WHAT IS NEW IN THE DIAGNOSIS OF TUBERCULOSIS?*

PART 1 : TECHNIQUES FOR DIAGNOSIS OF TUBERCULOSIS

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Despite the discovery of the tubercle bacillus more than a hundred years ago, and all the advances in our knowledge of the disease made since then, tuberculosis still remains one of the major health problems facing mankind, particularly in developing countries. Presently, about one third of the world’s population is infected with Mycobacterium tuberculosis. It is estimated that currently there are about 10 million new cases of tuberculosis every year with 3 million deaths occurring world-wide¹. Currently, more people die of tuberculosis than from any other infectious disease. Death from tuberculosis comprises 25% of all avoidable deaths in developing countries. Nearly 95% of all tuberculosis cases and 98% of deaths due to tuberculosis are in developing countries and 75% of tuberculosis cases are in the economically productive age group². In India, out of a total population of over 1 billion, each year about 2 million develop active disease and up to half a million die³. It implies that every minute, a death occurs due to tuberculosis in our country. It also imposes a cost on our economy in terms of current and future output losses because of premature deaths and ill health⁴. To add to the existing burden, the situation is compounded by the large scale increase of new TB cases associated with increasing HIV infection. India is estimated to have 3.5 million HIV patients, and about 1.8 million of these are co-infected with TB⁵. The HIV seroprevalence among TB patients in India ranges from around 2 to 20%, with an estimated 60% of HIV infected persons breaking down with active TB disease in their life-time⁶. The diagnosis of TB with HIV positive patients is more difficult than in those without HIV infection. These issues need to be scrutinized when laboratories are required to cater to this group of population.

Early diagnosis of tuberculosis and initiating optimal treatment would not only enable a cure of an individual patient but will also curb the transmission of infection and disease to others in the community. Of the several distinct components of the TB Control Programme, case finding remains the corner stone for effective control⁷. However, there are no definite guidelines available as of today as to how to use optimally the number of diagnostic tests ranging from simple AFB microscopy to complex molecular biological techniques which have become available over a period, to establish or rule out diagnosis of tuberculosis in a given patient. The present write-up gives, in two parts, a brief description of the important techniques available for the (i) early diagnosis of tuberculosis, and (ii) drug susceptibility testing.

There are two basic approaches for the diagnosis of tuberculosis. The direct approach includes detection of mycobacteria or its products and the indirect approach includes measurements of humoral and cellular responses of the host against tuberculosis.

The diagnostic modalities should have certain desirable features viz. sensitivity, specificity, predictive value, speed, reproducibility, cost effectiveness, safety, simplicity, robustness and easy application for wider use. Ideally, the tests should be quantitative, at least in some measure, so that the infectiveness of the individual cases can be measured. This is especially important for decisions to isolate hospitalized patients and to provide preventive therapy to contacts. Diagnostic modalities must also be tailored to needs of the population and epidemiology of TB in that region. Epidemiologically, the countries can be grouped as non-endemic or endemic. The diagnostic algorithms are planned as
per specific needs and resources available in individual countries.

The diagnostic needs in disease non-endemic countries include identification of latent infection in high risk groups, diagnosis of patients in early phase of disease, faster detection of outbreaks (nosocomial and community transmission), and finding out patients with non-tuberculous mycobacterial disease. The diagnostic needs in disease endemic countries include improved microscopy, usage of liquid culture for childhood and extra-pulmonary TB, chemical and physical detection of mycobacterial antigens in paucibacillary condition, antigen capture, antibody detection, cellular immune recognition, nucleic acid amplification, and phage assay.

The diagnosis in endemic countries depends more on the use of labour intensive, easy to use methodology with minimum infrastructure or equipment. The need is to find a viable alternative for smear microscopy. This method has to have the following desirable features: results within 2 hours, simple training, easy interpretation, should function well in HIV positive patients and allow start of treatment as early as possible. Currently, less than 20% of the nearly 10 million predicted annual cases of tuberculosis are identified as smear positive.

**DIRECT APPROACH**

*Microscopy:* Microscopy is the simplest and most rapid procedure currently available to detect acid-fast bacilli (AFB) in clinical specimens by Ziehl-Neelsen staining method or its modifications. The limit of detection with this method is that it requires at least $5 \times 10^3$ bacilli per ml of sputum. Fluorescent staining method offers the advantage of screening the smear under low power where a large number of slides is screened in less time.

The results of smear microscopy can be influenced by the type of specimens, thickness of the smear, extent of decolorisation, type of counter stain used, and training and experience of the person examining the smear. Several approaches are being made to enhance the sensitivity of the smear microscopy. Concentration of sputum sample by cytocentrifugation has been found to enhance the sensitivity to almost 100%. Liquefaction of sputum with sodium hypochlorite followed by concentration of bacilli by overnight sedimentations enhances the sensitivity of smear microscopy close to 70% compared to culture. Similarly, treatment of sputum samples with Zwitterionic detergent, also known as C$_{18}$ carboxy-prophylbetaine (CB18) interferes with the innate buoyancy of the bacilli and enhances the result of smear microscopy.

**The main advantages of smear microscopy:**

(i) It is inexpensive, simple.
(ii) It is relatively easy to perform and read and detects transmitters of tubercle bacilli.
(iii) Results can be reported within hours of receipt of the sample. Provides reliable epidemiological indicators needed for the evaluation of the National Tuberculosis Control Programme.

For our country, the smear microscopy is likely to remain for the foreseeable future, the only cost effective tool for diagnosing patients with infectious tuberculosis and to monitor the progress of treatment. Under the Revised National Tuberculosis Control Programme (RNTCP), Government of India has ensured good quality sputum microscopy in all aspects in the entire RNTCP implemented areas of the country. This includes training, enhancing manpower, developing manuals, establishing uniform laboratory set up, ensuring supply of good quality reagents and microscopes and instituting quality control measures, right from the microscopic centres up to the state level laboratories. The various national tuberculosis institutes of the country are made responsible for monitoring the above-mentioned activities.
Isolation of mycobacteria from clinical samples by culture still represents the cornerstone on which definitive diagnosis of tuberculosis and other mycobacterioses relies. At present, mycobacterial culture can be performed on conventional egg based solid medium such as Lowenstein-Jensen medium and agar based ones, such as Kirschner’s or Middlebrook 7H9 broth. The major constraint of culturing mycobacteria in conventional media is its slow growth which necessitates a mean incubation period of at least 4 weeks\(^{11}\). The drug susceptibility tests to antituberculosis drugs require additional 4 weeks. Most of the laboratories in the developing world rely on solid media for culture of mycobacteria. The choice and preparation of specimens by various pretreatment procedures has tremendous influence on the sensitivity of results. The positivity of culture largely depends on the technique of decontamination used by various laboratories, viz the chemicals used for decontamination and the centrifugation method adopted for processing specimens for culturing mycobacteria by inoculating into solid or liquid media.

