The decline of leprosy in the Republic of Korea; patterns and trends 1977–2013

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Summary

Background: Though the World Health Organization declared the ‘elimination of leprosy as public health problem’ in 2000, the disease remains endemic in many countries. Current trends in incidence of infection and disease are unclear.

Methods: Data on leprosy prevalence between 1977–2013 and data on new leprosy cases detected in the Republic of Korea between 1989–2013 were analysed by age, sex, clinical types, mode of detection, family history, disability grading and geographical distribution.

Results: Both prevalence and incidence have declined greatly. There has been a shift to an increased proportion of multibacillary disease, and older age groups, consistent with a dramatic decrease in infection transmission in recent decades. An increase in proportion of cases with family history of disease is consistent with these declines. There is evidence that declines in infection and disease have been greater in the north of the country, as revealed in patterns by place of birth over time. Cases in immigrants now form a substantial proportion of leprosy disease in the Republic of Korea.

Conclusions: Leprosy has declined dramatically in the Republic of Korea in recent decades, and transmission of M. leprae may have effectively stopped. There remains a burden of care for individuals whose disease developed in the past, and there may be some additional newly detected cases among immigrants and among older individuals who acquired autochthonous infections decades ago.

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Introduction

In 2000, the World Health Organization declared the ‘elimination of leprosy as public health problem’, as its reported prevalence had declined to less than 1 case per 10,000 of the global population. This announcement, based on an arbitrary threshold, led to much discussion of the actual patterns and trends of leprosy in the world. There is evidence that prevalence has declined much more rapidly than incidence, as a function of shortened treatment regimens, but there remains considerable uncertainty about trends in incidence of new infections and disease in different parts of the world.  

Though overall global incidence trends do not indicate a dramatic decline in recent years, there is evidence for significant decreases in some countries. Countries where leprosy is in decline provide a unique perspective on the natural history of this disease. Studies in Norway and in Japan, have revealed important trends relating to geography (shifts to lower latitudes), special populations at risk (increasing proportion of cases among household or family contacts), and changing patterns by age, sex and clinical manifestation (shifts to older cases, increases in proportions male and multibacillary). Insofar as these trends are seen in other countries with a declining epidemic they are likely to indicate inherent characteristics of this infection and disease.

The Korean peninsula has been endemic for leprosy for at least 700 years, and the earliest existing data refer to 17,458 prevalent cases in 1953. The disease declined dramatically in recent decades, and the Republic of Korea reported just 255 prevalent and five newly detected cases in 2012. Just how and why this decline occurred, and what were the characteristics associated with transmission of infection over time, remain important questions whose answers may provide insights for leprosy control in other settings. We report an analysis of routinely collected data to explore in detail what has happened to leprosy in the Republic of Korea in recent decades.

Materials and Methods

Data were obtained from records of the Korean Hansen Welfare Association/Institute of Leprosy Research (KHWA/ILR), an NGO that was founded in 1948 and has been responsible for most case finding, treatment, and rehabilitation of leprosy patients in the Republic of Korea since 1977. KHWA maintains the national register of leprosy patients and is closely affiliated to the Institute of Leprosy Research, making the Association also capable of laboratory testing and clinical diagnosis. It is supervised by the Ministry of Health and Welfare (MOHW) and the Korea Centers for Disease Control and Prevention, and currently runs 12 outpatient clinics, 17 mobile clinics, three short-term admittance and treatment clinics, and six care facilities for people affected by leprosy in close collaboration with other NGOs. Other than the KHWA-affiliated institutions, there is only one national hospital specialising in leprosy remaining in the Republic of Korea, located in Sorok-do where the largest leprosarium was once located. There are still 91 ‘settlement villages’ around the nation. Many who may not necessarily be prevalent cases but are aged and with some degree of disability as the aftermath of leprosy still live in these villages. The villages are now being reintegrated into society.

The KHWA/ILR register of prevalent cases includes not only all those on chemotherapy of leprosy (as in most countries) but also all those ever diagnosed with leprosy who are still
undergoing treatment for leprosy-related illness or injury. Thus the figures of prevalent cases in the Republic of Korea, as reported to WHO, include individuals described as being ‘in care’ in many leprosy programmes. Prevalence figures from year 1977 were taken from annual summary reports of the KHWA.4

‘Incidence’ (case detection) data were extracted from electronic records of all cases newly detected between 1989 and 2013, held by the KHWA/ILR. Names and exact birth dates had been removed by KHWA/ILR to preserve confidentiality.

