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ORIGINAL ARTICLE

Arsenicosis in bladder pathology and schistosomiasis in Eggua, Nigeria

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Background: Chronic schistosomiasis and arsenic exposure through drinking water are some of the risk factors for bladder cancer. To determine the association of schistosomiasis and arsenicosis with bladder pathologies, 122 individuals from Eggua in southwest Nigeria were recruited for this study.

Methods: Prevalence of schistosomiasis was determined by urine microscopy and PCR. Total urinary arsenic concentration and arsenic levels in three different water sources in the community were assessed by flame atomic absorption spectrometry. Bladder pathologies were investigated by ultrasonography. The data collected were evaluated with chi-square (χ^2) and ANOVA tests to examine the relationships among demographic factors, infection, bladder pathologies and urinary arsenic concentrations.

Results: The prevalence and mean intensity of schistosomiasis were 21.3% and 20.7 eggs/10 mL urine, respectively. Arsenic concentration in two of the water sources, River Yewa (0.46 mg/L) and borehole (0.52 mg/L), were above the WHO standard (0.01 mg/L); and the mean concentration in urine samples, 1.17 mg/L, was also above the WHO standard (0.2 mg/L). There was no evidence of an association between bladder pathology and arsenicosis, or between schistosomiasis associated-bladder pathology and arsenicosis (p=0.66).

Conclusions: Arsenicosis is a public health concern in the study population. At the moment no clear roles are envisaged for it in the development of bladder pathologies or urinary schistosomiasis-associated bladder pathologies in Eggua.

Keywords: arsenic contamination, bladder tumour, potable water, rivers, urogenital schistosomiasis

Introduction

Schistosomes are parasitic blood flukes. About 779 million people in 76 tropical and subtropical countries are at risk of schistosomiasis, and over 207 million people in these countries are infected and require treatment.[1] However, more than 90% (187/207) of this infection occurs in Africa;[1] Nigeria records the largest number of infection with about 29 million cases in 2008,[2] but this number may have increased going by recent studies.[3] Infection with *Schistosoma haematobium* affects the urinogenital tract and, as a result of the eggs' high antigenic character, the different bladder pathologies, including granuloma and fibrosis are induced.[4] Many studies have indicated that schistosomiasis associated with urinary bladder cancer is a multistage process involving several mechanisms, with chronic inflammation being a central theme.[5]

The development of schistosoma-associated bladder cancer often requires exposure to the parasite for many years. The resulting chronic inflammation of the tissue and bladder pathologies are usually the precursors of bladder cancer.[6] Other factors can also play a role in bladder carcinogenesis, including positive family history for cancer, parents' consanguinity, exposure to pesticides, smoking, and xenobiotics such as aflatoxin and arsenic.[7] Genetic polymorphisms in some genes involved in detoxification such as the glutathione S-transferases M1 and T1, and the *AS3MT* gene are also risk factors for bladder cancer.[8] Variants of these genes affect the body's ability to metabolize and detoxify exogenous substances, and increase susceptibility to bladder cancer. The prevalence of bladder pathologies as a result of urinary schistosomiasis in Eggua, Nigeria, was reported previously.[9]

Arsenic (As), a toxic metalloid, has been classified as a class 1 carcinogen by the International Agency of Research on Cancer.[7] It is released into the aquatic environment by natural erosion processes, sewage, refuse and industrial discharges,[10]

and may enter drinking water through dissolution in rain and groundwater. The World Health Organization (WHO),[11] the United State Environmental Protection Agency (USEPA) and the Nigeria standard for Drinking Water Quality,[12] have set the maximum concentration limit for arsenic in drinking water as 0.01 mg/L. In humans, an increased level of arsenic or chronic exposure to arsenic in the body is known as arsenicosis, a condition that has been reported in different countries of the world.[8,13,14] However, few published reports exist in Nigeria, and the available studies have only examined arsenic in water bodies.[10,13] To our knowledge, there is no available study on the relationship between arsenicosis and schistosomiasis, each of which may promote bladder cancer. Thus, the aim of this study was to explore the association between schistosomiasis, arsenicosis and bladder pathology in a rural community in Nigeria.

