BMC Research Notes

RESEARCH NOTE Open Access

Onchocerciasis is not a major cause of blindness in two endemic villages in Sierra Leone

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Abstract

Objective Sierra Leone, a country where onchocerciasis is endemic in 14 of the 16 districts, was the focus of our investigation. Despite 17 rounds of annual ivermectin treatment since 2005, a report circulated by a local politician indicated an increase in cases of suspected onchocerciasis-related vision impairment in two villages (Mangobo and Petifu) in Tonkolili district. In response, the National Neglected Tropical Disease Program conducted a comprehensive investigation. Ophthalmological, parasitological, and serological tests were conducted using standard procedures to determine the relationship between self-reported vision loss and onchocerciasis in adults. In addition, serological tests were carried out on children aged 5 to 9 years to assess the recent status of exposure to onchocerciasis in the two villages.

Results Reported vision loss in 37 patients was mainly due to cataracts (35.1%), allergic conjunctivitis (18.9%), refractive error (10.8%), and other conditions not related to onchocerciasis. There were 40.7% of all adults ($N=54$) tested and 29.0% of 31 persons with self-reported vision loss who were positive for Ov-16 IgG4 antibodies, suggesting a history of exposure to onchocerciasis. However, otoscopic eye examinations and microscopic skin snip tests were all negative for *Onchocerca volvulus* microfilariae, indicating no active or low-intensity infection among adults and a low or zero risk of serious ocular morbidity in the two villages. Onchocerciasis may no longer be a major cause of blindness in these two villages. Apparently, 4.6% of 153 children aged 5 to 9 years tested positive for Ov-16 IgG4 antibodies, suggesting that onchocerciasis transmission is likely still ongoing in the two villages. The data presented here suggest that more annual rounds of mass treatment with ivermectin with high coverage are needed to eliminate onchocerciasis transmission in this area.

Keywords Onchocerciasis, Vision loss, Ov-16 IgG4 antibodies, Skin snip, Sierra Leone

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Introduction

Onchocerciasis, or river blindness, is caused by infection with *Onchocerca volvulus*, transmitted by *Simulium* blackflies. It is a leading infectious cause of blindness and skin disease. The global objective is to eliminate the transmission of onchocerciasis through regular treatment of all at-risk populations with ivermectin [1]. The disease is endemic throughout Sierra Leone, with the exception of the capital, Freetown, and the island of Bonthe [2, 3]. The country was part of the Onchocerciasis Control Program for West Africa from 1998 to 2002 [4] and the African Program for Onchocerciasis Control from 2003 to 2007 [5]. Baseline surveys, using skin snip biopsy and microscopic examination to detect microfilariae (mf), showed that 88% of villages were either meso- or hyper-endemic (prevalence range: 47-88.5%) [4]. Onchocerciasis accounted for approximately 30% of all blindness in the country after cataracts, with some areas, such as the Taia river basin, having onchocerciasis blindness rates as high as 5.9% [4, 6, 7]. Vector control and ivermectin treatment were severely disrupted by the civil war from 1991 to 2002 [8]. The situation improved by 2005 but was interrupted again in 2014 by an outbreak of Ebola virus disease [3]. Impact assessments in 2010 after five rounds of ivermectin treatment using skin snip biopsy and in 2017 after six further rounds of treatment using the Ov-16 serological rapid diagnostic tests (RDTs) suggested that Sierra Leone was on track to achieve onchocerciasis elimination [2, 3]. Since 2017, six more rounds of mass treatment with ivermectin have been conducted by 2023.

In February 2023, a video of a local politician began circulating via email, suggesting a resurgence of cases of onchocerciasis blindness in two villages: Mangobo and Petifu in the Yoni Mamaila chiefdom of Tonkolili district in central Sierra Leone. In mid-February, the National Neglected Tropical Disease Program (NNTDP) attended a community meeting to gather more information. Residents reported more than 30 people with vision loss and an increasing blackfly nuisance in these villages. They also confirmed that the community health workers regularly distributed ivermectin and that communities were regularly participating in mass drug administration. In total, Tonkolili district as a whole had received 17 (16 effective) rounds of mass treatment with ivermectin since 2005 with effective coverage (≥65% epidemiological coverage) (Fig. 1).

