

Urogenital schistosomiasis in Nigeria post receipt of the largest single praziquantel donation in Africa

Egie E. Enabulele^{a,b,*}, Roy N. Platt^a, Ehizogie Adeyemi^c, Esther Agbosua^b, Martin S.O. Aisien^b, Oluwaremilekun G. Ajakaye^d, Mahmud U. Ali^e, Ebube C. Amaechi^f, Tolulope E. Atalabi^g, Timothy Auta^g, Oluwaseun B. Awosolu^h, Adamu G. Dagonaⁱ, Omoyemwen Edo-Taiwo^b, Chika E.P. Ejikeugwu^j, Christopher Igbeneghu^k, Victor S. Njom^l, Mary-Kate N. Orji^m, Funso O. P. Oyinloyeⁿ, Habib J. Ozemoka^o, Uchenna I. Ugah^p, Timothy J.C. Anderson^a

^a Disease Intervention and Prevention Program, Texas Biomedical Research Institute, San Antonio, Texas, USA

^b Department of Animal and Environmental Biology, University of Benin, Edo State

^c Department of Pathology, University of Benin Teaching Hospital, Edo State

^d Department of Animal and Environmental Biology, Adekunle Ajasin University, Ondo State

^e Department of Biology, Kano University of Science and Technology, Wudil

^f Department of Zoology, University of Ilorin, Kwara State

^g Department of Biological Sciences, Federal University Dutsin-Ma, Katsina State

^h Department of Biology, Federal University of Technology, Akure, Ondo State

ⁱ Department of Biological Sciences, Federal University, Gashua, Yobe State

^j Department of Applied Microbiology, Ebonyi State University, Abakaliki

^k Department of Medical Laboratory Science, Ladoko Akintola University of Technology, Osogbo, Osun State

^l Department of Applied Biology and Biotechnology, Enugu State University of Science and Technology

^m Department of Biological Sciences, Chukwuemeka Odumegwu Ojukwu University, Anambra State

ⁿ NTDs Division, Kwara State Ministry of Health

^o Department of Biological Science, Edo University Iyamho, Edo State

^p Department of Microbiology, Alex Ekwueme Federal University, Ndufu-Alike Ikwo, Ebonyi State.

ARTICLE INFO

Keywords:

Internally Displaced Persons
Nigeria
Praziquantel
Urogenital schistosomiasis

ABSTRACT

Schistosomiasis control efforts in Nigeria received a boost in 2016 when Merck Group made the largest single donation of praziquantel to an African country. We examined urine samples from 2,023 school age children from 15 locations in 10 states and an Internally Displaced Person's (IDP) camp in Nigeria. We recorded an overall *Schistosoma haematobium* prevalence of 10.4% in the 10 states that ranged between 6 – 37%, while prevalence in the IDP camp was 2.9%. The highest infection prevalence (37%) recorded was from the population in Wasai Dam area in Minjibir (Kano State), while five locations had no positive urine samples. We observed heavy intensity of infection (≥ 50 eggs/10 ml urine) in 87.9% of infected samples and co-occurrence of the eggs of *S. haematobium* and *S. mansoni* in urine for two participants. The overall prevalence we recorded is slightly above the national average (9.5%) reported in 2015. Our findings indicate that despite the ongoing administration of praziquantel in Nigeria, urogenital schistosomiasis is still prevalent with heavy intensity of infection. Large-scale epidemiological monitoring is required to monitor the efficacy of schistosomiasis control in Nigeria.

1. Introduction

In Nigeria, schistosomiasis is caused by both *S. haematobium* and *S. mansoni* and presently Nigeria has the largest schistosomiasis infected population in Africa. Despite all efforts Nigeria has made towards the

control of schistosomiasis both through national control programs and participation in several internationally funded projects, the disease is still prevalent in the country (Nduka et al., 2019). In 2016, Nigeria's schistosomiasis control efforts received a major boost when the largest single praziquantel donation to an African nation was provided by the

* Corresponding author.