Materials and methods

Study area and participants

The study was carried out in Sagbon, a farming settlement in Eggua, Yewa North Local Government Area of Ogun State in the southwest of Nigeria, as described in previous work.[15] The main sources of water in the area are flowing rivers, including River Iju and River Yewa, which are used for domestic purposes, including drinking, bathing and cooking by a majority of inhabitants of Sagbon. Ethical approval for the study was given by the Ogun State Ministry of Health; study objectives and plan were discussed with village heads and residents in order to obtain their cooperation. Language translations were carried out as necessary. All the residents who agreed voluntarily to participate were included in this study (universal sampling). Written informed consent was obtained from all participants, and personal information was anonymised.

Questionnaire survey

A structured, pre-tested questionnaire was administered to the participants in order to collect demographic data (age and gender), socio-economic background (educational level and occupation), and behavioural risks (water contact activities). The participants were interviewed by research assistants who received a specific training on how to apply the questionnaire.

Collection of samples

On-the-spot urine samples were collected in clear, clean, sterile universal containers by the participants upon instruction, in the morning hours. Aliquots were taken immediately for microscopic examination of *S. haematobium* eggs using the standard centrifugation method, and the other aliquots were kept immediately in an ice chest, transported to the laboratory and stored at −20°C. Water samples (1 L) were collected in duplicate from three water sources in Sagbon—River Yewa, River Iju and a borehole. The samples were collected into dark, clean sample bottles for determination of arsenic.

Determination of *S. haematobium* infection and urinalysis

Urine examination for *S. haematobium* eggs was carried out as described.[16] Each urine sample (10 mL) was centrifuged and the sediment examined microscopically. Eggs of *S. haematobium* were identified by their possession of a terminal spine, and the intensity of infection calculated as eggs/10 mL of urine. Samples negative for *S. haematobium* eggs were subjected to PCR using published Dra 1 primers and previously described methods.[17] Urinalysis reagent strips (Rapid Labs, UK) were used to make a rapid detection of blood and analytes, including glucose, ketone, specific gravity, pH, proteinuria and leukocytes in the urine samples, following the manufacturer's instructions.

Determination of arsenic levels in drinking water and urine samples

All the arsenic species were first converted to arsenic by acid digestion with perchloric and hydrogen peroxide (1:1) (Fisher Scientific, UK). This was followed by heating the samples on a hotplate for 10 min and filtering with Whatman No.1 filter paper. The water or urine samples were then analysed in replicates by Agilent 240 AA Flame Atomic Absorption Spectrometer with hydride generation accessory, along with three blanks.[18] Certified reference SRM 2668 standard was used and the standard solutions were also used for accuracy check after every five measurements. Analysis for total arsenic was carried out on three water sources in the community and 34 urine samples. The detection limit was 0.001 mg/L and limit of quantitation was 0.004 mg/L. Recoveries were between 95.1–100.8%. Total arsenic concentration was recorded in situ, rather than adjusted to creatinine, as previous research[19] had shown that correction of arsenic levels with creatinine in urine had no effect on measurements and does not necessarily provide maximum arsenic exposure to body tissues.

Ultrasound examination of the bladder for pathology

Using an ultrasound machine (Titan, Sonosite, WA, USA), each participant was examined by a radiologist. In the supine position, the well-distended urinary bladder was scanned and findings documented according to WHO protocol[20] for abnormal bladder morphologies, namely bladder wall thickness (≥5 mm), irregular bladder shape, bladder calculi, bladder polyps and bladder mass. Based on the analyses of infection and pathology, participants who had no infection or pathology were used as controls.

Statistical analysis

Descriptive statistics including percentage values was used to analyse data obtained from the questionnaire. The data collected were subjected to chi-square (χ^2) tests to examine the relationship between age group or gender, and prevalence of infection or bladder pathology, ANOVA tests to determine the association between arsenic concentration (dependent variable) and presence of bladder pathology and/or infection, ORs to examine risk of arsenic exposure; and p values less than 0.05 were considered to be significant.

