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Leprosy classification methods: a comparative study in a referral center in Brazil

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SUMMARY

Objectives: Different methods for the classification of leprosy have been proposed since the 1930s. The aim of this study was to compare the current methods at a referral center in Brazil.
Methods: The World Health Organization (WHO) operational classification was compared to the Ridley and Jopling classification, the Madrid classification, and a classification based on the number of body areas affected by skin and/or neural lesions (NBAA). The correlation between the clinical and histopathological components of the Ridley and Jopling classification was assessed.
Results: The agreement between the WHO operational classification and the Ridley and Jopling classification was 77.6% (kappa = 0.53). The WHO operational classification tended to overestimate the number of multibacillary patients. The WHO operational classification showed its best agreement with the NBAA. There was perfect agreement between the clinical and histopathological Ridley and Jopling classification in 46.9% of the patients.
Conclusions: The agreement between the WHO operational classification and the Ridley and Jopling classification was better than any other purely clinical classification, reinforcing the importance and simplicity of the operational method. Although major disagreement between the clinical and histopathological Ridley and Jopling classification was uncommon, perfect agreement occurred in less than half of the cases, and was even lower for the borderline lepromatous and tuberculoid forms. Possible reasons for the differences are discussed; these showed that there may be room for improvement in the Ridley and Jopling classification histopathological criteria.

1. Introduction

Leprosy presents a continuous spectrum of clinical and pathological manifestations that depend on the type and intensity of the patient's immune response to the bacterium *Mycobacterium leprae*.[1] An intense cellular response is associated with the containment of the bacillus and to the forms with a paucibacillary presentation, whose prototype is the tuberculoid form. A primarily humoral response is associated with intense agent replication and with multibacillary forms, with the lepromatous form at the extreme end.[2]

Several different leprosy classifications have been proposed since the 1930s, which consider these two ends of the spectrum and the intermediate (borderline) manifestations between them.[3] Based on clinical aspects, the Madrid classification, from 1953, includes the tuberculoid (TT), lepromatous (LL), borderline, and indeterminate (IND) forms. This classification was included in the recommendations of the World Health Organization (WHO) and was prevalent until 2002.[3,4] In 1966, Ridley and Jopling created a classification that is still considered essential for the standardization of leprosy research. The clinical, pathological, bacilloscopic, and immunological criteria of the Ridley and Jopling classification provide the basis for the most complete classification of the various forms of the

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disease, including IND, TT, borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and LL.[5,6]

However, while developing multidrug therapy for leprosy, it became critical for the WHO to establish a simplified operational classification to differentiate between paucibacillary and multibacillary patients and thus facilitate adequate treatment. Currently, patients are considered paucibacillary if they present up to five skin lesions and multibacillary if they present six or more lesions. This operational classification facilitates fieldwork, since it does not require expertise in assessing skin lesion morphology or applying the slit-skin smear examination (SSS); however different studies have indicated its flaws.[7–10]

On the other hand, studies on the Ridley and Jopling classification have shown great variations in agreement between its clinical and histopathological components.[5,11–18] In a study conducted in India involving 303 multibacillary patients, 73 of the 178 patients clinically classified as BT were classified into a different leprosy form following the histopathological examination. The biopsy classified two of these patients as LL and 32 as IND, both leprosy forms expected to be easily differentiated from BT.[19]

The aim of this study was to compare the WHO operational classification with the Ridley and Jopling classification at a leprosy referral center in Brazil. These classifications were also compared to the bacilloscopy results (SSS), the Madrid classification, and the NBAA classification (number of body areas affected). The latter is based on the number of body areas affected by skin or neural lesions.[7,20] Finally, the correlation between the clinical and histopathological components of the Ridley and Jopling classification was assessed.

2. Materials and methods

Forty-nine leprosy patients from the leprosy referral clinic of the Hospital Eduardo de Menezes (Fundação Hospitalar do Estado de Minas Gerais) agreed to participate and gave their signed consent.

