RESEARCH ARTICLE

The burden of physical disability among patients with newly detected leprosy in Yunnan, China, 1990–2020: A population-based, cross-sectional survey

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Abstract

Background

Physical disability is the main complication of leprosy. Although understanding the leprosy rate, prevalence, spatiotemporal distribution, and physical nerve characteristic trends is crucial for the implementation of leprosy control programs and identification of remaining challenges, these data are still unclear. We assessed physical disability trends among newly detected leprosy cases over the past 31 years in 129 counties and territories in Yunnan, China.

Methodology/Principal findings

We analyzed the data of newly detected leprosy cases from the Leprosy Management Information System in Yunnan, China, from 1990–2020. All available data related to physical disability were analyzed, including demographic characteristics (sex, age, ethnicity, education level); clinical characteristics (diagnosis duration, detection mode, contact history, leprosy reaction, skin lesions, nerve lesions, disability classification); World Health Organization (WHO) leprosy physical disability indicators; and nerve and eyes, hands and feet (EHF) involvement. A total of 10758 newly diagnosed leprosy cases were identified, and 7328 (65.60%), 1179 (10.55%) and 2251 (20.15%) were associated with grade 0, 1, and 2 disability (G0D, G1D, and G2D), respectively. Male sex, older age, Han ethnicity, urban employment, a longer diagnosis duration, a contact history, greater nerve involvement, and tuberculoid-related forms of leprosy were associated with increased prevalence rates of physical disability. The rates of physical disability in newly detected leprosy cases per 1 million population decreased from 5.41, 2.83, and 8.24 in 1990 to 0.29, 0.25, and 0.54 per 1 million population in 2020, with decreases of 94.64%, 91.17%, and 93.44% in G2D, G1D and total physical disability (G1D + G2D) rates, respectively. In the same period, the proportions of G2D, G1D and total physical disability decreased from 28.02%, 14.65%, and 42.67% in...
1990 to 10.08%, 11.76%, and 21.85% in 2020, with decreases of 64.03%, 19.73%, and 48.79%, respectively. Nerve thickening was more common than nerve tenderness, and claw hand, plantar insensitivity, and lagophthalmos were the most frequently reported EHF-related disabilities.

Conclusions

Despite general progress in reducing the prevalence of leprosy-related physical disability, the proportion of physical disability among leprosy disease remains high, especially in specific counties. This implies that leprosy cases are being detected at a later stage and that transmission in the community still exists. Further efforts focusing on early detection are crucial for leprosy control and the elimination of the disease burden.

Author summary

Leprosy, caused by Mycobacterium leprae (M. leprae), is a potentially disabling infectious disease. An understanding of the leprosy rate, prevalence, spatiotemporal distribution, and nerve characteristic trends are crucial for the implementation of leprosy control programs the identification of remaining challenges. The physical disability trends among newly detected leprosy cases were assessed over a 31-year period in Yunnan, a leprosy-endemic region in China. A total of 10758 newly diagnosed leprosy cases were reported, and 10.55% (1179) and 20.15% (2251) of patients were diagnosed with grade 1 (G1D) and grade 2 disability (G2D), respectively. Male sex, older age, Han ethnicity, urban employment, a longer diagnosis duration, a contact history, greater nerve involvement, and tuberculoid-related forms of leprosy were associated with increased prevalence rates of physical disability. Despite general progress in reducing the prevalence of leprosy-related physical disability, the proportion of those experiencing physical disability due to leprosy is still high. This implies that leprosy cases are being detected at a later stage and that transmission in the community remains. Further efforts focusing on early detection are crucial for leprosy control and the elimination of the disease burden.

Introduction

Leprosy, caused by Mycobacterium leprae (M. leprae), is a potentially disabling infectious disease, with over 200000 new cases reported annually worldwide. The involvement of certain peripheral nerves (neuritis) often leads to disability and devastating psychosocial consequences [1].

In 2019, 10813 leprosy cases associated with grade 2 disability (G2D) at diagnosis were reported globally, and the proportion of G2D cases among all new cases was 5.3%, corresponding to 1.2 people per million population [2]. In the absence of verifiable data, it is estimated that 3–4 million people are currently living with notable impairments or deformities due to leprosy [3].

Considering the Global Leprosy Strategy 2016–2020 targets [4], in this study, we assessed the geographic and clinical factors associated with the prevalence of physical disability. We also assessed World Health Organization (WHO) leprosy indicators of physical disability and the characteristics of nerve and eye, hands and feet (EHF) involvement associated with G2D,
G1D, and total physical disability (G1D+G2D) due to leprosy over the past 31 years in Yunnan, China.

**Methods**

**Ethics statement**

The data for this retrospective observational study were collected from the Leprosy Management Information System in China (LEPMIS). We systematically screened the case data of patients with leprosy from local hospitals and Centers for Disease Control and Prevention (CDCs) in Yunnan, China. The study design and data analysis protocol were approved by the Ethics Committee of the Yunnan Center for Disease Control and Prevention, Yunnan, China. Individual identifying information was not available and thus informed consent was not required.

**Data sources**

Patients with newly detected leprosy cases from 1990–2020 in Yunnan, China, were enrolled. The diagnosis of leprosy by clinicians met the diagnostic criteria issued by the Ministry of Health of the People's Republic of China [5]. Patients with newly detected leprosy cases were classified as having no disability (G0D), grade 1 disability (G1D) or grade 2 disability (G2D), forming the sample for this study.

**Disability classifications, nerve involvement and the EHF score**

All the patients included in this study with a confirmed diagnosis of leprosy were evaluated for physical disability level and nerve involvement according to the objective scale of physical impairment defined by the WHO [6]. The physical disability criteria were as follows: G0D: no impairment, G1D: loss of sensation, and G2D: visible impairment. Nerve involvement in leprosy was defined as signs of pain or nerve thickening upon palpation of the nerves [7]. The sum EHF score, which represents the sum of all disability scores (from 0 to 2 points) (Table 1) of the 6 sites investigated (both eyes, hands, and feet), ranged from 0 to 12 points; the EHF score is a reliable scoring tool representative of leprosy-related disability and a potentially more sensitive tool for the monitoring of disability changes and undetected disabilities than the WHO’s maximum impairment grade [8].

