Leprosy in Brazil: From the social developments to the diagnosis-therapeutic evolution of the disease

https://doi.org/10.56238/sevened2024.001-058

Arthur Kennedy Martins Costa[1], Dener Cleiton Souza e Silva[2], Paulo Henrique da Rocha Rosa[3], Roberani Borges Vaz Gonçalves[4], Vinícius Oliveira Santos[5], Yasmin Parreira Guimarães[6] and Viviane Santos Mendes Carneiro[7]

ABSTRACT

Few pathologies have marked the course of history as much as leprosy, in view of their geographical distribution, the level of contagion and the degree of involvement in the organism of the infected individual. To gather information on the epidemiology, origin and management of leprosy, this paper outlines an analysis of other bibliographies that have extensive relevance on this disease, including its biopsychosocial impacts on the patient's life. This is a bibliographic review in which works published in the last eight years were selected, with the aim of analyzing and disseminating the information captured. The results showed that the diagnosis of leprosy is based on clinical and epidemiological criteria, in addition to specific histological evaluation and sputum smear microscopy, emphasizing the importance of skin and serological tests. It is observed that the current treatment protocol consists of the use of drugs that cure the disease, with remission rates of up to 98%. Thus, the objective of this study is to identify the evidence available in the scientific literature about the main clinical manifestations of leprosy, the pathogenic mechanisms of the bacilli, as well as the methods of early diagnosis based on clinical and laboratory analyses and their therapeutic modalities. Despite the relevant considerations of the diagnosis-treatment dyad, Brazil is among the countries with the most registered cases, still placing this disease as a major public health problem, which confirms the continuous fight against the bacillary disease.

Keywords: Leprosy, Epidemiology, Diagnosis, Treatment.

[1] Studying for a degree in Medicine.
Mineiros University Center - UNIFIMES Campus Trindade.
[2] Studying for a degree in Medicine.
Mineiros University Center - UNIFIMES Campus Trindade.
[3] Studying for a degree in Medicine.
Mineiros University Center - UNIFIMES Campus Trindade.
[4] Studying for a degree in Medicine.
Mineiros University Center - UNIFIMES Campus Trindade.
[5] Studying for a degree in Medicine.
Mineiros University Center - UNIFIMES Campus Trindade.
[6] Studying for a degree in Medicine.
Mineiros University Center - UNIFIMES Campus Trindade.
[7] Advisor - Professor of Medicine at the University Center of Mineiros - UNIFIMES Trindade Campus.

INTRODUCTION

Leprosy, historically known as leprosy, is a chronic infectious disease that has intrigued the scientific community around the world for centuries. The discussion about the origin of leprosy being in the Asian or African continent is still ongoing among specialists, however, it is known that it has been reputed for more than four thousand years in India, China, Japan and Egypt. Over time, leprosy was grouped together with other skin pathologies, such as psoriasis, scabies, impetigo, and was also called "leprosy". Caused by the bacterium *Mycobacterium leprae*, leprosy has a unique complexity in its epidemiology and pathogenesis. *Mycobacterium leprae* has a special affinity for peripheral nerves, where it can replicate slowly and insidiously. The interaction between the pathogen and the host's immune system triggers a variety of clinical responses, from cutaneous and neurological lesions, to systemic manifestations. The diversity of clinical presentations of the disease is one of the main challenges in the diagnosis of leprosy.

In the global context, leprosy has been a public health concern in many countries, however, its epidemiological characteristics vary considerably. Brazil is considered an endemic country, occupying the 2nd position on the global scale among the federative units that register the most new cases of the disease. Due to its high incidence, the disease remains a significant public health problem in Brazil, where inspection agencies have compulsory notification and mandatory investigation in cases of leprosy. Beginning in the 1980s, the country implemented institutional initiatives that modified the care strategy for affected people, including the closure of colony hospitals that previously provided for compulsory hospitalization for those affected by the disease. In an innovative step in 1995, the State determined, through Law No. 9,010, that the term "leprosy" and its derivatives could not be used in the language described in official documents of the centralized and decentralized administration of the Union and the states. These advances were fundamental to broaden the understanding of the history of leprosy as a journey that does not belong only to the bacillus, but to the individuals and families affected by the pathology.

