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SCHISTOSOMIASIS HAEMATOBIA IN BRAZILIAN PATIENTS. CLINICAL AND RENAL FUNCTIONAL EVALUATION WITH ^{99m}Tc-DTPA

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ABSTRACT: The present study was carried out at the Army Central Hospital, Rio de Janeiro, Brazil, from September 2000 to December 2001, employing diethylenetriamine penta-acetic acid labeled with technetium-99m (^{99m}Tc-DTPA) to evaluate the renal function of nineteen symptomatic patients infected with *S. haematobium* during a peace mission in Mozambique. Results evidenced that the most frequent clinical manifestations were hematuria (68.4%) and low back pain (68.4%) and 73.7% patients had altered dynamic renal scintigraphy expressed by an increase in the excretory phase independently of the symptoms duration; furthermore, none of them had mechanical obstructive pattern. *Schistosoma haematobium* glomerulopathy could be considered a pathological finding without correlation with the disease clinical manifestations.

KEY WORDS: Schistosomiasis, *Schistosoma haematobium*, renal radionuclide imaging, Brazilian patients, ^{99m}Tc-DTPA.

CONFLICTS OF INTEREST: There is no conflict.

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INTRODUCTION

In 1852, the German physician Theodore Bilharz described a parasitic infection that would later be termed schistosomiasis. Currently, 200 million people in 74 countries have the disease; 120 million of them present symptoms and 20 million have severe illness (13). Schistosomiasis haematobia is caused by *S. haematobium*, parasitic trematode worms that reside in the venulas of vesical plexus of their vertebrate definitive host (11).

The classical tissue response to ova is granulomatous as consequence of a cascade of events due to release of soluble egg antigens through micropores of eggshell (3, 9). There is evidence that some of these lesions may predispose to malignancy (3). The urogenital system is the main target of *S. haematobium* infestation. Morbidity from urinary schistosomiasis is widely variable, probably due to differences in parasitic strains, intensity of infestation and host susceptibility (3, 11). The earlier reports of schistosomal glomerulopathy were from Brazil and further reports, also from Brazil and many other countries, confirmed it as a distinct disease entity (1). The syndrome is independent of oviposition and mediated by immune response to circulating antigens released by adult worms (10).

Clinical and laboratorial diagnosis of schistosomiasis haematobia included the presence of ova in the urine, hematuria, low back pain, dysuria, pollakiuria, nycturia and pain in the pelvic region (11, 14). Schistosomal antigens were detected in glomerular deposits, usually together with IgM, C3 and less frequently with IgG and IgA (3). The renal lesions of schistossomiasis reflect the two major pathogenetic mechanisms. First, there are focal lesions mostly affecting the lower urinary tract caused by local granulomatous response to *S. haematobium* ova. Second, there are lesions caused by immune-complex deposition in the glomeruli, usually associated with *S. mansoni* infections and with *S. haematobium* (4).

Radioisotope renography using ^{99m}Tc-DTPA is a safe, sensitive, simple and fast method which is widely accepted as a valuable tool for investigation, management, and follow-up of patients with renal disease. It also allows repeated examinations of individual renal function without any major inconvenience to the patient (8,9).

The aim of this work was to study renal dynamic scintigraphies with ^{99m}Tc-DTPA of male soldiers who went to Mozambique in a peace mission and were infected with *S. haematobium* which does not exist in Brazil.

PATIENTS AND METHODS

Renal dynamic scintigraphies were carried out for nineteen male soldiers aged from 26 to 36 years old, mean age of 30.05±2.97 years, who went to Mozambique for 15 months (from September 2000 to December 2001) and were infected with *S. haematobium*.

Clinical and laboratorial diagnosis of schistosomiasis haematobia was obtained within an interval between 10 months and seven years after exposition to the parasite. Inclusion criteria were: exposition to *S. haematobium* with clinical manifestations and presence of parasite eggs in the urine. This study was submitted and approved by the Committee of Ethics in Research.