**Variables**

Demographic and clinical data were collected in this study. Patient basic demographic information included sex, date of birth, ethnicity, occupation, and address at the county level. Clinical characteristics included age at diagnosis, date of symptom onset, date of diagnosis, and physical disability level.

| Disability | Eyes | Hands and Feet |
|------------|------|----------------|
| Grade 0    | No eye impairment due to leprosy; no evidence of visual loss | No sensory impairment, no visible impairment |
| Grade 1    | Eye problems due to leprosy present (irregular blink), but no vision impaired (can read fingers at six-meter distance) | Anesthesia present, but no visible deformity or damage, including muscle weakness without clawing |
| Grade 2    | Severe visual impairments (cannot read fingers at six-meter distance), lagophthalmos, uveitis, corneal opacities | Visible impairments present, including ulcers and atrophy |

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detection mode, skin lesions, nerve damage, contact history, leprosy reaction, disability classification (G0D, G1D, or G2D), Ridley-Jopling classification, and WHO classification. Diagnosis duration was defined as the time from the onset of symptoms to a confirmed diagnosis. “Early detection” was defined as a time between disease onset and diagnosis of within 2 years and the presence of G0D or G1D according to the WHO definition of leprosy disability [6].

Spatial distribution
Population data for the study area were obtained from the National Bureau of Statistics of the People’s Republic of China. The leprosy physical disability indicator was defined according to WHO criteria [9]. The WHO leprosy indicators were as follows: (a) numbers of new cases associated with G2D, G1D or G1D + G2D at diagnosis per 1 million population, and (b) proportions of new cases associated with G2D, G1D or G1D + G2D at diagnosis. The geographical distribution of newly detected leprosy cases was mapped with ArcGIS software version 10.1 (Environmental Systems Research Institute, Inc., Redlands, CA, USA). The study period was divided into time period 1 (1990–2003: MDT) and time period 2 (2004–2020: MDT + special funding for leprosy), as described previously [10].

Statistical analysis
Excel 2013 was used to compile the data of newly detected leprosy cases; calculate the ages of patients according to birth dates and diagnosis dates; and describe the basic demographic characteristics, time distribution trends and regional distribution characteristics of the cases. The data were subsequently analyzed using GraphPad Prism version 6 (GraphPad Software, La Jolla, CA, USA). The results of the descriptive analyses are presented as means ± standard deviations (SDs), minimum-maximum values, and medians and interquartile ranges (IQRs) for continuous variables and as counts and percentages in each category for categorical variables. The chi-square test and Fisher’s exact test were used to examine differences in the proportions of categorical variables between different groups.

Results
The prevalence of leprosy cases associated with physical disability
Table 2 shows the general characteristics of the study population. During the thirty-year study period, from 1990 to 2020, 11171 newly diagnosed leprosy cases were reported, and 96.3% of cases (n = 10758) were assessed for the level of physical disability at the time of diagnosis. A total of 7328 (63.60%), 1179 (10.55%) and 2251 (20.15%) were diagnosed with G0D, G1D and G2D, respectively (Table 2).

The distribution of cases according to sex demonstrated that 72.86% of the cases with G2D were males, who had a 1.141-fold higher prevalence of physical disability due to leprosy than females (p = 0.014). Regarding age groups, 83.56% and 15.02% of the reported patients with G2D were 15–59 years old and over 60 years old, respectively, and these patients had a 2.871- and 4.981-fold higher prevalence of disability than patients under 15 years old, respectively (p < 0.0001 and < 0.0001, respectively). Regarding ethnic groups, Han ethnicity was associated with a 1.219-fold higher prevalence of disability than patients belonging to minor ethnicity groups. Similar trends were also found for total physical disability (G1D+G2D) and G1D.

Regarding the diagnosis duration, 2–5 years, 5–10 years and over 10 years were associated with 2.368-, 3.652- and 4.233-fold higher G2D prevalence rates than a duration of less than 2 years, respectively (P < 0.0001, < 0.0001, and < 0.0001, respectively). Regarding the detection mode, other modes were associated with a 1.509-fold higher prevalence of G2D than self-
Table 2. The Characteristics and Prevalence Rates of Newly Detected Leprosy Cases Associated with Physical Disabilities in Yunnan, China, from 1990–2020.

