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# CORRELATION BETWEEN PREVALENCE RATES OF PULMONARY TUBERCULOSIS, TUBERCULOUS INFECTION AND NON-SPECIFIC SENSITIVITY

RAJ NARAIN, M.S. KRISHNAMURTHY, S. MAYURNATH and B.N. GOPALAN

Summary : Data from the initial examination of a BCG trial have been analysed to determine mathematical relationship, if any, between the prevalence of infection and disease. Also, because non-specific sensitivity otters protection against the development of tuberculosis and because there was high prevalence of nonspecific sensitivity in the area of the study, relationship between nonspecific sensitivity and tuberculosis had also been studied.

Results of the analysis showed that relationship between prevalence of tuberculous infection and disease is not amenable to any simple mathematical quantification. However, the values of the coefficients of correlation between the two were statistically highly significant suggesting that the prevalence of one varied directly with the prevalence of the other in the community, and that prevelence of infection may be used as an indicator for the prevalence of disease at different points of time. The analysis also showed the existence of an inverse relationship between prevalence of tuberculosis ane prevalence of non-specific sensitivity tending to confirm the previous finding that the latter offered protection against the other.

## Introduction

For assessment of the trend of tuberculosis in developing countries, little or no data are available. Notification data, wherever these exist, are grossly incomplete. Repeated prevalence surveys for morbidity are costly and difficult to organise. An easier way of assessing the problem could be by measuring infection rates in a representative sample of the population. Any change in these over a period of time could be assumed to represent a corresponding change in the prevalence of disease. Since infection in India is caused only by the open cases of the disease, *a priori* such a hypothesis should be acceptable. The ICMR has also recommended it under the New 20-point Program (ICMR, 1983). Prevalence of infection would appear to be almost the only practical measure for this purpose. A representative sample could be children, who are likely to be available for testing at different points of time more easily than most other groups.

For this *a priori* hypothesis, it could be desirable to assess the degree of correlation between prevalence of infection in some age groups and the prevalence of disease in the community. Therefore, we have analysed correlation between prevalence rates of pulmonary tuberculosis, tuberculous infection and non-specific sensitivity in the data of the initial round of the BCG trial (TB Prevention trial, 1980). Non-specific sensitivity was included in the analysis because it has been shown to offer protection against tuberculosis (Palmer et al, 1966; M.R.C., 1972 and Raj Narain, et al 1972) and because it was highly prevalent in the area of the study (Raj Narain et al, 1975). To the best of our knowledge such a relationship in mathematical terms has not been reported before.

## Material and Methods

The initial examination of the population in the BCG trial was carried out from July, 1968 to March, 1971. The design of the study and the methods adopted have been reported in detail earlier (TB Prevention trial, 1980). Briefly, the entire population 1 year or more by age was tested with 3 IU of PPD-S and 10 units of PPD-B. All persons aged 10 years or more were offered a 70 mm photofluorogram of the chest and those persons showing x-ray abnormality were offered examination of two specimens of sputum, both by smear and culture. The area consisted of 210 administrative units, namely, 209 panchayats* and a town. The data from the 210 units have been utilised to study the inter-relationship between the three parameters. The coverages for the examinations were of the order of 77% for skin testing, 82% for x-ray examination and 93% for sputum examination.

## Definitions

In this report the following definitions for the three parameters have been used.

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*A panchayat is a group of villages and hamlets and is the smallest administrative unit. The population may vary from less than 1000 to several thousand inhabitants.

1. For prevalence of pulmonary tuberculosis, the following three categories of cases have been considered. It is not easy to define a case of pulmonary tuberculosis (Raj Narain et al 1968). Possibly, one or the other definition may be acceptable to most workers.

(i) Cases in whom the culture growth from one or more of the specimens of sputum was classified as *M. tuberculosis,*

(ii) Cases in whom culture growths from at least two specimens of sputum were classified as *M tuberculosis,*

(iii) Cases under (i) who, in addition, had x-ray evidence of disease.