In early September 2023, the NNTDP conducted ophthalmological, parasitological, and serological investigations in the two villages. The objective was to investigate whether self-reported cases of visual impairment were onchocerciasis-related and to assess the current status of onchocerciasis transmission in these villages. This paper reports the findings and discusses the challenge of onchocerciasis elimination in Sierra Leone.

Methods

Study area and design

Mangobo is located along the Taia Riverbank, and Petifu is located about 3 km west of the river in the Yoni Mamaila chiefdom of Tonkolili district. The area is bordered to the west and east by Moyamba district (Fig. 2). These are hard-to-reach communities with a population of 322 in Mangobo and 789 in Petifu. These two villages had never been surveyed for onchocerciasis prevalence prior to this investigation, but are located in a meso-endemic zone at baseline [2, 3]. The area is upstream of the hyper-endemic Taia River basin in Mayamba district, where mf prevalence was 29.7–88.5% prior to the control intervention [9]. This was a cross-sectional investigation with convenience sampling of participants.

Ophthalmological examination

Village chiefs and community health workers mobilized both communities before the investigation team arrived. A community meeting was held, and residents who had self-reported vision loss were invited to participate in the examination, while some others volunteered for an eye

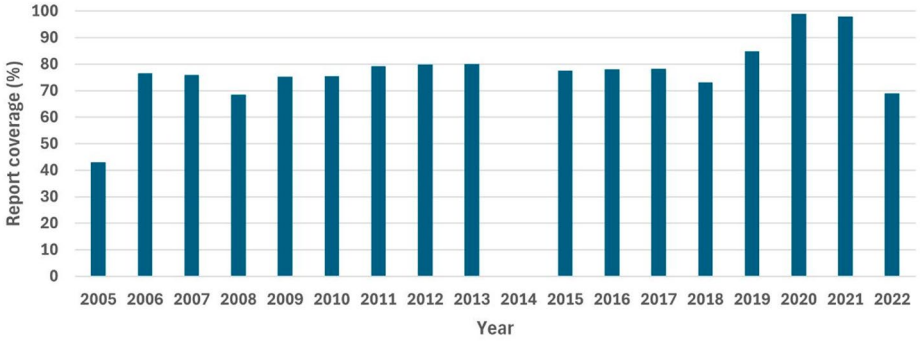

Fig. 1 Reported treatment coverage from 2005 to 2022 in Tonkolili district, Sierra Leone

