WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 13, Issue 3, 986-996. Research Article ISSN 2277–7105

MEASURING THE "TIME GAP" BETWEEN THE DATE OF DIAGNOSIS AND TREATMENT INITIATION AND ITS EFFECT ON THE TREATMENT OUTCOMES OF TUBERCULOSIS – A SECONDARY DATA ANALYSIS FROM CENTRAL RURAL INDIA

R. Naveen Shyam Sundar* and Mohnish Y. Giri

Senior Resident Doctors, Department of Community Medicine, MGIMS, Sevagram, Wardha, Maharashtra, India.

Article Received on
05 December 2023,

Revised on 26 Dec. 2023,
Accepted on 16 Jan. 2024

DOI: 10.20959/wjpr20243-31157

***Corresponding Author**
R. Naveen Shyam Sundar
Senior Resident Doctors, Department of Community Medicine, MGIMS, Sevagram, Wardha, Maharashtra, India.

ABSTRACT

Tuberculosis (TB) remains a significant public health challenge globally, with India bearing a substantial burden. This study, conducted in Wardha district, Maharashtra, aims to investigate the time gap between TB diagnosis and treatment initiation and its impact on treatment outcomes. Analyzing data from the Revised National Tuberculosis Control Programme (RNTCP) for the period January 2017 to August 2019, we focused on 4,551 patients. The study revealed that despite India's widespread adoption of the WHO Directly Observed Treatment Short course (DOTS) strategy, there is an ongoing challenge in achieving prompt treatment initiation. The age distribution of TB cases showed a predominance among adolescents and the working-age population, with males being more affected than females. The study identified a median time gap between diagnosis and treatment initiation, emphasizing the importance of timely intervention. The analysis of treatment outcomes, stratified by the time gap, revealed intriguing findings. Patients initiated on treatment within 7 days had lower odds of death and treatment completion within the first week compared to later initiation. However, the odds of being cured were higher when treatment was initiated after 7 days, suggesting a complex relationship between time and specific treatment outcomes. Stratifying the data by diagnosing health facility, sex, and age provided additional insights. Public health facilities demonstrated a significantly lower likelihood of initiating treatment within 7 days compared to private institutions, highlighting challenges within the public healthcare system.

Males had a slightly lower likelihood of early treatment initiation than females, and age stratification indicated variations, with the 18-60 age group showing a higher likelihood of timely initiation. In conclusion, the study underscores the need for targeted interventions to reduce delays in treatment initiation, particularly in public health facilities. Strengthening infrastructure, streamlining diagnostic processes, and implementing awareness campaigns, especially for demographic groups with lower odds of early initiation, are recommended. Collaborative efforts between public and private sectors, along with ongoing monitoring and evaluation, are crucial for achieving the goals outlined in India's National Strategic Plan for TB Elimination by 2025. Addressing disparities in treatment initiation is fundamental to enhancing overall TB treatment efficacy and reducing the burden of the disease in the region.

INTRODUCTION

Tuberculosis (TB) remains one of the major public health problems. According to the World Health Organization's Global TB report of 2019, India is one of the most affected countries by tuberculosis, sharing 27% of the total 10 million affected people globally in 2018 and with a mortality of 440 thousand individuals.[1] With such a magnitude of disease, it is imperative that all the diagnosed cases of tuberculosis must be initiated on anti-tubercular treatment at the earliest possible time.

India, under its Revised National Tuberculosis Control Programme (RNTCP), adopted the WHO Directly Observed Treatment Short course (DOTS) in 1997[2,3] and has reached country wide coverage, providing free medications and diagnostic services at the level of primary health facilities. This strategy treated more than 10 million people between 1997-2017.[4] The government of India has committed to the elimination of TB through rapid declining in disease burden, mortality, and morbidity by 2025 under The National Strategic Plan 2017-2025 for TB Elimination. It is made in line with the WHO's End TB Strategy.

In India's system of federal governance, health is a state subject and so the individual states remain responsible for the implementation of any national health programme. Further, the implementation of such health programmes depends upon the strength of health systems in individual states. Though the government of India is constantly working towards elimination of tuberculosis and has been able to increase the case detection and treatment success rates, there remains a constant increase in the incidence of the tuberculosis. The existing scientific evidence suggests that the best strategy to break the chain of transmission and to decrease the incidence of tuberculosis is early case detection, early initiation, and completion of

treatment.[5,6] It is presumed that after about 20 years of implementation of RNTCP, mechanisms and strategies are in place and functional to avoid any treatment delays.

