JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

https://doi.org/10.61919/jn1yn669

Original Article

Effect of a Physiotherapy Program Combined With Photobiomodulation on Neuropathic Pain, Disability, and Quality of Life in Leprosy Patients: A Randomized Controlled Trial

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"Cite this Article" Received: 15 December 2025; **Accepted**: 26 February 2026; **Published**: 15 March 2026

Author Contributions: Concept: MSK; Design: TZ; Data Collection: ABB, AM, VK, and AZ; Analysis: JNA; Drafting: MSK and TZ; Critical Review: ABB, AM, VK, AZ, and JNA. **Ethical Approval**: Jinnah Postgraduate Medical Centre, Karachi, Pakistan. **Informed Consent**: Written informed consent was obtained from all participants; **Conflict of Interest**: The authors declare no conflict of interest. **Funding**: No external funding; **Data Availability**: Available from the corresponding author on reasonable request; **Acknowledgments**: N/A.

ABSTRACT

Background: Neuropathic pain is a frequent and disabling complication among people treated for leprosy and may persist after completion of multidrug therapy because established peripheral nerve injury is not fully reversed by antimicrobial treatment. Physiotherapy is central to leprosy rehabilitation, but pain relief and functional recovery may remain incomplete. Photobiomodulation has been proposed as a non-invasive adjunctive intervention for neuropathic pain through anti-inflammatory and neuromodulatory mechanisms. Objective: To evaluate whether standardized physiotherapy combined with active photobiomodulation improves neuropathic pain, disability, participation, quality of life, and functional capacity more than standardized physiotherapy with sham photobiomodulation in adults with treated leprosy. Methods: In this parallel-group randomized controlled trial, 154 adults aged 18–65 years with confirmed leprosy, completed multidrug therapy, VAS pain ≥40 mm, and DN4 score ≥4 were allocated equally to physiotherapy plus sham photobiomodulation or physiotherapy plus active photobiomodulation for 12 weeks. The primary outcome was change in VAS pain score from baseline to week 12. Secondary outcomes included SALSA score, Participation Scale score, SF-36 pain domain, and hand grip strength. Results: VAS pain decreased from 60.2 ± 11.1 mm to 27.9 ± 10.4 mm in the active photobiomodulation group and from 62.1 ± 12.3 mm to 44.8 ± 13.1 mm in the sham group, with a between-group difference of 15.0 mm (95% CI, 11.8–18.2; $p < 0.001$; Cohen's $d = 0.93$). Clinical response occurred in 75.3% and 31.2% of participants, respectively (NNT = 2.27). Secondary outcomes also favored active photobiomodulation, including SALSA, participation, SF-36 pain, and grip strength. No serious adverse events were reported. Conclusion: Active photobiomodulation may be an effective and safe adjunct to physiotherapy for leprosy-related neuropathic pain, with clinically meaningful benefits across pain and functional outcomes. Multicenter trials with longer follow-up and verified dosimetry are warranted before broad implementation. Keywords: leprosy; neuropathic pain; photobiomodulation; low-level laser therapy; Hansen disease; physiotherapy; rehabilitation.

INTRODUCTION

Leprosy, or Hansen's disease, remains an important cause of preventable neurological disability despite major advances in multidrug therapy and global disease-control programs. The disease is caused by

Mycobacterium leprae and has a predilection for peripheral nerves, where direct bacillary invasion, Schwann-cell injury, demyelination, axonal damage, and immune-mediated inflammatory reactions may produce sensory loss, motor impairment, deformity, and chronic pain. Although multidrug therapy is effective in controlling infection, it does not reliably reverse established nerve injury or prevent persistent neuropathic symptoms after treatment completion. As a result, many treated patients continue to experience pain, activity limitation, participation restriction, and impaired quality of life, particularly when nerve damage has already progressed before diagnosis or during lepra reactions (1,2).

Neuropathic pain is among the most clinically burdensome late complications of leprosy. It commonly presents as burning, tingling, electric-shock-like pain, paresthesia, hyperalgesia, or allodynia, usually corresponding to affected peripheral nerve territories such as the ulnar, median, radial, tibial, and peroneal nerves. Previous studies have reported that neuropathic pain may affect a substantial proportion of people treated for leprosy, with estimates varying according to diagnostic criteria, disease severity, reactional history, and timing after multidrug therapy. The clinical importance of this pain extends beyond symptom burden because persistent neuropathic pain is associated with reduced hand and foot function, impaired mobility, sleep disturbance, psychological distress, reduced social participation, and poorer health-related quality of life (2–5).

Current approaches to leprosy-related neuropathic pain remain limited. Pharmacological management with agents such as tricyclic antidepressants, gabapentinoids, or serotonin-norepinephrine reuptake inhibitors may reduce symptoms in some patients, but pain relief is often incomplete and may be constrained by adverse effects, cost, availability, and long-term adherence challenges. Conventional physiotherapy is therefore an essential component of multidisciplinary leprosy care because it targets sensory re-education, muscle weakness, joint mobility, deformity prevention, protective education, gait and balance impairments, and functional task performance. However, physiotherapy alone may not adequately address the underlying inflammatory and neurophysiological mechanisms contributing to persistent neuropathic pain, creating a rationale for adjunctive non-pharmacological interventions that can improve both pain and function (6–8).

Photobiomodulation has emerged as a non-invasive therapeutic option for painful peripheral neuropathies. It uses red or near-infrared light to produce photochemical and photophysical effects in biological tissues, with cytochrome c oxidase in the mitochondrial respiratory chain considered an important photoacceptor. Experimental and clinical literature suggests that photobiomodulation may enhance mitochondrial activity, modulate oxidative stress, reduce pro-inflammatory signaling, influence nociceptor sensitization, and support tissue repair. These mechanisms are biologically relevant to leprosy-associated neuropathy because persistent pain may reflect both structural nerve damage and continuing neuroinflammatory sensitization even after the infectious component has been treated (9–11).

Evidence for photobiomodulation in neuropathic pain has grown in conditions such as diabetic peripheral neuropathy and other chronic pain states, where some studies have reported reductions in pain intensity, improvements in sensory function, and better quality-of-life outcomes. Leprosy-specific evidence is more limited but clinically promising. Previous trials evaluating physiotherapy combined with photobiomodulation in people affected by leprosy have reported improvements in pain, SALSA activity limitation scores, participation restriction, nerve tenderness, muscle strength, and selected quality-of-life domains compared with physiotherapy-focused care. Nevertheless, available studies have generally used small samples, have been conducted in limited geographic settings, and have not fully resolved questions about protocol standardization, treatment effect size, clinical response, or applicability to South Asian populations where leprosy persists in specific endemic pockets (12–15).

Pakistan has achieved substantial progress in leprosy control, but new cases and disability-related sequelae continue to occur, particularly in areas where delayed diagnosis, multibacillary disease, stigma, poverty, and restricted access to specialized rehabilitation may contribute to long-term impairment. In

this context, a safe, reproducible, and clinically feasible adjunct to physiotherapy could be valuable if it provides additional pain relief and functional improvement beyond standard rehabilitation alone. A combined physiotherapy and photobiomodulation protocol may be especially relevant in rehabilitation services because it integrates a symptom-modulating intervention with function-oriented training rather than treating pain and disability as separate problems (16,17).

