ESTIMATING MORTALITY FROM TUBERCULOUS MENINGITIS IN A COMMUNITY: USE OF AVAILABLE EPIDEMIOLOGICAL PARAMETERS IN THE INDIAN CONTEXT

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Summary: Occurrence of tuberculous meningitis (IBM) and deaths from it are related to the epidemiological situation of tuberculosis in a community. Since information from observational studies is lacking in India, a simple method of estimating these from available data is presented.

Transmission of infection, expressed as Annual Risk of Infection (ARI) is known to have a parametric relation with TBM deaths, among the 0-4 year aged: 1% of the ARI could be expressed as estimated IBM deaths. Applying this parameter to available data on natural dynamics of tuberculosis, derived from a 23 year epidemiological survey conducted in Bangalore district, it is estimated that in an average Indian district of 1.5 million population, about 25 TBM deaths are likely to occur annually (1.5/100,000 population). The reduction in the number of transmitters and consequently the ARI, as observed in the NTI Longitudinal Study area, is estimated and its possible effect on the estimated TBM deaths is discussed.

Key Words: Childhood tuberculosis, Meningeal tuberculosis. Epidemiology, Annual risk of tuberculosis infection.

INTRODUCTION

Transmission of tuberculosis infection is generally recognised as indicative of the tuberculosis situation in a community. It is measured by estimating the Annual Risk of Infection (ARI) i.e., the number of newly infected children in a year’s time. ARI is considered as the direct consequence of tuberculosis infectious cases prevalent in a community, the number infected per prevalence case giving the dimension of transmission. The latter could be expressed as 'contagion parameter' or 'infectivity' in a broader sense. It is important for paediatricians to observe that while incidence of infection is studied in children, the sources of transmission happen to be in the adult population. A working relationship between the two is described in the literature.

The incidence of tuberculous meningitis (TBM) is of great interest and concern, to paediatricians in particular because of the urgency in its clinical presentation. Its occurrence could also be taken as a marker for the size of tuberculosis situation in a community, because of the relatively stable relationship it is reported to have with ARI. In a recent study in South Africa, the incidence of TBM was observed to be higher among the comparatively marginalised people, socially as well as geographically, apart from predominantly occurring among those aged 0-4 years. The occurrence of TBM, and clinical tuberculosis of all forms in children have been mathematically related up in the above study, making it possible to estimate one from the other.

Following widespread BCG vaccination among children, under the Universal Immunization Programme (UIP), a reduction in the incidence of TBM is expected to occur in India. However, no baseline data on incidence of TBM seem to be available, in the absence of which it may not be possible to discern changes, if any. It is difficult to diagnose TBM accurately in the peripheral health/medical institutions in the country. The problem of 'confounders' of diagnosis or the so-called background illness-variables present in the hospital records, if available at all, would seriously come in the way of arriving at a reliable estimate. The disease is also not notifiable. It may be difficult to obtain an estimate of TBM incidence from the population based repeat surveys, in view of the acute nature of the illness and death supervening in a considerable proportion of children between surveys, besides the problems of diagnosing TBM. In this context, a mathematical model approach could be useful.
wherein deaths from TBM could be estimated by using the parametric relationship derived from some of the published studies. Estimates of death from TBM are useful for programme planning as well as assessment of the tuberculosis situation. Therefore, an attempt has been made to estimate tuberculosis transmission, and deaths from TBM, in young children in a community, using some of the epidemiological parameters, currently available.

**METHOD**

The present paper computes the contagion parameter, infectivity, mortality rate due to TBM and preventable mortality from TBM through District Tuberculosis Programme (DTP) intervention. The data used are from the following sources:
1. Longitudinal Survey conducted by the NTI
2. Tuberculosis Research & Surveillance Unit, The Hague (TSRU) - Report NO. 1
3. Report on monitoring of DTP

The hypothesis used in the paper is given under the broad heads A and B:

A. Sources of Infection in a community and extent of transmission

A.1 Prevalence of the infected persons, culture positive and smear positive cases

i) Population (Longitudinal Survey) 43,889
ii) Infected 29.5%
iii) Uninfected 70.5%
iv) Culture positive cases (178) (405/100,000)
v) Smear positive cases (83) 47% of culture positivity (189/100,000)
vi) ARI - 1.1% in 1961-62 1%

A.2 Two slightly different definitions are used:
For computing ‘infectivity’, all the culture positive cases, and for contagion parameter, only the smear positive cases (confirmed on culture) are considered.

i) Contagion Parameter

\[
\text{Annual Tuberculosis Infection Rate} = \frac{\text{Prevalence of culture + cases}}{\text{Prevalence of culture + cases in 100,000}} \times 1000
\]

