THE EFFECT OF REPEATED CHEMOTHERAPY ON THE PREVALENCE AND INTENSITY OF *ASCARIS LUMBRICOIDES* AND *TRICHURIS TRICHIURA* INFECTION

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Abstract. The prevalence and intensity of intestinal nematode infections were assessed during 3 anthelminthic interventions in an urban community in Malaysia. The prevalence levels of *Ascaris lumbricoides* at Interventions 1, 2 and 3 were 30.6%, 18.9% and 15.5%, respectively and the mean intensities were 1.9, 0.75 and 0.81 worms per person. For *Trichuris trichiura,* the prevalence levels at Interventions 1, 2 and 3 were 46.9%, 21.6% and 15.7%, respectively. The mean intensities for *T. trichiura* at Interventions 1, 2 and 3 were 3.30, 0.92 and 0.07 worms per person. No gender-related prevalence and intensity were observed for the two geohelminths in this community. Prevalences and intensity had convex age profiles. Although repeated chemotherapeutic intervention reduced both prevalence and intensity levels, intensity was a more sensitive indicator than prevalence. The results indicate that age-targetting treatment at school children of 7-12 years of age would be an appropriate strategy for this community.

INTRODUCTION

In endemic areas of high prevalence and intensity of intestinal nematode infections, it is usually not economically feasible to implement universal mass multi-intervention chemotherapeutic programs as a control strategy. Selective and age-targetting chemotherapy, may be more affordable alternatives (Warren and Mahmoud, 1976; Anderson and May, 1982); fewer people need to be treated compared with mass chemotherapy, a disproportionate reduction in morbidity is obtained (Anderson and Medley, 1985) and the risk of the development of drug resistent strains of the parasite is reduced since the lightly infected individuals are not treated (Anderson, 1986). However, the implementation of selective or age-targetting chemotherapy requires the detailed understanding of patterns of infection, particularly, the identification of the most highly infected individuals or age-classes.

Age-related prevalence and intensity patterns have been well-documented for *A. lumbricoides* and *T. trichiura* in other regions, such as the Philippines (Cabrera *et al,* 1989), India (Elkins *et al,* 1986) and the Caribbean (Bundy *et al,* 1987). Although data on the prevalence of parasitic infections in various geographical locations, socioeconomic groups and ethnic communities in the Malaysian context are voluminous (Barnes and Russell, 1925; Bisseru and Aziz, 1970; Kan, 1982; 1985a, b; 1986a, b; Sinniah, 1984), there is a paucity of epidemiological data such as age-related prevalence and intensity in communities of Malaysia. The objectives of this paper are to present the results of an investigation on gender-related and age-related prevalence and intensity of infection with *A. lumbricoides* and *T. trichiura* and the effect of three repeated chemotherapeutic interventions on prevalence and intensity levels in a Malaysian community.

MATERIALS AND METHODS

Study area and population

The study site is a large residential area, situated about 3 km from the prime business district of Kuala Lumpur, Malaysia. A large proportion of the study population are slum dwellers or squatters.

The houses are erected wherever there is land available. Most of the houses are made of wooden planks or zinc sheets with zinc roofs. The backyard, which is the children's playground, serves as a convenient waste disposal site.

Study design and protocol

The study was a longitudinal intervention assessment which charted the infection pattern and intensity of identified individuals over three succesive 6-monthly chemotherapeutic interventions (March 1989, September 1989 and March 1990). Before each intervention, infection status was assessed by stool examination. After each intervention, stool was collected and the number of worms expelled enumerated. Only a sub-sample of the community living in the study area who met the following criteria were recruited to the study: 1) Indian families living under slum or squatter conditions who are not likely to move out of the area for a year; 2) families with 3 to 7 children below 15 years of age. The criteria were set to select the ethnic group with the highest prevalence and intensity levels (Kan, 1982), to ensure the continuity of the project, and to reduce the known effects of factors, such as ethnicity (Kan, 1982) and family size (Forrester *et al,* 1988). The project design and protocol were approved by the Ethical Committee of the Medical Faculty of the University of Malaya, Kuala Lumpur and the Parkside Health Authority at the St Mary's Medical School, London. Consent was obtained from the participating families.