The population of interest in the present trial was adults with treated leprosy and confirmed neuropathic pain; the intervention was standardized physiotherapy combined with active photobiomodulation; the comparator was the same standardized physiotherapy protocol combined with sham photobiomodulation; and the primary outcome was change in neuropathic pain intensity measured by the Visual Analog Scale at 12 weeks. Secondary outcomes included activity limitation, participation restriction, quality of life, neurological function, and functional capacity. This trial was therefore designed to test the hypothesis that adjunctive photobiomodulation combined with standardized physiotherapy would produce greater reduction in neuropathic pain and superior functional and quality-of-life outcomes than standardized physiotherapy with sham photobiomodulation in adults with leprosy-related neuropathic pain.

MATERIAL AND METHODS

This study was designed as a parallel-group, participant- and assessor-blinded randomized controlled trial comparing standardized physiotherapy plus active photobiomodulation with standardized physiotherapy plus sham photobiomodulation in adults with treated leprosy and neuropathic pain. The trial was structured to evaluate superiority of the adjunctive active photobiomodulation protocol over an attention-matched sham procedure while ensuring that both groups received the same core physiotherapy program. The primary endpoint was change in neuropathic pain intensity from baseline to 12 weeks, and secondary endpoints included activity limitation, participation restriction, health-related quality of life, neurological function, and functional capacity. The design and reporting followed the principles of randomized trial methodology and CONSORT-based reporting, with prespecified allocation, blinded outcome assessment, standardized intervention delivery, intention-to-treat analysis, and adverse-event monitoring (18).

The study was conducted in leprosy treatment and rehabilitation settings in Karachi, Sindh, Pakistan, including Marie Adelaide Leprosy Centre–linked services, Civil Hospital–linked services, and National Leprosy Control Programme treatment units where patients received follow-up care for leprosy and related disability. Participants were recruited from outpatient leprosy and physiotherapy services after screening of clinic records and direct clinical assessment. Eligible individuals were adults aged 18–65 years with a confirmed diagnosis of paucibacillary or multibacillary leprosy according to accepted clinical criteria, completion of multidrug therapy at least three months before enrollment, and current neuropathic pain defined by a Visual Analog Scale score of at least 40 mm and a Douleur Neuropathique 4 score of at least 4. Participants were required to understand assessment instructions, provide written informed consent, attend scheduled treatment sessions, and have no clinical contraindication to physiotherapy or photobiomodulation.

Patients were excluded if they had an active lepra reaction requiring systemic corticosteroid therapy at enrollment, uncontrolled systemic disease likely to interfere with safe participation or outcome interpretation, pregnancy or lactation, open wounds or ulcers over planned treatment sites, malignancy in the treatment area, a photosensitivity disorder, current use of photosensitizing medication, epilepsy or seizure disorder, an implanted electronic device in the treatment region, photobiomodulation therapy during the preceding three months, cognitive impairment preventing valid consent or assessment, inability to comply with the intervention schedule, or concurrent participation in another interventional study. These criteria were applied to reduce clinical risk, minimize confounding from active

inflammatory reactions or competing neurological disorders, and ensure that changes in pain and function could be reasonably attributed to the allocated rehabilitation protocol.

Potential participants were identified by trained research staff through clinic lists, medical records, and routine visits. After preliminary eligibility screening, potentially eligible patients received verbal and written information about the study in a language they understood. The consent process explained the study purpose, procedures, possible benefits, foreseeable risks, voluntary participation, confidentiality protections, and the right to withdraw without affecting routine medical care. After written informed consent, baseline demographic, clinical, and outcome data were collected before random allocation. Randomization was performed using a computer-generated sequence with variable block sizes to maintain balanced allocation between groups. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes prepared by an independent individual who was not involved in recruitment, treatment delivery, or outcome assessment. Envelopes were opened only after baseline assessment had been completed.

Participants were allocated in a 1:1 ratio to receive either standardized physiotherapy plus sham photobiomodulation or standardized physiotherapy plus active photobiomodulation. Outcome assessors remained blinded to group allocation throughout data collection, and participants in both groups received the same session structure and treatment duration to reduce performance and expectation bias. The active and sham photobiomodulation procedures were delivered using identical-appearing procedures, with the sham device positioned and applied in the same manner but without therapeutic light emission. Treating physiotherapists could not be fully blinded because they administered the intervention; however, they were not involved in outcome assessment or statistical analysis. Participants were instructed not to discuss treatment sensations or device details with assessors.

Both groups received the same standardized physiotherapy protocol three times per week for 12 weeks, for a total of 36 planned sessions. Each session lasted approximately 45 minutes for physiotherapy and was delivered by trained physiotherapists using a written protocol to ensure consistency. The physiotherapy program included sensory rehabilitation, motor retraining, deformity-prevention strategies, functional task practice, and protective education. Sensory rehabilitation involved graded texture discrimination, thermal discrimination using safe warm and cool stimuli, two-point discrimination tasks where appropriate, and repeated sensory re-education activities directed to affected hand and foot regions. Motor retraining included active range-of-motion exercises, strengthening of clinically weak muscles, progressive resistance exercises as tolerated, hand function activities, ankle dorsiflexion and intrinsic foot muscle activation, balance exercises, and gait-related training when lower-limb involvement was present. Deformity-prevention care included stretching, positioning education, joint mobility exercises, protective sensation training, daily inspection of hands and feet, footwear advice, and education to prevent burns, pressure injury, and repetitive trauma. Functional training incorporated activities of daily living, grasp-and-release tasks, walking practice, balance and coordination tasks, and individualized task-specific activities based on the participant's functional limitations.

Participants allocated to the active photobiomodulation group received near-infrared photobiomodulation in addition to the same physiotherapy protocol. Treatment was applied using a Class IIIb laser device with a wavelength of 904 nm and output power of 70 mW. Application was performed in contact mode with the probe positioned perpendicular to the skin over clinically relevant superficial nerve pathways. Based on the stated output power and exposure time, each point received 0.63 J over 9 seconds; with a beam area of 0.04 cm^2, the corresponding fluence was 15.75 J/cm^2 per point. Six points were treated per affected nerve territory according to clinical involvement, including commonly affected regions along the ulnar, median, radial, tibial, peroneal, and plantar nerve distributions. The same treatment schedule was used as physiotherapy, with photobiomodulation administered three times per week for 12 weeks. Participants and therapists used appropriate laser eye protection during active treatment, and treatment sites were inspected before and after application.

Participants allocated to the control group received sham photobiomodulation in addition to the same standardized physiotherapy protocol. The sham procedure matched the active procedure in patient positioning, device appearance, probe placement, session duration, and therapist interaction, but the therapeutic light output was disabled. This approach was used to control for attention, expectation, contact time, and procedural effects while isolating the additional effect of active photobiomodulation. Both groups continued routine leprosy follow-up care, and participants were advised not to initiate new pain treatments during the intervention period unless medically required. Any changes in pain medication, intercurrent illness, lepra reaction, or additional therapy were recorded.

