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Morbidity hotspot surveillance: A novel approach to detect lymphatic filariasis transmission in non-endemic areas of the Tillabéry region of Niger

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A R T I C L E I N F O

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A B S T R A C T

The Niger Lymphatic Filariasis (LF) Programme is making good progress towards the elimination goal and scaling up morbidity management and disability prevention (MMDP) activities. Clinical case mapping and the increased availability of services has prompted patients to come forward in both endemic and non-endemic districts. The latter included Filingué, Baleyara and Abala districts of the Tillabéry region, and in 2019, 315 patients were found during a follow-up active case finding activity, suggesting it may have low transmission.

The aim of this study was to assess the endemicity status in areas reporting clinical cases, 'morbidity hotspots', in three non-endemic districts of the Tillabéry region. A cross-sectional survey was conducted in 12 villages in June 2021. Filarial antigen was detected using the rapid Filariasis Test Strip (FTS) diagnostic, and information obtained on gender, age, residency length, bed net ownership and usage, and presence of hydrocoele and/or lymphoedema. Data were summarised and mapped using QGIS software.

A total of 4058 participants between 5 and 105 years old were surveyed, with 29 (0.7%) participants found to be FTS positive. Baleyara district had significantly higher FTS positive rates than the other districts. No significant differences were found by gender (male 0.8%; female 0.6%), age group (<26 years 0.7%; ≥26 years 0. 7%), and residency length (<5 years 0.7%; ≥5 years 0.7%). Three villages reported no infections; seven villages <1%, one village 1.1% and one village 4.1%, which was on the border of an endemic district. Bed net ownership (99.2%) and usage (92.6%) was very high and there was no significant difference between FTS infection rates.

The results indicate that there are low levels of transmission in populations, including children, living in districts previously classified as non-endemic. This has implications for the Niger LF programme in terms of delivering targeted mass drug administration (MDA) in transmission hotspots, and MMDP services, including hydrocoele surgery to patients. The use of morbidity data may be a practical proxy to trigger mapping of ongoing transmission in low endemic areas.

Abbreviations: Lymphatic filariasis, LF; Neglected Tropical Disease, NTD; Global Programme to Eliminate Lymphatic Filariasis, GPELF; Mass Drug Administration, MDA; Morbidity Management and Disability Prevention, MMDP; Transmission Assessment Survey, TAS; World Health Organization, WHO; Filariasis Test Strip, FTS.

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Continued efforts to study morbidity hotspots, post-validation transmission, cross-border and cross-district endemicity are needed to meet the WHO NTD 2030 roadmap targets.

1. Introduction

Lymphatic filariasis (LF) is a mosquito-borne parasitic Neglected Tropical Disease (NTD) that is targeted for global elimination (World Health Organization, 2020). An estimated 51.4 million people worldwide were infected in 2018. The Global Programme to Eliminate Lymphatic Filariasis (GPELF) started in 2000, and aims to eliminate LF as a public health problem through two main components, namely transmission interruption through mass drug administration (MDA) and suffering alleviation among affected people through morbidity management and disability prevention (MMDP) (World Health Organization, 2021a). Many countries have achieved elimination or are reaching the post-MDA surveillance phase and need to develop strategies to detect transmission in low prevalence settings, and determine how to integrate care for patients into the health systems (World Health Organization, 2021b; Riches et al., 2020; Lammie et al., 2021). National level strategies need to consider both previously endemic districts and adjacent non-endemic districts and/or countries (cross-border) to account for changing demographics and mobility overtime.

