TRENDS OF EXTRA-PULMONARY TUBERCULOSIS UNDER REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME: A STUDY FROM SOUTH DELHI*  

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INTRODUCTION  

Extra-pulmonary tuberculosis (EPTB) is a milder form of disease in terms of infectivity as compared to pulmonary TB (PTB). Whereas sputum can be easily obtained for the detection of disease in lungs, diagnosis of EPTB is often difficult requiring invasive and expensive serological/radiological investigations. A category-wise drug treatment is similar for the two forms of disease¹. However, an assessment of end point of cure is a problem with EPTB. With the global rise of human immunodeficiency viral (HIV) infection over last decade, studies have reported increasing association of EPTB in HIV infected individuals²,³. Prevalence of EPTB has also been found to be high in paediatric TB cases⁴.  

In the past, treatment of EPTB has been carried out with a Short Course Chemotherapy (SCC), which has given successful results in tubercular affection of lymph nodes⁵, pleura⁶, male⁷ and female⁸,⁹ genitalia, ear¹⁰, skin¹¹, joints¹² etc. Even the more serious forms like tubercular meningitis (TBM) and miliary TB have been cured with it. However, the treatment in past needed to be given on a daily basis and delayed resolution, default or failure occurred frequently owing to incorrect prescriptions, inappropriate communication/drug intake, erratic medical supplies and inaffordability.  

A Directly Observed Treatment-Short Course (DOTS) strategy was recommended for National Tuberculosis Control Programmes globally by the WHO about a decade back¹¹, which was found to be successful in all types of TB cases¹³-²³. Reports have largely focused on smear positive pulmonary TB that posed greater infectivity threat and accounted for a higher morbidity and mortality than EPTB. In view
of the scarce data in respect of EPTB case-management with DOTS, especially in Indian context, a study was designed with the objectives: i) to determine prevalence of EPTB, ii) to draw comparison between annual case detection of PTB and EPTB, and iii) to assess outcome of DOTS in extra-pulmonary form of disease in a locality in Delhi.

MATERIAL AND METHODS

Present study is a retrospective analysis of the patients’ record among a population of Delhi living in the area catered by L.R.S. Institute of TB and Respiratory Diseases. The record comprised of parameters such as age, sex, site of disease (lymph node, pleura, abdomen, bone, joint, genitalia, kidney, skin, meninges and miliary), TB category (I, II or III) and treatment outcome (completion, default, failure, transfer out or death) for all consecutive cases, diagnosed as having EPTB at the Institute and administered DOTS at the area DOTS centres between January 1996 and March 2003.

The diagnosis of EPTB cases was established following the programme guidelines, which required one culture positive specimen from an extra-pulmonary site, or histological evidence, or strong clinical evidence consistent with active EPTB followed by a Medical Officer’s decision to treat with a full course of anti-TB therapy. The type of investigation necessary to prove the presence of disease depended upon the site of EPTB. Whenever needed, invasive procedures were carried out under an ultrasonic or a computed tomographic guidance and the specimen subjected to a culture or histopathology for evidence of TB. Following diagnosis and categorisation, EPTB cases were referred to their respective area DOTS centres, where regular drug administration and follow up visits took place as per the programme guidelines for a specified duration of therapy. Health education and motivation to them was imparted within Institute prior to the referral, as well as during the subsequent follow-up visits at DOTS centres. The trained staff of these centres, while administering the drugs, inquired about the tolerance and possible side-effects, if any. The number of PTB cases of area, who were diagnosed and treated with DOTS at the DOTS centres, was also recorded over the same study-period for a comparative analysis with EPTB cases. Analysis of treatment outcome was done for EPTB cases, whose data was available.

RESULTS

Of the overall 14,185 area cases treated under DOTS during study-period, 11,336 (80%) had pulmonary TB and 2849 (20%) suffered from EPTB. The latter comprised a higher number of females (1615 (57%)) than males (1234 (43%)) constituting a significantly different (p< 0.01) male: female ratio of 1: 1.3. Age-distribution of EPTB cases (Table 1) showed higher disease prevalence in the young age, with a mean ± standard deviation (SD) of 23.4 ±12.8 years. Case-distribution with regard to the age as well as the male: female ratio demonstrated respectively similar annual trends. Commonest site of EPTB involvement was lymph nodes followed by affection of pleura. The category-wise distribution placed highest number of study cases in Category III (1943 or 68%) followed by those in Categories I (537 or 19%) and II (369 or 13%).

