

Abstracts

1. Comparing outcomes in new pulmonary sputum positive and sputum negative cases under RNTCP in rural India.

Aghijit Mukherjee, Rupak Singla, Indrani Saha, et al. **India J Tuberc** 2009; 56 (3), 144-150

The study was undertaken to find out the different treatment outcomes of new sputum smear negative cases, in a low HIV prevalence population and to compare the results with new sputum smear positive cases in the same population.

It was a retrospective record based study carried out at the Bagula Tuberculosis unit (TU), Nadia, West Bengal, catering to a population of approximate 0.5 million, where most of the people belong to low socio-economic status. A total of 2884 patients registered between January 1999 and June 2005 were evaluated for the study. Diagnosis, classification & Chemotherapy were done and the outcomes following treatment were noted as per the RNTCP guidelines.

Favourable outcomes were less in new smear negative cases, compared to new smear positive (84 % vs 86 %, $P = 0.002$). Death and default were more in new smear negative cases compared to new smear positive cases (death 6.8 % vs 3.7 %; default: 6.02 % vs 4.18 %), ($P < 0.05$). Failure and transferred out were non-significantly higher in new smear positive group.

The study concludes that, the smear negative patients had a worse treatment outcome compared to smear positive patients including lower favourable outcomes, higher deaths and defaults.

2. Perception of Tuberculosis patients about private providers before and after implementation of RNTCP.

K. Jaggaranjamma, R. Balambal, M. Muniyand, et al: **Indian J Tuberc** 2009; 56 (4): 185-190

Most of the person with chest symptoms in India approach private providers (PPS) for health care. It has been observed that patients who start treatment with PPS for tuberculosis frequently switch over subsequently to the public sector.

This study was undertaken to document the perceptions about PPS India's RNTCP and the reasons for discontinuation of treatment with PPS and subsequent attendance at a public provider.

This was a cross sectional study on patients registered under TB programme during 1997 and 2005 in rural and urban areas. The rural area was Chengai MGR district and urban area was Chennai city. During this period patients who were initially diagnosed and treated for TB in a private clinic and subsequently shifted to public health facility were considered for the study. A semi-structured interview schedule was used to collect the factors related to patients perception on PPS, the factors responsible for initiating treatment with PPS, reasons for discontinuing treatment with PPS and their willingness to continue treatment with Govt. Health facilities were collected. This data was compared with data collected in 1997 before implementation of RNTCP.

A total of 1000 and 1311 TB patients were registered during 1997 and 2005 respectively. Among them, 203 (20 %) and 104 (8 %) patients were identified having been initially diagnosed and started on TB treatment by PPS and subsequently shifted to Government health facilities. There were significant changes in reasons for selecting PPS between two periods: being convenient (47% vs 10%; $P<0.001$), quality care (41% vs 19%; $P<0.001$), motivated by others (49% vs 19%; $P<0.001$), confidentially (19% vs 9%; $P<0.05$) and known (6% vs 28%; $P<0.001$) respectively. Financial problems were the most common reason for discontinuation of treatment in both periods. The use of sputum test for diagnosing TB by PPS was significantly increased after RNTCP implementation.

This study suggests that slowly, perceptions of patients have changed towards PPS and RNTCP has begun to gain acceptance among patients in terms of convenience, confidentiality and personal care.

3. Costs incurred by patients with pulmonary tuberculosis in rural India.

KR John, P Dalyey, N Kincler, et al: *Int J Tuberc Lung Dis*, 2009, 13 (10); 1281-1287

The study was undertaken to measure costs associated with diagnosis and the complete treatment of Tuberculosis (TB).

Prospective structured interview of 100 new smear- positive adult patients being treated for TB in Tamil Nadu, India were selected evenly from 10 peripheral and regional Government TB centres between July and November 2007, which represented both urban and rural settings and large and small clinics.

Costs were analysed according to time periods and reported using mean and standard deviation (SD). Pre-diagnosis was defined as period between first symptoms and final TB diagnosis (including collection and interpretation of sputum smears) and post-diagnosis was defined as the period between diagnosis and interview. All costs were reported in 2008 \$US (US \$1 = 44 Indian rupees). Direct (out of pocket) and indirect (lost time) costs were identified by period of illness using a standardized questionnaire and uni-variate regression investigated predictors of total cost.

