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Full Length Research Paper

Prevalence, epidemiological characteristics and predictors of occurrence of urinary schistosomiasis among 'Almajiri' school children in Sokoto, Nigeria

Yunusa, E. U.*, Awosan, K. J., Ibrahim, M. T. O. and Isah, B. A.

Department of Community Health, Usmanu Danfodiyo University, Sokoto, Nigeria.

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Schistosomiasis is a major public health problem and second only to malaria as the most devastating disease in tropical countries in Africa, East Asia and South America. 'Almajiri' children are known to be exposed to conditions that place them at high risk of infectious diseases including schistosomiasis. A cross-sectional study was conducted among 272 randomly selected children studying at the 'Almajiri' Integrated Model School, Sokoto, Nigeria, to determine the prevalence, epidemiological characteristics and predictors of occurrence of urinary schistosomiasis among them from December 2013 to January 2014. Urine samples were collected from the children and examined for microhaematuria (using reagent strips) and ova of *Schistosoma haematobium* (microscopically by sedimentation technique), in addition to questionnaire administration (to obtain information on epidemiological characteristics of participants). Mean age of participants was 9.2 ± 2.0 years. About a quarter (25.7%) of participants had urinary schistosomiasis, with the highest prevalence (27.2%) in the 10 to 14 years age group. Swimming in river/pond was found to be the sole predictor of occurrence of urinary schistosomiasis (OR = 3.284, $p = 0.020$, 95% CI = 1.210 to 8.911). There was a strong agreement between microhematuria and detection of ova of *S. haematobium* on urine microscopy (Kappa statistics = 0.895, $p = 0.0001$). These findings suggest the need for school based health education program and provision of potable water, in order to prevent schistosomiasis related exposures, break the chain of infection and reduce disease burden.

Key words: Prevalence, predictors, urinary schistosomiasis, 'Almajiri' school children.

INTRODUCTION

Schistosomiasis is a major public health problem and second only to malaria as the most devastating disease in tropical countries in Africa, East Asia and South America (USAID, 2016). Despite the high burden of the disease particularly in Africa that accounted for over 85 percent of the estimated 238 million people infected with the disease in 2010 (CDC, 2016; WHO, 2010), 90

percent of the estimated 261 million people requiring preventive treatment for the disease in 2013 (WHO, 2016), and an estimated 200,000 deaths per year (USAID, 2016), the paradox is that schistosomiasis remains a neglected tropical disease.

In areas endemic for the disease, it disproportionately affects poor and rural communities without access to safe

*Corresponding author. E-mail: dryunusausmanedzu@gmail.com.

drinking water and adequate sanitation, particularly agricultural and fishing populations, because people suffering from the disease contaminate freshwater sources with their urine and excreta containing parasite eggs which hatch in water and then enter into freshwater snails to develop into infective larval form of the parasite. Inadequate hygiene and contact with infected water (during which larval forms of the parasite released by freshwater snails penetrate the skin) make children especially vulnerable to infection; and women doing domestic chores in infested water, such as washing clothes, are also at risk (WHO, 2016).

Of serious concern is the fact schistosomiasis infection is usually acquired in childhood (when children tend to spend time swimming or bathing in water containing the larval form of the parasite), the increasing prevalence and intensity of infection with age (peaking in the 5 to 14 year age group), and the fact that children also suffer the most side effects of the disease, especially poor growth and impaired cognitive development. The disease also contributes to malnutrition and disrupts school attendance (USAID, 2016); in essence, the disease has become a double edged sword as it continues to exert huge socio-economic and health tolls on these children who grow up to bear the brunt of the complications of the disease.

The 30% prevalence of urinary schistosomiasis reported among school children in Zenu community of Ghana (Tetteh-Quarco et al., 2013), 64.3% prevalence in Zengerema District of Tanzania (Mazigo et al., 2010), and 73.3% prevalence in Eastern Cape province of South Africa (Meents and Boyles, 2010) among several other studies, perfectly mirror the reported overall high burden of the disease in Africa.

Similarly in Nigeria, the 30.5% prevalence of urinary schistosomiasis reported among school children in Keffi town, Nasarawa state (Ishaleku et al., 2012), 47.6% prevalence in two peri-urban communities in Osun state (Babatunde et al., 2013), 53.8% prevalence in Azumini, Abia state (Amechi, 2014), 60.8% prevalence in Sokoto metropolis, Sokoto state (Singh and Muddasiru, 2014), and 64.3% prevalence in Langai, Plateau state (Banwat et al., 2012), show the enormity of the burden of the disease in the country.

Almajirai (singular: Almajiri) is a Hausa word meaning immigrant children in search of Quranic education. In Nigeria, Almajirai are usually between the ages of seven and fifteen and mostly found in the Northern states including Kano, Kaduna, Katsina, Sokoto, Kebbi, and Zamfara among others. Sokoto state alone harbours about 1.1 million Almajiri children scattered around the state. Almajiri children are known for roaming the streets, farm lands, waste dumping sites and swimming in dirty and contaminated water. They are deprived of the basic necessities of life, plunged into poverty and may not be trained in the skills required to make them productive in future. They are known to face several social problems such as parental deprivation, food insecurity, and sleeping in overcrowded conditions that expose them to various

health hazards particularly communicable diseases (Christian, 2010; Kabir et al., 2005).

The enormous socio-economic burden of schistosomiasis on the affected population exposed to the disease, and the correlation between disease burden and host characteristics including age, lifestyles and occupation that contribute to exposure to infection (such as swimming in infected water, fishing), in addition to other ecological parameters, have been documented in several studies (Patz et al., 2000; Brouwer et al., 2003, 2004).

