

Contribution of Control Section (1959-2009) towards strengthening of Tuberculosis Control

The National Tuberculosis Institute (NTI), Bangalore was established in 1959 to formulate and evolve a practical, economically feasible and widely acceptable TB programme for the entire country. To fulfill the objectives, NTI had to carry out operation research activities in the field with relatively greater emphasis on rural areas. This was essential for formulating National Tuberculosis Programme (NTP) and evolving it further on the basis of experiences gained in its implementation to suit the changing scenario.

The Control Section derives its identity from the contribution it made towards various operational research to formulate and strengthen the TB control programme from time to time.

The major activities of the section are as follows:

Research:

- To formulate and evolve strategies for TB control programme after synthesizing the results of research studies, clinical trials on treatment for TB and to demonstrate its operational feasibility in field situation.
- To conduct operational studies related to case finding, treatment activities, modalities of management of TB patients with emphasis of Directly Observed Treatment to reinforce the TB control programme.

Training

- To impart training in communication and management skills to the state and district level officials involved in the tuberculosis control programme.

Supervision

- Periodical supervisions to evaluate the quality of the ongoing programme, field visits to districts for appraisal to assess the preparedness for starting the service delivery.

Staff Structure

Currently the section functions with one Sr. PHN, two Sister Tutors, four Health Visitors and supporting staff i.e, one Stenographer and a Group 'C' (Peon)

Research activities

The major responsibility of section is to conduct research for evolution of the programme. The section staff is involved in preparation of protocols, planning and execution of the fieldwork, data collection, maintenance of records, data analysis and preparation of the report for research studies undertaken by the Section.

In the formulation and evaluation of National Tuberculosis Programme, some assumptions were made which required to be tested under the normal administrative setup with minimum interference by the investigating team. At the time of formulation of the programme, several breakthrough studies on case finding, treatment and case holding were conducted. Subsequently, the section was responsible for development of Short Course Chemotherapy (SCC) regimens including intermittent regimens in collaboration with Tuberculosis Research Centre (TRC), Chennai.

Few of the important studies which have given valuable inputs to the programme are cited below:

In the late 60's the study on potential of case finding was undertaken in the neighboring districts to find out the optimum duration of cough for subjecting chest symptomatics for sputum microscopy for diagnosing TB cases¹. The objectives of the study were to understand some operational aspects of case finding in the Peripheral Health Institutions (PHIs) in an integrated programme. The questions addressed were, what is the frequency of persons having symptoms suggestive of pulmonary tuberculosis among the out patient attendees and how many cases could be found by direct sputum smear microscopy of these symptomatics and what would be the work load of TB case finding at the PHI. It was found that 2.5% of the 14881 total new outpatients of all age groups complained of cough for two weeks and more. From these chest symptomatic, 11% could be diagnosed as pulmonary TB cases. Each PHI had to examine only one or two sputum specimens in a day. The work load due to tuberculosis case finding was small and could be managed with the existing staff and case finding by direct smear examination of sputum at PHI had to be relied upon. Based on the study results, cough of two weeks with or without other symptoms was taken as optimum duration for case finding in the National Tuberculosis Programme.

In 1974, the potential efficiency of two standard regimens of one year duration - the daily self administered and the other supervised intermittent regimen was demonstrated². The relative merits of a fully supervised twice weekly regimen of streptomycin and INH twice weekly (SHtw) and an unsupervised daily regimen of INH and Thiacetizone (TH) in a routine programme condition were compared in terms of acceptability and response to treatment at one year. The acceptability was almost similar among patients with SHtw and with TH. However, the favourable response among the patients on SHtw and TH regimen was 68% and 60% respectively. Deaths among SHtw patients were 4% and 13.5% among TH patients, the difference being statistically significant. The response was directly related to the level of drug collection and supervised consumption. It was concluded that SHtw regimen was superior to TH as it prevented deaths and showed better bacteriological conversion. The superiority and importance of supervised regimen in obtaining better results in routine chemotherapy with available drug regimens was established. The operational feasibility and success of the intermittent supervised regimen which is the basis of directly observed treatment; now an important component of the DOTS strategy was thus established.

