

## RISK FACTORS FOR PHYSICAL DISABILITY IN PATIENTS WITH LEPROSY: A SYSTEMATIC REVIEW

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### Abstract

**Background:** Leprosy is also referred to as Hansen disease. It is a chronic granulomatous infection generally caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*, both of which primarily affects the skin and peripheral nerves. Physical disability (PD) can occur before leprosy diagnosis, during treatment and post-release from treatment. However, although patients may be exposed to risk factors that potentiate the risk of more severe PD they stop being routinely evaluated once the treatment of active leprosy has been completed.

**The aim:** This study aims to show about risk factor for physical disability in patients with leprosy.

**Methods:** By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

**Result:** In the PubMed database, the results of our search brought up 104 articles, whereas the results of our search on SagePub brought up 77 articles. The results of the search conducted for the last year of 2013 yielded a total 88 articles for PubMed and 48 articles for SagePub. The result from title screening, a total 7 articles for PubMed and 28 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.

**Conclusion:** Delayed diagnosis, nerve damage, no skin lesions, WHO and Ridley-Jopling classifications, leprosy reactions, advanced age, rural occupation, Han ethnicity, and male sex were associated with disability in leprosy patients. Identifying risk factors could help to prevent physical disability.

**Keyword:** Leprosy, Physical disability, Hansen disease.

## INTRODUCTION

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* that affects the skin and peripheral nerves, leading to progressive physical disability and deformities if not diagnosed and treated early. Despite a significant reduction in its global prevalence since the World Health Organization (WHO) implemented the free multidrug therapy program in 1995, leprosy remains a major cause of morbidity owing to its associated long-term disabilities and sequelae in an estimated 2 million people worldwide.<sup>1,2</sup>

The WHO goal is to reduce leprosy disabilities to a target of less than 1 per million population through the strengthening of strategies for the prevention and reduction of deformities. These strategies include the early recognition and prioritization of individuals with leprosy with characteristics associated with physical disability and the main focus of control programs and rehabilitation centers is to prevent and manage physical impairment to improve quality of life.<sup>1</sup>

Physical disability can occur before leprosy diagnosis, during treatment, and post-release from treatment. About 15% of the world's population has some form of disability. The Global Leprosy scheme 2016–2020 spotlights early case recognition before apparent incapacities happen. Target recognition among higher danger bunches through leading efforts in profoundly endemic regions or networks; and further developing inclusion and access for underestimated populaces. This will bring about prior recognition and decrease of patients with grade II disability (G2D) at the time of examination. The objective of G2D rate is less than one for every million populace.<sup>3,4</sup>

The WHO introduced a global target of reducing the rate of new cases with Grade 2 disabilities per 100,000 population by at least 35% at the end of 2015 compared to the baseline at the end of 2010. By focusing on interventions to reduce Grade 2 disability through early detection and treatment of leprosy, the spread of the disease in the community could be prevented. Grade 2 disability rate at the time of leprosy diagnosis has gained the attention of researchers, but data on Grade 1 disability are still lacking. Detection of disability at an earlier stage (Grade 1) and adoption of protective lifestyle measures may prevent further progression to Grade 2 disability and deformity. In this background, we decided to carry out a cross-sectional study in our tertiary care institution on the prevalence of Grade 1 and 2 disability in patients with newly diagnosed leprosy and tried to identify any clinical features that placed a patient at risk for developing the same.<sup>5</sup> The grade 2 deformities among newly detected leprosy patients still occur high. Claw hand was the most common deformity in the upper limb, whereas foot drop and trophic ulcer were the most common deformities in the lower limb. Although leprosy has been eliminated globally on study, the disease continues to be significant cause of peripheral neuropathy, deformity, disability and disfigurement in some developing countries.<sup>6</sup>

## METHODS

### Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

### Criteria for Eligibility

For the purpose of this literature review, we compare and contrast of risk factor for physical disability in patients with leprosy. It is possible to accomplish this by researching or investigating the risk factor for physical disability in patients with leprosy. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine the best time to perform emergency surgery for congenital diaphragmatic hernia. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

