MICRO-SPATIAL VARIATION IN FILARIAL DISEASE AND RISK OF DEVELOPING DISEASE ASSOCIATED WITH MICROFILAREMIA IN URBAN SITUATION

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Abstract. Clinical and parasitological surveys were carried out concurrently during 1986 in Pondicherry. The analyses showed that there was no significant micro-spatial variation in prevalence of total diseases (acute and chronic) and the manifestations such as hydrocele and lymphedema in the diferent zones and stations of Pondicherry urban area, a stable endemic area. Analyses on different filariometric indices in different stations showed a significant correlation between disease and mf prevalence ($r = 0.4106$; $p = 0.037$). The prevalence of disease and hydrocele in microfilaremic individuals (9.4% and 20.0% respectively) was higher compared to that observed in amicrofilaremic persons (6.4% and 11.2% respectively). The relative risk (RR) of parasite carriers developing disease (any manifestations) was marginally higher compared to amicrofilaremic persons (1.18). However, the RR of developing hydrocele manifestation due to microfilaremia was much greater (1.5) compared to amicrofilaremic persons. The attributable risk (AR) due to microfilaremia for developing hydrocele was 0.05. This suggests that although the risk is high in mf carriers, there might be alternate ways of developing disease without the infected person becoming microfilaremic. The limitations of point prevalence data on understanding complex dynamics of infection and disease are discussed.

INTRODUCTION

Filariasis is a major public health problem in India. About 50% of the world's population at risk of lymphatic filarial infection live in this country (WHO, 1992). Bancroftian filariasis due to *Wuchereria bancrofti* is the predominant form accounting for 98% of infection (Anonymous, 1990). Pondicherry is a known stable endemic area for periodic *W. bancrofti* (Nair, 1960; Rajagopalan *et al*, 1988; Pani *et al*, 1989). Earlier analyses on vector and human infection clearly showed that there is a considerable degree of micro-spatial variation in the study area of Pondicherry (Manoharan *et al*, 1993). The present analysis was carried out to study the micro-spatial variation in the prevalence of total disease (acute and chronic), clinical manifestations such as hydrocele and lymphedema, and, the relationship of prevalence of disease with microfilaremia (mf) and its intensity. The clinical and parasitological databases collected concurrently during 1986 at Pondicherry was used.

Further, our earlier study by application of a reversible catalytic model in a cohort of a population with both bancroftian and brugian forms of filariasis (Srividya *et al*, 1991; Sabesan *et al*, 1991) had shown that the progression of infection to chronic disease goes through 4 sequential compartments: uninfected; microfilaremic asymptomatic; amicrofilaremic asymptomatic; and amicrofilaremic with irreversible obstructive lymphatic disease. If this hypothesis is true one would expect more number of diseased cases than the microfilaremic cases in a stable endemic area. Therefore the data were analysed to study the relative and attributable risk of developing disease in relation to microfilaremia status.

MATERIAL AND METHODS

The study area and the filariasis situation in Pondicherry have been described elsewhere (Rajagopalan *et al*, 1977; Rajagopalan *et al*, 1989a). Clinical survey was carried out in 26 stations (representing all the seven operational zones) by house visits during 1986. Night blood survey for microfilaremia was also carried out in Pondicherry during the same period. The details of the study design for both the surveys have been described elsewhere (Rajagopalan and Das, 1987; Pani *et al*, 1991; Subramanian *et al*, 1989).

Statistical analyses: Zone and station specific prevalence rates for disease, hydrocele and lymphedema were obtained from clinical data, and, mf prevalence and intensity from parasitological data.

Analysis of variance was carried out to see the variation in clinical indices between the stations and the zones. The station specific data were also utilized to study the relationship between clinical and parasitological indices. To study the variations in filariometric indices, all the values were normalized by computing the Z-score. In the case of percentage values, all percentages were converted to arcsine values, which were again converted to Z-score. The risk of developing disease among those with and without microfilaremia was calculated by the method of Khan and Sempos (1989).