One of the indicators for the quality of the treatment provided under RNTCP is to start the treatment within 7 days of diagnosis.[4] Delay in the initiation of treatment accounts to a high rate of transmission and increased mortality rate.[7] These delays are common in middle- and low-income countries, accounting to high community transmission and high TB burden.[1]

Most of the patients first reach the informal private sector (chemists and unqualified practitioners) with symptoms and seek advices, then reach out to the private hospitals and finally reach the government sector for free treatment.[8] In India in 2018, among the 21 lakhs diagnosed patients of tuberculosis, 96% were initiated on treatment, 80% were cured and completed the treatment, 4% died, and 4% were lost to follow up. The proportion of patients with treatment failure and those for whom the regimen changed were 1% each while 7% of them were not evaluated.[9] There is very scarce to absolutely no evidence up to date published and available for the region of Maharashtra. Also, it is important to state that every region is unique when it comes to the health systems and the figures estimated for one region might be of no utility in another region. So, the aim of this study is to measure the time gap between the diagnosis and treatment initiation of TB for the patients registered under the RNTCP (now called the National Tuberculosis Elimination Programme or NTEP) in the Wardha district of Maharashtra and to assess its effect on their treatment outcomes.

OBJECTIVES

To find amongst all the tuberculosis patients registered in the RNTCP/NTEP programme under the district tuberculosis office of Wardha district, Maharashtra from January 2017 to August 2019:

1. The proportion of TB patients who had delay in initiation of treatment for more than seven days.
2. The effect of delay in initiation of treatment on the different treatment outcomes under RNTCP/NTEP
3. The potential risk factors causing treatment delay that are captured under the TB Notification Register.

METHODOLOGY

We used a retrospective cohort design for this study. We received the data of the tuberculosis notification register for Wardha district in Maharashtra, India with the authorization of the district tuberculosis office for all those patients who were registered from January 2017 to August 2019. All the tuberculosis patients registered under the RNTCP/NTEP from January 2017 to January 2020 whose details were updated in the TB notification register through the Wardha District Tuberculosis Office.

The data were collected from the TB Notification Register as updated on the Nikshay Portal (January 2017 – August 2019) by all the TB units under the Wardha District Tuberculosis Office. The personally identifiable information like the name of the patient, address, contact details, and case IDs were delinked, and a new case ID was allotted to anonymize the data.

The variables collected from the TB Notification register included the diagnosing facility district, diagnosing facility TB unit, diagnosing facility peripheral health institution type, date of diagnosis, patient status, age, gender, residential district, residential TB unit, HIV status, Diabetes status, basis of diagnosis, type of case, site of disease, treatment outcome and the treatment outcome date.

Data analysis

The collected data was screened for duplicates, 92 were found. Following this, we described the anatomy of the data frame to capture the completeness of data (Figure 1). Further, the data was cleaned for any wrong entries or missing entries, and if found, these were excluded from the further analysis. The clean data was entered into the Microsoft Excel (Office 365) which was then used as an input to analyse in R software version 4.2.1. The distribution of the data variables was analysed. The median with range was used to summarize the data on age, and time gap between the diagnosis and treatment initiation. To answer our first objective of determining the proportion of TB patients who had delay in initiation of treatment for more than seven days, we first calculated the difference in number of days from the date of diagnosis and the date of initiation of treatment. Further this was categorized into the time gap less than 7 days and time gap more than or equal to 7 days.

Ethical considerations

Because this study involved the review of records that the national program routinely collected and did not involve any patient interactions, informed consent was not required.

Information was entered in a structured format based on the information reported in the TB Notification Register. The data received was delinked and anonymized to prevent any possible identification of the TB patient. Data confidentiality was maintained by keeping the electronic data file kept only accessible to the principal investigator in a password protected computer. Required approvals for accessing records in the study district were obtained from the District Tuberculosis Officer (DTO).