The Niger LF Elimination Programme started in 2003 with endemicity mapping, which found that 54 out of 72 districts were endemic (Ministère de la Santé Publique et al., 2017). In 2007, the LF programme started MDA implementation activities across the endemic areas using ivermectin and albendazole, and by 2020 was able to report that 43 districts have successfully passed Transmission Assessment Surveys (TAS) (World Health Organization, 2015) and stopped the MDA campaign. The MMDP component of the Niger LF programme started early in 2009 with clinical case mapping and an increase in availability of care and services at community health centres. This encouraged patients to come forward in both endemic and non-endemic districts. The latter included several districts of the Tillabéry region, which was unexpected, and in 2010 a remapping survey was conducted in 3 districts of Niger including Filingué district (part of the Tillabéry region) to check its endemicity status, but no evidence of transmission was found. Despite this finding, over the past decade, patients have continued to come forward for MMDP services. In response, the Niger LF programme conducted an active clinical case finding activity across three districts of the Tillabéry region in 2019 and found 315 patients in Filingué (hydrocoele = 161; lymphoedema = 59), Baleyara (hydrocoele = 30; lymphoedema = 7) and Abala (hydrocoele = 38; lymphoedema = 20). This helped the LF programme to assess the MMDP needs and plan for health system integration, however, it also suggested that there may be low levels of transmission in areas previously considered to be non-endemic.

This study therefore aimed to assess the endemicity status in areas reporting significant levels of clinical cases, 'morbidity hotspots', in the three non-endemic districts of the Tillabéry region of Niger.

2. Material and methods

2.1. Study design

A cross-sectional survey was conducted in Filingué, Baleyara and Abala districts of the Tillabéry region. The selection of the villages was based on the number of clinical cases found in the active case finding survey conducted in 2019 and the security situation at the time of the implementation. In each village, the prevalence of infection and several risk factors were measured. The survey had a similar approach to the World Health Organization's (WHO) standard sentinel site surveys and aimed to sample between 300 and 350 individuals per village (World Health Organization, 2015). The survey team engaged with the community leader and traditional leaders of the village to gather residents in the centre of the town to inform them of the study. All residents aged 5 years and over were invited to participate in the survey, after providing informed consent.

Seroprevalence was determined by the Filariasis Test Strip (FTS), which detects circulating filarial antigen of *Wuchereria bancrofti* (World Health Organization, *2015*). The FTS is a standard rapid diagnostic test recommended by the WHO and used in endemic countries for LF surveillance. The FTS requires a finger prick blood sample (100 μl) from consenting individuals. For this study, if the FTS result was invalid or positive, it was repeated to confirm the result. The recommended night blood test to detect microfilaria in positive FTS participants was not conducted due to high levels of insecurity in the region due to presence of groups linked with Al-Qaeda and Islamic State, which did not allow safe visitation.

2.2. Variables collected

Demographic risk factors were collected for each individual and included gender, age, duration of residency (<5 years). In addition, information on other health interventions (bed net ownership and usage for malaria prevention) and presence of clinical conditions (lymphoedema and hydrocoele) was collected. For lymphoedema, the leg or arm affected and the stage (mild, moderate, severe) of the condition was recorded based on the WHO guidelines (World Health Organization, 2021b).

Survey data were collected electronically with phones and using the KoBoCollect open-source app (KoBo Toolbox, 2023). Geographical coordinates of each village were collected for mapping purposes using qGIS v.3.16.11 (QGIS, 2023).

2.3. Statistical analyses

Statistical analyses were conducted using the IBM SPSS Statistics 28 (IBM, 2023) calculating the prevalence of infection per village, district, gender, age, duration of residency and usage of bed net. The morbidity rate was calculated per village. Chi-square test was calculated to compare the prevalence of infection per each variable. Fischer's exact test used for the cross tabulations that had 1 or more cells with an expected count <5. Statistical significance was defined as a *P*-value of <0.05.

2.4. Ethics

Ethical approval was obtained from the Liverpool School of Tropical Medicine (LSTM) Research Ethics Committee (Research Protocol 19–116). The National Programme for the Onchocerciasis Control and Elimination of LF of the Ministry of Public Health of Niger formally approved this survey for programmatic purposes. This was accepted by LSTM Research Ethics Committee. During the study, participants found to have a positive for FTS were treated together with their family with the standard treatment regime of albendazole and ivermectin. Participants with lymphoedema or hydrocoele were referred to the nearest health centre where they were provided with information on morbidity management and disability prevention services, including hydrocoele surgery and management of lymphoedema.