Results

General characteristics of the respondents

The demographic and socioeconomic characteristics of the participants are shown in Table 1. Samples for this study were collected from 122 participants, comprising 47.5% males (58/122) and 52.5% females (64/122). Overall, 74% (90/122) of participants were farmers, while 42% (52/122) have at least one form of formal education. More than 70% (87/122) used the rivers as the main water source and 90% (105/122) of the participants visited their major water source more than once daily.

Prevalence and intensity of urinary schistosomiasis

A total of 21.3% (26/122) of the participants recruited were positive for *S. haematobium* infection. Participants between the ages of 31 and 35 years had the highest prevalence (42.9%) and intensity (23.1%) of infection, while the lowest prevalence was found in the age group 51–55 years (Table 2). There was a significant difference in the prevalence of schistosomiasis among the age groups ($p<0.05$, $\chi^2=19.97$).

The highest mean intensity of infection (62.3 eggs/10 mL of urine) was observed in the 36–40-year age group, while the lowest (3.0 eggs/10 mL of urine) occurred in the 61–70-year age group (Table 2). Although an overall mean intensity of 20.7 eggs/10 mL of urine was recorded in this study, a mean intensity of 30.4 eggs/10 mL of urine was recorded in male participants, while females had a mean intensity of 8.9 eggs/10 mL of urine. These differences in the intensity of infection among age groups or between genders, were statistically significant ($p<0.05$). Proteinuria occurred most frequently (48.4%) in the participants and only 1.6% of the participants had glucosuria.

Table 1. Demographics and descriptive statistics of a study population in Eggua, Nigeria

Variables	Frequency (M, F)	Percentage (%) (M, F)
Age		
<35	37 (16, 21)	30.3 (27.6, 32.8)
≥35	85 (42, 43)	69.7 (72.4, 67.2)
Gender		
Male	58	47.5
Female	64	52.5
Education qualification		
Primary school certificate	33 (24, 9)	27.0 (41.4, 14.1)
Secondary school certificate	15 (9, 6)	12.3 (15.5, 9.4)
First degree or equivalent	4 (2, 2)	3.3 (3.4, 3.1)
Vocational certificate	6 (5, 1)	4.9 (8.6, 1.6)
None of the above	64 (15, 49)	52.5 (25.9, 76.6)
Occupation		
Farmer	90 (47, 43)	73.8 (81.0, 67.2)
Fisherman	3 (2,1)	2.5 (3.4, 1.6)
Artisan	17 (6, 11)	13.9 (10.3, 17.2)
Civil servant	5 (3, 2)	4.1 (5.2, 3.1)
Student	6 (1, 5)	4.9 (1.7, 7.8)
Prefer not to say	1 (0, 1)	0.8 (0, 1.6)
Water supply		
River	87 (44, 43)	71.3 (75.9. 67.2)
River and borehole	19 (7, 12)	15.6 (12.1, 18.8)
Well	2 (0, 2)	1.6 (0, 3.1)
Borehole	8 (4, 4)	6.6 (6.9, 6.3)
River and well	3 (1, 2)	2.5 (1.7, 3.1)
Piped borehole water	2 (1, 1)	1.6 (1.7, 1.6)
River and piped borehole water	1 (1, 0)	0.8 (1.7, 0)
Visit to water source		
Once daily	8 (7, 1)	6.6 (12.1, 1.6)
Weekly	4 (1, 3)	3.3 (1.7, 4.7)
Monthly	5 (5, 0)	4.1 (8.6, 0)
More than once daily	105 (45, 60)	86.0 (77.6, 93.8)

Gender distribution in parenthesis. M, male; F, female.

Arsenic levels in water

The mean arsenic levels from the three water sources were 0.523 mg/L, 0.460 mg/L and 0.005 mg/L for the borehole, River Yewa and River Iju, respectively. The levels recorded in the borehole and River Yewa were above the WHO standard limit (0.01 mg/L) for drinking water.