| Characteristics                        | Total     | GB+1+2D | Grade 0 | Grade 1 | Grade 2 | G1D+G2D | G1D   | G2D   | G1D+G2D |
|----------------------------------------|-----------|---------|---------|---------|---------|---------|-------|-------|---------|
|                                        | 11171     | 10758   | 7328    | 1179    | 2251    | 3430    |       |       |         |
| Gender, No. (%)                        |           |         |         |         |         |         |       |       |         |
| Female                                 | 3338      | 3222    | 29.89%  | 2246    | 30.68%  | 611     | 28.45%|        |         |
| Male                                   | 7832      | 7536    | 70.03%  | 5082    | 69.65%  | 1841    | 71.55%| 0.838  | 0.988   |
| Age, Median (IQR), y                   |           |         |         |         |         |         |       |       |         |
| 0–14                                   | 453       | 440     | 4.06%   | 374     | 4.10%   | 34      | 2.88% | 32     | 1.42%   |
| IS–59                                  | 9700      | 9347    | 86.88%  | 6431    | 87.76%  | 1036    | 87.86%| 1881   | 1.065   |
| >60                                    | 1018      | 971     | 9.11%   | 523     | 7.14%   | 109     | 9.23% | 338    | 14.03%  |
| Ethnic Group                           |           |         |         |         |         |         |       |       |         |
| Han                                    | 5264      | 5085    | 52.88%  | 3287    | 44.86%  | 643     | 54.54%| 115    | 5.42%   |
| Minor ethinics                         | 5907      | 5673    | 52.73%  | 4041    | 51.54%  | 536     | 45.46%| 1096   | 43.78%  |
| Occupation                             |           |         |         |         |         |         |       |       |         |
| Urban                                  | 10254     | 9055    | 90.07%  | 6668    | 90.99%  | 1099    | 91.92%| 2198   | 9.43%   |
| City                                   | 918       | 854     | 8.22%   | 660     | 9.01%   | 80      | 6.79% | 113    | 5.02%   |
| Diagnosis Duration, y                  |           |         |         |         |         |         |       |       |         |
| <2                                     | 7168      | 6934    | 64.93%  | 5295    | 72.28%  | 747     | 63.36%| 892    | 47.78%  |
| 2–49                                   | 2924      | 2787    | 25.97%  | 1624    | 22.16%  | 321     | 27.23%| 842    | 33.91%  |
| 5–9.9                                  | 687       | 656     | 6.15%   | 273     | 3.73%   | 79      | 6.70% | 304    | 11.17%  |
| >10                                    | 392       | 381     | 3.51%   | 136     | 1.86%   | 273     | 2.11% | 213    | 7.14%   |
| Detection Mode                         |           |         |         |         |         |         |       |       |         |
| Passive Case Finding                   | 7152      | 6937    | 66.48%  | 4736    | 64.63%  | 795     | 67.43%| 1406   | 61.47%  |
| Active Case Finding                    | 4019      | 3821    | 35.52%  | 2592    | 35.37%  | 384     | 32.57%| 845    | 35.83%  |
| Self-reported illness                  | 2299      | 2058    | 20.38%  | 1594    | 21.73%  | 227     | 19.25%| 411    | 18.60%  |
| Out-patient clinic finding             | 3027      | 2931    | 27.14%  | 2066    | 28.19%  | 352     | 29.86%| 513    | 23.22%  |
| Other-reported illness                 | 1836      | 1775    | 16.50%  | 1076    | 14.68%  | 216     | 18.32%| 482    | 20.35%  |
| Contact examination                    | 1286      | 1259    | 11.70%  | 975     | 13.31%  | 135     | 11.45%| 149    | 6.62%   |
| Focus Survey                           | 360       | 345     | 3.22%   | 246     | 3.36%   | 3       | 2.54% | 66     | 2.93%   |
| Group examination                      | 114       | 113     | 1.05%   | 93      | 1.27%   | 2       | 0.17% | 6      | 0.27%   |
| Clear investigation                    | 1965      | 1855    | 17.24%  | 1089    | 14.86%  | 204     | 17.30%| 574    | 22.68%  |
| Leprosy Elimination Campaign (II.E)    | 137       | 127     | 1.18%   | 94      | 1.24%   | 10      | 0.85% | 23     | 1.02%   |
| Other ways                             | 157       | 141     | 1.34%   | 95      | 1.30%   | 3       | 0.25% | 27     | 1.20%   |
| Contact History                        |           |         |         |         |         |         |       |       |         |
| Unknown                                | 3572      | 3349    | 31.13%  | 2253    | 20.73%  | 349     | 29.00%| 747    | 31.95%  |
| Present                                | 7599      | 7408    | 68.87%  | 5075    | 69.23%  | 830     | 70.40%| 1504   | 68.05%  |
| With family                            | 3406      | 3327    | 30.93%  | 2403    | 32.79%  | 379     | 32.15%| 545    | 26.94%  |
| Out of family                          | 4195      | 4082    | 37.94%  | 2672    | 36.46%  | 451     | 38.25%| 959    | 41.11%  |

(Continued)
| Characteristics                          | Total   | G0+1+2D | Grade 0 | Grade 1 | Grade 2 | G1D+G2D | G1D | G2D | G1D+G2D |
|-----------------------------------------|---------|---------|---------|---------|---------|---------|------|------|---------|
|                                        | N       | Percent | N       | Percent | N       | Percent | N    | Percent | N       | Percent |
| **Leprosy Reaction**                    |         |         |         |         |         |         |      |       |         |         |
| Absent                                 | 10841   | 97.05%  | 10439   | 97.03%  | 7139    | 97.42%  | 1099 | 93.21% | 2201    | 96.21%  |
| Present                                | 330     | 2.98%   | 319     | 3.97%   | 189     | 2.58%   | 50   | 2.22%  | 150     | 3.79%   |
|                                        |         |         |         |         |         |         |      |       |         |         |
| **Skin Lesion**                         |         |         |         |         |         |         |      |       |         |         |
| 0                                      | 444     | 4.01%   | 440     | 4.09%   | 229     | 3.13%   | 44   | 3.73%  | 130     | 3.79%   |
| 1                                      | 1164    | 10.42%  | 1136    | 10.56%  | 808     | 11.03%  | 221  | 9.82%  | 328     | 9.56%   |
| (2–5)                                   | 3087    | 27.63%  | 3044    | 28.30%  | 2003    | 27.33%  | 715  | 2.22%  | 1301    | 3.79%   |
| Over 5                                  | 5749    | 51.46%  | 5643    | 52.43%  | 3923    | 53.53%  | 670  | 56.83% | 1071    | 3.79%   |
| Missing data                            | 723     | 6.47%   | 445     | 4.60%   | 176     | 2.40%   | 32   | 2.71%  | 77      | 3.42%   |
| **Nerve thickening and/or tenderness on palpation** |         |         |         |         |         |         |      |       |         |         |
| 0                                      | 1138    | 10.19%  | 1114    | 10.36%  | 970     | 13.24%  | 53   | 4.50%  | 91      | 4.04%   |
| 1                                      | 2173    | 19.45%  | 2130    | 19.80%  | 1455    | 19.86%  | 238  | 30.19% | 130     | 5.63%   |
| 2                                      | 7425    | 66.47%  | 7318    | 68.02%  | 4760    | 64.96%  | 871  | 11.63% | 1608    | 7.48%   |
| Missing data                            | 435     | 3.89%   | 196     | 1.82%   | 143     | 1.95%   | 17   | 1.44%  | 36      | 1.60%   |
| **Ridley-Jopling Classification**       |         |         |         |         |         |         |      |       |         |         |
| LL                                     | 1509    | 13.51%  | 1423    | 13.23%  | 1043    | 13.32%  | 223  | 9.92%  | 380     | 11.08%  |
| BL                                     | 4525    | 40.51%  | 4368    | 40.60%  | 3102    | 42.33%  | 549  | 46.56% | 717     | 11.08%  |
| BB                                     | 1080    | 9.67%   | 1053    | 9.79%   | 721     | 9.84%   | 121  | 10.26% | 332     | 9.68%   |
| BT                                     | 2661    | 23.82%  | 2581    | 23.99%  | 1597    | 21.79%  | 230  | 19.51% | 754     | 11.63%  |
| TT                                     | 1214    | 10.87%  | 1162    | 10.80%  | 719     | 9.81%   | 110  | 9.33%  | 333     | 12.92%  |
| Missing data                            | 435     | 3.89%   | 196     | 1.82%   | 143     | 1.95%   | 17   | 1.44%  | 36      | 1.60%   |
| **WHO Classification**                 |         |         |         |         |         |         |      |       |         |         |
| Multibacillary form                    | 7574    | 67.80%  | 7299    | 67.83%  | 5193    | 70.87%  | 875  | 74.22% | 1231    | 61.40%  |
| Paucibacillary form                    | 3580    | 32.15%  | 3452    | 32.09%  | 2131    | 29.08%  | 304  | 25.78% | 1017    | 38.51%  |
| Missing data                            | 17      | 0.15%   | 7       | 0.07%   | 4       | 0.05%   | 0    | 0.00%  | 0       | 0.00%   |

