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THE ANALYSIS STUDY OF DIAGNOSIS AND MANAGEMENT OF LEPROSY: A COMPREHENSIVE SYSTEMATIC REVIEW

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ABSTRACT

Background: *Leprosy, a major public health concern in middle-income countries, presents complex diagnostic and management challenges. Despite a decline in prevalence due to multidrug therapy, delayed diagnosis remains prevalent. Current diagnostic approaches rely on clinical evaluation, but molecular diagnostics offer promise. Management involves a multidisciplinary approach, including psychosocial support and rehabilitation. This study aims to systematically assess existing evidence on the diagnostic and therapeutic strategies in leprosy.*

Methods: *This systematic review followed PRISMA 2020 guidelines and included only full-text, peer-reviewed articles published in English between 2015 and 2025. Editorials and review papers without a DOI were excluded to ensure source quality. Relevant studies were identified through targeted searches in ScienceDirect, PubMed, and SAGE Publications.*

Result: *A preliminary search across multiple selected databases yielded over 8.000 studies deemed potentially relevant. Following a systematic three-tiered screening protocol, only eight articles met the strict inclusion criteria and were selected for in-depth analysis. Each of these studies underwent a thorough critical appraisal to evaluate their relevance and quality in addressing the diagnosis and management of leprosy. This methodical approach ensured that the final synthesis was grounded in high-quality evidence, providing valuable insights aligned with the review's objectives and enhancing the understanding of this multifaceted condition.*

Conclusion: *Leprosy treatment and management involve a comprehensive approach that includes clinical evaluation, bacteriological confirmation, and classification systems like Ridley-Jopling and WHO criteria. Accurate diagnosis is supported by skin lesions, peripheral nerve involvement, anesthesia, and positive slit-skin smears. Effective management involves early detection and prompt multidrug therapy to prevent complications and improve outcomes.*

Keyword: *Leprosy, accurate diagnosis, multidrug therapy, complication.*

INTRODUCTION

Leprosy, or Hansen's disease, remains a significant public health concern in several parts of the world, particularly in low- and middle-income countries.[1] Caused by Mycobacterium leprae, the disease primarily affects the skin, peripheral nerves, mucosa of the upper respiratory tract, and eyes.[2] Despite the global decline in prevalence due to multidrug therapy (MDT), the disease continues to present with complex diagnostic and management challenges, especially in endemic regions. Early detection and appropriate treatment are crucial to preventing long-term disability and breaking the chain of transmission.[3] However, delayed diagnosis is still prevalent, often due to a lack of awareness, stigma, and limitations in diagnostic accessibility.[4]

Current diagnostic approaches for leprosy rely heavily on clinical evaluation, which includes assessing skin lesions and peripheral nerve involvement. Slit-skin smear microscopy and histopathological analysis remain standard diagnostic tools but vary in sensitivity, especially in paucibacillary cases.[5] Advances in molecular diagnostics, such as polymerase chain reaction (PCR)-based tests, have shown promise in improving early and accurate detection.[6] However, their widespread implementation is limited by cost and infrastructure.[5] The lack of a reliable, point-of-care diagnostic test remains a significant barrier to timely intervention, particularly in resource-constrained settings.[7] Therefore, evaluating the accuracy, feasibility, and applicability of both conventional and novel diagnostic methods is essential for improving case detection and treatment outcomes.

Management of leprosy encompasses more than the administration of MDT. It requires a multidisciplinary approach that addresses not only the bacterial infection but also the associated complications, such as lepra reactions, nerve damage, and disability. WHO-recommended MDT regimens have been instrumental in reducing the disease burden, yet treatment adherence, drug resistance, and relapse rates pose ongoing concerns.[8] Furthermore, psychosocial support, rehabilitation, and community-based care are critical components of comprehensive leprosy management.[9] This review aims to systematically assess existing evidence on the diagnostic and therapeutic strategies in leprosy, identify gaps in current practice, and provide insights to strengthen future policy and clinical guidelines.

METHODS

PROTOCOL

This review was systematically designed following the PRISMA 2020 framework to maintain methodological accuracy and uphold the highest standards of research integrity. By adhering to these established guidelines, the study achieved greater transparency, consistency, and scientific credibility. Every stage of the review process—from extensive literature searching to detailed data extraction and synthesis—was conducted with a strong emphasis on reducing potential bias and ensuring dependable results. This rigorous approach reinforces the reliability of the conclusions and contributes meaningful perspectives to the broader evidence-based knowledge on the topic.