Most of the previous studies carried out in Sokoto state (Bello et al., 2003, 2014; Singh and Mudashiru, 2014; Kabiru et al., 2013) had focused majorly on disease burden and socio-demographic characteristics of the study subjects, there is dearth of literature on the epidemiological parameters that favor the transmission of the disease in the study area. This study was therefore conducted to determine the prevalence, epidemiological characteristics and predictors of occurrence of urinary schistosomiasis among 'Almajiri' school children in Sokoto, Nigeria. The findings would be invaluable in designing appropriate strategies for the prevention and control of the disease, particularly among this 'at risk' population.

MATERIALS AND METHODS

Study design and population

This was a cross-sectional study among children studying at the 'Almajiri' Integrated Model School at Tudun-Yandogo community, Dange-Shuni Local Government Area, Sokoto state, Nigeria, from December 2013 to January 2014. Most of the pupils were from the 23 Local Government Areas in Sokoto state, while a few came from the neighboring states.

The sample size was estimated at 272 using the statistical formula for estimating the sample size for descriptive studies (Ibrahim, 2009), 64.3% prevalence of urinary schistosomiasis among school age children from a previous study (Banwat et al., 2012), adjustment for a finite population of 800 pupils (obtained from the school records), precision level of 5% and an anticipated response rate of 90%. Children aged 5 years and above were considered eligible for enrolment into the study, those currently on treatment for urinary schistosomiasis or recently treated (less than 12 weeks) for the disease were excluded. The study subjects were selected proportionately in each of the 13 classes in the school by systematic sampling technique using the list of students in the respective classes to constitute the sampling frame.

Epidemiological characteristics

A set of pretested, semi-structured, interviewer administered questionnaire was used to obtain information on respondent's socio-demographic characteristics and schistosomiasis related exposures. It was reviewed by senior colleagues in the Department of Community Health, Usmanu Danfodiyo University, Sokoto; translated into Hausa version and then back translated into English by senior researchers in the social sciences department of the university to ascertain content validity. The Hausa translated version of the questionnaire was used for data collection. It was pretested among 15 students studying at the Federal Government

owned Almajiri school located in Sokoto metropolis, the necessary corrections were effected based on the observations made during the pretest. The questionnaires were numbered using the identification number issued to the participants. Five community health officers assisted in questionnaire administration after training on survey research, the objectives of the study, selection of study subjects and questionnaire administration.

Urine sample collection and analysis

Terminal urine samples were collected between 10:00 and 14:00 h, being the time of maximal egg output (Cheesbrough, 2005), into wide-mouthed, dry, sterile, clean bottles containing few drops of household bleach (as preservative), covered tightly and transported to the main microbiology laboratory of the Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria for analysis. The sample bottles were labelled using the identification number issued to the participants. The urine samples were examined for microhaematuria (using Medi-Test Combi 9 strips) and ova of *Schistosoma haematobium* (microscopically using standard sedimentation technique as described by Cheesbrough (2005)). All eggs were counted, recorded in the data sheet designed for the study, and the intensity of infection was graded based on the World Health Organization (WHO) criteria (WHO, 2002), as light (1 to 49 eggs per 10 ml of urine), heavy (≥ 50 to 499 eggs per 10 ml of urine), and severe (≥ 500 eggs per 10 ml of urine). Likewise, the community risk status was classified based on the WHO criteria (WHO, 2006) as low (<10% prevalence by parasitological method), moderate ($\geq 10\%$ but < 50% prevalence by parasitological method), and high ($\geq 50\%$ prevalence by parasitological method). Three laboratory technologists were recruited to assist in urine sample collection after training them on the objectives and conduct of the study.

Data analysis

Data entry, processing and statistical analysis were done using SPSS version 20 and Microsoft Excel computer statistical software packages after data cleansing. The chi-square test was used for bivariate analysis involving categorical variables. Kappa statistic was used to measure agreement between microhaematuria and diagnosis of urinary schistosomiasis. Logistic regression analysis was used to determine the variables that predict schistosomiasis infection. All levels of significance were set at $p < 0.05$.

Ethical consideration

Institutional ethical clearance was obtained from the Ethical Committee of Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. Permission to conduct the study was granted by the Sokoto state Ministry of Religious Affairs. The Principal of the school signed the parental informed consent on behalf of the children (and they also accented to participate in the study).

RESULTS

All the 272 questionnaires administered were retrieved and analyzed. All the participants were males and Moslem by religion. Their age ranged from 6 to 24 years (Mean = 9.2 ± 2.0), but majority (71.7%) were in the 10 to 14 years age group. For most of the respondents, their

father had only quranic education (62.5%), were either farmers (36.8%) or businessmen (39.0%). Majority of participants were from Sokoto state (74.7%), while about a fifth of them (22.3%) were from Zamfara state. A larger proportion of participants (57.6%) were from rural non-riverine areas (Table 1).

Schistosomiasis related exposures among participants

The participants reported high prevalence of schistosomiasis related exposures. Majority of participants wash their clothes and other items in river or stream (89.0%), and bath with water from the river (70.9%). Also, about half of participants (51.5%) swim in river or pond, while close to half of them (47.8%) work on swampy farm (Table 2).

Prevalence of urinary schistosomiasis among participants

Close to half of participants (49.0%) reported ever passing blood in urine at one time or the other, while about a quarter of them (26.9%) had microhaematuria (on urinalysis) as shown in Table 3.

