Epidemiology and spatial exploratory analysis of leprosy in the district of Toliara, Madagascar

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Accepted for publication 21 June 2016

Summary
Objectives: As leprosy case-notification is plateauing worldwide, a more targeted approach including contact tracing and possibly treating hotspots becomes necessary. This study aims to provide an update on the epidemiology of leprosy in the District of Toliara by comparing the local leprosy indicators to national data, along with a geographical exploration of patient’s origin and identification of hotspots.

Results: A cohort of 87 patients who started polychemotherapy (PCT) in 2013–2014 was identified at the principle hospital of Toliara. When compared with national findings, two-tailed z scores for proportions (95% confidence interval) indicate a significantly lower proportion of MB cases (79%, \( P = 0.01 \)), a higher proportion of females (39%, \( P = 0.001 \)) and a lower proportion of PCT completion in MB patients (59%, \( P = 0.00001 \)) in this cohort. Two maps were generated illustrating origin of patients by municipality and hotspots in the urban area and coastal rural regions along the Route Nationale 9 (RN9).

Conclusions: This study demonstrates the differences in leprosy indicators when comparing Toliara district to Madagascar’s national data with a significantly low PCT completion rate in this patient cohort. A geographical exploration on patient’s provenance reveals the appearance of hotspots especially in easily accessible municipalities. In interpreting hotspot analysis and eventually selecting appropriate strategies/interventions, care should be taken to take account of possible underestimation of leprosy burden in rural and difficult-to-reach areas.

Keywords: leprosy, epidemiology, spatial analysis, contact tracing, Toliara-Madagascar

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**Introduction**

From an epidemiologic perspective, morbidity due to leprosy continues to be an important problem with some degree of stagnation in leprosy case-notification being observed worldwide. The WHO Afro lists Madagascar as the country with the third highest case-notification rate in Africa, after the Democratic Republic of Congo and Ethiopia.\(^1\) Indeed, case-notification remains branched between 1474 and 1763 cases per year since 2006. The proportion of Grade 2 disability at the time of diagnosis is stagnating with 1·2 cases per 100,000 inhabitants in 2010 (14·6% of all leprosy cases) and 1·3 cases per 100,000 inhabitants in 2013 (17·3% of all leprosy cases).\(^2,3\)

The 2015 objective of the enhanced global strategy aims at a 35% reduction of Grade 2 disabilities at the time of diagnosis compared to 2010. This way, early diagnosis and treatment remains the main strategy in leprosy control. There is a need for more targeted approaches with campaigns tailored for persons at risk and with specific consideration for their local context.\(^4\)

Furthermore, the World Health Organization (WHO) has recently regained interest in contact-tracing and post-exposure prophylaxis (PEP) with single-dose rifampicin (SDR) and possibly blanket administration of rifampicin for so called ‘hotspots’ (high-incidence areas) and ‘hotpops’ (confined high-incidence populations).\(^5,6\) Pilot projects to assess contact tracing and PEP and their effect on leprosy transmission are currently being developed on an international scale. In South-East Asia, well-established contact-tracing programmes are already functional. Examples from Thailand and Cambodia include Rapid Village Surveys and Contact Drives (home visiting of patients and their neighbours), requiring supportive mapping of the targeted area.\(^6\)

Until the present time, contact tracing was not routinely integrated in the national leprosy services of Madagascar. In order to prepare for such campaigns, this study aims to provide an update on the epidemiology of leprosy in the District of Toliara with comparison of the local leprosy indicators to Madagascar as a whole, complemented by a geographical exploration of patient’s origin and identification of hotspots.

**STUDY AREA**

Madagascar is the world’s fifth poorest country as estimated by the per capita Gross Domestic Product. The total population in 2014 was 22,434,363.\(^7\) Madagascar’s Human Development Index (HDI) value for 2014 was 0·51 (category low HDI), ranking it globally at 154 out of 188 countries. For the same year, adult literacy rate was 64·5% and mean years of schooling was only 6.\(^8\) Religion consists of 50% indigenous beliefs, 42% Christianity and about 7% Islam.\(^9\) There are 22 regions and 114 districts, typically subdivided in five to 20 communities. The districts of Toliara I (urban zone) and Toliara II (rural zone) are located in the South-West of Madagascar (Atsimo Andrefana region). Toliara I counts 156,710 inhabitants and Toliara II has 264,301 inhabitants, 23 communities and 294 fokontany (the lowest administrative unit in Madagascar).\(^7\) The main way of travelling is by taxi-brousse over mostly degraded routes.

**Material and Methods**

**DATA COLLECTION**

The study was performed at the leprosy reference centre in the principal hospital of Toliara (Centre Hospitalier Régional aurea B) located in the city centre. Patient treatment cards of all
patients on polychemotherapy (PCT) who started treatment between 01.01.2013 and 31.12.2014 were studied. To receive treatment, patients had to fulfil the clinical criteria of leprosy according to the WHO (skin lesion consistent with leprosy and with definite sensory loss, with or without thickened nerves) and/or have positive skin smears. Diagnosis was made by well-trained health staff (one medical doctor and two nurses). Next, a two-tailed z-score for proportions for a 95% confidence interval was calculated to compare the epidemiological indicators in leprosy found for the district of Toliara with the national indicators.