### Search Strategy

We used "Risk factor for physical disability in patients with leprosy"; "Disability in patients leprosy" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: (*"Leprosy"[MeSH Subheading] OR "risk factor of leprosy"[All Fields] OR "incident of leprosy"[All Fields]*) AND (*"sign and symptom of leprosy"[All Fields] OR "complication of leprosy"[All Fields]*) AND (*"physical disability in leprosy"[MeSH Terms] OR ("risk factor of physical disability in leprosy"[All Fields]) OR ("risk factor of physical disability"[All Fields]) AND "incident of physical disability in patients with leprosy"[All Fields]*) used in searching the literature.

### Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

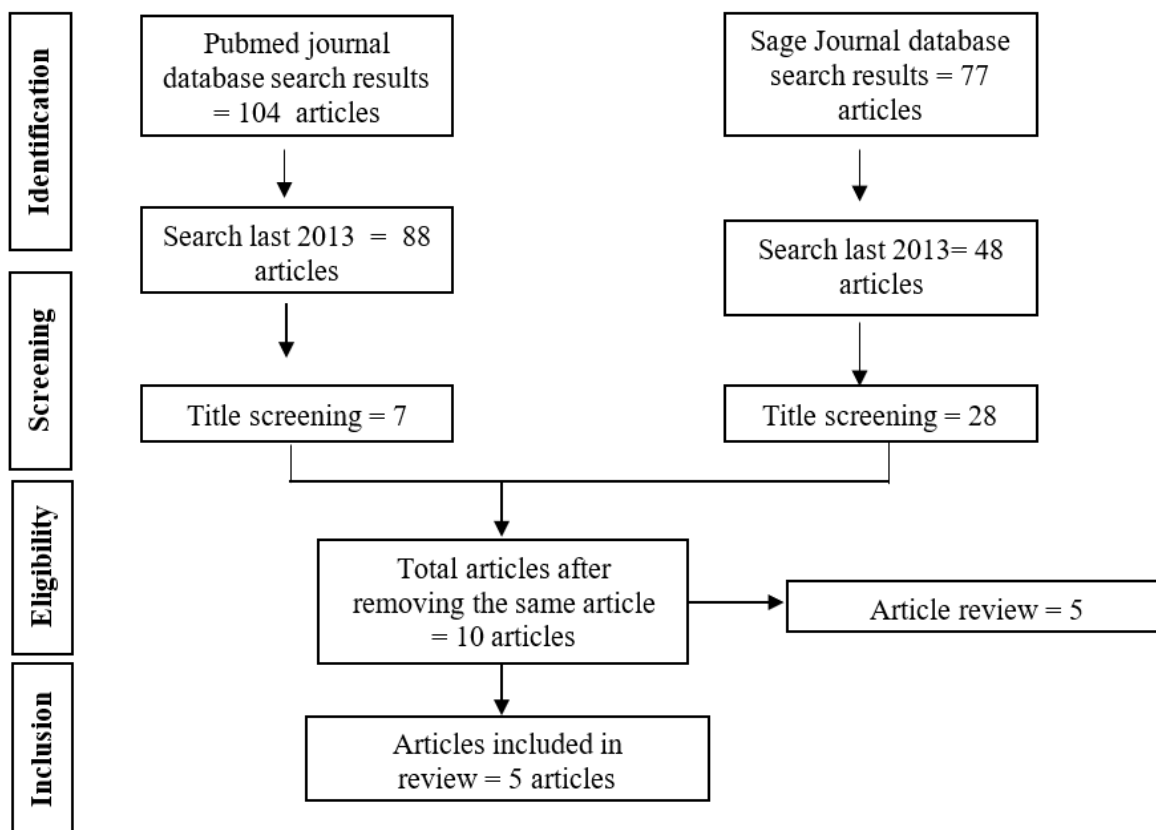


Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

**Quality Assessment and Data Synthesis**

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. In order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

**RESULT**

In the PubMed database, the results of our search brought up 104 articles, whereas the results of our search on SagePub brought up 77 articles. The results of the search conducted for the last year of 2013 yielded a total 88 articles for PubMed and 48 articles for SagePub. The result from title screening, a total 7 articles for PubMed and 28 articles for SagePub. In the end, we compiled a total of 10 papers. We included five research that met the criteria.

