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A retrospective study on the treatment outcomes of tuberculosis patients in tertiary care hospitals of Salem district, Tamil Nadu

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Abstract
Aim: To study the treatment outcomes of Tuberculosis patients in tertiary care hospitals of Salem District, Tamil Nadu.
Design: In the retrospective study conducted on 500 patients in tertiary care hospitals of Salem, district Tamil Nadu. The treatment outcomes and prescription analysis of patients were evaluated.
Results: From the total of 500 TB patients, 468 were PTB and 32 were EPTB cases. A total of 421 patient's treatment outcomes were cured. A total of 9 patients treatment outcome were died, in. A total of 11 patients treatment outcome were failure. A total of 60 patients treatment outcome were found to be in the defaulted. The percentage of deaths and defaulters were higher in males than in females. Being an older age group (p=0.0101), a rural resident (p=0.0001) and EPTB patients (p=0.001) were associated with a higher treatment success rate which shows improved public health and awareness on TB. On analysis of prescription higher incidence of drug interactions were found with Rifampicin + Pyrazinamide (36%) in which additive hepatotoxicity were observed
Conclusions: This study showed that TB patients' treatment success rate treated at the hospital DOTS clinic found above the national success rate. As a recommendation farther research should be done to identify causes of a common reason for unsuccessful treatment outcome in TB patients and working on the increasing awareness of the community.

Keywords: Tuberculosis, co-infection, DOTS therapy, medication adherence

Introduction
Tuberculosis is an infectious disease, usually of the lungs that kills nearly two million people annually. It is caused by *Mycobacterium tuberculosis*, bacteria that are spread in airborne droplets when people with tuberculosis cough. Most people infected with *M. tuberculosis* do not become ill; their immune system contains the infection. However, the bacteria remain dormant within the body and can cause tuberculosis years later if immunity declines because of, for example, infection with HIV [1]. A recent prevalence survey about TB reported that prevalence among 15–24-year-olds of 3.7 per 1000(95% confidence interval (CI) 2.2-6.2) among females and 1.8 per 1000 (95% CI 0.8-4.2) among males [2].
Pulmonary tuberculosis (TB) remains a major cause of morbidity and mortality worldwide, with about one-third of the world's population infected. Between 10% and 20% of those infected will progress to active TB, posing a serious health threat [3]. Extra pulmonary involvement can be seen in more than 50 percent of patients with concurrent AIDS and tuberculosis. The risk of extra pulmonary tuberculosis and mycobacteremia increases with advancing immunosuppression. Unique features of AIDS-associated tuberculosis include extra pulmonary disease, disseminated disease, rapid progression, visceral lymphadenopathy, tissue abscesses, and negative tuberculin skin test [4].
Both TB and HIV have profound effects on the immune system, as they are capable of disarming the host's immune responses through mechanisms that are not fully understood. HIV co-infection is the most powerful known risk factor for progression of *M. tuberculosis* infection to active disease, increasing the risk of latent TB reactivation 20-fold. Likewise, TB has been reported to exacerbate HIV infection. Various lines of evidence indicate that inborn errors of immunity, as well as genetic polymorphisms, have an impact on susceptibility to TB and HIV [5].

Sputum is the most common specimen obtained for the diagnosis of pulmonary infection with MTBC and nontuberculous mycobacteria (NTM). To enhance sensitivity by smear, current guidelines recommend the collection of early morning sputum specimens on 3 consecutive days with a minimum of 8 hours between collections [6].

DOTS geographical coverage reached 100% in 2006. However, the case detection rate is still below 50% [7]. In the country, the health facility coverage is 75% [8]. Although the WHO recommends routine culture and drug susceptibility testing for M. tuberculosis in order to effectively and timely follow-up on treatment outcomes, many developing countries including Ethiopia, do not perform it. It has been shown that patients taking drugs directly under the observation of health care providers have a paramount importance in achieving a high treatment success rate of 96.5% [9]. Studies from developing countries have also reported that DOTS was significantly associated with a higher treatment success rate than self-administered therapy, as well as a lower tuberculosis-related mortality rate [10]. Besides the association of DOTS with treatment success rate, DOTS also aims to significantly decrease the occurrence of primary and acquired drug resistance and relapse. Even though the objectives of TB treatment are curing the patient, preventing the spread of tuberculosis infection, and preventing the emergence of new drug resistant strains, these plans are not achieved in many regions of the world (WHO, 2003) due to several factors that affect treatment success. These include: the severity of disease, co-infection with HIV and/or other diseases, multidrug resistance, poverty, and also the support provided to the patient [11].

