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COMPARATIVE EFFECTS OF THERAPEUTIC ULTRASOUND AND HIGH INTENSITY LASER THERAPY ON NEUROPATHIC PAIN, STRENGTH AND QUALITY OF LIFE IN DIABETIC FOOT

Original Research

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ABSTRACT

Background: Diabetes mellitus is a major global health concern and a leading cause of morbidity, mortality, and long-term disability. One of its most disabling complications, diabetic peripheral neuropathy, adversely affects quality of life through neuropathic pain, sensory loss, gait disturbances, foot ulceration, and increased risk of amputation. Despite the widespread use of physical therapy modalities in neuropathy management, comparative evidence regarding the effectiveness of different adjunctive interventions remains limited, particularly in patients with diabetic foot involvement.

Objective: To compare the effects of therapeutic ultrasound and high-intensity laser therapy, each combined with routine physical therapy, on neuropathic pain, muscle strength, and quality of life in patients with diabetic foot.

Methods: A single-blinded randomized clinical trial (trial registration number NCT06479577) was conducted at Bahawalpur Medical and Dental Hospital. Using a non-probability convenience sampling technique, 44 patients with confirmed diabetic peripheral neuropathy were enrolled and randomly allocated into two groups. One group received therapeutic ultrasound with routine physical therapy, while the other received high-intensity laser therapy with routine physical therapy. Interventions were administered three times per week for eight weeks. Outcome measures included the Michigan Neuropathy Screening Instrument for neuropathic pain and the Foot and Ankle Disability Index for foot-related quality of life, assessed at baseline and after completion of the intervention. Data were analyzed using SPSS version 25.

Results: Baseline characteristics and outcome measures were comparable between groups ($p > 0.05$). Post-intervention analysis demonstrated statistically significant between-group differences in neuropathic pain, functional status, and muscle strength, favoring the high-intensity laser therapy group ($p < 0.05$). Within-group analysis showed significant improvements in all outcome measures in both groups ($p < 0.05$); however, the magnitude of improvement was consistently greater in the high-intensity laser therapy group.

Conclusion: High-intensity laser therapy combined with routine physical therapy was more effective than therapeutic ultrasound with routine physical therapy in reducing neuropathic pain, improving lower-limb strength, and enhancing quality of life in patients with diabetic foot.

Keywords: Diabetes Mellitus, Diabetic Neuropathies, Laser Therapy, Physical Therapy Modalities, Quality of Life, Rehabilitation, Ultrasonography.

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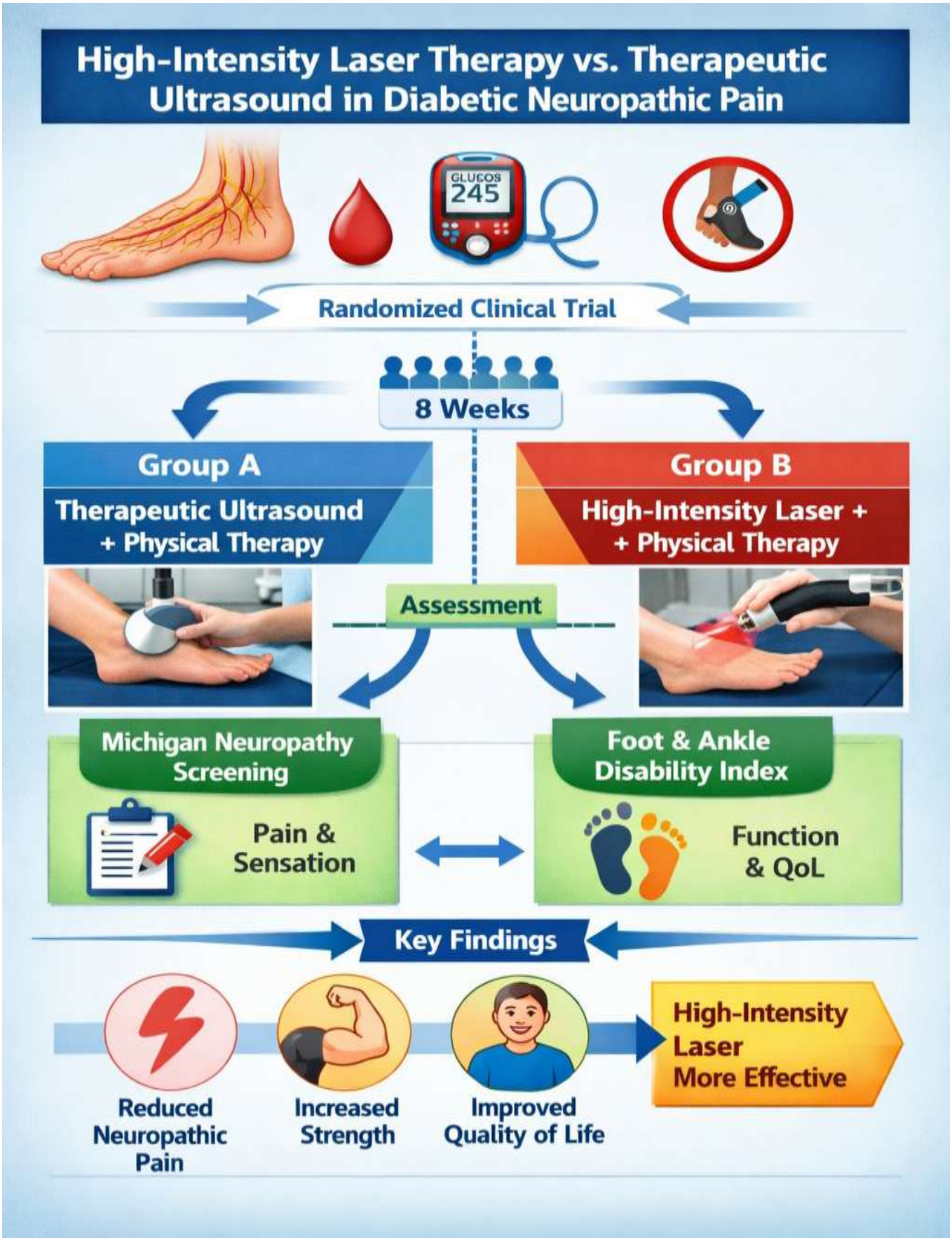