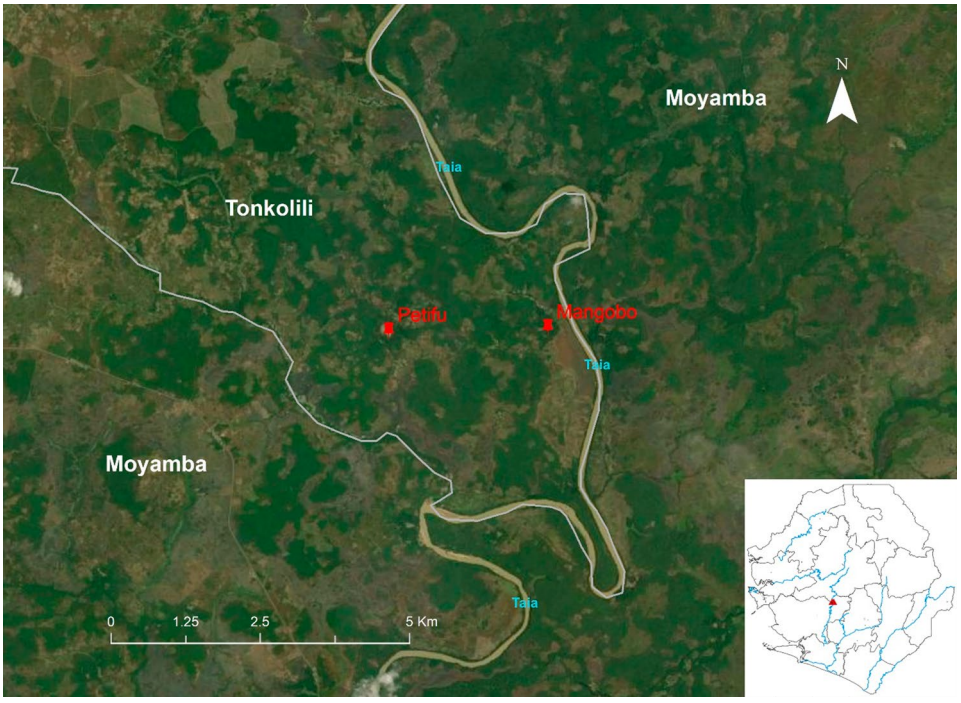

Fig. 2 Geographical locations of Mangobo and Petifu villages in Tonkolili district of Sierra Leone. World Imagery basemap source: Esri, Maxar, GeoEye, Earthstar Geographics, CNES/Arbus DS, USDA, USGS, AeroGRID, IGN, and the GIS User Community

examination. Two ophthalmologists from the National Eye Health Program in Bombali and Tonkolili districts conducted eye examinations to diagnose eye conditions and to detect mf in the anterior chamber of the eyes using a hand-held otoscope according to standard procedures [10]. Eye conditions and ocular mf findings for each patient were recorded on paper.

Parasitological examination

All individuals examined for eye conditions were asked to provide skin snip samples by skin snip biopsy to detect mf for *Onchocerca volvulus* infection. Thirty-four individuals gave verbal consent to provide skin snip samples. Two skin biopsies were taken from the right and left iliac crest of each volunteer. A sterilised 2 mm Holth corneoscleral punch was used to obtain the two bloodless skin snip biopsies. The skin snip samples were placed in normal saline for 24 h and then examined under a light microscope for *O. volvulus* microfilariae [11].

Serological examination

Volunteers undergoing ocular examinations also provided blood samples. Dried blood spot (DBS) samples were collected by finger prick for serological testing for the presence of Ov-16 IgG4 antibodies, an indicator of *O. volvulus* exposure. In addition, to assess the current situation of onchocerciasis transmission in the two villages, children aged 5–9 years were tested for Ov-16 IgG4 antibodies, as the presence of such antibodies in this group of children represents recent exposure and active infection [12], and WHO recommends testing this group of children for transmission assessment [13–15]. All children aged 5–9 years in the two villages were invited to participate. Those who volunteered were recruited, and DBS samples were collected from them. The DBS samples were then packed and transported according to standard protocols to the Central Public Health Reference Laboratory in Freetown for analysis [15]. DBS samples were eluted overnight at the laboratory and tested using Bioline Onchocerciasis IgG4 tests (Ov-16 RDT, Abbott Rapid Diagnostics, South Korea) to detect Ov-16 IgG4 antibodies per the manufacturer's instructions [15]. The final results were read and recorded after 24 h of incubation [16].

Data analysis

The results were entered into an Excel spreadsheet. Descriptive analysis and chi-squared test were used to compare the positivity rate between groups using SPSS statistics (IBM, version 23). The geolocation map of the two villages was created using ArcGIS version 10.8.2 (ESRI, Redlands, California, United States).

Results

Eye examination and *O. volvulus* infection in adults

Thirty-seven (37) persons aged 12 to 75 years (mean age: 51.4 years, standard deviation: 15.1 years) who reported vision loss presented themselves and were examined by