Globally, around 8.8 million people develop tuberculosis and 1.45 million people die every year due to TB, of which 0.35 million deaths are associated with HIV- TB co-infection [12]. An increased incidence of tuberculosis is found mostly in Africa and Asia, where the highest prevalence of co-infection with HIV and M. tuberculosis also occurs [13]. The global burden of death and disease caused by TB is concentrated particularly in low-income countries, Subsaharan Africa [14].

The study was aimed to analyze the treatment outcomes, incidence of co-infection, co-morbidities and patterns of prescription among tuberculosis patients in tertiary care hospitals of Salem district.

Materials and Methods

Study Location

The study was conducted at the tertiary care hospitals of Salem district, Tamil Nadu. In the hospital, DOTS clinic is operating under the National Tuberculosis and Leprosy Program (NTLCP), under which patients are diagnosed with tuberculosis by examination of morning sputum smears by Zeihel Nieelsen staining, for the presence of Acid fast bacilli (AFB), chest radiographs, and for EPTB, pathological investigations were used. Patients are referred to the DOTS clinic where they are registered and treated according to the National Tuberculosis and Leprosy Control Program (NTLCP).

Study Design and Data Collection

A retrospective study on the treatment outcomes and prescription analysis of tuberculosis patients in tertiary care hospitals of Salem district, Tamil Nadu was conducted during the period of November 2017 to April 2018. Total of 500 TB patients registered at the DOTS clinics were followed up during their course of treatment to assess treatment outcome and prescription analysis. Demographic data such as patient's age, sex, address, as well as the study subject's clinical data HIV serostatus, tuberculosis type, and treatment outcome were included in the registration form. Patients' treatment outcomes were evaluated in accordance with the NTLCP which is adopted from the WHO (MOH, 2008) and classified as Cured (patient completed treatment with negative bacteriology). Defaulted Treatment (patients who interrupted their treatment for two consecutive months or more after registration) Treatment Failure (remaining smear-positive at five months despite correct intake of medication) died (patients who died from any cause during the course of treatment). Patients were provided with free TB medications for a period of 6 to 8 months by the DOTS centre in the hospital. Patients were followed up regularly until completion of their treatment.

Results and Discussion

Demographic Characteristics of Study Subjects

Out of 500 patients recorded at the tertiary care hospitals of Tamil Nadu 415 (83%) cases were PTB and 6 (1.2%) were EPTB patients. Of the total TB patients registered, 363 (73%) were males and 137 (27%) were females. 390 (78.2%) of patients were in the age group 40 to 72 years. Figure 1 shows the general characteristics of the patients. Among the study subjects 5 (1%) were HIV seropositive. Three hundred and sixteen (63%) of the subset were from urban areas and one hundred and eighty four (37%) were from the rural regions.

Treatment Outcomes

The treatment outcomes of 500tuberculosis patients are shown in Table no 1. A Cured, finished treatment with negative bacteriology at the end of the treatment was achieved in 421 (84.2%) of the cases in the study. Meanwhile, 60 (12%) defaulters were found, 8 deaths (1.6%) and 11(2.2%) treatment failure were recorded. In this study a higher death rate (n=5) 1% was observed in male as compared of the female patients. Higher failure rate was recorded among females (n=6) 1.2% and higher defaulter rate goes to males (n=36) 7.6%.

Table 1: Treatment Outcomes of TB Patients

Characteristics	Cured	Died	Failure	Defaulted	Total
Gender					
Male	315	5	5	38	363
Female	106	3	6	22	137
Age (Years)					
18-28	23	0	1	4	28
29-39	42	0	0	3	45
40-50	74	0	2	7	83
51-61	208	1	2	7	218
62-72	56	3	2	29	90
73-83	18	4	4	10	36
Residence					
Urban	293	3	2	18	316
Rural	128	5	9	42	184
TB Type					
PTB	415	3	6	44	468
EPTB	6	5	5	16	32

