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Leprosy Reactions and Nerve Damage in Children and Adolescents: A Pediatric Evidence Synthesis with Verified Cohort Findings

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ABSTRACT

Leprosy in childhood is an indicator of ongoing transmission and may be complicated by inflammatory reactions, neuritis, and disability. Antimicrobial treatment is essential; however, completion of therapy alone does not guarantee the preservation of nerve function. Pediatric evidence remains dispersed across small observational cohorts, with inconsistencies in denominators and outcome definitions. This study prepared a pediatric evidence synthesis using publicly accessible full-text cohort reports that provided verifiable numerators and denominators for reactions, neuritis, nerve damage, or disability outcomes. The synthesis was structured according to PRISMA 2020 guidelines. Studies were eligible if they included children younger than 15 years with leprosy and reported clinically defined outcomes during diagnosis, multidrug therapy, or follow-up. Two Brazilian prospective cohorts from referral units were verified through full-text review. In a 2019 cohort, 18 of 34 children (52.9%) experienced a leprosy reaction and/or isolated neuritis; among these, 14 of 18 (77.8%) had type 1 reactions, 14 of 18 (77.8%) experienced two or more episodes, and 6 of 18 (33.3%) developed complications. In a 2024 two-year cohort, 38 of 77 children (49.3%) experienced reactions; among these 38 children, 16 (42.1%) showed progression with worsening nerve damage. At diagnosis, 29 of 38 children (76.3%) had nerve damage, 20 (52.6%) had physical disability, and 11 (28.9%) had grade 2 disability. The verified cohorts indicate a substantial burden of leprosy reactions and nerve impairment among children treated in referral settings. Reactions occurred both during and after multidrug therapy, highlighting the importance of continued neurological surveillance beyond the completion of antimicrobial treatment.

INTRODUCTION

Leprosy, also known as Hansen disease, is a chronic infection caused by Mycobacterium leprae and remains a public health concern in several endemic regions. The (Organization, 2018, 2021) global leprosy strategy and weekly epidemiological records provide important contexts for global policy and surveillance, with childhood cases remaining significant because they indicate recent or ongoing transmission within communities. The disease exhibits considerable clinical heterogeneity, ranging from limited paucibacillary disease to multibacillary disease associated with a higher risk of inflammatory complications. The World Health Organization recommends multidrug therapy as the cornerstone of treatment; however, antimicrobial therapy does not eliminate the risk of leprosy reactions or nerve impairment during and after treatment (Oliveira & Diniz, 2016) .

Childhood leprosy requires particular attention because diagnosis in children may indicate recent or ongoing community transmission. However, due to the long incubation period of the disease, the timing of infection cannot be determined solely based on age at

diagnosis. Pediatric leprosy also presents diagnostic challenges, as skin lesions may be subtle, sensory examinations may be difficult to perform, and children may receive alternative diagnoses before referral. Delayed diagnosis can increase the risk of nerve damage before appropriate management is initiated (Page et al., 2021; Santos et al., 2016) .

Leprosy reactions are acute inflammatory episodes that may occur at diagnosis, during multidrug therapy, or after treatment completion. Type 1 reactions commonly involve existing lesions and peripheral nerves, whereas type 2 reactions may manifest as systemic inflammation and erythema nodosum leprosum. Neuritis may be clinically apparent or asymptomatic, and both forms can contribute to progressive nerve impairment (Lockwood et al., 2014; Lockwood & Saunderson, 2012; Moet et al., 2006; van Brakel et al., 2012) . Disability grade at diagnosis should not be considered equivalent to incident disability during follow-up; these outcomes must be clearly distinguished when interpreting pediatric cohort findings (Ebenso et al., 2017; Kahawita et al., 2008; Walker et al., 2016; Walker & Lockwood, 2008) .

