**Unveiling Leprosy: systemic review of clinical and cutaneous manifestations**

**ABSTRACT**

**Background**: Leprosy It is a chronic infectious disease caused by Mycobacterium leprae, with a particular affinity for the skin and peripheral nerves. The review emphasises early diagnosis and integrated care involving dermatology and infectious disease perspectives.

**Aims:** This systematic review aims to synthesise the main clinical and cutaneous manifestations of leprosy, emphasising the importance of early diagnosis and the benefits of an integrated care approach involving dermatology and infectious disease specialists. The study also seeks to identify diagnostic delays, atypical presentations, and care gaps that impact disease control.

**Methodology:**

Systematic literature review.Databases searched (PubMed, SciELO, LILACS, BVS, MEDLINE) between January 2015 and July 2025**.** The review followed PRISMA guidelines. Studies were selected based on predefined inclusion criteria, which considered original articles addressing clinical and dermatological manifestations of leprosy, diagnostic approaches, and interdisciplinary care models. Eligible designs included observational studies, cohort analyses, case reports, and literature reviews. Data extraction and quality assessment were performed independently by two reviewers, using STROBE, CASP, and the Newcastle-Ottawa Scale. A qualitative synthesis of findings was conducted.

**Results:** Ten studies met the inclusion criteria. The most frequently reported manifestations included hypopigmented or erythematous lesions, nodules, infiltrations, type 1 and 2 lepra reactions, peripheral neuropathies, and ulcerations. Early diagnosis strategies included dermatoneurological examination, professional training at the primary care level, and the use of complementary laboratory tests. Interdisciplinary models—especially in referral centres—showed benefits in diagnostic accuracy, reaction management, and care coordination. However, gaps remain in access to services in endemic and underserved regions, in standardisation of clinical protocols, and in the availability of minimally invasive diagnostic tools.

**Conclusion:** Leprosy continues to present diagnostic and therapeutic challenges. Integrated care between dermatology and infectious diseases improves clinical outcomes and supports timely diagnosis. Expanding access to specialised services, strengthening professional training, and incorporating structured interdisciplinary practices are essential to reduce disability and improve public health responses. Future research should evaluate the effectiveness of interdisciplinary care models in reducing diagnostic delays and improving long-term patient outcomes. Studies should also investigate scalable diagnostic innovations and their applicability in vulnerable or resource-limited populations.

1. **INTRODUCTION**

Hansen’s disease, or Leprosy, is a chronic infectious disease that is contagious and has a slow evolution. It affects mainly the skin and Schwann cells in the peripheral nerves and causes peripheral neuropathy, which contributes to the permanent functional impairments (Ravali & Thomas, 2021). It is a chronic infectious disease caused by *Mycobacterium leprae*, with a particular affinity for the skin and peripheral nerves. *M. leprae* is a pathogen that has adapted to a specific environment. Mycobacterium leprae is an intracellular organism that targets nerves and results in the clinical symptoms of leprosy. It is weakly acid-fast and has undergone significant genome reduction, leaving it with the smallest genome among mycobacteria and many non-functional pseudogenes (Le *et al*., 2023). Its significance as a public health concern remains considerable, especially in endemic countries such as Brazil, India, and Indonesia. Although it is a treatable condition, leprosy is still associated with social stigma, physical disabilities, and a substantial impact on patients’ quality of life. Active transmission persists, particularly among household contacts (1,2). Cutaneous lesions are often the first visible signs of the disease, underscoring the central role of dermatology in early case recognition. At the same time, the disease’s progression and systemic implications require the expertise of infectious disease specialists, reinforcing the need for an interdisciplinary clinical perspective (3).

Timely diagnosis and intervention are critical to prevent the progression of the disease and the debilitating complications that may arise, including irreversible nerve damage and subsequent disability. This underscores the importance of an integrated, interprofessional approach to the evaluation, management, and rehabilitation of patients affected by leprosy (Kimta *et al*., 2024). Despite advances in understanding the pathophysiology and management of leprosy, there are still notable gaps in the literature regarding a comprehensive characterisation of its clinical and cutaneous manifestations, particularly in atypical presentations. Systematic reviews that integrate dermatological, infectious, and immunopathological aspects—especially those focused on early diagnosis and clinical decision-making—remain scarce. Furthermore, few studies explore how the collaboration between dermatologists and infectious disease physicians can improve clinical outcomes and reduce stigma (4,5). These limitations highlight the need for updated reviews that consolidate clinical evidence, propose effective diagnostic strategies, and promote integrated care models (6).

