Epidemiological Characteristics of Leprosy and the Effects of its Control in Chongqing, China, 1949-2018

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Research Article

Keywords: Leprosy, Epidemic characteristics, Delay period, Treatment, Course of disease

Posted Date: August 18th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-58136/v1

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Abstract

Objective: To analyse the epidemiological characteristics of leprosy in Chongqing from 1949 to 2018 and evaluate the prevention and treatment effects over time to provide a basis for improving leprosy prevention and treatment strategies in Chongqing.

Methods: Epidemiological indicators such as the incidence rate, prevalence rate, and annual estimated percentage change (EAPC) were used to evaluate the prevalence of leprosy. The prevention and treatment of leprosy patients were evaluated by indexes representing delay in diagnosis, the cure rate and the course of the disease. The statistical software used mainly include SPSS20.0, GraphPad Prism 8, ArcGIS 10.7.

Results: From 1949 to 2018, a total of 3698 cases of leprosy were reported in Chongqing, with a sex ratio (male:female) of 3.814:1. The incidence of leprosy in the city peaked at 0.848/10^5 people in 1960 and remained below 0.100/10^5 people after 2004, achieving the World Health Organization (WHO) standard for the elimination of leprosy. The mortality rate remained at or below 0.100 per 100,000 people. The median time between disease onset and diagnosis in the whole population was 3.576 (1.435, 7.621) years. The early detection rate was 31.314%, and the rate of patients with grade 2 disability was 31.989%, which decreased significantly over time (χ^2=5.063, P=0.024). Compared with dapsone (DDS), multidrug therapy (MDT) was associated with a higher cure rate and a shorter disease course (χ^2=608.346, P=0.000).

Conclusions: Currently, leprosy in Chongqing remains in a low epidemic state. However, to maintain the status of meeting the WHO standards for the elimination of leprosy, there are some challenges that should not be overlooked by leprosy prevention workers. For example, the early detection of leprosy and the prevention and treatment of related disability still need to be strengthened.

Background

Leprosy is a chronic infection caused by Mycobacterium leprae that affects the skin, peripheral nerves and upper respiratory tract. If patients are not treated in a timely manner, severe disability may occur [1]. After 1982, the World Health Organization (WHO) proposed multidrug therapy (MDT), which greatly improved the cure rate of leprosy [2]. However, more than 200,000 new cases are still reported globally every year. Therefore, leprosy remains a prominent public health and social problem in some parts of the world, especially in South East Asia and Africa [3–5].

In China, there were 6,032 leprosy cases at the end of 2010, with a prevalence of 0.450 per 100,000 people. Although China generally meets the WHO standards for the elimination of leprosy, the regional distribution of leprosy patients is extremely variable, and the provinces with high prevalence rates are mostly concentrated in southwest China and parts of Guangdong and Xizang [6–7]. Chongqing is a relatively new first-tier city in southwest China. There have been remarkable achievements in the
prevention and treatment of leprosy in Chongqing over the past 60 years [8]. By the end of 2010, a total of 3,561 leprosy patients had been diagnosed and treated for free in the city. From 1978 to 2010, the annual prevalence rate of leprosy decreased by 3.42 per 100,000 people. In recent years, the epidemic situation of leprosy in the city has been sporadic, and challenges such as early detection, professional training and team building still exist. Therefore, through the statistical analysis of epidemic leprosy data from the whole city after the existing leprosy data of the detection system, we elucidated the epidemic characteristics and control effects of leprosy to comprehensively evaluate the epidemic trend and the latest epidemic situation in Chongqing and provide a strong scientific basis for the follow-up prevention and treatment of leprosy.

1. Materials And Methods

1.1 Data sources

Data from leprosy cases (1949–2018) were obtained from the epidemic surveillance database of the Chongqing Center for Disease Control and Prevention. Epidemiological data included new cases, follow-up visits and case investigations over the years. Population data comprised the total population in major years, which was obtained from The Statistical Yearbook of Chongqing in 2019 [9].