The Brazilian situation is unique, since the country has an extensive geographical diversity, with different challenges in managing transmission. While some areas have been successful in controlling the disease, others still face significant challenges in terms of diagnosis, treatment, and prevention. Compared to other endemic countries, Brazil plays a respectable role in researching and implementing leprosy control strategies. The country's cultural and geographic diversity provides a unique opportunity to study variations in epidemiology and response to interventions, enriching scientific knowledge about the disease. However, the complexity of leprosy requires a multifaceted and collaborative approach that involves researchers, health professionals, and authorities in a joint effort to contain the progression of the bacillus.

Scientific research has projected a crucial role in the identification of diagnostic markers, in the development of effective treatments, and in the search for control strategies that can be implemented in different contexts. In Brazil, the evolution in bacillus research and the use of therapeutic modalities for leprosy have made remarkable progress over the last decades. New diagnostic approaches, such as molecular analysis, have improved the detection of the disease in early stages, by allowing effective resources to reduce the transmission of this pathology. The introduction of multidrug therapy and educational actions have also contributed to an effective intervention in patients.

Thus, the objective of this study is to identify the evidence available in the scientific literature about the main clinical manifestations of leprosy, the pathogenic mechanisms of the bacilli, as well as the methods of early diagnosis based on clinical and laboratory analyses and their therapeutic modalities.

METHODOLOGY

This article was constructed from a literature review, in which the analyses were produced and based on conjectures of the descriptive method. To carry out this investigation, the Health Sciences Descriptors (DeCS) were used, correlated to the English terms Hansen Disease, Epidemiology, Diagnosis and Treatment. Search combinations were performed by applying the Boolean operator "AND" in the databases, resulting in the following description: "Hansen Disease AND Epidemiology AND Diagnosis AND Treatment".

For this search, texts written in the last 8 years between 2015 and 2022 were selected, in English and Portuguese. The searches took place in the scientific databases PubMed, SciELO and Google Scholar, and 1,076 results were retrieved, which were selected for analysis 15 bibliographic materials that addressed the inclusion criteria. In addition, a search and analysis was carried out in the Ministry of Health database for the inclusion of public policies and recommended norms in relation to the management, treatment and biopsychosocial context of the disease under analysis. The exclusion criteria eliminated articles that did not include the proposed languages and were shorter than the given period.

RESULTS AND DISCUSSION

DIAGNOSIS

Clinical Diagnosis

The diagnosis of leprosy is primarily based on clinical and epidemiological criteria. Anamnesis, dermatological evaluation, identification of skin lesions, and application of tests to

evaluate the change in sensitivity are applied. Differential diagnosis, identification of neuritis, deformities, and reaction states are also included.

The leprosy manifestations that confirm the diagnosis should include one or more signs of the disease, namely: cutaneous lesion with modification of thermal or painful sensitivities, thickened or shortened peripheral nerve, cramps and pain, and confirmation of *M. leprae bacilli* evaluated by specific histological examinations. The forms of leprosy are grouped into 4 orders: indeterminate, tuberculoid, virchowian and dimorphic, and operational classifications are essential to support the clinical diagnostic criteria. The Madrid Classification (1953) evaluates the immunological pole in response to the infected individual and assumes the indeterminate and dimorphic forms as a stable therapeutic response and the tuberculoid and virchowian groups as the unstable spectrum. The Ridley & Jopling Classification (1962) describes the clinical, histopathological, and bacteriological manifestations of the subject with the disease.

Leprosy is recognized in 5 specimen specimens, according to the Ridley & Jopling Classification, among them, the polar forms: Tuberculoid (TT) and Lepromatous (LL) are mentioned and in intermediate forms: Dimorphs (D), also called Borderline, are named Borderline Tuberculoid (BT), Borderline (BB) and Borderline Lepromatous (BL). In addition, the virchowian form can be divided into Polar Virchowian (LLp) and subpolar Virchowian. The Indeterminate form (I) is classified as an initial or transitory response, which may course with healing or evolve with one of the spectres.

Investigation of peripheral nerve injury should include inspection of the eyes, palate, nose, hands and feet, and muscle strength. The sensitivity tests are applied in three moments: the thermal sensitivity should include the use of cold water (temperature around 25º C), hot water (around 45º C); Pain sensitivity should be provoked by means of a sterile and disposable needle, and the stimulus should be applied to the suspicious region; and tactile sensitivity is performed by touching the patient with a dry cotton pad and asking him to demonstrate the area touched.