Data on cases diagnosed before 1989 were not available. No data were available from the Democratic People’s Republic of Korea (North Korea). The following variables were extracted onto a Microsoft Excel file for analysis: year of diagnosis, birth year, sex, result of slit skin smear examination, clinical type (multibacillary/paucibacillary), mode of detection, disability status at diagnosis, family history record, birth area and address at the time of diagnosis. Most analyses were restricted to individuals born in the Republic of Korea, assumed to be autochthonous cases. There were in addition six foreign-born cases, all identified in the last three years; one in 2011, two in 2012, three in 2013. These were included and highlighted in separate analyses by age and time.


Age-specific incidence rates were calculated for 10-year age bands, (0–9, 10–19, . . ., 70–79, 80–89) by dividing the number of cases in each age band by the population of each age band at a year within the 5 years period when the national census was carried out (1990, 1995, 2000, 2005, 2010), divided by five to obtain an average per annum rate. They were expressed in linear and log scales using the statistical package R.

Cases were classified as multibacillary (MB) or paucibacillary (PB) based upon whether Acid-Fast Bacilli (AFB) were or were not seen in slit skin smears.

The mode of detection was broken down into five categories; intensive survey, contact examination, notification, voluntary, and others. Intensive survey refers to large or small scale case-finding surveys carried out in different target populations. Contact examination refers to examinations of household and family contacts of new cases. Notification refers to a method of contact tracing carried out by leprosy-specialist health workers prior to 1997, which involved asking villagers if they knew of individuals with certain symptoms of leprosy in order to identify new cases. After 1997, notification meant having been referred to a leprosy-specializing institution, by a health worker from general hospitals and health centers. Voluntary implies that the case self-reported to a leprosy-specialist institution or NGO on their own initiative. The others category was used when there was ambiguity or difficulty in determining the method of detection.

Disabilities were assessed upon diagnosis, employing a disability scale similar to that recommended by WHO,7,8 though in Korea those with disabilities classified as Grade 2 by WHO scale were further subdivided, making a Grade 3 with most severe disabilities.4 In this paper we refer to cases with any disability or Grade 2 (or greater) disabilities, which are thus comparable to the WHO definitions.8

Geographical distribution was analysed by birthplace and by address at the time of diagnosis. Geographical areas were based upon official national administrative areas: 9 provinces (Gyeonggi, Gangwon, Chungcheongbuk, Chungcheongnam, Jeollabuk,
Jeollanam, Gyeongsangbuk, Gyeongsangnam, Jeju) and 8 mega-cities with more than 1 million population (Seoul, Incheon, Daejeon, Gwangju, Daegu, Ulsan, Busan, Sejong).

The study was approved by the Ethics Committee of the London School of Hygiene and Tropical Medicine.

Results

OVERALL PREVALENCE AND INCIDENCE

Figure 1 shows the trend in prevalence in the Republic of Korea from 1977 to 2013.

There were 4,393 prevalent cases in 1977, implying a rate of 1·21 cases per 10,000 population. There was a steady decline of prevalence rate over time, falling to 0·57 by 1986, and to only 0·04 in 2013. There were 517 newly registered leprosy cases between 1989 and 2013; date of birth was missing for one case. Figure 2 shows the trend in new case detection, from 62 cases or 0·15 per 100,000 population in 1989, to 3 cases or 0·01 per 100,000 population in 2013.

AGE DISTRIBUTION

Figure 3 shows the age distributions of new cases detected over the five time periods since 1989. There is a general shift to older ages, with the average age shifting from approximately 45 years to 65 years as marked by tall bold lines on each distribution. The numbers and proportions of younger cases have declined considerably in later years.

There appear to be outliers in younger age groups in 2004–2008: three cases aged 12, 16 and 22 years old. The youngest of these, a girl born in 1993 and diagnosed at age 12 in 2005 is currently the youngest known autochthonous case. She was detected by voluntary reporting, was diagnosed with multibacillary disease, and had a family history of leprosy, having been born in Jeollanam Province in the southern part of the country.

Six foreign-born cases were diagnosed in the 5 years 2009–2013, and are marked separately in Figure 3. All were relatively young (aged 20, 22, 24, 28, 29 and 31 years) and
appear as outliers compared to the autochthonous cases diagnosed over that period. They were recorded as from Sri Lanka (two cases), Bangladesh, Nepal, Indonesia, and Myanmar. The duration of their stay in the Republic of Korea was unknown.

Figure 4 shows the trends in age-specific incidence rates over time. Incidence declined steadily in all age groups, and the peak age moved to the right, consistent with a birth cohort effect, reflecting the temporal decline in transmission.

Figure 2. New case detection numbers and new case detection rates per 100,000 of population in the Republic of Korea over years. 1989–2013.

