Chronic Schistosomiasis, a Clinical and Laboratory Diagnostic Challenge in Malawi

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Research note

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Abstract

Objective: Schistosomiasis cause significant morbidity and mortality worldwide. This is a retrospective cross-sectional study conducted at Mzuzu Central Hospital (MCH) from northern Malawi aiming at determining prevalence of schistosomiasis infection in cancer suspected patients. The data was collected from hospital files and the duration under review was from July 2013 to June 2018. A total of 790 Histopathological samples were analysed at University of North Carolina (UNC) Histopathology lab. Results were made available to the facility – Mzuzu Central Hospital.

Results: The overall prevalence of schistosoma (*S. mansoni* & *haematobium*) infection was 1.7% (14/790). About 93% (13/14) of schistosomiasis cases were observed in female patients while 7% (1/14) from male patients. Of the 14 cases from different histopathological pattern (Cervix, Ureter, Liver, Ovary, GIT and Urinary bladder), 43% (6/14) of cases were diagnosed from cervical tissues. Correlation between HIV infection and schistosomiasis infection was not reached as Serostatus for reasonable number of patients was unknown. Schistosomiasis chronic infection is highly prevalent in Malawi. This disease is neglected and underestimated due to lack of clinical skills and capacity in most of the public laboratories to accurately diagnose it as such, most cases are misdiagnosed as cancer.

Introduction

Schistosomiasis is one of the Neglected Tropical Diseases (NTDs) caused by five schistosome species; *Schistosoma haematobium*, *Schistosoma Japonicum*, *Schistosoma mansoni*, *Schistosoma intercalatum*, and *Schistosoma mekongi* (1,2). It is normally persistent and prevalent in people and communities living in poverty and social exclusion (3,4). Schistosomiasis is known to cause significant morbidity and mortality rate with an estimate of 600 million people living in the tropics being at risk of becoming infected and 200 million people are already infected with an annual death of 280,000. The disease ranks second beneath Malaria on the list of parasitic disease (1,5).

The chronic schistosomiasis is very devastating disease which causes granuloma due to Proteolytic enzyme activity. It occurs due to immune reaction against Schistosoma eggs trapped in tissue organs during migration via venous or lymphatic vessel. These cases are difficult to diagnose especially in developing countries where diagnostic tools are limited to miracidium/egg detection in urine or stool through microscopy (2,3,6,7).

The clinical manifestation of chronic schistosomiasis (in urinary, gastrointestinal tracts, genital including other organs) has often been nonspecific leading to mismanagement of cases and underestimated (8). It is thus not surprising to note that data for chronic schistosomiasis from developing countries is rare suggesting that a good number of cases are being missed (9).

Malawi is one of the countries in Sub-Saharan Africa where schistosomiasis cases (*S. haematobium* and *S. mansoni*) are being registered. However, prevalence of chronic schistosomiasis remains unknown. It is suspected that most of these cases are being misdiagnosed as cancer (4). Availability of chronic schistosomiasis data will help improve case detection and case management.

Therefore, the study aims at determining prevalence of chronic Schistosomiasis infection in cancer suspected patients with chronic infection of GIT, urogenital, extra urogenital and extra gastrointestinal organs.

Methods

Design, setting and population

This was a retrospective cross-sectional study which was conducted at MCH, in the northern part of Malawi. Mzuzu Central Hospital is a referral hospital for six districts supporting a population of 2.4 million people. The duration under review was from July 2013 to June 2018.

Inclusion criteria

Patients' files with complete information such as sex, age, race, clinical and histological diagnosis between July 2013 and June 2018, as well as patients' files with original biopsy reports were included in the study. Patients' files with missing demographic, clinical and histopathological data were excluded.

Specimen Collection and processing

Tissue specimens were collected and preserved in 10% buffered formalin solution and then transported to Kamuzu Central Hospital (KCH), KCH/UNC) pathology laboratory in Lilongwe. The KCH/UNC laboratory adheres to international quality assurance standards.

