Trends and spatial clustering of leprosy cases over a decade in a hyper-endemic area of western Maharashtra, India

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Summary  India accounts for 58.8% of globally reported new leprosy cases, wherein the Raigad district continues to report a high annual new case detection rate. The objective of this study was to assess the effect of integration of leprosy treatment into the public health system across 5 Public Health Centers (PHC) in this area. Spatial clustering and trends of leprosy cases prior to and post integration are reported. The study findings show a drop in prevalence rate (PR) was similar across all 5 PHC’s with a steeper drop post integration into the public health system. A higher PR in 2007–08 was the result of an active survey. Post 2005, a higher proportion of MB cases indicate delayed diagnosis. An average of 7.95% ± 2.4% cases presented with some form of deformity and 19.54% ± 5.6% of total cases were child cases both higher than the national average.

Some areas of high clustering before integration were not identified as clusters later, indicating reduced prevalence. The lack of high risk clusters in the post integration period may be due to passive detection of cases which is supported by an active survey that identified new cases.

Spatial scans enabled the identification of clusters across adjacent areas which overcome administrative boundaries. This emphasizes the need to analyze disaggregated data to get a broader perspective of leprosy. Thus, analyzing prevalence in conjunction with key indicators such as presence of MB cases, child cases and deformity and their spatial distribution provided a more comprehensive assessment of the situation of leprosy.

Keywords: Hyper-endemic leprosy, Mycobacterium leprae, spatial clustering, Sat Scan

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Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, affecting mainly the skin and peripheral nerves which can progressively worsen if left untreated, resulting in deformities and nerve damage. The introduction of Multi Drug Therapy (MDT) has resulted in a significant reduction in the number of leprosy cases reported worldwide.\(^1\) The WHO resolved to eliminate leprosy through the reduction of its prevalence rate (PR) to less than 1/10,000 by the year 2000.\(^2\) The assumptions underlying the leprosy elimination and control strategy is that MDT will reduce transmission by reducing the number of contagious individuals in the community. However, despite a decline in the number of cases reported, a few countries continue to remain endemic for leprosy with certain regions continuing to report a high Annual New Case Detection Rate (ANCDR).\(^1\) Thus, there remains the need to identify such regions in order to identify possible reasons for continued presence of cases and provide measures of early diagnosis in such areas. Even within endemic countries, different regions report significant variations in the prevalence of leprosy.\(^3\)–\(^5\)

India continues to report the highest number of cases with diverse statistics from various regions. India accounted for 58·81% of the cases reported globally in 2014 emphasizing the need for greater scrutiny of its epidemiology.\(^1\) The western state of Maharashtra, which achieved overall elimination levels of leprosy in 2010, has also been identified as one of the states with a high number of new cases in several of the districts.\(^2\)–\(^6\) The Raigad district in western Maharashtra continues to report a high prevalence rate (PR) of 1·8 per 10,000 and ANCDR of 32·48/100,000 in 2010.\(^6\)

The assessment of indicative factors, including prevalence, child cases and cases presenting with deformity, at a single time point may not suitably infer the relationship of these indicators to infection or disease progression considering the estimated long incubation period of leprosy. Nevertheless, a high ANCDR and the detection of child cases areas indicates active transmission and may be used to determine endemic areas.\(^2\)

The significance of spatial clustering techniques to identify clusters of leprosy cases has been demonstrated in different areas. In India, endemic areas were identified\(^5\) and leprosy was associated with dense urban populations.\(^7\) In Brazil, leprosy was associated with poorer sections of the population in Sao Paulo,\(^8\)–\(^9\) while migration of cases into the urban centers was also noted to affect the distribution of cases.\(^11\)–\(^13\) A study in Ethiopia showed that viability of *Mycobacterium leprae* is related to proximity to a water source and the temperature of the environment.\(^13\) On the other hand, mapping cases in Bangladesh did not reveal significant spatial clustering at the micro-level but overall clusters were detected over 15 years.\(^14\) Such an assessment may reveal clusters of cases within endemic areas and have an impact on monitoring and surveillance activities in such areas.

Observations of child cases and a high ANCDR in the selected study area suggests that this is an ideal locale to delineate spatial clustering.\(^2\)–\(^15\) The objective of this study was therefore to assess the effect of integration of leprosy treatment into the public health system in an endemic area by assessing trends of spatial clustering in conjunction with key leprosy indicators for 5 years prior and 6 years after integration. The assessment of temporal and spatial trends of leprosy was undertaken in Panvel block of Raigad district covered by 5 Public Health Centre’s (PHC) over 11 years from 1999 to 2010. This time frame covers leprosy prevalence trends 5 years prior and 6 years after the completion of integration of leprosy treatment into the public health system, as of 2004 and enables an evaluation of the same. Spatio-temporal trends were analyzed in combination with other indicators of leprosy
such as deformity and MB cases that may indicate a delay in diagnosis as well as the presence of new and child cases that may indicate continued transmission of the disease.