RESULTS

The different filariometric indices computed for the 7 zones in the study area are presented in Table 1. Analysis of variance indicated that the prevalence of total disease, hydrocele and lymphedema did not vary significantly between the zones. However, a significant variation in mf prevalence ($F = 2.435$; $p = 0.045$) and it's intensity ($F = 3.127$; $p = 0.015$) was observed.

Among the stations the disease prevalence ranged from 0 to 12.4%, hydrocele prevalence from 0 to 20.9% and lymphedema prevalence from 0 to 4.8%. These clinical indices also did not show a significant variation between different stations. However, variation in mf prevalence and intensity between stations was analysed in our earlier report (Manoharan *et al*, 1993). Analyses of data on filariometric indices in the different stations showed a significant correlation between disease and mf prevalence ($r = 0.4106$; $p = 0.037$, Fig 1). The zone specific data also showed a significant correlation between prevalence of hydrocele and mf prevalence ($r = 0.7691$; $p = 0.0432$).

A total of 3,124 individuals was surveyed both for disease and mf status. Disease prevalence among microfilaremic ($n = 202$) and amicrofilaremic individuals ($n = 2,922$) was 9.4% and 6.36% respectively ($p = 0.1233$). The risk of developing disease was 1.5 times among microfilaremic persons compared to those without microfilaremia. However, some of the observed amicrofilaremic persons could actually be parasite carriers due to sampling errors (Das *et al*, 1990). Therefore the proportion of true negative persons was calculated by applying the method of Das *et al*, (1990). The fitting of truncated negative binomial probability distribution of mf count among these 3,124 individuals was found to be good fit ($X^2 = 25.27$; $df = 17$; $p = 0.0888$) and the true amicrofilaremic individuals were estimated to be 2,337. The relative risk of developing disease in microfilaremic compared to true amicrofilaremic was 1.18 (0.75 - 1.85: 95% Confidence Limits). The prevalence of hydrocele, the predominant manifestation of bancroftian filariasis, was 20% and 11.2% in microfilaremic ($n = 85$) and amicrofilaremic ($n = 995$) males respectively ($X^2 = 5.048$; $p = 0.0246$). The risk of developing hydrocele among microfilaremic persons was 1.8 times that of amicrofilaremic individuals (before correcting for sampling error). The actual amicrofilaremic males was estimated by fitting truncated negative binomial distribution ($X^2 = 14.63$; $df = 8$; $p = 0.0668$) and found to be

Table 1

The observed values of filariometric indices in different zones of study area.

Filariometric indices	Zone No. 1	2	3	4	5	6	7	Overall values ± SE*
Mf prevalence[1]	4.83	8.69	6.82	10.51	5.84	7.71	14.63	6.3 ± 0.13
Mean mf count[2]	0.38	0.78	0.78	1.89	0.72	0.87	2.19	0.7 ± 0.05
Disease rate[1]	7.02	7.39	7.12	7.94	7.01	4.72	9.88	6.6 ± 0.33
Hydrocele rate[1]	9.50	14.07	9.18	12.42	13.40	10.88	17.19	11.9 ± 0.67
Lymphedema rate[1]	2.02	2.14	2.44	1.89	1.37	0.54	3.09	1.8 ± 0.17

* Standard error.
[1] Percentage.
[2] Per 20 mm^3

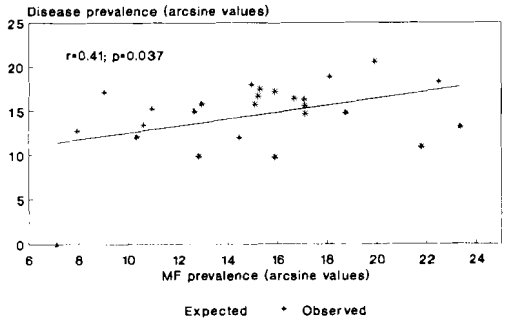

Fig 1—Relationship between prevalence of disease and mf in Pondicherry.