Seventy four percent of patients were male, with a mean age of 40.2 years. All were given a first line regimen, none had been previously treated. The mean direct cost was US\$ 34.91 (SD 46.94), the mean indirect cost was \$526.87 (SD \$ 375.71) and the total mean cost per patient was S 562.66 (SD \$ 287.48). Twenty five patients were admitted to hospital, at a mean cost of \$ 279.43 (SD \$ 142.88) per admission.

TB patients in India incur large cost associated with TB illness. The greatest single cost was time lost during admission. Total patients costs represent 193% of the estimated monthly income of a manual labourer.

4. Drug resistances in *Mycobacterium tuberculosis* isolated from tuberculosis patients in Kerala, India

BV Joseph, S Soman, I RadhaKrishnan et al: *Int J Tuberc lung Dis*, 2009, 13 (4): 494-499

This study was undertaken to analyse the extent of drug resistance in clinical isolates of *Mycobacterium tuberculosis* from patients attending various tuberculosis (TB) clinics in Kerala India. The study was conducted during the period 1998-2005.

Mycobacteria were isolated from sputum samples of TB patients. Isolates from 92 new and 104 retreatment cases were tested for resistance to four first - line drugs (isoniazid, rifampicin, ethambutol and streptomycin).

Twenty three percent of isolates from new cases and 14% from retreated cases were pan-susceptible and the rest were resistant to at least one of the drugs. Multidrug resistant isolates accounted for 5.4% among new cases noted that 18.5 % of the isolate were mycobacteria other than tuberculosis.

The study concludes that, there is an urgent need for statewide surveys to assess the level of drug resistance using quality assured culture and drug susceptible services. Considering that the RNTCP in India has been made operational nationwide, this kind of screening should be made mandatory under the programme to effectively control the spread of TB.

5. Risk of factors for new pulmonary tuberculosis patients failing treatment under the Revised National Tuberculosis Control Program, India.

R Singla, D Srinath, S Gupta, et al: *Int J Tuberc Lung Dis*, 2009, 13(4): 521-526

A prospective case control study was performed on patients enrolled from June 2006 to February 2008 in peripheral treatment centres under a tertiary level National TB Institute in south Delhi, India.

The objective was to study risk factors for new pulmonary TB patients failing treatment.

The profile of new pulmonary TB patients failing treatment (i.e. sputum smear positive at 5 months of treatment) and responders under the RNTCP were compared and risk factors associated with failures were analysed.

A total of 42 treatment failure cases and 76 controls were enrolled in the study. The presence of cavity on chest X-Ray (CXR), sputum acid fast bacilli (AFB) smear positivity at 2 months of treatment and the number of interruptions in treatment were independently associated with failures. Among failure patients at 5 months 17 (40.5 %) had negative sputum culture for *Micobacterium tuberculosis* and only 6 (14.3 %) had MDR-TB. When put on retreatment, patients with smear-positive, culture negative sputum had cure rates of 88.2% compared to 28.6% among culture positive patients.

The study concludes that the presence of cavity on CXR, sputum smear positivity at 2 months of treatment and the number of interruptions of treatment are risk factors for failure. Among failures based on smear examination the prevalence of MDR-TB is low and many patients have negative culture of *M. Tuberculosis*. Sputum positivity at the end of treatment may not be a reliable indicator of treatment failure.

6. The Bleach method improves the detection of pulmonary tuberculosis in Laos

S Ongkhammy, V Amstutz, H Barennes et al: **Ind J Tuber lung Dis, 2009, Vol 13 (9), 1124-1129**

Tuberculosis is a major health concern and the strategy of National Tuberculosis Programme is to reduce the transmission of infection by early detection of patients with pulmonary Tuberculosis and the use of DOTS. Case detection is based on direct sputum microscopy for AFB. It is observed that direct microscopy is less sensitive in patients with human immunodeficiency virus co-infection.