Pre-treatment fecal stool count

Self-sealing plastic bags (3.6 cm by 4.6 cm) and wooden applicator sticks for collection of a fecal specimen were issued to participating family members two weeks prior to treatment. The Kato-Katz Modified Thick Smear technique was used to determine the pre-treatment fecal egg-count of *A. lumbricoides* and *T. trichiura.*

Chemotherapeutic regimen

The therapeutic regimen was 400 mg albendazole (Zentel^{R}; Smith, Kline and Beecham plc) once per day for 3 consecutive days. Treatment was offered to the total study population with the exception of children under 2 years of age and pregnant or lactating women for whom treatment is contraindicated. To confirm that the anthelmintic was taken, children from 2 to 8 years were personally administered 20 ml (400 mg) of albendazole suspension by the investigator. Children between 9 to 15 years and adults were requested to take the two 200 mg (400 mg) chewable tablets under the observation of the investigator.

Worm count

To ensure that all the *A. lumbricoides* and *T. trichiura* worms were collected, the participants were requested to collect their 24-hour fecal output for 7 days (168 hours) in plastic containers. Three liter round plastic containers with 500 ml of 10% formol saline (Cheesbrough, 1987) were issued to participants aged 15 years and below while six liter plastic containers with 1,000 ml of 10% formol saline were given to subjects 16 years and above. The plastic containers were stored in a cold room at -6°C until all the worms had been retrieved from the fecal collection.

Data management and analysis

Prevalence was calculated using positive parasite egg count in feces. Although presence of eggs in feces is an acceptable way of estimating prevalence, the validity of egg counts as accurate measures of worm burden is less certain due to the non-linear relationship between worm count and eggs per gram (Croll *et al,* 1982; Bundy *et al,* 1987). The number of expelled worms was therefore used as a more reliable measurement of intensity. Data from individuals who had positive pre-treatment fecal egg-count but negative worm count were excluded from the analyses.

To obtain sample sizes appropriate for statistical analysis, it was necessary to group data. Due to the age distribution of prevalence, the age-classes were stratified to reflect the natural trend of this phenomenon. The following age-classes were adopted: 1) pre-school children of 2-6 years; 2) primary school children of 7-12 years; 3) secondary school students and teenagers of 13-17 years; 4) young adults of 18-29 years; 5) mature adults of 30-39 years; and 6) older adults of 40 years and above.

RESULTS

Efficacy of treatment was confirmed by post-treatment stool examination of 88 fecal samples. The cure rate of *A. lumbricoides* was 100% for all the three interventions. The cure rate of *T. trichiura* was 67.5% while the egg reduction rate after Intervention 1 was 96.0%. The sample size, n, of the study population involved at each intervention, is presented in parentheses.

Prevalence of *A. lumbricoides*

Of 723 persons recruited to the study, 589 (81.5% of initial recruitment) provided a stool specimen before the first intervention. Participation declined to 62.1% (n = 449) and 59.8% (n = 432) for Interventions 2 and 3, respectively. Children under 2 years were not treated, hence, the absence of data on individuals for the 0-1 age-class during Interventions 2 and 3. The age distribution of the sample size is shown in Table 1.

The data used to calculate the prevalence at the three interventions were not necessarily from a cohort, although the participants were all from the recruited population.

The prevalence of *A. lumbricoides* for the total study population at Intervention 1 was 30.6%; at Intervention 2, 18.9%; and at Intervention 3, 15.5%. The age-standardized prevalences were 30.3%, 18.9% and 15.6%, respectively. Using the X^2 test, the difference between the prevalence

Table 1

Age distribution of the participants contributing pre-treatment fecal samples for analysis of data on fecal egg-count of *Ascaris lumbricoides* and *Trichuris trichiura.*

Age class (Years)	Intervention		
	1	2	3
0 - 1	28	-	-
2 - 6	127	119	111
7 - 12	157	138	140
13 - 17	52	38	38
18 - 29	53	34	29
30 - 39	116	84	78
40 +	56	36	36
Total	589	449	432

