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Leprosy indicators and diagnosis delay in Mogovolas, Meconta and Murrupula district of Nampula Province, Mozambique: A baseline survey

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Summary
Objectives Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. The PEP4LEP project will compare two integrated skin-screening interventions combined with the distribution of a single dose of rifampicin as post exposure prophylaxis (SDR-PEP) for contacts of leprosy patients. To implement the study in Mozambique, it was necessary to assess recent epidemiological indicators of leprosy and to estimate case detection delay as a main outcome indicator at baseline.
Methods This was a descriptive study to establish the trend of epidemiological indicators of leprosy in the Nampula province districts Murrupula, Meconta and Mogovolas in Mozambique, between 2015 and 2019; and to calculate the average delay to diagnose leprosy cases in these districts. The National Leprosy Control Programme was also described. For the estimation of the case detection delay, 81 recently diagnosed patients were interviewed.
Results There were 939 new leprosy cases detected in the three districts from 2015 to 2019, with a high proportion of disability (17.0%). The mean diagnosis delay was 26.6 months (95% CI: 18.4–34.7), while the median was 17.0 months. Multibacillary cases had an average delay of 27.9 months (95% CI: 18.6–37.1), while those with grade 2 disability had an average delay of 47.8 months (95% CI: 15.4–80.2).
Conclusion The long case detection delay and high grade 2 disability rates indicate that there is a need for active case finding and chemoprophylaxis with SDR-PEP

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to help interrupt the chain of *Mycobacterium leprae* transmission in Nampula province.

Keywords: Leprosy, Hansen's disease, Mozambique, contact screening, delayed diagnosis, post-exposure prophylaxis, rifampicin

Introduction

Leprosy, or Hansen's disease, is a chronic infectious disease caused by *Mycobacterium leprae (M. leprae)*, mainly affecting the skin, peripheral nerves and eyes. An important challenge in leprosy control is the long incubation period, lasting from two to twenty years, during which transmission can occur.[1] Leprosy affects people of all ages and genders, particularly people living in poor resource settings.[2] The endemicity is highest in India, Brazil, Indonesia and also high in several countries in Sub-Saharan Africa.[1,3]

Treatment with multidrug therapy (MDT) has been the mainstay of leprosy control since the 1980s. Due to the stable case detection rate in many countries over the past 15 years, indicating ongoing transmission of *M. leprae*, novel preventive interventions have been developed.[4] An intervention proven to be effective is post-exposure prophylaxis (PEP) with single-dose rifampicin (SDR) given to contacts of leprosy patients.[5] In 2018, based on the available evidence, the World Health Organization (WHO) included a recommendation to implement chemoprophylaxis with SDR-PEP in their "Guidelines for the Diagnosis, Treatment and Prevention of Leprosy".[4]

Rifampicin as leprosy post-exposure chemoprophylaxis is currently subject to several implementation and feasibility studies, including the PEP4LEP study. This is a cluster-randomised implementation trial comparing two interventions of integrated skin-screening – community skin camps versus health centre based screening – combined with SDR-PEP distribution to contacts of leprosy patients in Ethiopia, Mozambique, and Tanzania.[6] The project compares the effectiveness of both interventions by assessing the period of delay in case detection and the rate of leprosy patients detected, as well as the feasibility in terms of cost-effectiveness and acceptability. To monitor the impact of the PEP4LEP study in the three countries, it is necessary to first assess baseline leprosy indicators and in particular the delay in detection of leprosy at baseline.