Arsenic levels in urine

Total concentration of arsenic in urine from this study ranged from 0.007 mg/L to 4.812 mg/L with a mean of 1.167 mg/L (Figure 1). Out of 34 urine samples analysed, 91% (31/34) had arsenic levels above the acceptable WHO limit (0.20 mg/L) and only 9% (3/34) of urine samples were within the limit. The differences in the urinary arsenic concentration among age groups was not significant ($p>0.05$), although age groups 36–40 and 41–45 had higher concentrations and higher proportion of arsenicosis (Table 3).

Bladder pathology in the sample population

Bladder pathology was observed in 22.1% (27/122) of participants examined (Table 4). All those with bladder pathology had abnormal wall thickness and 15% (4/27) had bladder calculi.

Fifteen per cent of the bladder abnormality was recorded in participants in the following age groups—36–40, 41–45, 61–70 and 70>years—while no pathology was found in age groups 26–30 and 56–60 years. There was a significant difference ($p<0.05$, $\chi^2=21.11$) in the bladder pathology among the various age groups. There was significantly higher ($p=0.004$) male preponderance (77.8%) of bladder pathology cases in this community, while females constituted 22.2% of the cases.

Bladder pathology in relation to schistosomiasis and arsenicosis

Among the participants with bladder pathology, 44% (12/27) had *S. haematobium* infection and 93% (25/27) of these participants had high levels of total urinary arsenic concentration

Table 2. Prevalence and intensity of urinary schistosomiasis in a study population in Eggua community, Nigeria

	Number examined (M, F)	Number infected (M, F)	Prevalence (%) (M, F)	Burden of infection (%) (M, F)	Mean egg intensity (egg/10 mL)
Age group (year)					
15–20	6 (3, 3)	0	0	0	0
21–25	5 (4, 1)	0	0	0	0
26–30	13 (5, 8)	2 (2, 0)	15.4 (40.0, 0)	7.7 (15.4, 0)	8 (8.0, 0)
31–35	14 (5, 9)	6 (3, 3)	42.9 (60, 30)	23.1 (23.1, 23.1)	11.3 (18.7, 4.0)
36–40	18 (8, 10)	4 (1, 3)	22.2 (12.5, 33)	15.4 (7.7, 23.1)	62.25 (116.0, 8.5)
41–45	14 (8, 6)	4 (1, 3)	28.6 (12.5, 50)	15.4 (7.7, 23.1)	4.0 (5.1, 3.0)
46–50	9 (2, 7)	1 (0, 1)	11.1 (0, 14.3)	3.8 (0, 7.7)	2.0 (0, 4.0)
51–55	12 (5, 7)	1 (1, 0)	8.3 (20, 0)	3.8 (7.7, 0)	12.0 (24.0, 0)
56–60	6 (2, 4)	2 (0, 2)	33.3 (0, 50)	7.7 (0, 15.4)	6 (0, 12.0)
61–70	12 (6, 6)	2 (2, 0)	16.7 (30, 0)	7.7 (15.4, 0)	3 (6.0, 0)
70>	13 (9, 4)	4 (3, 1)	30.8 (30, 25)	15.4 (23.1, 7.7)	32.5 (60.0, 5.0)
Gender					
Male	58	13	22.03	50.0	30.4
Female	64	13	20.30	50.0	8.9
Total	122	26	21.3	100	

Gender distribution for age group is in parenthesis: M, male; F, female.

(>0.20 mg/L). Participants with schistosomiasis-associated bladder pathology tended to have higher urinary arsenic levels (Figure 1), but the association was not statistically significant (p=0.83, F=0.043) or arsenicosis (p=0.78, F=0.08). Also, there was no statistical association between bladder pathology and total urinary arsenic concentration (p=0.72, F=0.129) or arsenicosis (p=0.83, F=0.042; Figure 1). In addition, bladder pathology cases in which *S. haematobium* infection was not detected, did not associate with urine arsenic concentration (p=0.9, F=0.08), or arsenicosis (p=0.66, F=0.197). Participants aged 70 years and above had equal frequency of bladder pathology, schistosomiasis and arsenicosis.