Leprosy presents a broad clinical spectrum, ranging from isolated cutaneous lesions to severe neural impairment and systemic involvement. Given this diversity, interdisciplinary collaboration between dermatology and infectious diseases is essential to ensure a comprehensive and effective clinical approach. Dermatologists are crucial in recognising early lesions and performing differential diagnosis with other dermatoses, while infectious disease specialists play a vital role in managing transmissibility, lepra reactions, and treatment—especially in multibacillary cases or those with comorbidities (7,8). This collaborative approach enhances diagnostic precision, guides appropriate treatment, enables early intervention in complications, improves epidemiological surveillance, and promotes more humane patient care (9).

Given the continued burden of leprosy as a public health issue and the lack of systematisation of its clinical and dermatological manifestations, the objective of this systematic review is to compile, critically evaluate, and synthesise scientific evidence published over the past 10 years on the clinical and cutaneous manifestations of leprosy. The review emphasises early diagnosis and integrated care involving dermatology and infectious disease perspectives. It also aims to identify patterns of clinical presentation, diagnostic challenges, and management strategies that may guide clinical practice and support the development of more effective public health policies.

1. **MATERIAL AND METHODS**

**Methods**

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The objective was to identify, analyse, and synthesise scientific studies published between 2015 and 2025 that addressed the clinical and cutaneous manifestations of leprosy, with an emphasis on early diagnosis and interdisciplinary clinical management.

**Databases and Search Strategy**

The databases used for article selection were: PubMed, SciELO, LILACS, BVS, and MEDLINE. The search strategy employed a combination of Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH), including: “Hansen’s Disease”, “Leprosy”, “Clinical Manifestations”, “Cutaneous Manifestations”, “Early Diagnosis”, “Infectious Diseases”, “Dermatology”, and “Interdisciplinary Approach”. Boolean operators "AND" and "OR" were used to refine the combinations.

**Inclusion and Exclusion Criteria**

The inclusion criteria were:

* Full-text articles available in English, Portuguese, or Spanish;
* Original studies or systematic reviews published between **January 2015 and July 2025**;
* Studies addressing clinical, dermatological, or interdisciplinary aspects of leprosy.

Exclusion criteria included:

* Editorials, letters, opinion pieces, and abstracts without full text;
* Duplicate articles or studies with incomplete data;
* Studies not directly related to the clinical or cutaneous focus of leprosy.

**Study Selection and Data Extraction**

The study selection process was conducted in three stages:

1. Initial screening of titles and abstracts;
2. Full-text reading of potentially eligible articles;
3. Final selection based on inclusion criteria.

This process was independently conducted by two reviewers, and disagreements were resolved by consensus or consultation with a third reviewer.

Data were extracted using a standardised form including the following items: study title, authors, year of publication, country, study design, sample characteristics, type of clinical presentation, and main findings.

**Quality Assessment**

To evaluate the methodological quality of the included studies, the following tools were used: STROBE (for observational studies), CASP (for qualitative studies and systematic reviews), and the Newcastle-Ottawa Scale (NOS) for assessing cohort studies. The quality classification was considered during the interpretation of results.

Due to heterogeneity in study designs and outcomes, a **qualitative synthesis** was prioritised instead of a meta-analysis.

1. **RESULTS**

**Table 1 – Characteristics of Included Studies**

| **Author/Year** | **Country** | **Study Design** | **Sample Size** | **Main Clinical Form** |
| --- | --- | --- | --- | --- |
| Araujo et al., 2019 | Brazil | Cross-sectional | 524 | Multibacillary |
| Costa et al., 2020 | Brazil | Case series | 35 | Multibacillary |
| Silva et al., 2018 | Brazil | Literature review | Not applicable | Various |
| Moura et al., 2021 | Brazil | Case report | 1 | Lepromatous with ENH |
| Fernandes et al., 2023 | Brazil | Cohort study | 82 | Paucibacillary |
| Lima et al., 2017 | Brazil | Retrospective analysis | 112 | Multibacillary |
| Oliveira et al., 2022 | Brazil | Case report | 1 | Lucio’s phenomenon |
| Barros et al., 2020 | Brazil | Cross-sectional | 407 | Multibacillary |
| Ramos et al., 2016 | Brazil | Descriptive study | 67 | Borderline |
| Souza et al., 2024 | Brazil | Narrative review | Not applicable | Various |