3. Results

A total of 4058 participants from 12 villages were surveyed in Filingué ($n = 6$), Baleyara ($n = 5$) and Abala ($n = 1$) districts with sample sizes ranging between 310 and 350 per village (Table 1). A total of 29 participants (0.7%; 95% confidence interval [CI], 0.4%–1.0%) were found to be FTS positive and ranged from 0 to 13 (4.1%; 95% CI, 1.9%–6.3%) per village. The distribution of villages and the percentage of FTS positives are shown in Fig. 1.

3.1. Infection rates and morbidity cases

The highest number of FTS positive cases and rates were found in Baleyara district ($n = 20$ cases; 1.2%; 95% CI, 0.7%–1.8%), which was significantly higher than Abala and Filingué districts as shown in Table 2. The village with the highest number of FTS positives and rate was Kossey village ($n = 13$; 4.1%; 95% CI, 1.9%–6.3%) in Baleyara district (Fig. 1). Faria Beri village had 4 positives (1.1%; 95% CI, 0%–2.3%); Kodey village had 3 positives (0.9%; 95% CI, 0%–1.9%); Kobi, Borgo Darey and Kabe villages had two positives (0.6%; 95% CI, 0%–1.4%); Abala, Bakin Toullou and Bonkoukou villages had one positive FTS (0.3%; 95% CI, 0%–0.9%), and the three villages of Dogongao, Garia Damana and Kokorbe Fandou had none (Table 1; Fig. 1).

Seven participants (0.2%) were found to have clinical conditions (hydrocoele = 6; lymphoedema = 1). The hydrocoele cases were found in men from Kossey ($n = 4$; 1.25%; age range 32–80 years, severe stages), Bakin Toullou ($n = 1$; 0.3%; age 40 years; moderate stage) and Dogongao (n = 1; 0.6%; age 7 years; mild stage) (Table 1). The lymphoedema case was found in a female (25 years of age) from Dogongao and classified as mild stage. All individuals with clinical conditions tested negative with FTS and were living in the same location for the last 5 years, except for the individual from Bakin Toullou who lived in Diffa region, Niger, classified as LF endemic. The number of morbidity cases found in this study may be under representative since surveyors notified that some patients did not want to participate in the survey due to stigma.

3.2. Age, gender, and duration of residence

The mean age of participants was 26 years and ranged from 5 to 105 years. The age distribution of participants by gender across all

Table 1
Summary of village samples, FTS positivity and clinical case results.

District	Village	FTS results			Clinical case numbers	
		No. tested	No. positive	% positive (95% CI)	Hydrocoele	Lymphoedema
Abala	Abala - Toudou	341	1	0.3% (0–0.9)	0	0
Filingué	Bakin Toullou	349	1	0.3% (0–0.9)	1	0
	Bonkoukou	350	1	0.3% (0–0.9)	0	0
	Dogongao	349	0	0.0% (0–0)	1	1
	Faria Beri	350	4	1.1% (0–2.3)	0	0
	Garia Damana	349	0	0.0% (0–0)	0	0
	Kobi	350	2	0.6% (0–1.4)	0	0
Baleyara	Borgo Darey	340	2	0.6% (0–1.4)	0	0
	Kabe	330	2	0.6% (0–1.4)	0	0
	Kodey	320	3	0.9% (0–1.9)	0	0
	Kokorbe Fandou	310	0	0.0% (0–0)	0	0
	Kossey	320	13	4.1% (1.9–6.3)	4	0
Total		4058	29	0.7% (0.4–1.0)	6	1