Rathod, SP *et al* (2020)<sup>7</sup> showed upon disability assessment by WHO grading system, 152 (76%) had no visible impairment, 21.25% of the patients had Grade 1 or above deformities and 16 (6.31%) had Grade 2 or more severe deformity. Of these deformities, deformities involving hand were 113 (44.48%), feet were 101 (39.76%) and involving face were 40 (15.74%) respectively. This suggests hand and feet are more commonly affected by deformities due to repetitive trauma due to work and house hold deeds. Deformities in Hansen's disease can be further sub-divided in the functional deformity and anatomical/morphological deformity. Most common functional deformity was trophic ulcer of hand or foot seen in 54 (29.34%) patients followed by claw hand 21 (11.41%), foot drop 2 (1.1%) and wrist drop 1 (0.54%). Amongst the morphological deformities, leonine facies 14 (7.60%), Ear deformity 13 (7.06%), resorption of digits 6 (3.20%), madarosis 6 (3.20%), sagging face 4 (2.17%), saddle nose 3 (1.63%), eye deformities 3 (1.63%). Of the 254 disabilities, 168 (66.14%) deformities were noticed at the moment of diagnosis, 20 (7.87%) deformities occurred while patient was on anti-leprosy treatment with Multidrug Therapy (MDT) for 1 year and (21.25%) deformities occurred in patients who were released from treatment and were diagnosed during the follow up period.

Shravani, B *et al* (2022)<sup>8</sup> showed analysis of the deformities showed 20% (n = 10) had trophic ulcers and 14% (n = 7) had claw hand. Out of the 10 patients with trophic ulcer, 70% (n = 7) belonged to the LL Spectrum. Lepromatous leprosy was significantly associated with trophic ulcer (p = 0.004) by Chi-square test. Out of seven patients with claw hand, three

(42.8%) belonged to BL spectrum. Three patients had both claw hand and trophic ulcer. All patients with claw hand and 80% of the patients with trophic ulcers presented to the healthcare facility at least 6 months after the onset of symptoms. The patients were divided into three groups using the WHO grading for disabilities of hands and feet. There were 28% (n = 14) patients with grade 1 disability and 32% (n = 16) patients with grade 2 disability. So, a total of 60% (n = 30) of our patients had either grade 1 or grade 2 disability. Majority (81.2%) of our G2D patients presented 6 months after the onset of symptoms of leprosy, which was not statistically significant. However, 41.9% of patients diagnosed after 6 months developed G2D, whereas only 15.7% of patients diagnosed before 6 months developed G2D. Among untreated patients, 30.7% developed G2D, similar to 30.6% of patients on treatment or completed treatment developed G2D. The proportion of lepromatous patients (56.2%) were the highest among G2D patients according to the clinical type. This was statistically significant (p = 0.012) by Chi-square test.