B. TBM Mortality

The following criteria were used for calculating the TBM mortality rate, and for estimating deaths in absolute numbers, including those preventable by intervention through DTP in an average Indian district:

B.1 TBM Mortality Rate

i) TBM mortality is considered only in 0-4 year age group.
ii) ARI is taken as 1% (see A.1)
iii) The ratio of annual mortality from TBM in 0-4 year age group to ARI: 0.7% - 1% (say 1%)
iv) Mortality rate due to pulmonary tuberculosis (NTI Survey area) - 90/100,000
v) Proportion of children aged 0-4 years in the total population - 15%

B.2 TBM mortality (absolute number) in an average Indian district:

i) Population - 1.5 million
ii) Population aged 0-4 years (15%) - 2,25,000
iii) Newly infected (at ARI - 1%) - 2,250

B.3 Preventable TBM mortality through DTP intervention

i) Efficiency of case-finding in an average DTP - 33% of the potential of 2,000 cases
ii) Average number of cases actually diagnosed in a DTP - 660
iii) Case per household - 1.0
iv) Size of average household - 10
v) 0-4 years aged among contacts at(iv) - 15%
vi) Infected among child contacts of case households - 26%
vi) Uninfected among (v) - 74%

RESULTS

Sources of infection in a community and extent of transmission
Table 1 shows that annually, on the average, about five persons are infected by a smear positive case and three by a culture positive case of tuberculosis.

Table 2 shows that the sources of infection would decline with time, as per the results of repeat surveys carried out in Bangalore rural district by the NTI, over a period of 23 years. Simultaneously, with the ARI declining on the average by 2.3% per year, the smear positive case prevalence is observed to have declined by 2.8% per year. This gives the estimate of a likely correlation between the extent of transmission and the size of sources of infection in the community.

**IBM Mortality**

As per the hypothesis B.I (lii), annual TBM mortality among 0-4 years old children is taken as 1% of ARI. With ARI itself being 1% (see A.I), there would be one TBM death in 10,000 children (0.01 x 0.01) (Table 3). The mortality rate from TBM in general population is thus calculated to be 1.5/100,000.

Comparing the data given in B.I (iv), the ratio of TBM mortality to pulmonary tuberculosis mortality in general population, could be expressed as 1.5 : 90.0 (or 1 : 60).

**Size of problem in an Indian district**

In an average Indian district of 1.5 million population, the likely number of deaths due to TBM could be 23 (say 25), at the rate of 1.5/100,000 (Table 3).

The likely occurrence of death from TBM among contacts of the cases in a DTP could be calculated as under:

- Population in case house holds = 660 x 5 = 3,300 (see B.3., I-iv).
- Uninfected among them in age group 0-4 years = 366 (see B.3., v and vi).
- Incidence of infection in 0-4 group (366 x 2%) = 7.0 (as per ARI given in B.3.viii)
- Deaths from TBM in a year 7 x 1% = 0.07, say 0.1 (see B.I, iii for the ratio of TBM deaths to ARI).
- Therefore, approximately one death is estimated to occur once in 10 years due to TBM among the household contacts of the smear positive cases diagnosed by the DTP, with a case-finding efficiency of 33%.

**DISCUSSION**

Tuberculosis infection rates in children, converted into a set of ARIs over time may reflect the trend of tuberculosis in the community as a whole. ARI could be correlated with incidence of sputum smear positive cases in the community, or the size of the transmitters of infection in the community who

<table>
<thead>
<tr>
<th>Table 1. Sources of Transmission of Infection</th>
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<tbody>
<tr>
<td>Prevalence of cases (per 100,000)</td>
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<tr>
<td>ARI %</td>
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<td>1</td>
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<th>Table 2. Decline in Transmission by Programme Efficiency*</th>
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<td>Time of Survey</td>
</tr>
<tr>
<td>SM</td>
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<tr>
<td>1962</td>
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<tr>
<td>1986</td>
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* Only pertains to the area surveyed repeatedly for 23 years
# Based on detailed calculation, given in Chakraborty et al
@ The area studied did not have District Tuberculosis Programme (DTP) upto 1971
** Average efficiency observed for DTP implemented in 1972 - hypothetical time of the efficiency calculation, middle of 1979
are the target for any tuberculosis control programme. The average number of persons infected by a case (smear positive and culture positive, separately) is also calculated, in this paper, making it possible to estimate the damage and its public health significance. The estimated decline in the prevalence of smear positive transmitters (by 2.8% per year) is reported to be related to that of the ARI (by 2.3% per year) in a population in south India, surveyed by the NTI, for the last 23 years. The above trend could be attributed to the natural dynamics, accentuated to some extent by socio-economic changes that are taking place in the area, along with the effects of intervention through DTP, if any.