The issue regarding treatment of smear negative but radiologically active pulmonary TB cases was also studied in late 70's³. The main objective was to know the proportion of suspect cases treated under the programme requiring specific treatment with anti-TB drugs. It was shown that about 30% of the 557 patients labeled as radiologically active TB at the start of study were genuine cases of tuberculosis. In addition, 20% of the cases broke down in one year with bacteriologically positive disease when treatment was not offered. Thus it was demonstrated that

nearly 50% of the radiologically active TB cases diagnosed in the programme required anti-TB treatment. It was concluded that it would be appropriate to treat radiologically active cases (suspect cases) from clinical and epidemiological point of view after taking due precautions to remove non-tubercular cases by doing repeat sputum examination.

Chemotherapy of TB underwent revolutionary changes in the 1970s owing to the availability of two potent bactericidal drugs: Rifampicin and Pyrazinamide and marked the era of SCC. The studies conducted at Tuberculosis Research Center, Madras (now Chennai) and in Hong Kong have shown that fully intermittent regimen were equally effective with near 100% efficacy at the end of treatment followed by a relapse rate of 2-7% and that the reduction in adverse reaction was significant. Fully intermittent treatment had also been found to be highly effective. The Section was then involved in collaborative clinical trials with TRC, Chennai from 1978-1983 to observe the efficacy of intermittent short course regimens. Fully intermittent treatment regimens of six months duration having four drugs in the intensive phase and two or three drugs in the continuation phase given twice, thrice or once weekly were studied and found to be very effective⁴. A regimen of HRZS given daily for 3 months in India achieved almost 100% culture conversion at 3 months but 20% of the patients had bacteriologically confirmed relapses. Two five months regimen (2HRZS/3HZS and 3HRZS/2H₂Z₂S₂) tried in south India were effective and had low relapse rates (4-5%). This was the only study that investigated 5 month regimens and acceptable results were achieved only by using streptomycin for the entire 5 months treatment⁵. It was concluded that at present there is no practical regimen of less than 6 months duration that has given acceptable results in smear positive tuberculosis. The operational aspects of implementing SCC in the programme were also taken up by the section during this period. Study on acceptability of two six-month regimens was conducted in 1989, which yielded results quite close to those of clinical trials⁶.

With the advent of Revised National Tuberculosis Control Programme (RNTCP) based on Directly Observed Treatment Short course (DOTS) strategy, to revitalize the existing programme, the focus on operational research was shifted largely to strengthen the RNTCP. The main thrust of RNTCP is treatment under direct observation to achieve a cure rate of more than 85%. The feasibility of providing Direct Observation of Treatment (DOT) by grass root level DOT providers was successfully demonstrated through a study carried out in two rural districts of Karnataka during Sept 1994 to March 1995⁷. This was conducted before the pilot phase of RNTCP. The objective of the study was to compare the treatment success as assessed by sputum microscopy when drug distribution was undertaken by Dais (Dai method) compared with that following the usual DTP procedures (PHI method). The outcome in terms of smear negativity at the end of treatment period was 86.9% and 72.2% by Dai and PHI method respectively. Level of compliance as well as favourable response to treatment was significantly higher in Dai method in comparison with PHI method.

The subsequent study related to RNTCP was taken up in the urban set up of Bangalore Mahanagara Palike (BMP) to assess the effectiveness of new and re-treatment intermittent SCC regimens supported with initial and final bacteriological profile including the drug susceptibility status under the programme situation⁸. One of the highlights of the study was the high default rate of 25% and 45% observed among the smear positive patients receiving Cat I and Cat II regimens respectively under DOT. This had vitiated the treatment success of the cohort. Attempts were then made to analyze the problem of default in depth to offer operationally effective measures to improve treatment adherence and treatment success⁹. The predictive risk factors identified for default in an urban setting were males and alcoholics. Those returning for treatment after default and those having poor knowledge regarding the disease emerged as

additional risk factors among retreatment patients. Devoting attention to those at potential risk of default from initiation of treatment with close supervision and repeated counselling was considered a major input to minimize default to achieve the desired goal of RNTCP.