Although a combination of solid and liquid media is currently the gold standard for the primary isolation of mycobacteria, a few modern, rapid methods are also available. These include micro colony detection on solid media (including the rapid slide culture technique), septi-check AFB method, microscopic observation of broth culture (MODS), the BACTEC 460 radiometric system, BACTEC MGIT 960 system (Becton Dickinson), MB/Bac T system (Organon Teknika), and the ESP II culture system.

**Micro colony detection on solid media:** In this method, plates poured with thin layer of Middlebrook 7H11 agar medium are incubated and examined microscopically on alternate days for the first 2 days and less frequently thereafter. In less than 7 days, micro colonies of slow growing mycobacteria such as *M. tuberculosis* can be detected. Though this method is less expensive and requires about half the time needed for conventional culture, the recovery of mycobacteria is less efficient and it is labour intensive. Since *M. tuberculosis* grows more rapidly in liquid medium forming strings and tangles, which can be observed under the inverted light microscope with 40x magnification, this method is a better alternative for culturing tubercle bacilli\(^{12}\).

**Septi-check AFB method:** The septi-check AFB system consists of a capped bottle containing 30.0 ml of Middlebrook 7H9 broth under enhanced (5-8%) CO\(_2\) a paddle with agar media enclosed in a plastic tube, and enrichment broth containing glucose, glycerine, oleic acid, pyridoxal, catalase, albumin, polyoxyethylene 40 stearate, azlocillin, nalidixic acid, trimethoprim, polymyxin B and amphotericin B. One side of the paddle is covered with non-selective Middlebrook 7H11 agar, the reverse side is divided into two sections: one contains 7H11 agar with para-nitro-á-acetylamino-ß-hydroxypropiophenone (NAP) for differentiation of *M. tuberculosis* from other mycobacteria, the other section contains chocolate agar for detection of contaminants. This non-radiometric approach has the potential to expedite processing, obviate CO\(_2\) incubation requirements and facilitates early detection of positive cultures. This method requires about 3 weeks of incubation. The unique advantage of this technique is the simultaneous detection of *M. tuberculosis*, non-tuberculous mycobacteria (NTM), other respiratory pathogens and even contaminants. A multicentric study conducted in the USA has shown that the system gives a better culture result when compared to other methods including BACTEC 460 TB system\(^{13}\).

**Radiometric BACTEC 460 TB method:** This technique is specific for mycobacterial growth, wherein \(^{14}\)C labelled palmitic acid in 7H12 medium is used. This system detects the presence of mycobacteria based on their metabolism rather than visible growth. When the \(^{14}\)C labelled substrate present in the medium is metabolized, \(^{14}\)CO\(_2\) is produced and measured by the BACTEC system instrument and reported in terms of growth index (GI) value. The BACTEC system is also useful in the identification of *M. tuberculosis* using specific inhibitor, para-nitro-á-acetylamino-ß-hydroxypro-
piophenone. Using the same system, drug susceptibility tests can also be performed for all the anti tuberculosis drugs when sufficient GI is observed. Mycobacteria in clinical samples can be detected in half the time compared to conventional culture methods14.

A comparison of the BACTEC radiometric method with the conventional culture and drug susceptibility testing methods undertaken at the Tuberculosis Research Centre (TRC), Chennai showed that the rate of isolation of positive cultures was significantly faster with the BACTEC method, with 87% of the positives being obtained by 7 days and 96% by 14 days. There was a good correlation in drug susceptibility tests and most of these results could be obtained within 8 days by the BACTEC method15. By facilitating early diagnosis, the BACTEC method may prove to be cost effective in a population with high prevalence of tuberculosis.

MGIT 960 mycobacteria detection system: It is an automated system for the growth and detection of mycobacteria with a capacity to incubate and continuously monitor 960 mycobacteria growth indicator tubes (MGIT) every 60 minutes for increase in fluorescence. Growth detection is based on the AFB metabolic O2 utilization and subsequent intensification of an O2 quenched fluorescent dye contained in a tube of modified MGIT. A series of algorithms are used to determine presumptive positivity and alert the operator to the presence and location of positive tubes.

In a multi-centre evaluation of the MGIT 960 system, three high volume testing sites in USA compared the growth and recovery of mycobacteria to that of BACTEC 460 TB and conventional culture methods16. Comparison of average time of detection between paired specimens showed that the BACTEC 460 and MGIT 960 systems were 8.7 versus 8.6 days for M. avium complex (MAC) and 13.4 versus 15.5 days for M. tuberculosis respectively. It was revealed that MGIT 960 system exhibits greater potential as a rapid, accurate and cost effective method for a high volume mycobacteriology laboratory.

MB/BacT system: This is a non-radiometric continuous monitoring system with a computerized database management. The system is based on colorimetric detection of CO2.

Comparison of the performance of MB/BacT system with that of BACTEC 460 showed that the mean time for detection of M. tuberculosis by the BACTEC system was 11.6 days vs 13.7 days by the MB/BacT system. It was concluded that the MB/BacT with the computerized data management system is an acceptable alternative for BACTEC 460 method despite some minor disadvantages such as increased contamination and slightly longer time for detection of growth17.

ESP culture system II: This is a fully automated continuous monitoring system based on the detection of pressure changes within the headspace above the broth culture medium in a sealed bottle, i.e. either gas production or gas consumption due to microbial growth. A special detection algorithm is present in this system for the detection of very slowly growing mycobacteria.

The system was evaluated in clinical specimens for the detection of mycobacteria against BACTEC 460 and 7H11 agar solid medium. The mean time for recovery of all mycobacteria, M tuberculosis complex and MAC was found to be 13.1, 15.5 and 10.9 days respectively. Hence the ESP II culture system seems to be a reliable non-radiometric less labour-intensive alternative to BACTEC 460 system for the growth and detection of mycobacteria. However, as with other liquid culture systems, ESP II should be used in combination with a solid medium, not as a stand-alone system18.