Urine arsenic exposure of up to ≥1 mg/L appear to elevate the risk for urogenital schistosomiasis (OR=6.88, 95% CI=1.35–35, p=0.02) more than schistosomiasis-associated bladder pathology (OR=3.6, 95%CI=0.76–17.01, p=0.11), and bladder pathology (OR=1.94, 95% CI=0.36–10.43, p=0.44; Table 5), although the precision of the calculated risks was low for all three outcomes and was only significant for urogenital schistosomiasis. Hence, the odds of urogenital schistosomiasis with a urine arsenic exposure of ≥1 mg/L was 6.8 times greater than without such an arsenic exposure.

Discussion

Schistosomiasis remains a major public health problem in many developing countries with Nigeria being considered as the most endemic country for schistosomiasis, with at least 29 million people infected and more than 100 million at risk.[2,3] Also, there are reports of arsenic exposure in parts of the country.[10,13] With scientific evidence showing that arsenic exposure or urogenital schistosomiasis are risk factors for bladder cancer, the current study examined the occurrence of arsenicosis, schistosomiasis and bladder pathologies in a rural population in Nigeria.

The prevalence and mean intensity of urinary schistosomiasis in this study, 21.3% (26/122) and 20.7 eggs/10 mL, respectively (Table 2), is close to that reported in an earlier study in Nigerian adults,[9] i.e. 25.7% (66/257) prevalence and 17 eggs/10 mL. However, it is lower than the mean prevalence of 39.1% and 34.7% (5166/14888) for Nigeria as estimated by Schur et al.[21] and Abdulkadir et al.,[3] respectively. In this study, the prevalence of urinary schistosomiasis was determined in adults and it is known that prevalence rates are often higher in children;[3,22] hence, the lower prevalence found in this study compared with other estimates, which include children, and is probably due to the ages of the participants, although the possibility of acquired immunity in adults would also reduce prevalence. With regard to specific age-groups, those aged 31–35 had higher prevalence than other groups (Table 2). Previous studies have reported a general decrease in prevalence with age, and school children are often the targets of treatment when possible.[3,22] The prevalence of schistosomiasis in the different decades of life depends largely on the frequency of a person's contact with contaminated water and the environmental sanitation activities.[1,21,23] Persons aged 31–35 are expected to maintain an active daily life, in a largely agrarian community, such as the population studied here, they would have frequent contact with water. In addition, within the age groups having the highest prevalence rates (age groups 31–35, 36–40 and 41–45) more women were infected than men especially in age groups 36–40 and 41–45 (Table 2). Gender-related factors could be contributing to the gender differences in prevalence rates because a greater