Materials and Methods

STUDY AREA
Panvel block includes 166 villages with a total population of 422,522 as per the 2001 census which increased to 570,216 in 2011. It extends over 50 sq. km and is covered by 5 PHC’s (indicated as Rural 1 – 5 respectively) and 1 Rural Hospital (RH). With the exception of Panvel city and parts of Rural 1 area, all the other areas of Panvel block are rural. Their primary source of healthcare is the PHC and 1 Rural hospital (RH) in Panvel city. Rural areas in Panvel have very few private medical practitioners so that most leprosy cases are thought to be registered by the PHC. Each PHC covers a population of 20,000 to 30,000 within which sub-centres cover a population of 5,000 to 8,000.

Prior to integration of leprosy diagnosis within the public health system, cases in this area were largely identified by health workers associated with an NGO dedicated to leprosy services in a vertical system. In addition to this, the system of active case detection as well as the practice of taking slit skin smears aided in the detection and appropriate diagnosis of cases. Post integration, the system relies on self-reporting of cases, diagnosis of cases is done mostly on the basis of clinical examination at the PHCs and treatment is home delivered through ASHA or Multipurpose workers (MPW).

DATA COLLECTION
Records available from 1999 to 2003 available with Kushthrog Nivaran Samiti (KNS) which is an NGO working with leprosy patients in the Panvel area. From 2003 onwards data collected from the Primary Health Centre (PHC) were examined. The time span of data collected ranged from April 1999 to March 2010. The information collected on each patient was coded to protect personal information. Cases detected by the Foundation for Medical Research (FMR) from this area were also included in this list. Data collected was entered manually by double entry verification.

ANALYSIS OF TRENDS
Trends of prevalence rates, clinical classification, age, gender, presence of deformity and number of cases seeking retreatment (recorded under zero registry by the PHC post 2004) over the years were assessed. The trends were analyzed over the 11 year period as well as separately for the pre (April 1999 to March 2005) and post (April 2005 to March 2010) integration in the year 2004. This time frame was selected in accordance with the PHC working year (1st April to 31st March).

STATISTICAL ANALYSIS
Comparison of data between pre and post integration period was assessed for clinical classification, age, gender, presence of deformity and number of cases seeking retreatment on all recorded leprosy cases, using Chi square test of significance (IBM SPSS Inc, USA).
SPATIAL ANALYSIS

The Kulldorff’s SaTScan Statistics\textsuperscript{14} was used to identify whether space-time disease clusters of leprosy exists and to examine if they are statistically significant. The space-time scan statistic is defined by a cylindrical window with a circular (or elliptic) geographic base and with height corresponding to time. The base is defined exactly as for the purely spatial scan statistic, while the height reflects the time period of potential clusters. The cylindrical window is then moved in space and time, so that for each possible geographical location and size, it also visits each possible time period. In effect, we obtain an infinite number of overlapping cylinders of different size and shape, jointly covering the entire study region, where each cylinder reflects a possible cluster. The scan statistic provides a measure of whether the observed number of leprosy cases is unlikely for a window of that size, using reference values from the entire study area.

SatScan in the study was performed using the Poisson model. Space-time clustering was examined using the centroid of each sub-centre as the location (coordinate) values. The data set was transformed into a Poisson model data set using each record with the spatial location, total number of cases per year compared to the base population of each village (between 1999 and 2010). (SatScan v 8.2.1, 2009).

Results

TEMPORAL TRENDS IN PREVALENCE OF LEPROSY IN PANVEL

A total of 2633 cases were recorded between Apr 1999 to Mar 2010. The prevalence rate of leprosy over 11 years across all PHC’s is depicted in Figure 1. The trend of a drop of PR of leprosy over the years was similar across all 5 PHC’s with a steeper drop in PR in 2004 when leprosy treatment was integrated into the public health system and when active case detection was discontinued. A higher PR reported in 2007–08 is the result of an active survey conducted where a high number of previously undetected cases of leprosy were observed (Figures 1 and 2).\textsuperscript{15}