In 2020, the African Region of WHO reported 16,690 new leprosy cases on the continent; giving a new case detection rate of approximately 14.9 per 1 million inhabitants.[7] It is important to highlight that the number of newly detected cases was substantially lower compared to 20,207 reported cases in the previous year, which is thought to be a result of the COVID-19 pandemic and the restrictive measures to control the pandemic.[1,7] According to the WHO, Mozambique detected 2,065 new cases of leprosy in 2020, of which 895 (43.3%) were female and 212 (10.3%) were children below the age of 15 years. Furthermore, 1,681 (81.4%) had multibacillary (MB) leprosy, and 399 (19.3%) had a grade 2 disability (G2D) of which 51 (12.8%) patients were children.[7] Mozambique has an estimated population of 31,255,000.[8]

Disability caused by peripheral nerve damage at time of diagnosis is considered an indicator for detection delay.[9] Early detection and timely treatment of leprosy is crucial to prevent disabilities.[10] Many barriers are known to impede early case detection, such as cultural or religious beliefs (e.g. leprosy being inherited or a divine punishment), social stigma or internalised stigma, lack of education and medical knowledge, fear of isolation and loss of identity.[11–13] These are all patient or community related factors associated with longer case

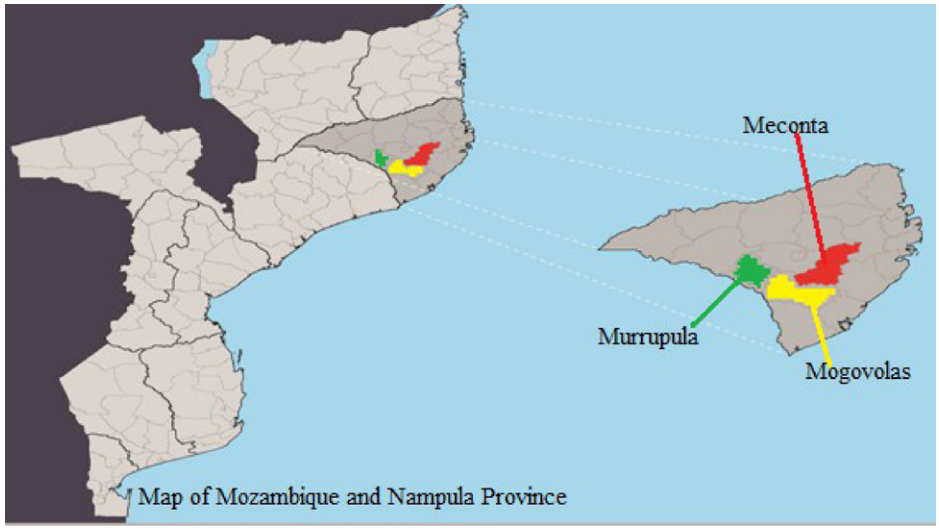

Figure 1. Map of Mozambique and Nampula Province.[14]

detection delays, but there are also health staff and health service related factors, such as lack of training on leprosy, stigmatisation by health workers, and inaccessibility of health services.

Material and methods

The National Leprosy Control Programme was described by consulting the National Leprosy Manual, and data from five consecutive years between 2015 and 2019 were analysed, using individual clinical records to establish the trend of leprosy evolution. Additionally, 81 recently diagnosed leprosy patients were interviewed using a questionnaire to estimate case detection delay, which was culturally validated and approved as part of the PEP4LEP project.[6] The survey took place between June and August 2021.

STUDY DESIGN

This was a descriptive, retrospective cross-sectional study, based on secondary data from the Provincial Leprosy Control Programme of Nampula between 2015 and 2019, and based on interviews with patients diagnosed preferably up to six months prior to inclusion.

STUDY POPULATION AND LOCATION

The survey was carried out in Meconta, Mogovolas and Murrupula, districts of Nampula province in Mozambique (Figure 1). Nampula has 23 districts and is located in northern Mozambique.[8] Selected districts are endemic for leprosy and co-endemic for other Neglected Tropical Diseases (NTDs) such as lymphatic filariasis and scabies.[15] The districts were purposely selected as part of the PEP4LEP project due to the high number of leprosy patients and because they are accessible by road.