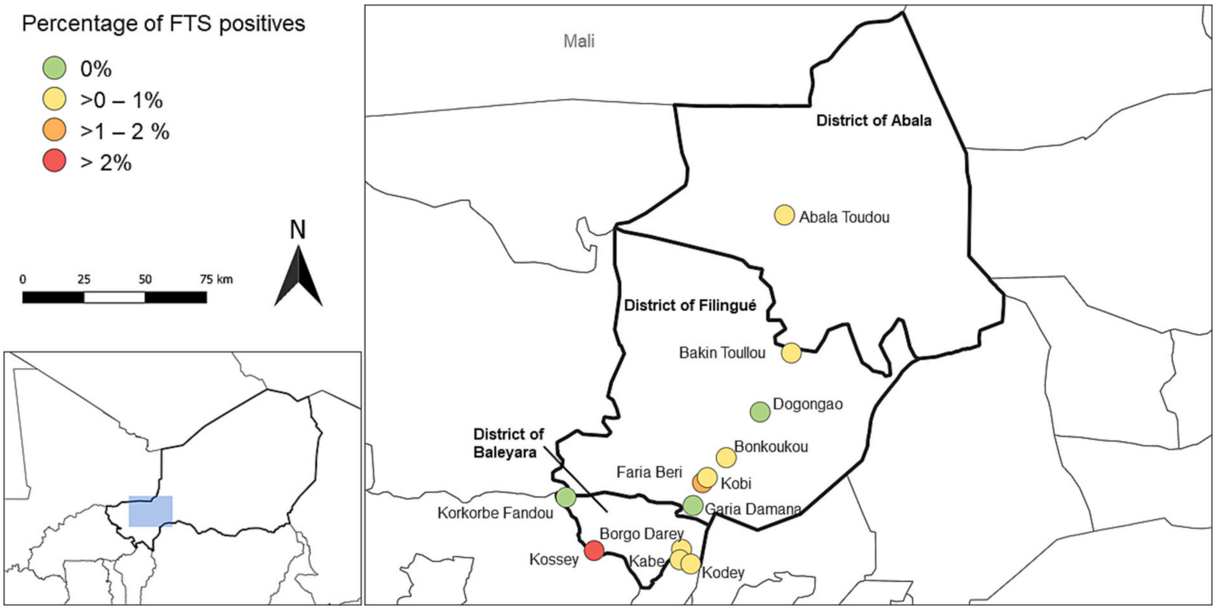

Fig. 1. Distribution of study villages and percentage of FTS positives.

Table 2
Comparison FTS positive and negative participants by demographic and intervention risk factors.

Variables	N	FTS No. positive (%)	Chi-square test§ / Fischer's exact test† (*P* value)
Abala District	341	1 (0.3%)	
Filingué District	2097	8 (0.4%)	
Baleyara District	1620	20 (1.2%)	P = 0.006*§
Male	1914	16 (0.8%)	*P* = 0.386§
Female	2144	13 (0.6%)	
<26 years old	2425	18 (0.7%)	*P* = 0.799§
≥26 years old	1633	11 (0.7%)	
Residency <5 years	140	1 (0.7%)	*P* = 1.000†
Residency ≥5 years	3918	28 (0.7%)	
Did own a bed net	4026	28 (0.7%)	*P* = 0.719†
Did not own a bed net	32	1 (3.1%)	
Did use a bed net	3729	27 (0.7%)	P = 1.000†
Did not use a bed net	297	1 (0.3%)	

Note. * Significant difference *p* value <0.05.

villages is shown in Fig. 2A and highlights that most were young and in the 5–14 ($n = 1524$) and 15–24 ($n = 814$) age groups. No positives were found in the 55–64 age group. In the other age groups, FTS positive rates ranged from 0.1% (90% binomial CI 0.2%–2.1%) in the 35–44 age group to 0.9% (90% CI 0.2%–2.8%) in the >65 age group. (Fig. 2B; Table 3).