CRITERIA FOR ELIGIBILITY

This systematic review is designed to thoroughly assess the diagnosis and management of leprosy by integrating findings from a diverse array of relevant studies. Through the identification of recurring patterns, emerging clinical trends, and notable research gaps, the review aims to generate insights that can support the refinement of diagnostic protocols and therapeutic strategies. Its primary goal is to deepen the understanding of current approaches while strengthening the evidence base that informs clinical decision-making and patient care practices.

To uphold a high standard of methodological rigor, the review applied carefully defined inclusion and exclusion criteria. Only peer-reviewed publications in English from the years 2015 to 2025 were considered eligible, with source authenticity verified using Digital Object Identifiers (DOIs). Editorials, review articles, and duplicate publications were intentionally excluded to preserve the review's focus on original, high-quality research. This rigorous selection process reinforces the reliability and academic validity of the findings.

By applying a structured and transparent research methodology, the review ensures its conclusions are rooted in dependable empirical evidence. The insights derived from this analysis aim to advance current practices in the diagnosis and management of leprosy, ultimately contributing to better clinical outcomes. This evidence-based approach not only enhances patient care but also promotes the continued development of standardized and effective medical protocols within the field.

SEARCH STRATEGY

An extensive and methodical search strategy was implemented to identify relevant literature for this review, using targeted keywords including "diagnosis," "management," and "leprosy." To capture a broad and balanced selection of academic sources, the search was conducted across three prominent databases: PubMed, SAGE Publications, and ScienceDirect. This approach ensured access to a diverse range of peer-reviewed studies, thereby enhancing both the depth and quality

of the evidence base. The use of a well-structured and academically rigorous search protocol reinforces the credibility of the findings and supports a more comprehensive and accurate assessment of leprosy diagnosis and management practices.

Table 1. Search Strategy

Database	Search Strategy	*Hits*
Pubmed	*("diagnosis" AND "management" AND "leprosy")*	552
Science Direct	*("diagnosis" AND "management" AND "leprosy")*	7.019
Sagepub	*("diagnosis" AND "management" AND "leprosy")*	1.108

DATA RETRIEVAL

The authors conducted a thorough and structured initial screening by critically reviewing the titles and abstracts of all retrieved articles to determine their alignment with the study's objectives. Only those that met the established inclusion criteria and demonstrated strong relevance to the core topic were selected for full-text assessment. This methodical approach enabled the identification of recurring patterns and critical themes across the literature, ensuring that the synthesis remained focused and directly addressed the central research question. By adopting a transparent and systematic selection process, the review effectively extracted high-quality data to support well-founded conclusions.

To maintain consistency and improve comparability across selected studies, only full-text articles published in English were considered. Each article underwent a strict eligibility check to confirm it met the study's criteria and contributed meaningfully to the research focus. Studies that failed to meet these standards—such as those lacking peer review or original data—were excluded, narrowing the pool to the most relevant and credible sources. This rigorous screening process helped reduce selection bias and bolstered the overall validity of the findings.

Furthermore, the evaluation incorporated a close analysis of study attributes including authorship, publication year, geographic context, and research methodology. This comprehensive review ensured the inclusion of studies that were both methodologically sound and contextually appropriate. The systematic and well-organized framework adopted for study selection significantly enhanced the reliability of the review, forming a solid foundation for drawing insightful conclusions that advance clinical knowledge and improve practice in the diagnosis and management of leprosy.

QUALITY ASSESSMENT AND DATA SYNTHESIS

The authors implemented a thorough and systematic screening procedure, beginning with a detailed evaluation of each study's title and abstract to determine its relevance and methodological soundness based on predefined criteria. Only those studies that aligned closely with the review's aims and exhibited a high standard of scientific quality were advanced to the full-text review phase. This selective approach ensured the inclusion of only significant and reliable research, thereby enriching the review's depth and analytical value. By concentrating solely on trustworthy and contextually relevant literature, the authors enhanced the clarity, consistency, and scholarly rigor of the analysis, reinforcing the credibility and academic integrity of the overall findings.