Briefly, Specimen was cut into 3-5mm slices put in the cassette and the lid covered. Up to 200 cassettes were then put in one of the containers of an automatic tissue processor. There are 12 containers each containing different reagents and the tissue moved from one to another. This process takes 24hours. The tissue was then embedded using Leica Histocore Arcadia H-Heated Paraffin embedding station. A manual rotary microtome was used to cut the tissue into 3-5µm thin slices. A floatation bath and a slide warmer are then used to fix the tissue slice onto the microscope slide. The tissue slices were then stained with hematoxylin and eosin thereafter mounted ready for analysis by pathologist. Immunohistochemically or special stains requested depending on primary differential diagnoses

Statistical analysis plan

Data were entered in Microsoft excel 2016, validated and cleaned before importing into Stata, version 13.0 (Stata Corp. LP, College Station, TX, United States of America) for analysis. Descriptive analyses were performed to summarise patients' sociodemographic and clinical characteristics. Chi Square (or Fisher's exact) test was used to look for significant associations between predictor and outcome variables at p-value of less than 0.05 being statistically significant. A binomial logistic regression was used to quantify the association between predictor variables and outcome variables.

Results

Retrospectively, the study enrolled a total of 790 histopathological samples which were from six different histological patterns. A total of 14 Schistosomiasis cases were registered from six histopathological patterns. Of the six histopathological patterns, schistosomiasis cases from cervix constituted (6/14) 43% of the total cases, followed by GIT, Ureter and Liver with (2/14) 14% each. Cases of schistosomiasis were highly registered in female patients than in male patients with 93% (13/14) and 7% (1/14) respectively.

Table 1: Patient Demographic and clinical data on HIV sero-status and Schistosomiasis infection.

<i>Sex</i>	<i>Total Number of Biopsies</i>	<i>HIV positive</i>	<i>HIV negative</i>	<i>HIV unknown status</i>	<i>Schistosomiasis cases in HIV positive Patients</i>	<i>Schistosomiasis cases in HIV negative patients</i>	<i>Schistosomiasis cases in unknown HIV sero-status</i>
<i>M</i>	192	21	83	88	0	0	1
<i>F</i>	598	97	272	229	1	3	9
<i>Total</i>	790	118	355	317	1	3	10

The total (790) enrolled patients, 192 and 598 were male and female respectively. About (104/192) 54% of men had HIV Serostatus known while (369/598) 62% for female. Overall, about 40% of patients had unknown Serostatus and registered 71% (10/14) of schistosomiasis cases.

Table 2: Histopathological patterns from six organs with positive Schistosomiasis.

<i>Histopathology sites</i>	<i>Total number of biopsies</i>	<i>Cases of schistosomiasis</i>	<i>Percentage</i>
<i>Cervix</i>	501	6	1.2
<i>Ovary</i>	52	1	2
<i>GIT</i>	165	2	1.2
<i>Ureter</i>	42	2	5
<i>Liver</i>	13	2	15
<i>Urinary Bladder</i>	22	1	4.5
<i>Total</i>	790	14	1.7

About (14/790) 1.7% of the total samples suspected of cancer were positive for schistosomiasis.

Discussion

Schistosomiasis remains a public health challenge in most of the developing countries including Malawi where it is nationally represented (9). This was a retrospective study conducted at Mzuzu Central Hospital northern part of Malawi. In this study, a total of 790 histopathological samples from six different patterns (Cervix, Ovary, GIT, Ureter, Liver and Urinary bladder) were analysed and 14 schistosomiasis cases out of 790 cases were identified representing prevalence of 1.7% (14/790). Detection of schistosoma in these mentioned organs, directly correlate with the findings of other studies which equally revealed schistosomiasis infection in the mentioned organs (1,10–14).

In this study, schistosomiasis cases were highly noted in cervical tissues (6/501) followed by GIT (2/265), Ureter (2/42) and Liver (2/13). These findings are in support of the data from similar studies which equally detected schistosomiasis infection from cervix and suggestively to be the possible cause of tissue lesions (15,16).