Factors Associated with TB Treatment Success

Out of 500 patients, male patients had significantly higher success rate than the female patients who were being treated for TB, making a treatment success rate of 63% (RR=1.53,

95% CI= 1.6907-1.3868, p = 0.0101). The Patients with mean age group greater than 50 had significantly higher success rate when compared to other age groups, that is success rate of 56.4% (RR = 0.25, 95% CI = 0.2739-0.2365, p = 0.0001). Among the urban and rural patients, urban patients had higher success rate than rural patients, making a treatment success rate of 58.6% (RR=0.42, 95% CI= 0.4655-0.3808, p = 0.0158)**,** Patients who were treated with PTB has a higher success rate than that of patients being treated for EPTB (RR = 2, 95% CI = 4.1170- 0.9715, p = 0.001). (Table no: 2).

Table 2: Association between different factors, which may affect treatment outcomes among tuberculosis patients

Characteristics	Successful	Unsuccessful	Total	Risk ratio	P- Value
	Treatment (N%)=421	Treatment (N%) =79	N =500	95% CI	
Gender					
Male	315(63%)	48(9.6%)	363(72.6%)	1.53125	0.0101
Female	106(21.2%)	31(6.2%)	137(32.4%)	(1.6907-1.3868)	
Age					
≤50	141(28.2%)	15(3%)	156(31.2%)	0.2539	0.0001
>50	282(56.4%)	62(12.4%)	344(68.8%)	(0.2739-0.2365)	
Residence					
Urban	293(58.6%)	23(4.6%)	316(63.2%)	0.4210	0.0158
Rural	128(25.6%)	56(11.2%)	184(36.8%)	(0.4655-0.3808)	
TB Type					
PTB	415(83%)	53(10.6%)	468(93.6%)	2 (4.1170-0.9715)	0.001
EPTB	6(1.2%)	26(5.2%)	32(6.4%)		

Prescription Analysis

Out of 500 cases, about 77.4% (387) of prescriptions contain more than 10 drugs and about 16.2% (81) prescriptions contain 7-9 drugs (Figure no: 2). The four anti-tubercular drugs were prescribed from the Essential Drug List of India 2017-18(Figure no:3), out of which Isoniazid, Ethambutol and Rifampicin (27%) were prescribed more. Among 500 cases, all the patients were treated with combination therapy, of which 69 % (343) were AKT-4 and 31 % (157) were AKT-3 respectively (Figure no: 4). Out of 500 prescriptions, higher incidence of drug interactions were found with Rifampicin + Pyrazinamide (36%) in which additive hepatotoxicity were observed (Figure no: 5).

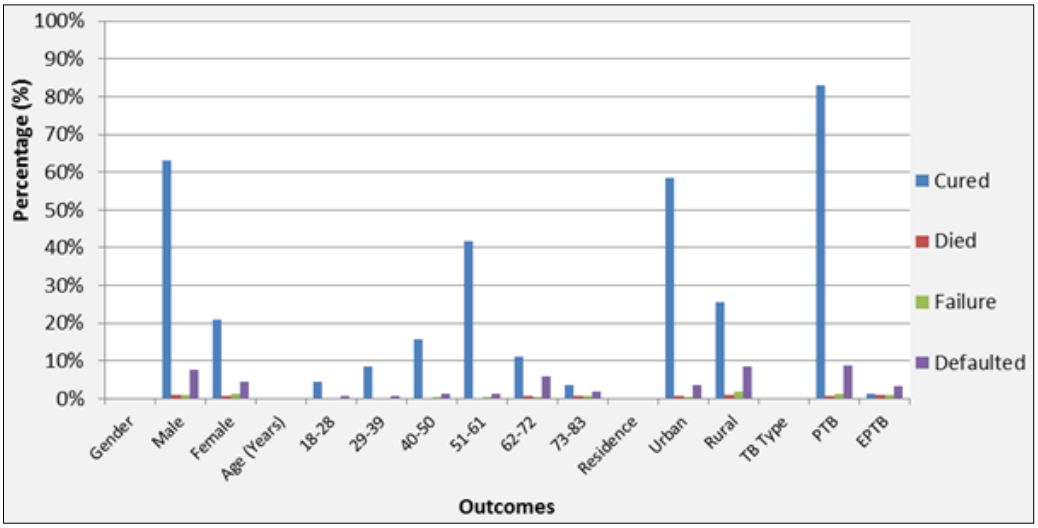

Fig 1: Treatment Outcomes of TB Patients by Gender, Age Groups, Residence and TB Type

