

The morbidity of schistosomiasis mansoni in the highland focus of Lake Cohoha, Burundi

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Abstract

Morbidity due to infection with *Schistosoma mansoni* was investigated in a recently discovered highland focus around Lake Cohoha, Burundi. The distribution of the infection was very focal and morbidity patterns in populations from an endemic area A (prevalence 38%, mean egg load of positive subjects 231 eggs per gram [epg]), a less affected area B (16%, 90 epg) and a virtually non-endemic area C (5%, 45 epg), were compared; apart from schistosomiasis, the profiles of these populations were highly similar. The overall frequencies of diarrhoea were 36%, 25%, and 19%, respectively; of abdominal pain 86%, 78%, and 83%; of fatigue 7%, 2%, and 1%; of left lobe hepatomegaly 30%, 18%, and 9%; of right lobe hepatomegaly 18%, 10%, and 5%; of splenomegaly 18%, 10%, and 7%. Organomegaly was generally mild, even in area A. Within area A, the association between the presence of infection and diarrhoea, fatigue, hepatomegaly and splenomegaly was significant, but far less impressive than the results of the community-based comparison with areas B and C. The correlation with intensity was limited to an increased prevalence of diarrhoea and fatigue in the highest egg count group, and a more gradual increase (varying with age) in hepatomegaly and splenomegaly. The data are compared to other morbidity studies in subsaharan Africa, in particular one in the nearby Rusizi Plain. The lesser impact of malaria, the higher egg loads, the recent establishment of the focus and possibly parasite strain differences may account for the more apparent and more important schistosomiasis morbidity in the Cohoha focus. It is concluded that morbidity due to *S. mansoni* infection is better demonstrated by comparing endemic with non-endemic communities than by relating morbidity to egg counts. Individual egg counts are not always a reliable measure for actual pathology, and their use as a discriminative screening tool for treatment may therefore be questioned.

Introduction

Studies on the morbidity of schistosomiasis mansoni in subsaharan Africa (reviewed by CHEN & MOTT, 1988 and GRyseELS, 1989) have given variable, even conflicting results and are often difficult to compare. Different parasitological, clinical and

epidemiological methods have been applied; the interference of confounding socio-economic, ethnic and nutritional factors, and other diseases (e.g. malaria and intestinal parasitism), is variable and difficult to measure; valid control populations can generally not be defined. It becomes also increasingly difficult to evaluate 'pure' morbidity, as efficacious drugs are becoming widely available.

In this study, we present the results of a morbidity study in a recently discovered focus without these drawbacks. The distribution of the infection is still very focal in an otherwise homogeneous area; valid control populations can thus easily be defined; other parasites have a homogeneous distribution and malaria is hypoendemic; the epidemiological situation has so far been untouched; and the standardized methods have been applied by our group in other foci (GRyseELS & POLDERMAN, 1987a; GRyseELS, 1988), so data can be compared.

Area and population

The Cohoha area has been described in detail by GRyseELS *et al.* (1987). In short, Lake Cohoha is the most important of a series of lakes and marshes in the valleys of the Bugesera, a depression in the north-eastern part of the Burundese highlands. It is situated on the border with Ruanda, at an altitude of 1350 m; the climate is temperate-tropical (mean temperature 21°C, average rainfall 1100 mm). The shoreline is long and irregular and largely inaccessible by road. The hilly peninsulas generally form administrative units (*collines*) and are inhabited by about 20 000 people, mainly farmers and fishermen; the houses are scattered in the fields and not grouped into villages. Rivers, streams or water sources are scarce; nearly all water contact takes place in the lake.