In addition, we examined Kossey village given the high number of cases. The age distribution of participants by gender is shown in Fig. 2C and highlights also that most were young and in the 5–14 ($n = 126$) and 15–24 ($n = 70$) age groups. No positives were found in the 55–64 or >65 age groups. In the other age groups, FTS positive rates were much higher and ranged from 2.1% (90% CI 0.1%–9.7%) in the 25–34 age group to 5.7% in the 15–24 age group (90% CI 2.0%–12.6%) and >65 age group (90% CI 1.0%-17.0%) (Fig. 2D; Table 3).

Most participants had lived in the village ≥5 years ($n = 3918$). Of the 140 participants that had been resident <5 years, one third had come from other parts of Niger (n = 39), followed by Benin, Burkina Faso, Mali, Cote d'Ivoire, Nigeria, Libya and Ghana. Only one participant (from Cote d'Ivoire) was found to be FTS positive.

The comparison between the FTS positive and negative participants by the demographic risk factors found only significant

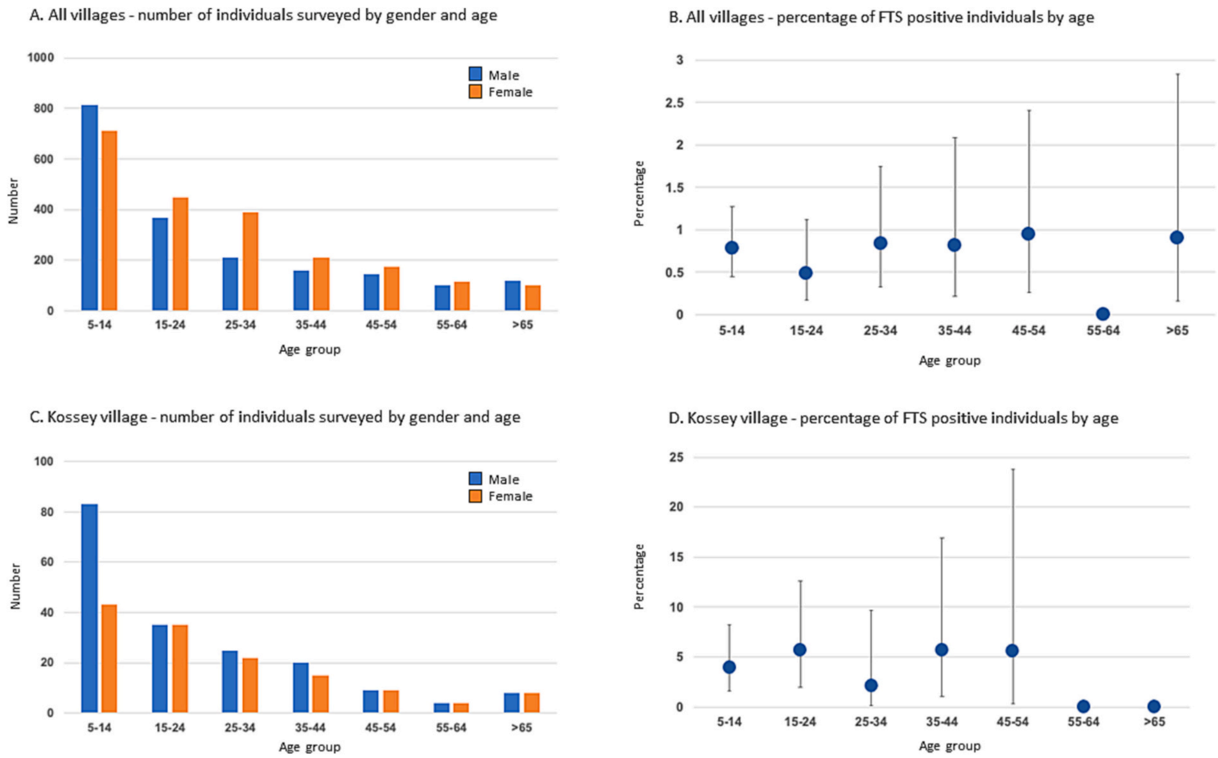

Fig. 2. Summary of number and percentage FTS positive participants by gender and age in all villages and in Kossey village.