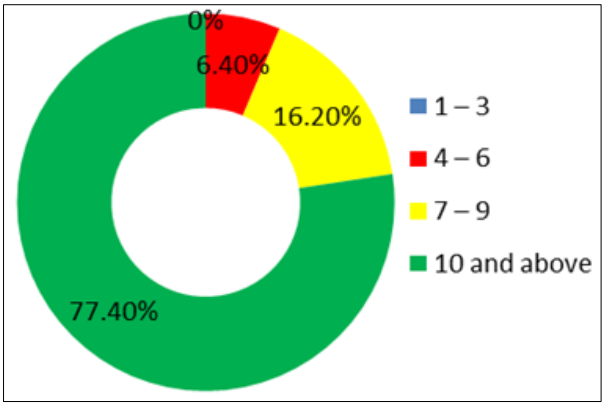

Fig 2: Evaluation of Prescription on the Number of Drugs per Prescription

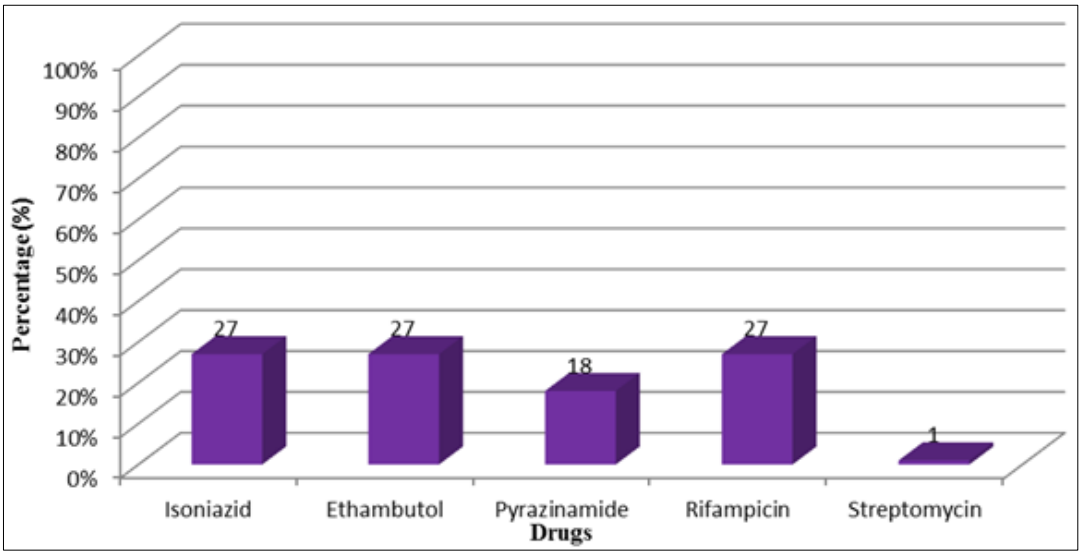

Fig 3: Analysis of Prescription for the Number of Drugs in the Essential Drug List of India 2017-18