The primary outcome was neuropathic pain intensity measured using a 100-mm Visual Analog Scale, anchored by “no pain” at 0 mm and “worst imaginable pain” at 100 mm. The primary comparison was the between-group difference in change in VAS score from baseline to week 12. Secondary outcomes included activity limitation measured by the Screening of Activity Limitation and Safety Awareness scale, participation restriction measured by the Participation Scale short version, health-related quality of life measured by the SF-36, neurological function assessed through simplified neurological examination of affected nerves, and functional capacity assessed using hand grip strength and clinically relevant muscle strength measures. Neuropathic pain eligibility and symptom classification were assessed using the Douleur Neuropathique 4 questionnaire. Outcomes were assessed at baseline, mid-intervention where appropriate, post-intervention at 12 weeks, and follow-up according to the trial schedule. All assessments were performed by trained assessors using standardized instructions in a private clinical setting.

The main exposure variable was treatment allocation, categorized as physiotherapy plus sham photobiomodulation or physiotherapy plus active photobiomodulation. The primary dependent variable was change in VAS pain score from baseline to 12 weeks. Secondary dependent variables were change in SALSA score, Participation Scale score, SF-36 domain scores, neurological function findings, and grip strength. Baseline covariates included age, sex, leprosy type, duration since multidrug therapy completion, baseline pain severity, disability grade, and baseline functional limitation. A clinically meaningful pain response was defined as at least 30% reduction in VAS score from baseline. Treatment adherence was defined as the proportion of scheduled sessions attended, and participants attending at least 80% of planned sessions were included in the per-protocol sensitivity analysis.

Several procedures were used to reduce bias and improve reproducibility. Random sequence generation and allocation concealment were separated from recruitment and assessment. Outcome assessors and the statistician were blinded to treatment assignment. Both groups received equal session frequency, treatment duration, therapist contact, and standardized physiotherapy content. Intervention delivery was guided by a written manual, and treating physiotherapists received protocol training before recruitment. Case report forms were used for all assessments, and data were checked for completeness, range errors, and logical inconsistencies before analysis. Data were entered into an electronic database using participant identification codes rather than personal identifiers, and access was restricted to authorized research personnel.

The sample size was determined for a two-group comparison of change in VAS pain score at 12 weeks. The calculation was based on detecting a clinically meaningful between-group difference using a two-sided alpha level of 0.05, 80% power, and equal allocation between groups. A medium effect size was selected to ensure the trial was powered to detect a practical treatment effect while allowing for expected attrition. The required sample size was increased by 20% to compensate for dropout, yielding a final target sample of 154 participants, with 77 participants in each group. This sample also allowed estimation of secondary outcomes and clinical response rates with acceptable precision, although subgroup analyses were treated as exploratory.

Statistical analysis was performed using standard statistical software. Continuous variables were summarized as mean and standard deviation when approximately normally distributed and as median

and interquartile range when distributional assumptions were not met. Categorical variables were summarized as frequencies and percentages. Baseline comparability between groups was assessed descriptively, with standardized differences considered alongside inferential tests where appropriate. The primary analysis compared change in VAS pain score from baseline to 12 weeks between groups using an independent-samples approach when model assumptions were satisfied; otherwise, an appropriate non-parametric alternative was used. Repeated-measures analysis was used to evaluate group-by-time effects across baseline, mid-intervention, and post-intervention assessments. Effect sizes and 95% confidence intervals were reported to support clinical interpretation.

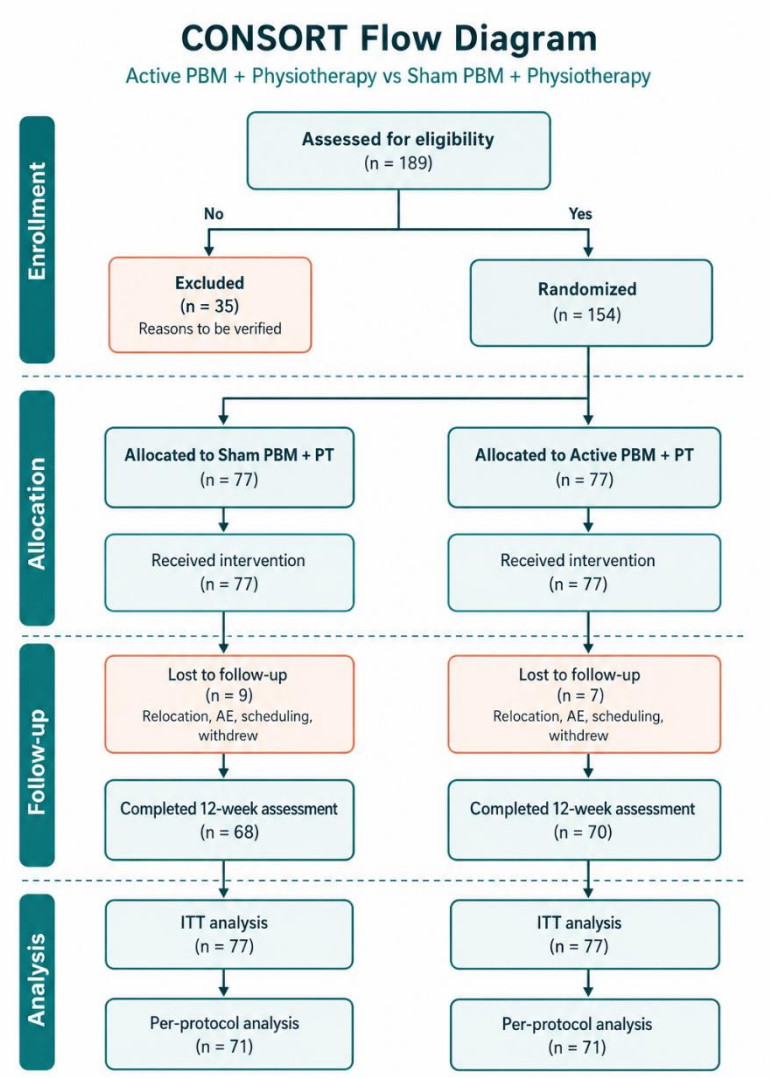

Figure 1 CONSORT Flowchart

Secondary outcomes were analyzed using between-group comparisons of change scores and repeated-measures models where outcomes were collected at multiple time points. Categorical clinical response was compared between groups using risk differences, relative measures, and number needed to treat where data permitted. Regression models were used to examine whether treatment allocation predicted pain reduction after adjustment for baseline pain severity and clinically relevant covariates. Subgroup analyses by leprosy type, baseline pain severity, and duration since multidrug therapy completion were considered exploratory and interpreted primarily through interaction terms rather than isolated within-subgroup p-values. Missing outcome data were handled using a prespecified intention-to-treat approach; sensitivity analysis compared the primary results with a per-protocol analysis among participants who completed at least 80% of sessions. Statistical significance was set at $p < 0.05$, with interpretation guided by effect size, confidence intervals, clinical relevance, and multiplicity of secondary analyses.