1.2 Evaluation Indexes

The prevalence of leprosy in Chongqing was evaluated by the annual incidence, prevalence, mortality over time, population and area. The time variation trend of each indicator was estimated with the estimated annual percentage change (EAPC) [10]. Taking incidence rate as an example, the EAPC calculation method was as follows: after logarithmic conversion of incidence rate of leprosy in each year, which was the dependent variable, and considering the year as the independent variable, the following fitting line was calculated: \( Y = b + aX, \ Y = \log(\text{incidence rate}), \) where \( X = \text{year} \). The, the EAPC was calculated as \((10^a - 1) \times 100\%\). A t test was used to judge whether it was a contingent change, that is, whether the annual change was sustained and stable.

The prevention and treatment effects of leprosy in each period were evaluated by the delay in diagnosis, disability ratio, cure rate and cure course in leprosy patients. Because leprosy is a chronic disease with a low mortality rate, it is of little practical significance to evaluate the mortality rate of leprosy, which is described in only a temporal epidemiological profile.

1.3 Statistical Methods

SAS 9.4 and Excel were used for data collection, SPSS 20.0 was used for data analysis, GraphPad Prism 8 was used for graph construction, and ArcGIS 10.7 was used to create the heat map of cumulative incidence. Descriptive analyses were always applied to the data. Chi-square tests were used for the comparison of rates. The test level was set at 0.05.

2 Results
2.1 Overview of leprosy cases over time

A total of 3698 leprosy patients were registered in Chongqing from 1949 to 2018. As seen in Fig. 1(1), the incidence of leprosy in the whole city increased rapidly from a low level and then decreased to a stable low level. The incidence of leprosy increased rapidly from $0.006/10^5$ people in 1949 to a peak of $0.848/10^5$ people in 1960. The incidence of leprosy fluctuated within the range of $0.085/10^5$ and $0.848/10^5$ people from 1959 to 2002 and the decreased to $0.048/10^5$ people in 2003. After that, the incidence of leprosy remained below $0.100/10^5$ people. According to the above, the onset of leprosy was divided into three periods. After analyzing the change in the morbidity rate and the EAPC, it was calculated that the EAPC in incidence from 1949 to 1958 was $12.460\% (P = 0.238)$; the change in morbidity in that period was not significant. From 1959 to 2002, the EAPC in the incidence was $-4.281\% (P = 0.000)$, that is, the incidence rate decreased at a rate of $4.281\%$ per year during that period. From 2003 to 2018, the incidence rate remained at a low level, at less than $0.100/10^5$.

By the end of 2018, the city reported 98 leprosy patients. As shown in Fig. 1(2), the number of cases rose rapidly in 1959 and peaked at 1021 in 1977, with a prevalence of $3.938/10^5$ people. By 2003, the number of cases had dropped to 169, with a prevalence of $0.540/10^5$ people. Since then, the prevalence rate has remained below $0.600/10^5$ people, achieving the WHO standard for the elimination of leprosy (a prevalence rate below $1/10^5$). Moreover, the mortality rate of leprosy remained below $0.100$ per 100,000 people, and the change trend was consistent with the incidence rate.

2.2 Regional Prevalence

A heat map was constructed according to the cumulative incidence of leprosy in each region from 1949 to 2018. As shown in Fig. 2, the Hechuan district had the most cases (351), followed by Fengjie County (304). According to the regional distribution, leprosy cases were more densely distributed in the northern and eastern areas than in the southern and western areas of the city. The incidence rate increased with distance from the main urban area.

2.3 Population Prevalence

2.3.1 Sex distribution

By the end of 2018, there were 2930 cases reported in males and 768 cases reported in females. The sex ratio was 3.814 to 1. As shown in Fig. 1(3), the annual incidence rate in males was significantly higher than that in females ($P = 0.000$). There were 73 male and 25 female leprosy patients in the whole city. The annual prevalence was significantly higher in males than in females ($P = 0.000$). The mortality rate in both male and female patients with leprosy remained low, and the mortality rate in male patients was significantly higher than that in female patients. The variation trends of the three rates were consistent with that of the total population rate.

