The Relationship between Bilharziasis and Typhoid Fever employing the Widal Test as a Screening Procedure

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INTRODUCTION

The purpose of this study was to investigate whether an association existed between bilharziasis and enteric fever organisms. The association between bilharziasis and salmonellosis (the salmonellosis group includes over 200 types of intestinal pathogens in addition to *S. typhi* and *S. paratyphi*) has been described before in Egypt (1949) and Brazil (1967). As typhoid fever and bilharziasis (*S. haematobium* and *S. mansoni*) are both common in Africans in Rhodesia, it seemed worth investigating a possible relationship between them.

METHODS AND MATERIALS

Selection of Cases

Four groups of cases were selected in the University Medical Unit at Harare Hospital, which caters only for African in-patients.

Group A

Group A consisted of patients diagnosed as having typhoid fever with a Widal 1/480, rising titre or positive stool and/or blood culture for *S. typhi* in whom *S. mansoni* or *S. haematobium* existed as well in stool or urine.

Group B

Group B consisted of those found to harbour ova of *S. mansoni* in the stool or *S. haematobium* in the urine.

Group C

In this category of cases diffuse bilharzial lesions were present on cystoscopy.

Group D

Random samples of in-patients acting as controls for the investigation. In this group a battery of tests were done irrespective of the clinical diagnosis.

The following tests were carried out on all the patients of the four groups:

(1) Widal agglutination reaction.
(2) Routine microscopical examination of urine.

(3) Routine microscopical examination of stool.
(4) Stool culture.
(5) Blood culture, using both a typhoid and ordinary medium for each specimen.
(6) A rectal snip was taken in those in whom no ova of *S. mansoni* or *S. haematobium* were found in either urine or stool.

The Widal agglutination reaction is a test designed to detect both quantitatively and qualitatively antibody in the serum against one of the enteric fever organisms. Anything below a titre of 1/160 H or O antigen is reported as not being of likely significance. For a more definite diagnosis a titre between 1/320 and 1/640 should be obtained. (Professor Cruickshank, personal communication, 1973).

Findings

Group A (26 cases were considered to have typhoid fever). Seventeen had ova of *S. mansoni* in stools as determined by routine stool or rectal snip. Three had *S. mansoni* ova plus *S. haematobium* ova. Two had *S. haematobium* ova only. Four had neither *S. haematobium* nor *S. mansoni* ova.

Group B (in-patients in whom *S. mansoni* or *S. haematobium* had been found on routine investigation of stool or urine). None of these patients showed clinical signs of typhoid fever. Fifty-nine cases were investigated as outlined previously. The findings were as follows:

(a) Positive *S. mansoni* ova in stools with a Widal test of less than 1/480 — 20 cases eight of which had H or O > 1/960).
(b) Positive *S. mansoni* ova in stools with Widal test greater than 1/480 — 10.
(c) With *S. haematobium* ova in urine with Widal test greater than 1/480 — 3; Widal test less than 1/480 — 0.
(d) With *S. haematobium* ova in stools with Widal test greater than 1/480 — 2; Widal test less than 1/480 — 1.
(e) With *S. haematobium* ova and *S. mansoni* ova, Widal test greater than 1/480 — 4; Widal test less than 1/480 — 2.
(f) With *S. haematobium* ova only, negative Widal test — 4.
(g) With *S. mansoni* ova only, negative Widal test — 12.
(h) With *S. mansoni* ova and *S. haematobium* ova, negative Widal test — 1.

Group C (bilharziasis evident on cystoscopy with or without bladder calcification on X-ray). There were 10 cases: Widal test greater than 1/480 — 4; Widal test less than 1/480 — 3; Negative Widal — 3.

Group D 47 cases (control group in whom the battery of tests was done irrespective of their clinical diagnosis). These were subdivided as follows:

(a) Negative Widal test, negative stool, negative urine — 31 cases.
(b) Widal test greater than 1/480, negative stool, negative urine — 6 cases.
(c) Widal test less than 1/480, negative stool, negative urine (not diagnosed as typhoid) — 2 cases.
(d) Negative Widal test, positive *S. mansoni* in stools, negative urine — 5 cases.
(e) Negative Widal test, negative stool, positive *S. haematobium* in urine — 2 cases.
(f) Negative Widal test, positive *S. mansoni*, positive *S. haematobium* — 1 case.

Discussion and Interpretation

In analysing our results, only those considered positive, e.g., 1/960, was compatible with a diagnosis of typhoid fever. The results discussed apply only to our hospital in-patients and although they may also be true of the general population, as a whole, our conclusions were restricted to our hospital in-patients.

In comparing Group A (those with a positive Widal test) with Group D (our control), we found:

	Positive Widal	*Negative Widal*	
Positive Bilharziasis	22	8	30
Negative Bilharziasis	6	31	37
	28	39	67

$$\therefore X^2 \text{ with Yates correction} = \frac{67\,(682 - 48) - 33\tfrac{1}{2}^2}{28 \times 39 \times 37 \times 30} = \frac{24120000}{1212120} = 19{,}90.$$

In comparison, Group B (those showing either *S. mansoni* or *S. haematobium*) were subjected to a Widal test and their results were:

	Positive Widal	*Negative Widal*	
Bilharziasis	23	17	40
No bilharziasis	2	31	33
	25	48	73

$$\therefore X^2 \text{ with Yates correction} = \frac{73(1713 - 34) - 36\tfrac{1}{2}^2}{1000 \times 48 \times 33} = \frac{30181777}{1584000} = 19{,}054.$$

It might be argued that a few of our cases had an amnestic reaction, giving rise to the

high Widal result, but if this were so, one might have expected the same to have occurred in the control series.