![Figure 1. Temporal trends in the prevalence of leprosy from April 1999 to March 2010. The trends observed by the Public Health system across all 5 PHC’s with a reduction in PR in the post 2004–2005 period. The peak observed at the time period of 2007–2008 is the result of an active survey.](image-url)
The classification of cases reported in the pre and post 2004 period is reported in Table 1. The proportion of MB cases increased from an average of 47·8 ± 4·4% to 56·05 ± 3·8% in the post 2004 time period (Figure 2; Table 1). Although the number of child cases (< 15 yrs) significantly reduced post 2004 from 23·84 ± 1·7% to 15·95 ± 5·1, it is still high compared to the national average of 9·7 ± 0·17% between 2008 and 2012.6,16

There was no significant variation between the pre and post integration period in the categories of gender, cases presenting with deformity and those seeking retreatment. An overall average of 56·7 ± 4·9% cases were male. Over the past 11 years the Panvel block has reported a higher number of cases presenting with some form of deformity 7·95 ± 2·5% compared to the National average of 3% ± 0·1% observed between 2008 and 2012 as well as a higher proportion of cases seeking retreatment (Table 1).

**SPATIAL ANALYSIS**

Applying Kulldorff Space time Scan Statistics17 to the spatial data set and scanning for high and low rates using the Poison model for the time period from 1999 to 2010 identified statistically significant clusters of areas under “most likely cluster” and “secondary clusters”. The Table 2 gives a detailed list of Panvel areas under “most likely cluster” and “secondary

**Table 1.** Comparison of case distribution observed in the time period pre and post integration of leprosy case care with public health services

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Overall average over 11 years</th>
<th>Pre 2004</th>
<th>Post 2004</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of MB cases (%)</td>
<td>50 ± 7·9</td>
<td>47·8 ± 4·4</td>
<td>56·05 ± 3·8</td>
<td>&lt;0·05</td>
</tr>
<tr>
<td>Proportion of cases &lt; 15 yrs (%)</td>
<td>19·53 ± 5·6</td>
<td>23·84 ± 1·7</td>
<td>15·95 ± 5·1</td>
<td>0·173</td>
</tr>
<tr>
<td>Proportion of male cases (%)</td>
<td>56·7 ± 4·91</td>
<td>56·83 ± 1·5</td>
<td>56·60 ± 6·8</td>
<td>0·167</td>
</tr>
<tr>
<td>Deformity (%)</td>
<td>7·95 ± 2·5</td>
<td>7·50 ± 1·6</td>
<td>8·33 ± 3·1</td>
<td>0·224</td>
</tr>
<tr>
<td>Previously treated cases (%)</td>
<td>13·39 ± 16·2</td>
<td>&gt; 1%</td>
<td>24·2 ± 14·7</td>
<td>&lt;0·05</td>
</tr>
</tbody>
</table>
### Table 2: Summary of most likely clusters observed in the Panvel area

<table>
<thead>
<tr>
<th>Location</th>
<th>Cluster</th>
<th>Villages covered</th>
<th>Area radius (km)</th>
<th>Time</th>
<th>No of observed cases</th>
<th>No of expected cases</th>
<th>RR*</th>
<th>LLR^</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>Most likely</td>
<td>4.71</td>
<td>2005 to 2010</td>
<td>180</td>
<td>585.33</td>
<td>0.26</td>
<td>230.76</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Secondary clusters</td>
<td>45 villages (Adjacent area of Rural 4 and 5)</td>
<td>15.3</td>
<td>1999 to 2003</td>
<td>382</td>
<td>142.59</td>
<td>2.96</td>
<td>148.93</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 villages (Rural 1)</td>
<td>3.96</td>
<td>1999 to 2003</td>
<td>306</td>
<td>106.13</td>
<td>3.13</td>
<td>132.29</td>
<td>0.001</td>
</tr>
<tr>
<td>Rural 1</td>
<td>Most likely</td>
<td>22 villages</td>
<td>7.52</td>
<td>1999 to 2003</td>
<td>454</td>
<td>111.42</td>
<td>6.76</td>
<td>374.72</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Secondary clusters</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural 2</td>
<td>Most likely</td>
<td>26 villages</td>
<td>6.85</td>
<td>1999 to 2002</td>
<td>106</td>
<td>42.54</td>
<td>3.21</td>
<td>41.1</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Secondary clusters</td>
<td>3 villages</td>
<td>1.16</td>
<td>2005 to 2010</td>
<td>0</td>
<td>27.79</td>
<td>0</td>
<td>29.25</td>
<td>0.001</td>
</tr>
<tr>
<td>Rural 3</td>
<td>Most likely</td>
<td>6 villages</td>
<td>3.5</td>
<td>1999 to 2003</td>
<td>75</td>
<td>21.16</td>
<td>4.34</td>
<td>46.31</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Secondary clusters</td>
<td>10 villages</td>
<td>2.91</td>
<td>2005 to 2010</td>
<td>26</td>
<td>68.28</td>
<td>0.33</td>
<td>20.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Rural 4</td>
<td>Most likely</td>
<td>17 villages</td>
<td>5.96</td>
<td>2005 to 2010</td>
<td>36</td>
<td>100.21</td>
<td>0.31</td>
<td>31.81</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Secondary clusters</td>
<td>1 village</td>
<td>0</td>
<td>2005 to 2010</td>
<td>21</td>
<td>3.9</td>
<td>5.56</td>
<td>18.52</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 villages</td>
<td>6.03</td>
<td>2005 to 2010</td>
<td>33</td>
<td>68.1</td>
<td>0.45</td>
<td>12.46</td>
<td>0.004</td>
</tr>
<tr>
<td>Rural 5</td>
<td>Most likely</td>
<td>14 villages</td>
<td>2.91</td>
<td>2005 to 2010</td>
<td>11</td>
<td>46.13</td>
<td>0.21</td>
<td>21.96</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Secondary clusters</td>
<td>2 villages</td>
<td>1.06</td>
<td>2002 to 2006</td>
<td>33</td>
<td>8.39</td>
<td>4.34</td>
<td>21.76</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 villages</td>
<td>1.41</td>
<td>1999 to 2001</td>
<td>30</td>
<td>9.87</td>
<td>3.29</td>
<td>14.02</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*RR - Relative risk.