E-mail address: eenabulele@txbiomed.org (E.E. Enabulele).

<https://doi.org/10.1016/j.actatropica.2021.105916>

Received 19 December 2020; Received in revised form 1 April 2021; Accepted 2 April 2021

Available online 18 April 2021

0001-706X/© 2021 Elsevier B.V. All rights reserved.

Merck Group for mass distribution and administration (Merck KGaA, 2016). We report here the epidemiological and parasitological data on urogenital schistosomiasis prevalence recorded while collecting materials for genomic study of *S. haematobium* in Nigeria. We discuss our findings in the light of ongoing mass drug administration of praziquantel in Nigeria.

2. Methods

2.1. Sample Population

School-aged children from 15 locations in 10 states across Nigeria (Anambra, Ebonyi, Edo, Enugu, Kano, Kastina, Kwara, Ondo, Osun and Yobe) were sampled for urogenital schistosomiasis, while collecting material for a *S. haematobium* genomic study. Sampling of the schools was done based on schistosomiasis case information obtained from the health centers and previous epidemiological studies (Ezeh et al., 2019). Samples were also collected from children and adults from 10–20 years old in the International Christian Center (ICC) internally displaced person's (IDP) camp in Uhuogua, Ovia North East LGA of Edo State (6°43'11" N and 5°57'10" E). The ICC is a religious organization involved in Christian missionary and humanitarian activities in rural communities in different states in Nigeria. Most of the IDPs are people from the north-east region of Nigeria where there has been prolonged insecurity due to the insurgent activities of Boko Haram as well as persons displaced due to ethno-religious conflicts. The first batches of IDPs were received in 2014 and since then, more displaced persons have been admitted to the camp every year. Currently, over 2,000 IDPs children and young adults < 20 years are registered in the camp. Ethical clearance and study protocols were approved by the National Health Research Ethics Committee of Nigeria (NHREC) (protocol number: NHREC/01/01/2007- 30/10/2020 and approval number: NHREC/01/01/2007- 29/03/2021) and the Institutional Review Board

(IRB) of University of Texas Health, San Antonio Texas, United States of America (protocol number: HSC20180612H).

2.2. Sample collection

Participation involved obtaining informed consent after briefing the participants of the objectives of the investigation and only consenting participants were requested to provide samples of their urine. We obtained consent by administering to parents and guardians of the participants a designed consent form approved by the IRB and NHREC. Only participants with endorsed consent forms were enlisted for the study. We collected mid-stream urine from participants in universal bottle containers between 10 am and 2 pm and transported them to the laboratory for microscopic examination. Identification of *Schistosoma haematobium* eggs was based on their characteristic terminal spine and prevalence percentage and infection intensity calculated. Infection intensity was determined as the number of eggs detected per 10 ml of urine (eggs/10 ml) where light infection is categorized as 1–49 eggs/10 ml and heavy infections ≥ 50 eggs/10 ml (Montresor et al., 1998). We also visually examined the collected urine for macrohematuria.

3. Results

We collected urine from 2,023 participants which comprised of 1,267 school pupils from 15 locations (n=44–102 per location) in 10 states (Figure 1 and Table 1) and 756 from the IDPs camp (Table 2). The overall prevalence of *S. haematobium* infection from the states was 10.4% with the highest record in Kano (37%) and followed by Ipogun in Ondo State (21.6%). We detected no positive urine samples from five locations in five different states (Anambra, Ebonyi, Enugu, Katsina, and Kwara). In the IDPs camp, the overall prevalence was 2.9%. We observed macrohematuria in the urine of 4.2% of the samples from the 10 states and in 1.72% of the samples from the IDPs camp. However,