**Table 1. The literature include in this study**

Author	Origin	Method	Sample Size	Result
Rathod, SP <i>et al.</i> , 2020 <sup>7</sup>	India	Retrospective cohort study	200 patients	Of the 200 patients followed up in the study, 134 (67%) were males and 66 (33%) female. Lepromatous Leprosy was the most common type of leprosy in the current study with 61 (30.5%) followed by Tuberculoid Leprosy 54 (27%), borderline lepromatous leprosy 42 (21%), borderline tuberculoid leprosy 29 (14.5%), pure neuritic leprosy 6 (3%) respectively and mid-borderline leprosy 1 (0.5%), indeterminate leprosy 1 (0.5%) each. Proportion of Multibacillary (MB) cases was 67% as compared to 33% Paucibacillary (PB) cases.
Shravani, B <i>et al.</i> , 2022 <sup>8</sup>	India	Cross-sectional study	50 patients	Grade 2 disability was found among 32% of the patients with leprosy, whereas a total of 60% of our patients had either grade 1 or grade 2 disabilities. Trophic ulcer was found among 20% and claw hand among 14% of leprosy patients. We found significant associations of lepromatous leprosy with trophic ulcer (p = 0.004) and grade 2 disability (p = 0.012). All patients with claw hands and 80% of the patients with trophic ulcers presented to the healthcare facility at least 6 months after the onset of symptoms.
Mulugeta, SS <i>et al.</i> , 2022 <sup>9</sup>	Ethiopia	Retrospective cohort study	205 patients	In total, 205 (66.3%) completed records revealed patients with leprosy were disabled. Among these, 64.88% of them were males. In multilevel binary logistic regression analysis, the individual-level variables, such as median age (AOR = 1.1; 95% CI: 1.043, 1.13) of patients, patients with duration of symptom [7–12 months (AOR = 2.26; 95% CI: 1.50, 3.39), 13–24 months (AOR = 2.13; 95% CI: 1.44, 3.15), and more than 24 months (AOR = 2.67; 95% CI: 1.8, 4.02)], the absence of sensory loss (AOR = 0.84; 95% CI: 0.72, 0.96), and patients with asymmetry lesion distribution (AOR = 0.74; 95% CI: 0.65, 0.85), were the most significant determinant factors of disability. The default leprosy patient (AOR = 15.53; 95% CI: 1.82, 134.96) and new leprosy patient (AOR = 0.51; 95% CI: 0.33, 1.68) were the significant determinant factors of disability due to leprosy patients.
Chen X <i>et al.</i> , 2021 <sup>10</sup>	China	Retrospective observational study	10644 patients	The following factors were associated with the development of physical disability in these patients with leprosy: delayed diagnosis [odds ratio (OR): 5.652, 4.399, and 2.275; 95% confidence intervals (CIs): 4.516–7.073, 3.714–5.212, and 2.063–2.509; for ≥ 10, 5–10 y, and 2–5 years, respectively], nerve damage (OR: 3.474 and 2.428; 95% CI: 2.843–4.244, and 1.959–3.008; for 2 and 1 damaged nerves, respectively), WHO classification of PB (OR: 1.759; 95% CI: 1.341–2.307), Ridley-Jopling classification (OR: 1.479, 1.438, 1.522 and 1.239; 95% CI: 1.052–2.079, 1.075–1.923, 1.261–1.838, and 1.072–1.431; for TT, BT, BB, and BL when compared with LL, respectively), advanced age (OR: 1.472 and 2.053; 95% CI: 1.106–1.960 and 1.498–2.814; for 15–59 and over 60 years old, respectively), zero skin lesions (OR: 1.916; 95% CI: 1.522–2.413), leprosy reaction (OR: 1.528; 95% CI: 1.195–1.952), rural occupation (OR: 1.364; 95% CI: 1.128–1.650), Han ethnicity (OR: 1.268; 95% CI: 1.159–1.386), and male sex (OR: 1.128; 95% CI: 1.024–1.243).
Santos AR <i>et al.</i> , 2020 <sup>11</sup>	Brazil	Retrospective cohort study and survival analysis	618 participants	The mean time for progression of the PD grade was 162 months for PB and 151 months for MB leprosy patients. The survival curve showed that 15 years after the release from treatment, the probability of PD grade progression was 35%, with no difference between PB and MB or age groups. Leprosy reactions and registered medical complaints of any kind during treatment were identified as risk factors with Hazard Ratios of 1.6 and 1.8 respectively.

Mulugeta, SS *et al* (2022)<sup>9</sup> showed the distribution of disability among leprosy patients was not consistent across clusters. A two-level mixed-effects binary logistic regression model was used to analyze the effect of individual characteristics and community-level factors in determining disability among leprosy patients. The intraclass correlation coefficient (ICC) value was 39.4%, indicating that about 39.4% of the total variability of disability among leprosy patients was attributed to community-level factors, whereas the individual variation explained the remaining 60.6% of the total variability. According to the PCV results, the full model explained approximately 79.2% of the disability in clusters. Moreover, the MOR confirmed that disability was attributed to community-level factors. In the null model, the MOR for disability due to leprosy patients was 4.5, indicating that there was variation between communities.