Scintigraphies were done employing DTPA labeled with ^{99m}Tc, both produced by Nuclear and Energetic Research Institute [Instituto de Pesquisas Energéticas e Nucleares - IPEN/CNEN, São Paulo, Brazil]. A two-headed gamma-camera (Nucline DH – MB950 – Mediso, Budapest) was used, with low-energy, all-purpose collimator, and 20% window in peak for ^{99m}Tc (140 keV).

Test was carried out 30min after hydration of the patient with 300–500ml water at room temperature. The patient was in supine position, the collimator was underneath and close to the patients' back and the kidneys were in the center of the image. Sequential images were obtained following the bolus injection of a small volume of ^{99m}Tc-DTPA with high-activity (370MBq; 10mCi) into the antecubital vein.

Data were obtained using 60 frames of 1s followed by 87 images of 20s each. Activity/time curves were generated for regions of interest: cortical, pelvic and whole kidney, bladder and aorta. Background was determined by a C-shaped perirenal area. Fifteen to 20min after radiotracer, an injection of 40mg furosemide was intravenously administered to patients who presented a plateau or an ascending pattern in the excretory phase of the nephrogram.

The following values were considered normal: time to peak activity (T_{max}) lower than 6min (8), $T_{1/2}$ of the renogram lower than 14min, and parenchymal transit time index (PTTI) lower than 2:36min (6).

RESULTS

Table 1 shows the age and the time interval between the exposition to the parasite and the beginning of the clinical manifestations (signs and/or first symptoms) of all nineteen patients. Hematuria was the first sign in 13 patients (68.42%) and low back

pain also in 13 patients; association of both signs was identified in 11 patients (58%). Isolated or in association, all two symptoms had no relation to the time interval between exposition and clinical manifestations. Low back pain was the unique and first symptom in two patients (one after twelve months and one after eighty-four months of infection); both patients presented a prolonged excretory phase (PEP) in the nephrogram. Dysuria was the third most common symptom (42.10%) and was the unique symptom in one patient (after less than twelve months of exposition–clinical manifestation), who had PEP in the nephrogram. Among the five patients that did not present hematuria, three had twelve months or less of infection, one had forty-eight months, and two had eighty-four months of infection. Pollakiuria was present in four patients (21%).

Table 2 shows the time interval between exposition to the parasite and clinical manifestations, the relative function of each kidney, and the result of renogram. Six patients with twelve months or less of infection had already a PEP (four patients for both kidneys; two for the right kidney); in contrast, eight patients with more than twelve months of infection had PEP (four patients for both kidneys; three for the left kidney; and one for the right kidney). Five patients (26%) had normal nephrograms for both kidneys (one patient with twelve months; two with twenty-four months; one with 48 months; and one with eighty-four months of infection). Only five patients (26%) had normal nephrograms for both kidneys; out of the remaining fourteen patients (73.7%), eight had bilateral and six unilateral PEP. There was no tendency for left or right kidney alteration; both were equally compromised. All fourteen patients with abnormal renogram (100%) presented PEP and none of them had obstructive pattern.

Patients with bilateral normal renogram had random clinical manifestations and infection duration. The kidneys relative function was calculated between 60–120s; the mean value for the right kidney was 49% and that for left kidney was 51%.

T_{max} was higher than 6min in 42% of the patients; $T_{1/2}$ was higher than 14min in 68.5% of them; and PTTI was higher than 2:36min in 58% patients.

Figure 1A evidences a normal curve for both kidneys of Patient 6, who presented pollakiuria as first clinical manifestation. Figure 1B shows a curve with PEP for both kidneys of Patient 13.

Table 1. Patients' number, age and time interval between exposition to the parasite and initial manifestation (symptoms or signs).