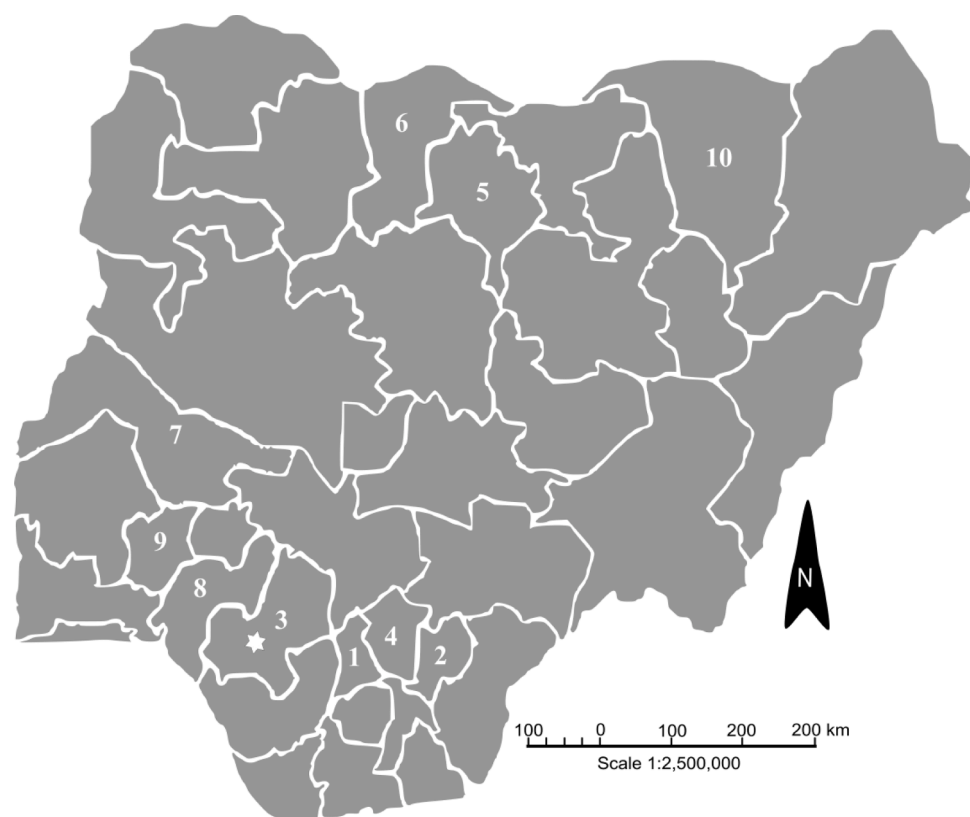


Figure 1. Map of Nigeria showing state locations where urine samples were collected from school children. 1-Anambra, 2-Ebonyi, 3-Edo, 4-Enugu, 5-Kano, 6-Kastina, 7-Kwara, 8-Ondo, 9-Osun, 10-Yobe. Star-Location of internally displaced persons' camp.

Table 1Prevalence of *Schistosoma haematobium* infection in children from 10 states in Nigeria.