STUDY SETTING: NATIONAL LEPROSY CONTROL PROGRAMME IN MOZAMBIQUE

Three levels of governmental departments are involved in the National Leprosy Control Programme in Mozambique: national level, provincial level and district level. The Ministry

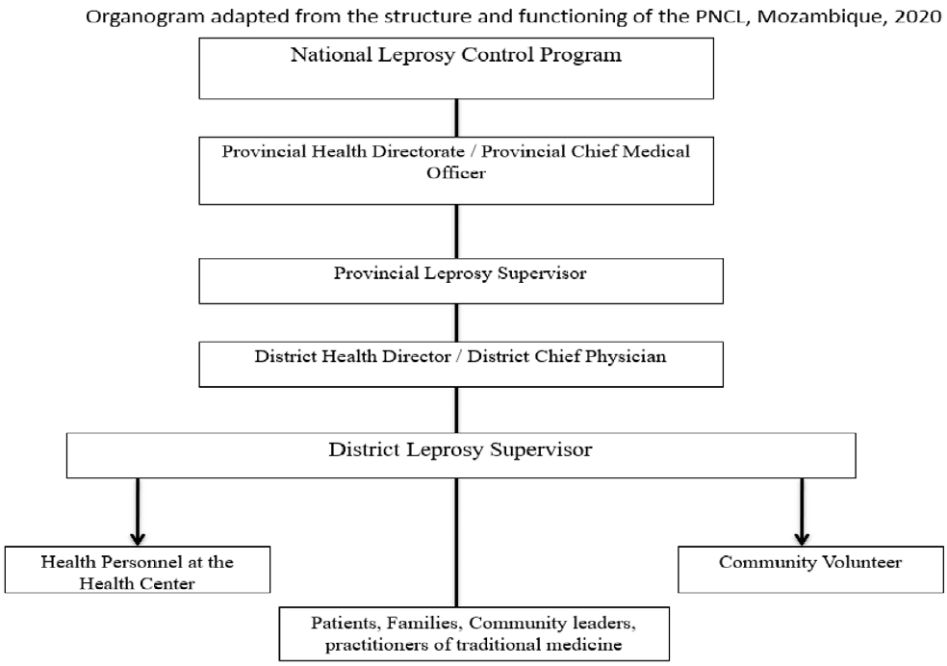

Figure 2. National Leprosy Control Programme organisational chart, Mozambique.[16] Abbreviation: PNCL (Programa Nacional de Controlo da Lepra).

of Health (*Ministerio da Saúde – MISAU*) is responsible for health services provided to the public and accessible to the Mozambican population at all health network levels.[16] Active case detection activities already being performed in PEP4LEP districts during 2015–2019 included searching for suspected cases, registering and reporting them to the district supervisor, and mobilising field workers to go to the communities to administer treatment with MDT. MISAU supervises and executes the largest part of health services provided to the Mozambican population.

Over the past five years, responsibilities for the execution of health activities were increasingly transferred from the central level of the MISAU to the Provincial Health Directorates (DPS) and to the Health District Services Women's and Social Action (SDSMAS).[17]

The National Leprosy Control Programme (*Programa Nacional de Controlo da Lepra - PNCL*) is responsible for the preparation, distribution and updating of leprosy training, treatment, prevention, and the availability of leprosy control materials in the country. The PNCL cooperates with international private and public organisations in disease control activities. Their aims are to reduce leprosy transmission and morbidity; to eliminate leprosy as a public health problem at a subnational level; and to prevent, reduce and rehabilitate persons living with physical disabilities and the psychosocial consequences caused by leprosy (Figure 2).[16]

SAMPLE AND SELECTION CRITERIA

All data from patients registered from January 1, 2015, to December 31, 2019 in the three districts were included for the evaluation of epidemiological indicators. In total, 81 recently

diagnosed patients, preferably within six months prior to inclusion, were interviewed to estimate the delay in case detection at baseline. Sampling was performed systematically based on availability of recently diagnosed patients in PEP4LEP study districts. Population data were obtained from the National Institute of Statistics (INE) of Mozambique based on the 2017 Population Census data and population estimates for 2018 and 2019.[17,18]

OUTCOME MEASURES

The outcome measures chosen are in line with the indicators of the WHO Leprosy Monitoring Guide:[15]

- Number of newly detected cases of leprosy.
- Proportion of newly diagnosed grade 2 disability patients.
- Proportion of children (age-specific detection).
- Proportion of multibacillary (MB) cases.
- The proportion of women (sex-specific detection).