2.3.2 Age Distribution
According to the existing literature, demographic data regarding the age distribution were available from only 1982 onwards. Leprosy affects residents of all ages. Among the 3698 patients, 117 children aged 1–14 years accounted for 3.164%, with an average annual incidence of 0.082/10^5 people. There was a total of 3445 patients who were 15–64 years old, accounting for 93.158% of the total sample, and the average annual incidence was 0.904/10^5 people. Among the elderly population aged 65 years and older, 136 cases occurred, accounting for 3.678%, and the average annual incidence was 0.240/10^5 people. Clearly, leprosy mainly occurred in people aged 15–65 years, and the average annual incidence was significantly higher in this age group than the other two age groups, as shown in Fig. 1(4).

2.4 Diagnosis, Treatment And Disease Course Of Leprosy

2.4.1 Diagnosis

The median time between the onset and diagnosis of leprosy in the whole city was 3.576(1.435, 7.621) years. A total of 1158 cases were diagnosed within 2 years, with an early detection rate of 31.314%. A total of 1170 cases were diagnosed within 2 ~ 5 years, with a detection rate of 31.639%. A total of 1370 cases were diagnosed within 5 years, with a detection rate of 37.047%. The distribution of leprosy patients with different diagnosis delay times was significantly different in different years ($\chi^2 = 133.852, P = 0.000$). As shown in Table 1, the proportion of patients diagnosed within 2 years of onset fluctuated greatly in the first 10 years but increased starting in 1964. The proportion of patients with a delayed diagnosis of 5 years or more reached a maximum of 42.395% in 1979 to 1983, followed by a downward trend.

From 1949 to 2018, a total of 1709 leprosy patients were registered as without disability at the time of diagnosis, with a disability-free rate of 50.413%. There were 598 patients with grade 1 disability, and the rate of grade 1 disability was 17.640%. There were 1083 patients with grade 2 disability, and the rate was 31.947%. The distribution of leprosy patients with different degrees of disability was significantly different in different years ($\chi^2 = 71.885, P = 0.000$); 310 patients with an unknown degree of disability were not included in the analysis. The chi-square trend test for pairwise comparison showed that compared with the prevalence of grade 1 disability, the prevalence of grade 2 disability showed a significant downward trend over time ($\chi^2 = 9.562, P = 0.002$). Correlation analysis showed that disability grade was closely related to the delay in diagnosis of leprosy ($r = 0.275, P = 0.000$).
### Table 1
Delayed diagnosis and abnormal disability in leprosy patients in the whole city from 1949 to 2018