Microscopic observation of broth culture: This is a rapid and relatively inexpensive method which compares very well with other well established systems in terms of both sensitivity and specificity, and also to some extent with speed when compared to solid media. Although this technique may be appropriate for disease endemic high-burden countries, it requires P2 Bio-safety cabinets, relatively expensive Middlebrook 7H9 broth, oleic acid dextrose catalase (OADC) and anti-microbial supplements and
IDENTIFICATION OF MYCOBACTERIAL SPECIES

Mycobacterial speciation is carried out by various methods ranging from conventional biochemical tests to modern high-tech molecular biological methods. These can be broadly classified as:

(i) Phenotypic characterization
(ii) Biochemical typing
(iii) Analysis of lipid: By gas chromatography, mass spectrum and high pressure liquid chromatography (HPLC).
(iv) Probe based identification: It includes peptide nucleic acid (PNA) fluorescence in situ hybridization assay for identification of mycobacterial species. PNA is a novel DNA mimic in which sugar phosphate backbone of DNA has been replaced by a polyamide backbone. The uncharged nature and high conformational flexibility of PNA allows PNA probes to hybridize DNA or RNA with excellent affinity and specificity. The sensitivity of the *M. tuberculosis* (MTB) probe targeting MTB complex was reported to be 98%. The sensitivity of NTM probes targeting NTM species, however, was only 57% since these do not target all non-tuberculous mycobacterial species.
(v) Sherlock mycobacteria identification system (SMIS): It uses computerized software to identify mycobacterial species on the basis of mycolic acid pattern generated by HPLC.
(vi) PCR restriction enzyme analysis: It exploits the 65 kDa hsp gene and 16s rRNA gene for identification purposes.
(vii) DNA chips: A technology still under development that appears promising involves oligonucleotide arrays or DNA chips (molecular biology coupled with computer technology), which have been designed to determine the specific nucleotide sequences diversity of the rpoB and 16S rRNA genes for species identification.

Detection and identification of mycobacteria directly from clinical samples

Both genotypic (molecular) and phenotypic methods are available with newer modifications for the diagnosis of tuberculosis as an alternative for smear microscopy.

Genotypic methods

*Polymerase chain reaction*: PCR allows sequences of DNA present in only a few copies of mycobacteria to be amplified *in vitro* such that the amount of amplified DNA can be visualized and identified. If appropriate sequences specific for *M. tuberculosis* are selected, 10-1000 organisms can be readily identified. The PCR methodology is rapid; results are available within a day of DNA extraction from the sample. A number of target genes of mycobacterial DNA have been evaluated for diagnosis by PCR and various other genotypic methods. The most common target used in the PCR is IS6110. This sequence is specific for *M. tuberculosis* complex and is present up to 20 times in the genome, thus offering multiple targets for amplification. PCR detection of IS6110 in sputum (in pulmonary TB) and peripheral blood (in extra-pulmonary TB), when compared to culture has a sensitivity, specificity and positive predictability of 83.5, 99.0 and 94.2% respectively. A variety of PCR methods have been described in the search for a sensitive and reliable screening test for tuberculosis in clinical specimens. Species-specific and genus-specific PCR methods are being used with various targets and modifications of PCR. The following are some of the methods used for identification of...
Transcription mediated amplification (TMA) and nucleic acid amplification (NAA): This approach identifies the presence of genetic information unique to *M. tuberculosis* complex directly from pre-processed clinical specimens. The NAA technique uses chemical, rather than biological amplification to produce nucleic acid, so that within a few hours these tests distinguish between *M. tuberculosis* complex and NTM in an AFB positive specimen. It is currently used only for respiratory specimens; use for non-respiratory specimens is likely in the near future.

A positive direct amplified test in conjunction with an AFB-positive smear is highly predictive of tubercular disease. However, the results of NAA are preliminary; mycobacterial culture is still needed for species identification/confirmation and for drug-susceptibility testing. A negative NAA with an AFB-positive smear indicates that the AFB is probably NTM. The *M. tuberculosis* direct test (MTD) and amplified mycobacterial direct test (AMDT) are highly sensitive (96%) and specific (100%) for *M. tuberculosis* on specimens that are smear positive for AFB. However, there are occasional false-negative or false positive results being reported, which are either due to the presence of fewer bacilli or due to contamination. Another disadvantage of the technique is that both viable and dead bacilli can give positive results as the DNA of both can be amplified.

The ligase chain reaction: It is a variant of PCR, in which a pair of oligonucleotides are made to bind to one of the DNA target strands, so that they are adjacent to each other. A second pair of oligonucleotides is designed to hybridize to the same regions on the complementary DNA. The action of DNA polymerase and ligase in the presence of nucleotides results in the gap between adjacent primers being filled with the appropriate nucleotides and ligation of the primers. The LCX *M. tuberculosis* assay kit (Abbot) is mainly being used for respiratory samples, and has a high overall specificity and sensitivity for smear positive and negative specimens.

**Table 1. Targets in commercially available kits**

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Method</th>
<th>Target</th>
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<tbody>
<tr>
<td>1</td>
<td>PCR</td>
<td>IS 6110</td>
</tr>
<tr>
<td>2</td>
<td>TMA</td>
<td>16 S r RNA</td>
</tr>
<tr>
<td>3</td>
<td>SDA</td>
<td>IS 6110</td>
</tr>
<tr>
<td>4</td>
<td>NASBA</td>
<td>16 S r RNA</td>
</tr>
<tr>
<td>5</td>
<td>b DNA</td>
<td>As for PCR</td>
</tr>
<tr>
<td>6</td>
<td>LiPA</td>
<td>As for PCR</td>
</tr>
</tbody>
</table>

**Phenotypic method**

**FAST Plaque TB**: This is an original phage based test, which uses the mycobacteriophage to detect the presence of *M. tuberculosis* directly from sputum specimens. It is a rapid, manual test, easy to perform and has a higher overall sensitivity as compared to sputum smear microscopy, in newly diagnosed smear positive TB patients. The test has a specificity of 98.7 – 99.0% and a sensitivity of 70.3 – 75.2%, as compared to smear microscopy, which has a specificity of 97.3 – 97.4% and a sensitivity of 61.3 – 63.4%.

**Serological diagnosis of Tuberculosis**

Most of the serological tests have low turn around time, high negative predictive value and are useful as screening tests. The limitation of these tests is low sensitivity in smear negative patients, HIV positive cases, and in disease endemic countries with a high infection rate. The tests are also expensive, require trained personnel and often have difficulty in distinguishing between *M. tuberculosis* and NTM.
Development of antigen detection assay for diagnosis of TB using sputum samples

Capture ELISA: A quantitative test to detect lipoarabinomannan (LAM) has been developed for the detection of TB in urine specimens. Another test being used in a field trial is the dipstick method (semi-quantitative) for the detection of LAM in both pulmonary and extra-pulmonary specimens. Preliminary reports have shown a sensitivity and specificity of 93 and 95% respectively.