^LLR - Log likelihood ratio.
clusters” with their levels of significance of villages with high and low relative risk. Map 1 shows the significant “most likely” and “secondary” clusters of villages with high and low risk.

The space-time analysis of leprosy indicated the highest prevalence was reported over 1999 to 2003 across Rural 1 (Table 2, Map 1) with a spatial dependency of 7·52 km covering 22 villages with a relative risk of 6·76. Similarly, most likely cluster and secondary clusters across Rural 2, Rural 3, Rural 4 and Rural 5 of varying radius of spatial dependency are also shown.

The pre 2004 period identified significant high risk clusters in Rural areas 1, 2 and 3. Most likely clusters identified in the post 2004 time frame were in Rural areas 4 and 5 (Map 1). Compared to the time period from 1999 to 2004, a lower relative risk of disease was statistically interpreted in the time period 2005 to 2010 based on the data collected by the PHC and cases identified by active surveillance in 2008 (Table 2). No clusters with a high relative risk were identified in 2007 to 2008, despite an active survey which covered 90·8% of the population.

Map 1. Distribution of significant clusters of leprosy cases identified with high and low relative risk (RR). Map source - Village boundary map from Survey of India.
Discussion

This study assessed temporal and spatial trends of leprosy, between the year 1999 and 2010 in Panvel block, Raigad district. Most countries have reported a decline of the disease and India reported the achievement of elimination by 2005.\textsuperscript{18,19} Whilst the prevalence of leprosy reduced sharply following the introduction of MDT treatment, the PR of leprosy in India has remained similar since 2007 at 1·1/10,000.\textsuperscript{6,16} This study attempts to examine the paradox of a decline in PR in context of the current finding of a high number of MB cases, child cases as well as a high proportion of cases reporting with deformity in certain areas.

We found that the temporal trend of leprosy prevalence was similar across 4 of the 5 PHC’s (except Rural are 2 where prevalence remained low) with a drop in prevalence in 2004 when leprosy treatment was integrated into the public health system. The prevalence also remained low as expected for the referral hospital (Figure 1). While elimination campaigns and increased coverage in blocks were thought to have resulted in significant reduction in cases in Maharashtra,\textsuperscript{20} an active survey carried out in Panvel block showed the prevalence to be comparable to that in 2004 at 6·72 per 10,000 (Figure 2). This reinforced the need for active surveys for early diagnosis of leprosy and to examine that status of leprosy prevalence in a disaggregated manner.\textsuperscript{15}

As with most infectious diseases, clusters of leprosy cases have been detected in areas with previously reported cases\textsuperscript{13,14} as well as in areas with lower socio-economic status.\textsuperscript{7,8,12} Spatial scans have been useful in the identification of clusters of leprosy cases over a decade in this study. They have also enabled the identification of clusters across adjacent PHC areas which aids in overcoming administrative boundaries. It should also be noted that SaTScan does not identify irregularly shaped windows of the study area, which conflicts with the natural phenomenon of disease spread seldom taking a fixed shape such a circle. Secondly it does not take heterogeneity into consideration, thus spatial objects (leprosy cases) which may be part of a circle shaped window may not necessarily have anomalous behavior but by virtue of proximity to anomalous entities may be considered as a part of the anomalous window.