Several improvements have been suggested to improve the yield of microscopic detection. Among the many that have been suggested, Sodium hypochlorite (NaOCL) or bleach method as is commonly known has been used for over a century. The method uses a concentration of 2-5 % NaOCL to digest the sputum material and also to inactivate the mycobacterium without altering the structure of mycobacterium. So even when killed they can be stained and examined. This method also provides great security for persons doing the smear. Further centrifugation increases the bacterial concentration in the smear thereby increasing the positivity rate.

The National reference Hospital, Vientiane took up the study to assess the gain due to the bleach method and its feasibility in Laos. From the sample a direct sputum smear was made and stained by Ziehl-Neelsen method. To the remaining sample bleach method was used. It was added to an equal volume of sputum in the container. The mixture was homogenised by shaking and then incubating for 15 minutes at room temperature. Then a volume of 2-15ml was transferred to a disposable plastic conical tube with equal volume of distilled water. After centrifugation for 15 minutes at 2000 rpm, a drop of the pellet was transferred on the slide, dried, heat fixed and stained. Microscopic examination was done by two experienced technicians for 20 minutes per smear under 200 high-power microscopic fields.

Findings of the study showed that the positive rates were higher in bleach method. The bleach method increases the effectiveness of TB case finding, detecting 24 patients who were not detected by direct method. The bleach method yielded an overall increase in positivity of 33.5% besides being simple and very easy to use as highlighted by the author of this paper.

7. Performance of MTBDR plus for detecting high/ low levels of *Mycobacterium tuberculosis* resistance to isoniazid.

F Brossier, N Veziris, V Jarlier et al: **Int J Tuberc Lung Dis, 2009, 13 (2); 260-265**

Rifampicin (RMP) and isoniazid (INH) are the two main drugs used in treatment of TB. The rapid identification of drug resistance, particularly of multidrug resistance (MDR), in clinical isolates of *Mycobacterium tuberculosis* is the main challenge that needs rapid and adequate chemotherapy besides preventing the spread of resistant strains.

Several molecular methods have been designed to detect the drug-resistance in *M.tuberculosis*. A commercial DNA chip assay, Genotype, is a new version of MTBDR plus, which detects resistance to RMP and INH. The test is based on reverse hybridization of *rpoB* and *katG* amplicons to immobilized membrane-bound probes, allowing the detection of the most frequent mutations in *rpoB*.

A study was taken-up in National Reference Centre for Mycobacteria, Paris, to evaluate the performance of the Genotype MTBDR plus assay, an upgraded version of Genotype MTBDR in the detection of RMP and INH resistance, and to assess its advantages over the earlier version of the test.

The conventional method of drug susceptibility test (DST) by Proportion method on Lowenstein- Jensen media was used as standard control. One hundred and thirteen strains were used for the test and the amplification reactions. The genotype MTBDR plus test were performed as recommended by the manufacturer. The results obtained for rpoB in the 76 RMP-resistant strains were in total agreement with the sequencing results.

MTBDR plus retains the accuracy shown by MTBDR in detecting RMP resistance and is more sensitive in detecting INH resistance, particularly at low levels (minimum inhibitory concentration). The MTBDR kit as claimed by the researchers is an easy and rapid tool for genotypic detection of RMP and INH resistance in *M. tuberculosis*. It is efficient for detecting mutations causing RMP resistance, a surrogate for multidrug resistance, and significantly improves the detection of strains displaying low level of INH resistance.

8. Rapid, accurate determination of multidrug resistance in *M. tuberculosis* isolates and sputum using a biochip system.

Y Guo, Y Zhou, C Wang et al: *Int J Tuberc Lung Dis*, 2009, 13 (7), 914-920

Rapid identification of drug resistant strain would facilitate early administration of appropriate treatment and is crucial to reduce the spread of MDR-TB. Conventional drug susceptibility testing is time consuming. The automated system such as the BACTEC / BacTAlert though widely used, it takes 14 days to get result from the day the culture is obtained.

The biochip-based assay system, which includes a biochip, apparatus for sample preparation, chip hybridization, washing and data acquisition, and dedicated software for automated diagnosis, is designed to detect the most frequent observed mutations for RMP and INH resistance in the rpoB and katG genes and a promoter of the inhA gene. The total process is semi-automatic, and the automatic software analysis for the diagnosis of drug resistance eliminates some elements of operator error.