State/Location	Coordinate	% prevalence (95% CI) N	Mean infection intensity (range)	Light /Heavy infection intensity	% macro-hematuria
Anambra , Aguleri, Anambra East	6°19'49" N 6°52'53" E	0 (0) 76	0	0	0
Ebonyi					
Nigercem, Ishielu	6°47'75" N 7°77'56" E	0 (0) 100	0	0	0
Abakaliki	6°19'43" N 8°4'56" E	6 (1.35 - 10.65) 100	65.8 (60 - 120)	0/6	0
Edo					
Aden, Ovia South West	6°27'52" N 5°18'24" E	18.2 (6.8 - 29.6) 44	93.5 (112 - 186)	0/8	11.36
Siluko, Ovia South West	6°32'7" N 5°9'35" E	18.6 (8.67 - 28.53) 59	85.6 (80 - 147)	0/11	16.95
Enugu , Amagunze, Nkanu East	6°28'13" N 7°43'29" E	0 (0) 84	0	0	2.38
Kano , Wasai Dam, Minjibir	12°8'20" N 8°39'57" E	37 (27.54 - 46.46) 100	108.7 (78 - 310)	0/37	26
Katsina					
Safana	12°24'45" N 7°24'51" E	12.9 (5.77 - 20.03) 85	63.5 (30 - 69)	8/3	1.18
Sokoto Rima, Dutsin-ma	12°28'25" N 7°29'44" E	0 (0) 100	0	0	3
Kwara					
Lafiagi, Edu	8°53'32" N 5°27'5" E	7.3 (1.67 - 12.93) 82	66.8 (43 - 90)	3/3	3
Shonga, Edu	9°0'52" N 5°9'5" E	0 (0) 68	0	0	0
Ondo					
Ipogun, Ifedore	7°18'52" N 5°4'35" E	21.6 (13.61 - 29.59) 102	84.5 (82 - 124)	0/22	2.94
Ogbese, Akure North	7°15'38" N 5°22'29" E	12 (5.36 - 18.64) 92	84.9 (56 - 118)	0/11	0
Osun , Ore, Odo-Otin	7°57'50" N 4°33'50" E	14 (7.2 - 20.8) 100	76.6 (92 - 130)	0/14	0
Yobe , Gashua	12°52'4" N 11°0'56" E	8 (1.86 - 14.14) 75	61.2 (36 - 76)	5/1	0
Overall		10.4 (8.72 - 12.08) 1,267	86.7 (36 - 310)	16/116	4.2

N, number of persons sampled; CI, confidence interval.

Table 2Prevalence of *Schistosoma haematobium* infection in children residing in an internally displaced persons' camp in Benin City, Nigeria.

State of origin	% prevalence (95% CI) N	Mean infection intensity (range)	Light /Heavy infection intensity	% macro hematuria
Adamawa	0 (0) 29	0	0	0
Abuja	0 (0) 6	0	0	0
Borno	2.4 (1.18-3.62) 601	93.2 (80 - 102) 14	0/14	1.66
Delta	0 (0) 8	0	0	0
Edo	8.3 (-4.63-6.63) 12	95 (0)	0/1	0
Enugu	0 (0) 5	0	0	0
Gombe	0 (0) 1	0	0	0
Kaduna	0 (0) 8	0	0	0
Kebbi	15.6 (3.03-28.17) 32	70.6 (45 - 90) 3	2/3	6.25
Kogi	0 (0) 1	0	0	0
Nasarawa	0 (0) 24	0	0	0
Plateau	0 (0) 6	0	0	0
Taraba	8.7 (-2.82-20.22) 23	77 (56 - 98) 2	0/2	4.35
Overall	2.9 (1.7-4.1) 756	86.7 (45 - 102)	2/20	1.72

N, number of persons sampled; CI, confidence interval.

S. haematobium eggs were not recorded in the urine samples of five children with observable macro hematuria (Edo 3. Enugu 2). Although prevalence was low in our study population, most infected individuals carried heavy infection intensity (≥ 50 eggs/10 ml of urine). In the urine samples from Osun State, two of 14 patients infected with *S. haematobium* also had *S. mansoni* eggs in their urine with light infection intensity (≤ 5 eggs/10 ml of urine).

4. Discussion

Although mass distribution and administration of praziquantel across Nigeria commenced in 2016 immediately after receipt of the drug donation from Merck Group, there is yet to be a nationwide assessment

of the level of impact of the drug intervention on schistosomiasis prevalence. The overall prevalence of *S. haematobium* we recorded in the 10 states studied (10.4%) is slightly above the national average (9.5%) reported in 2015 during the last epidemiological study on urogenital schistosomiasis across 19 states in Nigeria (Nduka et al., 2019). We observed heavy intensity of infections (≥ 50 eggs/10 ml urine) in most of the patients from all infected populations sampled (Table 1). 14/15 of the communities sampled in this study except for the population from Kano have at least received one round of treatment with praziquantel since 2016 and prior to our sampling (October/November 2018). The high intensity observed suggests that transmission is still high, and that the infected children reported here have been re-infected after treatment or missed treatment.