Methods

The population sample was selected by choosing every tenth household on updated census lists. From each member of these households, duplicate 28 mg Kato slides were prepared in the field and examined in Bujumbura 24-72 h later; the results were not available to the clinical observer until after the study. Mean egg loads of groups were calculated as the geometric means of positive individual counts and expressed as eggs per gram of faeces (epg). Each participant was submitted to a standardized protocol (GRyseELS, 1988) by the same observer (L.K.), unaware of the infection status of the subjects and the endemicity level in the *collines*. The case history focused on intermittent (bloody) diarrhoea (defined as at least 3 episodes, each lasting one day or more, in the last 2 months), abdominal pain (analogous defini-

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tion), and general fatigue or weakness. Abdominal palpation and inspection were done in the supine position; spleen enlargement was measured according to HACKETT (1944), liver enlargement at the midsternal and right midclavicular lines in cm below the costal arch.

Results

The distribution, epidemiology and transmission of *Schistosoma mansoni* around Lake Cohoha have been described by GRYSSELS *et al.* (1987). Geographically, a 'core' area, area A (Figure), was recognized with local prevalences ranging from 30 to 51%, an intermediate area B in neighbouring *collines* (prevalences 15–21%), and a peripheral area C with only sporadic cases (4–9%). Ecological conditions (including the presence of the intermediate host, *Biomphalaria stanleyi*) and socioeconomic factors were comparable for all 3 areas. Based also on other observations, the epidemiological situation can probably be explained by assuming that the parasite has been introduced recently and is still spreading (GRYSSELS *et al.*, 1987).

The composition of the population samples in each area is given in Table 1, and the age-specific prevalences and mean *S. mansoni* egg loads in Table 2. In each area, infection rates and intensities were highest in the group aged 10 to 19 years; they decreased considerably in adults, even in area A. Prevalences were significantly higher in males than in females in all 3 areas; the sex ratios were slightly different, but this did not affect the conclusions about endemicity or morbidity. Prevalences of other helminthiases, as far as could be measured, were comparable in the 3 areas (Table 3). There were no reliable statistics for malaria in the area; at this altitude it is generally hypoendemic in Burundi and according to local health workers cases were not very frequent.

The frequencies of (bloody) diarrhoea, abdominal pain, fatigue, hepatomegaly and splenomegaly for the 3 areas are compared in Tables 4 and 5. In all age groups, except those aged 20–39 years, diarrhoea was considerably and significantly more frequent in area A than in areas B or C (Table 4). In area A, the diarrhoea was reported as 'bloody' by 28% of those presenting this complaint, in area B by 18%, and in area C by 10%. Abdominal pain was a very frequent complaint in all age groups of all areas, and can probably not be related to any single infection. Fatigue was complained of by only a minor proportion of the population, but it was nevertheless 3–7 times as frequent in area A than in the other areas; this increased frequency was significant in all age groups except the oldest. Hepatomegaly of the left lobe was almost twice as frequent in area A as in area B, and 3 times more frequent as in area C (Table 5). In the 10–19 years age group, the frequency of hepatomegaly in area A was 10 times as high as in area C. Right lobe hepatomegaly was less frequent but still clearly associated with schistosomiasis endemicity. Splenomegaly was up to 3 times as frequent in children and adolescents in area A than in areas B or C. The trend was present, but not significant, in those aged 20 to 39 years, and was absent in the oldest age group.

Organomegaly was mostly mild. Even in area A,

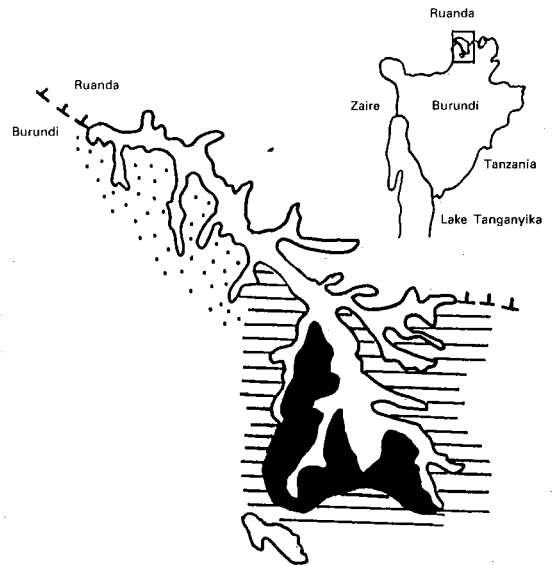


Figure. Geographical situation of Lake Cohoha and study areas. Black=area A, prevalence 38% (see text and Table 2); hatched=area B, prevalence 16%; stippled=area C, prevalence 5%.