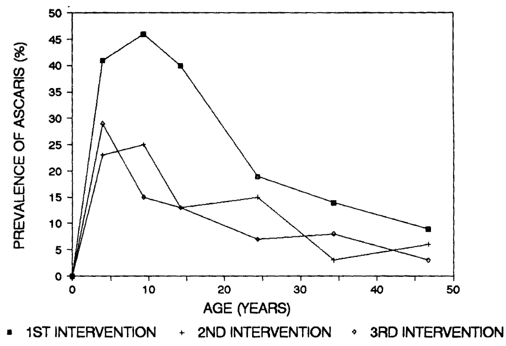

Fig 1—Age-stratified prevalance of *Ascaris lumbricoides* at Interventions 1, 2 and 3.

immediately prior to Interventions 1 and 2, and Interventions 1 and 3, was found to be highly significant ($p < 0.001$). The difference in the prevalence levels between Interventions 2 and 3 was not significant.

The prevalence of *A. lumbricoides* in females prior to Interventions 1, 2 and 3 were 29.2% (n = 312), 19.9% (n = 246), and 11.7% (n = 230) while the figures for males were 32% (n=277), 21.7% (n=203), and 19.8% (n=202). The X^2 test indicated that there was no significant difference in the prevalence levels of the two genders at all the three interventions.

The prevalence of *A. lumbricoides* showed marked age-convexity at the beginning of the investigation and the convexity was maintained throughout the three interventions (Fig 1). The highest prevalence was seen in the 7-12 year age-class at Interventions 1 and 2. At Intervention 3, the 2-6 age-class had the highest prevalence. A distinct decrease in prevalence was observed between Intervention 1 and 2 in all the age-classes.

Intensity of *A. lumbricoides*

482 participants (66.7% of the initial recruitment population) returned stool collection after intervention 1. Compliance declined marginally to 59.6% (n = 431) and 57.4% (n = 415) for Interventions 2 and 3. The age distribution of the participants is presented in Table 2. Negative worm counts from individuals who had positive pre-treatment fecal egg-counts were excluded from the analysis.

Table 2

Age distribution of the participants contributing fecal output for analysis of *Ascaris lumbricoides* worm count.

Age class (Years)	Intervention		
	1	2	3
0 - 1	-	-	-
2 - 6	113	111	103
7 - 12	154	142	136
13 - 17	44	42	39
18 - 29	33	24	26
30 - 39	94	75	76
40 +	44	37	35
Total	482	431	415

The mean intensity (worms per person) of *A. lumbricoides* for the total study population was 1.90, 0.75, and 0.81, retrieved after Interventions 1, 2 and 3, respectively. The data were log (x + 1) transformed. The equality of variance between the intensities of *A. lumbricoides* of the total population at Interventions 1 and 2, at Interventions 1 and 3, and Interventions 2 and 3 was tested, using the *F*-test (Elliot, 1983). The three variances were found to be significantly different from each other at the 5% level since the calculated values of *F* were greater than the tabulated values.

The mean intensities (worms per person) of *A. lumbricoides* for females at Interventions 1, 2 and 3 were 1.32 (n = 250), 0.38 (n = 219) and 0.50 (n = 223), respectively. For Interventions 1, 2 and 2, the mean intensities of *A. lumbricoides* for males were 2.51 (n = 236), 1.12 (n = 212) and 1.18 (n = 192), respectively. Using the *t*-test to compare the mean intensities, the difference in intensities between the genders was insignificant at the 1% level for all the interventions.

Convexity was also seen in the age-stratified intensity graph of *A. lumbricoides*. The 2-6 year age-class consistently had the highest mean intensity throughout the interventions. Between Intervention 1 and Intervention 2, a sharp drop in mean worm intensity was recorded in all the age-classes. The differences in the mean intensities of the age-classes between interventions 2 and 3 were not consistent: some showed an increase (2-6 years; 13-17 years; 30-39 years); two experienced a decrease (7-12 years; 40 and above years); and one showed no change (18-29 years) (Fig 2).

Prevalence of *T. trichiura*

The fecal egg-counts of *A. lumbricoides* and *T. trichiura* were read from the same fecal sample, hence, statistics for the sample sizes are the same as for *A. lumbricoides* presented in Table 1.