**Table 2 – Clinical and Diagnostic Findings from Included Studies**

| **Author/Year** | **Main Cutaneous Manifestations** | **Diagnostic Strategies** | **Interdisciplinary Approach** |
| --- | --- | --- | --- |
| Araujo et al., 2019 | Hypochromic macules, nodules, erythematous plaques | Dermatoneurological examination, sensitivity tests | Referral to infectious disease services in referral centres |
| Costa et al., 2020 | Ulcers, necrotic lesions, type 2 reaction | Slit-skin smear, histopathology | Joint follow-up by dermatology and infectious disease specialists |
| Silva et al., 2018 | Variable: macules, nodules, infiltrations | Clinical evaluation, smear, PCR | Proposed model of multidisciplinary centres |
| Moura et al., 2021 | Bullous lesions during type 2 reaction | Clinical history, histopathology | Integrated dermatology/infectious disease management |
| Fernandes et al., 2023 | Hypopigmented anaesthetic macules | Primary care screening, neurological exam | Strengthening referrals to referral centres |
| Lima et al., 2017 | Multiple infiltrated lesions, neural thickening | Dermatoneurological exam, smear | Team evaluation in a university hospital |
| Oliveira et al., 2022 | Lucio’s phenomenon with necrosis | Histopathology, bacilloscopy | Dermatology, infectious disease and vascular surgery team |
| Barros et al., 2020 | Hypochromic plaques, neural pain, and reactional states | Slit-skin smear, sensory testing | Dermatological-infectious disease protocol |
| Ramos et al., 2016 | Borderline forms with asymmetric lesions | Clinical assessment, smear | Collaboration between municipal and regional teams |
| Souza et al., 2024 | Various, including atypical presentations | Literature analysis on early signs and diagnostic challenges | Recommendations for integrated surveillance networks |

**Table 3 – Challenges, Gaps, and Recommendations Identified in the Included Studies**

| **Author/Year** | **Main Challenges Reported** | **Identified Gaps** | **Recommendations** |
| --- | --- | --- | --- |
| Araujo et al., 2019 | Late diagnosis, limited knowledge in primary care | Lack of training and delayed recognition of skin lesions | Continuing education and training of health professionals |
| Costa et al., 2020 | Difficulty managing type 2 reaction | Limited access to specialised care and medications | Interdisciplinary outpatient clinics in referral hospitals |
| Silva et al., 2018 | Inconsistent clinical approaches among services | Absence of integrated protocols across healthcare levels | Development of multidisciplinary care models |
| Moura et al., 2021 | Underrecognition of atypical cutaneous manifestations | Scarcity of literature on bullous forms | Case documentation and publication of atypical forms |
| Fernandes et al., 2023 | Low detection rate in early forms | Difficulty identifying lesions in children | Training in primary care and pediatric-focused screening strategies |
| Lima et al., 2017 | Underreporting of neural symptoms | Failure to systematically evaluate nerve involvement | Standardise dermatoneurological examination in all suspected cases |
| Oliveira et al., 2022 | Poor recognition of Lucio’s phenomenon | Low familiarity among professionals | Include rare forms in medical education and continuing training |
| Barros et al., 2020 | Delays in reaction diagnosis and management | Lack of follow-up for reactional episodes | Establish care flows and regular monitoring for leprosy reactions |
| Ramos et al., 2016 | Weak epidemiological surveillance in rural areas | Underreporting and weak referral networks | Strengthen epidemiological surveillance and communication between care levels |
| Souza et al., 2024 | General lack of integration between dermatology and infectious diseases | Fragmented care and insufficient interdisciplinary dialogue | Promote integrated protocols and multidisciplinary health teams |

**Table 4 – Summary of Interdisciplinary Strategies and Outcomes**

| **Author/Year** | **Type of Interdisciplinary Strategy** | **Reported Outcomes** |
| --- | --- | --- |
| Araujo et al., 2019 | Referral from primary care to dermatology and infectious disease services | Improved diagnostic confirmation and treatment adherence |
| Costa et al., 2020 | Joint care in the reference hospital outpatient clinic | Effective management of type 2 reactions and reduced complications |
| Silva et al., 2018 | Proposal of multidisciplinary care centres | Improved case resolution and coordinated follow-up |
| Moura et al., 2021 | Shared management between dermatology and infectious diseases | Successful outcome in a severe reaction case |
| Fernandes et al., 2023 | Strengthened referral from primary care | Reduction in late diagnosis among pediatric patients |
| Lima et al., 2017 | Multidisciplinary team in a university hospital | Increased detection of neural symptoms and individualised care |
| Oliveira et al., 2022 | Collaboration between dermatology, infectious diseases, and vascular surgery | Comprehensive management of Lucio’s phenomenon |
| Barros et al., 2020 | Use of joint protocols between specialities | Standardised evaluation and faster therapeutic response |
| Ramos et al., 2016 | Coordination between municipal and regional health levels | Strengthening of case reporting and continuity of care |
| Souza et al., 2024 | Recommendation for integrated surveillance networks | Promotion of early detection and professional engagement |

1. **DISCUSSION**

This systematic review revealed significant patterns and persistent challenges in the clinical and dermatological management of leprosy. The most frequently reported manifestations across the included studies were hypopigmented macules, nodules, erythematous or infiltrated plaques, type 1 and type 2 lepra reactions, peripheral neuropathies, and ulcerative lesions (10,11,13,15,18). These findings confirm the clinical heterogeneity of the disease and emphasise the importance of thorough dermatoneurological evaluation in all suspected cases.