Chen, X *et al* (2021)<sup>10</sup> showed results of risk factors associated with physical impairments graded as G1D and G2D separately when compared with G0D. Han ethnicity, rural occupation, nerve damage, delayed diagnosis, leprosy reaction, zero skin lesions, and Ridley-Jopling classification were associated with a higher risk of G1D.

Santos, AL *et al* (2020)<sup>11</sup> showed the Cox proportional risk model indicated no significant difference in the risk of progression of the PD grade post-release from treatment between age groups and operational leprosy classifications. Leprosy reactions during the treatment period represented a 1.6 times greater risk of PD progression (HR: 1.6; 95% CI: 1.1–2.4). A record of leprosy-related complaints during treatment was associated with almost twice the risk of progression of the PD post-release from treatment (HR: 1.8; 95% CI: 1.3–2.4). The mean time until progression of the PD grade was 130 months for patients with documented leprosy reactions during treatment. For individuals with recorded complaints during treatment the average time of progression of the PD grade was 139 months.

## DISCUSSION

Leprosy is also referred to as Hansen disease. It is a chronic granulomatous infection generally caused by *Mycobacterium leprae* and *Mycobacterium lepromatosis*, both of which primarily affects the skin and peripheral nerves. "Mycobacterium leprae complex" comprises *M. leprae* and *M. lepromatosis*. Though both mycobacteria are classified as different species because of their DNA sequences, they both are obligate intracellular organisms and have many similar features causing the same clinical disease. Leprosy is of great concern in the medical community. This disease is not highly contagious, contrary to belief, and treatment is readily available for this ailment. Through awareness and early medical intervention, significant reduction causing disability in the eyes, hands, and feet is possible. Relapses tend to be rare, but any damage caused by neuropathy is irreversible and may require lifelong care.<sup>12,13</sup>

Global attention to eliminating leprosy has focused on curative efforts. Additionally, leprosy is well known as one of the most frequent causes of disability, even years after the patient is cured. People affected by leprosy are prone to have physical disability grade progression with a probability of 35%. According to WHO, disability is an umbrella definition for impairment of bodily function and structure, activity limitation, and participation restriction.<sup>14</sup>

The delayed presentation is a recognised risk factor for disability in leprosy and is the result of complex interactions between physical, social, economic and psychological factors. Assessing the potential factors associated with delays in seeking care and diagnosis of leprosy is essential to identify program impediments and devise appropriate strategies to promote early diagnosis and prevent disability. The present study was conducted to determine the risk factors associated with disability (G2D and G1D) among adult new leprosy cases and to measure their strength of association. We hypothesized that adult leprosy cases who have a delay in diagnosis are at a greater risk of developing disability (G2D and G1D). In the present study, we quantified the delay in terms of patient delay and health care provider delay.<sup>15</sup>

Data on the magnitude of the problem of leprosy-related impairments are not easily available. The targets under WHO, Global Leprosy Strategy (2016–2020) are number of children diagnosed with leprosy and deformities are zero, the rate of newly diagnosed cases with deformities are <1 per million and number of countries with legislation allowing discrimination on leprosy are zero. A progressive increase in grade 2 deformities seems to indicate an increasing delay in the detection of cases, which itself is indicative of operational failure. In leprosy, the disability assessment is a very important factor in the evaluation of the effectiveness of the National Leprosy Elimination Program (NLEP).<sup>6</sup>

## CONCLUSION

Delayed diagnosis, nerve damage, no skin lesions, WHO and Ridley-Jopling classifications, leprosy reactions, advanced age, rural occupation, Han ethnicity, and male sex were associated with disability in leprosy patients. Identifying risk factors could help to prevent physical disability.<sup>6</sup>

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