Adverse events were monitored throughout the intervention period and recorded at each treatment session and assessment visit. Events of interest included skin redness, warmth or discomfort at the treatment site, fatigue, musculoskeletal soreness, worsening pain, lepra reaction, burn, ulceration, or any event requiring medical care. Serious adverse events were defined as events resulting in hospitalization, persistent disability, life-threatening illness, or death, whether or not they were judged related to the intervention. All adverse events were reviewed for severity, duration, relatedness, action taken, and outcome.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and good clinical practice. Written informed consent was obtained before enrollment, and participants were informed that refusal or withdrawal would not affect their routine medical care. Confidentiality was protected by coded data collection, secure storage of consent documents separately from research data, and restricted access to study records. The trial was conducted after institutional ethical approval, and all study procedures were designed to minimize risk while addressing an important source of pain and disability in people affected by leprosy.

RESULTS

A total of 154 participants were randomized in a 1:1 ratio to receive standardized physiotherapy plus sham photobiomodulation or standardized physiotherapy plus active photobiomodulation. Each group included 77 participants. Post-intervention assessment at 12 weeks was completed by 138 participants, while 16 participants were lost to follow-up. Loss to follow-up occurred in 9 participants in the physiotherapy plus sham photobiomodulation group and 7 participants in the physiotherapy plus active photobiomodulation group. All randomized participants were retained in the intention-to-treat analysis.

Table 1. Baseline Demographic and Clinical Characteristics of Randomized Participants

Variable	Physiotherapy + Sham PBM (n = 77)	Physiotherapy + Active PBM (n = 77)	Test Statistic	p-value
Age, years, Mean ± SD	42.3 ± 11.8	41.7 ± 12.1	0.32	0.749
Male, n (%)	52 (67.5)	48 (62.3)	0.41	0.522
Female, n (%)	25 (32.5)	29 (37.7)	0.41	0.522
Paucibacillary leprosy, n (%)	18 (23.4)	21 (27.3)	0.89	0.345
Multibacillary leprosy, n (%)	59 (76.6)	56 (72.7)	0.89	0.345
Duration since MDT, years, Mean ± SD	2.6 ± 1.9	2.4 ± 1.7	0.68	0.498
WHO Grade 2 disability, n (%)	42 (54.5)	39 (50.6)	0.26	0.610

PBM, photobiomodulation; MDT, multidrug therapy; SD, standard deviation; WHO, World Health Organization. Test statistics are reported as provided in the source manuscript.

The randomized groups were comparable at baseline across demographic and clinical variables. Mean age was 42.3 ± 11.8 years in the physiotherapy plus sham PBM group and 41.7 ± 12.1 years in the physiotherapy plus active PBM group. Multibacillary leprosy was the predominant disease type in both groups, affecting 59 participants in the sham PBM group and 56 participants in the active PBM group. WHO Grade 2 disability was present in 42 participants in the sham PBM group and 39 participants in the active PBM group, indicating a clinically relevant disability burden at enrollment.

Table 2. Baseline Outcome Measures by Treatment Group

Outcome Measure	Physiotherapy + Sham PBM (n = 77), Mean ± SD	Physiotherapy + Active PBM (n = 77), Mean ± SD	Test Statistic	p-value	Cohen's d
VAS pain, mm	62.1 ± 12.3	60.2 ± 11.1	1.02	0.309	0.16
SALSA score	18.2 ± 6.1	17.4 ± 5.6	0.87	0.386	0.14
Participation Scale score	72.4 ± 18.2	70.1 ± 17.3	0.79	0.431	0.13
SF-36 pain domain score	42.3 ± 14.1	44.2 ± 13.2	-0.86	0.392	-0.14
Hand grip strength, kg	28.1 ± 8.2	29.0 ± 7.6	-0.69	0.492	-0.11

VAS, Visual Analog Scale; SALSA, Screening of Activity Limitation and Safety Awareness; SF-36, 36-item Short Form Health Survey; PBM, photobiomodulation; SD, standard deviation.

Baseline outcome scores showed similar pain intensity, disability, participation restriction, quality of life, and grip strength between groups. Mean VAS pain was 62.1 ± 12.3 mm in the sham PBM group and 60.2 ± 11.1 mm in the active PBM group. Baseline SALSA, Participation Scale, SF-36 pain domain, and grip strength values showed small between-group differences, with Cohen's d values ranging from -0.14 to 0.16.

Table 3. Intervention Completion and Adherence

Variable	Physiotherapy + Sham PBM (n = 77)	Physiotherapy + Active PBM (n = 77)	Total (N = 154)	Test Statistic	p-value
Completed 12-week assessment, n (%)	68 (88.3)	70 (90.9)	138 (89.6)	0.41	0.522
Lost to follow-up, n (%)	9 (11.7)	7 (9.1)	16 (10.4)	0.41	0.522
Attended ≥30 sessions, n (%)	—	—	142 (92.2)	—	—
Mean session attendance, %	94.2	95.1	—	0.89	0.375

PBM, photobiomodulation. The denominator for participants attending ≥30 sessions was reported for the total randomized sample only in the source manuscript.

Completion rates were high in both groups. The 12-week assessment was completed by 68 participants in the sham PBM group and 70 participants in the active PBM group. The difference in loss to follow-up between groups was small, with 9 participants lost in the sham PBM group and 7 lost in the active PBM group. Treatment attendance was also high, with 142 randomized participants attending at least 30 of 36 planned sessions.

Table 4. Neuropathic Pain Intensity Over Time

Time Point	Physiotherapy + Sham PBM (n = 77), Mean ± SD	Physiotherapy + Active PBM (n = 77), Mean ± SD
Baseline	62.1 ± 12.3	60.2 ± 11.1
Week 6	52.7	44.9
Week 12	44.8 ± 13.1	27.9 ± 10.4

VAS values are reported in millimeters on a 0–100 mm scale. Week 6 standard deviations were not provided in the source manuscript. PBM, photobiomodulation; SD, standard deviation.

Pain intensity decreased over time in both groups, with a larger reduction in the active PBM group. In the sham PBM group, mean VAS pain decreased from 62.1 mm at baseline to 44.8 mm at week 12. In the active PBM group, mean VAS pain decreased from 60.2 mm at baseline to 27.9 mm at week 12. The week 6 values indicated earlier separation between groups, with mean VAS pain of 52.7 mm in the sham PBM group and 44.9 mm in the active PBM group.

Table 5. Primary Outcome: Change in VAS Pain Score from Baseline to Week 12

Outcome	Physiotherapy + Sham PBM (n = 77)	Physiotherapy + Active PBM (n = 77)	Between-Group Difference	95% CI	Test Statistic	p-value	Cohen's d
VAS change, mm	-17.3 ± 10.8	-32.3 ± 11.2	15.0	11.8 to 18.2	9.18	<0.001	0.93
VAS reduction, %	27.8	53.7	—	—	—	—	—

Negative change values indicate reduction in pain from baseline. VAS, Visual Analog Scale; PBM, photobiomodulation; CI, confidence interval; SD, standard deviation.

The active PBM group demonstrated greater reduction in neuropathic pain than the sham PBM group. Mean VAS reduction was -32.3 ± 11.2 mm in the active PBM group compared with -17.3 ± 10.8 mm in the sham PBM group. The between-group difference in pain reduction was 15.0 mm, with a 95% confidence interval from 11.8 to 18.2 mm and a Cohen's d of 0.93.