Previous pediatric studies have often been limited by small sample sizes, referral-based selection, inconsistent follow-up periods, or the inclusion of both children and adults within the same analysis. Leprosy reactions are acute inflammatory episodes that may occur at diagnosis, during multidrug therapy, or after treatment completion. Type 1 reactions commonly affect existing lesions and peripheral nerves, whereas type 2 reactions may present with systemic inflammation and erythema nodosum leprosum. Neuritis may occur with or without clinical symptoms, and both forms may contribute to progressive nerve impairment. Disability grade at diagnosis does not represent incident disability occurring during follow-up; therefore, these outcomes should be differentiated when interpreting pediatric cohort studies (Alberts et al., 2011; Richardus & Croft, 1995; Saunderson et al., 2000) .

METHOD

Reporting approach and review question

The manuscript was organized according to the PRISMA 2020 framework [10]. The review question examined the reported frequencies of leprosy reactions, neuritis, nerve damage, and disability among children and adolescents with leprosy during diagnosis, multidrug therapy, and post-treatment follow-up.

Eligibility criteria

We considered studies eligible when they included children younger than 15 years with clinically diagnosed leprosy and reported at least one prespecified outcome: leprosy reaction, isolated neuritis, nerve damage, physical disability, grade 2 disability, or progression of neurological impairment. Studies with mixed-age populations were eligible only when pediatric data were separately extractable. Case reports, narrative reviews, and reports without a verifiable numerator and denominator were not used for the quantitative descriptive results presented here.

Information sources and verification

Public full-text sources were examined through PubMed Central and the publisher’s open-access article page. The verified evidence consisted of two prospective Brazilian cohorts: a 2019 cohort from a leprosy referral unit in the Brazilian Amazon and a 2024 two-year prospective cohort from the same regional referral context. A separate urban Brazilian study

was used only for contextual epidemiological findings and not for reaction or nerve-damage estimates.

Data items

The extraction fields were country and setting, recruitment period, age threshold, design, sample size, disease classification, outcome definition, follow-up duration, reaction type, nerve-damage measure, disability grade, numerator, denominator, and reported limitations. Denominators were retained exactly as reported. We did not reconstruct missing 2×2 tables or convert descriptive proportions into comparative measures.

Risk of bias and interpretation

The cohorts were interpreted as observational evidence. Key concerns included referral-center selection, small sample size, loss to follow-up, absence of an unexposed comparison group, possible overlap of the regional study populations, and variation in outcome ascertainment. Because only two regional cohorts were verified for the principal outcomes, formal small-study effect testing and a pooled random-effects estimate were not justified.

Statistical synthesis

We reported exact numerators, denominators, and calculated percentages where these were explicitly available in the full text. We did not pool the cohorts. The 2019 reaction/neuritis estimate used 34 participating children as the denominator. The 2024 progression estimate used 38 children who had already developed reactions as the denominator. These estimands are not interchangeable. Progression among children with reactions cannot be pooled with the prevalence of reactions among all children without creating a clinically incoherent outcome.

RESULTS AND DISCUSSION

Characteristics of verified cohorts

Table 1. Characteristics of verified cohorts

Study	Setting and design	Participants	Follow-up	Main outcomes
(Bandeira et al., 2019)	Prospective referral-unit cohort, Brazilian Amazon	34 children <15 years	During diagnosis, MDT, and post-treatment monitoring	Reaction/isolated neuritis, reaction type, recurrence, complications
(Bandeira et al., 2024)	Prospective longitudinal referral-unit cohort, Brazilian Amazon	77 children <15 years; 38 with reactions	Two years, assessments every six months	Reaction progression, nerve damage, physical disability, grade 2 disability, silent neuritis
Santos et al., 2016	Urban descriptive study, Salvador, Brazil	145 registered cases; 76 interviewed	Case ascertainment period 2007–2011	Contact pattern, age group, PB/MB classification

Reactions and neuritis in the 2019 cohort

Among 34 participating children, 18 (52.9%) experienced a leprosy reaction and/or isolated neuritis at some point during the disease course. Type 1 reactions accounted for 14 of 18 cases (77.8%), while type 2 reactions accounted for 4 of 18 (22.2%). Fourteen of 18 children (77.8%) experienced two or more reaction episodes.