Patients underwent a complete dermato-neurological examination by a dermatologist with expertise in leprosy. Skin lesions were counted and the affected body areas were recorded on the appropriate form. All patients underwent SSS from four sites (ear lobes, elbows, and skin lesions). Ziehl–Neelsen staining and SSS bacilloscopy index assessment were conducted in the same referral center by an experienced microbiologist. All patients underwent a skin lesion biopsy. Hematoxylin–eosin and Wade staining were performed in the Experimental Neuroimmunopathology Laboratory of the Instituto de Ciências Biológicas (UFMG), where two pathologists with expertise in leprosy interpreted the histopathological examinations. When there was divergence between their reports, discussions were held between the two pathologists at a new session until a consensus diagnosis was reached.

For the Madrid classification, patients with the borderline and LL forms were considered multibacillary. For the Ridley and Jopling classification, patients with the BB, BL, and LL forms were considered multibacillary. The histological classification was the one outlined by Ridley.[6] For the NBAA classification, two thresholds for the multibacillary status were tested: patients with two or more body areas involved and patients with three or more body areas involved. For this purpose, the body surface was divided into nine areas, as described by Gupta et al. and van Brakel et al.[7,20]

To assess the agreement between any two classification methods, 2×2 tables were created and the kappa coefficient calculated, as well as the percentage of cases in which there was agreement. Kappa values between 0.20 and 0.40 were considered 'reasonable', those between 0.41 and 0.60 were considered 'moderate', those between 0.61 and 0.80 were considered 'good', and values above 0.81 were considered 'excellent'. Data were analyzed using SPSS 15.0 software (SPSS Inc., Chicago, IL, USA).

The discrepancy between the clinical and histopathological components of the Ridley and Jopling classification was classified as minimal or major disagreement. Cases in which discrepancy resulted in a change in the pauci/multibacillary status of the patient were considered major disagreement. Otherwise, the disagreement was considered minimal. Histopathological examinations showing non-specific inflammation were diagnosed as IND to permit the disagreement analysis.

The final Ridley and Jopling classification included the clinical presentation, the histopathological findings, and the SSS results.

3. Results

This study included 49 new leprosy cases. Seventeen (34.7%) patients had been undergoing treatment for at least 1 day and at most 30 days; the remaining patients were not undergoing treatment at the time of inclusion. According to the final Ridley and Jopling classification, the incidence of the different leprosy forms was IND = 9 (18.4%), TT = 5 (10.2%), BT = 21 (42.9%), BB = 1 (2%), BL = 6 (12.2%), and LL = 7 (14.3%). Table 1 presents a descriptive analysis of the patients.

Twenty-one (42.9%) patients had six or more skin lesions and 16 (32.7%) patients had a positive SSS. Table 2 shows that most patients were classified as paucibacillary (with the exception of the Madrid and NBAA classifications). When compared to the operational classification, the Madrid and NBAA classifications resulted in higher numbers of multibacillary patients, while the Ridley and Jopling classification resulted in a higher percentage of paucibacillary patients.

The different classification systems were compared in terms of their ability to define a patient's multibacillary status. The operational classification was more sensitive for the multibacillary status diagnosis than the clinical component of the Ridley and Jopling classification alone, but the addition of the histopathological examination resulted in a significant improvement in the sensitivity of the Ridley and Jopling classification (see Table 2).

When compared with the Ridley and Jopling classification, the Madrid and NBAA classifications showed lower specificity for the multibacillary diagnosis. The purely clinical classification system that best agreed with the Ridley and Jopling classification was the

Table 1
Descriptive analysis of 49 new leprosy cases at a referral center in Minas Gerais, Brazil[a]

Variable	*n*	(%)
Sex		
Male	27	(55.1)
Female	22	(44.9)
Age, years		
<15	2	(4.0)
15–30	12	(24.5)
31–45	10	(20.4)
46–60	13	(26.5)
61–75	12	(24.5)
Number of skin lesions		
≤5	28	(57.1)
>5	21	(42.9)
Number of impaired nerves[b]		
≤1	41	(83.7)
>1	8	(16.3)

[a] Source: research data.
[b] Impaired nerves means thickened or painful peripheral nerves or sensory or motor functional impairment in their area of innervation.