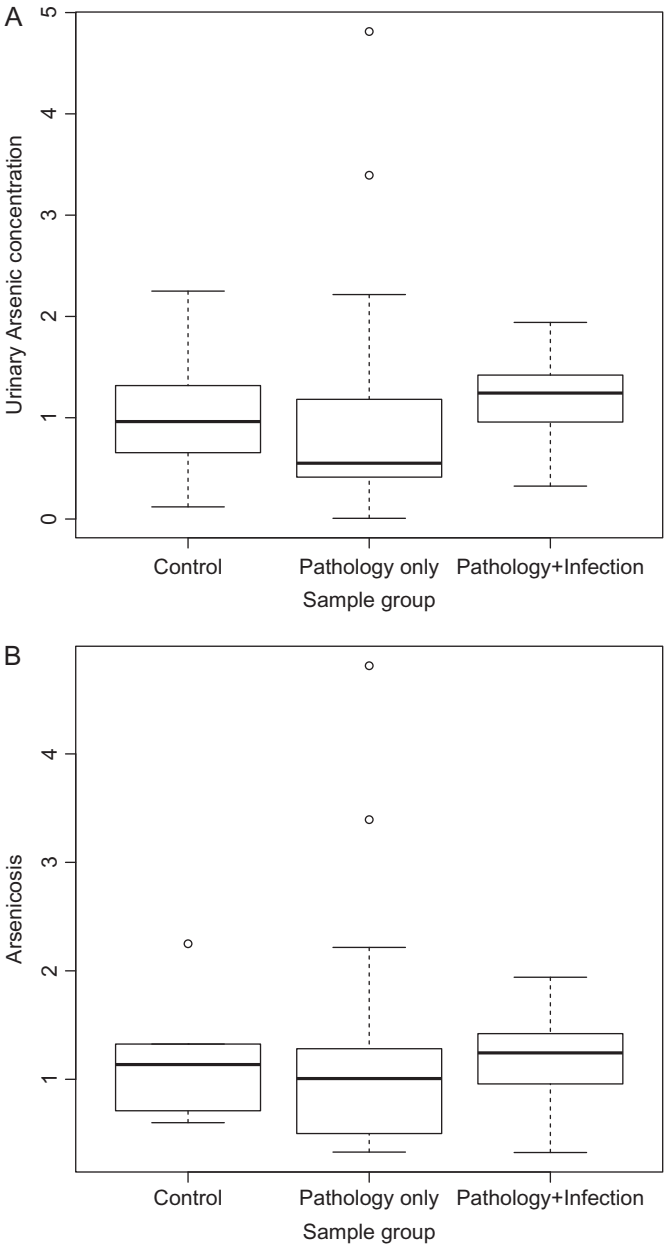

Figure 1. Arsenic concentrations in urine of individuals with no pathology or infection (Control), bladder pathology (Pathology-only) and schistosomiasis associated-bladder pathology (Pathology+Infection). (A) Plot of total urinary arsenic concentration. (B) Plot of urinary arsenic concentration higher than 0.2 mg/L (arsenicosis).

percentage of women (94%) visit domestic water source more than once daily compared with men (77%; Table 1). Additionally, more women (76%) lacked a formal education than men (25%; Table 1). Women in the highest prevalence age groups had contact with water more frequently for domestic purposes. The poor educational level of the women in the age group might have reduced their levels of awareness on schistosomiasis prevention measures.

The mean intensity observed in this study was much lower than that reported by Ugbomoiko et al.[24] in two communities of Osogbo, Nigeria. Mean egg intensity in the current study was highest among the age group 36–40 years old, and decreased with increasing age. For all age groups except 46–50 and 56–60, males had a far higher intensity than females (Table 2). The high egg intensity in the 36–40 year age group could be attributed to greater exposure to infection since these years are very active periods of life. The decrease of intensity with age could be due to reduced parasite egg shedding. Adeoye and Ipeajeda[25] reported that chronic infections could lead to fewer eggs being excreted in the urine. There is a need for control programmes and development-aid agencies to also focus control efforts on adults.

In this study, males had more infection, and greater intensity and pathology than females, despite the fact that more females were examined across most age groups (Tables 1, 2 and 4). There are other studies with similar findings. Although prior studies indicate that there was almost equal prevalence of schistosomiasis in males and females,[4] more reports in Africa, as reviewed in Adenowo et al.,[2] indicate higher prevalence in males or male children. Higher prevalence of bladder pathology and infection were also observed in males in Eggua.[9] These studies attributed these observations to the higher predisposition of males to contact with infected water due to more frequent daily activity and less inclination to quickly seek medical attention when ill.

The high levels of arsenic in both River Yewa and the borehole in Eggua community are most probably due to contamination from anthropogenic activities such as mining, in and around the community. The study area has large deposits of limestone and hosts cement manufacturing companies, whose activities maybe the major anthropogenic factors increasing arsenic levels in water bodies of Eggua community. The high levels in water may be responsible for the high levels in urine; even participants aged 61–70 and >70 years old who are not likely to have a current occupational exposure to arsenic, also had high urine arsenic. The high arsenic concentration of the two water bodies in the current study is of concern, since these are major sources of drinking water and water for other domestic purposes, for many among the study population. Also, these values were higher than that recorded for sunken boreholes (0.03 mg/L) in Maiduguri in northern Nigeria.[26]

The total urinary arsenic concentration in this study ranged from 0.07 mg/L to 4.8 mg/L with a mean of 1.17 mg/L (Figure 1). This was much higher than the standard limit of 0.05 mg/L. Navas-Acien et al.[27] found that very high total arsenic concentration (50 μg/L or higher) in individuals of their study population, was due to ingestion of organic arsenic in seafood such as shellfish, which is less toxic. In the current study, there was no indication of increased availability of seafood in the village. However, mining activities and rice cultivation, which could be sources of inorganic arsenic exposure,[28] are common activities in the study area; and farmers were a majority among the participants. There is need for further research to determine the effect of rice farming conditions and/or mining as important sources contributing to increased urine arsenic in the study population. Also, men in the sample population studied tend to have higher arsenic levels than women (Table 3), especially in