RNTCP with emphasis on high cure rate of 85% and case detection of 70% is expected to have an impact on TB situation especially on the level of drug resistance. There was paucity of information regarding the pattern of drug resistance among new and retreatment cases. The level of drug resistance among new smear positive cases and its trend is a sensitive indicator of the TB control programme efficiency and is an indirect reflection of the quality of TB control services in the area. In the above study in the metropolis of Bangalore in a cohort of smear and culture positive patients¹⁰, the pattern of drug resistance was examined in a cohort of 324 new smear and culture positive patients initiated on CAT I regimen under RNTCP from April to Dec 1999. The study findings showed that the resistance to streptomycin was highest (22.5%) followed by INH (13.7 %) and Multi Drug Resistance (MDR) was 2.2%. The age specific drug resistance was highest in those aged <25 years and declined significantly in the higher age group. Even among 226 smear positive retreatment patients the MDR was 12.8%. As the study was undertaken soon after RNTCP implementation in the area the results were expected to serve as the baseline information to subsequently assess the impact of the DOTS on the level of drug resistance particularly, the MDR during subsequent surveys.

To reduce the problem of default and ensure treatment success, models for involvement of Non-health workers for community based treatment observation in an urban setting were identified¹¹. Out of 300 patients who opted for treatment for shopkeeper, 244 took treatment continuously and the success rate was 89.3%. It was concluded that the shopkeepers could be effectively used as DOT providers because of the accessibility, availability and convenience to the patients.

The risk of relapse is the key indicator of the effectiveness of a regimen. Limited reports were available on long term follow-up of new and re-treatment cases treated under DOTS in India. However, data from various SCC control clinical trials on both daily and intermittent regimens has shown that majority of the relapses occurred in the first two years after treatment initiation and more so within 6 months after treatment completion. In this direction, a cohort of 271 new smear and culture positive patients treated under DOT with Cat I regimen was followed up after 2 years of treatment completion to know the relapse rate¹². The relapse rate in this cohort was 11.4%. The study demonstrated that fully intermittent Cat I regimen was effective in programme conditions irrespective of the pretreatment drug susceptibility status.

Diagnosis of smear negative but radiologically active patients has always remained an enigma. A prospective follow up of smear negative patients was subsequently undertaken to study the adherence to the recommended diagnostic algorithm, return rate of smear negative chest symptomatics begun on antibiotics and proportion of patients positive by culture among those declared as smear negative TB in an urban setting.

With highly effective treatment regimen available for TB, the role of Sanatoria is gradually becoming limited. In this context, the present status of Sanatoria in Karnataka state and its cost effectiveness was studied in detail¹³. The study findings suggested a need to redefine the role of sanatoria all over the country. Also, stringent guidelines for admission of seriously ill TB patients or those having post tubercular complication have to be formulated and complied with. Training of medical and paramedical staff in RNTCP may be made mandatory. Budget conserved after judicious utilization of the beds may be made to treat seriously ill TB patients at CHC / Taluk hospital.

The RNTCP has now attained the phase of consolidation, the research is focused on sustaining the programme performance, particularly, the cure rate. In this context, a Nation-wide study was undertaken covering different geographic, demographic and cultural settings to assess the problem of treatment non-adherence from patient and provider perspective¹⁴. The objective was also to identify predictors of defaults among new smear positive TB patients to suggest possible interventions to rectify the problem of default. The risk factors identified were alcoholism, illiteracy, having commitments during treatment, inadequate knowledge, poor patient provider interaction, lack of support from health staff, side effects to anti TB drugs and dissatisfaction with services provided. Majority of the risk factors for default were treatment and provider oriented and rectifiable with appropriate interventions. The study provided an insight into the various other issues involved in the delivery of DOT services by the providers and its utilization by patients keeping in view the treatment adherence to achieve the desired cure rate. Despite the vastness and diversities particularly, in the health infrastructure within the country, DOT was being followed in a considerable proportion of cases which was being translated to high treatment success rate.