Although category (i) is used for diagnosis of disease in most surveys, it was felt that categories (ii) and (iii) established the diagnosis of pulmonary tuberculosis with greater certainty than category (i). It may be noted that the three categories of cases are not mutually exclusive, but overlapping.

2. For prevalence of infection with *M. tuberculosis,* all persons with a size of reaction of 12 mm or more to PPD-S have been considered as infected (TB Prevention Trial, 1980).

Prevalence of infection has been studied, separately, for three overlapping age groups, namely 1-9 years, 1-14 years and all ages.

3. For non-specific sensitivity, persons with 7 mm or smaller reaction to PPD-S and showing 10 mm or bigger reaction to PPD-B, have been considered to have non-specific sensitivity (Raj Narain et al 1975). Prevalence of non specific sensitivity in the three age-groups, as for infection with *M. tuberculosis,* has been studied.

**Results**

Data for each of the 210 units were studied in detail (not shown); variation in the size of the units and in the prevalence rates of the three parameters between units was great.

Values of coefficients of correlation between prevalence rates of tuberculous infection and the three categories of disease are shown in Table 1. Although the numerical values of the coefficients of correlation were not large, the correlation between the prevalence rates of infection and disease, for each of the three age groups and the three categories of disease was positive and highly significant.

Correlation between prevalence rates of non-specific sensitivity and the 3 categories of cases is shown in Table II; the correlation in each case was negative and highly significant. Again, the numerical values of the co-efficients of correlation were not large.

Table III shows the values of the coefficient of correlation between prevalence of infection and the prevalence of non-specific sensitivity. All the values were very small and none was statistically significant.

A better way to consider inter-relationship between 3 variables is to consider the variables, two by two, after eliminating the effect of the third i.e., to consider partial correlation co-efficients.

Partial correlation coefficients between prevalence of infection and disease and between prevalence of non-specific sensitivity and disease are presented in Tables IV and V respectively. Values of the partial coefficients were highly significant. But the values, though higher, were still small.

TABLE 1

*Coefficients of correlation between prevalence rates of infection (≥12 mm to PPD-S) and disease*

| Category of case (aged ^ 10 years) | Age-group considered for infection | | |
|---|---|---|---|
| | (1-9) years | (1-14) years | All ages |
| 1. *M.tub* on atleast one culture | 0.35** | 0.38** | 0.41** |
| 2. *M.tub* on atleast two cultures | 0.35** | 0.36** | 0.32** |
| 3. *M.tub* on atleast one culture and x-ray evidence of disease | 0.39** | 0.40** | 0 40** |

**P<0.01

TABLE 2

*Coefficients of correlation between prevalence rates of non-specific sensitivity* (0—7 *mm to PPD-S and* ≥ 10 *mm to PPD-B) and disease*

| | Age-group considered for non-specific sensitivity | | |
|---|---|---|---|
| | 1-9 years | 1-14 years | All ages |
| 1. *M.tub* on at least one culture | — 0.27** | —0.28** | —0.31** |
| 2. *M.tub* on at least two cultures | — 0.27** | —0.26** | —0.30** |
| 3. *M.tub* on at least one culture and x-ray evidence of disease | — 0.22** | —0.22** | —0.25** |

P<0.01

TABLE III

*Coefficients between prevalence rates of infection and non-specific sensitivity*

| Age-groups considered | Coefficients of correlation |
|---|---|
| 1-9 years | 0.11 |
| 14 years | 0.10 |
| All ages | 0.09 |