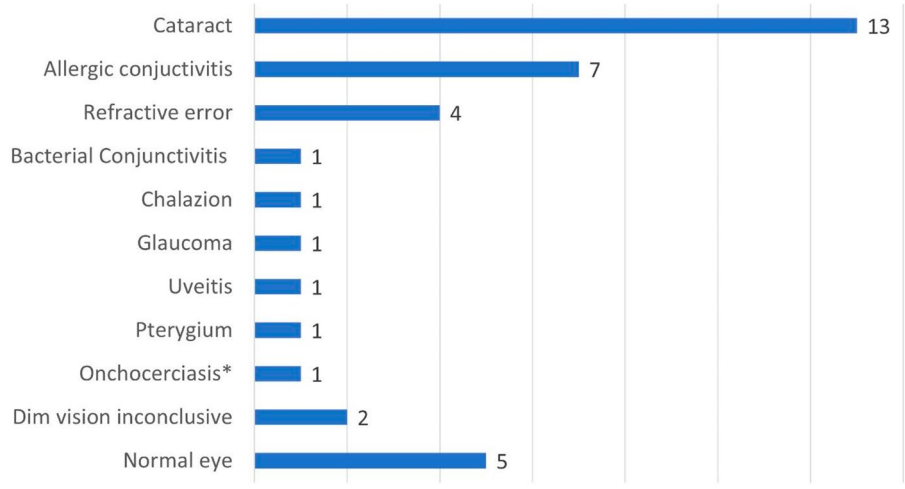

Fig. 3 Number of eye conditions observed in the 37 volunteers who self-reported vision loss. * One case suspected of onchocerciasis-related blindness

Table 1 Results of skin snip biopsy in adults in the two villages (Mangobo and Petifu)

	Number of people tested	Number of people mf-positive	Positivity rate (%)
Patients self-reporting vision loss	18	0	0
Other volunteers	16	0	0
Female	18	0	0
Male	16	0	0
≤ 55 years	9	0	0
> 55 years	25	0	0
Total	**34**	**0**	**0**

ophthalmologists. Various eye conditions were diagnosed, as shown in Fig. 3. Of 37 persons, the main eye conditions were cataracts (35.1%), allergic conjunctivitis (18.9%), refractive error (10.8%), and other eye conditions. Five people had normal eyes, and two reported dimmed vision with inconclusive diagnosis. In addition, one case of blindness in a 60-year-old man may have been caused by *O. volvulus* due to suspected uveitis, optic atrophy, and punctate keratitis. No mf was observed in the anterior chamber of any of the patients examined. Individuals with ocular morbidity were referred to the eye health program for management.

Of the thirty-seven (37) adults who self-reported vision loss and were examined for eye conditions and anterior chamber mf, 18 (48.6%) persons aged 35–80 years were examined for *O. volvulus* mf by skin snip biopsy. In addition, 16 other community members who did not report vision loss also volunteered for skin snip biopsy. None of these 34 adults tested were reported to be positive for mf (Table 1). This was not a community-wide survey, so the community microfilarial load (CMFL) was not calculated.

Blood samples were collected from a total of 54 adults, including 31 (83.8%) of 37 who self-reported and were examined for eye conditions and 23 other community members who did not report vision loss (Table 2). Among the 31 patients, 9 were positive for Ov-16 IgG4 antibodies by Ov-16 RDT, with a positivity rate of 29.0% (95% CI: 13.1–45.0%). This was significantly lower than the positivity rate for Ov-16 IgG4 antibodies of 56.5% (95% CI: 36.3–76.8) in the other 23 residents who did not report vision loss ($\chi^2=4.133$, $p=0.042$). Among all subjects, the positivity rate was significantly higher in male adults, 55.6% (95% CI: 36.8–74.3%), than in female adults, 25.9% (95% CI: 9.4–42.3%) ($\chi^2=4.909$, $p=0.027$). There was no statistically significant difference in Ov-16 antibody prevalence between age groups ($\chi^2=1.72$, $p=0.190$).

A subset of 17 patients with self-reported vision loss underwent ophthalmic examination, skin snip biopsy, and serological testing by Ov-16 RDT. No mf was found in the anterior chamber or skin snip biopsy, and five of 17 patients were positive for Ov-16 IgG4 antibodies, 29.4% (95% CI: 7.8–51.1%). The single case of blindness probably related to onchocerciasis was both mf and serologically negative.