Table 3
Summary of FTS positivity by age group in all villages and the Kossey village.

Age group	All villages			Kossey village		
	No. tested	No. positive	% positive (90% CI)	No. tested	No. positive	% positive (90% CI)
5–14	1524	12	0.8% (0.5–1.3)	126	5	4.0% (1.6–8.2)
15–24	814	4	0.5% (0.2–1.1)	70	4	5.7% (2.0–12.6)
25–34	597	5	0.8% (0.3–1.8)	47	1	2.1% (0.1–9.7)
35–44	369	3	0.1% (0.2–2.1)	35	2	5.7% (1.0–17.0)
45–54	319	3	0.9% (0.3–2.4)	18	1	5.6% (0.28–23.8)
55–64	215	0	0	8	0	0
>65	220	2	0.9% (0.2–2.8)	16	0	0

difference between the district variable ($p = 0.006$) (Table 2).

3.3. Bed nets

Most participants owned a bed net (99.2%) and usage (92.6%) was very high. The main reasons for not owning a bed net were reported to be the lack of money ($n = 19$) and the heat (n = 6). Of those who did own a bed net, 297 (7.4%), but did not sleep under it the previous night, reported that the main reasons were because of the heat ($n = 171$; 57.6%), and lack of presence of mosquitoes ($n = 102$; 34.3%).

There was no significant difference between the FTS positive rates between the participants who owned and used bed nets, and those who did not (Table 2).

4. Discussion

Our results indicate that there are low levels of *W. bancrofti* transmission in areas previously considered as non-endemic districts of the Tillabéry region. Villages in the southern areas of Filingué and Baleyara districts had the highest prevalence rates, which were above the 1% threshold set by the WHO to classify a district as endemic (World Health Organization, 2015), and in close proximity to the endemic districts of Kollo and Boboye that are now under post-MDA surveillance (Ministère de la Santé Publique et al., 2017; World Health Organization Regional Office for Africa, 2023). Especially, the locality of Kossey, which borders the district of Baleyara and the district of Kollo. Kossey village had a population of 871 people in 2021, the environment is similar to other neighbouring villages as they are located in the Sahelian zone. The primary occupations are agriculture, livestock and trade.

This has implications for the Niger LF Elimination Programme as it may need to conduct further assessments to delineate risk along non-endemic/endemic district areas, where local population movements may facilitate transmission and targeted MDA may be required (Ramaiah, 2013). Additional assessments in the northern area of Abala district bordering endemic areas of Mali should also be considered, as this was a limitation of the study due to security concerns, along with the development of a cross-border strategy to optimise surveillance.

Overall, we found no differences between males and females, or between the younger and older age groups. Interestingly, however, the prevalence rate in children ≤14 years of age were similar to or higher than other age-groups. This indicates that local transmission is endemic rather than imported, especially as most children had lived in the villages all their lives. To assess the extent of transmission in these younger age-groups it may be beneficial for the LF Programme to follow-up and conduct specific surveillance activities in children using WHO recommended TAS survey or the WHO confirmatory mapping tool (target age 9–14 years) as these methods have helped to determine endemicity status in a number of different settings, and moved programmes forward towards the elimination goal (World Health Organization, 2015; Gass et al., 2017; Rebollo et al., 2015; Shamsuzzaman et al., 2017; Sime et al., 2018; World Health Organization, 2014).

The hydrocoele and lymphoedema patients found in the case finding activity in 2019 and through the routine register of patients in the health facilities highlight the need to provide MMDP services and care to all patients, including those in areas considered to be non-endemic districts (World Health Organization, 2021b). The Niger LF Elimination Programme is developing a strategy to include training of health personnel in non-endemic areas where patients are found and has already initiated surgeries for men with hydrocoele in 33 districts, 9 of them classified as non-endemic. These data on the number of patients, availability of treatment for lymphoedema and hydrocoele will be included in the WHO validation dossier as additional data (World Health Organization, 2017). However, the programme will still need to consider that there may be other causes of these clinical condition, as we show here with a 7-year-old boy with a mild hydrocoele in a village with no FTS positivity, which suggests it may be non-filarial.