RESULTS

The total participants considered for the study is 4551 out of the total 4881 entries in the TB notification register from January 1st 2017 to January 31st 2020. This is because of removing of the duplicates in the patient unique ID, neglecting the patients whose treatment outcome were not assigned and those whom treatment was not been evaluated, patients without date of initiation of treatment also were not considered. (Fig 1)

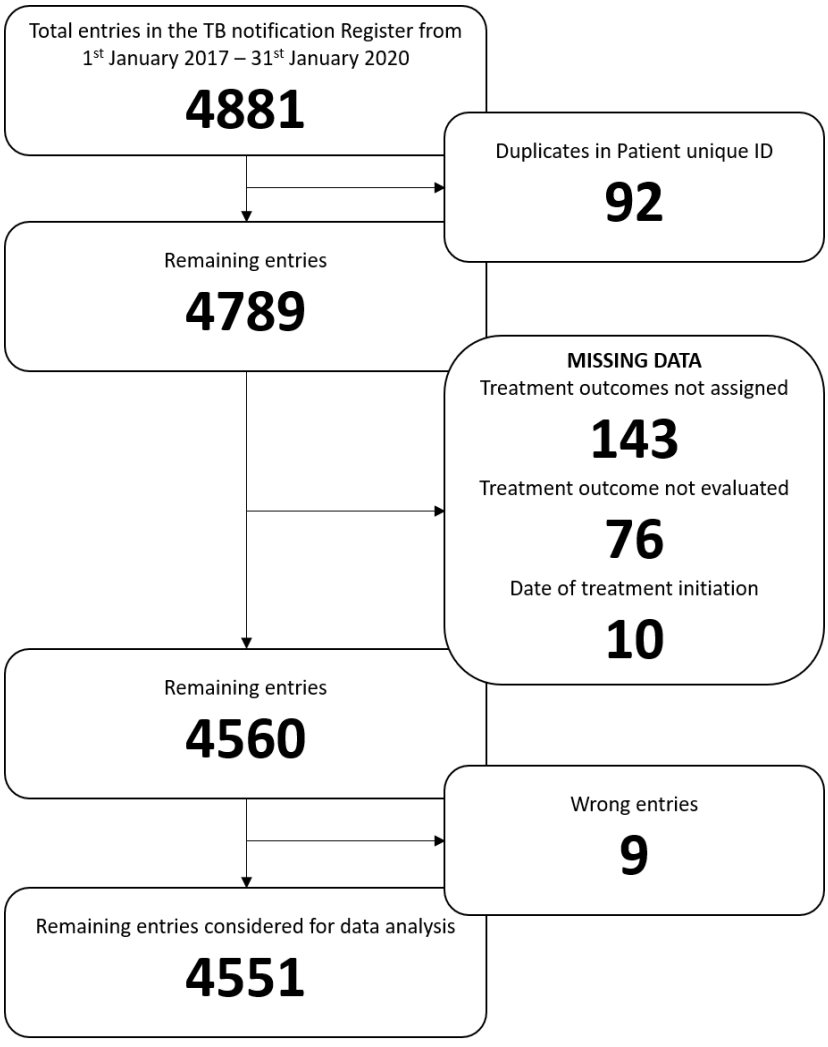


Figure 1: Data Analysis outline.

Overall, the age distribution of TB diagnosed cases shows predominance among the adolescents and working age population between 15-40 years of age. However, there is a wide variation in the age distribution pattern showing exclusively skewed occurrence. And also, males are more affected than females. (Fig 2)

