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EPIDEMIOLOGICAL, CLINICAL AND THERAPEUTIC ASPECTS OF HEPATIC SCHISTOSOMIASIS AT THE UNIVERSITY HOSPITAL OF TAMBOHOBE FIANARANTSOA MADAGASCAR

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ABSTRACT

Background: Hepatic schistosomiasis is a severe clinical form of *Schistosoma mansoni* infection. It is one of the main causes of portal hypertension and it is responsible of high morbidity and mortality. The aim of this study was to describe the epidemiological, clinical and therapeutic aspects of hepatic schistosomiasis. **Patients and method**s: A retrospective study has been conducted during 5 years, including 1137 patients with liver schistosomiasis at the University Hospital of Tambohobe Fianarantsoa. **Results:** The mean age was 37.90 years. Medical history revealed gastrointestinal bleeding in 10.29 %. Splenomegaly associated with portal hypertension syndrome were the main clinical sign. The majority of patients (72.03%) received an

antiparasitic drug, praziquantel. The surgical treatment was splenectomy in 3.51 %. Mortality was 0.52%, mainly due to hemorrhagic recurrence. **Conclusion:** Liver schistosomiasis is common in the University Hospital of Tambohobe Fianarantsoa and mainly affects young adults. A therapeutic combination of praziquantel and propranolol reduces the mortality rate. Splenectomy would reduce the risk of recurrent bleeding.

KEYWORDS: gastrointestinal bleeding, hepatic schistosomiasis, *Schistosoma mansoni*, splenomegaly.

INTRODUCTION

Bilharzia or schistosomiasis is a parasitic disease caused by a flatworm, a hematophagous trematode.[1] It affects about 300 million people worldwide, and 800 million people are at risk of this disease. Ten percent of patients have severe forms of the disease and there are 250.000 death each year.[2] Schistosomiasis caused by *S. mansoni* affects 74 countries.[3] In many regions of Africa, in the Middle East and Asia, it is the most common cause of portal hypertension, far ahead of ethylic cirrhosis.[4] Hepatic schistosomiasis is a severe clinical manifestation of *S. mansoni* infection, characterized by an increase in liver and spleen size and histological modifications in these organs.[5] Liver damage is delayed.[4] In Madagascar, Schistosomiasis caused by S. *mansoni* is an endemic disease that occurs in the highlands, east, and southeast.[3] More than 2 million people are estimated to be carriers of schistosomiasis *in S. mansoni*.[6] "Haute Matsiatra Region", located in southern Madagascar, is an endemic area for intestinal schistosomiasis.[7] However, there is a lack of data in hepatic schistosomiasis in this region which justify this study. This study aims to describe the epidemiological, clinical and therapeutic aspects of hepatic schistosomiasis.

MATERIALS AND METHODS

A retrospective study carried out over 5 years from January 2011 to December 2015 in the visceral surgery, intensive care and internal medicine departments of Tambohobe University Hospital.

All patients with hepatic schistosomiasis whose medical records were complete were included in this study.

The criteria adopted to define hepatic schistosomiasis[8,9] were the positivity of Schistosoma serology and/or the presence of *Schistosoma mansoni* eggs in the stool during parasitological

examination and/or during biopsy of the rectal mucosa, associated with the mandatory presence of periportal fibrosis and one or more signs of portal hypertension on abdominal ultrasound which are: atrophy of right liver lobe, hypertrophy of left liver lobe and main portal vein dilatation.

The following parameters were analyzed: epidemiological data, clinical and paraclinical findings, treatments and outcome.

The first step of the study was the development of the study protocol. Patient recruitment was carried out by consulting hospital registers. A patient with a diagnosis of gastrointestinal bleeding in all three departments was identified. Epidemiological data included age, gender, home (0-25 km from the University Hospital, 26 to 50 km and greater than 50 km); profession sectors (primary: breeder, farmer; secondary: craftsman, industrial employee; tertiary: service sector), medical history represented by the notion of dysentery, gastrointestinal bleeding (hematemesis and/or melaena and/or hematochezia), and a known schistosomiasis infection. Clinical data included: gastrointestinal bleeding, splenomegaly, pale skin.

Paraclinical data were: eggs detection on stool examination or rectal biopsy, hepatitis B and C serology and imaging (abdominal ultrasound and upper digestive endoscopy).

Data were analyzed using Epi Info software version 3.5.