Table 1. Composition of study populations^a

Age (years)	Total	Area A	Area B	Area C
0–9	474	149	220	105
10–19	313	146	121	46
20–39	457	144	194	119
≥40	330	108	127	95
Total	1574	547	662	365
Males	774	289	305	180
Females	800	258	357	185

^aBased on a 10% sample.

Table 2. Prevalences of *S. mansoni* infection and egg loads in different areas

Age (years)	Prevalences (%)			Mean egg loads ^a		
	A	B	C	A	B	C
0–9	30	11	0	195	90	0
10–19	64	38	20	347	101	51
20–39	37	15	7	179	79	38
≥40	14	6	2	78	77	36
Total	38	16	5	231	90	45
Male	50	21	7	235	102	47
Female	24	12	3	223	73	38

^aGeometric mean eggs per gram of faeces of positive individuals.

Table 3. Prevalences (%) of other helminthiases in the Cohoha area^a

	A	Area B	C
<i>Ascaris</i>	28	25	26
<i>Trichuris</i>	43	44	38
<i>Taenia</i>	3	3	5

^aHookworm and *Strongyloides* cannot be reliably measured with delayed Kato slides.

Table 4. Age-related percentage frequencies of complaints in the three areas^a

Age (years)	Diarrhoea			Abdominal Pain			Fatigue		
	A	B	C	A	B	C	A	B	C
0-9	37**	28**	14	71	62	71	4*	1	0
10-19	43**	23	22	93	86	87	8*	0	0
20-39	26	24	19	88	82	89	5*	2	0
≥40	39*	23	23	94	80	87	7	9	2
Total	36*	25*	19	86	78	83	7*	2	1

^aStatistically significant differences (χ^2) indicated thus: A>B+C or B>C: * $P<0.05$, ** $P<0.01$.

Table 5. Age-related percentage frequencies of organomegaly in the three areas^a

Age (years)	Hepatomegaly						Splénomegaly		
	(left lobe)			(right lobe)			A	B	C
	A	B	C	A	B	C	A	B	C
0-9	34**	25**	8	20**	13*	5	14 [†]	10	5
10-19	41**	19*	4	25**	10*	0	31**	12	11
20-39	19*	9	9	10*	5	2	14	10	7
≥40	22 [†]	19	11	16 [†]	14*	3	10	10	8
Total	30**	18**	9	18**	10**	5	18**	10	7
Enlargement ^b									
>2	12*	6*	2	2	0.5	0	6*	3	2
>4 cm	2	0.5	0	0	0	0	3	1	1

^aStatistically significant differences (χ^2) indicated thus: *A>B+C or B>C, $P<0.05$; **A>B+C or B>C, $P<0.01$; [†]A>C $P<0.05$.

^bHepatomegaly measured in midsternal line beneath costal arch; for splénomegaly, these rows refer to Hackett's scales 1 and 2, respectively.

Table 6. Percentage frequency of symptoms in different egg output groups in area A^a

	Age (years)	Percentage of subjects with complaint in egg output group				
		All positive	0	1-100	101-350	>350 epg
Diarrhoea	0-9	48	32*	29*	46	69*
	10-19	46	36	27	24	61*
	20-39	30	24	29	14	47*
	≥40	47	38	46	50	50
	Total	43	32*	31	28	60**
Fatigue	0-9	4	4	6	8	0
	10-19	10	4	0	0	17*
	20-39	8	3	4	7	13
	≥40	20	5	27*	0	0
	Total	9	4*	7	4	13**
Hepatomegaly	0-9	54	26**	41	69**	56**
	10-19	53	23**	36	35**	63**
	20-39	30	13*	25	21	47**
	≥40	27	22	18	50	50
	Total	45	21**	31	41**	59**
Splénomegaly	0-9	20	12	12	23	25
	10-19	31	25	14	29	44*
	20-39	14	11	8	21	33
	≥40	10	9	18	50	0
	Total	18	13**	12	26*	38**
Number of subjects in egg output groups	0-9	45	104	16	13	26
	10-19	93	53	22	17	54
	20-39	53	91	24	14	15
	≥40	15	93	11	2	2
	Total	207	345	74	46	87