About a quarter, 70 (25.7%) of the 272 participants had ova of *Schistosoma haematobium* in their urine (Figure 1). Although, all the participants had light-intensity infection, as none of them had up to 50 ova of *S. haematobium* per 10 ml of urine, with a 25.7% prevalence of urinary schistosomiasis, the school ('Almajiri' Integrated Model School, Sokoto, Nigeria) was classified as 'moderate-risk community'.

There was a strong agreement between microhaematuria and detection of ova of *S. haematobium* on urine microscopy (Kappa's statistics = 0.895, $p < 0.001$).

Factors associated with occurrence of urinary schistosomiasis among participants

Urinary schistosomiasis was statistically significantly more prevalent among children in the 10 to 14 years age group compared to those in the other age groups ($\chi^2 = 1.974$, $p = 0.043$), and less prevalent among children whose fathers were farmers compared to those whose fathers were businessmen, civil servants or artisans ($\chi^2 = 9.357$, $p = 0.021$) as shown in Table 4. However, in logistic regression analysis there was no predictor of occurrence of urinary schistosomiasis among the socio-demographic variables.

Similarly, urinary schistosomiasis was statistically significantly more prevalent among children that swim in river or pond (26.4%) compared to those who do not (14.6%); $\chi^2 = 12.76$, $p = 0.001$ (Table 5). Logistic

Table 1. Socio-demographic profile of participants.

Variables	Number	Percentage
Age groups (in years) n = 272		
5-9	29	10.7
10-14	195	71.7
15-19	47	17.3
>19	1	0.4
Father's level of education (n = 264)		
None	2	0.8
Quranic only	165	62.5
Primary	9	3.4
Secondary	78	29.5
Tertiary	10	3.8
Father's occupation (n = 244)		
Farming	100	36.8
Business	106	39.0
Civil servant	35	12.9
Artisan	3	1.1
State of origin (n = 206)		
Sokoto	154	74.7
Zamfara	46	22.3
Kano	3	1.5
Others	3	1.5
Nature of place of residence (n = 257)		
Rural riverine	109	42.4
Rural non-riverine	148	57.6

Table 2. Schistosomiasis related exposures among participants

Type of exposure*	Number (n = 272)	Percentage
Swim in river or pond	140	51.5
Wash clothes/other items in river/stream	242	89.0
Bath with water from the river	192	70.9
River as main source of water for drinking	12	4.4
Work on swampy farm	130	47.8

*Multiple responses allowed.

regression analysis also shows that children who swim in river or pond were three times more likely to have urinary schistosomiasis compared to children who do not (Odds ratio (OR) = 3.284, $p = 0.020$, 95% Confidence Interval (CI) = 1.210 to 8.911) as shown in Table 6.

DISCUSSION

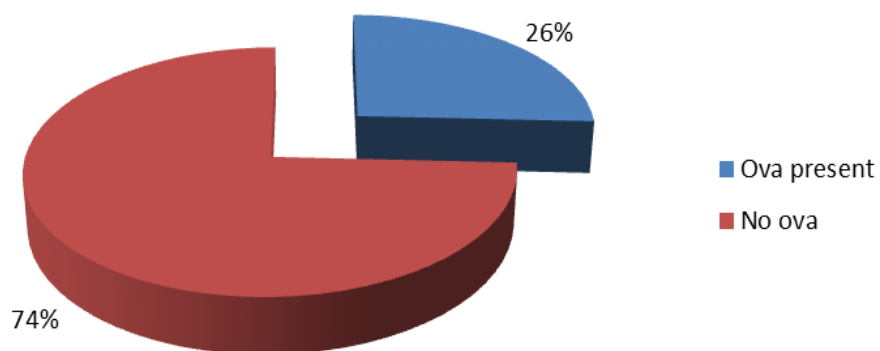
Schistosomiasis related exposures were very prevalent

among the participants; majority of participants wash their clothes and other items in river or stream (89.0%), bath with water from river (70.9%), and swim in river or pond (51.5%). This is of public health concern as it exposes the prevailing lack of access to potable water in the rural communities in Sokoto and Zamfara states where most of the participants resided before migrating to the city.

About a quarter (25.7%) of the participants in this study had urinary schistosomiasis, this may be attributed to the fact that a sizable proportion of the participants (42.4%)

Table 3. Prevalence of hematuria among participants

Hematuria	Number	Percentage
Ever passed blood in urine (n = 271)		
Yes	134	49.0
No	135	50.0
I can't remember	2	1.0
Microhaematuria (on urinalysis, n = 268)		
Present	72	26.9
Absent	196	73.1

**Figure 1.** Prevalence of urinary schistosomiasis among participants.**Table 4.** Distribution of occurrence of urinary schistosomiasis by socio-demographic profile of participants.

Variables	Presence of ova of <i>Schistosoma hematobium</i> in urine		Test of significance
	Yes [Number (%)]	No [Number (%)]	
Age groups (in years)			
5-9	7 (24.1)	22 (75.9)	$\chi^2 = 1.974$, df = 1, p = 0.043
10-14	53 (27.2)	142 (72.8)	
15 and above	10 (21.3)	38 (79.7)	
Education status of father			
Quranic	43 (26.1)	122 (73.9)	$\chi^2 = 1.037$, df = 4, p = 0.904
Primary	3 (33.3)	6 (66.7)	
Secondary	20 (25.6)	58 (73.4)	
Tertiary	2 (20.0)	8 (80.0)	
None	1 (50.0)	1 (50.0)	
Occupation of father			
Farmer	15 (15.0)	85 (85.0)	$\chi^2 = 9.357$, df = 3, p = 0.021
Business	34 (32.1)	72 (67.9)	
Civil servant	12 (34.3)	23 (65.7)	
Artisan	1 (33.3)	2 (66.7)	
Nature of place of residence			
Rural riverine	32 (29.4)	77 (70.6)	$\chi^2 = 2.009$, df = 1, p = 0.156
Rural non-riverine	32 (21.6)	116 (78.4)	

Table 5. Distribution of occurrence of urinary schistosomiasis by exposure status of participants.