TBM, being one of the serious consequences of tuberculosis infection, is of major concern to paediatricians as well as programme planners. Its occurrence or TBM mortality is sometimes taken as a ‘marker’ of the tuberculosis situation in the area and effect of the intervention effort. Since notification of TBM, or tuberculosis of any other form is not practised in India, it would be desirable to estimate the size of the TBM from the ARI, to review the tuberculosis situation.

It is possible to estimate, from ARI of 1% (as observed in the south Indian district, data from which are used in this model), that TBM mortality rate in the population could be 1.5/100,000 (cf: pulmonary tuberculosis mortality rate : 90/100,000). For an average Indian district (population considered as 1.5 million), nearly 25 TBM deaths could occur in a year. The estimated number would vary, depending on the ARI (1.7% in Tamil Nadu) which is not likely to be uniform throughout the country. The range of TBM deaths could be appropriately calculated from the area-specific ARI, as per the method shown in this paper.

It is believed that TBM deaths could largely be prevented by BCG vaccination of the newborns and the non-infected children (provided, the hypothesis is true that BCG vaccination is highly effective in preventing haematogenous dissemination). However, those who recommend chemoprophylaxis and treatment of child contacts of smear positive index cases should note that by carrying out surveillance and preventive treatment, only among the child contacts of the tuberculosis cases registered under DTP, one could possibly prevent just one death from TBM in 10 years with DTP’s current efficiency, and an un-estimated morbidity in them provided chemoprophylaxis is delivered at 100% efficiency and is truly effective in preventing disseminated disease. The operational feasibility of undertaking such a surveillance and preventive treatment activity in the country, under the current socio-economic constraints, can only make it an illusory objective for any health programme to achieve.

TBM deaths are shown as directly proportional to ARI, the latter showing a reduction at 2.3% per year, as reported in the NTI Longitudinal Study area over a period of 23 years. This reduction could have brought down TBM deaths as well. Correlating the reduction of smear positive transmitters to the decline in ARI and TBM deaths, it would appear reasonable to say that an efficient DTP could prove effective in reducing TBM deaths in the community as well, over the long term, especially when supported by BCG vaccination, as done at present.

There is paucity of reliable information on incidence of TBM and mortality from it in general population. The data available from a recent observational study from South Africa show that out of the infected children, in 0-4 year age group, 15.7% had suffered from clinical tuberculosis and 0.5% had developed TBM (ARI - between 2% and 3%). Our TBM mortality rate (at 10/100,000 children or 1.5/100,000 population) compares favourably with that observed among the 0-4 year old coloured children.

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**Table 3. Computation of Mortality due to Tuberculous Meningitis**

<table>
<thead>
<tr>
<th>Distt. population all ages (in Millions)#</th>
<th>Annual Risk of Infection</th>
<th>Death from TBM in children 0-4 years (in 10,000)*</th>
<th>TBM Mortality (per 100,000 population)</th>
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<tbody>
<tr>
<td>1.5</td>
<td>1</td>
<td>1</td>
<td>15(22-23)**</td>
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# Children aged 0-4 years 15%
*1% of ARI
**No estimated bmi 1.5 million (col.1)
of the predominantly rural areas in South Africa (incidence rate of TBM: 29.0/100,000 in 0-4 year old children with 24% deaths) because black children below the age of five years, living away from the urban and peri-urban areas, expectedly had higher TBM deaths. It is also worth noting that only 44% of the TBM cases identified were found in the records of the South Africa health department. These findings indicate the seriousness of the problem among underprivileged sections of the community, apart from underlining the constraints in the measurement of the problem through health services data. In the Indian context, the proportion of TBM fatalities out of all tuberculosis deaths was reported to be as high as 18.6%, from the vital statistics records of Nagpur Municipal Corporation. But city hospitals attract serious emergencies like TBM more than the insidiously dying tuberculosis cases, besides the problems encountered in diagnosing TBM. Hence, sentinel centres data have their own limitations in projecting these to the community at large.

It may not be out of context to mention the process of arriving at ARI in Great Britain, from the notification data on TBM. Even though Vynnycky’s model is, in a manner, converse application of the parameters compared to the use made in our analysis, both are essentially similar approaches as they illustrate the feasibility of arriving at a set of data, not readily found, from those which are available.

Even though the data on TBM mortality presented in this paper are only preliminary estimates, which also do not permit cross classifications of any sort, these could still be used in planning for services for the paediatric age group. Needless to say that the estimates require to be validated on the lines of the study carried out in South Africa.

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