The prevalences of *T. trichiura* for the total population prior to Interventions 1, 2 and 3 were 46.9%, 21.6% and 15.7%. The difference between the prevalences prior to Interventions 1 and 2, and Interventions 1 and 3 was found to be significant by the X^2 test, but not between Interventions 2 and 3.

The prevalence of *T. trichiura* for females was 48.7% (n = 312), 18.3% (n = 246) and 10.9% (n = 230) while for males, the prevalence was 44.8% (n = 277), 25.6% (n = 203), and 21.3% (n = 202), at Interventions 1, 2 and 3, respectively. The calculated X^2 value for all three interventions was smaller than the tabulated value of 3.84 ($v = 1$; $p = 0.05$). The difference between the prevalences of *T. trichiura* for females and males was, therefore, not significant.

The prevalence of *T. trichiura* increased with age up to the 7-12 year age-class and remained at a plateau until it slowly decreased from the 30-39 year age-class (Fig 3). With repeated intervention, the prevalence was reduced. The 7-12 year age-class maintained the highest prevalence throughout the intervention period.

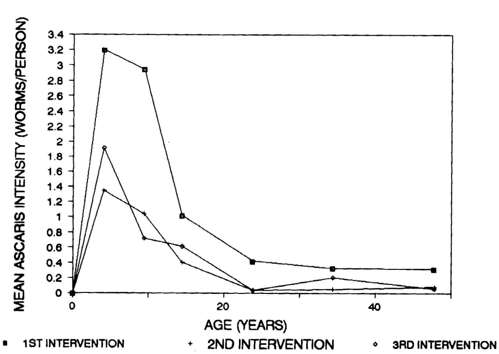

Fig 2—Age-stratified mean intensity of *Ascaris lumbricoides* at Interventions 1, 2 and 3.

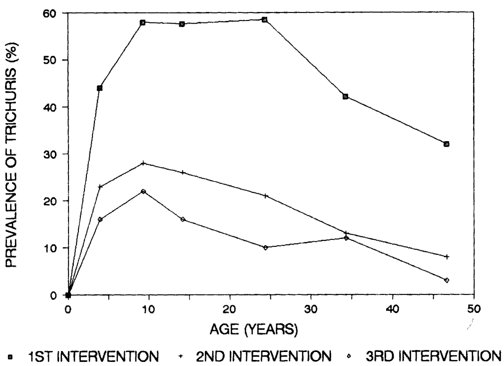

Fig 3—Age-stratified prevalance of *Trichuris trichiura* at Interventions 1, 2 and 3.

Intensity of *T. trichiura*

The age-stratified sample sizes are listed in Table 3. The sample sizes for worm counts of *T. trichiura* were less than those of *A. lumbricoides*. This is because albendazole is less efficacious against *T. trichiura*, and hence more cases of negative worm count/positive pre-treatment fecal egg-counts were excluded from the data set used in the analysis.

The mean intensities of *T. trichiura* for the total study population were 3.30, 0.92 and 0.07 worms per person, after Interventions 1, 2 and 3, respectively. Using the *F*-test to test the equality

Table 3

Age distribution of the participants contributing fecal output for analysis of *Trichuris trichiura* worm count.

Age class (Years)	Intervention 1	2	3
0 - 1	-	-	-
2 - 6	95	97	96
7 - 12	136	128	122
13 - 17	39	36	35
18 - 29	27	21	25
30 - 39	79	71	72
40+	42	37	34
Total	418	390	384

of variances for Interventions 1 and 2, Interventions 1 and 3, and Interventions 2 and 3, it was found that all the three comparisons were significant.

The mean intensities of *T. trichiura* for females were 3.28 (n = 211), 0.07 (n = 203) and 0.03 (n = 213) worms per person after Interventions 1, 2 and 3 while males had mean intensities of 3.32 (n = 211), 1.83 (n = 187), and 0.12 (n = 171). The differences in mean intensities were not significant at the 5% level for all the interventions at p = 0.05.

The age-stratified mean intensity graph showed an increase up to the 7-12 year age-class, followed by a sharp decrease which tapered off gradually. The 7-12 year age group which had a much higher mean intensity than any of the other age-classes at Intervention 1, retained its high position throughout the period of investigation (Fig 4). The mean intensities of all the age-classes were reduced with each subsequent intervention.