Detection of LAM in sputum: The test is based on the capture antibody derived from murine source (murine monoclonal antibody against LAM). The rabbit antiserum against M. tuberculosis is used as a source of detector of the antibody. The specific and sensitive assay for the detection of LAM in sputum is potentially useful for the diagnosis of TB.

Antigen detection in body fluids: The advent of nucleic acid amplification technology (especially PCR) has overshadowed recent developments in antigen detection. However, free mycobacterial antigen at a concentration of 3-20 ng/ml can be detected in biological fluids such as cerebrospinal fluid (CSF) or pleural fluid. The most commonly used antigens include mycobacterial sonicates, extracted glycolipids, PPD, Ag5 (38kDa), Ag A60, 45/47 kDa Ag, Ag Kp90, 30 kDa Ag, P32 Ag, cord factor (trehalose dimycolate) and lipoarabinomannan. Most of the tests use polyclonal antibodies raised against crude mycobacterial antigens except for antigen 5 and LAM. The sensitivity of tests ranges from 40-50% and specificity 80-95%. The methods used for antigen detection are: the sandwich ELISA, inhibition ELISA, latex agglutination and reverse passive haemagglutination tests.

INDIRECT APPROACH

Detection of Antibodies for diagnosis of TB

Antibodies to mycobacterial antigens in sera of patients are detected either by using monoclonal or polyclonal antibodies. Cross-reaction by environmental mycobacteria is likely to produce false-positive results. Reproducible methods for purification of mycobacterial antigens have yet to be evolved; hence the results of most assays available at present are variable in different settings. It is also important to note that the immune response in mycobacterial disease appears to be associated with HLA Class II allotypes and different patients appear to recognize different antigens. It is thus unlikely that all tuberculosis patients will recognize a single antigen, and hence prove to be a handicap for the development of antibody-based detection systems for mycobacteria. Some of the newer approaches are as follows:

TB STAT-PAK: Immunochromatographic test based on the detection of antibodies has been evolved with a capability to differentiate between active or dormant TB infection in whole blood, plasma or serum. Its value in disease endemic countries such as India is yet to be ascertained.

Enzyme immuno assay for the detection of anti-mycobacterial superoxide dismutase antibody: Superoxide dismutase is an important secretory protein of M. tuberculosis and has been evaluated for the serodiagnosis of tuberculosis. It is found to be useful only in low prevalence countries (93-94% positive predictive value), compared to high prevalence countries like India and Egypt, where the positive predictive value drops to 77-88%.

Insta test TB: It is a rapid in vitro assay for the detection of antibody in active TB disease using whole blood or serum. The test employs an antibody binding protein conjugated to a colloidal gold particle and a unique combination of TB antigens immobilized on the membrane.

Some of the other commercially available antibody tests for pulmonary TB are listed in Table 2.

Miscellaneous diagnostic methods

To overcome the poor specificity of the existing skin test based on tuberculin, newer tests with defined antigens are needed to discriminate...
between the infected individuals from those with active disease. The latest of these is the MPB 64 patch test.

**Table 2. Some commercially available antibody tests for diagnosis of pulmonary TB**

<table>
<thead>
<tr>
<th>Name of the assays</th>
<th>Antigen used</th>
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<tbody>
<tr>
<td>MycoDot (Dot-blot)</td>
<td>Lipo arabino mannan (LAM)</td>
</tr>
<tr>
<td>Detect-TB (ELISA)</td>
<td>Recombinant protein Peptide</td>
</tr>
<tr>
<td>Pathozyme Myco (ELISA)</td>
<td>38 kDa (recombinant Ag) and LAM</td>
</tr>
<tr>
<td>Pathozyme TB(ELISA)</td>
<td>38 kDa (recombinant)</td>
</tr>
<tr>
<td>Antigen A60 (ELISA)</td>
<td>Antigen – 60</td>
</tr>
<tr>
<td>ICT diagnostics (membrane based)</td>
<td>38 kDa (recombinant)</td>
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</table>

**TB MPB 64 patch test:** MPB 64 is a specific mycobacterial antigen for *M.tuberculosis* complex. This patch test becomes positive in 3-4 days after patch application and lasts for a week. The test has a specificity of 100% and a sensitivity of 98.1%\(^3\). This promising test has been reported so far only in one setting in Philippines and needs to be carried out in other settings.

Another approach is the use of defined antigens for an accurate and rapid test for tuberculosis infection based on the detection of T cells sensitized to *M.tuberculosis* either by blood tests *in vitro* or skin tests *in vivo*\(^2\). Mononuclear cells from the peripheral blood are stimulated *in vitro* and production of IFN gamma from the sensitized T cells is measured by ELISA\(^3\). The antigens used are ESAT 6 (early secretory antigen TB) and CFP 10 (culture filtrate protein), which are being used as alternatives for PPD, for use in skin test (tuberculin testing) *in vivo*.

**Measurement of IFN gamma producing cells**

The ESAT 6 (6 kDa) is a specific antigen and a strong inducer of IFN gamma production by T cells of TB patients. The *M.tuberculosis* genome encompasses regions of differences (RD). These RD may encode potential antigens relevant for protection or diagnosis. The RD1 region is responsible for the secretion of ESAT-6 in response to TB. This antigen is recognized by T cells of TB patients and is not recognized by BCG vaccinated or healthy unvaccinated individuals. The levels of IFN gamma increases in treated compared to untreated patients, and is associated with improved immunity against TB. Hence this may be useful for monitoring TB patients\(^4\).

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HOW TO QUIT SMOKING?

The very first step for quitting is to shun ambivalence about quitting. And, making a firm resolve to quit at any cost. No sacrifice is big enough to justify giving up in midstream.

First, list all the perceived reasons why you must continue to smoke. Some of the common reasons listed by smokers are: fear of suffering caused by the withdrawal; frequent bouts of anger; weight gain or loss; less than usual appetite; lower mental concentration while at work.

Then, list all the benefits that accrue from quitting: that irritating whacking cough gone; fresh non-foul smelling breath; lower risk of developing lung cancer or other respiratory disorders; avoiding the considerable damage which tobacco use (smoking, sniffing, chewing) inflicts on heart and blood vessels; the money saved would become available for buying nutritional supplements, education of children, purchase of medicines for minor sickness, etc.