Variables	Presence of ova of <i>Schistosoma hematobium</i> in urine		Test of significance
	Yes [Number (%)]	No [Number (%)]	
Swim in river/pond			
Yes	46 (26.4)	128 (73.6)	$\chi^2 = 12.76$, df = 1 p = 0.001
No	21 (14.6)	140 (85.3)	
Source of water for washing			
River	6 (42.9)	8 (57.1)	$\chi^2 = 2.854$, df = 3 p = 0.415
Stream	0 (0)	2 (100)	
Well	44 (22.7)	150 (77.3)	
Tap	17 (25.0)	51 (75.0)	
Source of water for bathing			
River	5 (38.5)	8 (61.5)	$\chi^2 = 1.756$, df = 2 p = 0.416
Well	51 (26.6)	141 (73.4)	
Tap	14 (73.7)	5 (26.3)	
Source of water for drinking			
River	4 (33.3)	8 (66.7)	$\chi^2 = 1.246$, df = 3 p = 0.742
Stream	0 (0)	2 (100.0)	
Well	49 (26.8)	134 (73.2)	
Tap	17 (33.9)	54 (76.1)	
Work on swampy farm			
Yes	36 (27.7)	94 (72.3)	$\chi^2 = 0.741$, df = 2 p = 0.779
No	33 (25.8)	95 (74.2)	

Table 6. Logistic regression analysis for predictors of occurrence of urinary schistosomiasis among participants.

Type of exposure	Odds ratio (OR)	p value	95% Confidence Interval (CI)	
			Lower	Upper
Swim in river or pond	3.284	0.020	1.210	8.911
Wash clothes/other items in river/stream	1.428	0.433	0.586	3.481
Bath with water from the river	1.721	0.360	0.539	5.499
River as main source of water for drinking	0.567	0.436	0.136	2.366
Work on swampy farm	0.845	0.778	0.262	2.724

in this survey were from rural riverine areas where children have unrestricted access and exposure to schistosoma breeding bodies of water. This finding is in concordance with that obtained in a study among school age children in the lower river Volta basin in Ghana by Nkegbe et al. (2010) that reported a prevalence of 21%, but it is much lower than the 60.8% prevalence reported in a study among school children in Sokoto metropolis by Singh and Mudashiru (2014).

Although, all the participants in this study had light-intensity infection as none of them had up to 50 ova of *S.*

haematobium per 10 ml of urine (WHO, 2002), with a 25.7% prevalence of urinary schistosomiasis, the school ('Almajiri' Integrated Model School, Sokoto, Nigeria), was classified as 'moderate-risk community' (WHO, 2006), and all the school-age children in the school are expected to have preventive chemotherapy by mass administration of praziquantel, at a dose of 40 to 60 mg/kg body weight, in single or divided doses, every 2 years (WHO, 2006).

Almost equal proportion of participants that currently pass blood in urine (26.9%) had urinary schistosomiasis (25.7%), and there was a strong agreement between self-

reported current hematuria and detection of ova of *S. haematobium* on urine microscopy (Kappa's statistics = 0.895, $p = 0.001$). This finding is consistent with the pathophysiology of the disease (with hematuria accompanying shedding of ova from the bladder), and it supports the use current hematuria for a presumptive diagnosis of the disease especially in resource poor settings endemic for the disease. This would facilitate prompt treatment of those infected, reduce their risk of developing complications of the disease and halt transmission of the disease in the community.

The prevalence of urinary schistosomiasis among the participants in this study, rose from 24.1% among those in the 5 to 9 years age group, to a peak of 27.2% among those in the 10 to 14 years age group and then dropped to 21.3% among those aged 15 years and above. This is similar to the findings in the study by Brouwer et al. (2003) where the prevalence of urinary schistosomiasis rose from 23.6% in the 5 to 9 years age group, to a peak of 29.2% in the 10 to 14 years age group and then dropped to 20.1% in the 15 to 19 years age group.

Another study by Amadu et al (2001) in Wurno, Sokoto state, also reported a similar pattern with the prevalence rising from 6.5% in the 5 to 9 years age group, reaching a peak of 30.3% in the 10 to 14 years age group and then dropped to 8.7% in the 15 to 19 years age group. These findings could be due to the agricultural practices in these communities and the fact that grown up children (10 years and above) were more likely to be involved in farming, fishing and other forms of contact with contaminated water that expose them to the risk of the disease than those in the younger age group.

An intriguing finding in this study was the lower prevalence of urinary schistosomiasis among children of farmers (15.0%) as compared to children of businessmen (32.1%), artisans (33.3%) and civil servants (34.3%). This is explainable in the context of the fact that the children of farmers were not unlikely to have been exposed to the disease and could have been educated on the preventive measures for the disease in the course of accessing healthcare services. Swimming in infected pools of water and streams/rivers could have been the major source of infection among children whose fathers were non-farmers.

In sharp contrast to the similarity in the prevalence of urinary schistosomiasis among children from rural riverine (29.4%) and rural non-riverine areas (21.6%) in this study, Phiri et al. (2000) observed a very high prevalence of urinary schistosomiasis among children resident in rural riverine (86.1%) compared to those resident in rural non- riverine areas (12.1%).