A study was taken up in National Reference Laboratory, Beijing, China, to assess the system. For this purpose, 330 mycobacterial isolates and 129 sputum samples for rifampicin (RMP) and 205 isolates and 105 sputum samples for isoniazid (INH) were taken. They were compared to DNA sequencing and conventional drug susceptibility testing. 5ml of sputum was first liquefied by adding equal volume of 10% NaOH and then incubated at 37° C before centrifugation for 5 minutes to get the pellets. Then after discarding the supernatant, the pellet was resuspended in 1 ml of 0.9 % saline and then centrifuged. Again after discarding supernatant the pellet was resuspended in 50 µl of 10mm Tris-EDTA Buffer, then transferred to an extraction tube. The extraion materials and reagents were supplied in the CapitalBio Universal Kit for bacterial DNA extraction. The total DNA was isolated by vortexing for 5 minutes. The extraction tube was then incubated at 95° C for 5 minutes, centrifuged briefly and then stored at -20° C until use. For cultured strains, 80 µl of DNA extraction buffer was added to a bacterial DNA extraction tube, and the bacterial colony was collected with a sterile tip and transferred into the tube. It was extracted in the same way as that was done for the sputum samples. The mycobacteria sample was heated at 85° C for 30 min to decontaminate before use.

A set of 210 non-*M. tuberculosis* cultures and 586 non-*M. tuberculosis* sputum specimens were used for threshold determination. DST was performed using the proportional and absolute methods in parallel using indirect DST. The genotypic results were found in agreement with the DST results.

The study indicates that the biochip system has a good overall performance. The biochip system has several clinically advantageous differences compared to other molecular diagnostic assays. First, the extraction of DNA has been simplified by using a bacterial DNA extraction kit. Secondly, the biochip contains probes for most of the frequently seen mutation types. Third a modified spotting buffer and a newly developed advanced hybridization system were employed in this study. Fourthly, a higher sensitivity was achieved by improving the MAPCR process. Lastly, the process is semi-automatic, and the interpretation software set to predetermined detection ranges was used to analyse scan data and to generate test reports. The biochip system provides a rapid, simple semi-automatic and reliable diagnostic tool for the simultaneous detection of *M. tuberculosis* as well as the most prevalent form of MDR-TB from culture isolates or sputum samples within 6 hours.

9. Cross-referral between HIV counselling and testing centres and smear microscopy centers in Tamil Nadu.

R Ramachandran, V Chandrasekaran, M Muniyandi et al: *Int J Tuberc Lung Dis* 2009, 13 (2): 221-225

The combined tuberculosis and human immunodeficiency virus (TB-HIV) epidemic demands effective and urgent action. The Objective of this study was to assess the effectiveness of the system of referral of TB suspects from the integrated HIV counselling and testing centres (ICTCs) to the designated microscopy centres (DMCs) in Tamil Nadu, and to identify reasons for dropping out.

The ICTC counsellors identified TB suspects among clients (excluding pregnant women and children) in six districts of Tamil Nadu in 2007 and referred them to DMCs, irrespective of their HIV status. From the records at ICTCs and DMCs, information was collected on the number of referrals to the DMCs, TB suspects attending DMCs and smear-positive TB cases with or without HIV. Clients who did not attend the DMCs were interviewed to elicit reasons for dropping out.

Out of 18329 clients counselled, 1065 (6%) were identified as TB suspects and referred to DMCs. Of these, 888 (83%) attended and 177 (17%) dropped out; 81% of the drop-outs were interviewed. Reasons for dropping out were multiple: 51% were due to the health system, 62% due to the disease and 62% due to personal reasons. Twelve per cent of DMC attendees were smear-positive.

The finding of this study indicates the ICTC-to-DMC referral system makes a significant contribution to the detection of TB cases. Reasons for dropping out were multiple, but are correctable. This study also probes into current policies on programme coordination and recommends strategies for strengthening the collaboration between the TB and HIV programmes.

10. A multidisciplinary method to map potential tuberculosis transmission 'hot spots' in high-burden communities.

EJ Murray; BJ Marais, G Mans et al: *Int J Tuberc Lung Dis*, 2009, 13 (6): 767-774

The Global control of the tuberculosis (TB) epidemic remains poor, especially in high-burden settings where ongoing transmission sustains the epidemic. In such settings, a significant amount of transmission takes place outside the household, and practical approaches to understanding transmission at community level are needed.

