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BILHARZIA INDUCED PATHOLOGIES AND TECHNIQUES OF DETECTION IN UGANDA: A REVIEW
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BILHARZIA INDUCED PATHOLOGIES AND TECHNIQUES OF DETECTION IN UGANDA: A REVIEW

E. I. ODONGO-AGINYA and E. DOEHRING

ABSTRACT

Background: *Schistosoma S. mansoni* **was observed and reported in Uganda in 1902.** *Schistosoma S. mansoni* **is widely distributed in Uganda along permanent water bodies.**
Objective: **To review the literature on previous techniques and conventional ones used for the assessment and comparison of morbidity due to** *schistosomiasis* **in Uganda.**
Design: **Retrospective study.**
Setting: **Gulu University, Faculty of Medicine, Department of Microbiology and Immunology.**
Results**: Since its first detection in 1902** *Schistosomiasis mansoni* **and later** *Schistosomiasis haematobium* **in Uganda, morbidity assessment was based on physical examination and intensity of eggs excretion. The first field study in Uganda of schistosomiasis pathologies using ultrasound was that conducted in West Nile in Obongi, Rhino Camp and Pundu in 1991 and reviewed in 1992. These armless and none invasive method of pathologies detection has the advantage of repeatability. It showed that after treatment there was reversibility of pathological conditions introduced by the parasites in the hosts.**
Conclusion**:** *Schistosomiasis mansoni* **pathologies as detected by the none invasive ultrasound findings compared well with those of the more risky invasive liver biopsy. The detection of pathologies by clinical examination was less sensitive. Pathological lesions due to *S. haematobium* correlated with abnormalities of the urinary tract and intensity of eggs in urine.**

INTRODUCTION

Pathological changes resulting from *schistosomiasis* have been recognised for more than a century. In 1856, Bilharz found lesion due to *S. haematobium* in the autopsy material in Cairo (1). Symmers described a new form of liver cirrhosis due to *S. haematobium* (2). In that time liver cirrhosis due to *S. mansoni* and *S. haematobium* were not distinctly separated. The introduction of *in vivo* cystoscopy in 1879 made it possible to visualise bladder pathology in *S. haematobium* infection (3). Biopsy of the liver and the lower gastrointestinal tract were performed to demonstrate *S. mansoni* related pathology (4). Modern radiological techniques provided a variety of methods for detection and follow up of *schistosomiasis* related morbidity (5). Methods available today include various radiographic techniques isotope investigation of the kidneys and liver, computed tomography (CT) and recently ultrasonography (6). The introduction of ultrasonography in the late 70s was an improvement on the previous morbidity detection methods due to schistosomiasis (7). This is an important step forward in the development of imaging diagnosis of *schistosomal* lesions. The method is non invasive, simple to perform in experts' hands, does not have the disadvantage of radiation and it is relatively cheap (7). Therefore it can be used in field studies to investigate large communities in endemic areas. This can be applied in epidemiological research. Sonography has become more and more popular for the assessment of *schistosome* related morbidity on community basis (8). It is therefore a tool to follow the course of infection in the community during and after the control intervention (9). If the full benefit of this invaluable technique is to be realised, it is important that a reliable and well standardised methods for examination and reporting should be developed so that the results from different workers can be compared (9).

This short review on evolution of bilharzias morbidity detection in Uganda covers literatures of the fundamental work on *schistosomiasis* in Uganda from 1902 to date. The inclusion of the application of ultrasound in assessing schistosome related morbidity aims at pointing out the advantages and limitation of the method and in particular, points out the issues that have been classified in order to make ultrasound a truly efficient tool for use at field level.

General review of schistosomiasis pathologies: The ancient Egyptians recorded comprehensive clinical accounts of bilharziasis as laid down in the papyrus Pfister (10). Ruffer (11) in 1910 proved the presence of Schistosoma ova in mummies and in Canopic jars of mummified viscera. The first published record of the causative agent was after the post-mortem discovery of the worm in the mesenteric veins of a patient in Kasr el Aini Hospital in Cairo by Bilharz (1). The introduction of cystoscopy by Leite (2) made it possible to visualise bladder pathology in *S. haematobium*. Radiographic techniques for monitoring morbidity due to schistosomiasis are available, but all these methods have been superseded by introduction of portable ultrasound in the study of schistosomiasis pathology in 1970. Since then, ultrasonography became one of the most efficient tools for the diagnosis of morbidity due to *schistosomiasis* at the community level (1). It is a tool being used to follow the course of infection in the community during and after control programme (12). Doehring *et al*. (12) in 1986 using ultrasonographical investigation in Sudanese children showed that reversibility of liver fibrosis was observed 23 months after praziquantel treatment. However the reporting of the reversibility by ultrasound studies varied considerably so that it was difficult to make valid comparisons between results obtained in different places or at different time points (9). Therefore the Cairo workshop was held to standardise the use of ultrasongraphy in the public health context. The emphasis was on the visualisation of the organs most commonly affected by the schistosomes and recording of the observations. The criteria considered were based on lesions with tendency to develop severe pathology, lesions which are characteristic of schistosomiasis, lesions which are commonly observed in these organs, but more so to monitor reversibility of pathological conditions before and after treatment (9).