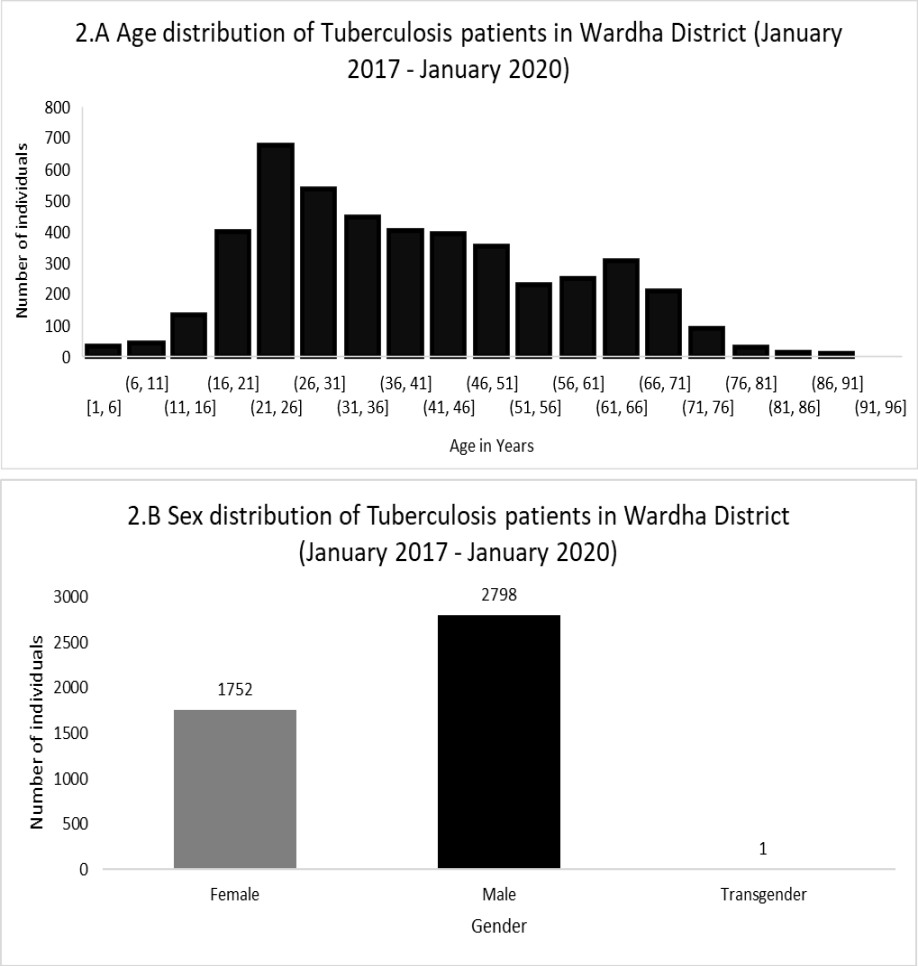
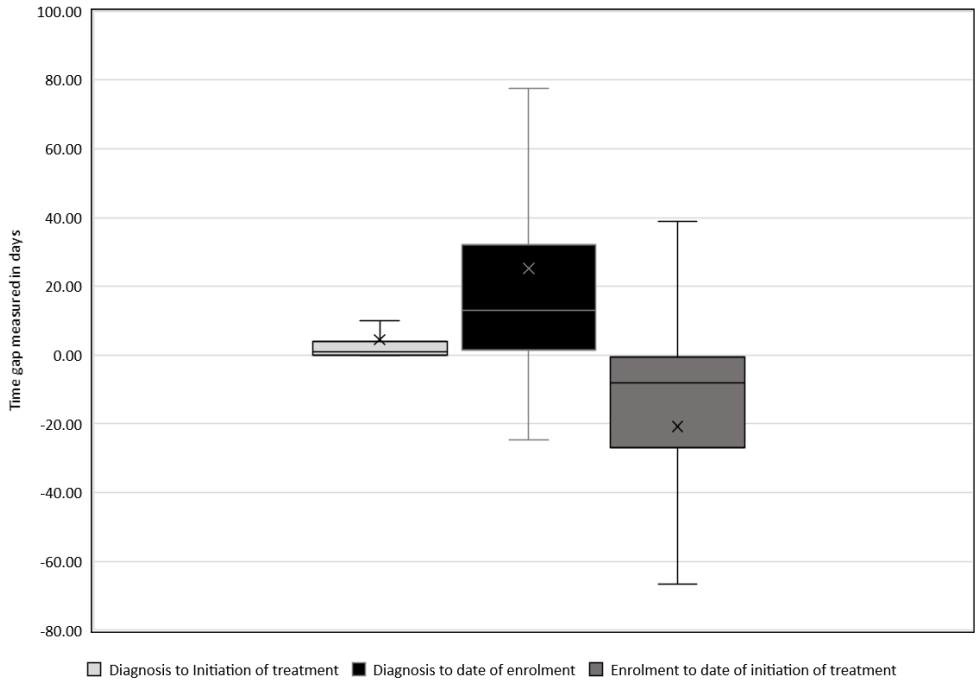


Figure 2: Age and sex distribution of the Tuberculosis patients in Wardha District (January 2017 to January 2020).

By comparing the time gap between three variables namely diagnosis time, time of initiation of treatment and date of enrolment on a boxplot as shown in fig.3, the median time gap between the diagnosis to date of enrolment is more. Its evident that the initiation of treatment is done even before the enrolment. The diagnosis to initiation of treatment gap is comparatively less.