O. volvulus infection in children

A total of 182 children from two villages voluntarily provided blood samples, including 153 children aged 5–9 years: 19 from Mangobo and 134 from Petifu (Table 2). Twenty-nine (29) children aged 10–13 years were excluded from the analysis. Of the 153 children aged 5–9 years, 7 were positive for Ov-16 IgG4 antibodies (4.6%, 95% CI: 1.3–7.9%). The positivity rate of Ov-16 IgG4 antibodies was similar in boys at 5.9% (95% CI: 0.3–11.5%) and girls at 3.5% (95% CI: 0-7.5%) ($\chi^2=0.479$, $p=0.489$). Seropositivity for Ov-16 IgG4 antibodies in children aged

Table 2 Results of Ov-16 RDT tests in the two villages (Mangobo and Petifu)

	Number of people tested	Number of people positive	Positivity rate (%) (95% CI)	*P* value
Adults				
Patients self-reporting vision loss	31	9	29.0 (13.1–45.0)	0.042
Other volunteers	23	13	56.5 (36.3–76.8)	
Female	27	7	25.9 (9.4–42.3)	0.027
Male	27	15	55.6 (36.8–74.3)	
≤ 50 years	19	10	52.6 (30.2–75.1)	0.190
> 50 years	35	12	34.3 (18.6–50.0)	
Total	**54**	**22**	**40.7 (27.6–53.8)**	
Children aged 5–9 years				
Boys	68	4	5.9 (0.3–11.5)	0.489
Girls	85	3	3.5 (0-7.5)	
Mangobo	19	0	0	0.308
Petifu	134	7	5.2 (1.5–9.0)	
Total	**153**	**7**	**4.6 (1.3–7.9)**	

5–9 years by village was 5.2% (95% CI: 1.5–9.0%) in Petifu and 0% in Mangobo ($\chi^2 = 1.040$, $p = 0.308$).

Discussion

Eye examination revealed that self-reported vision loss in the two villages was mainly due to cataracts, ocular allergy, refractive error, and other non-onchocerciasis eye conditions, with cataracts remaining the most common cause of blindness. This was consistent with previous findings in Sierra Leone [17]. Twenty-two adults, 29.0% of those with self-reported vision loss and 56.5% of other community volunteers, tested positive for Ov-16 IgG4 antibodies, indicating likely exposure to *O. volvulus* infection during their lifetime, possibly in their residential villages. The absence of skin and/or ocular mf in these individuals suggests either no active infections or very low-intensity infections. Blindness caused by onchocerciasis is directly related to the microfilarial load [18] and is predicted in communities with a mf prevalence of ≥40% and a community microfilarial load (CMFL) of ≥5 mf/skin snip [19, 20]. Annual ivermectin treatment sharply reduces the incidence of blindness after two years of mass treatment with ivermectin [21]. The current situation of no or very low-intensity infections in these villages poses a low or zero risk of serious new ocular morbidity. The first large-scale ivermectin mass treatment in endemic villages in the Taia river basin started in 1990 [22]. A study of patients at an eye hospital patients in 1992 showed that onchocerciasis blindness was estimated to be 15% of all blindness, a reduction from 30% before 1990 [6]. More recently, a rapid assessment of avoidable blindness in Siera Leone in 2021 showed that the main causes of blindness were cataracts, glaucoma, other corneal opacities, and other eye conditions, and that no cases of blindness found were attributed to onchocerciasis in the populations surveyed [17]. Therefore, after many years of intervention, onchocerciasis may no longer be a significant cause of blindness in these villages.