Sputum smear microscopy diagnosis

This technique is indicated in suspected cases of recurrence, differential diagnosis with other dermatological diseases or in case of doubt about the classification of leprosy before starting treatment. Sputum smear microscopy is a complementary test to classify cases as paucibacillary (PB) or multibacillary (MB) and has a low degree of complexity compared to other techniques, requires few financial resources, and is easily accessible. The collection of biological samples from the ear lobes, elbows or lesions allows microscopic identification of *M. leprae*. In laboratory terms, diagnostic specificity is 100%, although sensitivity is limited to 34% (Soneja et al., 2016; Maymone et al., 2020).

Histological diagnosis

Histopathological evaluation requires biological samples of skin and nerve fragments, collected from the edges of lesions that have recently appeared and are symptomatic. In this examination, the type of bacillus, the extent and characteristics of the infiltrate, and the presence of Hansen's bacilli are analyzed. Although it has good clinical application, histological examination should not be considered the gold standard for diagnosis, because the disease has a diverse morphological presentation.

Diagnosis by Skin Test

In this examination, the patient receives an inoculation of 0.1ml of lepromine – a suspension of leprosenomas containing *M. leprae*, – applied intradermally. The appearance of a papule greater than or equal to 5 mm suggests the reactive effect of the test. Its use is predictive in the patient's prognosis, since it is capable of studying the individual's immune response to lepromine suspension.

Serological diagnosis

Mycobacterium leprae is capable of producing several immune mediators, including phenolic glycolipid-1 (PGL-1), which stimulates the production of IgM antibodies when mediated by enzyme-linked immunosorbent assays. Through the available techniques that identify leprosy forms, such as Enzyme Linked Immunosorbent Assay (ELISA), Gelatin Particle Agglutination Test (MLPA), dipstick and Rapid Lateral Flow Test (ML-Flow), it is possible to apply serological tests for anti-M. *leprae antibodies.* This test is widely used on a diagnostic scale due to the detection of the patient's bacillary load, in addition to having facilitated application methods, such as the independence of the dispensing of enzyme reagent refrigerators.

Diagnosis by Molecular Biology

From the development of sequencing in the genome of *M. leprae*, tests capable of evaluating the structure of DNA and RNA were created by means of Polymerase Chain Reaction (PCR) of the various biological samples for the diagnosis of leprosy. The genetic markers hsp65, 18 kDa, 36kDa, 16S rRNA and sodA have high predictive value in the identification of species-specific sequences, confirming the high specificity and sensitivity of this test.

TREATMENT

The institution of the therapeutic plan is based on the adequacies of the World Health Organization (WHO), which establishes clinical classifications of the disease to select the best treatment regimen. The number of skin lesions and the confirmation of bacterial presence in the skin

smear are taken into account. The first line of leprosy treatment recommended by the WHO is the outpatient administration of rifampicin, dapsone and clofazimine. The primary objective of leprosy treatment is to cure the disease, where remission rates reach 98%.

This treatment regimen consists of 6 monthly doses for paucibacillary leprosy or 12 monthly doses for multibacillary leprosy. In addition, the recommendation of anti-inflammatory and immunosuppressive drugs can be prescribed in conjunction with the baseline plan, even after the end of antibacterial treatment with rifampicin, dapsone, and clofazimine, in order to achieve symptomatic control of the disease. The main adverse effects of multidrug pharmacotherapy include hemolytic anemia, methemoglobinemia, agranulocytosis, thrombocytopenia, drug-induced hepatitis, pseudoflu-like syndrome, dapsone syndrome, erythroderma, exfoliative dermatitis, among others.

Non-pharmacological treatment presupposes a psychosocial approach, aiming to combat the stigmatization of leprosy patients, both due to possible physical alterations and the development of physical disabilities.

SOCIAL IMPACTS OF THE DISEASE

Created by the WHO, the Global Leprosy Strategy 2021-2030 has as its main approach the confrontation of social stigmas that result in psychological consequences for the patient. On a global scale, the obstacles to be overcome involve the impact that discrimination projects on diagnosis and treatment, social distancing and expanded dissemination in the community due to the lack of information and early diagnosis of the pathology.