All rates are calculated with a common denominator of 1 million inhabitants according to the latest WHO update.[1] Disability grading of leprosy is assigned according to WHO definitions.[14]

CASE DETECTION DELAY

Delay in case detection is defined as the period between the onset of the first sign and/or symptom of leprosy and the moment of diagnosis. This includes 'patient delay' and 'health system delay' as defined by Muthuvel *et al.* (2017).[12] The delay (in months) between patient recognition of symptoms and diagnosis is based on individual records and/or interviews of a sample of patients. In the context of the study, patients diagnosed preferably within six months prior to inclusion were interviewed to estimate the average delay in the diagnosis of leprosy in the PEP4LEP project districts.[6] For the baseline study, the detection delay survey component of PEP4LEP, a structured questionnaire was used consisting of 10 questions (including information on when signs were first noticed and the subsequent steps taken prior to diagnosis) to determine delay in case detection.[19] The patient's case detection delay is then calculated in total number of months, based on the dates/periods reported to each question. A country and cultural context-specific version of the questionnaire was validated in Mozambique, based on the conceptual framework of Herdman et al., and translated into Portuguese.[19,20] The questionnaire also contains two annexes: a set of clinical photos showing signs of leprosy and a context-specific calendar indicating important local dates. A 'Question by Question' guide was available to provide additional guidance to the interviewers.[20] The questionnaire can be found online via the international leprosy knowledge centre Infolep: https://www.leprosy-information.org/resource/case-detection-delay-questionnaire.[21]

STATISTICAL ANALYSIS

The epidemiological characterisation was based on leprosy surveillance data collected during the study period. Data were analysed using the statistical programme Statistical Package for the Social Sciences (SPSS) version 22.[22] A descriptive analysis was performed of all variables presented in absolute and relative frequencies by gender, age group, clinical form and disability grade.

Table 1. Yearly leprosy indicators per study district, Mozambique, 2015 to 2019

Year	Population	New cases detected	New cases/ million population	Female cases (%)	MB cases (%)	Child cases (%)	G2D cases (%)	G2D cases per million population
				Meconta				
2015	190,642	36	188.8	11 (30.6)	27 (75.0)	1 (2.8)	5 (13.9)	26.2
2016	194,540	20	102.8	9 (45.0)	18 (90.0)	0 (0)	4 (20.0)	20.6
2017	198,318	73	368.1	33 (45.2)	65 (89.0)	6 (8.2)	6 (8.2)	30.3
2018	201,975	36	178.2	10 (27.8)	34 (94.0)	0 (0)	4 (11.1)	19.8
2019	205,517	37	180.0	7 (18.9)	32 (86.0)	4 (10.8)	2 (5.4)	9.7
				Mogovolas				
2015	419,593	40	95.3	9 (22.5)	31 (77.5)	11 (27.5)	6 (15.0)	14.3
2016	448,044	89	198.6	26 (29.2)	76 (85.4)	9 (10.1)	27 (30.3)	60.3
2017	479,382	115	239.8	53 (46.1)	90 (78.3)	21 (18.3)	20 (17.4)	41.7
2018	513,813	148	288.0	61 (41.2)	117 (79.1)	23 (15.5)	19 (12.8)	37.0
2019	551,518	94	170.4	49 (52.1)	52 (55.3)	17 (18.1)	15 (16.0)	27.2
				Murrupula				
2015	173,619	24	138.2	10 (41.7)	20 (83.3)	4 (16.7)	4 (16.7)	23.0
2016	177,044	29	163.8	13 (44.8)	21 (72.4)	1 (3.4)	9 (31.0)	50.8
2017	177,044	45	254.1	20 (44.4)	40 (88.9)	3 (6.7)	6 (13.3)	33.9
2018	183,493	93	506.8	45 (48.4)	59 (63.4)	15 (16.1)	19 (20.4)	103.5
2019	186,534	60	321.6	22 (36.7)	52 (86.7)	4 (6.7)	14 (23.3)	75.1

Abbreviations: MB: multibacillary; G2D: grade 2 disability.