Recognizing the association of TB and HIV the programme initiated the TB-HIV collaborative activities. To enhance and streamline these activities, a pilot study was taken up in two districts in South India with high HIV prevalence between July 2007 and March 2008^{15,16}. The objective was to assess the feasibility of Provider Initiated HIV Testing and Counselling (PITC) of all TB patients prior to implementation of this policy in the programme. Of the 4701 with unknown HIV at the time of TB treatment initiation, 3368 (72%) were referred to ICTC, and 3111 (66%) were newly tested for HIV. PITC implementation resulted in the ascertainment of HIV status for 70% of TB patients. Overall 8.8% of all registered TB patients were HIV infected and 37% were documented to have received Anti-Retroviral Therapy (ART). To conclude, though implementation of PITC could successfully ascertain HIV status for 70% of TB patients, ART uptake was poor. This suggested PITC implementation should include measures to strengthen and support ART referral, evaluation and initiation.

The cohort of HIV infected positive TB patients detected in the above study are now being followed up prospectively to evaluate their treatment outcome and survival status of eighteen months after treatment initiation. In addition, treatment related factors that could be associated with unfavourable outcome (death, default and failure) and mortality are also being studied.

The control section was thus involved in many operational research studies and focused on priority areas according to the need of the evolving programme. The knowledge gained from the research studies is disseminated through publications in the national and international journals and by presentations in the conferences. The section also has actively participated in research dissemination workshops organized by the institute as well as those held at the state and national level.

The section has contributed to research activities by reviewing the research proposals submitted to the programme by various organizations. The articles and papers submitted to various journals have been reviewed to assess its suitability for publication.

Planned future research studies

As mentioned earlier one of the priority areas in research is assessing the relapses after intermittent short course chemotherapy regimens given under direct observation in the

programme. It is proposed to participate in the multi-centric study to assess long term relapses among new smear positive cases treated with intermittent regimen under the programme.

Training activities

Training the work force at different levels for the TB control programme is one of the major activities entrusted to NTI. The Section plays a dominant role in all the training activities conducted in the Institute for various categories of health staff from within and outside the country. The emphasis now is on the modular training in RNTCP, exposure to fieldwork and development of interpersonal communication skills. Brief sensitization on the TB control programme and orientation was given to students of Pharmacology, B.Sc nursing, Microbiology, Health Assistants, Social work, etc., as and when required during their brief visit to the Institute.

The necessity to revise the training modules was felt in view of the experience gained from the evolving programme particularly, after the country wide coverage in March 2006, and the introduction of newer initiatives like TB-HIV collaborative activities, DOTS Plus, involvement of medical college and NGOs etc. The section is actively involved in periodic revision of the training modules.

Supervision activities

Supervision visits to districts within and outside the state from time to time also form an important activity undertaken by the Section staff as one of the key personnel in the supervisory team right from the inception of the National Tuberculosis control Programme. Before the districts embarked on starting RNTCP service delivery, appraisal visits were made to assess the preparedness of the district for launching the programme. In addition to periodic supervisory visits the section participated in the internal evaluation of districts to assess the quality of the ongoing programme.

The operational research studies and the training activities undertaken by the Section from time to time befits the changing scenario in TB control programme and offers continuous inputs for its further improvement. The Section, right from the inception has contributed enormously for the TB control programme and towards the fight against TB.