RESULTS

We recruited 1137 patients representing a prevalence of 11.04% in a hospital-based population (Fig.1). Male gender were 67.88% (n = 680) and female were 40.20% (n = 457) giving a sex ratio of 1.48. The mean age was 37.90 years. Six hundred and fifty-five patients (57.60%) were in the primary sector (Table I). Almost half of the patients (41.63%) (n=473) lived more than 50 km from the hospital. Besides, 34.03% (n=387) had a medical history of dysentery and 10.29% (n=117) had a digestive bleeding. The causes of hospital admissions were dysentery (52.15%; n=593); abdominal pain (21.02%; n=239) and digestive bleeding (19.26%; n= 219).

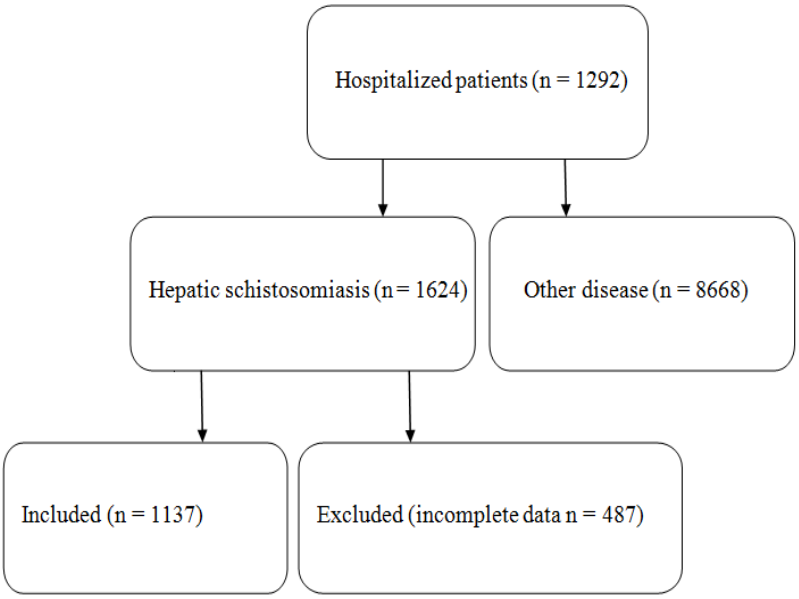

Figure 1: Flowchart of the study.

Table I: Epidemiological data of patients (n = 1137).

Data	
Mean age (years)	37.90 (Extreme: 12-81)
Gender n (%)	
• Man	680 (59,80)
• Woman	457 (40,20)
Profession n (%)	
• Primary sector	655 (57,60)
• Secondary sector	380 (33,40)
• Tertiary sector	102 (9)

On physical examination, splenomegaly was present in 315 patients (27.70%), pale skin in 199 patients (17.50%) and ascites in 70 patients (6.15%) (Table II). One hundred and fifty-five patients (13.63%) had anemia. Hepatitis B serology was positive in 20.58% of cases (n=21/102) and hepatitis C in 3.92% of cases (n=4/102). Nine hundred and twenty-five patients out of 1020 (90.68%) had positive Schistosoma serology. The rectal biopsy found *Schistosoma mansoni* eggs in 67.63% (n=468/692). Four hundred and twenty-five patients performed a parasitological examination of the stool and 134 revealed schistosoma eggs (31.52%; n = 134/425). In abdominal ultrasound 18.82% (n=214) presented ascites; 98.50% (n=1120) had splenomegaly; 99.38% (n=1130) presented portal dilatation and 98.76% (n=1123) had a periportal fibrosis. The endoscopy has been performed in 2 patients (0.17%) and found grade III esophageal varices (Table III). The majority of our patients (72.03%; n=819) with positive schistosoma serology or eggs in the stool were treated by Praziquantel 600 mg. Then, 24.45 % (n=278) of patients received a propranolol beta-blocker. Forty

patients (3.51%) underwent a splenectomy. Thirty-seven patients (3.26%) received blood transfusion (Fig. 2). The outcome was favorable in 99.47% of cases. A recurrence of digestive hemorrhage was observed in 6 patients and caused death.

Table II: Clinical data of patients (n = 1137).

Clinical signs	Number (%)
Splenomegaly	315 (27,70)
Pale skin	199 (17,50)
Ascite	70 (6,15)
Collateral venous circulations	9 (0,79)
Edema of the lower limbs	7 (0,61)

Table III: Paraclinical data of patients (n=1137).