TABLE IV

*Partial correlation coefficients between prevalence rates of infection and disease (after eliminating the effect of non-specific sensitivity)*

| Category of case (aged 10 years) | Partial correlation coefficient |
|---|---|
| 1. *M.tub* on at least one culture | 0.45** |
| 2. *M.tub on* at least two cultures | 0.40** |
| 3. *M.tub* on at least one culture and x-ray evidence of disease | 0.41** |

a Age group 1—14 years has been considered for the prevalence of infection

** P<0.01

TABLE V

*Partial correlation coefficients between prevalence rates of non-specific sensitivity and disease ( after eliminating the effect of infection )*

| Category of case (aged ≥10 years) | Partial correlation coefficient |
|---|---|
| 1. *M.tub* on at least one culture | —0.35** |
| 2. *M.tub* on at least two cultures | —0.31** |
| 3. *M. tub* on at least one culture and x-ray evidence of disease | —0.34** |

a A.ge group 1—14 years has been considered for the prevalence of NSS

** P<0.01

Scatter diagrams and regression lines, between infection and disease and between non-specific sensitivity and disease were drawn. These did not show any definite pattern of correlation (not shown). Attempts were made to obtain closer fits (than with the linear regression model) by using transformations (log, arcsine) and by including a quadratic term. None of these, however, proved beneficial.

## Discussion

The highly significant values of the coefficients of correlation between infection and the 3 categories of cases of pulmonary tuberculosis (Table 1) suggest that if prevalence of infection with *M. tuberculosis* is high, the number of cases of pulmonary tuberculosis is also likely

to be high. However, the numerical values of the coefficients of correlation were not large. This is probably not surprising as disease may develop during a greatly varying period after infection. The link between disease and infection is spread over a long period. Furthermore, the link was incomplete in the sense that the infected persons at any time were not necessarily infected by the patients of tuberculosis found at the time. Many patients responsible for spreading infection might have died or be no longer patients or migrated to other areas before the survey. Further, some persons might have been infected during their visits to places outside the study area or during short visits by patients from outside the study area to their relations in the study area. Also, in the vast majority, disease does not always develop after infection. Whatever the reason for the low numerical values of the coefficients of correlation, these do not encourage one to make an attempt to evolve an exact mathematical relationship between infection and disease or between non-specific sensitivity and disease. All the same, since the values of the coefficients of correlation are highly significant, infection rates could serve as a far simpler indicator of the prevalence of disease for at least certain purposes. For example, it should be permissible to indicate changes in the prevalence of disease by repeated tuberculin surveys rather than by the costly and time consuming repeated tuberculosis prevalence surveys for disease.

Negative and significant values for the coefficients of correlation between non-specific sensitivity and cases of tuberculosis (Table 11) support earlier reports of the association of non-specific sensitivity with lower incidence rates of pulmonary tuberculosis (Palmer et al 1966; M.R.C., 1972 and Raj Narain et al 1972).

The values of the coefficients of correlation between prevalence rates of infection with *M. tuberculosis* and non-specific sensitivity are very small and not statistically significant (Table III). Thus, the two parameters would seem to be independent of each other. Non-specific sensitivity cannot prevent infection with *M. tuberculosis,* but possibly (as suggested by the data presented in Table II), it would seem to prevent the development of disease after infection, much in the same way as BCG vaccination, thus earning for non-specific sensitivity the name 'natural vaccination'.

The values of the coefficients of correlation, though statistically significant, were numerically small. Any value of the correlation coefficient less than 0.7 may not normally be used to decide the linear relationship between two variables (Oldham, 1968). Furthermore, the large residual or unexplained relationship would seem to point out to the great and important role of several other parameters such as the immunological factors, nutritional aspects or the low virulence of the organisms, etc.. in addition to the two considered in this report on the development and prevalence of pulmonary tuberculosis in a community.

Possibly, incidence rates of infection could be more directly associated with existing disease in the community. Incidence rates are, however, more difficult to estimate. Even the definition of infection is not agreed upon (Narain et al, Amrican Thoracic Society 1981; Comstock et al 1978; Thompson et al 1979 and Narain 1980) and the time lag between infection and disease shows great variation.

To sum up, the results presented show that the relationship between prevalence of tuberculous infection and disease, though highly significant, is not amenable to any simple mathematical quantification. All the same, it may not be unjustifiable to use prevalence rates of infection as indicators of the prevalence of disease in the community at different points of time. Further, the inverse relationship between prevalence of tuberculosis and prevalence of non-specific sensitivity supports the earlier finding that the latter offered protection against the former.

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