Figure 3. Age distributions at diagnosis of leprosy cases detected in the Republic of Korea, shown with mean ages as thick lines and relative frequency distributions (density estimation) as shaded areas, 1989–2013. Six foreign-born cases reported in the 2009–2013 period are plotted but not included in the density estimation, because they are not considered autochthonous.
OTHER VARIABLES (SEX, CLASSIFICATION, MODE OF DETECTION, DISABILITY GRADING AND FAMILY HISTORY)

Among the newly detected autochthonous cases since 1989, 279 were male (54%). There was no evidence of any significant change in sex ratio over this period.

Three hundred and seventy-seven (73%) of the cases were classified as multibacillary. The proportion of multibacillary cases increased steadily from 61% in 1989–1993 to 96% in 2004–2008 (with a slight decrease to 89% over the subsequent five years, based on only 18 cases) (Figure 5).

There were interesting trends in mode of detection over the years since 1989. As shown in Figure 6, the proportion of cases who self-reported (‘voluntary’) declined and the proportion found by ‘notification’ increased over this period. All of the cases detected by contact tracing

Figure 4. Age specific incidence rate for new leprosy cases detected in Korea in linear scale (a) and log scale (b). 1989–2013.

Figure 5. Numbers of new cases of Leprosy in the Republic of Korea, and proportions by clinical types Multibacillary/ Paucibacillary. 1989–2013.
had a family history, and more than half (10 out of 16) were less than 20 years of age. No cases have been identified by contact tracing since 1999, and by intensive survey since 2001 (official policy of having a health worker designated only for leprosy control was discontinued in 1997).

Out of 517 cases, 303 (59%) had leprosy-attributable disability at the time of diagnosis, and 113 (23%) were recorded to have disability Grade 2 or greater. Analysis by year of diagnosis (Figure 7) shows that the proportions of new cases with any disability and of those with disability Grade 2 or greater increased in the most recent decade.

Overall, 101 (20%) cases were reported to have a family history of leprosy, 146 (28%) cases were reported as having no such history, and 270 (52%) had no information on family history. When this variable is examined by year of birth, as in Figure 8, it shows a clear increase in proportion with family history over time. Out of 33 cases born after 1970, 24 cases (73%) had family history.
GEOGRAPHICAL DISTRIBUTION

The geographic patterns of cases over time are shown by address at birth (Figure 9a, b) and by address at time of diagnosis (Figure 9c, d), showing that the distribution of leprosy shifted towards the south over this period. The distributions by address at birth suggest a stronger association with the southern provinces than do the distributions by address at time of diagnosis.

Discussion

In this paper we describe epidemiological characteristics of the decline of leprosy in the Republic of Korea over a 36-year period (1977–2013). Several factors have contributed to this trend. WHO Multi Drug Therapy (MDT) was introduced in the Republic of Korea in 1982, and the national standard for completion of MDT treatment was officially established in 1985. At this time, those who completed the recommended MDT regimen were excluded from the registry data, if there were no more signs or symptoms and the skin smear was negative.4 Since then, the Ministry of Health and Welfare (MOHW) of the Republic of Korea has recommended MDT regimens longer than the WHO-recommended 1 year for multibacillary cases and 6 months for paucibacillary cases. In Korea, multibacillary cases receive MDT until their skin smear result turns negative, and paucibacillary cases receive treatment for 2 years.6 It should be noted that the longer treatment period will inflate prevalence data in Korea compared with other countries which use the shorter WHO-recommended regimen.

Incidence data as expressed by the case detection rate provide a better measure of transmission of \textit{M. leprae} than do prevalence data.9 The decline in case detection numbers has been consistent over the study period, with temporary excursions (i.e. 2000, 2001) most likely attributable to chance (Figure 2). Such dramatic decline in case detection in recent decades in the Republic of Korea is likely due to a combination of socio-economic and ecological factors.3 Socio-economic status influences general level of hygiene, crowding within households, and general health conditions including nutritional status and skin health, all of which have been suggested as possible contributing factors.10 The Republic of Korea has experienced a tremendous improvement in standard of living in recent decades, which is
Figure 9. Annual incidence rates of leprosy in the Republic of Korea by address at the time of diagnosis (a,b) and by birth place (c,d) over two period of time 1989–2000 (a,c) and 2001–2013 (b,d).
consistent with this decline in leprosy. In addition, The Bacille de Calmette et Guérin (BCG) vaccine has been administered since 1954 in the Republic of Korea, and might have had some effect on those born after 1954, though few data exist on its coverage until 1990 when 70% coverage was recorded. There may have been some underestimation of case numbers due to less intense case detection and lack of awareness on leprosy of health staff in most recent years associated with the decline of the disease. However, the overall effect of such under-recognition is likely to have been small.