^aStatistically significant (χ^2) indicated thus: * $P<0.05$, ** $P<0.01$, referring to comparisons between all positive and negative (0 epg) groups, and between each epg output group and total of positive lower egg output groups; epg=eggs per gram of faeces.

Table 7. Review of *S. mansoni* morbidity patterns in subsaharan foci

Focus ^a	Prevalence	Mean epg ^b	Diarrhoea (%) ^c			Hepatomegaly (%) ^d		
			+	-	C	+	-	C
Rusizi (Burundi) ¹	33%	98	26	21	-	26	19	-
Rusizi ^a	53%	118	32	27	19	>2 6	4	17
Cohoha (A) (Burundi) ³	38%	231	43	32	19	>2 8	8	9
Tana (Ethiopia) ⁴	43%	117	16	10	11	≥2 12	6	12
Kisumu (Kenya) ⁵	47%	87	13	10	-	>2 34	22	-
Gezira (Sudan) ⁶	52%	300-600	39	17	-	33	26	-
Machakos (Kenya) ⁷	82%	499	5	4	-	≥3 34	21	-
West Nile (Uganda) ⁸	89%	400-1100	49	-	-	46	-	-
Maniema (Zaire) ⁹	96%	791	55	-	5	>4 32	0	9

^aSuperscript numbers indicate references as follows: ¹GRYSEELS, 1988; ²GRYSEELS & POLDERMAN, 1987b (areas of the Rusizi plain with prevalences >50% only); ³this paper; ⁴HIATT, 1976; ⁵SMITH *et al.*, 1979; ⁶OMER *et al.*, 1976; ⁷ARAP SIONGOK *et al.*, 1976; ⁸ONGOM & BRADLEY, 1972; ⁹GRYSEELS & POLDERMAN, 1987.

^bepg=eggs per gram of faeces.

^cVarying definitions; +=positive subjects, -=negative subjects, C=control subjects.

^dMidsternal measurement (if specified): >2=over 2 cm below costal arch and >4=over 4 cm below costal arch; +=positive subjects, -=negative subjects, C=control subjects.

only 7% of the enlarged livers extended more than 4 cm below the costal arch; 17% of the splenomegaly cases were in grade 3 or more of Hackett's scale. In areas B and C, no gross organomegaly was seen.

Relevant symptoms are related to the presence and intensity of infection in individuals from area A in Table 6. For all ages combined, diarrhoea, fatigue, hepatomegaly and splenomegaly were all significantly associated with the presence of infection. However, the differences between positive and negative subjects in area A were much less dramatic than the differences between the populations of area A and area C or even B, as shown in Tables 4 and 5. When analysed by age group, the difference (if any) between positive and negative individuals was not significant for fatigue or splenomegaly in any group; for diarrhoea it was significant only in the group aged 0-9 years. For hepatomegaly, the association was present in all age groups except those aged over 40 years. The correlation of frequency of diarrhoea with intensity of infection (Table 6) was limited to a significant increase in infections over 350 epg, over the whole population and in all age groups up to 40 years. For fatigue, a significant increase was observed in the highest egg output group over the whole population, and in the 10-19 years age group. Hepatomegaly increased gradually with intensity of infection for the whole population. The extent of the correlation varied with age: in children aged 0 to 9 years, there was a significant association with infections over 100 epg, and in adolescents and adults under 40 years with infections over 350 epg. In older adults, the apparent correlation with intensity related to a few cases only and was not significant. Splenomegaly also correlated significantly with presence and intensity of infection in the total population. The trend was consistent in

each age group, but significant only for heavy infections in adolescents.