Excluding an insignificant (p >0.05) dip in number of cases detected in 1998 as compared to the preceding year, detection of total, as well as, of PTB and EPTB cases increased progressively over the successive study years (Figure 1).

Table 1: Age distribution of extra-pulmonary tuberculosis cases

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Case-number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;14</td>
<td>611 (21)</td>
</tr>
<tr>
<td>15-24</td>
<td>1074 (38)</td>
</tr>
<tr>
<td>25-34</td>
<td>725 (25)</td>
</tr>
<tr>
<td>35-44</td>
<td>274 (10)</td>
</tr>
<tr>
<td>45-54</td>
<td>92 (3)</td>
</tr>
<tr>
<td>55-64</td>
<td>45 (2)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>28 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>2849 (100)</td>
</tr>
</tbody>
</table>
of annual EPTB case detection (Figure 2) increased significantly (p < 0.01) through 16 in 1996 to 22 in 2002, whereas that of PTB decreased significantly (p < 0.01) through 84 to 78 during same time, though change for the either was not uniformly similar over intervening years. A further comparison of EPTB to PTB case detection ratio between the base and final years of study showed a significant (p < 0.05) fall in the value of PTB cases from 1:5 to 1:3.5 (Figure 3).

The available outcome for the 1885 EPTB cases, ranging from the milder lymphadenopathy to the serious ones like meningeal or miliary TB etc, who were treated with DOTS from January 1996 to December 2001, showed treatment completion in 1775 (94%), default in 69 (3.7%), failure in 18 (1%), transfer-out in 12 (0.7%) and death in 11 (0.6%) cases. Drug tolerance was good. No significant drug modifications were required due to side-effects such as drug induced hepatitis etc.

**DISCUSSION**

The present study has shown a rising trend of annual TB case detection in the area over recent years for both PTB and EPTB cases. This rise is believed to have occurred due to the extensive case management efforts undertaken within the area under
Due to the DOTS programme over the last decade, which has enhanced the case enrollment of both forms of TB, the overall number of cases is also expected to rise. HIV could be another contributory factor. However, a recent study from LRS Institute has found a low HIV sero-prevalence (0.9%) in area TB cases (unpublished data) in comparison to other regions of the country outside Delhi, implying thereby, that the factor is less likely to have played a significant role in the observed trend of disease. Exact cause for the rise in annual TB cases in area needs to be better defined.

The study has shown that the percentage of annual case detection has been gradually declining for PTB (from 84 in 1996 to 78 in 2002) and rising for EPTB (from 16 in 1996 to 22 in 2002). Both observations appear to be linked because high cure rate for new smear positive cases with DOTS over last decade is likely to have reduced the TB transmission level in area, thereby, accounting for the decline in percentage of observed annual PTB cases, as well as, the change in EPTB:PTB ratio (from about 1:5 at start to about 1:3.5 at conclusion of study). The decline of annual PTB case detection percentage is assumed to have contributed in a relative rise of the annual EPTB case percentage from the expected prevalence of 7.4% (10/135) under DOTS programme to the significantly higher (p<0.01) observed level of 22%. More studies need to be carried out, in order to determine the trend change of EPTB and the factors responsible for this especially desirable in developing countries, where more TB cases exist and HIV is also on the rise.

Demographic characteristics of EPTB cases have shown higher detection in females and in patients of young age. Similar observations have been made in past. Recent Indian studies have also noted a higher prevalence of EPTB in children than adults (47% vs 16% respectively), with greater affection.
of females (63% vs 33% respectively)\(^4\). In contrast, a higher prevalence of PTB has been observed in elderly than younger patients (16:1 respectively), with male preponderance of disease (3:1 respectively)\(^2\). Thus, demography of disease has not changed over the years.