Studies carried out in countries where leprosy has declined have found several factors associated with the declines, in particular shifting to older age groups, increases in multibacillary cases, increases in proportion of male cases, more cases with family history, and lower latitude regions being the last to have evidence of transmission. The patterns observed here for newly detected cases in the Republic of Korea in 1989-2013 are generally consistent with these trends and add new observations to be explored and explained.

The changes in age distribution of newly detected cases, shown in Figures 3 and 4, are entirely consistent with a dramatic decline in \textit{M. leprae} transmission in recent decades in this population. The great decline in young cases and steady increase in average age of newly detected cases, from approximately 45 to approximately 65 years, are consistent with the most recently detected cases having arisen from infections acquired many years ago. The high proportion of MB disease, which is known to have a relatively long incubation period, is consistent with this observation. The proportion male among newly detected cases has not changed appreciably in this population in recent years.

It is useful to consider the outliers in these age distributions. Those under 40 years of age during 2004–2013 stand out as being unusual. Three outliers in the period 2004–2008 were autochthonous cases (Figure 3). The case with the latest birth year (1993) is recorded as having a family history of the disease. The other two cases were reported as unknown family history, which means that either it was not actively asked or was not answered, perhaps due to the sensitivity that arises from social stigma. In this context it is important to note that almost half of the total cases were marked with no information on family history. It is likely that some cases that are marked as having no family history have hidden this history due to the same issue. Those detected due to contact tracing are more likely to have accurate records of family history, as all of 16 cases detected through contact examination were recorded as having a family history.

The six youngest cases detected in 2009–2013 were all foreign-born but residing in the Republic of Korea. Considering that there were only 18 autochthonous new cases between 2009 and 2013, the six foreign born cases were an appreciable proportion of all the new leprosy in the country. Similar declines in leprosy in recent years have reported elsewhere in East Asia. For instance, in Japan, a substantial proportion of new cases detected between 2001–2007 were recorded to be foreign-born, comprising 74% of total cases. In the case of the Republic of Korea, it is noticeable that all six cases came from countries with a relatively high burden of leprosy (Sri Lanka, Bangladesh, Nepal, Indonesia, and Myanmar). The Republic of Korea is experiencing increasing numbers of foreign workers in various sectors of its industries. Out of 985,923 foreigners officially residing in the Republic of Korea, 637,548 (65%) are from the 16 ‘high burden’ countries (i.e. with more than 1,000 new cases of leprosy detected yearly). While this is unlikely to affect the decline of transmission of \textit{M. leprae} in the Republic of Korea, it is appropriate to be aware of this trend when considering any future control strategy.
It is notable that records of family history according to birth year (Figure 8) show an increasing proportion of cases with family history over time. This too is consistent with an overall decline in transmission, as those with family history or close contact with leprosy are those most likely to have whatever are the risk factors for infection and disease.\(^2,3,13,17\)

It is interesting that the proportion identified by notification (identified by health professionals and referred to leprosy-specialised institutes) appears to have increased compared to those reporting voluntarily in recent years. Numbers are small, but this might reflect declining awareness of leprosy in the population, and confusion as to whether someone who reports for an unknown skin condition, which is later recognised by a health worker to be leprosy and then notified, should be classified in the voluntary or notification category.

Analysis of the proportion of cases with disability according to disability grading by year of diagnosis (Figure 7) showed a slight increase in the recent decade in proportions of new cases with any disability and of those with disability Grade 2 or greater. This may be attributable to chance, as numbers are small, but it also may have been influenced by the increase in age and a possible apparent increase in the delay to diagnosis of the more recent cases.

The geographic distributions of newly detected cases indicate that leprosy has declined most rapidly in the north of the country (Figures 9). The fact that this trend appears more clearly in analyses by place of birth, than by address at the time of diagnosis, is one further indicator of the decline in \textit{M. leprae} transmission in this population, as it is suggests that many of the recent cases were infected early in their lives. What has driven this geographic shift is unclear, but it may include ecological, climatic and socio-economic influences. It is important to note that a very similar shift has been documented in Japan where \textit{M. leprae} transmission may now have stopped, having last occurred in the southernmost island of Okinawa.\(^3\)

Taken together, these observations suggest that \textit{M. leprae} transmission may now have effectively stopped in Korea. A few new cases may be detected in years to come, almost all of them either immigrants infected in other countries, or older people whose autochthonous infections were acquired decades ago. It is appropriate to consider measures to tackle this issue of new incident cases among foreigners and in older age groups, even if they may be small in numbers.

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\textbf{Authors' contributions}

JL designed the study, wrote the protocol, analysed the data and drafted the paper. JPK advised on data collection and analysis and assisted in drafting the paper; NN advised on the protocol and assisted in the analysis and in drafting the paper. PF suggested the study, advised on protocol and an analysis, assisted in drafting the paper, and is the guarantor. All authors have read and approved the final submitted paper.
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