Reactions were identified at diagnosis in 10 of 18 children (55.6%), during multidrug therapy in 13 of 18 (72.2%), and after treatment in 13 of 18 (72.2%). The percentages describe the distribution among children with reactions and are not cumulative incidence estimates across separate time intervals. Six of 18 children (33.3%) developed complications associated with reactional episodes or prolonged corticosteroid treatment. Reported complications included decreased hand strength, ulnar claw, ulcers, foot drop, necrotizing erythema nodosum, and Cushing syndrome.

Nerve damage and progression in the 2024 cohort

The 2024 cohort followed 77 children for two years; 38 (49.3%) had leprosy reactions. Among these 38 children, 16 (42.1%) experienced progression with worsening of the initial nerve damage, whereas 22 (57.9%) had non-progression. Non-progression included unchanged neurological status or improvement.

Nerve damage was observed in 29 of 38 children (76.3%), including peripheral nerve damage in 23 (60.5%). Twelve children (31.6%) had two or more nerves affected at diagnosis. Physical disability at diagnosis was present in 20 (52.6%), grade 2 disability in 11 (28.9%), and silent neuritis in 16 (42.1%). Twenty-eight children (73%) had two or more reactional episodes, with a reported mean of 2.3 episodes.

Contextual epidemiological findings

In the Salvador study, 145 cases in children younger than 15 years were registered during 2007–2011, and 76 were located and interviewed. Among interviewed children, 40 of 76 (52.6%) reported household contact, 19 (25.0%) social contact, 4 (5.2%) both household and social contact, and 13 (17.1%) unknown or no contact. Children aged 10–14 years represented 59.3% of the cases, those aged 5–9 years 30.3%, and those aged 0–4 years 10.3%. Paucibacillary disease accounted for 60.7% and multibacillary disease for 39.3% of registered cases [9]. These findings are descriptive and do not provide an association measure comparing children with and without household exposure.

Why no pooled estimate is presented

The verified cohorts were not pooled. First, both principal cohorts were conducted in a related Brazilian referral context, creating a reasonable concern about overlapping populations. Second, their denominators differed: 34 participating children in the 2019 cohort and 38 children with reactions for the 2024 progression outcome. Third, the outcomes differed. The 2019 study measured reaction and/or isolated neuritis during the disease course, whereas the 2024 study measured progression among children already identified with reactions. A pooled estimate would therefore combine different populations and estimands and could mislead readers.

This pediatric evidence synthesis identifies a consistent clinical signal: reactions and neurological complications are common among children managed in referral settings. In the 2019 cohort, more than half of participating children developed a reaction or isolated neuritis, and in the 2024 cohort almost half of the total cohort had reactions. These estimates should not be generalized directly to all children with leprosy because referral units are likely to receive patients with more complex, delayed, or multibacillary disease. They nevertheless demonstrate the clinical burden that pediatric services must be prepared to manage.

The distribution of reaction timing is particularly important. In the 2019 cohort, reactions were reported during multidrug therapy and after treatment completion. This finding supports

the principle that antimicrobial completion and neurological safety are different outcomes. A child who has completed MDT may still require assessment for new weakness, sensory loss, pain, swelling of peripheral nerves, or recurrent inflammatory lesions.

The 2024 cohort adds a longitudinal dimension. Among children with reactions, 42.1% experienced progression with worsening nerve damage during two years of follow-up. More than half had physical disability at diagnosis, and nearly one third had grade 2 disability. These findings indicate that baseline neurological assessment is not a formality; it establishes the reference point against which improvement, stability, or deterioration should be assessed.

The high proportion of type 1 reactions in the 2019 cohort is clinically plausible in a pediatric population with a substantial proportion of borderline disease. Type 1 reactions may threaten nerve function even when systemic symptoms are limited. Their clinical recognition may be difficult in young children, particularly when sensory testing is inconsistent or when caregivers interpret weakness as an ordinary childhood problem. Standardized neurological examination and caregiver education are therefore important components of care.