Parameters	Number (%)
Biology	
- Anemia	155/1137 (13.63)
- Bicytopenia	88/1137 (7.77)
- Pancytopenia	105/1137 (9.23)
- Positive Ag HBS	21/102 (20.56)
- Positive Ac Anti-VHC	4/102 (3.92)
- Positive schistosoma serology	925/1020 (90.68)
- Positive rectal biopsy	468/692 (67.63)
- Positive stool examination	134/425 (31.52)
Ultrasound	
- Ascites	214/1137 (18.82)
- Splenomegaly	1120/1137 (98.50)
- Portal vein dilatation	1130/1137 (99.38)
- Periportal fibrosis	1123/1137 (98.76)
Endoscopy	
- Esophageal varices Grade III	2/1137 (0.17)

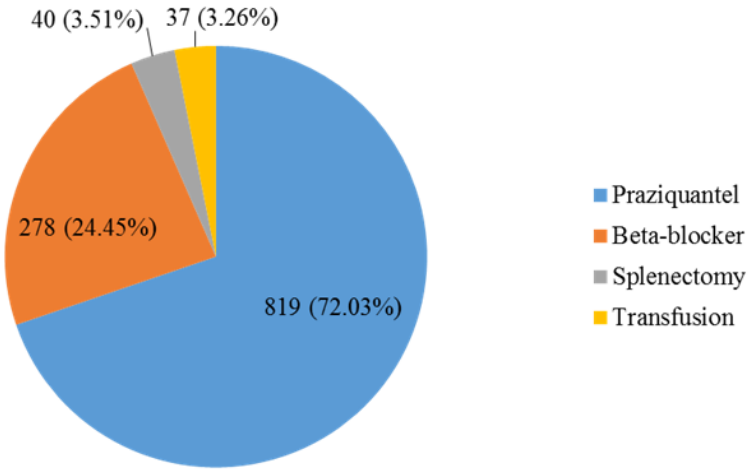

Figure 2: Distribution of therapeutic modalities.

DISCUSSION

The population of this study is young. Besides, schistosomiasis-hepatitis B co-infection was common. Splenomegaly, dilatation of the portal vein and periportal fibrosis were almost constant. The outcome was mostly favorable. In our study, the frequency of hepatic schistosomiasis is relatively low (11.04%). However, this data is probably underestimated considering the importance of schistosomiasis in the "Haute Matsiatra "a region of Fianarantsoa. Indeed, a Malagasy study in public primary schools in 7 districts showed that out of the 2 million patients infected by intestinal schistosomiasis, 25% come from the "Haute Matsiatra" region.[10] Another Malagasy study reports that the hepatic and intestinal manifestation, due to *Schistosoma mansoni,* extends over the central highlands and to the east of Madagascar. It is estimated that 3 million people are exposed, and 2 million are infected. This disease is expanding, favored by population movements, seasonal work, and hydro-agricultural developments. Moreover, it is found that most of the hyperendemic villages are located near 7 th National Road and the zebu trail.[11]

In Turkey, a hospital-based study found a frequency of 10% of hepatic schistosomiasis.[3] In Zambia, the rate was higher because schistosomiasis was present in 30% of hospitalized patients.[12]

Regarding the age, the hepatic schistosomiasis predominated in young adults found in our study and it is traditionally reported in the literature. The frequency of this disease increased with the age, the peak frequency was between 25-35 years and then gradually decreased. Young adults are most at risk because of their professional activity and swimming in fresh water.[6] However, children are not spared because in Senegal one study reported a high frequency (78%) of hepatic schistosomiasis in children under five years of age. The children were exposed because most of the time their bathing took place in the backwater.[14] A study in Ivory Coast reported that within the urban area, 20.6% of schoolchildren are carriers of *S. mansoni.*[15] The Lack of hygiene and playing in contaminated water make children particularly vulnerable.[13] The older children have more risk to be infected, confirming the chronic nature of the schistosomiasis.[16]

The majority of our patients works in the primary sector (57.60%). Their work exposed them to schistosomiasis contamination. Rice farming is one of the dominant activities of the population in "Haute Matsiatra"region. The rice field and the hydraulic installations used for the irrigation are high-risk areas.[17] This result is consistent with other studies.[10] Liver

schistosomiasis particularly affects poor farmers and fishermen. During the physical examination, we found 27.70% of splenomegaly while on abdominal ultrasound, the rate of splenomegaly was higher (98%). In practice, this discordance between the clinic and the abdominal ultrasound is common; the ultrasound is an operator and material-dependent examination.[9]