The comparison is so overwhelming in favour of quitting that almost any one could resolve to quit and gather the required motivation and self-confidence to do so.
COMMUNITY MEDIATED DOMICILIARY DOTS EXECUTION – A STUDY FROM NEW DELHI*

V.K. Arora¹, Neeta Singla² and Rajnish Gupta³

Summary:
Background: Directly Observed Treatment-Short Course (DOTS) strategy has been successful in global tuberculosis (TB) control. However, a few patients may have their reasons for non-acceptance of Directly Observed Treatment (DOT) despite the agreement with strategy in principle. A need exists for identifying the community DOTS providers for such patients, who could assist in their treatment delivery at the either-one’s residence.

Aim: The study was carried out to determine feasibility, acceptability and efficacy of domiciliary DOTS execution to TB patients through services of community DOTS providers.

Method: The study was prospectively carried out on those TB patients residing in New Delhi, who visited Institute between February 2001-January 2002 and were unable to accept DOTS due to a specific reason. Each of them identified a provider from the community, who could assist in a domiciliary DOTS execution at the residence of patient or provider.

Result: Out of 3127 TB patient-registrations over 1 year study-period, community DOTS providers were identified for the domiciliary DOTS treatment of 52 patients (about 2%), who were themselves unable to visit the centres owing to either inconvenient centre-timings mingling with job, study or household work (43), unavailability of nearby DOTS centres (4), social stigma (3) or physical disabilities (2). Most providers volunteering for such treatment executions were neighbours of patients and did so owing to human considerations. The DOTS was self-indicated as treatment of disease by 25 (48%) patients and 24 (46%) providers. Existing TB knowledge of incumbents increased significantly following the motivation by physicians. Sputum conversion at end of intensive phase occurred in 10 (91%) patients, while overall treatment success of study was observed to be 98% which was significantly better than that observed in the other patients treated at DOTS centres of Institute. No major problem was encountered during the treatment execution through providers.

Conclusion: Community DOTS providers were able to carry out a successful domiciliary DOTS execution in TB patients, who were unable to accept the treatment due to specific reasons. Number of incumbents having DOTS awareness was noteworthy and knowledge about disease increased further through physician’s motivation.

Key words: Tuberculosis, community, DOTS provider, RNTCP

INTRODUCTION

DOTS has currently become the essential operational strategy of global TB control. Many countries have been either able to meet the WHO targets (85% cure among new sputum positive cases and 70% case-detection) or have come close to meeting them.¹⁻¹⁰ Employing the strategy, Indian Revised National TB Control Programme (RNTCP), too, achieved a treatment success rate of 81% for new smear-positive, 82% for new smear-negative and 89% for extra-pulmonary TB (EPT) cases.⁷ The programme has been implemented across more than 670 million population of country by May 2003 (personal communication) and extensive efforts are on to cover the entire population as soon as operationally feasible.

As of now, DOTS programme has targeted the ambulatory population of country, which has been attending the Government health facilities for symptoms and getting themselves enrolled for a treatment institution. This section of patient-population has constituted back-bone of the country’s acclaimed DOTS-successes. However, people visiting the private providers get excluded as does un-estimated population facing the problems owing to inconvenient centre-timings (that menace with work), unavailability of nearby DOTS centres, unbearable travel costs, social stigma, disabilities etc. Efforts are already underway to effect a private-public mix in RNTCP¹¹, but care needs to be taken in respect of the remaining left-over patient-population. This section may constitute a formidable size for a particular area. There is a need, therefore,

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Studies, utilising provider services, have been sporadically carried out to deliver the DOT in past. A study from New York, involving coalition of public and private health care providers in a TB DOT Provider Network, was shown to facilitate the DOT delivery.12 Not much provider data is available in Indian context. Hence, present study was designed with the aim to determine a feasibility, acceptability and efficacy of domiciliary DOTS execution through a service-utilisation of community DOTS providers, who were identified by patients themselves for having reasons of treatment non-acceptance.

MATERIAL AND METHODS

The present study was prospectively carried out over 1½ year period between February 2001 and August 2002 at L.R.S Institute of Tuberculosis and Respiratory Diseases, New Delhi. It enrolled all those consecutive residents of city, who got diagnosed as TB patients at the Institute (between February 2001 and January 2002) and fulfilled the under-mentioned selection criteria.

Patient selection

The study-group was primarily constituted by those TB patients attending out-patient department of Institute, who were offered and even motivated to take DOTS but on their own gave reasons for the non-acceptance. These comprised of either inconvenient centre-timings (menacing with loss of hours of job, study or house-hold work), unavailability of nearby DOTS centres (resulting in unbearable travel costs), patient disabilities (making regular centre-visits difficult) or social stigma. There was no selection bias in respect of age, sex, race, religion or quality of living.

Provider identification

Each patient was told to identify a provider from community, who lived within <100 yards of his residence and could assist in DOTS execution at the either-one’s residence. Providers were selected amongst the friends, neighbours, employers, landlords or even distant relatives of patients. Upon identification, their details comprising of names, addresses and relationship with patients were entered individually on treatment cards. Their ability to collect drugs from centres and make regularly available for the patient-usage was appropriately assessed by physicians.

Assessment, motivation, training and data-recording

Knowledge of the enrolled patients and providers with respect to TB was initially assessed by a senior resident of specialty using ‘Motivation Assessment Scoring Scale’ (MASS) parameters13 that pertained to the cause, mode of transmission and treatment of disease. An additional determinant of the assessment was their awareness about DOTS. Subsequently, the health education and motivation was provided to all incumbents by the resident and consultant of specialty in order to rationalise their ideas both with regard to the disease and its treatment.

Specially designed questionnaire-based performa were filled by a staff-member at the RNTCP section of Institute for both patients and providers in order to record their socio-demographic profiles, mutual relationships, reasons for DOTS non-acceptance (by patient) or volunteering (by provider) and knowledge, attitude and practice (KAP) about TB. The last determinant was meant to assess a comprehensive ability of incumbents in respect of the education about disease earlier provided by physicians. The type and category of TB was entered separately for each case.

Community DOTS providers were trained to recognise the commonly possible undue effects of therapy, and accordingly, notify the same to either doctors or staff of programme. Subsequently, they were required to assist in the provision of requisite remedial measures. They were also trained to fill the patient treatment cards for purpose of record-keeping. In case of default, they were required to effect the defaulter retrieval in congruency with programme staff.
At 2 months of treatment, an incumbent’s experience of DOTS acceptance / provision was recorded in terms of the problems faced or satisfaction obtained by each of them. A provider’s expectation to receive an incentive (financial or certificial) in lieu of the service performed was also entered in record.