Figure 3: Time gap from diagnosis to initiation of treatment, from diagnosis to enrolment, and from enrolment to initiation of treatment



The table 1 illustrates treatment outcomes for tuberculosis (TB) patients categorized by the time gap between diagnosis and treatment initiation, with time intervals "<7 days" and ">7 days." It presents counts and percentages of patients who either died, were cured, or completed treatment within each time gap. The odds ratios with corresponding 95% confidence intervals provide a comparative measure of the likelihood of these outcomes within 7 days compared to more than 7 days. Notably, the odds ratios for death and treatment completion are both 0.80, suggesting a slightly lower likelihood of death and treatment completion within the first week compared to later initiation. However, the odds ratio for being cured is 1.35, indicating a higher likelihood of cure when treatment is initiated after 7 days. These findings underscore the importance of timely treatment initiation in improving certain TB treatment outcomes.

Table 1: Treatment Outcomes Based on Time Gap between Diagnosis and Treatment Initiation for Tuberculosis Patients.

Time gap	Death (%)		ODDs Ratio	Cured (%)		ODDs Ratio	Treatment completed (%)		ODDs Ratio
	yes	No		yes	no		yes	no	
<7 days	182 (6.70)	2535 (93.30)	0.80 (0.55-1.20)	810 (29.81)	1907 (70.19)	0.80 (0.64-1.01)	1522 (56.02)	1195 (43.98)	1.35 (1.10-1.68)
>7days	32 (8.21)	358 (91.79)		135 (34.62)	255 (65.38)		189 (48.46)	201 (51.54)	

The table 2 provides odds ratios, confidence limits (95%), and patient counts stratified by diagnosing health facility, sex, and age, with a focus on the time gap between tuberculosis (TB) diagnosis and treatment initiation. The "Time gap" column indicates two categories: "<7 days" and ">7 days," representing the duration from diagnosis to treatment initiation. Diagnosing Health Facility: The first section stratifies patients based on the diagnosing health facility, distinguishing between public and private institutions. The odds ratio (ODDs Ratio) suggests a significantly lower likelihood of initiating treatment within 7 days in public health facilities compared to private ones (ODDs Ratio = 0.12, 95% CI: 0.06-0.22). Sex: The second section categorizes patients by sex, with odds ratios indicating that males have a slightly lower likelihood of initiating treatment within 7 days compared to females (ODDs Ratio = 0.87, 95% CI: 0.70-1.09). Age: The final section stratifies patients by age, with odds ratios for both <18 and >60 age groups suggesting no significant difference in treatment initiation within 7 days compared to their respective counterparts. However, the odds ratio for the 18-60 age group indicates a higher likelihood of treatment initiation within 7 days (ODDs Ratio = 1.36, 95% CI: 1.04-1.76). These findings underscore variations in treatment initiation based on diagnosing health facility, sex, and age, providing insights into potential areas for targeted interventions to improve timely TB treatment initiation.

Table 2: Odds Ratios for TB Treatment Initiation within 7 Days Compared to >7 Days, Stratified by Diagnosing Health Facility, Sex, and Age.

		Time gap		ODDs Ratio	Confidence limit	
		<7 days	>7 days		Lower	Upper
Diagnosing health facility	Public	2195	379	0.12	0.06	0.22
	Private	522	11			
sex	Male	1683	254	0.87	0.70	1.09
	Female	1033	136			
Age	<18	165	28	0.84	0.56	1.29
	>18	2552	362			
	<60	2261	306	1.36	1.04	1.76
	>60	456	84			

DISCUSSION

The state of Maharashtra has a population of 11,23,72,972 and is located in the west-central India. For administrative purposes, it is divided into six divisions namely Amaravati, Aurangabad, Konkan, Nagpur, Nashik and Pune; that includes a total of 36 districts, 109 sub-divisions and 358 tehsils.

Geographically, the Wardha district is a part of Nagpur division and consists of 8 tehsils with a total population of 1,300,774 with a population density of 210/km2 (530/sq. mi.). The literacy rate is 86.99% and around 0.31% of population live homeless. The district consists of 3TB units, and 15 designated microscopy centres.