No cases with a history of oesophageal bleeding, ascites or other apparent signs of portal hypertension were found in the study sample. However, 2 male adolescents in area A, who had not been included in the sample, presented gross ascites, *caput medusae*, stunted growth and cachexia. Both excreted *S. mansoni* eggs, 120 and 280 epg respectively, but had no history of haematemesis.

Discussion

The much higher frequencies of diarrhoea, hepatomegaly, splenomegaly and fatigue in the 'core area', when compared to the more peripheral hills, can be due only to the higher infection rates and intensities of *S. mansoni*. Ecological, socio-economical and sanitary conditions were similar along the lake shore. The prevalence of intestinal helminthiasis was comparable; malaria was probably hypoendemic and there was no obvious reason why its distribution would be heterogeneous. Observer bias is unlikely, as the clinical observer was not aware of the infection status of the individual or even of the prevalence in the *colline* in which he was working; the slides were examined far away and the focal distribution of the infection became apparent only when the data were analysed. This study thus clearly demonstrates the important morbidity due to schistosomiasis mansoni in the Cohoha area. Diarrhoea was twice as frequent in the endemic *collines* than in the (still) non-endemic ones; fatigue, 7 times more frequent; and hepatomegaly and splenomegaly, 2-3 times.

The present results are compared with those of other community-based studies of *S. mansoni* morbidity in subsaharan Africa in Table 7 (other studies

relating to schoolchildren only are not included). Diarrhoea and hepatomegaly can generally (though not always) be related to the presence and—to a lesser extent than is generally accepted (GRYSEELS & POLDERMAN, 1988)—the intensity of infection. De-compensated portal hypertension is very infrequent in most study areas (for further review see GRYSEELS, 1989). In terms of frequencies of symptoms, the morbidity pattern in the Cohoha focus seems close to the dramatic situations described in intense foci such as Maniema in Zaire and West Nile in Uganda rather than to more comparable, moderate foci. However, variations in quantification methods must be allowed for in this comparison. In the Kenyan study, for example, only livers extending more than 2 cm below the costal arch (in the midsternal line) were considered as significantly enlarged. As shown in the Table, applying this criterion reduces our results to much lower levels. Gross hepatomegaly or splenomegaly was indeed infrequent in the Cohoha area, in contrast to West Nile and Maniema, and also Gezira or Machakos. Criteria for diarrhoea or fatigue are even more variable, and depend on the attitude of both interviewer and population. The association between diarrhoea and schistosomiasis may have been striking in the Cohoha focus, but severe dysenteric syndromes, as described by our group in the Maniema focus and by others in the West Nile and Gezira foci (references in Table 7), are certainly not very frequent. Although we found 2 suspected cases, de-compensated portal hypertension appears to be uncommon. The absence of dramatic clinical pictures indeed partly explains the late discovery of the Cohoha focus (GRYSEELS *et al.*, 1987).

The most relevant and interesting comparison can be made with the Rusizi plain. The characteristics of the populations are comparable, and an identical protocol was followed by the same observers. Nevertheless, intestinal and hepatic morbidity are more important and more clearly related to schistosomiasis in the Cohoha area than in the Rusizi plain, even when only high-prevalence areas in the latter area are included (Table 7). The varying morbidity patterns may be due to several factors. (i) Malaria is highly endemic in the Rusizi plain (COOSEMANS *et al.*, 1984), and confuses the nevertheless significant association between organomegaly and schistosomiasis (GRYSEELS, 1988); the hepatomegaly rate in control subjects was twice as high in the Rusizi plain as in the Cohoha focus. (ii) Egg loads were higher in the Cohoha area than in the Rusizi plain, particularly in younger age groups. These higher egg loads may furthermore be due to recent, massive infection rather than a gradual superinfection (see item iii). These differences appear to lead to higher frequencies and intensities of hepatomegaly in the Cohoha area, in spite of the lower impact of malaria. Also the higher frequency of diarrhoea can be explained by the higher intensities of infection; diarrhoea was equally frequent in control populations from both areas (Table 7). (iii) The Rusizi plain is an older, established focus (GRYSEELS, 1984; GRYSEELS & NKULIKYINKA, 1988), whereas in the Cohoha area the parasite has presumably been introduced during the last decade or so (GRYSEELS *et al.*, 1987). Adults in this focus have probably had no contact with the parasite in their youth, and may not yet have developed the immuno-