The results from children aged 5–9 years showing 4.6% seropositivity with Ov-16 IgG4 antibodies seem to indicate a recent exposure to *O.volvulus* infection. This is possibly an indication of continuing transmission of *O.volvulus*. However, recent exposure does not necessarily indicate that transmission is ongoing. Entomological information on blackfly infectivity would help to confirm the likely continuing transmission of *O.volvulus* infection in these two villages. This would validate the decision to continue mass treatment with ivermectin to eliminate onchocerciasis in Tonkolili district. The 2010 national impact assessment suggested good progress in mf prevalence reduction from 60.4 to 16.1% in Tonkolili district [2]; however, it was still one of the areas with the highest Ov-16 antibody prevalence (2.5%) in the country in 2017 [3]. The duration of ivermectin treatment required to achieve onchocerciasis elimination depends on the baseline endemicity levels, the force of infection, an inadequate strategy, or the quality of mass treatment [23, 24]. The two villages are located in an area with meso-endemicity at baseline, and the current seroprevalence of 4.6% by Ov-16 IgG4 antibodies is in line with the predicted mf prevalence after 16 years of treatment in Africa for hypo- to meso-endemic areas [21].

Together with program information across the country, it is recommended that the NNTDP continue at least annual mass treatment with ivermectin and ensure effective treatment coverage in all endemic communities by taking extra measures to improve program quality. This will help achieve the national goal of eliminating onchocerciasis transmission.

Limitations

The investigation focused on the community members who self-reported vision loss to confirm whether these

were onchocerciasis-related. Participation was voluntary and the results may not be representative of all the community members who may have vision impairment either due to onchocerciasis or other eye conditions. The sample size for mf by skin snip was relatively small and not from the wider community. The mf results may not be representative of the true situation in the population in the two villages. However, the relatively low prevalence of Ov-16 IgG4 antibodies in children aged 5–9 years suggests that the level of transmission in the two villages is relatively low, although we did not conduct an entomological investigation to confirm this.

Abbreviations

CI	Confidence interval
CMFL	Community microfilarial load
DBS	Dried blood spot
MDA	Mass drug administration
Mf	Microfilariae
RDT	Rapid diagnostic test

Acknowledgements
The authors would like to thank two ophthalmologists (Gibrilla Bah and Issa Kamara) for performing eye examinations for diagnosis of eye conditions and laboratory technicians (Ali Tia, Sam Saffa and others) for sample collection and examination. We also thank Sightsavers for providing the Ov-16 RDT tests to the NNTDP for testing the DBS samples in the laboratory.

Author contributions
IKL is the National NTDP Manager; YZ and AMW conceived and designed the study; VRS, MSB and AC led the field data collection and managed the data; DH coordinated laboratory testing. YZ drafted the manuscript; YZ, AMW, AK and DE critically revised the manuscript for intellectual content. PH and SJ reviewed the manuscript. All authors approved the final manuscript.

Funding
Sierra Leone onchocerciasis elimination received funding from the United States Agency for International Development (USAID). The funding was granted to Helen Keller International under the Act to End Neglected Tropical Diseases | West Program, led by FHI 360 in partnership with Helen Keller International, Health and Development International, Deloitte, World Vision, and the American Leprosy Missions under Cooperative Agreement No. 7200AA18CA00011. This investigation was supported by Helen Keller International with funds from Albert Parvin Foundation. The contents are the responsibility of the authors and do not necessarily reflect the views of USAID or the United States Government. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Data availability
All data generated or analyzed during this investigation are included in this published article and can be made available on reasonable request from the National Neglected Tropical Disease Program with permission from the Ministry of Health and Sanitation, Sierra Leone.

Declarations

Ethical approval
The onchocerciasis elimination was part of the national neglected tropical disease elimination program, and this investigation was in response to community requests and conducted by the NNTDP of the Ministry of Health Sierra Leone. Prior to the surveys, permission was received from the traditional authorities and the Paramount Chief of the chiefdom. A community meeting was held, and oral informed consent/assent was obtained from village chiefs and adult participants themselves before they were examined, and samples collected. For children, permission was given from parents/guardians on behalf of each child before DBS samples were collected. All participants were eligible for inclusion without discrimination on gender, social status, religion, or ethnicity. Participation was entirely voluntary, and they could participate and/or withdraw at any time. The data were securely stored in the NTDP database and no identity of participants can be revealed upon publication of this paper.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 28 March 2024 / Accepted: 19 December 2024
Published online: 17 January 2025

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