Table 6. Repeated-Measures Analysis for VAS Pain Scores

Effect	df	F	p-value	Partial η^2
Time	2, 304	284.73	<0.001	0.652
Group	1, 152	84.32	<0.001	0.357
Group × Time	2, 304	67.89	<0.001	0.309

VAS, Visual Analog Scale.

Repeated-measures analysis showed a clear group-by-time pattern for VAS pain scores. The group × time interaction had an F value of 67.89 and partial η^2 of 0.309, indicating that the trajectory of pain reduction differed between groups across baseline, week 6, and week 12. The active PBM group showed a steeper reduction in pain over time than the sham PBM group.

Secondary outcomes consistently favored the active PBM group. SALSA score decreased by -5.6 ± 4.1 in the active PBM group and -3.3 ± 4.2 in the sham PBM group. Participation Scale score decreased by -24.5 ± 14.8 in the active PBM group and -14.3 ± 15.2 in the sham PBM group. SF-36 pain domain score increased by 18.9 ± 11.2 in the active PBM group compared with 10.5 ± 11.8 in the sham PBM group. Hand grip strength increased by 10.8 ± 7.1 kg in the active PBM group and 6.2 ± 6.8 kg in the sham PBM group.

Table 7. Secondary Outcome Changes from Baseline to Week 12

Outcome	Physiotherapy + Sham PBM, Mean ± SD	Physiotherapy + Active PBM, Mean ± SD	Between-Group Difference	95% CI	Test Statistic	p-value	Cohen's d
SALSA change	-3.3 ± 4.2	-5.6 ± 4.1	2.3	1.1 to 3.5	3.71	<0.001	0.56
Participation Scale change	-14.3 ± 15.2	-24.5 ± 14.8	10.2	5.8 to 14.6	4.54	<0.001	0.68
SF-36 pain domain change	10.5 ± 11.8	18.9 ± 11.2	8.4	5.1 to 11.7	5.01	<0.001	0.73
Hand grip strength change, kg	6.2 ± 6.8	10.8 ± 7.1	4.6	2.4 to 6.8	4.10	<0.001	0.66

Negative change values for SALSA and Participation Scale indicate reduction in limitation or restriction. Positive change values for SF-36 and grip strength indicate improvement. SALSA, Screening of Activity Limitation and Safety Awareness; SF-36, 36-item Short Form Health Survey; PBM, photobiomodulation; CI, confidence interval; SD, standard deviation.

Table 8. Clinical Response Based on ≥30% Reduction in VAS Pain Score

Outcome	Physiotherapy + Sham PBM (n = 77)	Physiotherapy + Active PBM (n = 77)	Absolute Difference	95% CI	NNT
Clinical response, n (%)	24 (31.2)	58 (75.3)	44.1	—	2.27
NNT 95% CI	—	—	—	1.82 to 3.05	—

Clinical response was defined as ≥30% reduction in VAS pain score from baseline. VAS, Visual Analog Scale; PBM, photobiomodulation; NNT, number needed to treat; CI, confidence interval.

A greater proportion of participants achieved clinically meaningful pain reduction in the active PBM group. Clinical response occurred in 58 of 77 participants in the active PBM group and 24 of 77 participants in the sham PBM group. The absolute difference in response rate was 44.1 percentage points, corresponding to a number needed to treat of 2.27.

Table 9. Improvement in SALSA Limitation Category

Outcome	Physiotherapy + Sham PBM (n = 77)	Physiotherapy + Active PBM (n = 77)	Odds Ratio	95% CI	χ^2	p-value
Moderate/severe to mild/no limitation, n (%)	25 (32.5)	45 (58.4)	2.94	1.58 to 5.47	10.67	0.001

SALSA, Screening of Activity Limitation and Safety Awareness; PBM, photobiomodulation; CI, confidence interval.

Improvement in SALSA limitation category was more frequent in the active PBM group. A shift from moderate or severe limitation to mild or no limitation occurred in 45 participants in the active PBM group and 25 participants in the sham PBM group. The reported odds ratio was 2.94, with a 95% confidence interval from 1.58 to 5.47.

Exploratory subgroup analyses showed numerically greater VAS reduction with active PBM across leprosy type, baseline pain severity, and duration since MDT completion. The between-group difference was 13.6 mm among participants with paucibacillary leprosy and 16.2 mm among those with multibacillary leprosy. Among participants with moderate baseline pain, the between-group difference

was 12.3 mm, while among those with severe baseline pain it was 17.7 mm. The treatment difference was similar among participants with shorter and longer duration since MDT completion.

Changes in pain were associated with changes in disability, participation, quality of life, and grip strength. VAS change correlated with SALSA change at r = 0.68 and with Participation Scale change at r = 0.72. The correlation between VAS change and SF-36 pain domain change was -0.74, reflecting the inverse scoring direction of pain reduction and quality-of-life improvement. VAS change also correlated with grip strength change at r = -0.48.

Table 10. Subgroup Analysis of VAS Pain Reduction

Subgroup	Physiotherapy + Sham PBM, Mean ± SD	Physiotherapy + Active PBM, Mean ± SD	Difference	95% CI	Test Statistic	p-value	Cohen's d
Paucibacillary leprosy	-14.8 ± 9.2	-28.4 ± 10.1	13.6	8.9 to 18.3	5.71	<0.001	1.14
Multibacillary leprosy	-17.9 ± 11.2	-34.1 ± 11.5	16.2	12.6 to 19.8	8.89	<0.001	0.83
Moderate baseline pain	-12.4 ± 8.1	-24.7 ± 9.3	12.3	7.8 to 16.8	5.39	<0.001	0.90
Severe baseline pain	-20.1 ± 11.4	-37.8 ± 11.2	17.7	13.8 to 21.6	8.92	<0.001	0.91
MDT duration <2 years	-15.2 ± 9.8	-30.1 ± 10.4	14.9	10.5 to 19.3	6.69	<0.001	0.95
MDT duration ≥2 years	-19.1 ± 11.6	-34.2 ± 11.8	15.1	10.7 to 19.5	6.74	<0.001	0.76

Negative values indicate reduction in VAS pain score. VAS, Visual Analog Scale; PBM, photobiomodulation; MDT, multidrug therapy; CI, confidence interval; SD, standard deviation.

Table 11. Correlations Between Changes in Clinical Outcomes

Variable Pair	r	p-value
VAS change and SALSA change	0.68	<0.001
VAS change and Participation Scale change	0.72	<0.001
VAS change and SF-36 pain domain change	-0.74	<0.001
SALSA change and Participation Scale change	0.65	<0.001
SALSA change and SF-36 pain domain change	-0.61	<0.001
VAS change and grip strength change	-0.48	<0.001

VAS, Visual Analog Scale; SALSA, Screening of Activity Limitation and Safety Awareness; SF-36, 36-item Short Form Health Survey. Direction of correlation depends on change-score coding, where lower VAS, SALSA, and Participation Scale scores indicate improvement and higher SF-36 and grip strength scores indicate improvement.