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reporting (P < 0.0001). In detail, contact examination, Leprosy Elimination Campaign (LEC), disease focus investigation, and suspected disease clue investigation were associated with 2.187-, 3.244-, 3.490-, and 5.695-fold higher prevalence rates of G2D than group examination, respectively (P < 0.05). However, there was no association between passive and active detection modes and the development of G2D (P = 0.0505). Regarding traceable infectious sources, infection from sources outside the family was associated with a 1.429-fold higher prevalence of G2D than infection from sources within the family (P < 0.0001).

Regarding skin lesions, 2–5 skin lesions and 0 skin lesions were associated with 1.225- and 1.964-fold higher prevalence rates of G2D than 1 skin lesion, respectively (P = 0.0023 and < 0.0001). Regarding nerve lesions, 1 nerve lesion and 2 nerve lesions were associated with 2.693- and 3.051-fold higher prevalence rates of G2D than no nerve lesions (P < 0.0001, and < 0.0001). Regarding the Ridley-Jopling classification, the mid-borderline (BB), mid-borderline (BT) and tuberculoid (TT) forms were associated with 1.285-, 1.821- and 1.797-fold higher prevalence rates of G2D than the lepromatous (LL) form of leprosy, respectively (P = 0.0040, < 0.0001, and < 0.0001). Regarding the WHO classification, paucibacillary (PB) form was associated with a 1.686-fold higher prevalence of G2D than the multibacillary (MB) form of leprosy (P < 0.0001).

Temporal distributions of WHO leprosy indicators of physical disability

The diagnostic durations and rates of early detection are shown in Fig 1A and 1B. The diagnostic duration decreased from 37.63 months in 1990 to 14.19 months in 2020 (S1 Table and Fig 1A). During the same period, the rate of early detection increased from 43.10% in 1990 to 75.63% in 2020 (S1 Table and Fig 1B).

The rates and proportions of physical disabilities in newly detected cases of leprosy are shown in Fig 1C and 1D. With the dramatic decreases in the rates of newly detected leprosy cases, the rates of G2D, G1D, and G1D + G2D (cases per 1 million population) also decreased from 1990 to 2020 (S2 Table and Fig 1C). The rates of G2D, G1D, and G1D + G2D among patients with newly detected leprosy cases decreased from 5.41, 2.83, and 8.24 per 1 million population in 1990 to 0.25, 0.29, and 0.54 per 1 million population in 2020, respectively. However, the proportion of new cases with physical disability at diagnosis remained over 20% (S2 Table and Fig 1C). The proportion of new cases with total physical disability initially decreased from 42.67% in 1990 to 30.22% in 2009, increased to the highest rate (48.68%) in 2010, and finally decreased to 21.85% in 2020. The proportion of cases associated with G2D showed a similar trend, ranging from 10.08% to 32.02%, with the highest and lowest rates observed in 2010 and 2020, respectively. The proportion of cases associated with G1D ranged from 4.82% to 18.39%, with the highest and lowest rates observed in 2003 and 2018, respectively (S2 Table and Fig 1D).

Spatial distributions of WHO leprosy indicators of physical disability

Figs 2 and 3 and S3 Table show the spatial distributions of G1D, G2D, and total physical disability among newly detected leprosy cases in Yunnan, China. A total of 98.45% (127/129) of counties in Yunnan reported leprosy cases during the study period, and 96.85% (123/127) of counties registered new cases of leprosy associated with G2D over the study period.

Regarding the G2D rate per 1 million population, 29.27% (36/123) of counties with new cases had very low rates (0.0–1.9), 16.26% (20/123) had low rates (2.0–3.99), 27.64% (34/123) had moderate rates (4.0–7.99), 17.89% (22/123) had high rates (8.0–14.99), and 8.94% (11/123) had very high rates (≥15 cases per 1 million population) (S3 Table and Fig 2). Regarding the proportion of new leprosy cases associated with G2D at diagnosis, 35.77% (44/123) of counties
had a low proportion (0.00%-19.99%), 53.66% (66/123) of counties had a moderate proportion (20.00%-39.99%), 8.94% (11/123) of counties had a high proportion (40.00%-60.00%), and 1.62% (2/123) of counties had a very high proportion (60.00%-100.00%) (S3 Table and Fig 3).