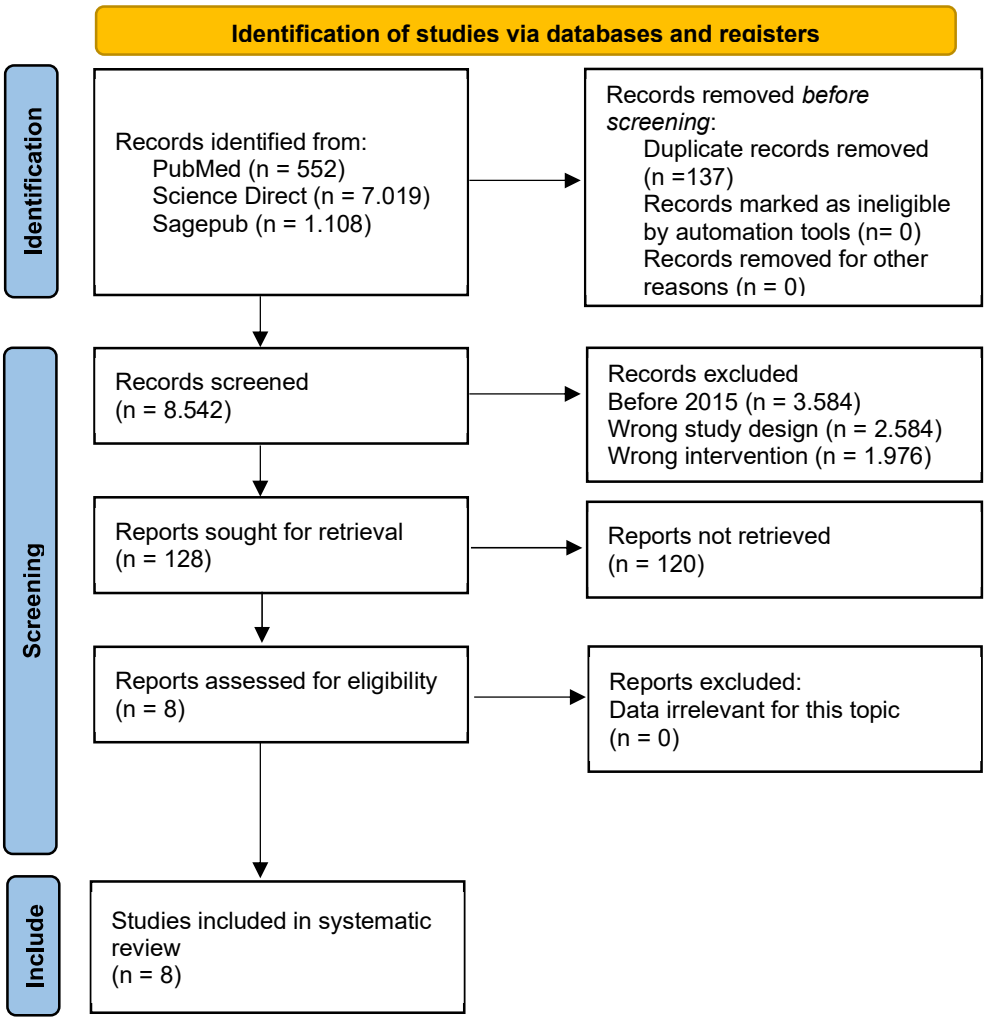

Figure 1. Article search flow chart

Table 2. Critical appraisal of Study

Parameters	(Reibel et al., 2015)	(Yap et al., 2015)	(Fischer et al., 2017)	(Akpolat et al., 2019)	(Maymone et al., 2020)	(Alinda et al., 2020)	(Chen et al., 2022)	(Hsieh et al., 2023)
1. Bias related to temporal precedence								
Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation								
Was there a control group?	No	No	No	No	No	No	No	No
3. Bias related to confounding factors								
Were participants included in any comparisons similar?	No	Yes	No	No	No	No	No	Yes
4. Bias related to administration of intervention/exposure								
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No.	Yes.	No.	No.	No.	No.	No.	Yes.
5. Bias related to assessment, detection, and measurement of the outcome								
Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	No	No	No	No	No	No	No	No
Were the outcomes of participants included in any comparisons measured in the same way?	No	No	No	No	No	No	No	No
Were outcomes measured in a reliable way?	No	Yes	No	No	No	No	No	Yes
6. Bias related to participant retention								
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	No	No	No	No	No	No	No	Yes
7. Statistical conclusion validity								
Was appropriate statistical analysis used?	No	Yes	No	No	No	No	No	Yes

RESULT

The research commenced with a structured literature search across reputable academic databases such as ScienceDirect, PubMed, and SAGE Publications to gather studies aligned with the review's objectives. A meticulous three-phase screening process was then implemented to refine the search results, ultimately narrowing them down to eight studies that fulfilled the established inclusion criteria. These selected studies were subjected to in-depth analysis to extract key insights and identify recurring themes. For clarity and ease of reference, the synthesized data have been systematically presented in Table 3, facilitating coherent comparison and interpretation of the findings across the selected literature.