SPATIAL EXPLORATORY ANALYSIS

A database was constructed with all patients’ addresses as recorded at the beginning of PCT. This database was linked to the official INSTAT municipality list of Madagascar, allowing calculation of the number of patients for each municipality. For the region of Atsimo Andrefana, where all the patients but two are based, a map was developed in ArcGIS representing the provenance of the patients. Next, the Getis-Ord G statistic was applied to identify possible hot spots. For this exploratory analysis, the null hypothesis (H0) was random distribution of leprosy patients across the study area based on uniform probability. Statistical significance is then determined by the degree in which the detected distribution has deviated from a complete random spatial pattern. Due to the continuous nature of the case-notification rates and the strong influence of spatial proximity, the inverse distance method is preferred for the conceptualisation of spatial relationships.

Results

Epidemiology

The total number of patient treatment cards was 87 with 45 patients starting PCT in 2013 and 42 in 2014. Case detection rate as calculated with a denominator including inhabitants of both Toliara I and II (a total of 421,011 inhabitants) was 11 per 100,000 in 2013 and 10 per 100,000 in 2014. The female proportion was 39% (n = 34). Multibacillary leprosy (MB) as defined clinically (five or more skin lesions) and/or as demonstrated with a positive skin smear was found in 79% of the cases (n = 68). The proportion of children aged 0–14 years was 10% with nine children identified, of which seven were MB. The youngest patient was 5 years old, median age was 26 and the average age was 31. Figure 1 shows the age distribution for this cohort.

Out of 87 patients, 85 were assessed for disabilities (98%). Five patients (6%) were identified with disability Grade 1 and 16 (18%) were found to have a disability Grade 2 at the time of diagnosis (or 3·8 per 100,000). In 77% (n = 10) of cases, patients with paucibacillary leprosy (PB) diagnosed in 2013 completed their 6-month treatment regimen. For MB patients who started PCT in 2013, 59% (19 out of 32) completed a 12-month treatment. Among MB patients not completing PCT (n = 13), the average duration of treatment was 5 months, and the median time 3·5 months. Women represented 69% (n = 9) of non-completers. We noted two patients completing treatment for PB before, who were enrolled during the current study for MB-PCT (relapse proportion of 2·3%). Table 1 summarises the epidemiological indicators found in Toliara district in comparison with the whole of Madagascar. A significant difference was found for MB proportion (lower in Toliara district with P = 0·01), female
proportion (higher in Toliara district with $P = 0.001$) and PCT completion for both MB and PB (lower in Toliara district with $P = 0.00001$).

**Spatial Exploratory Analysis**

Two maps were generated. Figure 2 represents the provenance of leprosy patients and detection rate per municipality.

At a glance, the highest detection rates are seen in the urban area of Toliara I and along the coastal rural areas of Toliara II. Hotspot analysis (Figure 3) confirms that these detection rates are significantly higher than expected merely based on random distribution.

For the rural municipalities, the minimal distance (as measured from the centre of each municipality) to the study hospital was 4 kilometers, the maximum distance was 181 kilometers and the median distance was 62 kilometers (average 68 kilometers).

**Discussion**

**Limitations**

Due to practical considerations, this study was performed as a one-off analysis. It does not allow any detection of trends of the epidemiological data. Reliability of data depends both on the accuracy of file completion by health staff and on correct patient information. For the

| Table 1. Summary of leprosy indicators of the Toliara cohort compared with national data |
|-----------------------------------|--------------------------------------|----------------|----------------|
|                                   | Hospital B, Toliara                  | Madagascar total (2) | Z-score | P-value |
| Detection rate 2013              | 11 per 100'000                       | 7 per 100'000      | 0.04   | 0.97    |
| MB proportion                    | 79%                                  | 88%               | 2.58   | 0.01    |
| Child proportion                 | 10%                                  | 9%                | 0.33   | 0.74    |
| Female proportion                | 39%                                  | 24%               | 3.28   | 0.001   |
| Disability grade 2 proportion    | 18%                                  | 18%               | NA     | NA      |
| PCT completion (MB)              | 59%                                  | 85%               | 6.79   | 0.00001 |
| PCT completion (PB)              | 76%                                  | 95%               | 8.13   | 0.00001 |
| Relapse proportion               | 2.3%                                 | 1%                | 1.22   | 0.22    |
Figure 2.