Table 12. Correlations Between VAS Change and Baseline Characteristics

Baseline Characteristic	r	p-value
Age	0.12	0.142
Duration since MDT	-0.08	0.321
Baseline VAS	0.34	<0.001
Baseline SALSA	0.29	<0.001
Baseline SF-36 pain domain	-0.31	<0.001

VAS, Visual Analog Scale; SALSA, Screening of Activity Limitation and Safety Awareness; SF-36, 36-item Short Form Health Survey; MDT, multidrug therapy.

Baseline pain, disability, and SF-36 pain domain scores were associated with subsequent VAS change, whereas age and duration since MDT completion were not. Baseline VAS showed a correlation of r = 0.34 with VAS change, and baseline SALSA showed a correlation of r = 0.29. Baseline SF-36 pain domain showed an inverse correlation with VAS change at r = -0.31.

Table 13. Multiple Linear Regression for Predictors of VAS Pain Reduction

Predictor	B	SE	β	t	p-value	95% CI
Constant	8.42	3.21	—	2.62	0.010	2.08 to 14.76
Group	-15.24	1.42	-0.52	-10.73	<0.001	-18.04 to -12.44
Baseline VAS	-0.28	0.05	-0.34	-5.60	<0.001	-0.38 to -0.18
Age	-0.04	0.03	-0.07	-1.33	0.186	-0.10 to 0.02
Duration since MDT	-0.82	0.38	-0.11	-2.16	0.032	-1.57 to -0.07
Leprosy type	-2.14	1.58	-0.07	-1.35	0.178	-5.27 to 0.99

Model statistics: $R^2 = 0.612$; adjusted $R^2 = 0.600$; $F = 46.82$; $p < 0.001$; Durbin-Watson = 1.98. Group was coded as active PBM relative to sham PBM. Leprosy type was coded as multibacillary relative to paucibacillary. Negative B values indicate greater reduction in VAS pain score. VAS, Visual Analog Scale; PBM, photobiomodulation; MDT, multidrug therapy; SE, standard error; CI, confidence interval.

Regression analysis showed that treatment allocation was the strongest predictor of VAS pain reduction. Allocation to active PBM was associated with an additional 15.24 mm reduction in VAS score after adjustment for baseline pain, age, duration since MDT completion, and leprosy type. Baseline VAS score was also associated with pain reduction, with a B coefficient of -0.28. The model explained 61.2% of the variance in VAS change.

Table 14. Multiple Linear Regression for Predictors of SF-36 Pain Domain Improvement

Predictor	B	SE	β	t	p-value	95% CI
Constant	12.34	2.87	—	4.30	<0.001	6.67 to 18.01
Group	6.82	1.28	0.31	5.33	<0.001	4.29 to 9.35
VAS change	-0.42	0.06	-0.45	-7.00	<0.001	-0.54 to -0.30
SALSA change	0.58	0.11	0.38	5.27	<0.001	0.36 to 0.80
Baseline SF-36 pain domain	-0.18	0.04	-0.29	-4.50	<0.001	-0.26 to -0.10

Model statistics: $R^2 = 0.687$; adjusted $R^2 = 0.678$; $F = 80.12$; $p < 0.001$; Durbin-Watson = 2.02. Group was coded as active PBM relative to sham PBM. VAS, Visual Analog Scale; SALSA, Screening of Activity Limitation and Safety Awareness; SF-36, 36-item Short Form Health Survey; PBM, photobiomodulation; SE, standard error; CI, confidence interval.

Improvement in the SF-36 pain domain was associated with treatment allocation, VAS change, SALSA change, and baseline SF-36 pain domain score. VAS change had the largest standardized coefficient, with $\beta = -0.45$. Active PBM allocation remained associated with SF-36 pain domain improvement after accounting for pain and disability change, with $B = 6.82$ and $\beta = 0.31$.

Table 15. Logistic Regression for Clinical Response

Predictor	B	SE	OR	95% CI	Wald χ^2	p-value
Constant	-2.14	0.48	—	—	19.89	<0.001
Group	2.48	0.42	11.94	5.23 to 27.26	34.82	<0.001
Baseline VAS	0.028	0.011	1.03	1.01 to 1.05	6.45	0.011
Duration since MDT	0.18	0.09	1.20	1.01 to 1.42	4.00	0.046
Age	-0.012	0.009	0.99	0.97 to 1.01	1.78	0.182
Leprosy type	0.34	0.38	1.41	0.67 to 2.96	0.80	0.371

Model statistics: -2 log likelihood = 142.38; Cox and Snell $R^2 = 0.284$; Nagelkerke $R^2 = 0.381$; model $\chi^2 = 72.84$; $p < 0.001$; classification accuracy = 78.6%. Clinical response was defined as ≥30% reduction in VAS pain score. Group was coded as active PBM relative to sham PBM. Leprosy type was coded as multibacillary relative to paucibacillary. OR, odds ratio; VAS, Visual Analog Scale; MDT, multidrug therapy; PBM, photobiomodulation; SE, standard error; CI, confidence interval. Logistic regression showed that treatment allocation was associated with clinical response. Participants allocated to active PBM had an odds ratio of 11.94 for achieving at least 30% VAS pain reduction compared with participants allocated to sham PBM. Baseline VAS and duration since MDT completion were also retained in the model, while age and leprosy type were not.

Table 16. Per-Protocol Analysis Among Participants Attending ≥80% of Sessions

Outcome	Physiotherapy + Sham PBM (n = 71), Mean ± SD	Physiotherapy + Active PBM (n = 71), Mean ± SD	Between-Group Difference	95% CI	Cohen's d
VAS change, mm	-16.8 ± 10.2	-33.1 ± 10.8	16.3	12.8 to 19.8	0.96
SALSA change	-3.1 ± 4.0	-5.8 ± 3.9	2.7	1.4 to 4.0	0.62
SF-36 pain domain change	11.2 ± 11.1	19.8 ± 10.6	8.6	5.1 to 12.1	0.75

Negative change values for VAS and SALSA indicate improvement. Positive change values for SF-36 indicate improvement. VAS, Visual Analog Scale; SALSA, Screening of Activity Limitation and Safety Awareness; SF-36, 36-item Short Form Health Survey; PBM, photobiomodulation; CI, confidence interval; SD, standard deviation.

The per-protocol analysis was consistent with the intention-to-treat results. Among participants who attended at least 80% of planned sessions, VAS pain reduction was -33.1 ± 10.8 mm in the active PBM group and -16.8 ± 10.2 mm in the sham PBM group. SALSA and SF-36 pain domain changes also favored active PBM, with between-group differences of 2.7 points and 8.6 points, respectively. No serious adverse events were reported in either group. Any adverse event occurred in 10 participants in the sham PBM group and 16 participants in the active PBM group. The most frequent events were musculoskeletal

soreness, treatment fatigue, temporary warmth sensation, and mild skin redness. Events reported in the source manuscript were mild and self-limiting.