Children who swim in river/pond were three times more likely to have urinary schistosomiasis compared to those who do not (OR = 3.284, $p = 0.020$, 95% CI = 1.210 to 8.911). This finding is consistent with the documented pathogenesis of the infection in which schistosome cercariae penetrate the body following exposure to cercarial contaminated water. The higher risk (40.1%) of

schistosoma infection among children who had contact with stream/pond in a study by Satayathum et al. (2006) further corroborate the finding in this study.

The higher prevalence of urinary schistosomiasis among participants whose source of water for washing was river/pond in this study (although not statistically significant) compare well with the findings in the study by Kloos et al. (2006), that reported 58.9% prevalence of urinary schistosomiasis among participants whose source of water for washing was river, 42.1% prevalence among those whose source of water for bathing was stream, and 32.0% prevalence among those whose source of water for drinking was stream/river. This finding highlights the risks rural populations are exposed to as a result of lack of access to potable water, and it underscores the need to make provision of potable water in the rural populations a top priority.

Conclusion

This study demonstrated high prevalence of urinary schistosomiasis among children in "Almajiri" Integrated Model School, Sokoto, Nigeria, with the highest prevalence in the 10 to 14 years age group. Similarly, schistosomiasis related exposures were very prevalent among them, particularly swimming in river/pond which was found to be the sole predictor of occurrence of urinary schistosomiasis. These findings suggest the need for school based health education program and provision of potable water, in order to prevent schistosomiasis related exposures, break the chain of infection and reduce disease burden. In addition, being a moderate-risk community, all the school-age children in the school should have preventive chemotherapy by mass administration of praziquantel once in 2 years.

Conflict of interests

The authors have not declared any conflict of interests.

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Full Length Research Paper

Persistent proteinuria among sickle cell anaemia children in steady state in Ilorin, Nigeria

Emmanuel Ademola Anigilaje^{1*} and Olanrewaju Timothy Adedoyin²

¹Department of Paediatrics, College of Health Sciences, University of Abuja, Abuja, Nigeria.

²Department of Paediatrics, University of Ilorin, Ilorin, Kwara State, Nigeria.

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Sickle cell disease (SCD), the commonest single gene disorder amongst Nigerian children, may present as sickle cell nephropathy (SCN). SCN is detectable by persistent proteinuria, a “nephrotoxin” that contributes to progression of SCN to end stage renal disease. Unfortunately, screening for persistent proteinuria is an uncommon practice among Nigerian children with SCD, even when reduction of proteinuria is a proven renoprotective therapy. Dipstick urinalysis was done to detect persistent proteinuria (proteinuria of trace and above, on first contact and a month on follow-up in the same subject) among consecutive steady state sickle cell anaemia (haemoglobin SS confirmed using cellulose acetate paper electrophoresis) children attending sickle cell clinic at the University of Ilorin Teaching Hospital between October, 2004 and July, 2005. Subjects with persistent proteinuria were also assessed for estimated glomerular filtration rate (eGFR) using the method described by Schwartz et al. A total of 75 children aged between 1 to 17 years, comprising 35 males and 40 females, were studied. Proteinuria was found in 6 (8%) subjects (5 males, 1 female) and in 5 (6.7%) subjects (3 males, 2 females) on first contact and one month on follow-up, respectively. Persistent proteinuria was only seen in 3 (4%) male subjects (older than 10 years age) whose eGFR was not impaired. Although proteinuria occurred more commonly among male subjects than females on first contact and at follow-up, this observation was not statistically significant ($p = 0.175$ at first contact, $p = 0.224$ at follow-up). Proteinuria also occurred more among subjects older than 10 years of age at both contacts, this association was also not significant ($p = 0.071$ on first contact, p value = 0.10 at follow-up). Although, a low prevalence of persistent proteinuria was found among the sickle cell anaemia children studied, its screening should become a routine to identify children who will benefit from antiproteinuric treatment.

Key words: Persistent proteinuria, steady state sickle cell anaemia, children, Ilorin, Nigeria.

INTRODUCTION

Nigeria, by virtue of her population, is the most sickle cell disease (SCD) endemic country in the world, with over 40 million people (24% of its population) being a carrier of

the Haemoglobin “S” gene; and the prevalence of sickle cell anaemia (SCA) being about 20 per 1000 births and about 150,000 children born each year with the disorder

*Corresponding author. E-mail: demolaanigilaje@yahoo.co.uk. Tel: +2348033833839.

(Sickle Cell Foundation, 2016). The cause of the SCD is the substitution of valine for glutamic acid at the sixth position of the β -globin chain of the haemoglobin (Nath and Hebbel, 2015). The immediate consequence of the mutation is that deoxygenated haemoglobin S polymerizes and distorts the shape of the erythrocytes (Manwani and Frenette, 2013). Sickled haemoglobin also causes oxidative damage of the erythrocyte membrane, cellular dehydration, abnormal phospholipid asymmetry and increased adherence to endothelial cells (Francis and Johnson, 1991; Hebbel, 1991). The net result of these alterations is a shortened erythrocyte life span from chronic haemolysis and episodic microvascular occlusion that cause tissue ischaemia and acute and chronic dysfunction of virtually all the organs of the body including the kidney (Oral and George, 1993; Alhwiesh, 2014). The kidney's microvasculature is particularly vulnerable because of absence of collateral circulation and the characteristic sickling promoting features of the renal medulla including the low oxygen tension, acidosis and hypertonicity (Alhwiesh, 2014).