Patient Number	Age (years)	Time Interval (months)	Initial Symptoms/Signs
1	33	84	Dysuria, pain in the pelvic region.
2	29	84	Low back pain.
3	26	72	Hematuria, low back pain, dysuria.
4	27	72	Hematuria, low back pain, dysuria.
5	28	48	Hematuria, low back pain, dysuria.
6	30	48	Pollakiuria.
7	29	36	Hematuria, low back pain.
8	30	36	Hematuria, low back pain, dysuria, pollakiuria.
9	30	36	Hematuria, low back pain, pollakiuria, nycturia.
10	34	36	Hematuria, low back pain.
11	27	24	Hematuria, low back pain.
12	28	24	Hematuria, low back pain.
13	27	12	Hematuria, low back pain, dysuria, pollakiuria.
14	28	12	Hematuria, low back pain.
15	30	12	Pollakiuria, dysuria.
16	30	12	Hematuria.
17	34	12	Hematuria.
18	35	<12	Low back pain.
19	36	<12	Dysuria.

Table 2. Time interval between exposition to the parasite and initial symptoms and/or signs; renal relative function; and the renogram results.

Patient Number	Time Interval (months)	Relative Function		Renogram	
		LK (%)	RK (%)	LK	RK
1	84	52.2	47.8	N	N
2	84	49.5	50.5	N	PEP
3	72	51.9	48.1	PEP	PEP
4	72	53.0	47.0	N	PEP
5	48	52.1	47.9	PEP	PEP
6	48	50.3	49.7	N	N
7	36	50.1	49.9	PEP	N
8	36	49.1	50.9	PEP	PEP
9	36	60.3	39.7	PEP	PEP
10	36	56.6	43.4	N	PEP
11	24	53.8	46.2	N	N
12	24	50.2	49.8	N	N
13	12	51.4	48.6	PEP	PEP
14	12	44.2	55.8	PEP	N
15	12	46.4	53.6	PEP	N
16	12	47.6	52.4	N	N
17	12	47.6	52.4	PEP	PEP
18	10	52.9	47.1	PEP	PEP
19	10	50.0	50.0	PEP	PEP

Renogram: whole kidney function curve; LK: left kidney; RK: right kidney; N: normal curve; PEP: prolonged excretory phase.

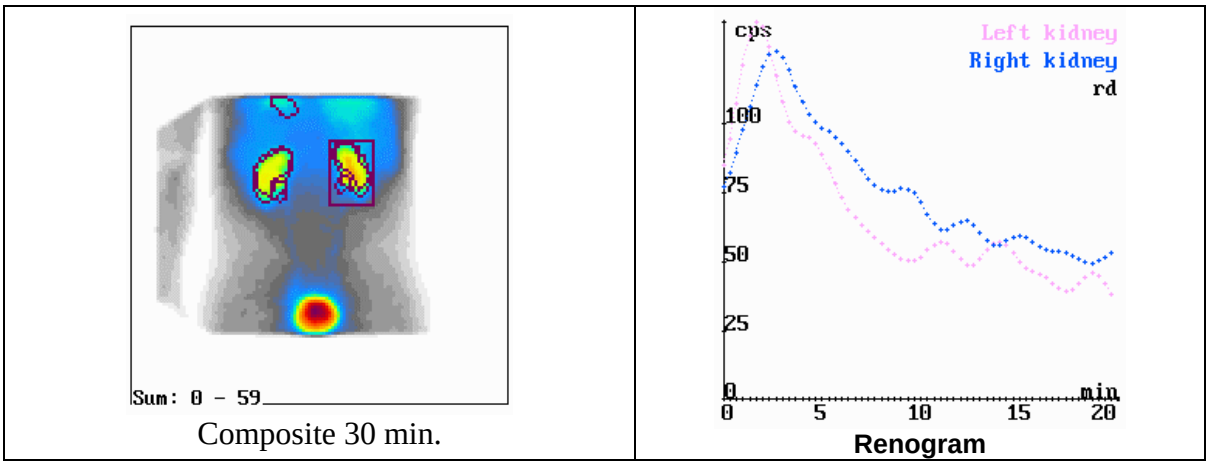

Figure 1A: Normal scintigraphy with diethylenetriamine penta-acetic acid labeled with technetium-99m (^{99m}Tc-DTPA) (Patient 6).