Table 17. Adverse Events by Treatment Group

Adverse Event	Physiotherapy + Sham PBM (n = 77), n (%)	Physiotherapy + Active PBM (n = 77), n (%)	Total (N = 154), n (%)
Mild skin redness at treatment site	0 (0.0)	3 (3.9)	3 (1.9)
Temporary warmth sensation	0 (0.0)	5 (6.5)	5 (3.2)
Treatment fatigue	4 (5.2)	3 (3.9)	7 (4.5)
Musculoskeletal soreness	6 (7.8)	5 (6.5)	11 (7.1)
Any adverse event	10 (13.0)	16 (20.8)	26 (16.9)

PBM, photobiomodulation.

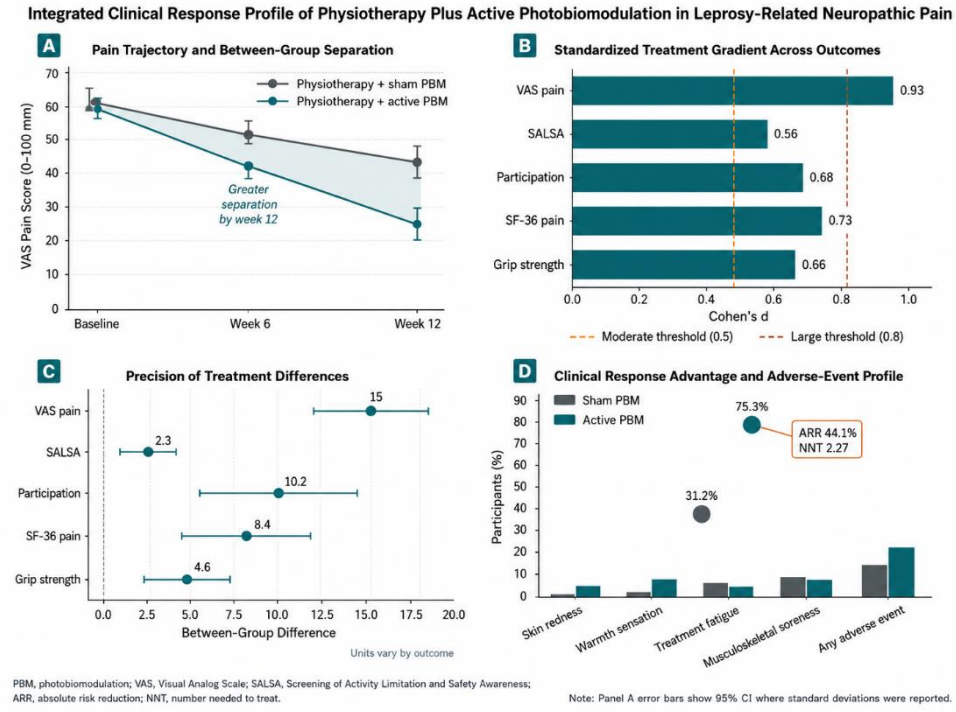

Figure 2 Clinical Response Profile of Physiotherapy Plus Active Photo-biomodulation in Leprosy

The panelled figure summarizes the integrated clinical response profile of physiotherapy plus active photobiomodulation compared with physiotherapy plus sham photobiomodulation in leprosy-related neuropathic pain. Panel A shows progressive separation in VAS pain scores, with active PBM decreasing from 60.2 mm at baseline to 27.9 mm at week 12, compared with 62.1 mm to 44.8 mm in the sham PBM group. Panel B demonstrates a consistent standardized treatment gradient across outcomes, with Cohen's d ranging from 0.56 for SALSA improvement to 0.93 for VAS pain reduction. Panel C shows that all reported between-group differences favored active PBM, including a 15.0 mm VAS advantage, 10.2-point Participation Scale difference, 8.4-point SF-36 pain-domain difference, and 4.6 kg grip-strength difference. Panel D integrates clinical response and tolerability, showing a higher ≥30% pain-response rate with active PBM than sham PBM, 75.3% versus 31.2%, with an absolute risk reduction of 44.1% and NNT of 2.27, while adverse events remained mild and were reported in 20.8% and 13.0% of participants, respectively.

DISCUSSION

This randomized controlled trial evaluated whether adding active photobiomodulation to a standardized physiotherapy protocol produced superior clinical outcomes compared with standardized physiotherapy with sham photobiomodulation in adults with leprosy-related neuropathic pain. The findings showed a clinically and statistically meaningful reduction in neuropathic pain after 12 weeks, with the active photobiomodulation group showing a larger decrease in VAS pain score than the sham photobiomodulation group. Pain declined from 60.2 ± 11.1 mm to 27.9 ± 10.4 mm in the active photobiomodulation group and from 62.1 ± 12.3 mm to 44.8 ± 13.1 mm in the sham photobiomodulation group, corresponding to reductions of 53.7% and 27.8%, respectively. The between-group difference of

15.0 mm, with a 95% confidence interval of 11.8 to 18.2 mm and Cohen's d of 0.93, indicates that adjunctive photobiomodulation produced an additional analgesic effect beyond the improvement achieved with physiotherapy alone. This effect is clinically relevant because a 30% or greater reduction in pain is commonly interpreted as a meaningful response in chronic pain research, and this threshold was achieved by 75.3% of participants in the active photobiomodulation group compared with 31.2% in the sham photobiomodulation group.

The direction and magnitude of the primary outcome were supported by the repeated-measures analysis, which demonstrated a significant group-by-time interaction for VAS pain scores. This indicates that the treatment groups did not merely improve in parallel over the intervention period; rather, the active photobiomodulation group showed a steeper reduction in pain from baseline to week 12. The separation between groups was already evident at week 6 and became more pronounced by week 12, suggesting that the adjunctive intervention may have both early and cumulative effects. The observed number needed to treat of 2.27 further supports the clinical efficiency of the combined approach, although this estimate should be interpreted within the context of a controlled trial and should be confirmed in larger pragmatic studies before broad policy implementation.

Secondary outcomes showed a consistent pattern favoring active photobiomodulation. Activity limitation measured by the SALSA scale improved by 32.2% in the active photobiomodulation group compared with 18.1% in the sham group, and the proportion of participants shifting from moderate or severe limitation to mild or no limitation was also higher in the active intervention arm. Participation restriction decreased by 35.0% versus 19.8%, while the SF-36 pain domain improved by 42.8% versus 24.8%. Hand grip strength also improved more in the active photobiomodulation group, with a 37.2% increase compared with 22.1% in the sham group. The consistency of these findings across pain, activity limitation, participation, quality of life, and functional capacity suggests that the intervention effect was not limited to symptom reporting but extended to clinically important dimensions of rehabilitation.

These findings are aligned with previous leprosy-specific studies that examined photobiomodulation as an adjunct to physiotherapy. Duarte et al. reported improvements in pain, SALSA limitation, nerve palpation, strength, sensitivity, and neurological disability when photobiomodulation was combined with physiotherapy in people affected by leprosy (2). Bonazza et al. similarly reported improvements in SALSA categories, participation, SF-36 pain-related domains, and selected nerve function outcomes after combined treatment, although their sample size was smaller and some between-group pain comparisons were less definitive (1). The present study extends that evidence by using a larger sample, a standardized 12-week treatment schedule, and a broader analytical framework including repeated-measures analysis, clinical response, regression, and per-protocol sensitivity analysis. However, comparisons with earlier trials must remain cautious because differences in study setting, participant characteristics, dosimetry, comparator procedures, and outcome timing may influence the magnitude of treatment effects.