Compared with that in time period 1, the number of counties with high and very high rates (over 8 cases per 1 million population) of G2D decreased dramatically from 20 to 4 counties, while the number of counties with high and very high proportions (over 40.00%) of G2D decreased only slightly from 21 to 19 counties during time period 2 (Figs 2 and 3, and S3 Table).

Characteristics of nerve and EHF involvement

At the time of diagnosis. A total of 69.99% (7819/11171) of cases were assessed for nerve (Table 3) and EHF involvement (Table 4). Nerve thickening and nerve tenderness examined by nerve palpation were evaluated in the study population, and the positivity rate for nerve thickening (13.29%, 8314/62552) was higher than that for nerve tenderness (3.96%, 2477/7819) (P<0.05) (Table 5). The most common thickened nerves were the ulnar (1679/7819, 21.47%; and 1651/7819, 21.12% for the right and left sides, respectively), common fibular (1204/7819, 15.40%; and 1189/7819, 15.21% for the right and left sides, respectively) and greater auricular (822/7819, 10.51%; and 824/7819, 10.54% for the right and left sides, respectively) nerves (Table 5). The most common nerves with tenderness were also the ulnar (501/
Detection rate of new detected leprosy cases with physical disability in general population

Fig 2. Proportions of Physical Disability Among Newly Detected Leprosy Cases in Yunnan, China, 1990–2020. The proportions of newly detected leprosy cases associated with G1D (A, D), G2D (B, E), and total physical disability (C, F) in the general population in time period 1 (1990–2003) (A, B, C) and time period 2 (2004–2020) (D, E, F). Map from Naive Map developed in AMAP with data from the National Catalogue Service For Geographic Information. https://www.naivemap.com/admin-cn-downloader/

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7819, 6.41%; and 513/7819, 6.56% for the right and left sides, respectively), common fibular (355/7819, 4.54%; and 348/7819, 4.45% for the right and left sides, respectively) and greater auricular (208/7819, 2.66%; and 207/7819, 2.65% for the right and left sides, respectively) nerves (Table 3). Regarding the grade of disability, the positivity rate for G1D was higher than that for G2D (Table 3).

Table 4 shows the total disabilities of the EHF. Among disabilities of the EHF, the hands were the most affected (1561/15638, 9.98%), followed by the feet (1150/15638, 7.35%) and the eyes (377/15638, 2.41%). Table 4 shows the deformities of the EHF. The most frequent eye disabilities were lagophthalmos (295/15638, 0.70%), insensitivity (94/15638, 0.60%), and decreased visual ability (79/15638, 0.51%). The most frequent hand disabilities were palmar
The burden of physical disability among leprosy in Yunnan, China

Proportion of new detected leprosy cases with physical disability at diagnosis

Fig 3. Detection Rates of Physical Disability Among Newly Detected Leprosy Cases in Yunnan, China, 1990–2020. The detection rates of G1D (A, D), G2D (B, E), and total physical disability (C, F) among newly detected leprosy cases in the general population in time period 1 (1990–2003) (A, B, C) and time period 2 (2004–2020) (D, E, F). Map from Naive Map developed in AMAP with data from the National Catalogue Service For Geographic Information. https://www.naivemap.com/admin-cn-downloader/.

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insensitivity (677/15638, 4.33%) and claw hand (485/15638, 3.10%). The most frequent foot disabilities were palmar insensitivity (744/15638, 4.76%) and simple plantar ulceration (162/15638, 1.04%).

Table 5 shows the diagnosis duration of and physical disabilities associated with leprosy. A total of 76.37% (5294/6932) of leprosy cases associated with G0D were diagnosed within 2 years. With the prolongation of the diagnostic duration, the proportions gradually decreased, with proportions of 58.25% (1624/2788), 41.64% (274/658) and 35.79% (136/380) for diagnosis durations of 2–4.99 years, 5–9.99 years, and over 10 years, respectively. In contrast, the proportions of leprosy cases associated with G2D diagnosed within 2 years, 2–4.99 years, 5–9.99 years
and over 10 years were 8.92% (892/6932), 30.20% (842/2788), 46.35% (305/658), and 55.79% (212/380), respectively.

**Discussion**

This survey found that 31.88% (3430/10758) of newly detected leprosy cases had different degrees of disability. In 2018, the prevalence of leprosy-related disability in Yunnan (10.34%) was lower than that in China (19.0%) [11]. This may be due to the effective multistrategy for leprosy control in Yunnan, China [10].

The WHO leprosy-related physical disability indicators are commonly used by control programs to monitor and evaluate the epidemiological situation of leprosy, reveal the changes in the transmission chain and form conclusions regarding the quality of the health care services.

Table 3. The Characteristics of Nerve Involvement Among Leprosy Patients in Yunnan, China, 1990–2020.