Table 3. Arsenicosis burden in a study population (n=34) in Eggua community, Nigeria

	Number examined (M, F)	Arsenicosis (M, F)	Burden of arsenicosis (%) (M, F)
Age group (year-old)			
15–20	2 (1, 1)	2 (1, 1)	7 (5.0, 9.1)
21–25	2 (1, 1)	2 (1, 1)	7 (5.0, 9.1)
26–30	0		0
31–35	3 (2, 1)	3 (2, 1)	10 (10, 9.1)
36–40	6 (4, 2)	6 (4, 2)	17 (20.0, 18.2)
41–45	6 (4, 2)	5 (4, 1)	17 (20.0, 9.1)
46–50	3 (2, 1)	2 (2, 0)	7 (10.0, 0)
51–55	3 (1, 2)	3 (1, 2)	10 (5.0, 18.2)
56–60	0		0
61–70	4 (2, 2)	4 (2, 2)	13 (10.0, 18.2)
>70	5 (3, 2)	4 (3, 1)	13 (15.0, 18.2)
Gender			
Male	20	20	61
Female	14	11	39

Gender distribution for age group is in parenthesis: M, male; F, female.

Table 4. Prevalence of bladder pathologies in a study population in Eggua, Nigeria

	Number examined (M, F)	Number positive (M, F)	Prevalence (%) (M, F)	Proportion of pathologies (M, F)
Age group				
15–20	6 (3, 3)	2 (0, 2)	33.3 (0, 66.7)	7.4 (0, 30.0)
21–25	5 (4, 1)	2 (2, 0)	40.0 (50.0, 0)	7.4 (30.0, 0)
26–30	13 (5, 8)	0	0	0
31–35	14 (5, 9)	3 (3, 0)	21.4 (60.0, 0)	11.1 (14.3, 0)
36–40	18 (8, 10)	4 (4, 0)	22.2 (50.0, 0)	14.8 (19.0, 0)
41–45	14 (8, 6)	4 (3, 1)	28.6 (37.5, 16.7)	14.8 (14.3, 16.7)
46–50	9 (2, 7)	1 (1, 0)	11.1 (50.0, 0)	3.7 (4.8, 0)
51–55	12 (5, 7)	3 (1, 2)	25.0 (20.0, 28.6)	11.1 (4.8, 30.0)
56–60	6 (2, 4)	0	0	0
61–70	12 (6, 6)	4 (3, 1)	33.3 (50.0, 16.7)	14.8 (14.3, 16.7)
70>	13 (9, 4)	4 (4, 0)	30.8 (44.4, 0)	14.8 (19.0, 0)
Gender				
Male	58	21	36.2	77.8
Female	64	6	9.4	22.2
Total	122	27	22.1	100

Gender distribution for age group is in parenthesis: M, male; F, female.

the age groups 41–45 and 46–50. This gender difference in arsenic levels in urine may be explained if the occupational exposure from cultivation or mining is the main source of the urinary arsenic because men in the study population practice farming more than women (Table 1) and would be more exposed.

The levels of urinary arsenic observed in this study differ in some important ways from earlier studies. For instance, total urinary arsenic was not significantly associated with age group (Table 3). This is contrary to an earlier study[26] carried out in northern Nigeria, which reported an increase in arsenic with respect to age and concluded that arsenic accumulation is

Table 5. Risk association of arsenic exposure and stages of urogenital schistosomiasis in a study population from Eggua, Nigeria