| Year   | Onset - Diagnosis time (T) | Disability |
|--------|-----------------------------|------------|
|        | $T < 2$ (year)              | $2 \leq T < 5$ (year) | $T \leq 5$ (year) | No disability | Grade 1 disability | Grade 2 disability |
| 1949~  | 17 (89.474%)                | 1 (5.263%) | 1 (5.263%) | 7 (58.333%)  | 1 (8.333%)      | 4 (33.333%)      |
| 1954~  | 20 (55.556%)                | 8 (22.222%) | 8 (22.222%) | 9 (31.034%)  | 7 (24.138%)     | 13 (44.828%)    |
| 1959~  | 194 (38.569%)               | 159 (31.610%) | 150 (29.821%) | 242 (58.173%) | 41 (9.856%)     | 133 (31.971%)   |
| 1964~  | 128 (24.758%)               | 170 (32.882%) | 219 (42.360%) | 241 (51.386%) | 84 (17.91%)     | 144 (30.704%)   |
| 1969~  | 150 (30.060%)               | 148 (29.659%) | 201 (40.281%) | 202 (45.291%) | 97 (21.749%)    | 147 (32.960%)   |
| 1974~  | 132 (29.011%)               | 133 (29.231%) | 190 (41.758%) | 200 (47.281%) | 69 (16.312%)    | 154 (36.407%)   |
| 1979~  | 81 (26.214%)                | 97 (31.392%) | 131 (42.395%) | 141 (49.301%) | 50 (17.483%)    | 95 (33.217%)    |
| 1984~  | 121 (24.200%)               | 168 (33.600%) | 211 (42.200%) | 239 (50.743%) | 71 (15.074%)    | 161 (34.183%)   |
| 1989~  | 74 (32.456%)                | 84 (36.842%) | 70 (30.702%) | 114 (50.220%) | 51 (22.467%)    | 62 (27.313%)    |
| 1994~  | 56 (35.669%)                | 60 (38.217%) | 41 (26.115%) | 60 (39.735%)  | 45 (29.801%)    | 46 (30.464%)    |
| 1999~  | 55 (33.951%)                | 43 (26.543%) | 64 (39.506%) | 76 (49.351%)  | 25 (16.234%)    | 53 (34.416%)    |
| 2004~  | 44 (33.333%)                | 43 (32.576%) | 45 (34.091%) | 75 (58.140%)  | 23 (17.829%)    | 31 (24.031%)    |
| 2009~  | 48 (45.714%)                | 36 (34.286%) | 21 (20.000%) | 62 (59.615%)  | 20 (19.231%)    | 22 (21.154%)    |
| 2014~  | 38 (50.000%)                | 20 (26.316%) | 18 (23.684%) | 41 (56.164%)  | 14 (19.178%)    | 18 (24.658%)    |

#### 2.4.2 Treatment

Before 1982, the treatment of leprosy mainly consisted of dapsone (DDS). In 1982, the WHO issued a standard regimen for the treatment of leprosy: multidrug therapy (MDT) \[11\]. Therefore, considering 1982
as the boundary, the data were analysed by classification and treatment plan in each period. Among the 3702 registered patients, 3274 patients had multibacillary (MB)-type leprosy (88.486%), and 426 patients had paucibacillary (PB)-type leprosy (11.534%). During the whole period, the number of MB-type patients was much higher than that of PB-type patients, with an MB:PB patient ratio of 7.685:1. As shown in Table 2, before 1982, the two leprosy treatment regimens were dominated by DDS therapy, accounting for 91.815% of the total therapeutic regimens, which was consistent with the situation during that period. After 1982, MDT-MB was the main treatment regimen for MDT-MB patients, and MDT-PB was the main treatment regimen for MDT-PB patients.

### Table 2
Treatment types in and treatment plans for leprosy patients in different periods in Chongqing

| Treatment | 1949~1981 | 1982~2018 |
|-----------|-----------|-----------|
|           | MB        | PB        | MB        | PB        |
| Untreated | 20(1.033%)| 3(1.200%) | 16(1.197%)| 4(2.273%) |
| DDS       | 1794(92.617%) | 214(85.600%) | 306(22.887%) | 50(28.409%) |
| MDT-MB    | 61(3.149%) | 1(0.400%) | 965(72.177%) | 40(22.727%) |
| MDT-PB    | 3(0.155%) | 17(6.800%) | 24(1.795%) | 68(38.636%) |
| Other     | 59(3.046%) | 15(6.000%) | 26(1.945%) | 14(7.955%) |

The cure rate is shown in Fig. 1(5). From 1949 to 1981, the overall 5-year cure rates in leprosy patients in the city were lower than 30%, though they began to increase rapidly after the WHO announced the MDT treatment plan in 1982. The cure rate reached its maximum value of 41.18% in 1998 and fluctuated by approximately 20% thereafter. In terms of sex, the cumulative cure rate in males was 81.809%, and that in females was 84.245%, which was slightly higher than that in males ($t = -0.616, P = 0.539$). In terms of age, the cumulative cure rate was 87.179% in children aged 0–14 years old, 82.714% in patients aged 15–64 years old, and 67.647% in elderly patients aged 65 years and older. The cumulative cure rate decreased significantly with increasing age ($\chi^2 = 17.836, P = 0.000$).