logical mechanisms which modulate pathology. This would explain the relatively important impact of schistosomiasis on the frequency of diarrhoea and hepatomegaly in adults. Splenomegaly, on the other hand, cannot be related to schistosomiasis in the older age groups of Cohoha, whereas such a relation could be shown in the Rusizi plain. Splenomegaly as a late consequence of liver fibrosis and portal hypertension may not yet have developed in the Cohoha focus; if no more serious morbidity may develop in coming years, (iv) The intermediate host in lake Cohoha is *Biomphalaria stanleyi* (GRYSEELS *et al.*, 1987); in the Rusizi plain it is *B. pfeifferi*, which is also present but not (yet) transmitting *S. mansoni* in the Burundese highlands (GRYSEELS, 1985). Possibly the isolation of the Cohoha focus in these highlands can be explained by parasite strain differences, which may then also account for different morbidity patterns.

In the present study, morbidity was far more apparent from the comparison of endemic communities with control populations (area A vs areas B and C) than from its analysis as related to presence or intensity of infection within the endemic community (area A). Even the parasitologically negative group in area A showed higher morbidity rates than the populations from areas B and C. Within area A, a significant correlation of morbidity with intensity of infection was, in most age groups, limited to the highest egg output group.

Community-based, and certainly one-to-one, comparisons may easily be biased by confounding factors (BLUM & FEACHEM, 1983). This problem may also lead to an overstatement of the strength of the statistical significance for comparisons between areas. However, in this and other morbidity studies by our group in Burundi and Zaire (POLDERMAN, 1984; GRYSEELS & POLDERMAN, 1987a, 1987b; GRYSEELS, 1988), we believe we have identified groups of study and control populations which differ only in their exposure to schistosomiasis transmission. In each of these studies, the inter-population comparisons reveal more important morbidity than intra-population analysis; these results also are summarized in Table 7. This apparent discrepancy may be partly explained by the insensitivity of a single stool examination; many 'negatives' may prove to be 'positive' on repeated examination (GRYSEELS & NKULINKYA, 1988), with the use of more sensitive methods (MARSHALL *et al.*, 1989), or by detection of circulating worm antigen in the serum (DE JONGE *et al.*, 1988). In chronic schistosomiasis there is, furthermore, a time lag between (heavy) infection and development of pathology; HOMEIDA *et al.* (1988) have recently shown, by ultrasound, that many patients with proved Symmers' fibrosis are parasitologically negative. CHEEVER (1968) in his famous autopsy studies also indicated that, though high worm loads may be a prerequisite for the development of Symmers' fibrosis, this would not necessarily be reflected in high faecal egg counts. Presence and number of eggs of *S. mansoni* in the stools are thus not always reliable indicators of actual pathology on the individual level, as was suggested by, among others, WHO (1985) and MOTT (1987). On the community level, (mean) egg counts may be a useful tool to assess the 'population worm burden' and overall risk of morbidity; within an endemic community, however, it can be expected that schisto-

schistosomiasis pathology is present also in individuals with low or even negative egg counts. Even on the population level, important variations do occur: prevalences and mean egg counts in the foci of Rusizi (Burundi), Tana (Ethiopia) and Kisumu (Kenya) are comparable (Table 7), but the respective morbidity patterns are quite different.

The conclusions of this comparative study in a focus with moderate prevalences and intensities of infection are similar to those in the highly endemic Maniema focus (GRYSEELS & POLDERMAN, 1987a). First, by not including control populations in morbidity studies, the impact of schistosomiasis on public health may be considerably underestimated. Second, the use of egg counts for discriminative screening in targeted or even selective population-based chemotherapy is arguable; indiscriminate mass treatment may be the most efficient way to achieve morbidity control.

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