Throughout India, after diagnosis, all patients report to their local DOTS Centres to begin the treatment where the patient is enrolled under the system for treatment and the drugs are distributed to them in patient wise boxes to ensure that all drugs are provided on day one for full course of treatment. The DOTS centres are highly decentralized. Currently, to the extent possible, over 400,000 DOTS centres have been located near the patients' residence. These serve as a service delivery point from which a DOTS provider operates (e.g. home of a rural health worker, community volunteer, local sub-centre, where a nurse or accredited social health activist (ASHA) operates, Anganwadi Worker (AWW)), in addition to this, the NGOs, and the private practitioners are also involved under the RNTCP to serve as a DOTS centre / provider. The DOTS provider who covers the region under the DOTS Centre receives the anti-TB drugs from the Peripheral Health Institute, performs an Initial Home Visit (IHV) to check the address, and provides counselling to the patient. She / he subsequently identifies a suitable DOTS Provider for the patient who is located nearer to the patient's residence to start the patient on treatment.

The findings from our study offer crucial insights into the factors influencing the initiation of tuberculosis (TB) treatment and its subsequent outcomes. Detailing treatment outcomes based on the time gap between diagnosis and initiation, highlights the critical importance of early treatment in achieving positive results. Notably, the odds ratios for death and treatment completion suggest a slightly lower likelihood of these outcomes within the first week of diagnosis. In contrast, the odds ratio for being cured is higher when treatment is initiated later. These observations underscore the intricate relationship between timely treatment and different treatment outcomes. Examining stratified factors like health facility, sex, and age, further emphasizes disparities in treatment initiation. Public health facilities demonstrate a significantly lower likelihood of initiating treatment within 7 days compared to private institutions, indicating potential challenges in the public healthcare system. Additionally, differences in initiation by sex and age highlight the need for targeted interventions to address specific demographic factors. Overall, these findings collectively stress the importance of timely diagnosis and treatment initiation, while also underscoring the necessity of tailored

strategies to overcome disparities in various healthcare settings and demographic groups for improved TB treatment outcomes.

CONCLUSION

This study provides valuable insights into the complexities of tuberculosis (TB) treatment initiation and outcomes, emphasizing the pivotal role of timely intervention. Public health facilities exhibit challenges in achieving prompt treatment initiation, and variations based on sex and age indicate the need for targeted interventions. Overall, these findings emphasize the intricate interplay of factors influencing TB treatment outcomes and underscore the importance of addressing disparities to enhance overall treatment efficacy.

Recommendations

Based on the study findings, several recommendations can be made to improve TB treatment outcomes. Firstly, there is a crucial need for interventions aimed at reducing delays in treatment initiation, particularly within public health facilities. Strengthening infrastructure, resource allocation, and streamlining diagnostic processes can contribute to more timely treatments. Additionally, targeted awareness campaigns could be developed to address specific demographic groups with lower odds of early treatment initiation, such as males and older individuals. Collaborative efforts between public and private healthcare sectors are essential to ensure uniform access to timely and effective TB care. Finally, ongoing monitoring and evaluation programs should be implemented to track and address disparities, enabling a dynamic and responsive healthcare system that continuously strives to improve TB treatment outcomes for all segments of the population.

REFERENCES

1. World Health Organisation (2019), Global Tuberculosis report 2019.
2. Mahadev B. Kumar. History of tuberculosis control in India. J Indian Med Assoc.
3. World Health Organisation. Brief history of tuberculosis control in India. World Health Organisation, 2010.
4. Central TB division. National strategic plan 2017-2025, 2017.
5. Stop TB Partnership and World Health Organization, Geneva (2006) Global Planto Stop TB2006–2015. Available: http://www.stoptb.org/assets/documents/resources/publications/plan_strategy/The_Stop_TB_Strategy_Final.pdf, Accessed on 15th May, 2011.

6. World Health Organisation, Geneva (2010) Treatment of Tuberculosis: Guidelines-4th edition.
7. Goel K, Kondagunta N, JoyceeSoans S, Ramachandra Bairy A, Goel P. Reasons for patient delays and health system delays for tuberculosis in South India. Indian Journal of Community Health, 2012; 23(2): 87-89.
8. Finnie RK, Khoza LB, van den Borne B, Mabunda T, Abotchie P, Mullen PD. Factors associated with patient and health care system delay in diagnosis and treatment for TB in sub-Saharan African countries with high burdens of TB and HIV. Tropical Medicine & International Health, 2011; 16(4): 394–411.
9. India TB report 20 http://tbcindia.gov.in