**DOTS – execution**

Providers were supposed to collect medications regularly for the patient administration from respective DOTS centres on showing the empty blister pack of previous week’s / month’s supply. The centre-staff interacted with them to determine difficulties faced during patients’ treatment execution and to suggest remedial measures. DOTS was administered either at the residence of patient or of provider that was decided at with their mutual consent although the latter trend was encouraged as far as possible. Programme-guidelines were followed in respect of treatment-execution, follow-up and defaulter-tracing of patients with the difference that services were mediated through community DOTS providers. During entire course of therapy, a resident doctor made regular telephonic enquiries from providers in order to deliver them any requisite assistance in respect of desired DOTS execution of patients. Providers were not paid anything by the Institute for services carried in respect of their patients.

Entire DOTS provider-related data was subjected to the analysis for statistical significance with Z-test for age and chi square test for other parameters. It was also compared with corresponding data in respect of patient-distribution and treatment outcome from the DOTS centres under Institute. Further, rates of sputum conversion and treatment success between the ‘domiciliary’ and ‘centre’ based approaches of DOTS execution were analysed for statistical significance by Z test.

**RESULTS**

Out of the overall 3127 TB patients registered within Institute between February 2001 and January 2002, 52 (about 2%) were unable to accept DOTS owing to: (a) the inconvenience due to unsuitable centre-timings (43 cases or 82.7%) menacing with loss of hours of job (28 cases or 65%), study (13 cases or 30%) and household work (2 cases) or due to unavailability of nearby DOTS centres (4 cases or 8%) resulting in unbearable travel costs (b) the social stigma (3 cases) holding therapy-institution particularly in young unmarried females and (c) the disability (2 cases) making regular centre-visits difficult. The disabilities in two cases were poliomyelitis and bilateral optical atrophy, with latter presumptively occurring due to birth trauma.

Thirty patients (58%) had EPT with the 10 being of pleural effusion, 14 of lymphadenopathy, 1 each of abdominal, tonsillar and bone & joint involvement, 1 of combined bone and lymph node affection, and 1 of discharging para-umbilical sinus. The remaining 22 patients (42%) had pulmonary TB, of whom, 11 had sputum positive disease (all being new cases). Category-wise patient-distribution was 25 (48%) for Category I, 4 (8%) for Category II and 23 (44%) for Category III.

**Provider -patient relationship**

The community DOTS providers were identified either as neighbours (24 cases or 46.2%), friends (11 cases or 21.2%), distant relatives (12 cases or 23%), employers (4 cases) or landlord (1 case) of patients. Majority of them volunteered for DOTS provision on account of the sympathetic neighbourly considerations, moral grounds and service concern for community. 87% of patients, when asked to identify the alternative DOTS provider other than enrolled one, did not give any other option.

**Socio-demographic profile**

The socio-demographic profile of patients and providers has been outlined in table 1. No incumbent existed in the age-category of <10 or >60 years. Both groups predominantly comprised of middle-aged males. The ratio of males to females was 1.2:1 for patients and 3:1 for providers. Servicemen significantly constituted majority in both groups. Further, 47 (90%) of DOTS providers were found to be literate.
Prior to motivation, awareness was found in 16 (31%) patients for ‘germ’ being a TB cause. 15 (29%) knew about the inhalation being a mode of transmission. However, knowledge with respect to the curability, need for prolonged and regular treatment and the possible outcome in case of disruption was possessed by two-third of patients. 25 (48%) self-indicated DOTS as the specific treatment and 31 (about 60%) recollected hearing previously of it at the provision of reference. Patient-survey performed at RNTCP section of Institute showed that 47 (90%) were aware of the TB cause and 31 (about 60%) identified cough and fever as the symptoms of disease. 50 (96%) knew that medication could provide the cure. An equal number was aware of the need for a minimum of 6-months therapy and for a regular treatment intake. 51 (98%) identified ‘morning’ as the correct time of drug-intake and 46 (89%) did not think it necessary to take special diet, exercise or alternative medication for getting cured from disease. An almost three-fourth (73%) favoured the re-start in case of treatment-interruption. 42 (81%) opined that coverage of mouth during coughing and sneezing procedures could prevent the spread of disease to house-hold members. 8 (19%) proposed the observation of additional precautions like proper sputum disposal and maintenance of distance with family members and

<table>
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<th>Parameters</th>
<th>Patients</th>
<th>DOTS providers</th>
</tr>
</thead>
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<tr>
<td>Age (in years):</td>
<td>Number</td>
<td>Percentage(%)</td>
</tr>
<tr>
<td>≤ 10</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>11 – 20</td>
<td>13</td>
<td>25</td>
</tr>
<tr>
<td>21 – 30</td>
<td>19</td>
<td>36.5</td>
</tr>
<tr>
<td>31 – 40</td>
<td>6</td>
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<td>8</td>
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<td>24</td>
<td>46.2</td>
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<tr>
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<td>Service personnel</td>
<td>25</td>
</tr>
<tr>
<td>Businessmen</td>
<td>3</td>
<td>5.8</td>
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<td>Students</td>
<td>13</td>
<td>25</td>
</tr>
<tr>
<td>Retired personnel</td>
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<td>1.9</td>
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<tr>
<td>Housewives</td>
<td>8</td>
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<tr>
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<td>Post graduate</td>
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* Statistical analysis: Z – test for age (significant for both patient and provider at 1% level) and Chi square test for sex (significant only for provider at 1% level), occupation (significant for both patient and provider at 1% level) and education (significant for provider at 1% level).

** Data available in respect of DOTS provider only.

Patient- KAP
children. However, 24 (46%) were of opinion that there was no need for a follow-up during the treatment.

At 2 months of treatment, 51 (98%) patients were found to be taking therapy regularly and 50 (96%) were satisfied with it. 45 (87%) did not undergo any adverse drug effects and the remaining experienced effects of only mild nature. The survey demonstrated an overall tolerance of therapy by 47 (90%) patients.

**DOTS provider-KAP**

Assessment of provider’s knowledge prior to motivation showed results not significantly different from those of the patients in relation to MASS parameters. 24 (46%) self-indicated DOTS as the specific treatment and 31 (62%) recollected hearing of it on provision of reference. Provider-survey carried out at the RNTCP section of Institute revealed that 49 (94%) were aware about ‘germs’ being the TB cause and a nearly half suggested the cough and fever as identifiable symptoms of disease. All, except one, knew about ‘medicine’ being the cure and an equal number was aware of the need for a minimum treatment of 6-months, a ‘morning’ intake of medication and a regularity of therapy. 47 (90%) did not feel it necessary to take a special diet, exercise or alternative medication for the cure. 36 (69%) favoured the re-start of therapy in case of treatment-interruption. Coverage of mouth during coughing and sneezing procedures for the prevention of spread to household members was proposed by 44 (85%), one-fourth of whom, mentioned the similar observation of additional precautions as in patient-survey. An essentiality of follow-up was validated by the two-third of providers.