Our study confirmed the value of splenomegaly in the diagnosis of hepatic schistosomiasis. In Brazil, studies had reported a clinical manifestation dominated by hepatosplenomegaly and signs of portal hypertension.[18]

In our population, the blood count data were used to detect one of the complications of hepatic schistosomiasis. A minority (13.63%) of our patients had normocytic normochromic anemia. African studies have suggested that the discovery of anemia should lead to a systematic search for hepatic schistosomiasis in a hyperendemic area.[19]

The search for eggs in the stool is used in the diagnosis of schistosomiasis, it is traditionally performed simultaneously with serology.[20] A rectal biopsy is also a sensitive research method, equivalent to a series of three stool analysis.[9] Besides, bilharzia and hepatitis co-infection were frequent with 20.58% for HBV and 3.92% for HCV respectively. In Madagascar, the prevalence of acute or chronic carrying of Ag HBS is estimated at 23% in the population living in rural areas, placing the country at a high level of endemicity.[21] A Meta-analysis reported that hepatitis B was present in 9 to 60 % of patients infected with schistosomiasis.[22] This is related to polytransfusion in patients with portal hypertension, to the superposition of schistosomiasis and hepatitis endemic areas[23]; or to parenteral therapy using reusable and poorly sterilized needles.[24]

In our study, abdominal ultrasound remained the key examination to confirm liver schistosomiasis and almost all our patients benefited from it. However, no classification could be used. Several Malagasy studies had been carried out on abdominal ultrasound results using international classifications, proving the possibility of using them in current practice in Madagascar.[25] Abdominal ultrasound is, therefore, the gold standard in practice. The prevalence of Symmers fibrosis determined by abdominal ultrasound is 2 to 3 times higher than splenomegaly and/or hepatomegaly determined by clinical examination.[26]

In our study, a large proportion of our patients did not perform an endoscopic examination because it has not been yet available in our center at the time of the study.

However, upper gastrointestinal endoscopy is a key examination in the management of hepatic schistosomiasis to establish the esophageal varices grade and the severity of portal hypertension.[2]

In our patients, single-dose praziquantel therapy was administrated.

In Sudan, a study showed a total regression of periportal fibrosis in 35.6% of patients after 39 months of praziquantel. Praziquantel would reduce the severity of infection by eliminating the parasite, reducing the number of eggs in the liver tissue, thus reducing granuloma formation and fibrosis.[27] During portal hypertension (PH) in liver schistosomiasis, propranolol has been poorly studied. It would significantly reduce azygos venous flow and prevent hemorrhagic recurrence in the short period before surgical treatment, and carvedilol is even better than propranolol.[28] Variceal banding is also indicated. A recent randomized study did not show any significant difference between sclerotherapy and variceal banding.[2,9] Other author proposed a splenectomy associated with variceal banding.[29]

In our study, splenectomy was performed because it is a habit of our team and it is the cheapest technique.

However, the ineffectiveness of splenectomy alone has been demonstrated in Brazil. The authors reported that esophagogastric devascularization associated with splenectomy is more effective in terms of hemorrhagic recurrence.[30,31] A study concerning the effectiveness of splenectomy associated with endoscopic banding would be interesting.

The death in our study was the result of hemorrhagic shock likely due to variceal bleeding of the esophagus. In the literature, the mortality is observed in 11.4% of patients with hepatosplenic schistosomiasis who had an episode of gastrointestinal bleeding and in whom sclerotherapy was not performed.[4]

A Brazilian study showed bleeding in 14.4% and mortality in 5.4% of patients who underwent splenectomy, followed by anastomosis of the left gastric vein, after 30 months of follow-up.[31] The implementation of a department dedicated to the management of gastrointestinal bleeding would reduce the mortality.

CONCLUSION

Hepatic schistosomiasis is common at the University Hospital of Tambohobe Fianarantsoa and mainly affects young adults. Splenomegaly was the most feature encountered in clinical examination. Drug treatment combined antiparasitic praziquantel with beta-blocker propranolol. The surgical treatment was the splenectomy.

Given the high prevalence of hepatic schistosomiasis in our region, studies concerning the different stages of the disease, from diagnosis to treatment, would be interesting to realize.

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