	Schistosomal-associated bladder pathology (M, F)	Control (M, F)	Bladder pathology (M, F)	Control (M, F)	Urogenital schistosomiasis (M, F)	Control (M, F)
Exposure to urine arsenic>1 mg/L	9 (7, 2)	3 (2, 1)	16 (13, 3)	11 (6,5)	10 (7, 3)	4 (3,1)
Non-exposure	10 (6, 4) OR=3.6 p=0.11	12 (5, 7)	3 (1, 2) 0R=1.94 p=0.44	4 (1, 3)	9 (6, 3) OR=6.88 p=0.02	11 (4, 7)

age-dependent. Also, the total urinary arsenic concentration from this present study was higher than those from other studies in various parts of the world, even when highly sensitive methods were used. For instance, Gomez- Rubio et al.[14] recorded a range of 0.0–0.227 mg/L in Sonora, Mexico; and 0.01–1.200 mg/L in Argentina, while 0.05–1.200 mg/L was recorded in Bangladesh.[8] We propose that increased total urinary arsenic concentration observed in this sample population is probably due to increased bioavailability and biomagnification from drinking contaminated water or occupational exposure.

In this study, 22.1% (27/122) of the study subjects were found to have abnormal bladder morphologies or pathologies (Table 4). This is lower than 71% prevalence in Edo state, Nigeria,[4] 33% prevalence in nearby villages of Eggua, Nigeria[9] and 51% prevalence in Roudwan village, Sudan.[29] It was reported by Van der Welf et al.[30] that ultrasonography detects more bladder pathology in children than in adults and this was also found by Nmorsi et al.[4] The reason given for this was the higher prevalence of urinary schistosomiasis in children than in adults. Although it is possible that subtle bladder pathologies may be missed in ultrasound scans, the prevalence of bladder pathology can be expected to be higher in children or those with higher prevalence of schistosomiasis. With regard to gender and age groups, males had higher prevalence of bladder pathologies in the current study in almost all age-groups (Table 3). Such observations may be linked to the well-known gender disparity in bladder cancer studies, and the major reasons for this are not clear yet.

No association between bladder pathology and high urinary arsenic concentrations was observed (Figure 1). This was the case whether *S. haematobium* eggs were detected with the bladder pathology or not. The data suggests that high arsenic levels may be common in the study population irrespective of urinary schistosomiasis. It has been proposed that high urinary arsenic levels, as observed in this study, may not necessarily lead to clinical problems. Chanda et al.[31] argued that increased urinary arsenic denotes a decrease in the body's burden, therefore decreasing the risk for arsenic-associated clinical symptoms, i.e. arsenic is being metabolized almost completely in the body; while reduced arsenic in urine denotes an increase in the body burden of arsenic. Such an argument may explain the non-association of arsenicosis with bladder pathology or schistosomiasis-associated bladder pathology. In addition, genetic polymorphisms in the Arsenic(III)methyltransferase gene (AS3MT) influence arsenic metabolism[8] and polymorphisms in the GST influence metabolism of exogenous substances,[32] hence, it is possible that AS3MT or GST variations in our study population would modulate tolerance to arsenic in the population and reduce occurrence of complications due to arsenic exposure. Still, higher than limit levels occurred in 31 of 34 samples analysed. Also, high urine arsenic levels associated strongly with schistosomiasis infection, with participants almost 7 times more likely to record >1 mg/L and be positive for infection, rather than have only infection (Table 5). Both arsenicosis and urogenital schistosomiasis are of serious concern in the study population.

A limitation of the observations on arsenicosis in the current study may be the small sample size examined for arsenic levels. A very large sampled population tends to improve immediate usage of the results of a study. Also, urine samples were collected at a single time-point and this may only reflect recent arsenic exposure or dosage, rather than chronic exposure. It is also possible that some bladder pathologies may have been missed. Nevertheless, the current study has provided important results that may be validated in larger studies.

It is concluded here that high arsenic levels in water bodies and human urine, and its concordance with urogenital schistosomiasis, are of serious concern in the Eggua community, although arsenicosis or urinary arsenic levels may not have any influence on bladder pathologies or progression of urinary schistosomiasis.

Author contributions: SB undertook the experiments and the initial data analysis. AA , SB and RI were involved in the data analysis. SB, AA, HA, OO,CA did field sampling and grouping of participants. AMA did the ultrasound. RI and CA designed and planned the work. SB, AA, HA, RI and CI, were involved in writing and editing the manuscript.

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