Most commonly involved EPTB site was lymph node in more than one-half of patient-population followed by the pleural effusion in more than one-fourth of study cases. This finding is in accordance with the epidemiological trend seen in developed countries over past couple of decades, where a rise in tubercular lymphadenitis cases has been noticed after the onset of HIV era\(^2^9\). Although a pre-dominance of lymphadenopathy among EPTB cases in HIV and TB co-infected cases has been recently reported from the capital\(^3^1\), more studies need to be carried out, in order to ascertain the association of tubercular lymphadenitis and HIV infection within the region as well as within the country.

It is notable that the observed outcome of area, with a treatment completion of 94%, default of <4% and failure of 1%, was better than that reported for the country under the past and the present NTP\(^1^7-1^9\). Although, treatment outcome is likely to have been influenced by the presence of a large number of EPTB cases with the Category III disease (as compared to the Categories I or II), the observation of quality assurance in case management is also believed to have been contributory. Whereas, information, education and communication (IEC) campaigns were conducted for the community awareness, funds and administrative will adequately supported the DOTS programme.

It was encouraging to note that DOTS could satisfactorily treat all forms of EPTB without requiring significant treatment modifications due to drug-induced hepatitis. Its absence has been reported earlier during the treatment of EPTB from the hilly region of Himachal Pradesh, where presence of hypoxia was believed to exist as an additional contributory factor in causation of hepatic impairment\(^3^2\). Exact reason for the observation in EPTB needs to be explored. However, the absence of side-effects is likely to have contributed in a good treatment compliance.

**Future Issues**

The EPTB cases employed in service tend to ignore their disease by giving priority to occupational compulsions. Recent study from Delhi has reported a high treatment success with service utilisation of DOTS providers for those TB cases engaged in job, study or household work \(^2^5\). Utility of providers in delivering DOTS to TB cases has been reported in other studies as well.\(^3^3,3^4\) Similarly, an involvement of private practitioners (PPs) in DOTS programme has been suggested as another way of increasing the case enrollment and treatment success in TB control because usual PP practices have been found to be ill advised and poorly performed. Recent efforts to bring about a PP participation in Delhi resulted in EPTB case detection of 23% (143 out of 612 cases) and a treatment completion of 68% (13 out of 19 cases in just 1 quarter)\(^3^5\). Feasibility of improved case detection through involvement of PPs has been similarly reported from Vietnam.\(^3^6\) In a probable changing scenario of disease, with an increasing EPTB prevalence, role of DOTS providers and private practitioners could become even greater, for, they could assist in the further enhancement of case enrolment, as well as, treatment success.

As of now, EPTB cases continue to be referred for the management from a DOTS centre to the tertiary institute. However, future health policies may necessitate the placement of EPTB at a greater level of priority than that in existence. DOTS centres could be also strengthened to play a greater role in EPTB case management.

**In conclusion, annual case detection has improved for both pulmonary and extra-pulmonary TB under Revised National TB Control Programme employing a DOTS strategy. Cure of infectious disease is likely to have contributed in a relative rise of the annual EPTB case detection. DOTS effected an acceptable treatment outcome in EPTB case management.**

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Limitations

Present study did not undertake a carriage of the HIV serology that has been presumed to be responsible for the rise in the number of tubercular lymphadenitis cases in developed countries. Another limitation of this study related to the difficulty in declaring an EPTB case cured in the absence of objective evidence at end of treatment. A prolonged follow-up of the treated cases could provide data with regard to the number of relapses.

ACKNOWLEDGEMENTS

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REFERENCES


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**Essay Competition For Medical Students-2006**

The Tuberculosis Association of India awards every year a cash prize of Rs. 500/- to a final year medical student in India for an original essay on tuberculosis. The subject selected for the year 2006 competition is ‘HIV and Tuberculosis’. The essay should be written in English, typed double spaced, on foolscap size paper and should not exceed 15 pages (approximately 3,000 words, including tables, diagrams, etc.). Four copies of the typescript should be forwarded through the Dean or Principal of a College/University to reach the Secretary-General, Tuberculosis Association of India, 3 Red Cross Road, New Delhi-110 001, before 30th June, 2006 along with a certificate that the author is a final year medical student.