Silent neuritis deserves particular emphasis. The 2024 cohort reported silent neuritis in 42.1% of children with reactions. The absence of pain should not be interpreted as the absence of nerve injury. Regular measurement of muscle strength and sensory function may identify deterioration before the child or caregiver reports symptoms. This has implications for training, documentation, and the timing of referral.

The contextual Salvador findings suggest that household contact is important but not exclusive. More than one quarter of interviewed children reported social contact, and a further group had unknown or no reported contact. These categories may be influenced by recall, stigma, and incomplete ascertainment, but they support a broader public-health approach that combines household examination with attention to social and neighborhood transmission.

The findings also highlight the need for harmonized pediatric outcome definitions. Reaction at diagnosis, reaction during MDT, reaction after MDT, incident nerve damage, persistent nerve damage, progression, and disability grade are different endpoints. Future studies should report each with a clear denominator and follow-up period. Without this information, even apparently similar percentages cannot be pooled safely.

A further priority is duplicate-cohort recognition. When several publications arise from the same referral region, investigators should report recruitment dates, participant counts, and overlap explicitly. Reviewers should not treat each publication as an independent sample. This is especially important in rare diseases and small pediatric cohorts, where one population may generate multiple outcome reports.

From a programmatic perspective, pediatric leprosy services should link MDT delivery to reaction education, neurological monitoring, rehabilitation referral, and post-treatment follow-up. Caregivers should receive clear instructions about weakness, loss of sensation, pain, swelling, new lesions, eye symptoms, and functional changes. Children may not independently seek care, and delayed recognition can lead to preventable disability.

Strengths and limitations

The main strength of this synthesis is its conservative use of verified full-text numerators and denominators. It preserves the distinction between reaction prevalence, progression among children with reactions, and baseline disability. It also identifies why a pooled estimate would currently be misleading. Limitations include the small number of verified cohorts, referral-

center selection, potential overlap between the Brazilian studies, heterogeneous outcome definitions, and absence of a global search result set that would justify a complete PRISMA flow count. The findings should therefore be read as a verified pediatric evidence summary rather than a completed global meta-analysis.

Conclusions/Significance

The available verified pediatric cohorts show substantial frequencies of leprosy reactions, nerve damage, silent neuritis, and disability in referral settings. Reactions may occur at diagnosis, during multidrug therapy, and after treatment completion. Pediatric care should therefore include longitudinal neurological surveillance and caregiver education rather than relying on antimicrobial completion as the sole treatment endpoint. A defensible global meta-analysis remains dependent on additional non-overlapping full-text studies using standardized outcome definitions and transparent denominators (Associations, 2019; Britton & Lockwood, 2004; Organization, 2023; Scollard et al., 2006) .

CONCLUSION

The verified pediatric cohorts demonstrated that leprosy reactions, neuritis, nerve damage, and disability remained clinically important despite the availability of multidrug therapy. The evidence supports a care model in which treatment completion is accompanied by systematic neurological assessment and post-treatment surveillance. Because the available cohorts were small and potentially overlapping, their findings should be interpreted as clinically important indicators rather than as estimates of global prevalence.

First, pediatric leprosy programs should document neurological function at diagnosis and during regular follow-up visits throughout and after multidrug therapy. Second, caregivers should receive practical education regarding signs of nerve impairment, including weakness, sensory loss, nerve pain, new inflammatory lesions, and functional changes. Third, referral services should integrate reaction management with rehabilitation and growth monitoring. Fourth, future cohorts should apply standardized definitions of reactions, baseline disability assessment, follow-up duration, treatment regimens, and separate reporting of numerators and denominators for incident reactions, recurrent reactions, neuritis, and disability progression. Finally, researchers should identify potentially overlapping cohorts before combining publications in systematic reviews.

Future pediatric cohorts should use standardized neurological examinations, predefined reaction criteria, and follow-up intervals that capture events occurring after treatment completion. Reporting should distinguish children lost to follow-up from children who completed surveillance without experiencing adverse outcomes. This distinction is essential for accurately interpreting treatment outcomes and designing services aimed at preventing avoidable disability among children with leprosy.

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