. Indian J Tuber. 2001;48;123-7.
30. Ahmad Z, Shameem M. Manifestation of Tuberculosis in HIV Infected Patients. J Indian Acad Clin Med. 2005;6:302-5.
31. Demissie M, Lemma E, Gebeyehu M, Lindtjorn B. Sensitivity to anti-tuberculosis drugs in HIV-positive and

–negative patients in Addis Ababa. Scand J Infect Dis. 2001;33:914-9.
32. Kebede D, Mitike G, Yeneneh H. HIV infection and Anti Tuberculosis Drug Resistance among Pulmonary Tuberculosis Patients in Harar Tuberculosis Centre, Ethopia; East African Med J.1997;74:154-7.
33. National AIDS Control Organization. Antiretoviral therapy guidelines for HIV-infected adults adolescents including post-exposure prophylaxis(Section A7) New Delhi, India: National AIDS Control Organization;2007.
34. Central TB Division. www.tbcindia.nic.in/showfile.php?lid=3180.
35. [Internet]www.who.int/tb/challenges/hiv/scaling_up_tb-hiv_in_india_what_ is_ achieved_and_what_is_remaining.pdf.
36. Crofton J, Chaulet P, Maher D. Guidelines for management of drug resistant Tuberculosis. Geneva:WHO;1997.pp. 31-7.
37. Migliori G."125 years after Robert Koch's discovery of tubercle bacilli: the new XDR threat. Is "science" enough to take the epidemic?" European Respiratory Journal. March 1,2007. http://ersjournal.com.
38. World Health Organization. The WHO/IUTALD Global Project on Anti-tuberculosis Drug Resistance Surveillance. Report No.3. Geneva: WHO; 2003.
39. World Health Organization. Global Tuberculosis Report.Geneva.WHO;2009.
40. Atemnkeng MA, Decock K, Plazier-Vercammenn J. Quality control of active ingredients in artimisnin-derivative antimalarials within Kenya and DR Congo. Trop Med Int Health.2007;12:68-74.
41. Onwujekwe O, Kaur H, Dike N, Shu E, Uzochukwu B, Hanson K, et al. Quality of Anti-malarial drugs provided by public and private health care providers in South-East Nigeria. Malar J.2009;8:22.
42. ANI. Homeopathy doesn't help in HIV,TB, Malaria. The Times of India. http://timesofindia.indiatimes.com/life-style/health-fitness/ health/ Homeopathy- doesn't- help-in-HIV-Tb-malaria/articleshow/4918285.cms.