The highest infection prevalence of urogenital schistosomiasis (37%) recorded in this study was from the population in Wasai Dam area in Minjibir (Kano State) and it is far above the current national average of 9.5% recorded in 2015 (Nduka et al., 2019). This indicates the study area is highly endemic for schistosomiasis and appears to be among the hotspots for transmission of urogenital schistosomiasis in Nigeria. The location of a dam in the locality is a major contributing factor of infection transmission. We note that even higher infection prevalence (42.7% and 70%) has previously been reported in the same study location (Abdullahi et al., 2009; Ali et al., 2016).

Two of the 14 infected children in Osun State had both *S. mansoni* and *S. haematobium* eggs in their urine (≤ 5 eggs/10 ml of urine). A prevalence of 2.2% of *S. mansoni* eggs in urine has been previously reported in one study in Nigeria (Okoli and Odaibo, 1999). Although we recorded a low prevalence of *S. mansoni* eggs in urine, higher prevalence $>10\%$ has been reported by investigators working elsewhere in Africa (Meurs et al., 2012). Coinfection of *S. haematobium* and *S. mansoni* may have pathological significance. It has been suggested that ectopic presentations result in a lower liver morbidity in mixed infections compared to single infections, and higher bladder morbidity in mixed compared to single *S. haematobium* infections (Koukounari et al., 2010). Since Nigeria is endemic for both *S. haematobium* and *S. mansoni*, it is important that researchers and public health workers are careful to report any co-occurrence of the eggs of both species during microscopic examination of urine/stool samples. The data collected will help in

understanding predisposing factors driving mixed occurrences of *S. haematobium* and *S. mansoni* in Nigeria.

Our examination of children in the IDPs camp for urogenital schistosomiasis revealed 2.9% prevalence with most of the infected children (63.64%) from Borno State where the insurgent group Boko Haram is most active (Table 2). In similar urogenital schistosomiasis studies in IDPs camps elsewhere in Nigeria, prevalence of 35.5% and 62% have been reported (Balla et al., 2016; Yauba et al., 2018). The low prevalence reported in the current study may be connected to the anti-helminthic treatment often provided to the IDPs during intermittent humanitarian visits by several medical non-governmental organizations. Our investigation was limited to children and adults from 10–20 years. However, younger pre-school age children and infants should also be screened for both urinary and intestinal schistosomiasis.

Despite the ongoing schistosomiasis control efforts in Nigeria using donated praziquantel, the disease is still prevalent with heavy intensity of infection. Our investigation involved data from 15 communities in 10 Nigerian states; it therefore may not provide an accurate representation of the current urogenital schistosomiasis prevalence status in the country. Detailed nationwide epidemiological monitoring of schistosomiasis is urgently needed to allow direct evaluation of the impact of the ongoing mass administration of praziquantel on schistosomiasis prevalence and intensity. Also crucial is sustained praziquantel administration across the country covering all categories of people at risk including pre-school children, nomadic communities and IDPs.

Competing interest

None

Author contributions

Egie Enabulele: Conceptualization, Methodology, Data curation, Investigation, Validation, Writing- Original draft preparation, Writing- Reviewing and Editing. Timothy Anderson: Conceptualization, Supervision, Writing- Reviewing and Editing. Mahmud Ali, Victor Njom: Methodology, Investigation, Validation, Writing- Reviewing and Editing. Roy Platt, Ehizogie Adeyemi, Esther Agbosua, Martin S. O. Aisien, Oluwaremilekun Ajakaye, Ebube Amaechi, Tolulope Atalabi, Timothy Auta, Oluwaseun Awosolu, Adamu Dagona, Omoyemwen Edo-Taiwo, Chika Ejikeugwu, Christopher Igbeneghu, Mary-Kate Orji, Funso Oyinloye, Habibata Ozemoka, Uchenna Ugah: Methodology, Investigation, Validation.