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INTRODUCTION

Diabetes mellitus has emerged as one of the most pressing global public health challenges, contributing substantially to morbidity, mortality, and long-term disability worldwide. In 2017, an estimated 451 million individuals were living with diabetes, a figure projected to rise dramatically to nearly 693 million by 2045, reflecting the relentless expansion of this metabolic disorder across both developed and developing regions (1). The disease predominantly affects adults between 18 and 65 years of age, a demographic that represents the core of the productive workforce, thereby amplifying its socioeconomic and healthcare burden. Beyond glycemic dysregulation, diabetes is characterized by a spectrum of chronic complications that progressively impair functional capacity and quality of life. Among these complications, diabetic peripheral neuropathy (DPN) stands out as one of the most common and disabling, affecting approximately half of all individuals with diabetes during the course of the disease (2). DPN develops as a consequence of sustained hyperglycemia, which induces peripheral nerve damage and disrupts normal nerve fiber regeneration (3). Clinically, neuropathy may remain asymptomatic in its early stages or present with distressing sensory symptoms as the disease advances (4). In low- and middle-income countries such as Pakistan, where healthcare access and preventive awareness remain uneven, the impact of diabetes and its complications is particularly profound. National estimates suggest a diabetes prevalence of approximately 6.8%, with nearly 87,000 diabetes-related deaths occurring annually (5). Projections further indicate that by 2030, around 9.2 million Pakistanis may be living with diabetes, underscoring the urgency of addressing its complications at both clinical and public health levels (6). Globally, diabetes has reached epidemic proportions. Reports from international agencies estimated 425 million people with diabetes in 2017, with expectations of an increase to 628 million by 2045 (7). Parallel projections suggested that by 2023 alone, nearly 360 million individuals worldwide would be affected (8).

Obesity, a rapidly escalating epidemic in its own right, remains one of the most significant modifiable risk factors for the development and progression of diabetes (9). As obesity rates climb, the incidence of diabetes-related complications such as DPN is expected to rise correspondingly. One of the most serious clinical consequences of DPN is diabetic foot syndrome, with lifetime ulceration risk estimated at 15–25% among patients with type 2 diabetes. These foot complications not only predispose individuals to infections and amputations but also significantly increase the risk of falls, which is reported to be two to three times higher in patients with DPN due to muscle weakness, sensory loss, and foot pathology (10). Effective foot care and early recognition of neuropathy are therefore central to preventing disability, making patient awareness and education critical components of diabetes management (11). Neuropathic pain is a particularly burdensome manifestation of DPN, often described as burning, tingling, shooting, or electric-like sensations. Validated tools such as the Douleur Neuropathique 4 (DN4) questionnaire, originally developed and validated in France, have been widely used to identify neuropathic pain in clinical and research settings (12). Painful diabetic neuropathy frequently interferes with sleep, daily activities, and social participation, and is commonly associated with psychological distress, including anxiety and depression (13). Despite advances in understanding diabetes-related nerve damage, a striking clinical paradox remains: pain severity often does not correlate with the extent of nerve damage, and some individuals develop severe pain in the absence of overt neuropathic deficits, while others with advanced neuropathy remain pain-free (14). This unexplained variability highlights a critical gap in current knowledge.