ETHICAL CONSIDERATIONS

The study was part of the baseline research component of the PEP4LEP study protocol.[6] The PEP4LEP project was approved on August 16, 2019 by the National Bioethics Committee for Health (CNBS) of Mozambique with the reference IRB00002657 under Ref. 385/CNBS/19 and for the second extension, Ref. 476/CNBS/21.[23] The project has been registered at the Netherlands Trial Register under the number Trial NL7294 (NTR7503).[24] All participants signed the informed consent form to express their voluntary participation in the research.

Results

LEPROSY INDICATORS PEP4LEP DISTRICTS

During the 5-year period from 2015 to 2019, a total of 939 new leprosy patients were detected (Tables 1 and 2). The proportion of children affected by leprosy was highest in the district of Mogovolas, 16.7%, followed by Murrupula, 10.8% and Meconta, 5.4% (Table 2). Affected women were 43.8% of the leprosy patients in Murrupula district, 40.7% in Mogovolas and 34.7% in Meconta district. Regarding MB leprosy, the district of Meconta had the highest percentage (87.1%), followed by Murrupula (76.6%) and Mogovolas (75.3%). Grade 2 disability was high in Murrupula district with 20.7%, compared to Mogovolas with 17.9% and Meconta with 10.4%.

The districts of Mogovolas and Murrupula showed an increasing trend of 54 and 36 cases respectively between 2015 and 2019, with peak growth achieved in 2018. Meconta district showed a trend of stable incidence of leprosy over these five years, with a detection peak in 2017 (Figure 3).

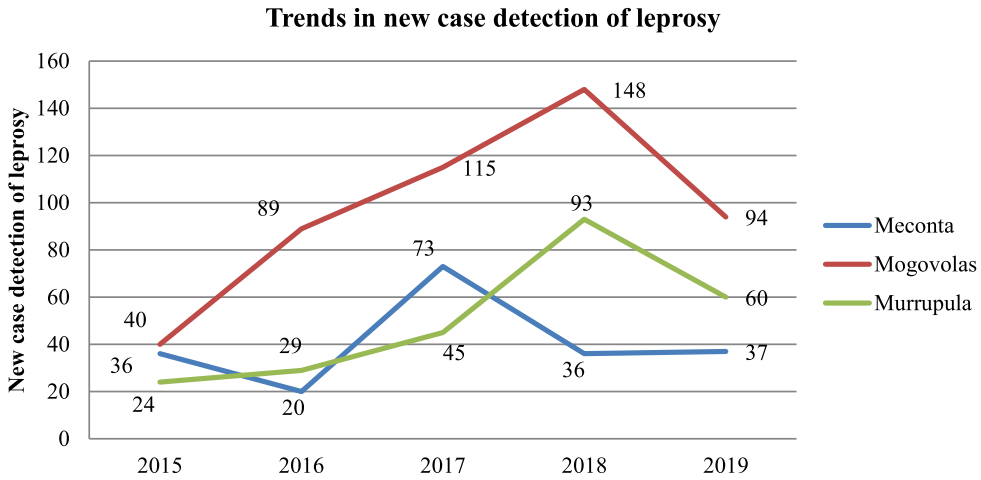

Figure 3. Trends in new case detection of leprosy in the Mogovolas, Murrupula, and Meconta districts of Nampula, Mozambique, 2015–2019.