References

1. Baily GVJ, Savic D, Gothi GD, Naidu VB & Nair SS: Potential yield of pulmonary tuberculosis cases by direct microscopy of sputum in a district of south India; **Bull WHO 1967, 37, 875-92.**
2. Baily GVJ, Rupert Samuel GE & Nagpaul DR: A concurrent comparison of an unsupervised self-administered daily regimen and a fully supervised twice weekly regimen of chemotherapy in a routine out-patient treatment programme; **Ind J TB 1974, 21, 152-167.**
3. Aneja KS, Gothi GD & Rupert Samuel GE: Controlled study of the effect of specific treatment on bacteriological status of "suspect cases"; **Ind J TB 1979, 26, 50-57.**
4. Balasubramaniam R: Fully intermittent six months regimens for pulmonary tuberculosis in south India; **Ind J TB, 1991, 38:51-53**

5. Tuberculosis Research Center, Madras, National Tuberculosis Institute, Bangalore: A control clinical trial of three and five months regimens in treatment of sputum positive pulmonary tuberculosis in south India; **American Rev of resp dis** 1986, **134**, 27-33
6. Jagota P, Gupta EVV, Nagaraja Rao BS, Parimala N & Baily GVJ: The acceptability and efficacy of two regimens of Short Course Chemotherapy under conditions of an urban tuberculosis programme; **Ind J TB** 1989, **36**, 18-26.
7. Jagota P, Balasangameshwara VH, Jayalakshmi MJ & Islam MM: An alternative method of providing supervised short course chemotherapy in District Tuberculosis Programme; **Ind J TB** 1997, **44**, 73-77.
8. Sophia Vijay, Balasangameshwara VH, Jagannatha PS, Saroja VN, Shivashankar BA & Jagota P: Re-treatment Outcome of smear positive tuberculosis cases under DOTS in Bangalore city; **Ind J TB**, 2002 ,**49**,**195**.
9. Sophia Vijay VH Balasangameswara, Jagannatha PS, Saroja VN, Kumar P: Defaults among tuberculosis patients treated under dots in Bangalore city - a search for solution; **Ind J TB**, 2003, **50**, 185-196.
10. Sophia Vijay, Balasangameshwara VH, Jagannatha PS, Kumar P: Initial Drug Resistance among Tuberculosis Patients under DOTS Programme in Bangalore City; **Ind J Tub**, 2004, **51/1**, 17-22.
11. Mahadev B, Kumar P, Sharada MA : How effective are shopkeepers as DOT providers ? A study under RNTCP in Bangalore Mahanagar Palike Karnataka; **Ind J Tub**, 2006, **53**, 18-26.
12. Sophia Vijay, Balasangameswara VH, Jagannatha PS, Saroja VN, Kumar P: Treatment Outcome and Two Year Follow-up Status of New Smear Positive Patients Treated Under RNTCP in Bangalore City; **Ind J Tub**, 2004, **51**, 199-208.
13. Suryanarayana L, Kumar P, Sumathi G: Current status of functioning of Tuberculosis Sanatoria and Chest Disease hospitals in Karnataka; **Ind J Tub**, 2005, **3 (52)**, 162. (Summary of the paper published)
14. Sophia Vijay, Kumar P, Chauhan LS, Balasangameshwara HV, Unnikrishnan KP: Risk Factors Associated with Default among New Smear Positive TB Patients Treated Under DOTS in India; PLoS ONE | www.plosone.org April 2010 | Volume 5 | Issue 4 | e10043
15. Beena E, Thoma, Puneet K Dewan, Sophia Vijay, Aleyamma Thomas, Chauhan LS, Chandrasekaran V, Preetish Vaidyanathan, Soumya Swaminathan: Perceptions of Tuberculosis Patients on Provider-Initiated HIV Testing and Counseling - A Study from South India; PLoS ONE | www.plosone.org 1 December 2009 | Volume 4 | Issue 12 | e8389
16. Sophia Vijay, Soumya Swaminathan, Preetish Vaidyanathan, Aleyamma Thomas, Chauhan LS, Kumar P, Sonali Chiddarwar, Beena Thomas, Puneet K Dewan: Feasibility of Provider-Initiated HIV Testing and Counselling of Tuberculosis Patients under the TB Control Programme in Two Districts of South India; PLoS ONE | www.plosone.org 1 November 2009 | Volume 4 | Issue 11 | e7899