At the end of 2 month-treatment, it was found that 25 (48%) providers were executing the DOTS at patient’s residence itself, whereas patients were visiting them for a drug intake in 22 (43%) cases. The drug collection and administration occurred either way in remaining 5 cases. Treatment boxes were retained by 46 (89%) of DOTS providers in comparison to the retention by patients. 51 (98%) providers imparted the therapy regularly. A three-fourth number did not face any problem with DOTS provision, while the remaining experienced only minor hurdles that could be sorted out through mutual adjustment with their patients and through assistance provided by doctors during telephonic conversations or by staff at times of drug-collection. All providers were satisfied with the way their mediation brought about the domiciliary DOTS execution. Further, 43 (83%) did not expect incentives either monetary or certificial for their services despite the minority aspiring for latter. No change was noticed in the manner of DOTS execution between patients and providers even at the end of treatment.

**Treatment outcome**

Sputum conversion at end of intensive phase in provider-mediated DOTS execution was found to occur in 10 (91%) cases. Outcome for all 52 study-enrolled patients at end of treatment is presented in table 2. Excluding 1 defaulter, all others either satisfactorily completed the treatment or got cured resulting in overall success rate of the study at 98%. Attempts to trace the defaulter did not meet with success, since he shifted the residence without a prior knowledge of the either provider or

<table>
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<th>Outcome*</th>
<th>New smear positive pulmonary</th>
<th>Smear negative pulmonary</th>
<th>Extra-pulmonary</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Cured</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>Completed</td>
<td>-</td>
<td>11</td>
<td>30</td>
<td>41</td>
</tr>
<tr>
<td>Defaulted</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>11</td>
<td>30</td>
<td>52</td>
</tr>
</tbody>
</table>

* No patient existed in the outcome-categories of ‘died’, ‘failure’ and ‘transfer out’

Table 2: Treatment outcome of patients

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programme staff.

Comparative data from Institute’s DOTS centers

In comparison to the 52 patients identified for a DOTS execution through community providers, other 3075 accepted DOTS at the Institute’s DOTS centers over the same time-period of study and were distributed as 554 (18%) cases of EPT and 2521 (82%) cases of pulmonary TB. Of latter, 1718 were sputum positive cases, with 1065 (62%) having a new smear positive disease. An overall number of 1406 (46%) patients belonged to Category I, 836 (27%) to Category II and 833 (27%) to Category III type of TB.

Sputum conversion at end of intensive phase, as observed in the Institute’s DOTS centres, occurred in 947 (89%) new smear-positive patients of Category I. 941 (88%) new and 436 (67%) belonging to Category II got cured during the corresponding 1-year period of centre-based DOTS execution. While there were 1207 others who completed treatment in the either category of disease resulting in overall treatment success rate of 84% for patients receiving DOTS at centres, remaining fell under the outcome of either ‘died’, ‘failure’, ‘default’ or ‘transfer-out’.

A comparison of the treatment outcomes of patients treated with DOTS via ‘domiciliary’ and ‘centre’ based approaches showed that their rates of sputum conversion ($Z_{calc} = 0.23$) were insignificantly different at 5% level of significance, whereas the treatment success ($Z = 6.6$) was significantly higher in former at 1% level of significance.

DISCUSSION

Analysis of reasons, for which the enrolled patients were unable to visit DOTS centres, suggests that the bulk of group was either employed in service or was constituted by students and house-wives and found the centre-timings inconvenient owing to resulting loss of work-hours. The unavailability of a nearby DOTS centre was observed in only 8% of cases and highlights existence of a satisfactory programme-network within metropolis. Whereas two disabilities, namely poliomyelitis and bilateral optical atrophy, made the regular centre-visits genuinely difficult for concerned patients, it is unfortunate that TB stigma prohibited therapy-institution in at least 3 young females for fear that their marriages could get jeopardised. This number would perhaps have been higher but for a successful persuasion of many others towards the centre-based DOTS acceptance. Even recent Indian studies have reported the stigma persistence in both rural and urban populations of country.14,15 There is a need, therefore, to address such social concern during the carriage of Information, Education and Communication (IEC) campaign within communities of even metropolitan areas.

46% of patients selected their ‘neighbours’ for the requisite DOTS provision. All providers lived within close proximity of their patients that facilitated the process of DOTS execution in present study. The fact, that most providers opted for job out of humane considerations without any monetary aspiration, appreciably highlights concern of society towards the ailing TB patients and shows its readiness to participate in the process of their cure from disease. It was further encouraging to note that during a treatment execution, only minor problems were faced by the one-fourth of providers, which could be appropriately sorted out through assistance of doctors and staff and through mutual adjustment with their patients.

The knowledge about cause of TB was found to be relevantly possessed by 31% of enrolled patients that was better than the 8% reported in a past Indian study on metropolitan TB patients.16 Treatment-perceptions in two-third of patients appropriately reflected the curability of disease as well as period of therapy. The observed values were lower for former and of the same order for latter in comparison to those correspondingly reported earlier.14 However, the post-motivational KAP survey of enrolled patients revealed that almost 90% or more were able to correctly mention the cause, preventive measures and treatment of TB (in terms of availability, duration and rhythm). This suggests that physician efforts at patient’s education had a significant impact.
on recipient’s general awareness about disease. Similarly, the overall results of pre-motivational assessment and post-educational KAP survey in respect of providers’ TB knowledge were not different from those observed under patient-survey. Yet, the misconception of a large number of patients with regard to the follow-up during treatment requires careful addressal of issues in the programmes concerning patient-education.

A notable fact with regard to perception of disease was the prevalence of specific DOTS awareness amongst nearly 60% of patients and 62% of providers in respective surveys. The observations give a fairly reasonable account of community awareness about DOTS against the hind-sight of a scantily available literature on it. Underlying reasons for such appreciable DOTS awareness within metropolis appear to be the regular conduction of IEC campaigns, propaganda-carriage by popular print and electronic media of communication and message-spread through banners, advertisements, hoardings, seminars and continuing medical education programmes. Assumably, satisfactory existence of a community DOTS awareness along with health education provided by RNTCP staff played the key role in effecting a good overall DOTS acceptance (98%) by the patients at Institute’s DOTS centres.