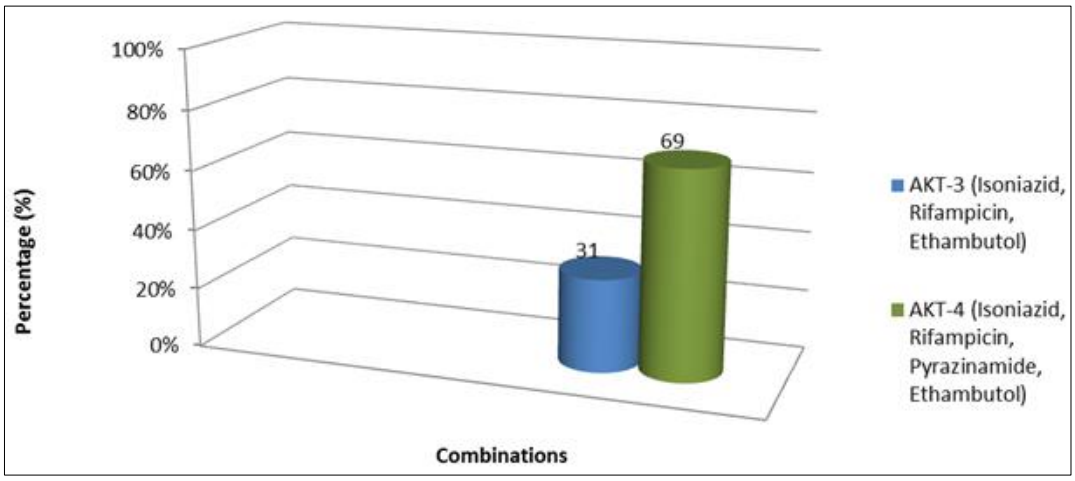

Fig 4: Analysis of the Prescription Based on the Combination Therapy

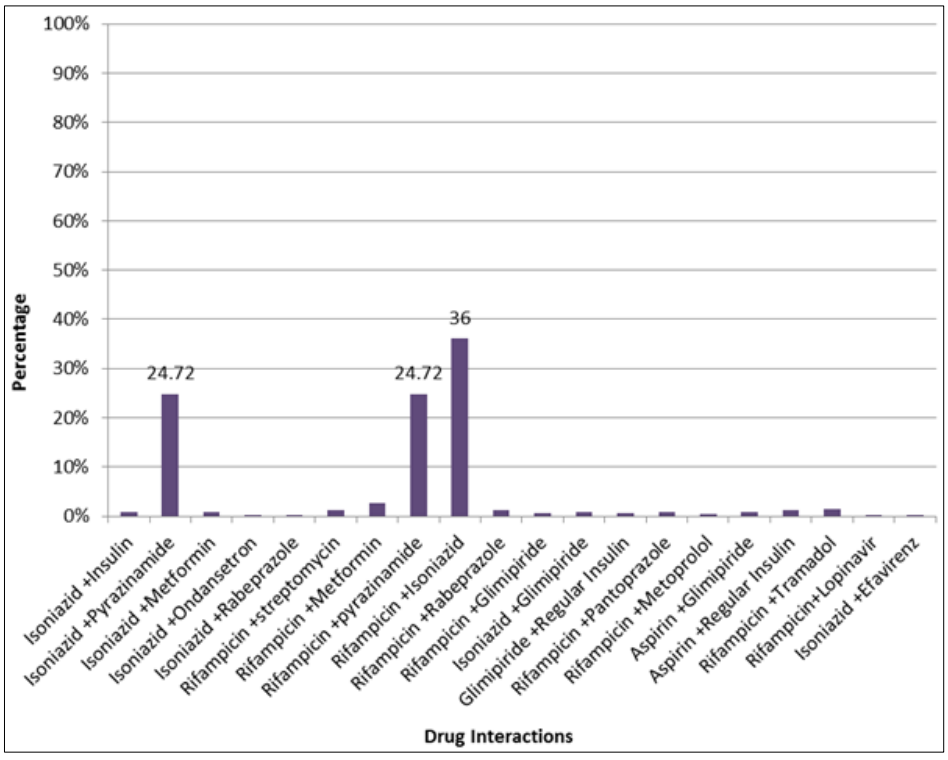

Fig 5: Analysis of Prescription based on Drug - Drug Interactions

Summary

Majority of the tuberculosis patients were males (73%). Concurrent to other studies conducted in southern Ethiopia (Gebremedhin Gebrezgabiher *et al.* [15]) and North West Ethiopia (Fauntahun Biadglegne *et al.* [16]) showed higher incidence in male tuberculosis patients of 61.35% and 58.5% This could be due to underutilization of the DOTS service by females or higher proportion of males being exposed to the infection in the area.

In this study, 41.6% of the registered TB patients fall in the age range between 51–61 years. This may pose challenges to the social and economic development of the community in the area and the nation at large. Older age has been reported to be a risk factor for death, partly due to co-infection and general physiological deterioration with age, and thus it is crucial to exercise close monitoring of TB treatment also in older patients.

The tuberculosis patients were classified according to the area of their residence. Majority of the patients were from urban area 63% and 37% patients were from rural area. Concurrent studies conducted in southern Ethiopia (Gebremedhin Gebrezgabiher *et al.* [15]) and North West Ethiopia (Fauntahun Biadglegne *et al.* [16]) showed higher incidence of patients, 66% and 98% respectively from urban area than rural areas. The lower treatment rate in rural patients is probably due to lower awareness of TB treatment and the long distance between their homes and the treatment center. Therefore, close monitoring and health education for rural patients is of great importance.