Table 2. Summary of leprosy epidemiological indicators, Mozambique, 2015–2019

District	Total new cases detected	Average yearly new cases per million population	Female cases (%)	MB cases (%)	Child cases (%)	G2D cases (%)	Average yearly G2D cases per million population
Meconta	202	203.6	77 (38.1)	176 (87.1)	11 (5.4)	21 (10.4)	21.3
Mogovolas	486	198.4	198 (40.7)	366 (75.3)	81 (16.7)	87 (17.9)	36.1
Murrupula	251	276.9	110 (43.8)	192 (76.5)	27 (10.8)	52 (20.7)	57.3

Abbreviations: MB: multibacillary; G2D: grade 2 disability.

DELAY IN THE DIAGNOSIS OF LEPROSY

A total of 81 patients were interviewed, 39.5% in Mogovolas, 38.3% in Murrupula and 22.2% in Meconta (Table 3). Among them, 54.3% were men and 45.7% women, with an average age of 38 years, in the range of 9 to 78 years. Multibacillary leprosy was present in 87.7% of the cases, 22.2% patients presented with G2D and a total of 85.1% presented with a delay of more than six months. The total mean delay in case detection was 26.6 months (95% CI, 18.4–34.7); the district of Meconta had 55.1 months of delay on average, Murrupula 19.3 months and 17.4 months in Mogovolas. Women had a slightly longer delay in diagnosis (27.5 months) compared to men (25.8 months). Those with MB leprosy had longer delays (27.9 months) compared to paucibacillary (PB) leprosy (17.3 months), however only 10 PB patients were interviewed. The delay in diagnosis grew substantially according to disability rate, with an average delay of 18.3 months for patients with G0D, 38.1 months for those with grade 1 disability (G1D) and 47.8 months for patients presenting with G2D. Of the 81 patients, 21 (25.9%) visited a health facility at least one time before receiving their diagnosis.

Table 3. Case detection delay according to patient characteristics, diagnosis and type of delay

Characteristics	*n* (81)	Mean case detection delay (months)	95% CI for mean		Median case detection delay (months)	Range	
			Lower bound	Upper bound		Min.	Max.
District							
Mogovolas	32	17.4	13.3	21.5	15.5	3	42
Murrupula	31	19.3	13.5	25.1	15.0	5	73
Meconta	18	55.1	20.7	89.4	31.0	3	292
Sex							
Female	37	27.5	11.7	43.2	17	5	292
Male	44	25.8	17.6	34.1	16.5	3	137
Age group							
Children <15 years	5	22.2	13.6	58	9	5	73
Adults ≥15 years	76	26.9	18.2	35.5	17	3	292
Clinical subtype							
MB	71	27.9	18.6	37.1	18	3	292
PB	10	17.3	2.4	32.2	9	3	73
Disability grade							
G0D	56	18.3	14.5	22.1	15.0	3	73
G1D	7	38.1	−8.6	84.9	14.0	3	137
G2D	18	47.8	15.4	80.2	28.5	9	292
Total	**81**	**26.6**	**18.4**	**34.7**	**17.0**	**3**	**292**

Abbreviations: CI: confidence interval; MB multibacillary; G0D grade 0 disability; G1D grade 1 disability; G2D grade 2 disability; max: maximum; min: minimum; *n*: number.

Discussion

In addition to describing the National Leprosy Control Programme in Mozambique, this study aimed to assess the trend of epidemiological indicators of leprosy in the districts of Murrupula, Meconta and Mogovolas in Nampula province, and to determine the average delay in detection of cases in these areas before the start of the PEP4LEP project.

The socio-political and economic situation in Mozambique over recent years has drastically affected the national health system, especially the activities of NTD control programmes, including leprosy. As a result, the detection of leprosy patients has been suboptimal in the three districts, influenced by several factors such as less effective promotion and awareness activities in the community, the lack of health professionals and ability to correctly diagnose leprosy, a reduction of quality of monitoring and supervision activities, and decreased coverage of the leprosy control programme to provide services to the entire population.[25] Moreover, delay in leprosy diagnosis is multifactorial and internalised stigma may be a major cause. Health education could also be helpful to reduce delay in diagnosis, together with enhanced access to health services. Additionally, the COVID-19 pandemic has negatively impacted routine leprosy control and case finding activities in Mozambique and other endemic countries.[6,7,24,26]