In a survey carried out by Neva (1949) in Cairo, Egypt, in 76 cases of salmonellosis, 14 failed to respond to treatment and continued for many months as chronic carriers of salmonella in the urine. Out of these 14, eight had *S. haematobium* in the urine and three gave a history of bilharziasis. Because of the very high incidence of urinary bilharziasis in Egypt, some speculation has arisen on the possible lesions which may be found with urinary enteric carriers. These include pylonephritis, pyonephrosis or a perinephric abscess. Rupture of the focal lesions into the kidney tissues may be the main cause of the bacilluria.

Neves *et al* (1969) observed that prolonged salmonellosis in Brazil was invariably associated with an *S. mansoni* infection which was resistant to treatment with chloramphenicol until a course of Niridazole was given. Halawani *et al* (1960) in Egypt found that the incidence of urinary carriers of salmonellosis was greater than in intestinal carriers (as is not the case in other parts of the world). They studied two groups of persistant urinary carriers of salmonella. In one, bilharzial ova were present in the urine and in the other they were absent. Fifty per cent. of those with evidence of bilharziasis in the urine failed to respond to chloramphenicol and the urine cultures remained positive. Following treatment for the bilharzial infection, however, a second course of chloramphenicol was administered and the 50 per cent. which failed to respond previously showed sterile urine cultures for salmonella. These results confirm the observation that by treating urinary bilharziasis, the response of carriers to therapy with chloramphenicol is increased; they serve to emphasise the important role active bilharziasis can play in the persistent carrier state.

It has also been pointed out that a previous urinary tract anomaly may often predispose to the urinary carrier state. While doing an extensive study of urinary bilharziasis, Lehman, Farid, Smith, Bassily and El-Masry (1973) found significant bacteriuria in 73 out of 186 patients. By far the most common organism isolated was that of *Salmonella* species; others included coliforms, *Klebsiella* and *Pseudomonas*. This superimposed bacterial urinary tract infection upon primary urinary bilharziasis has significance in that the concentrating powers of the kidney are further decreased in the presence of a bacteriuria (Lehman *et al*, 1971).

More recently Gentilini, Roubineau, Letonturier, Boussougant and Domart (1972) of France have demonstrated the existence of a urinary tract infection with *Paratyphi C* in the presence of *S. haematobium* without any clinical manifestations being shown. This patient underwent a nephrectomy and from the culture of the ground calculus *S. paratyphi C* was isolated — an exceptional micro-organism in Europe. In the same patient, although urine culture for *S. paratyphi C* was high, the Widal remained persistently negative.

Our findings show that an individual infected with either *S. mansoni* or *S. haematobium* is more liable to contract an infection with typhoid organisms than one who is not infected. A significant difference is noted in those found harbouring the bilharzial infection. If this association exists, as our evidence appears to indicate, where in the body are the salmonella organisms located? It may be that the pathogenesis of this type of typhoid fever is different to that contracted by ingesting infected water or food in which the lesions of the small bowel are characteristically present. In view of the findings of Young *et al* (1973), it would seem that the organisms are present in the tegument of the worms, which live in close relationship to the blood stream, thus infecting it. Patients who develop symptoms of this type of typhoid fever may run bouts of fever of varying severity, on and off, for long periods, but haemorrhage and perforation of the small intestine are not to be expected.

This study as shown by Wicks *et al* (1971) also throws some doubt on the reliability of the Widal agglutination reaction as a screening test for the diagnosis of typhoid fever, since, in our series, many patients, who had no clinical evidence of typhoid fever had a Widal test H or O or H and O $>$ 1/960, which in the past has been accepted as being diagnostic.

Most of our cultures for *S. typhi* from stool and blood were negative. This might have been because we were seeing the cases late or because they were being treated sub-therapeutically before arrival and hence result in a negative culture. If the Widal cannot be used as a screening test in this country, where the concurrent presence of bilharziasis may give false findings, what index or indices are we to use to diagnose typhoid fever, which is so endemic in our local African population?

Should all cases of suspected typhoid be treated concurrently for bilharziasis if ova are

found in the faeces or urine? The long, protracted course of salmonellosis is possibly seen here as often as has been seen described elsewhere. There seems to be no doubt from our series that the presence of *S. mansoni* or *S. haematobium* (and in particular *S. mansoni* in faeces) causes a higher Widal agglutination reaction than in patients with no bilharziasis. The exact pathogenicity between salmonellosis and bilharziasis is not known.

Some observers might be tempted to explain the high positivity of our Widal testing as an anamnestic reaction, but this is not the case since our control group showed no similar reaction to the Widal test.

Summary

Our results are statistically significant. They show good reason to support the finding that an association exists between bilharziasis and salmonellosis. How and why the association exists is not known.

In our work, *S. mansoni* would appear more important although *S. haematobium* is the more prevalent parasite (Gelfand, 1967). We have included *S. haematobium* in our results but our findings apply particularly to *S. mansoni.*

Patients with bilharziasis have a higher Widal positivity than those without the disease. Whether this has any bearing on the future management of typhoid fever is not known. Many patients admitted to our hospital have a low grade pyrexia and their illness assumes a chronic protracted course. Our results may be of importance for such patients because the existence of bilharzial ova in the urine or stool may draw attention to the presence of a salmonella septicaemia for which prompt treatment for both diseases will result in a more speedy recovery and decrease in mortality.

The question also arises as to the role played by the sufferer with chronic urinary bilharziasis (as in Group C) as a carrier of salmonellosis. In regions where bilharziasis and typhoid fever are endemic the reliability of the Widal as a diagnostic test for the recognition of typhoid fever may be of limited value in those with negative cultures in blood or excreta.

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