Provenance of leprosy patients treated in Hopital B, Toliara
Region: Atsimo Andrefana

Legend
- Leprosy center
- District capital
- Secondary road
- Primary road (RN)
- Region
- District
- Municipality

Detection rate (/10000 inhabitants)

DISTRICT TOLIARA
Avg. detection rate: 2.57/10000

0 25 50 100 150 200 km
cartography section especially, we cannot exclude patients giving false addresses as stigma remains a considerable burden for leprosy patients;\textsuperscript{13} e.g. two patients gave an address outside the Atsimo-Andrefana region. Also the denominator used for the calculation of the detection rate might not be fully realistic as patients are not \textit{stricto sensu} from Toliara district.
Concerning the hotspot analysis, an option would be to take travel time and travel cost into account to conceptualise the spatial relationships between the municipalities. However, local affordable transportation is extremely unpredictable, especially during the rainy season, while the travel cost is proportional to the distance travelled. The poor road infrastructure implies that the closer an area is, the easier it is to reach. This way, the inverse physical distance is a reliable data source to reflect the spatial interaction between the municipalities.

**Discussion**

When comparing data from Tulear with Madagascar as a whole, significant differences were found for MB proportion, female proportion and PCT completion.

The lower MB proportion found in Tulear could be a consequence of the fairly young age of the cohort as children tend to be less affected by MB leprosy. The female proportion in our study was well above 30%, whereas national data state only 24%. This finding suggests that in other areas in the country women might have even more difficulty accessing leprosy services. This subject however, merits an in-depth exploration per se and is beyond the scope of this study. Interestingly, when a cohort is studied in a prospective way, with follow-up and examination on a regular basis, more women and less MB cases are also generated. This similarity might be explained by high awareness among health staff and the population in our area of interest and by less gender inequality in access to health care. Next in this study, 76% of PB patients completed the 6-month treatment regime, and 59% of MB patients completed the 12-month treatment. Our study does not include details on whether these unacceptably low proportions are due to incorrect treatment registration, stock breaks, patient death or defaulting. Remarkably, women represent almost 70% of MB treatment defaulters. Albeit interpreting only very small numbers, women still seem to have suboptimal access to continuous medical care. With a median treatment time of 3.5 months, an effort to reduce defaulters in this programme is expedient.

**SPATIAL EXPLORATORY ANALYSIS**

A comparison was made on the level of municipalities because of scale related issues when comparing fokontany’s, the lowest tier of administrative divisions in Madagascar. The Atsimo-Andrefana region alone officially counts 1,527 of such divisions. Furthermore, the official division often differs from its local interpretation.

The hotspot analysis demonstrates a statistically significant higher detection rate in Toliara I (urban region) and in the Toliara II rural coastal regions of Anakao, Betsinjaka, Mitsinjo Betanimena, Belalanda and Manombo Sud. These findings should be interpreted with caution, as the definition of hotspots is only vague at this exploratory stage and the association between patients is subjected to spatial proximity and cannot be interpreted as a formal analysis. We do note that all hotspots north of Toliara I are located along the ‘Route Nationale 9’ (RN 9). Additionally, the hotspot of Anakao has an easily accessible free boat connection on a daily basis to urban Toliara. On the other hand, municipalities along the ‘route nationale 10’ (RN 10) seem cold spots as patients there most probably go to the well-known leprosy treatment centre near Betioky. In the Atsimo-Andrefana region, the mean proportion of the population living below the poverty line of 1.25 US$ purchasing power parity (PPP) is 82%.
National data show a tendency of higher proportions of poverty in the rural areas and lower proportions in the urban zones. We also emphasise that the roads in rural Toliara are heavily degraded and almost impassable after the rainy season. This way, we cannot exclude an underestimation of the detection rate of other rural cold spots, as they are sometimes extremely difficult to reach and poor.

Conclusion

This study demonstrates the differences in leprosy indicators when comparing Toliara district to Madagascar’s national findings. Worryingly low PCT completion rates in our patient cohort urge an effort to reduce defaulters. A geographical exploration on patient’s origin reveals the appearance of hotspots especially in easily accessible municipalities. When interpreting hotspot analysis and eventually planning contact tracing, we warn of the underestimation of leprosy cases in rural and difficult to reach areas.

List of abbreviations

HDI: Human Development Index
INSTAT: Institut National de la Statistique de Madagascar
MB: multibacillary leprosy
PB: paucibacillary leprosy
PCT: Polychemotherapy
PEP: post-exposure prophylaxis
PPP: Purchasing Power Parity
RN: Route Nationale
SDR: single-dose rifampicin
USD: United States Dollar
WHO: World Health Organization

Ethical clearance

Ethics approval was not required for this study.

Authors’ contributions

VS analysed and interpreted the cohort data and is the principal author of the manuscript. TL was responsible for the geographical exploration and mapping in ArcGIS.

Acknowledgements

The authors declare no sources of funding for this study. We would like to thank Dr. Bertrand Cauchoix MD, specialist in public health and medical counsellor, Fondation Raoul Follereau, for introducing us to the leprosy program of Madagascar and inspiring us for this research.
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