Recommended reporting and recording in the Cairo workshop: Observations such as the diameter of the lumens of veins and echo-texture of liver parenchyma were recommended. These observations are both quantitative and qualitative respectively. Basically they depend on the experiences of the observers. Quantitative ultrasound data provide better information that can be compared. Nevertheless qualitative ultrasound data can be converted into quantitative data by assigning 'grades' like 0, 1, and 2 to the qualitative date which mostly are described as normal, moderate or severe lesions respectively. These grades correspond to measurements which normally diverge from the normal measurement. That is either it decreases or increases from the normal. For example the shrinking or enlargement of the liver in *schistosomiasis.* Staging is yet another recommended quantitative way of reporting in ultrasonography. This system is important in the assessment of lesions in the organs before and after treatment which include the progression of the disease. Therefore staging defines different ultrasound observations at different time point of the disease. It is recorded as 0 = normal; stage I = low; stage II = moderate and stage III = severe.

Detection of schistosoma mansoni pathologies in Uganda protectorate and other British colonies: Case report by Dey (13) 1924 in Nyasaland (Malawi) and Trim (14) 1936 in Kenya confirmed cirrhosis and splenomegaly to be prevalent in areas of *S. mansoni* (15). Strong (15) in 1944 indicated that in Egypt and other parts of East Africa, splenomegaly was a common feature in *Schistosoma mansoni* infection. Schwert (16) in 1951 in Lango district, now Lira district, reported vesical bilharzias in the community living in Aloi, Ayer along River Okole and other tributaries of River Acwa. Haematuria was common among both adults and children in this community (17). In 1953, Williams reported a case of Cor pulmonale in schistosomiasis in a 15 year old Ganda boy from Masaka near the lake. His clinical examination showed oedema and ascites and enlarged palpable' liver. Nevertheless the patient had several haemoptyses while in the hospital and died a month later after such an episode. The post mortem examination (89/53 Professor J.N.P.Davies) however showed that the cause of the death to be schistosomiasis (17). Nelson (18) in 1958 found that intensity of infection with S. *mansoni* was highest immediately along the banks of the River Nile in North Western Uganda and decreased with altitude and distance from the Nile. Nelson (18) further observed clinically that enlarged spleens and anaemia were a common feature among children around ten years old with high intensity of infection. It was earlier believed the splenomegaly and anaemia were features associated with *Schistosoma mansoni* infection. (15). In the same year 1958 Wydell (19) working from Ukerewe Island in Lake Victoria found cases of small intestinal obstruction due to *S. mansoni*. He also reported peritoneal tumours which on section were found to contain a large number of *S. mansoni* eggs (19). Investigations of the bilharzial bladder have been made by Kirkland-Willis (20) in 1960 who described the cystoscopic appearance. Langlo and Walter (21) in Kirkland 1962 made cystomanometric observation on bladder of *S. haematobium* infections

persons. They found that in the later stages of the disease the bladders became more irritable, and when a certain pressure was reached the contents were expelled in a sudden mass contraction, which explains urgency of micturition associated with this stage of the disease (21). Turner (22) in 1964 reported three cases of *schistosomiasis mansoni* pulmonary arterial hypertension which was confirmed to be a common finding at autopsy in Nairobi (22). Forsyth and Bradley (23) in 1964 did much to clarify the position in relation to *Schistosoma haematobium* infection. They, under field condition combined X-ray and intravenous pyelography and demonstrated high prevalence of urinary tract lesions due to *S. haematobium* in Mwanza primary school children. Moreover as high as 8% of those lesions were hydronephrosis (23). Hamilton et al (24) in 1965 investigated this association in inpatients in research ward at Mwanza and found out that eggs out put were related to the presence of liver and spleen enlargement. A direct relationship between intensity of infection and lesions of urinary tract was demonstrated by Forsyth and Macdonald (25) in 1965 who showed that calcified bladders, deformed ureters and hydronephrosis were significantly more common in children with an egg output above 250 per 10ml of urine than in children with egg counts below this figure. These urological changes were found to be a common finding in Zanzibar, Tanga on the coast of Tanzania and most of East Africa (25). Ongom and Bradley (26) in their field study on the epidemiology and consequences of *Schistosoma mansoni* infection in Panyagoro community in West Nile in Northern Uganda observed that there was a wide range of physical signs due to *S. mansoni.* This included distended abdomens, ascites and anaemia. Nevertheless hepatosplenomegaly was very common in all cases of *schistosomiasis mansoni;* the same patients also had malaria. Liver enlargement was more common in males than females. Splenomegaly occurred at an earlier age and equally in both sexes. Splenomegaly, however, showed association with intensity of egg output in adults. Ongom and Brandley (27) in 1972 concluded that the clinical examinations and symptoms observed in their studies were due to *S. mansoni*.