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

We thank all participants and field assistants during sample collection. The support of the Parasitology and Public Health Society of Nigeria (PPSN) is also appreciated.

Funding

This work was supported by a Cowles Postdoctoral Fellowship to the corresponding author. TJCA and RNP are supported by NIH grants 1R01AI123434 and 1R01AI133749.

References

- Abdullahi, M.K., Bassey, S.E., Oyeyi, T.I., 2009. A comprehensive mapping of urinary schistosomiasis using Geographic Information System (GIS) in Kano State, Nigeria. *Bayero J. Pure Appl. Sci.* 2 (1), 41–46. <https://doi.org/10.4314/BAJOPAS.V2I1.73453>.
- Ali, M.U., Umar, A.U., Hamza, I.U., Yahaya, A., Dambazau, S.M., 2016. Schistosoma haematobium infections: prevalence and morbidity indicators in communities around Wasai Dam, Minjibir, Kano State, Northern Nigeria. *Int. J. Trop. Dis. Health* 17 (2), 1–8. <https://doi.org/10.9734/IJTDH/2016/23448>.
- Balla, H.J., Bulama, A.A., Kutdang, E.T., Babagana, M., 2016. Survey of urinary schistosomiasis among internally displaced persons (idps) in Borno State. *Borno Med. J.* 13 (2), 117–124. http://bornomedicaljournal.com/pdfs/BALLA%20HJ_2%20et%20al.pdf.
- Ezeh, C.O., Onyekwelu, K.C., Akinwale, O.P., Shan, L., Wei, H., 2019. Urinary schistosomiasis in Nigeria: a 50 year review of prevalence, distribution and disease burden. *Parasite* 26, 19. <https://doi.org/10.1051/parasite/2019020>.
- Koukounari, A., Donnelly, C.A., Sacko, M., Keita, A.D., Landouré, A., et al., 2010. The impact of single versus mixed schistosome species infections on liver, spleen and bladder morbidity within Malian children pre- and post-praziquantel treatment. *BMC. Infect. Dis.* 10, 227. <https://doi.org/10.1186/1471-2334-10-227>.
- Merck KGaA, 2016. News release. Merck KGaA. <https://www.emdgroup.com/en/news/csr-nigeria-pariquantel-24-05-2016.html>, 2016. accessed 10 November 2020.
- Meurs, L., Mbow, M., Vereecken, K., Menten, J., Mboup, S., Polman, K., 2012. Epidemiology of mixed *Schistosoma mansoni* and *Schistosoma haematobium* infections in northern Senegal. *Int. J. Parasitol.* 42 (3), 305–311. <https://doi.org/10.1016/j.ijpara.2012.02.002>.
- Montresor, A., Crompton, D.W.T., Hall, A., Bundy, D.A.P., Savioli, L., 1998. Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level: a guide for managers of control programmes, 1988. WHO. <http://www.who.int/iris/handle/10665/63821> (accessed 12 August 2020).
- Nduka, F., Nebe, O.J., Njebuome, N., Dakul, D.A., Anagbogu, I.A., et al., 2019. Epidemiological mapping of schistosomiasis and soil-transmitted helminthiasis for intervention strategies in Nigeria. *Nig. J. Parasitol.* 40 (2), 218–225.
- Okoli, E.I., Odaibo, A.B., 1999. Urinary schistosomiasis among schoolchildren in Ibadan, an urban community in south-western Nigeria. *Trop. Med. Int. Health* 4 (4), 308–315. <https://doi.org/10.1046/j.1365-3156.1999.00388.x>.
- Yauba, S.M., Rabasa, A.I., Farouk, A.G., Elechi, H.A., Ummate, I., Ibrahim, B.A., Ibrahim, H.A., Baba, A.S., Boda, T.A., Olowu, W.A., 2018. Urinary schistosomiasis in Boko Haram-related internally displaced Nigerian children. *Saudi J. Kidney Dis. Transpl.* 29 (6), 1395–1402. <https://doi.org/10.4103/1319-2442.248286>.