The common clinical presentations and findings in about 90% of the positive schistosomiasis cases were; inflammation, mass, lesions, endometriosis, dyspareunia, nodular and hydronephrosis. Lack of specificity of these clinical features have made Clinicians misdiagnosing the schistosomiasis disease as cancer or other related diseases ignoring schistosoma infection. Our study confirms this as most extra urogenital and extra GIT lesions were clinically diagnosed as cancer and were sent to pathology lab for confirmation. According to (17)

found out that chronic schistosomiasis infection has frequently been misdiagnosed as cancer due to nonspecific conditions as some mimic cancer. This directly correlate with the above narrative.

The chronic schistosomiasis disease has always been neglected or misdiagnosed due to limited clinical skills and laboratory diagnostic tools especially in developing countries (4,18). Currently, available diagnostic methods for schistosomiasis include those that are relying on stool and urine for miracidium or egg detection, serum antibodies, antigen detection and the detection of Deoxyribonucleic Acid (DNA). However, most developing countries including Malawi rely on microscopy technique as it is a cheap test and easy to use (3). Unfortunately, microscopic examination of eggs in urine or stool is less sensitive as it takes about two months from the time of infection for eggs to appear in stool or urine. The method is again less sensitive to detect oviposition infection. In addition, the test is known to be less sensitive in non-endemic areas (3).

The detection of schistosomiasis infection in regions rather than urogenital and gastrointestinal organs such as ureter, ovary, liver and cervix, highlights the complexity of the disease and act as a recommendation to Clinicians to consider investigation of *Schistosoma* infection in such clinical cases. Despite the fact that this is the first ever presented data from Malawi, findings of studies conducted elsewhere have indicated similar findings confirming presence of escalating disease of chronic organ schistosomiasis (11).

Prompt diagnosis and management of schistosomiasis is of paramount importance as the disease has strongly been linked to cancer. According to Zepeda et al., 2015, *S. haematobium* is being recognised as a group 1 carcinogen due to the strong evidence linking chronic infection to bladder cancer. Similarly, Mostafa & Sheweita, 1999 indicated that of 11,626 cancer cases of all types recorded at Cairo Cancer Institute from 1970 to 1974, 27.6% were bladder cancer cases associated with schistosomiasis and that of 2,500 new cancer patients, 27% had cancer of the bladder associated with schistosomiasis. Furthermore, the following studies have strongly linked schistosomiasis to various malignancies (1,6,10,11,20).

In the current study, it was very limited to ascertain total cases of *S. haematobium* and *S. mansoni* as histological reports did not specify species. It was again limited to associate HIV sero status to schistosomiasis infection as only 29% (4/14) of the patients with schistosomiasis had sero status known.

The study has revealed high prevalence of chronic schistosomiasis prompting for more consideration in management of cancer suspected diseases. It is recommended to consider targeted screening of schistosoma infection in chronic cancer suspected patients. The microscopy test should be replaced or support by the most sensitive, accurate and rapid antigen or antibody test for quality, reliable and rapid results. Further studies at a large scale are recommended to determine responsible species.

Limitations

The study could not determine whether schistosomiasis was due to *haematobium* or *mansoni* type as species were not reported. However, based on literature, *mansoni* is known to cause GIT schistosomiasis while *haematobium* is responsible for urinary and other productive organs.

List Of Abbreviations

MCH – Mzuzu Central Hospital

UNC – University of North Carolina

NTD – Neglected Tropical Disease

KCH – Kamuzu Central Hospital

UG – Urogenital

GIT – Gastrointestinal Track

DNA – Deoxyribonucleic Acid

Declarations

Authors' contributions:

PSK, FWS, CSC worked on study design, data collection and write up, MC, AK, JW, BMC worked data analysis. All authors read and approved the final manuscript.

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Competing interests:

The authors declare that they have no competing interests.

Availability of data and materials:

All original or analysed data for this study is available on request from the corresponding author.

Consenting for publication:

Not applicable to all

Ethical approval and consent to participate:

Ethical approval for the study was obtained from National Health Sciences Research Committee (NHSRC), approval number 19/05/2316. Mzuzu Central Hospital authorities cleared the authors to access the patients' records for data extraction. Privacy and confidentiality was observed by removing patient identifiers such as names, surnames and using coded information.

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Figures

Figure 1

Represents schistosomiasis infection in Urogenital and GIT (UG) and Extra Urogenital and Extra GIT (Extra UG) organs.