Out of 500 tuberculosis patients, the incidence of PTB was found to be 94% and EPTB was to be 6%. This might be due to the infectious nature of PTB. Concurrent study was conducted in Kocaeli TB dispensary; Turkey (Aysun sengul *et al.* [17]) found 92.6% to be PTB patients.

The average number of drugs per prescription is an important index for identifying the pharmacy practice in a health care setting. Our present study showed that more than 10 drugs were prescribed in 77.4% of prescriptions.

Use of drugs from Essential Drug List should be promoted for the optimal use of limited resources, for maximum safety and satisfy the health care needs of the majority of the population. In the present study for anti- tubercular drugs were prescribed according to Essential drug list of India 2017-18, of which isoniazid, ethambutol and rifampicin were prescribed more.

Patients with tuberculosis mostly undergo combination therapies that include drugs such as isoniazid, ethambutol, rifampicin and pyrazinamide. In the combination therapy for drug combination (AKT-4) was used in majority as approach in management.

Drug interactions were found in the prescription, the interaction between isoniazid + pyrazinamide were found in maximum that augments additive hepatotoxicity. These drug interactions maybe caused due to polypharmacy. Diabetes is a common comorbidity found in people with TB. A screening for all tuberculosis patients should be made mandatory. Out of 500 tuberculosis patients 35% were observed to have diabetes mellitus. HIV infection increases the chance of tuberculosis reactivation and infection. In our present study out of the 500 tuberculosis patients observed there is a low incidence of coinfection.

The tuberculosis patients on a minimum scale need to complete a treatment period of 6 months. In the present study, most of the patients were hospitalized for 5 – 7 months which increase the chances for problems such hospital acquired infections.

The present study found that the successful treatment rate of all tuberculosis cases 421 (84.2%) treated at the DOTS clinic in tertiary care hospital Salem district, Tamil Nadu was satisfactory. These findings can be contrasted to the study conducted in the year 2015 by (Muthukumar shanmugham *et al.* [18]) in the district of Kanyakumari has reported a treatment success rate of 84.59%.

The high treatment success rate observed in the present study might be due to the patient awareness and compliance towards DOTS therapy, the decreased amount of defaulted among (7.6%) the tuberculosis patients. It is more viable to treat when patients show more adherences to the therapy. Concurrent to other studies conducted in the Kanyakumari district (Muthukumar shanmugham *et al.* [18]) this study also found a low default of 9%, low rate of death 6% and lower rate of treatment failure 2%. The lower defaulter and death rate in the study is mainly due to the proper supervision and health education in the study area.

There is a high cured (58.6%) rate to patients from urban areas as compared with that of the rural areas (25.6%), the lower success rate in the rural patients is probably due to the lower awareness of tuberculosis treatment and the long distance between their homes and treatment center.

Close monitoring and health education for rural patients is of great importance. The patients in the mean age group greater than 50 had a higher treatment success rate compared to the age groups other age groups; older age has been reported to be a risk factor for death, partly due to coinfection and general physiological deterioration with age, and thus it is crucial to exercise close monitoring of tuberculosis treatment in older patients. Patients with PTB had a significantly higher treatment success rate compared with EPTB patients. This might be due to the delayed diagnosis of EPTB patients, which we suspect increases tuberculosis mortality.

HIV infection increases the chances of tuberculosis reactivation and infection. In this study HIV prevalence rate was 1% recorded among TB patients is much lower than in previous reports from Kanyakumari district 2.6%.

Conclusion

Adequate education to the community and family members on DOTS strategies is recommended. DOTS program should be introduced in all private clinics as a priority as suggested by the WHO. Home visits by the DOTS workers should be encouraged especially targeting the working, elderly and severely ill patients. TB will remain a major cause of morbidity and mortality, because of social issues like poverty, alcohol consumption, illiteracy, distance from health centers and stigma about the disease. These issues need to be addressed appropriately and aggressively so that the country could contribute significantly in achieving the WHO goal of reducing the global burden of TB and use of comprehensive approach will enhance the RNTCP programme.

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