Introduction of ultrasonograpy to detect *Schistosoma mansoni* related pathologies in the Uganda and neighbouring countries:

CONGO

Morphological aspects of the urinary tract in haematobium infection have been provided by Dittrich and Doehring in 1986 (28). Fifty four percent of *S. haematobium* infected patients had bladder abnormalities and 23% revealed urinary tract obstruction. Urinary egg excretion correlated with the degree of pathological involvement and high proteinuria was an indicator of bladder wall enlargement and vesical pseudopolyps. There were reversibility of the pathological lesion of the lower urinary tract as early as three months after therapy with praziquantel but upper urinary tract, were not reversible (29). Reversibility of pathological lesions was more pronounced one year after treatment. Similar results have been provided from Tanzania and Niger. Reversibility of minor lesions was found within six months (30).

SUDAN

In 1990 Doehring *et al.* (31) for the first time used ultrasonography in *S. mansoni* infected patients under field conditions. High morbidity was detected in children and adults in Gezira Province of Central Sudan. Between 13% and 18% of the complete community in two villages had signs of periportal fibrosis, while in schoolchildren, this rate reached almost 40%. Clinical examination was of limited value as an indicator of periportal fibrosis. A hospital based study indicated high diagnostic accuracy of ultrasound in advanced cases of *S. mansoni* infection when compared with liver biopsy. This was later confirmed in Egypt as well. Ultrasound parameters were useful to indicate the risk of upper gastro oesophageal bleeding (31).

TANZANIA

Hatz *et al.* (30) in 1990 assessed the value of ultrasonography in *Schistosoma haematobium* infection in comparison with radiological techniques and cystoscopy in Tanzania. Both imaging techniques were comparable in their sensitivity and specificity to detect *S. haematobium* induced morbidity of the urinary tract. The prevalence of *S. haematobium* infection in 231 schoolchildren was 62% and 29% of these had congestive changes of the kidneys (32). Bladder lesions were even more prevalent (68%). There was a clear correlation between abnormalities of the urinary tract and schistosomiasis. They also evaluated ultrasound within the framework of Primary Health Care Services. They considered ultrasound as cost effective except for the initial investment (around 15,000 US Dollars) and appropriate for research purposes, but not for individual patient care in endemic areas (30).

UGANDA

The first evaluation study using ultrasound on reversibility of *Schistosoma (S) mansoni* induced morbidity before treatment in 1991 and the review after treatment in 1992 with praziquantel, 40mg/kg body weight was carried out in Rhino Camp, Obongi and Fundo all in West Nile district in Northern Uganda.

A complete abdominal scan was performed as well as sonomorphometrical documentation (assessment of all parenchymal organs in the abdomen plus great abdominal vessels) (33). For assessment of morbidity due to schistosomiasis, Managil-Hannover and the WHO Cairo 1990 systems of classification were used (9). Previously in Rhino Camp, Obongi and Fundo in 1991, 1562 fishermen and women, school pupils, teachers, and civil servants were studied for *S. mansoni* using Kato / Katz stool smear method. One thousand two hundred and seventy three (81.5%) were found to be excreting *S. mansoni* eggs in their faeces. Abdominal ultrasonography was performed on all patients who had *S. mansoni* eggs in their faeces. It was found that 46.1% of those had various stages of periportal fibrosis (PF) as revealed by the ultrasound scores. In 1992 the periportal fibrosis (PF) was reduced to 21.9%. This study observed that among the patients retrieved in 1992 a great reduction in severe PF reversed to normal liver parenchyma. In substantial cases the reduction of PF was closely related to intensity of infection previously seen in children (33).

In a similar study at Butiaba on Lake Victoria, Kabatereine *et al.* (34) in 2004 used Aloka SSD-500 potable scanner with a 3.5MHZ convex transducer, applied WHO guideline to scan 247 who were stool positive for *S. mansoni*. The sonographical examination included assessment of the liver and spleen size. In this study a total of 92.3% of the people in ultrasound cohorts had organomegaly. Most patients 53.4% had both hepatomegaly and splenomegaly. Hepatomegaly or splenomegaly only was detected in 26.3% and 12.6% respectively (34).