A variety of renal structural and functional abnormalities have been consistently found in patients with SCD in what is now termed sickle cell nephropathy (SCN) (Allon, 1990; Lopez and Andres, 2011; Alhwiesh, 2014). The structural changes in the cortex and the medulla include vascular dilatation and engorgement of glomerular capillaries with sickled erythrocytes, glomerular hypertrophy, glomerular sclerosis, mesangial proliferation as well as focal scarring and papillary necrosis in the medulla (Allon, 1990; Lopez and Andres, 2011; Alhwiesh, 2014). The functional alterations manifest clinically as proteinuria with or without nephrotic syndrome, haematuria, impaired urinary concentration, increased susceptibility to urinary tract infection, incomplete distal tubular acidosis, impaired potassium excretion abilities, increased glomerular filtration rate and renal plasma flow in young patients but with progressive decline of these values after the third decades of life (Allon, 1990; Lopez and Andres, 2011; Alhwiesh, 2014).

In Nigeria, studies on SCN among sickle cell anaemia (SCA) children in the steady state had involved measurement of proteinuria/microalbuminuria and the glomerular filtration rate (GFR). Persistent proteinuria of 7% was reported in Port Harcourt, Southern Nigeria, by Ugwu and Eke using the dipstick urinalysis (Ugwu and Eke, 2002). Solarin et al. (2014) in Lagos, Southern Nigeria reported microalbuminuria prevalence rates of 11.3 and 38.8% using the albumin creatinine ratio (ACR) and the micral test, respectively. In addition, using the micral method, a respective microalbuminuria of 42.7 and 20.3% was reported by Yaguo-Ide et al. (2010) in Port-Harcourt, Southern Nigeria and Abhulimhen-Iyoha et al. (2009) in Benin-city, Southern Nigeria.

Although the dipstick proteinuria is not sensitive for the detection and quantitation of microalbuminuria; the persistent proteinuria detectable by it is a signal indicator of a glomerular lesion (Kallen et al., 2013). Persistent

proteinuria is nephrotoxic and it plays a central role in the progression of glomerular lesions to later stages of chronic kidney disease (Kallen et al., 2013). Furthermore, Oyinade (1973) in Lagos Western Nigeria demonstrated a significantly higher mean GFR in SCA children compared to age-matched controls without SCA. Other Nigerian researchers (Aikhionbare et al., 1988; Okoro and Onwuameze, 1991; Olowu et al., 2002) did not find a significant difference in the mean GFR between the two groups.

Whereas, infection is the leading cause of death among children with sickle cell anaemia, deaths from chronic renal failure takes prominence after the first three decades of life (Platt et al., 1994). This becomes important because with improvement of knowledge of medical management of the disease and in better living standards, a longer survival is expected among these children and hence the risk of death from renal failure may become more frequently encountered (Anigilaje and Adedoyin, 2013).

This study determined the prevalence rates of persistent proteinuria and its association with age and gender among SCA children attending the sickle cell clinic at the University of Ilorin Teaching Hospital, Ilorin, Nigeria. SCA subjects with persistent proteinuria were also assessed for estimated GFR to determine the extent of renal impairments.

MATERIALS AND METHODS

Study area

The study took place at the Sickle cell clinic of the Department of Paediatrics and Child Health of the University of Ilorin Teaching Hospital (UIITH), Ilorin, Kwara State, Northern Nigeria. The UIITH provides tertiary health care services to the people in Ilorin metropolis and the adjoining cities and communities. UIITH also serves as a referral Centre for the surrounding States of Kogi, Niger, Ekiti, Oyo and Osun.

Consent and ethical approval

Permission to embark on the study was gotten from the Research and Ethics Committee of the University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria. Written informed consent was obtained from the parents/legal care providers of the children that constitute the study population. The study design complied with the Helsinki declaration. The study's objectives were explained to the parents/legal care providers of the study population and it was emphasized that the information obtained from the study would be treated with the utmost confidentiality. It was also underscored that anyone was at liberty to decline participation and that declination to participate would not affect the care and treatment of the children.

Study population

Subjects were SCA children (haemoglobin, HbSS, determined by electrophoresis using cellulose acetate paper) in the steady state.

Table 1. Age-group and gender distribution of the subjects.

Age group (years)	Male	Female	Total (%)
< 5	10	12	22 (29.3)
6-10	11	15	26(34.7)
11-15	10	8	18(24.0)
≥ 16	4	5	9(12.0)
Total	35	40	75(100)

We had earlier reported the burden of haematuria in the same cohort of subjects (Anigilaje and Adedoyin, 2013). Included in the study were SCA children between 9 months and 18 years of age. They were assumed to be in the steady state when they satisfied the following criteria (Ojuawo et al., 1994): (i) No fever at presentation and for 4 weeks preceding clinical attendance, (ii) No complaints of skeletal and/or abdominal pain at presentation and within the 4 weeks preceding the investigation, (iii) Not on any medication apart from routine folic acid and proguanil, (iv) Otherwise well and going about their routine activities. Exclusion criteria included subjects with: (i) Symptoms and signs suggestive of urinary tract infections, (ii) At least 4 weeks history of exposure to radio-opaque dye and some drugs that decrease the reactivity of dipstick reagents including nitrofurantoin, cephalexin, cephalothin, captopril and tetracycline (Davis and Avner, 2004; Bayer Diagnostics, 2004), (iii) Menstruation or vaginal/penile discharge (Davis and Avner, 2004; Bayer Diagnostics, 2004), (iv) Fever (Davis and Avner, 2004; Bayer Diagnostics, 2004), (v) Involvement in competitive sport/exercise in the previous 24 h (Davis and Avner, 2004; Bayer Diagnostics, 2004).