Table 3. The literature included in this study

Author	Origin	Method	Sample	Result
Reibel et al.[10] (2015)	France	Review	-	Leprosy, a chronic infection affecting skin and peripheral nerves, presents with various presentations correlated with immune response, bacillary load, and delay before diagnosis. Multidrug therapy, recommended since 1982, has contributed to a decline in new cases, but resistance persists, necessitating further monitoring.
Yap et al.[11] (2015)	Malaysia	Cross Sectional	52 participants	The study found that pre-intervention knowledge of FMS improved significantly post-intervention, with a mean confidence of 4.0 out of 10 for diagnosis and 3.3 out of 10 for management. Knowledge on pathogenesis and clinical features improved the most, while leprosy reactions showed the least improvement. This improvement aims for earlier detection and prevention of clinical and epidemiological sequelae.
Fischer, M.[12] (2017)	Germany	Review	-	Leprosy, a chronic infectious disease caused by Mycobacterium leprae, is primarily affecting the skin and peripheral nervous system. Treatment options include early remission, multibacillary treatment, and preventive measures, with the highest incidence in India, Brazil, and Indonesia.
Akpolat et al.[13] (2019)	Turkey	Review	-	Leprosy, a chronic infection caused by Mycobacterium leprae, has been reported for over 2000 years. Despite its decline due to multidrug therapy, resistance remains a challenge, necessitating ongoing monitoring and

				identification by public health workers.
Maymone et al.[14] (2020)	USA	Review	-	Leprosy, a curable infectious disease, is endemic in over 140 countries worldwide. Despite being declared eradicated in 2000, 200,000 new cases were reported in 2017. Widespread migration and autochthonous transmission may bring leprosy to nonendemic areas, including North America.
Alinda et al.[15] (2020)	Indonesia	Review	-	Leprosy is a chronic granulomatous infectious disease caused by Mycobacterium leprae. It is grouped into six forms using the Ridley-Jopling classification. Treatment is categorized into paucibacillary (PB) and multibacillary (MB). Diagnosis is often clinical, but a higher sensitivity test may be needed. Multi-Drug Therapy (MDT) is adjusted based on leprosy type, with PB patients receiving rifampicin and dapsone.
Chen et al.[16] (2022)	China	Review	-	Leprosy, a neglected infectious disease, requires therapeutic and diagnostic approaches for diagnosis and treatment. Despite progress in adult and childhood leprosy, the disease remains largely neglected. This review updates diagnostic and therapeutic recommendations, emphasizing the importance of control and prevention in the ongoing development of leprosy management strategies.
Hsieh et al.[17] (2023)	Taiwan	Retrospective Study	28 participants	Leprosy diagnosis and treatment have improved significantly, with a lower rate of dapsone resistance compared to the World Health Organization's report from 2009 to 2015. Advances in drug-resistant gene mutations, post-exposure prophylaxis, vaccination, and coronavirus disease 2019 have also been reported.

DISCUSSION

DIAGNOSTIC CRITERIA AND CLINICAL CLASSIFICATION OF LEPROSY

Leprosy remains a significant global health challenge, particularly in tropical and subtropical regions, despite advances in diagnostic and treatment modalities.[18] Accurate and timely diagnosis is fundamental to controlling disease transmission and preventing disability. The diagnosis of leprosy is primarily clinical, based on the presence of hypopigmented or reddish skin lesions with definite sensory loss, thickened peripheral nerves, and a positive skin smear for acid-fast bacilli (AFB).[16] These criteria, when used systematically, form the cornerstone of case detection in endemic settings.

Leprosy is classified in two key ways: the WHO operational classification and the more detailed Ridley-Jopling classification.[19] The WHO classification, designed for treatment purposes, categorizes patients into paucibacillary (PB) and multibacillary (MB) leprosy based on the number of skin lesions and the results of slit-skin smear examinations. Patients with up to 5 skin lesions and negative smear results are considered PB, while those with more than 5 lesions or positive smears are classified as MB. This simple system is highly practical in field conditions.[20]

The Ridley-Jopling classification, however, offers a more nuanced understanding by considering the host immune response, histopathological features, and bacillary load.[21] It identifies five types of leprosy across a spectrum—tuberculoid (TT), borderline tuberculoid (BT), borderline (BB), borderline lepromatous (BL), and lepromatous (LL)—each with distinct clinical, bacteriological, and immunological features. For instance, TT leprosy presents with sharply demarcated lesions and marked anesthesia due to a strong cell-mediated immune response, while LL leprosy shows numerous, symmetrical, poorly defined lesions with minimal sensory loss early on and a high bacillary load due to immune energy.[19,21]