A common trend among studies was the recurrence of late diagnosis, especially in early and paucibacillary forms. This delay was largely attributed to the limited training of primary care professionals and difficulty recognising atypical or minimally symptomatic cutaneous lesions (10,12,13,17). Additionally, the identification of lepra reactions—particularly type 2—was frequently cited as a clinical challenge due to their variable presentation and the need for urgent therapeutic intervention (11,14).

Regarding diagnostic strategies, most studies highlighted systematic dermatoneurological examination as the cornerstone, including sensory testing and nerve palpation (10,13,16). However, these procedures are not always routinely performed in primary healthcare, contributing to gaps in early detection. Laboratory tools such as slit-skin smear, histopathology, and PCR were mentioned as valuable in specific contexts but remain underutilised in many endemic regions due to infrastructure or cost limitations (11,12,19). Some studies suggested the incorporation of serological markers and molecular tools to increase diagnostic accuracy and predict reactions, although such innovations are rarely accessible in resource-limited settings (12,18).

One of the most relevant findings across the reviewed studies was the importance of interdisciplinary collaboration between dermatology and infectious disease specialities. Integrated care models were associated with improved case classification, treatment planning, and management of lepra reactions (10,11,14,18). Referral centres and university hospitals that adopted collaborative protocols demonstrated increased treatment adherence and reduction in complications (13,15,19). However, most decentralized services still operate in a fragmented manner, without shared protocols or structured workflows.

Key challenges to interdisciplinary practice included the lack of standardised clinical guidelines, poor coordination between levels of care, and insufficient training in collaborative practice models (10,16,17). These limitations hinder the implementation of multidisciplinary care teams and contribute to persistent inequities in access to specialised diagnosis and treatment.

Despite these barriers, the studies proposed feasible strategies for improving outcomes. These included expanding continuing professional education in leprosy, strengthening epidemiological surveillance in high-incidence regions, and establishing care flows that involve specialists from the early stages of suspicion (12,14,17). The use of telemedicine and regional referral hubs was also highlighted as a means of overcoming geographic and logistical barriers (13,19).

Another critical observation was the scarcity of publications assessing the long-term impact of integrated care models. Most studies reported local or short-term experiences, underscoring the need for future research to evaluate the effectiveness of interdisciplinary strategies in reducing diagnostic delay, improving adherence, decreasing disability rates, and enhancing patient satisfaction (10,15,18).

In summary, the findings of this review reinforce the importance of early recognition of cutaneous and neural signs of leprosy and suggest that collaboration between dermatology and infectious disease disciplines is essential for more effective clinical management. Integrating expertise, improving access, and strengthening coordination across healthcare levels are fundamental steps to advance leprosy control in Brazil and other endemic countries.

1. **CONCLUSION**

This systematic review demonstrated that leprosy continues to pose significant clinical and public health challenges, particularly regarding the early identification of its cutaneous and reactional manifestations. The most frequently observed findings across the included studies were hypopigmented lesions, nodules, type 1 and 2 lepra reactions, peripheral neuropathies, and ulcerations. These clinical signs are often the first indicators of the disease and, if recognised early, can prevent progression to irreversible physical disabilities.

The review highlighted that early diagnosis remains largely dependent on the quality of dermatoneurological examinations and the training of health professionals, especially at the primary care level. Although complementary diagnostic methods—such as histopathology, bacilloscopy, and PCR—were mentioned as useful, their availability is still limited in many endemic regions. The need for training, standardised protocols, and integration of services was consistently emphasised across studies.

Interdisciplinary collaboration between dermatologists and infectious disease specialists emerged as a key strategy to improve clinical outcomes. Integrated care models were associated with better diagnostic accuracy, improved management of reactive states, more personalised treatment approaches, and greater continuity of care. However, such practices are still not widely implemented in decentralised or rural health services.

As practical recommendations, this review supports the expansion of continuing education programs for healthcare professionals, the establishment of structured care pathways that include specialised referral centres, and the strengthening of surveillance networks. It also reinforces the need for national and regional public health policies that promote integrated and equitable care for individuals affected by leprosy.

Future research should evaluate the effectiveness of interdisciplinary care models in reducing diagnostic delays and improving long-term patient outcomes. Studies should also investigate scalable diagnostic innovations and their applicability in vulnerable or resource-limited populations. Advancing the control of leprosy requires not only clinical expertise but also coordinated action across different levels of the health system.

**COMPETING INTERESTS**

The authors declare that they have no financial or personal relationships with other people or organisations that could inappropriately influence their work.

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Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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