The findings are biologically plausible in light of proposed photobiomodulation mechanisms. Near-infrared photobiomodulation has been described as a non-invasive modality that may influence mitochondrial activity through cytochrome c oxidase absorption, with downstream effects on cellular energy metabolism, oxidative stress modulation, inflammatory signaling, and nociceptor sensitization (3,11,28). These mechanisms are relevant to leprosy-related neuropathic pain, which may persist after multidrug therapy because structural nerve injury, demyelination, axonal damage, immune-mediated reactions, and altered somatosensory processing can continue after the infectious burden has been controlled (6,14,26). The current trial did not measure biomarkers, nerve conduction parameters, cytokines, or imaging markers; therefore, mechanistic explanations should be interpreted as plausible biological pathways rather than mechanisms directly proven by this study.

The physiotherapy component likely contributed to improvement in both groups by addressing sensory impairment, weakness, joint mobility, deformity prevention, protective education, gait, balance, and functional task performance. The improvement observed in the sham photobiomodulation group

supports the value of structured physiotherapy in leprosy rehabilitation. This is consistent with prior literature emphasizing physiotherapy as a core component of disability prevention and functional recovery in people affected by leprosy (7,8). The greater improvement in the active photobiomodulation group suggests that pain modulation may have enabled more effective participation in rehabilitation activities, while the functional program may have converted symptom relief into measurable gains in activity, participation, and grip strength. This interpretation is consistent with a biopsychosocial model in which pain reduction, physical rehabilitation, confidence in movement, and improved daily function interact rather than operate as isolated treatment effects.

The regression analyses further support the independent contribution of treatment allocation. Active photobiomodulation was the strongest predictor of VAS pain reduction after adjustment for baseline VAS, age, duration since multidrug therapy completion, and leprosy type. The adjusted coefficient indicated an additional 15.24 mm reduction in VAS pain associated with active photobiomodulation. Baseline VAS also predicted pain reduction, suggesting that participants with greater initial pain had more room for absolute improvement. Logistic regression similarly showed that active photobiomodulation was strongly associated with achieving at least 30% pain reduction. These analyses strengthen the primary finding, although the regression models should be interpreted as supportive rather than definitive causal modeling because all modeled predictors were analyzed within the context of a single clinical trial.

The correlation analyses indicated that reduction in pain was associated with improvement in disability, participation, quality of life, and grip strength. These relationships are clinically coherent because neuropathic pain can restrict hand use, walking, self-care, occupational function, and social participation. The strongest associations were observed between VAS change and Participation Scale change and between VAS change and SF-36 pain-domain change, suggesting that pain relief may be an important pathway through which patients experience broader functional and quality-of-life benefit. The mediation analysis should be reported cautiously. Pain reduction accounted for part of the relationship between treatment assignment and SF-36 pain-domain improvement, but because VAS and SF-36 changes were measured over the same treatment interval, the analysis should not be interpreted as proving a causal mediation pathway. It is more appropriate to state that pain reduction statistically explained part of the observed quality-of-life improvement, while residual treatment effects may reflect other clinical pathways such as functional gains, improved confidence, reduced disability burden, or unmeasured neurological changes.

Subgroup analyses showed that the direction of benefit favored active photobiomodulation across leprosy type, baseline pain severity, and duration since multidrug therapy completion. The treatment difference was observed in both paucibacillary and multibacillary disease, in moderate and severe baseline pain, and in shorter and longer durations since multidrug therapy. These findings suggest that the intervention may be applicable across a clinically heterogeneous treated leprosy population. However, subgroup analyses were exploratory and should be interpreted primarily through interaction testing rather than isolated within-subgroup p-values. The study was not specifically powered to establish differential treatment effects within small subgroups, particularly among participants with paucibacillary leprosy.

The safety profile was favorable. No serious adverse events were reported, and adverse events were mild and self-limiting. Mild skin redness, warmth sensation, treatment fatigue, and musculoskeletal soreness were the main events recorded. Although any adverse event was numerically more frequent in the active photobiomodulation group, the events were minor and did not indicate major tolerability concerns. This is clinically important because people affected by leprosy may already have sensory impairment and tissue vulnerability, making careful monitoring essential when introducing device-based or exercise-based interventions. The use of standardized treatment parameters, skin inspection, protective positioning, and safety precautions should therefore remain integral to implementation.

This study has several strengths. It used randomized allocation, equal group sizes, blinded outcome assessment, standardized intervention delivery, intention-to-treat analysis, and validated clinical outcomes. The inclusion of pain, disability, participation, quality of life, and functional capacity provided a multidimensional view of treatment response. The sample size was larger than previous leprosy-specific photobiomodulation trials, improving precision for the primary outcome. The use of both clinical response and continuous change scores also improved interpretability for clinicians.

Several limitations should be acknowledged. First, participant blinding may not have been complete because active photobiomodulation can produce warmth or other subtle sensations, which may influence expectation or reporting. Second, the study was conducted in a limited geographic and service context, which may reduce generalizability to other regions, rural settings, or health systems with different rehabilitation capacity. Third, long-term durability of treatment effect remains uncertain because the main reported endpoint was 12 weeks, and extended follow-up data were not emphasized in the presented results. Fourth, the trial excluded patients with active lepra reactions requiring systemic corticosteroids, so the findings should not be generalized to that clinically important subgroup. Fifth, the manuscript should ensure full consistency in reporting the control condition as sham photobiomodulation when a sham device was used. Finally, the photobiomodulation dosimetry must be checked carefully in the final manuscript because the reported power and exposure time must mathematically align with the stated energy per point.

The clinical implications are meaningful but should be framed cautiously. The findings support active photobiomodulation as a promising adjunct to standardized physiotherapy for treated leprosy patients with neuropathic pain. The intervention may be particularly relevant in settings where leprosy-related disability persists despite infection control and where non-pharmacological rehabilitation options are needed. However, before recommending routine guideline-level adoption, the findings should be replicated in multicenter trials with longer follow-up, formal cost-effectiveness analysis, verified dosimetry, and implementation evaluation in routine clinical care. Future research should also examine biomarkers, nerve conduction outcomes, recurrence of pain, medication reduction, adherence, patient-reported acceptability, and effects in patients with lepra reactions or more advanced disability.

CONCLUSION

In adults with treated leprosy and neuropathic pain, standardized physiotherapy combined with active photobiomodulation produced greater 12-week improvement in pain, activity limitation, participation restriction, SF-36 pain-domain score, and hand grip strength than standardized physiotherapy with sham photobiomodulation. The intervention was associated with a large between-group effect for VAS pain reduction, a higher clinically meaningful response rate, and no serious adverse events. These findings suggest that photobiomodulation may be a useful adjunct to physiotherapy in leprosy rehabilitation, particularly for patients with persistent neuropathic pain after multidrug therapy; however, broader implementation should be supported by multicenter confirmation, longer follow-up, verified dosimetry, and cost-effectiveness evaluation.

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