SUPPORTING EXAMINATIONS AND THE GOLD STANDARD

Confirmatory investigations play an essential role in supporting the clinical diagnosis of leprosy, especially in ambiguous or early cases. The gold standard remains the histopathological examination of skin or nerve biopsies, which reveals granulomatous inflammation and the presence of Mycobacterium leprae.[22] This method allows for definitive classification within the Ridley-Jopling spectrum and can detect subclinical cases, particularly in contacts of index patients.

In routine clinical settings, slit-skin smear microscopy is widely used due to its simplicity, specificity, and ability to quantify bacterial load via the bacteriological index (BI). However, its sensitivity is limited, especially in PB leprosy.[16] To overcome this, molecular diagnostic techniques such as polymerase chain reaction (PCR) have been introduced, enabling early and accurate detection even in smear-negative cases. Though promising, their utility is limited in low-resource areas due to cost and infrastructure demands.[23]

Other diagnostic tools include:[15,16]

- Lepromin test: Useful for immunological classification but not for diagnosis.
- Nerve conduction studies: Assess the extent of peripheral neuropathy.
- High-resolution ultrasound and thermography: Detect early nerve damage and inflammation.
- Serological assays (e.g., anti-PGL-1 antibodies): Provide insights into exposure and disease activity but lack specificity for clinical use.

MANAGEMENT OF LEPROSY

Effective management of leprosy requires more than antimicrobial therapy—it demands a comprehensive, patient-centered approach that encompasses drug treatment, complication management, rehabilitation, and psychosocial support.[19] The World Health Organization's Multidrug Therapy (MDT) remains the cornerstone of treatment. PB leprosy is treated for 6 months with rifampicin and dapsone, while MB leprosy is treated for 12 months using a combination of rifampicin, dapsone, and clofazimine.[24]

Prompt recognition and management of lepra reactions—Type 1 (reversal reaction) and Type 2 (erythema nodosum leprosum, ENL)—are vital to prevent irreversible nerve damage.[25] Type 1 reactions, due to cell-mediated immune response shifts, are managed with systemic corticosteroids, while Type 2 reactions, immune complex-mediated, often require thalidomide, especially in severe or recurrent cases. Other immunosuppressants like azathioprine or methotrexate may be considered in refractory cases.[25,26]

A holistic approach also includes:

- Disability prevention and rehabilitation, with physiotherapy and provision of protective footwear or orthoses.
- Surgical correction of deformities when needed (e.g., tendon transfer surgeries).
- Psychological counseling and community reintegration programs to combat stigma and social exclusion.

COMPLICATIONS OF LEPROSY

Leprosy complications are predominantly a consequence of delayed diagnosis and inadequate management, often resulting in irreversible nerve damage and permanent disabilities. The most common complications include:[27,28]

- Peripheral neuropathy, leading to loss of sensation, muscle atrophy, and motor deficits such as claw hand or foot drop.
- Recurrent ulcers, particularly in anesthetic feet, which may become chronic and secondarily infected.
- Facial nerve involvement, causing lagophthalmos and corneal exposure, increasing the risk of blindness.
- Ocular involvement, including iridocyclitis, keratitis, and scleral melting, particularly in LL leprosy.
- Chronic lepra reactions, which can lead to systemic complications such as orchitis, nephritis, and amyloidosis.

Addressing these complications requires integrated care involving dermatologists, neurologists, ophthalmologists, physiotherapists, and social workers. Rehabilitation, community education, and long-term surveillance are vital to reducing the burden of disability and enhancing the quality of life for affected individuals.[29]

CONCLUSION

In conclusion, the diagnosis and management of leprosy require a comprehensive approach that integrates clinical evaluation, bacteriological confirmation, and classification systems such as Ridley-Jopling and WHO criteria. Accurate diagnosis is supported by characteristic skin lesions, peripheral nerve involvement, anesthesia, and positive slit-skin smears, while the gold standard remains the identification of Mycobacterium leprae through bacteriological examination. Effective management relies on early detection and prompt multidrug therapy (MDT) to prevent complications, reduce transmission, and improve outcomes. Understanding the distinctions among leprosy types and their respective diagnostic features is crucial for guiding treatment decisions and minimizing long-term disability.

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