Despite finding no significant difference between use of bed nets and FTS positivity in the current study, the very high bed net coverage for malaria is likely to have reduced and/or helped to maintain low levels of *W. bancrofti* transmission, especially if the *Anopheles* mosquito species are the primary vector, and considering that the three non-endemic districts had not conducted MDA campaigns (World Health Organization, 2021a; Wilson et al., 2020; Kelly-Hope et al., 2013). The WHO advocates that mosquito control is an important supplementary strategy (World Health Organization, 2021a), and studies have shown that it may facilitate elimination (Rebollo et al., 2015; Webber, 1979) or accelerate the interruption of LF transmission in the absence of large-scale preventive chemotherapy (Nsakashalo-Senkwe et al., 2017; Davis et al., 2021). Communication and coordination between the LF and malaria programmes will help to understand barriers to bed net use (e.g., heat), optimise human and financial resources, and develop integrated strategies, which will be important for low prevalence settings and the post-validation surveillance phase of the Niger LF Elimination Programme (World Health Organization, 2020; Riches et al., 2020; World Health Organization, 2011; van den Berg et al., 2013).

The main limitation of the study was not being able to conduct microfilaria night blood in FTS positive participants to determine if they had active infection with microfilariae in their blood (World Health Organization, 2015; Kelly-Hope et al., 2018). However, specificity of the FTS is high at 98–100% according to the manufacturer, which has been supported by a variety of field studies (Weil et al., 2013). In addition, microfilaria tests are not required to validate the results of FTS, as on its own is a WHO recommended method to inform programmes when to stop MDA or to map endemic districts (World Health Organization, 2017). This activity was not done due to the concerns of security and safety of the field teams. This is an increasingly important consideration for all NTD programmes, especially in the Sahel region of West Africa where there are high levels of insecurity and conflict due to presence of groups linked with Al-Qaeda and Islamic State causing difficulty in implementation of surveys, MDA, and MMDP. New approaches may be required to collect the data required for validation and surveillance (Al-Lami, 2020; Kelly-Hope et al., 2021).

The GPELF advocates to eliminate LF as a public health problem (World Health Organization, 2020), which means that low levels of transmission may occur in hypo-endemic areas or during the post-MDA and validation phases (Riches et al., 2020), and that clinical cases will need to be integrated into health system for long term care and monitoring (World Health Organization, 2021b). National programmes will need to develop practical surveillance systems to detect areas with transmission and recrudescence potential. Given the chronic nature of lymphoedema and hydrocoele, it is feasible that a clinical case reporting could identify areas where LF remains a public health problem as shown in this study, and could be used together with other recommended epidemiological surveillance strategies (World Health Organization, 2015; World Health Organization, 2014).

5. Conclusion

The study highlights the value of assessing areas reporting an unusual number of clinical cases or 'morbidity hotspots' in non-endemic areas to trigger surveys for evidence of infection. This novel approach may also be used in endemic areas where clinical case data are available, and transmission is low or uncertain. It is practical due to the chronic life-long nature of LF, especially lymphoedema, and high burden areas provide a proxy of where transmission may be occurring or was occurring before the implementation of MDA. This may help LF Programmes to direct assessments to risk areas, which can supplement the WHO TAS and/or confirmatory mapping tool. Continued efforts to study morbidity hotspots, post-validation transmission, and cross-district and cross-order endemicity are needed to meet the WHO NTD 2030 Roadmap targets.

Author contributions

XB-R and LK-H conceived and designed the study, wrote the first draft of the manuscript. LK-H and MJT obtained the resources. SA and XB-R conducted and supervised the field work. All authors contributed to the article and approved the submitted version.

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Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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