A reduction in the prevalence of leprosy in the time period post 2004; as indicated by lower relative risks reflect cases detected by the PHC and not cases that may seek private or alternative treatment. The detection of statistically likely clusters also varied between the pre 2004 period where villages in Rural areas 1, 2 and 3 were identified and post 2004 where clusters in Rural areas 4 and 5 were identified.

Some villages of high risk clustering in Rural areas 1, 2, 3 and 5 identified in the time period 1999 to 2004 were interpreted as low risk clusters in the later years indicating a reduction in prevalence in these areas. A lower relative risk in the post 2004 period in Rural area 1 may partly be explained by urbanization and the presence of private doctors, where cases may seek treatment from sources other than the PHC. A higher risk in Rural areas 4 and 5 in the post 2004 period may be explained by a higher tribal population largely served by the public health services. A rise in the number of MB cases largely from Rural areas 4 and 5 may indicate a delay in diagnosis following integration. Additionally, one village in the Rural 4 area was identified which continued to report a higher number of cases in the pre and post 2004 period. The lack of high risk clusters in the 2005 to 2010 period may also be due to passive detection of cases by the health system which is supported by an active survey in the area which identified cases\textsuperscript{15} but these were not identified as a spatial cluster indicating that cases were not reported from any particular area.
Overall, the rise in the number of MB cases may be a result of a delay in diagnosis. Although the number of cases reporting with deformities has reduced post 2004, it continues to remain higher than the national average. A consistent proportion of child cases reported from this area over 11 years may indicate continued transmission of leprosy. This trend of higher MB and child cases is similar to that observed among an urban population in India\textsuperscript{20–22} and in Brazil.\textsuperscript{23,24}

Additionally, a higher number of cases seeking retreatment post 2004 (24·2% ± 14·7%) may be due to a change in data recording measures in the pre and post 2004 period as mentioned previously. From the records it was not clear whether these were treatment drop-outs or relapse cases. Alternatively, this may be due to the cessation of the practice of taking slit skin smears to evaluate the response of patients to treatment.

Our findings emphasize the need to analyze disaggregated data to get a broader perspective of leprosy trends. The prevalence of leprosy in combination with spatial information along with key indicators such as number of MB cases, child cases and cases presenting with deformity has an added advantage in accurately assessing the situation of leprosy. Spatial distribution has aided in evaluating the status of leprosy in endemic areas.\textsuperscript{25} This has an additional advantage combined with other clinical and epidemiological data.\textsuperscript{24–27} However, since SatScan uses a fixed cylindrical window to assess spatial information, it may be slightly overestimate the burden of leprosy. Hence, it may be more appropriate to use spatial information in combination with other indicators of leprosy in order to gauge the situation of disease. Considering the continued reports of new cases, the National Leprosy Elimination Programme now aiming to undertake more intensive monitoring for early detection of new cases as well as IEC activities. Such an approach can aid in the identification of high risk areas and implementation of appropriate strategies for the same for the control of leprosy.

**Funding**

This study was financially supported by the Corpus grant awarded to FMR by the Jamsetji Tata Trust (Grant no: JTT/IG/SNB/JP/sdm/C/12/H/2006-07).

**Acknowledgements**

The authors gratefully acknowledge Nilesh Shahsane, Pratik Chaudhary and Mandar Raut (FMR) for assistance in data collection. Mr. Uday Thakar (KNS) and all field KNS staff and PHC staff for assistance in data collection. Dr. A. Ladda (District Health Officer) for permission to carry out this study.

**Contributors**

Sanjana Kuruwa – planned study, undertook fieldwork, analyzed data and wrote manuscript, Vasna Joshua – planned study, analyzed data and wrote manuscript, Vanaja Shetty – planned study and reviewed manuscript, Nerges Mistry - planned study and reviewed manuscript,
Nilesh Shahasane – undertook fieldwork and data entry, Pratik Chaudhary – undertook fieldwork and analyzed data, Mandar Raut – Undertook filedwork and data entry, Uday Thakar – planned fieldwork, KNS staff – assisted in fieldwork.

Guarantor

Nerges Mistry/Vanaja Shetty.

Ethical considerations

This study was approved by the Institutional Ethics Committee (No: FMR-IEC-LEP02-2010). Patient data was collected following permission from the district health officer.

Competing interests

All authors declare that the answer to the question on competing interest form are all ‘No’, and therefore have nothing to declare.

Independence of funders

We state that researchers and funders are independent.

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