Sample size

A minimum sample size of 42 for the subjects was calculated using the Leslie Kish's method (Kish, 1965) at a standard normal deviate of 1.96, assuming 2.8% target population (Adewuyi and Akintunde, 1990) and tolerating 5% sampling error. We limited response rate to 80%, giving a rounded figure of 53. Although a total of 80 SCA children met the inclusion criteria, a total of 75 were evaluated at follow-up (five subjects were lost to follow-up). These 75 subjects comprised 35 males and 40 females with a male to female ratio 1:1.1. Their age range was between 1 to 17 years, with a mean age of 8.9 ± 4.5 years. The age group and gender distribution of the subjects were as shown in Table 1

Study design

A prospective longitudinal study in which consecutive SCA patients (HbSS) who came for routine follow-up clinic over 10 months between October, 2004 to July, 2005 were recruited. In order to define a persistent proteinuria on dipstick urinalysis findings, two clinical contacts were required, the second contact being a month after the first one.

Specimen collection

All enrolled subjects were provided with a properly labeled universal bottle for the collection of early morning urine. Subjects were instructed on how to collect early morning mid-stream urine depending on the age. The care givers collected for subjects who could not collect on their own. Urine samples so brought were

accepted when subjects still satisfied the inclusion criteria. The lead investigator was available as early as 7.00 a.m. to receive urine specimens. Early morning urine is expected to be concentrated and therefore most suitable for biochemical analyses (Clinical and Laboratory Standards Institute, 2001). When tests could not be performed within the first hour of urine collection, urine was stored in the refrigerator (at 4°C) and tested within two hours of storage in the refrigerator. Urine refrigerated was kept at room temperature for 15 min before tests were performed. Dipstick urinalysis was done using Multistix 10SG by Bayer Diagnostic (Bayer Diagnostics, 2004). All instructions regarding the storage, handling of reagent strip and the performance of the dipstick urinalysis were observed as stipulated by the manufacturer. The grades of findings on colour chart and their corresponding quantitative values were as follows; negative, trace (15 mg/dl), 1+ (30 mg/dl), 2+ (100 mg/dl), 3+ (300 mg/dl) and 4+ (2000 md/dl).

Glomerular filtration rate measurement

GFR was estimated for all subjects with persistent findings on dipstick urinalysis. The GFR in ml/min/1.73 m² was estimated using the formula described by Schwartz et al. (1987).

$$\text{GFR} = \frac{\text{KL}}{\text{Sc}}$$

Where K = constant of proportionality
 = 0.55 for children and adolescent girls (13-21 years of age)
 = 0.70 for adolescent boys (13-21 years of age).
 L = body height in cm.
 Scr = Serum creatinine in mg/dl.

About 4 ml of blood was collected into a plain ethylene diamine tetra-acetic acid EDTA bottle for Scr estimation using the Jaffe's method on Corning colorimeter reading at 520 nanometers (Newman and Prize, 1999). The height was measured by a standard method to the last 0.1 cm. Hyperfiltration; eGFR value more than 140 ml/min/1.73m² (Aloni et al., 2014)

Statistical analysis

Data analysis was done with the Epi-info Software package (version 6.04) and SPSS 11.1. Subjects were grouped into increasing age-groups of four (1 to 5, 6 to 10, 11 to 15, and ≥ 16 years). Descriptive statistics were tabulated as numbers and percentages for categorical variables. The prevalence of persistent proteinuria was calculated. Chi square (χ²) test was adopted to test for association between the age groups and gender and proteinuria. P value of < 0.05 was regarded as significant.

RESULTS

Table 2 shows the proteinuria on dipstick urinalysis for subjects on first contact and at follow-up. Proteinuria was found in 6 (8%) subjects (5 males, 1 female) and in 5 (6.7%) subjects (3 males, 2 females) on first contact and at follow-up, respectively. Persistent proteinuria was only seen in 3 (4%) male subjects. Although proteinuria occurred more commonly among male subjects than females on first contact and at follow-up, this observation

Table 2. Proteinuria for subjects on first contact and at follow-up.

Age groups (years)	Subjects without proteinuria		Subjects with proteinuria		Subjects with Persistent proteinuria	
	Male	Female	Male	Female	Male	Female
1-5	9 (10)	11 (12)	2 (0)	1 (0)	0	0
6-10	11 (11)	15 (14)	0 (0)	0 (0)	0	0
11-15	8 (8)	8 (8)	2 (2)	0 (0)	2	0
≥16	3 (3)	4 (4)	1 (1)	0 (2)	1	0
Total	31 (32)	38 (38)	5 (3)	1 (2)	3	0
Prevalence rates in %	41.3 (42.7)	50.7 (50.7)	6.7 (4)	1.3 (2.6)	4	0

Table 3. The estimated glomerular filtration (eGFR) rates of the three male subjects with persistent proteinuria.

Serial number	Age	eGFR (ml/min/1.72 m ²)
7	14	114
12	15	107
55	17	140

was not statistically significant ($p = 0.175$ at first contact, $p = 0.224$ at follow-up). Proteinuria also occurred more among subjects older than 10 years of age at both contacts, this association was also not significant ($p = 0.071$ on first contact, p value = 0.10 at follow-up). Figures in parenthesis were findings at follow-up. Relationship between gender and proteinuria on first contact ($X^2 = 4.963$, $df = 3$, p value = 0.175) and at follow-up; ($x^2 = 4.376$, $df = 3$, p value = 0.224). Relationship between age and proteinuria on first contact ($X^2 = 15.814$, $df = 9$, p value = 0.071) and at follow-up ($X^2 = 21.479$, $df = 9$, p value = 0.10).