| Characteristics | Nerves involved | Grade 0 | Grade 1 | Grade 2 | Total |
|-----------------|-----------------|---------|---------|---------|-------|
|                 | N   | %    | n      | %      | n      | %     |
| Nerve Thickness |     |      |        |        |        |       |
| Greater auricular | Right | 490 | 10.08% | 138 | 15.08% | 174 | 10.15% | 822 | 10.51% |
|                  | Left  | 491 | 10.10% | 137 | 14.97% | 172 | 10.04% | 824 | 10.54% |
| Supra-orbital    | Right | 81  | 1.67%  | 36  | 3.93%  | 42  | 2.45%  | 168 | 2.15%  |
|                  | Left  | 87  | 1.79%  | 34  | 3.72%  | 39  | 2.28%  | 169 | 2.16%  |
| Ulnar            | Right | 928 | 19.08% | 266 | 29.07% | 441 | 25.73% | 1679 | 21.47% |
|                  | Left  | 902 | 18.55% | 278 | 30.38% | 421 | 24.56% | 1651 | 21.12% |
| Common fibular   | Right | 687 | 14.13% | 207 | 22.62% | 281 | 16.39% | 1204 | 15.40% |
|                  | Left  | 663 | 13.63% | 219 | 23.93% | 275 | 16.04% | 1189 | 15.21% |
| Median           | Right | 45  | 0.93%  | 32  | 0.71%  | 50  | 0.75%  | 127  | 1.57%  |
|                  | Left  | 43  | 0.88%  | 31  | 0.66%  | 56  | 0.81%  | 130  | 1.65%  |
| Tibial           | Right | 45  | 0.93%  | 32  | 0.71%  | 50  | 0.75%  | 127  | 1.57%  |
|                  | Left  | 48  | 0.99%  | 36  | 0.64%  | 51  | 0.75%  | 135  | 1.70%  |
| Radial           | Right | 16  | 0.33%  | 9   | 0.22%  | 23  | 0.35%  | 48   | 0.61%  |
|                  | Left  | 17  | 0.35%  | 9   | 0.22%  | 26  | 0.38%  | 49   | 0.62%  |
| Facial           | Right | 4   | 0.08%  | 1   | 0.02%  | 3   | 0.05%  | 9    | 0.11%  |
|                  | Left  | 6   | 0.12%  | 2   | 0.04%  | 2   | 0.03%  | 10   | 0.13%  |
| Nerve Tenderness | Greater auricular | Right | 130 | 2.67% | 32 | 0.50% | 40 | 0.63% | 208 | 2.66% |
|                  | Left  | 120 | 2.47% | 31 | 0.49% | 47 | 0.70% | 207 | 2.65% |
| Supra-orbital    | Right | 32  | 0.66% | 13 | 0.38% | 15 | 0.24% | 60 | 0.75% |
|                  | Left  | 35  | 0.72% | 15 | 0.42% | 15 | 0.23% | 65 | 0.83% |
| Ulnar            | Right | 258 | 5.13% | 86 | 2.14% | 137 | 2.23% | 501 | 6.42% |
|                  | Left  | 264 | 5.43% | 90 | 2.33% | 135 | 2.30% | 533 | 6.93% |
| Common fibular   | Right | 187 | 3.65% | 63 | 1.69% | 86 | 1.38% | 355 | 4.54% |
|                  | Left  | 176 | 3.52% | 67 | 1.79% | 84 | 1.32% | 348 | 4.45% |
| Median           | Right | 18  | 0.37% | 10 | 0.25% | 18 | 0.28% | 46 | 0.60% |
|                  | Left  | 18  | 0.37% | 8  | 0.21% | 16 | 0.24% | 40 | 0.52% |
| Tibial           | Right | 20  | 0.41% | 7  | 0.18% | 7  | 0.11% | 34 | 0.44% |
|                  | Left  | 19  | 0.39% | 7  | 0.19% | 9  | 0.14% | 45 | 0.58% |
| Radial           | Right | 8   | 0.17% | 3  | 0.08% | 7  | 0.11% | 18 | 0.23% |
|                  | Left  | 9   | 0.19% | 4  | 0.11% | 6  | 0.09% | 20 | 0.26% |
| Facial           | Right | 2   | 0.04% | 0  | 0.00% | 0  | 0.00% | 2  | 0.03% |
|                  | Left  | 4   | 0.08% | 2  | 0.03% | 1  | 0.02% | 7  | 0.09% |

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Table 4. Characteristics of Disabilities of the EHF Among Leprosy Patients in Yunnan, China, 1990–2020.

|                | Total EHF (n, %) | Right (n, %) | Left (n, %) | Total |
|----------------|-----------------|--------------|-------------|-------|
| **Eye**        |                 |              |             |       |
| Total eye      | 7819 50.00%     | 7819 50.00%  | 15638 100.00% |       |
| Insensitivit y | 48 0.61%        | 47 0.60%     | 94 0.60%    |       |
| Lagophthalmos  | 56 0.72%        | 56 0.72%     | 109 0.70%   |       |
| Ectropion      | 8 0.10%         | 8 0.10%      | 16 0.10%    |       |
| Trichiasis     | 3 0.04%         | 3 0.04%      | 6 0.04%     |       |
| Exposure keratitis | 12 0.15% | 12 0.15% | 24 0.15% |       |
| Iritis (Iridocyclitis) | 17 0.22% | 18 0.23% | 35 0.22% |       |
| Decrease of vision | 39 0.50% | 44 0.56% | 79 0.51% |       |
| Blindness      | 6 0.08%         | 8 0.10%      | 14 0.09%    |       |
| **Hand**       |                 |              |             |       |
| Total hand     | 816 10.44%      | 784 10.03%   | 1561 9.98%  |       |
| Insensitivit y | 338 4.32%       | 353 4.51%    | 677 4.33%   |       |
| Claw hand      | 261 3.34%       | 238 3.04%    | 485 3.10%   |       |
| Ape hand       | 49 0.63%        | 45 0.58%     | 91 0.58%    |       |
| Wrist drop     | 6 0.08%         | 7 0.09%      | 13 0.08%    |       |
| Keratosis and chapped wound | 44 0.56% | 35 0.45% | 79 0.49% |       |
| Palmar ulcer   | 24 0.31%        | 11 0.14%     | 33 0.21%    |       |
| Stiff joint    | 45 0.58%        | 40 0.51%     | 84 0.54%    |       |
| Absorption     | 49 0.63%        | 55 0.70%     | 101 0.65%   |       |
| **Foot**       |                 |              |             |       |
| Total foot     | 585 7.48%       | 595 7.51%    | 1150 7.35%  |       |
| Insensitivit y | 379 4.85%       | 388 4.96%    | 744 4.76%   |       |
| Foot drop      | 13 0.17%        | 9 0.12%      | 21 0.13%    |       |
| Skin chapped wound | 51 0.65% | 43 0.55% | 93 0.59% |       |
| Simple planter ulcer | 78 1.00% | 87 1.11% | 162 1.04% |       |
| Complex planter ulcer | 19 0.24% | 19 0.24% | 36 0.23% |       |
| Clowed toes slight absorption | 38 0.49% | 44 0.56% | 82 0.52% |       |
| Equinus        | 5 0.06%         | 3 0.04%      | 8 0.05%     |       |
| Amputation     | 2 0.03%         | 2 0.03%      | 4 0.03%     |       |
| **EHF Total**  |                 |              |             |       |
| EHF = 0        | 7680 98.22%     | 7671 98.11%  | / /         |       |
| EHF = 1        | 41 0.52%        | 40 0.51%     | / /         |       |
| EHF = 2        | 98 1.25%        | 108 1.38%    | / /         |       |
| EHF = 3        | 53 0.68%        | / /          | / /         |       |
| EHF = 4        | 261 3.34%       | / /          | / /         |       |
| EHF = 5        | 24 0.31%        | / /          | / /         |       |
| EHF = 6        | 103 1.32%       | / /          | / /         |       |
| EHF = 7        | 11 0.14%        | / /          | / /         |       |
| EHF = 8        | 53 0.68%        | / /          | / /         |       |
| EHF = 9        | 7 0.09%         | / /          | / /         |       |