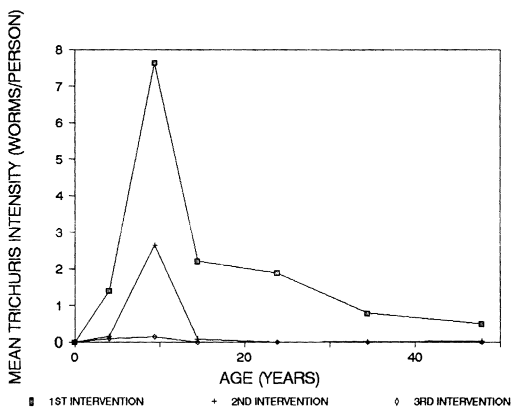

Fig 4—Age-stratified mean intensity of *Trichuris trichiura* at Interventions 1, 2 and 3.

DISCUSSION

The observed age-convexity patterns concur with previous observations (Thein-Hlaing *et al*, 1984; Elkins *et al*, 1986; Bundy *et al*, 1987).

The prevalence and mean intensity of *A. lumbricoides* and *T. trichiura* increased in children and declined in adults (Figs 1-4). This convexity relationship is stable as it was maintained through three interventions. Although this pattern has been described for the major gastro-intestinal helminths of humans (Bundy, 1986), the precise cause has yet to be elucidated. Age-related change in exposure or susceptibility or a combination of both have been postulated (Anderson and May, 1985).

Prevalence and intensity were reduced significantly by the interventions. This indicated that the 6-monthly chemotherapeutic intervention regimen is effective in reducing both prevalence and intensity, and hence, transmission of *A. lumbricoides* and *T. trichiura.* Although there was no significant difference in the prevalence levels between Interventions 2 and 3 for both *A. lumbricoides* and *T. trichiura,* significant reductions were found in the intensity levels. This shows that intensity is a more sensitive indicator than prevalence and argues for the measurement of intensity in the evaluation of the effect of parasite control methods.

In this study, there was no statistically significant difference between the prevalence and mean intensity of infection in females and males in all the three interventions. This suggests that gender-related behavior or immunity does not contribute significantly to the transmission of these two geohelminths in the present study site. Two field studies elsewhere, however, showed that females were more often infected and were re-infected more rapidly than males (Elkins *et al,* 1988; Holland *et al,* 1989).

The rate of increase in prevalence with age between the 2-6 and 7-12 age-classes was similar for *A. lumbricoides* and *T. trichiura,* perhaps because of their similar modes of transmission. However, for age-classes above 13 years, a marked decrease in prevalence was noted in *A. lumbricoides* while a plateau followed by a modest decline was observed in *T. trichiura.* It has been demonstrated that for high degrees of parasite aggregation, large changes in mean worm burden will cause relatively small changes in prevalence, and that prevalence is more sensitive to changes in mean intensity when the numerical value of the worm burden is low (Anderson and May, 1985).

The difference in the age-prevalence patterns of the two species despite their similar modes of transmission could, hence, be attributed to the differences in the absolute magnitude of their intensities.

The results indicate that *A. lumbricoides* and *T. trichiura* are common parasites in the study community and exhibit age profiles of prevalence and intensity which resemble those described elsewhere: for *A. lumbricoides,* the most prevalence and intensely-infected age-classes were the 2-6 year and the 7-12 year age classes while for *T. trichiura,* it was the 7-12 year age-class. The results also indicate that the age and gender relationships observed prior to intervention remained essentially of the same form despite repeated and successful treatment. Both *A. lumbricoides* (Stephenson, 1987) and *T. trichiura* (Cooper and Bundy, 1986) have been shown to cause stunting in children. Since the most intensely infected age-class (7-12 year) also coincides with the period of maximum growth spurt (Tanner, 1962), the growth velocity of children who are heavily infected would be adversely affected. In the Malaysian context, based on these epidemiological and clinical findings, treatment would have most impact on transmission and morbidity if targetted at primary school children, of both sexes between 7-12 years of age.

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