The Objective of this study was to identify and map potential TB transmission 'hot spots' across high-burden communities. The method draws on data that qualitatively describe a high-burden community in Cape Town, South Africa. Established transmission principles are applied to grade the potential TB transmission risk posed by congregate settings in the community. Geographic information systems (GIS) technology then creates a visual map, locating potential transmission 'hot spots' in the community. The finding of this study indicates that the places like Drinking places, clinics and churches (often gatherings in confined homes) emerge as gathering places that potentially pose a high transmission risk, particularly if located in overcrowded and impoverished areas of the community.

This proof-of-concept study demonstrates that combining qualitative techniques with GIS mapping may improve our understanding of potential TB transmission within a community and guide public health interventions to enhance TB control efforts.

11. Economic evaluation of public-private mix for tuberculosis care and control, India. Part I. Socio-economic profile and costs among tuberculosis patients.

A Pantoja, K Floyd, KP Unnikrishnan et al: *Int J Tuberc Lung Dis*, 2009, 13 (6): 698-704

The objective were to assess the socio-economic profile, health-seeking behaviour and costs related to tuberculosis (TB) diagnosis and treatment among patients treated under the Revised National TB Control Programme (RNTCP).

A total of 1106 new TB patients registered for treatment under the RNTCP in the second quarter of 2005 participated. Interviews at the beginning and at the end of treatment were conducted. A convenience sample of 32 patients treated outside the RNTCP also participated. The finding of this study indicates that among the TB patients, respectively 50% and 39% were from low and middle standard of living (SL) households, and 77% were from households with a per capita income of less than US\$1 per day. The first health contact was with a private practitioner in the case of >70% of patients. Mean patient delay was low, at 21 days, but the mean health system delay was 52 days. The average cost incurred by patients before treatment in the RNTCP was US\$145, and during treatment it was US\$21. Costs as a proportion of annual household income per capita were 53% for people from low SL households and 41% for those from other households. Costs during treatment faced by patients treated outside the RNTCP averaged US\$127. Patients treated under the RNTCP through a public-private mix approach were predominantly poor. Many of them experienced considerable health expenditures before starting treatment. Additional efforts are required to reduce the delays and the number of health care providers consulted, and to ensure that patients are shifted to subsidised treatment within the RNTCP.

12. Utilization of RNTCP services in rural areas of Bellary District, Karnataka, by gender, age and distance from health centre.

J Ahmed, VK Chadha, S Singh, B Venkatachalappa and P Kumar: **Indian J Tuberc**, 2009, 56: 62-68

Knowledge on utilization pattern of RNTCP shall provide important inputs towards its strengthening in rural areas. The objective of this study is to find out the utilization of RNTCP services by age, sex and distance from the residence to designated microscopy centres and treating Health centers. The study was carried out in Sandur TU of Bellary District, Karnataka. Information on age, sex and residence of persons with pulmonary symptoms and detected new sputum smear positive cases during the quarter 2003 to second quarter 2004 and their treatment outcome was obtained from the respective RNTCP records. Age and sex distribution of out-patients was collected from OPD Registers of one randomly selected DMC and its PHCs. A lesser number of males accessed the health care services. However, large no of males with pulmonary symptoms and new sputum smear positive cases utilized RNTCP services than female in the ratio of 1.6:1 and 2.5:1 respectively. This was due to higher prevalence of persons with pulmonary symptoms and sputum positivity rate among males. Sputum positivity rates were also lower among the elderly. Male symptomatics and cases were on an average older than females. About 70% symptomatics and 53% cases resided at more than four kilometers from the respective DMCs and treating Health centers. Treatment outcome was poorer among males with higher proportion of initial defaulters and among those residing at more than 20 Kms. The finding of this study indicates that there is need to make health services available to the male working population at convenient hours and to be more vigilant to screen persons with pulmonary symptoms among the elderly. Collection of the sputum specimen from eligible persons may be undertaken at PHCs which may later be transferred to DMC. Supervision and motivation of treatment for male TB Cases and those residing more than 20 Kms from the treating health centers requires to be strengthened.