(Continued)
This study evaluated the trends of the WHO physical disability leprosy indicators in Yunnan, China, using historical data from a period of 31 years. Our data showed that the rates of physical disabilities among patients with newly detected leprosy cases per 1 million population decreased dramatically by 94.64%, 91.17%, and 93.44% for G2D, G1D and total physical disability, respectively. In the same period, the proportions of G2D, G1D and total physical disability decreased by 64.03%, 19.73%, and 48.79%, respectively. Despite the relatively low rate of physical disability evaluation among leprosy patients per 1 million population, the data revealed a high proportion of physical disability at diagnosis among newly detected leprosy cases.

The global strategy for the control of leprosy from 2011 to 2015 aimed to reduce the rate of new cases with G2D worldwide by more than 35% by the end of 2015 compared with the baseline at the end of 2010 [7]. Our findings revealed that the proportions of G2D among newly detected leprosy cases were 32.02% in 2010 and 16.04% in 2015, with a decrease of 49.91% in Yunnan, China, which was over the 35% target considering the baseline at the end of 2010.

The global strategy for the control of leprosy from 2016 to 2020 aimed to reduce the number of newly diagnosed leprosy patients with visible deformities to less than 1 per million population [4]. The rate of new leprosy cases with G2D per 1 million population is an impact indicator that reflects delayed diagnosis. According to the current study, this indicator has been less than 1 case per 1 million population since 2013 in Yunnan, China, indicating a high level of early detection of leprosy cases in the study region. The proportion of G2D cases among newly detected leprosy cases, another indicator, also reflects a delay in diagnosis. The G2D proportion ranges from 1.8% in the Federated States of Micronesia to 18.6% in China and 42.1% in Somalia [13]. The global average of this indicator is 6.7%. Generally, figures above 5% are considered to reflect delayed case detection. However, in this study, the prevalence rates of G2D and total physical disability were 10.08% and 21.85% in 2020 in Yunnan, China, implying that delayed leprosy diagnosis is still a problem in the study region.

The high proportion of new leprosy cases associated with G2D at diagnosis may reflect operational problems and barriers in access to health care services and supports evidence that the transmission chain is being maintained in the community since, in general, leprosy patients with visible disabilities have advanced forms of the disease (e.g., MB leprosy) [12]. In Yunnan, China, 17.07% (21/123) of counties had a G2D proportion of over 40.00% from 1990–2003, and 15.45% (19/123) of counties had a G2D proportion of over 40.00% from 2010–2015.
2004–2020. These results indicates that the transmission chain is still active in communities in certain regions.

In this study, nerve thickening has a higher positivity rate than nerve tenderness (13.29% vs. 3.96%). Regarding disabilities of the EHF, the hands (9.98%) were more affected by disabilities than the feet (7.35%) or eyes (2.41%). Claw hand, plantar insensitivity and simple plantar ulceration were the most frequent disabilities in the hands and feet. In our previous studies, nerve enlargement in the peripheral upper limbs detected by ultrasound [14] and claw hand were the most frequently reported symptoms in leprosy patients [15]. Lagophthalmos, insensitivity and decreased visual ability were the most frequent disabilities of the eyes. It has been reported that when neuritis occurs in individuals who do not receive proper treatment, the condition may become chronic, leading to the development of characteristic physical disabilities associated with leprosy [16]. In addition, medical personnel are not very familiar with leprosy because of its low prevalence, which could lead to a delay in diagnosis. During this time, peripheral nerve damage develops, leading to disability [17]. Thus, understanding the characteristics of nerve involvement would help medical personnel identify leprosy in the early stage, avoiding a delayed diagnosis and preventing irreversible deformities. We also observed that although G0D was generally associated with a shorter diagnosis duration among newly detected leprosy cases and G2D was mainly associated with a longer diagnosis duration, some cases rapidly progressed to irreversible deformity within 2 years after symptom onset, while other cases did not progress to physical disability even with a disease duration of over 10 years. This may imply that there are risk factors in addition to early detection that influence physical disability.

Our study has some limitations. A proportion of leprosy patients had an unknown degree of physical disability, which may have had little effect on the WHO leprosy indicators used in this study. In addition, physical disabilities remained after completion of multidrug therapy (MDT) and frequently recurred in an endemic area in Brazil [18]. Systematic follow-up of patients after treatment completion should be assessed in the study area in the future. The coronavirus disease 2019 (COVID-19) pandemic had a significant impact on health services in all countries, and leprosy programs were clearly affected, as evidenced by the substantial reduction in the number of cases detected and reported by countries in 2020 [19]; this may be a potential source of bias in 2020 leprosy data from Yunnan, China.