Table 3 depicts the estimated glomerular filtration rates of the three subjects with persistent proteinuria. None of the 3 male subjects with persistent proteinuria had impaired GFR as their eGFRs were all above 60 ml/min/1.73 m².

DISCUSSION

The prevalence of proteinuria of 8.0% noticed on the first contact among our subjects dropped off to 6.7% on follow-up, one month after, but persisted in 3 male subjects with a persistent proteinuria prevalence rate of 4%. This finding differed from that of Aikhionbare et al. who did not find persistent proteinuria among the 22 SCA subjects studied (Aikhionbare et al., 1988). However, the prevalence of persistent proteinuria of 4.0% in this study was higher than the persistent proteinuria of 6.2% reported both, in the USA and in Congo by Wigfall et al. (2000) and Aloni et al. (2014), respectively among SCA children, even though the subjects of Aloni et al. (2014) appear to be younger (2 to 13 years old).

Furthermore, the prevalence of persistent proteinuria in this study was lower than 12.3% reported by Morgan among 407 Jamaican SCA patients and the 7% reported by Ugwu and Eke among 72 SCA children in Port Harcourt, Nigeria (Morgan, 1982; Ugwu and Eke, 2002). While the discrepancy in this study and that of Morgan may be due to the difference in age composition of the two studies (1 to 17 years in this study and 1 to 70 years in Morgan's); that of Ugwu and Eke may not be easily explained as they also studied children in a relatively similar age groups with ours (16 months to 16 years).

In general, inter-observer differences in the reading of dipstick urinalysis cannot be totally ignored and may also be responsible for the different rates of proteinuria observed in our study and those of Wigfall et al. (2000), Aloni et al. (2014), Morgan (1982) and Ugwu and Eke (2002). We are very careful in comparing our study with those of other Nigerian researchers (Solarin et al., 2014; Yaguo-Ide et al., 2010; Abhulimhen-lyoha et al., 2009) as these researchers measured microalbuminuria in Nigerian children with SCA in contrast to dipstick proteinuria measured in this study. Although, the dipstick urinalysis mainly detects albumin among the various proteins in urine and it is sensitive to albumin concentrations as low as 15 mg per deciliter; it is not sufficiently sensitive for detecting albumin in the range of microalbuminuria (that is, albumin excretion of 30 to 300 mg per day) (Kallen et al., 2013).

Although proteinuria occurred more commonly among male subjects than females on first contact and at follow-up, this observation was not statistically significant. The pathophysiology of proteinuria among SCA patients is not gender dependent and the observed gender related differences in this study may therefore be due to a chance

chance occurrence as more male subjects were seen during the study period.

Proteinuria was found more among subjects older than 10 years in this study, this trend was not statistical significant. Furthermore, the three subjects with persistent proteinuria were also older than 13 years of age. Nicholson had earlier reported that proteinuria did not occur in SCA children below the age of 10 years but affected older age group (Nicholson, 1977). Wigfall et al also noted that the prevalence of proteinuria in SCA patients increased with increasing age, ranging from 0.0% in children 1 to 6 years to 12.0% in older teenagers (Wigfall et al., 2000). Medullary and cortical infarctions resulting from incessant vaso-occlusive crises gets cumulatively worsened with age and this may probably explain the reason why proteinuria is commoner in older SCA patients (Allon, 1990; Yaguo-Ide, 2010; Lopez and Andres, 2011; Alhwiesh, 2014).

Luckily, the eGFR in all the three subjects was relatively normal, perhaps in keeping with the fact that the proteinuria is yet to damage the glomeruli in these subjects. However, hyperfiltration of eGFR greater than 140 ml/min/1.73 m² cannot be rule out as one of the subjects was having eGFR of 140 ml/min/1.73 m². Recently, an intrinsic glomerulopathy related to endothelin (ET)-1 production and signals and nitric acid synthesis have been reported and may also explain the proteinuria seen in SCD patients (Tharoux, 2011; Lopez and Andres, 2011; Aloni et al., 2014).

Proteinuria in SCN has been attributed to glomerular capillary hypertension. This concept of glomerular hypertension induced proteinuria is supported by the reduction in protein excretion that is observed with the administration of angiotensin-converting enzyme inhibitors (Sharpe and Thein, 2014; Scheinman, 2009). Proteinuria may also accompany the membranoproliferative lesions of SCN (Nath and Hebbel, 2015). The membranoproliferative lesion has been thought to result from an autologous immune-complex nephritis, although the nature of antigens triggering the immune response remains speculative and even when known, such immune reactants are often considered non-specific (Nath and Hebbel, 2015).

Conclusion

The study reveals that the prevalence of persistent haematuria is low in this cohort of SCA children in steady state. Although not statistically significant, proteinuria is commoner among boys than girls who are often older than age of 10 years. Although microalbuminuria detects renal impairment much earlier than the dipstick urinalysis, SCA children can still benefit from screening with dipstick urinalysis, especially when the proteinuria is found to be persistent. Progression of SCN to end stage renal disease can be achieved through the prevention of incessant crises and the control of proteinuria with angiotensin-1-

converting enzyme inhibitors (Anigilaje and Adedoyin, 2013). The three children with persistent proteinuria in this study also benefited from lisinopril on follow-up at the sickle cell clinic.

Conflict of interest

The authors have not declared any conflict of interest.

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