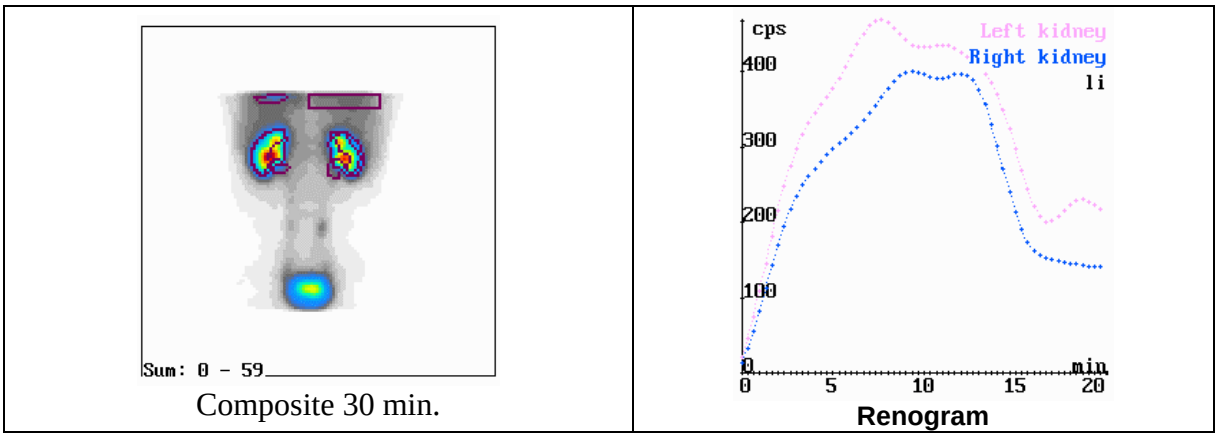

Figure 1B: Scintigraphy with diethylenetriamine penta-acetic acid labeled with technetium-99m (^{99m}Tc-DTPA) (Patient 13). Note the prolonged excretory phase.

DISCUSSION

The clinical manifestations of schistosomiasis haematobia observed in this study agreed with those described by Rey *et al*. (11,12).

Fourteen patients had abnormal scintigraphies evidencing an increase in the excretion time; none of them had obstructive pattern. Bahar *et al*. (2) studied 92 patients presenting schistosomiasis haematobia and urinary symptoms from endemic areas (Nile Valley, East Africa, Saudi Arabia, and Yemen) and reported that 68% of them showed altered excretory phase in ^{99m}Tc-DTPA dynamic renal scintigraphy and 71% had PEP without obstructive pattern.

The current results corroborated the studies of Barsoum (3) who mentioned that *S. haematobium* glomerulopathy could be considered a pathological finding without correlation with the disease clinical manifestations indicating subclinical glomerular

involvement. In the present study, scintigraphy showed close relationship with physiopathologic alterations induced by individual immunologic response to *S. haematobium.*

Despite the small number of patients, the present results are not in agreement with the predominance of post-renal obstruction (7) in different progression degrees of schistosomiasis haematobia. Infected patients often present few or no clinical signs of serious disease until very late stages of the infection. Therefore, it has been difficult to establish a clinical gradient with respect to *S. haematobium* infections (3,9).

The evaluation of renal scintigraphies of infected patients added a new dimension to the understanding of the problem by revealing severe functional abnormalities in some patients who were apparently well (3, 5, 9).

In this study, increased PTTI and PEP cannot be due to the improper hydration of the patients since the hydration protocol before the test was strictly followed.

Results showed 14 patients with PEP instead of the common post-renal obstruction. There was no correlation between the alterations observed and the clinical manifestations of the disease. The obvious task ahead for health authorities in the developing world is to detect and treat kidney diseases at the earliest possible stage (5, 14). For this purpose, renal scintigraphy using ^{99m}Tc-DTPA in *S. haematobium* infected patients would help to discriminate those with a major probability to develop schistosomal glomerulopathy, which does not depend on the duration of the disease.

Prolonged excretory phase in 73.7% patients and increased PTTI in 58% of them suggested parenchymal compromising consistent with schistosomal glomerulopathy. So far, scintigraphy has shown to be important to evaluate the outcome of infected patients. Further longitudinal studies of infected patients are desirable and should yield useful information particularly in patients whose renographic abnormalities persist despite good parasitologic response to specific chemotherapy.

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