**Conclusion**

In Yunnan, China, the rate of leprosy-related physical disability per 1 million population has decreased dramatically. Despite general progress in reducing the prevalence of physical disability associated with leprosy, the proportion of leprosy-related physical disability remains high, and leprosy-related physical disability still imposes a substantial burden on patients and societies. Strengthening health systems to improve early case detection and improving the quality of leprosy care, including prompt and accurate diagnostics, early initiation of treatment, and routine follow-up, are priorities. Counties for which the leprosy-related physical disability burden is high should investigate the reasons for the high burden and address them appropriately.

**Supporting information**

S1 Table. Diagnostic Durations and Early Detection Rates of Newly Detected Leprosy Cases in Yunnan, China, 1990–2020.
(XLS)
S2 Table. Rates and Proportions of Physical Disabilities Among Newly Detected Leprosy Cases in Yunnan, China, 1990–2020.
(XLS)

S3 Table. WHO Leprosy Indicators of Physical Disability Among Newly Detected Leprosy Cases in Yunnan, China, 1990–2020.
(XLS)

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References
1. White C, Franco-Paredes C. Leprosy in the 21st century. Clin Microbiol Rev. 2015; 28: 80–94. https://doi.org/10.1128/CMR.00079-13 PMID: 25567223
2. World Health Organization. Global leprosy (Hansen disease) update, 2019: time to step-up prevention initiatives. Wkly Epidemiol Rec. 2020; 95: 417–440.
3. World Health Organization. Towards zero leprosy. Global leprosy (Hansen’s disease) strategy 2021–2030. New Delhi, India: World Health Organization; 2021.
4. World Health Organization. Global leprosy strategy 2016–2020: accelerating towards a leprosy-free world. New Delhi, India: World Health Organization; 2016.
5. National Health and Family Planning Commission of the People’s Republic of China. Diagnosis for leprosy (WS 291–2018). 2018.
6. World Health Organization. World health organization expert committee on leprosy: seventh report. Technical report series 847. Geneva: World Health Organization; 1998.
7. Oliveira DT, Sherlock J, Melo EV, Rollemberg KC, Paixão TR, Abuawad YG, et al. Clinical variables associated with leprosy reactions and persistence of physical impairment. Rev Soc Bras Med Trop. 2013; 46: 600–604. https://doi.org/10.1590/0037-8682-0100-2013 PMID: 24270251
8. Heldinger M, Simonnet E, Karippadathu SF, Puchinger M, Pfeifer J, Grisold A. Analysis of social determinants of health and disability scores in leprosy-affected persons in Salem, Tamil Nadu, India. Int J Environ Res Public Health. 2018; 15: 2769. https://doi.org/10.3390/ijerph15122769 PMID: 30563301
9. World Health Organization. Global leprosy strategy 2016–2020. Accelerating towards a leprosy-free world. Monitoring and evaluation guide. Geneva: World Health Organization; 2016.

10. Shui TJ, Long H, Xiong L, Zhang XH, He J, Chen X. Towards the elimination of leprosy in Yunnan, China: a time-series analysis of surveillance data. PLoS Negl Trop Dis. 2021; 15: e0009201. https://doi.org/10.1371/journal.pntd.0009201 PMID: 33725010

11. Wang L, Sun PW, Gu H, Wang HS, Chen XS. Epidemiological characteristics of leprosy in China, 2018. Int J Dermatol Venereol. 2020; 3: 27–30.

12. Souza CDF, Tavares DLC, Tavares CM, Almeida A, Accioly S, Paiva JPS, et al. Physical disabilities due to leprosy in Alagoas State, Northeast Brazil: a temporal and spatial modeling. Rev Soc Bras Med Trop. 2019; 52: e20180540. https://doi.org/10.1590/0037-8682-0540-2018 PMID: 31340360

13. World Health Organization. Global leprosy update, 2015: time for action, accountability and inclusion. Wkly Epidemiol Rec. 2016; 91: 405–420.

14. Chen X, Zhang L, Huang M, Zhai X, Wen Y, Pan C. Coexistence of nerve enlargement and neuratrophic detected by ultrasonography in leprosy patients. Sci Rep. 2018; 8: 7812. https://doi.org/10.1038/s41598-018-26085-1 PMID: 29773868

15. Chen X, Zha S, Shui TJ. Presenting symptoms of leprosy at diagnosis: clinical evidence from a cross-sectional, population-based study. PLoS Negl Trop Dis. 2021; 15: e0009913. https://doi.org/10.1371/journal.pntd.0009913 PMID: 34813585

16. Lana FC, Amaral EP, Lanza FM, Saldanha AN. Physical disabilities resulting from Hansen's disease in Vale do Jequitinhonha/state of Minas Gerais, Brazil. Rev Lat Am Enfermagem. 2008; 16: 993–997. https://doi.org/10.1590/s0104-11692008000600009 PMID: 19229402

17. Cakiner T, Yüksel A, Eğit AS, Çağrı G, Karaçorlu M, Kültür A. The extent of leprosy-related disabilities in Istanbul Leprosy Hospital, Turkey. Lepr Rev. 1997; 68: 43–49. https://doi.org/10.5935/0305-7518.19970007 PMID: 9121331

18. Raposo MT, Reis MC, Caminha AVQ, Heukelbach J, Parker LA, Pastor-Valero M, et al. Grade 2 disabilities in leprosy patients from Brazil: need for follow-up after completion of multidrug therapy. PLoS Negl Trop Dis. 2018; 12: e0006645. https://doi.org/10.1371/journal.pntd.0006645 PMID: 30011288

19. World Health Organization. Weekly epidemiological record. Global leprosy (Hansen disease) update, 2020: impact of COVID-19 on the global leprosy control. Wkly Epidemiol Rec. 2021; 96: 421–444.