The disease course in clinically cured patients is shown in Fig. 1(6); from 1949 to 1981, DDS therapy was mainly used for the treatment of leprosy. A total of 79.470% of the patients had a disease course, from diagnosis to cure, longer than 5 years, and 42.245% of the patients had a disease course longer than 10 years. After the introduction of MDT therapy in 1982, 94.741% of leprosy patients were cured within 10 years. Among these patients, 51.570% had a duration of disease less than 5 years, and the disease course in patients receiving MDT was significantly shorter than that of patients receiving DDS treatment ($\chi^2 = 608.346, P = 0.000$).
3 Discussion

(1) General epidemic profile

The incidence rate is the most effective indicator to evaluate the prevalence of leprosy [12]. From the existing leprosy data of the detection system, the incidence of leprosy in Chongqing increased rapidly and then decrease to a stable low level. The peak incidence occurred in 1960, and the variation trend of the incidence over the time was similar to that of leprosy in China [7, 13–15]. In the 1960s, the country strengthened efforts in the active detection of leprosy, and Chongqing actively implemented detection strategies, resulting in the detection rate peaking (0.848/100,000 people) in 1960. Since 1959, leprosy detection in Chongqing has decreased at a rate of more than 4% per year. The reason is that Chongqing attached great importance to the prevention and control of leprosy and is constantly improving its ability to detect leprosy in these years. The epidemic situation of leprosy from 2003 to 2018 was further analyzed, showing that the incidence rate was below 0.100/10⁵ people and the prevalence rate was below 0.6/100,000 people in all years. This indicates that the incidence of leprosy in Chongqing is stable and has achieved the standard for the elimination of leprosy stipulated by the WHO. Leprosy is a chronic infectious disease with a low mortality rate and a disease course that can last for years or even decades. Some studies have shown that the actual incidence of leprosy may be much higher than the reported incidence because many cases are still not detected by the national surveillance system [16–18]. Therefore, strengthening the detection of leprosy symptoms and succeeding in early detection, diagnosis and treatment of leprosy patients are the primary tasks for the prevention and control of leprosy in Chongqing.

(2) Region And Patient Distribution Characteristics

According to the regional distribution, the disease incidence in the northern and eastern areas was more densely distributed than those in the southern and western regions of the city. The incidence rate increased with distance from the main urban area. This may be related to the lack of transportation, relatively underdeveloped economies, and poor allocation of and access to health resources in remote areas. Some studies have shown that leprosy cases are likely to cluster in small areas and that poverty, access to health care and an area's economic development level may be important drivers of its persistence [19–22]. This suggests that for the development of new leprosy prevention and treatment measures, priority should be given to strengthening the allocation of health resources in remote and economically underdeveloped areas to increase access to health care for patients. This will not only decrease the burden of leprosy but also help strengthen the tertiary prevention of other related infectious diseases.

In terms of population distribution, the sex ratio of leprosy patients in the whole city was 3.814:1, and there were far more male patients than female patients. Most researchers believe that since men engage in extensive social activities, they have more opportunities to be exposed to sources of infection than women. Some experts also believe that women have poorer access to health services than men and report their illness later than men [6, 23]. A total of 93.158% of the affected patients were aged 15–64
years; this age group is the main source of social productivity. Leprosy often causes multiple morbidity, resulting in an inability of patients to care for themselves; this may cause substantial economic losses to and medical burdens on leprosy patients' families and society as a whole. Therefore, it is of great significance to provide effective rehabilitation of leprosy patients and combine health care and nursing services. Childhood leprosy is a sensitive indicator that reflects the prevalence of leprosy [12]. In 2016, the WHO proposed the goal of zero cases of leprosy among children by 2020 [24], which established additional requirements for the prevention and treatment of leprosy. The prevalence of leprosy in children aged 0–14 years in Chongqing has been sporadic since 1996, indicating that the prevalence of leprosy is declining.