Despite the progressive advances in medicine in containing the spread of Hansen's bacillus, high rates of confirmation of the disease are still observed worldwide. Although multidrug treatment is highly effective in combating leprosy, the triple regimen is not able to prevent the transmission of the bacillus. Measures that require early diagnosis of the disease, continuous antibiotic therapy, identification of the first signs and symptoms of the disease, and a medical service specialized in the diagnosis of leprosy will be able to promote the regression of the global picture of this pathology.

CONCLUSION

From the brief discussion about the subject that involves this theme, and given the importance of this approach in the social context, it is understood that knowledge about the bacillary clinical picture provides an understanding of the pathogenic mechanisms that involve leprosy, in order to add technical and operational skills in medical diagnosis. Early diagnosis is capable of benefiting all population segments, especially those who are economically and socially disadvantaged, allowing early access to diagnostic health and efficacy in polychemotherapy treatment.

Despite the relevant considerations of the diagnosis-treatment dyad, which provides a valuable reduction of the community impacts of leprosy, such as a reduction in cases of permanent disabilities, it is of paramount importance to understand the current situation in the country. Currently, Brazil is among the countries with the most registered cases, still placing this disease as a major public health problem, which confirms the continuous fight against the bacillary disease.

REFERENCES

1. Aamir, M., et al. (2018). Recent Advancement in the Diagnosis and Treatment of Leprosy. *Current Topics in Medicinal Chemistry*, 18(18), 1550-1558. doi:10.2174/1568026618666181025100434

2. Avanzi, C., et al. (2020). Molecular epidemiology of leprosy: An update. *Infection, Genetics, and Evolution: Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases*, 86, 104581. doi:10.1016/j.meegid.2020.104581

3. Brasil. (2022). *Protocolo Clínico e Diretrizes Terapêuticas da Hanseníase*. Brasília: Ministério da Saúde.

4. White, C., & Franco-Paredes, C. (2015). Leprosy in the 21st Century. *Clinical Microbiology Reviews*, 28(1), 80–94.

5. Chen, K.-H., et al. (2022). Leprosy: A Review of Epidemiology, Clinical Diagnosis, and Management. *Journal of Tropical Medicine*, 2022, 8652062. doi:10.1155/2022/8652062.

6. Conceição, R. S. C., et al. (2017). Leprosy: current situation, clinical and laboratory aspects, treatment history and perspective of the uniform multidrug therapy for all patients. *Anais Brasileiros de Dermatologia*, 92(6), 761–773. doi:10.1590/abd1806-4841.20176724

7. Silva Ferreira, I., & Zanon Lopes Ribeiro, A. (2021). Prejuízos do Diagnóstico Tardio em Hanseníase: Uma Revisão Integrativa. *Revista De Patologia Do Tocantins*, 8(2), 65–69. doi:10.20873/uft.2446-6492.2021v8n2p65

8. Mungroo, M. R., et al. (2020). *Mycobacterium leprae*: Pathogenesis, diagnosis, and treatment options. *Microbial Pathogenesis*, 149, 104475. doi:10.1016/j.micpath.2020.104475

9. Salipante, S. J., & Hall, B. G. (2011). Towards the molecular epidemiology of *Mycobacterium leprae*: strategies, successes, and shortcomings. *Infection, Genetics, and Evolution: Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases*, 11(7), 1505-13. doi:10.1016/j.meegid.2011.06.003

10. Sugawara-Mikami, M., et al. (2022). Pathogenicity and virulence of *Mycobacterium leprae*. *Virulence*, 13(1), 1985-2011. doi:10.1080/21505594.2022.2141987

11. Vitório, E. J., et al. (2020). Leprosy: epidemiology of the morbidity, mortality, and public spending in the northeast of Brazil. *Revista de Pesquisa Cuidado É Fundamental Online*, 12. Available at: https://doi.org/10.9789/2175-5361.rpcfo.v12.8022

12. White, C., & Franco-Paredes, C. (2015). Leprosy in the 21st century. *Clinical Microbiology Reviews*, 28(1), 80-94. doi:10.1128/CMR.00079-13.