Present study reveals a predominance of EPT cases over pulmonary type of disease, an observation, which is at variance from the general trend of disease reported in Indian population with an 8 times more common occurrence of the latter. A higher prevalence of pulmonary TB than EPT (82% vs 18% respectively) was also observed in the patient-distribution pattern of Institute’s DOTS centres. An underlying factor for higher EPT occurrence in a provider-mediated DOTS execution could be the enrollment criteria of patients, who were selected randomly at ‘as and when come basis’ without following any consecutive (as done for the centre-based approach) or periodic norm of case selection. The randomness of case-entries would obviously give a less meaningful data for comparison than that obtained with degree of regularity. However, in the same context, another consideration deserves mention since most EPT cases possess a milder form of disease as compared to those with pulmonary affection. At least a few of them may give greater priority to their occupational compulsion than the necessity of treating basic ailment with DOTS through regular centre-visits. Since large number of our cases were servicemen or students, a few with EPT might have taken an undesirable course of DOTS non-acceptance eventually resulting in the provider-recruitment for them.

As compared to ‘centre’ based approach, the DOTS execution of TB patients done via ‘domiciliary’ approach through services of community DOTS providers had a significantly better treatment success rate (84% vs 98% respectively) despite the observed difference in number of incumbents between them. Several reasons may contribute to the observations. Foremost of these appears to be the convenience of a ‘domiciliary’ DOTS delivery to these patients that saved the hours of job, study or household work for concerned majority. Secondly, the patient-provider-physician rapport created through telephonic conversations and the regular staff-interaction with providers during drug collection not only helped to sort out minor problems of therapy-execution, but also assured the observation of DOT component over entire treatment course against the ‘appropriate’ supervision observed during continuation phase in a ‘centre’ based approach. Finally, apart from a free delivery of drugs, investigations and physician-consultations to the patients attending either DOTS centres or receiving treatment at homes, the latter also did not have to spend anything on their travelling to respective DOTS centres. As the Institute did not make any payment to providers for their services, travelling costs in majority of cases were apparently borne by them out of a humane consideration for their patients, though possibility of a few recovering the same either in part or in totality from treatment beneficiaries is not entirely ruled out. Yet, it is obvious that the ‘domiciliary’ DOTS execution remained a cheaper option of treatment acceptance not only for the 4 study-enrolled patients required to travel distantly but also possibly for many others who did not mention the ‘travel’ expenses as chief reason of treatment non-acceptance.

Although results of the ‘provider’ mediated DOTS execution were found to be better than the
standard ‘centre’ executed treatment, former should not be seen as the replacement for latter. This is because such arrangement would take away from health system the essential factor of ‘supervision’ of a patient’s intensive phase of treatment, and in absence of the regular provider-interaction, could result in greater number of defaults. Eventually, it might end-up in putting the strain upon existing resources and complicating the scenario of disease. Therefore, community DOTS providers should be identified selectively only for those TB cases who cannot accept DOTS on genuine grounds. Though our study enrolled only about 2% of these cases, other programme-areas within country could have a greater number of such kind. Since enhancement of programme-coverage would always be desirable, all cases with the limiting factors for DOTS acceptance should be subjected to suggested ‘provider’ mediated alternative strategy of DOTS delivery. A need also exists for the further carriage of similar studies that could bring out more facts on the subject in Indian programme conditions.

ACKNOWLEDGEMENTS

Authors are grateful to Dr. Rohit Sarin (Assistant Medical Superintendent of Institute), Dr. Khalid (Epidemiologist) and entire programme staff for having made valuable contributions towards the conduct of study.

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**HIV INFECTION SEROPREVALENCE IN TUBERCULOSIS PATIENTS**

Zuber Ahmad¹, Rakesh Bhargava², D.K Pandey³ and K. Sharma³

**Summary:**
Setting: Department of Tuberculosis and Chest Diseases, JN Medical College, Aligarh.

Objective: To find out (1) the prevalence of HIV infection in tuberculosis patients in and around Aligarh and (2) clinical presentations of tuberculosis in HIV infected patients and the associated complications.

Methodology: All tuberculosis patients diagnosed between August 1996 and June 2001 were screened for HIV infection by ELISA technique after informal consent and the positive results were re-confirmed by repeat ELISA test.

Results: Prevalence of HIV infection rose from 0.8% in 1996-97 to 0.91% in 1997-98, 1.24% in 1998-99, 1.8% in 1999-2000 and 2.82% in 2000-2001. Out of total 91 HIV positive patients, 78 (85.71%) were males and 13 (14.29%) were females. Eighty seven (95.60%) patients had contracted HIV infection through sexual contact, 3 by blood transfusion and one by sharing of needles. Sixty eight (74.73%) patients had pulmonary tuberculosis, 12 (13.19%) had pleural effusion, 4 (4.4%) had lymphadenitis, 5 (5.5%) had both pulmonary and extrapulmonary tuberculosis and 2 (2.2%) had miliary tuberculosis. Associated complications were present in 68 (74.73%) patients: oral candidiasis in 57 (62.64%), chronic or recurrent diarrhoea in 7 (7.69%), herpes zoster in 2 (2.2%) and pyrexia of unknown origin in 2 (2.2%) patients.

Conclusion: The trend of dual infection with HIV and tuberculosis in the area is rising. Pulmonary tuberculosis is the commonest lesion followed by pleural effusion. Oral candidiasis is the commonest associated complication.

**Key Words:** HIV, Tuberculosis, ELISA.

**INTRODUCTION**

Tuberculosis, a major public health problem in most of the developing world, is posing a still bigger threat with the worldwide epidemic of Human Immunodeficiency Virus (HIV). There are more than 14 million dually infected persons globally and India accounts for more that 1 million of them¹. HIV sentinel surveillance among TB patients is being carried out in many countries in order to ascertain the level of HIV prevalence and the trend. Substantial evidence exists that the consequences of HIV and tuberculosis coinfection are greater than either of these conditions singly¹. Tuberculosis exerts a detrimental effect on the course of HIV infection and the risk of death in HIV infected persons with tuberculosis is twice as high as that in HIV infected patients without tuberculosis².

HIV seroprevalence among tuberculosis patients in Uganda and Zambia was found to be 50-70%³ and in Tanzania 40%⁴; in Thailand, HIV seroprevalence rose from 2.4% in 1989 to 10.8%⁵ and 22.0% in 1996⁶. In India, so far, this information remains patchy as reports from Delhi⁷, Chennai⁸, Mumbai⁹, Pune¹⁰ and Pondicherry¹¹ only are available, recording rates varying from less than 1% to around 30%.

**OBJECTIVES**

Since Aligarh is a noted educational centre in north India, where students and teachers from different parts of India and other countries...