815. The relative risk of developing hydrocele due to microfilaremic cases compared to true amicrofilaremic persons (as estimated) was 1.5 times (0.93 - 2.32: 95% Confidence Limits). The attributable risk (AR) for hydrocele due to parasitemia in males was 0.05, suggesting that only about 5% of the hydrocele prevalence in the study area can be attributed to microfilaremic males. Since there was only one case of lymphedema among microfilaremic persons, the above analysis could not be carried out.

DISCUSSION

Variations in the spectrum and prevalence of clinical manifestations are known to occur in larger geographical areas (Hawking 1976; Rao, 1977). Analyses of micro-spatial variation within an endemic area has not been carried out earlier. The present analysis in Pondicherry shows that in a stable endemic area there is no micro-spatial variation in prevalence of disease, hydrocele and lymphedema at a given point of time. Significant variations in mf prevalence and intensity were observed between zones in the present analysis and between stations as reported earlier (Manoharan *et al*, 1993) suggest the variations in levels of intensity of transmission potential. Prior to 1986, different types of vector control measures (Rajagopalan and Das, 1987, 1989) were undertaken in Pondicherry and these have influenced not only the prevalence of infection (Subramanian *et al*, 1989) but also the spatial varia-tion in course of time (Manoharan *et al*, 1993). However, these variations in parasite indices were not reflected in disease indices observed in present analyses. It is known that the impact of vector control operations is observed in a short period on mf prevalence, where as the indirect impact on disease takes even decades to be observed (Rajagopalan *et al*, 1989b). Considering the long fecundic life span of adult worm (Vanamail *et al*, 1989a) and the complicated transmission dynamics of disease (Srividya *et al*, 1991), the 5 years period may be the short duration to observe the spatial variation in clinical manifestations. Infection status is relatively shorter duration but chronic disease is permanent and there fore prevalence of this cumulates over time. Also our earlier analyses have shown that the distribution of clinical cases are random and the distribution of mf carriers is clustered in the households where family size is more than five individuals (Vanamail *et al*, 1989b, 1992).

The significant positive correlation between prevalence of mf and disease obtained in these analysis corroborates with observations made earlier (Joseph and Prasad, 1967; Iyengar, 1938). Though a majority of clinical cases are amicrofilaremic at given point of time (Vanamail *et al*, 1989a; Srividya *et al*, 1991; Pani *et al*, 1991), the increase of disease rate along with mf prevalence in different areas is epidemiologically important for considering the natural history of disease in the population.

Contrary to general belief that there is usually a negative relationship between microfilaremia and chronic disease the present analyses has shown that the relative risk for total disease is more or less same for both microfilaremic and amicrofilaremic individuals. However, there was a high risk of developing hydrocele among microfilaremic males. In spite of this higher risk, at a given point of time mf carriers contributed only 5% of the total hydrocele individuals. This suggests that although the risk is high in mf carriers (Michael *et al*, 1994), there might be alternate way of developing disease without becoming microfilaremic though infected. This implies that probable single sex adult worm infections may also result in progression of disease, as suggested earlier (Hairston and Jackowski, 1968). Analysis carried out in the study area (Das *et al*, 1994) showed that there is a good correlation between challenge with infective stage and prevalence of acute attack and primary grade edema. Further work needs to be carried out to understand these intricate aspects of the dynamics of infection and disease.

There are however, certain limitations of using point prevalence data for understanding the dynamics of infection and disease. Although a majority of

clinical cases are amicrofilaremic at a given point of time, in no way it is possible to know, if these cases did not harbor parasites earlier. Carrying out longitudinal studies on microfilaremic persons for development of disease though ideal, is not realistic, because of ethical reasons (since treatment cannot be avoided). Further, one also needs to understand that due to inherent problems in the sampling technique and due to possible single sex infection (Hairston and Jackowski, 1968) or to L3 larave (Das *et al*, 1994), there may be a very high proportion of false negative cases as far as infection is concerned (Das *et al*, 1990).

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