Dunne *et al* (35) in 2006 working in Paiida fishing village on Lake Albert in North Western Uganda were some of the early investigators who used the ultrasound in Uganda to demonstrate the pathology due to *Schistosoma mansoni*. They used the newly developed protocol under the auspices of World Health Organisation (WHO) for staging periportal fibrosis to study 462 inhabitants aged 5 to 60 years (9).

In addition to commonly reported diarrhoea and abdominal pain they found organomegaly as assessed by ultrasonography to be frequent. Hepatomegaly was associated with heavy *S. mansoni* infection but spenomegaly was not correlated to schistosome observed earlier in the studies used in physical and clinical examination. Cases of liver fibrosis (PF) were identified and scored according to severity of fibrosis as normal, (A) and severe (F) periportal fibrosis. The advantage of this new protocol differentiated cirrhosis due to other causes from periportal fibrosis attributable to *S. mansoni*. The Paiida study revealed an overall periportal fibrosis of 30% with a strong age dependency (35).

DISCUSSION

The conclusions from these reviews indicate that in the fortieth century when the knowledge about schistosomiasis was unfolding, it was not easy to differentiate the liver and spleen pathologies due schistosomiasis from those caused by other diseases such as malaria and Kala azar. For example in most parts of East Africas malaria, Kala azar and schistosomiasis co-existed. It was difficult to distinguish hepatomegaly and splenomegaly due in these parasites by mere clinical and physical examination of the patients (36). However in the early fifties convincing observation began to immerge to point out that schistosomiasis was indeed responsible for increased hepatosplenomegaly and a considerable increase spleen rate (19). In 1962, Rosanelli (37) performed liver biopsies in 23 cases of schistosomiasis mansoni and compared with liver biopsies from presumably ten normal subjects.

There was no major difference in incidence of portal fibrosis although a slight increase was recorded among those with schistosomiasis mansoni (37). The west Nile observation further provided stronger evidences that suggested that *Schistosoma mansoni* actually was associated with splenomegaly in children (18, 26, 27). Nevertheless contradiction arose when they further observed that in adults living in relatively *S. mansoni* free areas splenomegaly and liver cirrhosis were common. For these reasons it was then concluded that in the districts where there were great variations in the incidence of malaria and schistosomiasis the presence of an enlarged spleen even including gross splenomegaly was of little significance in the diagnosis of *S. mansoni*. Ongom and Bradley (2) used liver and rectal biopsies to demonstrate presence of *S. mansoni* eggs in such ambiguous cases. These invasive techniques needed experience to take the biopsies accurately and safely. Because of these risks, the biopsies were mainly reserved for adult patients (27).

The introduction of ultrasonography, a non invasive method for detecting pathology in the late 70s was an improvement on the previous morbidity detection methods due to schistosomiasis. This is an important step forward in the development of imaging diagnosis of schistosomal lesions. The method is simple to perform in experts' hands, does not have the disadvantage of radiation and it is relatively cheap (8). Therefore it can be used in field studies to investigate large communities in endemic areas. This can be applied in epidemiological research.

Sonography has become more and more popular for the assessment of schistosome related morbidity in a large community. It is therefore a tool to follow the course of infection in the community during and

after the control intervention. If the full benefit of this invaluable technique is to be realised, it is important that a reliable and well standardised method for examination and reporting should be developed so that the results from different workers can be compared (9). This short review on evolution of bilharzias morbidity detection, including ultrasound: in Uganda, Tanzania, Sudan and Congo reviews the literatures on application of ultrasound in assessing schistosome related morbidity in East and Central Africa and other endemic areas with the aim of pointing out the limitation of the method and in particular point out the issues that have been classified in order to make ultrasound a truly efficient tool for use at field level (12,28,31).

Ultrasonography has been established as a valuable tool to conduct screening studies of the population of endemic areas in order to establish prevalence rates of hepatosplenic lesions and urinary tract abnormalities (30-34). Research in several African countries presently concentrates on the detailed analysis of morbidity patterns in various geographical areas. It seems to emerge from these data, despite different parasitological and epidemiological conditions that East Africa is a high morbidity area as opposed to other countries, where severe hepalosplenic morbidity has been found less extensively mainly West Africa (7, 12,31,32).

Concerning *S. haematobium* studies, ultrasound was used mainly to follow up treatment and to establish adequate time intervals for morbidity control. This will not only supply health services with invaluable information necessary to modify health care strategies, but will also improve our understanding of the development of organ lesions induced by schistosomiasis haematobium (28, 32).

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