(3) Diagnosis And Disability

From 1949 to 2018, the median time from onset to diagnosis was 3.576 years (1.435, 7.621). After years of active prevention and treatment, the 2-year detection rate of leprosy has been increasing annually. This reflects an improvement in the leprosy detection system and an improvement in the ability to identify leprosy. The disability ratio reflects the severity of delayed detection [25]. Our results indicate that there has been no significant change in the proportion of non-disabled patients at the time of diagnosis since 1949. Over the last 5 years, the rate of grade 2 disability was 24.658%, which was slightly higher than that in previous years. This may be attributed to the increase in the detection rate of grade 2 disability due to the strengthening of leprosy monitoring by the health system in recent years. This is consistent with the conclusion of Kyra H. Grantz et al. [22], who found a slight increase in the detection rate of grade 2 malformation cases in an epidemiological study of leprosy in India. It has been reported that the quality of life of patients with functional limitations is adversely affected in both physical health and environmental domains. In addition, sequelae caused by leprosy, such as disability and nerve damage, are major risk factors for Parkinson's disease [26–29]. Therefore, in the future, the city should improve the early detection of leprosy, strengthen prevention and treatment efforts, reduce the incidence of disability in patients, and eliminate the harm of leprosy [30].

(4) Treatment Of The Patient

Before 1982, the treatment of leprosy was mainly based on DDS. The clinical cure rate of leprosy patients in the city was less than 10%, and the proportion of cured patients with a disease course of more than 10 years was 42.245%. After the establishment of MDT therapy by the WHO in 1982 [31], that the annual cure rate increased rapidly and stabilized at approximately 20%. Cured patients with a disease course exceeding 10 years accounted for 5.259% of the patient population, indicating that MDT therapy significantly improved the cure rate in leprosy patients and shortened the course of the disease. This has important implications for reducing the disease burden of leprosy and the social pressures it imposes. Since the cure rate of leprosy is higher in women than in men, it can be considered that the risk of exposure in men is higher than that in women and that women adhere to medical treatment better than men. The cure rate decreased significantly with increasing age, which may be related to the deterioration of the body's development, metabolism and repair function.
4 Conclusion

In summary, the prevalence of leprosy in Chongqing is currently low. However, to maintain the status of meeting the WHO standards for the elimination of leprosy, there are some challenges that should not be overlooked by leprosy prevention workers. For example, patients’ onset-diagnosis times and disability status at diagnosis are still prolonged and severe, respectively. In this regard, Chongqing health workers are committed to strengthen the monitoring of leprosy, improve the ability of early detection of leprosy, in order to effectively reduce the rate of patients with disability. At the same time, attention to disease recurrence and health education is also one of their priorities. It is helpful to achieve early detection, early diagnosis and early treatment that can eliminate the harm of leprosy and improve the quality of life of leprosy patients.

Deficiencies

In this study, we focus on analyse the epidemiological characteristics of leprosy in Chongqing from 1949 to 2018 and evaluate the prevention and treatment effects over time. And these contents have not been published in the existing literature. For more in-depth analysis, such as disease influencing factors and patients’ quality of life, etc., will be presented in subsequent studies.

Declarations

Availability of data and materials

All data are available in the citations.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare they have no competing interests.

Funding

Chongqing Basic Research and Frontier Exploration Project (cstc2018jcyjA0135)

Authors’ contributions

All authors contributed to data acquisition, analysis, and writing. All authors read and approved the final manuscript.
Acknowledgements

We thank the study participants for their time and collaboration.

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**Figures**

![Figure 1](image-url)

**Figure 1**
Changes in indicators of leprosy from 1949 to 2018

Figure 2

Distribution of the cumulative incidence in Chongqing from 1949 to 2018. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.