From the data presented here, we observe a clear discrepancy in case detection between districts. The district of Mogovolas detected more cases, mainly in 2018. However, in relation to the detection rate, all three districts reported a very high level. According to information collected from the provincial supervisor of leprosy control in Nampula, only the PEP4LEP study districts had active case-finding activities in 2017 and 2018, with financial support

from non-governmental organisations. With regards to the leprosy detection in children under 15 years of age, recent transmission seems to be high in Mogovolas. The number of cases in Meconta and Murrupula also remains high, although a slight reduction was observed over time in all districts. The G2D rate in the population was higher in Murrupula district compared to the other two districts, indicating that delayed diagnosis is an ongoing problem.

The results of this study also showed that the district of Meconta had longer delays in diagnosis on average, which may be explained by the lack of active case finding activities, aimed at early diagnosis. There was a high proportion of patients with the MB form of leprosy in both the epidemiological and case detection delay component of the study (78.2% and 87.7% respectively), with longer delays observed in these patients. In relation to disability, people with G2D experienced the longest delay, an association confirmed in a study by Dharmawan *et al.*[11] The interviews to determine the delay in the diagnosis of leprosy in this study involved more men than women and more people over 15 years of age than children below that age. The mean delay in diagnosis in our study was 26.6 months, much shorter than described in China at 64.1 months or in Colombia at 35.5 months, but longer than in India at 23.2 months, in Brazil at 25.5 months and over 12 months observed in Mozambique in 2013.[12,25,27–29] A recent study in Ethiopia using the PEP4LEP questionnaire reported a mean delay of 22.0 months.[30]

The delay observed in our study was also shorter than the mean case detection delay of 31.4 months reported in a recent systematic review that collected data on leprosy cases across several low-endemic countries.[31] However, we observed a very broad range of delays in the PEP4LEP study districts, with the longest delay reported at 292 months. In our survey, most patients (85.1%) reported a late diagnosis of more than six months after noticing the first signs/symptoms. Similar results were reported by Henry et al. in Brazil, who stated that 121 participants (99.2%) reported seeing a doctor within five years of the onset of symptoms in the community.[32]

Importantly, we used a newly developed and validated cultural context-specific questionnaire to determine delay in case detection in Mozambique, which differs from other studies in which delay in detection is typically estimated by basic questioning as part of the history of the disease during the clinical examination.[11,19] A strength of this study was that field activities were conducted by researchers with an understanding of the health system, access to national/district-level data and the ability to perform interviews using the local language. On the contrary, the design of the protocol and data collection had limitations determining factors associated with delayed diagnosis. This was mainly due to the limited sample size of 81 participants who were interviewed, insufficient to perform a meaningful subgroup analysis.

Conclusion

The National Leprosy Control Programme (Programa Nacional de Controlo da Lepra – PNCL) has faced serious challenges in their efforts to establish adequate control of leprosy in the PEP4LEP study areas. The districts of Meconta, Mogovolas and Murrupula would benefit from the implementation of increased active case finding activities, contact screening and chemoprophylaxis with SDR-PEP to help interrupt the chain of *M. leprae* transmission.

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Contributorship

All authors contributed to the study design and planning. AS, RvW, LM and JHR were responsible for the conceptualisation of the study. AS, RvW and LM did the overall project coordination. AM, YS, PHNMP, AMM and FM were involved in the coordination of local data collection and field work activities. AM, TH and RvW performed the data analysis. Drafting of the manuscript was performed by AM, TH and JHR. All authors read, revised and approved the manuscript.

Patient consent

Consent was collected from all study participants interviewed.

Data sharing statement

The data set generated and analysed during current study will be stored for a period of 25 years, according to the European Union regulation 536/2014, considering clinical medication related research projects and will be made available on reasonable request.[33]

Conflict of interest

All authors declared no conflict of interest.

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