At the mechanistic level, metabolic disturbances driven by chronic hyperglycemia play a central role in the development of diabetic neuropathy. Activation of the polyol pathway during hyperglycemia increases aldose reductase activity, leading to intracellular sorbitol accumulation, osmotic stress, and cellular dysfunction (15). The pathogenic significance of this pathway is further attributed to depletion of key cofactors such as NADPH and NAD+, resulting in impaired glutathione regeneration, enhanced oxidative stress, increased formation of advanced glycation end products (AGEs), and activation of diacylglycerol-dependent protein kinase C (PKC) isoforms (16). Oxidative stress is additionally amplified through glucose autoxidation, AGE-receptor interactions, mitochondrial dysfunction, hexosamine pathway overactivity, and sustained PKC signaling, collectively contributing to neural injury (17). Beyond somatic neuropathy, diabetes is increasingly recognized to disrupt autonomic balance between sympathetic and parasympathetic systems, a disturbance associated with heightened cardiovascular risk and adverse outcomes (18,19). Microvascular injury, a hallmark of diabetes, further compounds neural damage and affects multiple organ systems, including the kidneys, retina, nervous system, skin, and oral tissues (20). While numerous studies have demonstrated that diabetes adversely affects overall quality of life across physical, psychological, and social domains, comparatively fewer investigations have focused specifically on the impact of painful diabetic peripheral neuropathy on health-related quality of life (HRQoL) (21). This represents an important gap, particularly in populations where disease burden is high and supportive care resources are limited. Given the rising prevalence of diabetes, the high frequency of DPN, and the disproportionate functional and psychosocial burden imposed by neuropathic pain, there is a clear need to better understand how painful DPN influences patients' health-related quality of life. The objective of the present study is therefore to evaluate the impact of

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diabetic peripheral neuropathic pain on HRQoL among individuals with diabetes, and to identify the extent to which neuropathic pain contributes to functional impairment beyond glycemic control and neuropathy severity.

METHODS

This randomized, single-blinded clinical trial was conducted at Bahawalpur Medical and Dental Hospital over a seven-month period from December to July, following formal approval of the study synopsis by the institutional ethical review authorities. Ethical clearance was obtained from the Institutional Review Board of Bahawalpur Medical and Dental Hospital prior to participant recruitment, and the study was carried out in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants after a detailed explanation of study objectives, procedures, potential benefits, and risks. The sample size was calculated using G*Power software version 3.1, based on previously reported Michigan Neuropathy Screening Instrument (MNSI) mean ± standard deviation values of 4.8 ± 1.9 and 2.8 ± 2.2 for the two intervention groups. With an effect size of 0.973, a significance level (α) of 0.05, and a statistical power of 0.95, the required sample size was estimated. To compensate for an anticipated attrition rate of 20%, the final sample size was set at 44 participants. A non-probability convenience sampling technique was employed. Eligible participants were randomly allocated into two equal groups (n = 22 per group) using a computerized randomization method. Participants included diagnosed cases of type 2 diabetes mellitus aged between 50 and 75 years, with a disease duration of at least seven years and confirmed diabetic peripheral neuropathy. Neuropathy confirmation was performed using the Diabetic Neuropathy Symptom (DNS) score and Diabetic Neuropathy Examination (DNE) score prior to enrollment. Individuals with a history of lower-limb amputation, coexisting neurological or musculoskeletal disorders, implanted medical devices such as pacemakers, metallic implants, or a history of major surgery were excluded to minimize confounding influences and ensure participant safety.

All enrolled participants received routine physical therapy consisting of stationary cycling and progressive resistance exercises targeting major lower-limb muscle groups. These exercises were performed three times per week throughout the eight-week intervention period. Group A additionally received therapeutic ultrasound using a continuous mode at a frequency of 1 MHz for a duration of 20–25 minutes per session. Group B received high-intensity laser therapy with a wavelength of 905 nm for 15–20 minutes per session, followed by the same routine physical therapy protocol. Both interventions were administered three times weekly, resulting in a total of 24 treatment sessions per participant. The study followed a single-blinded design in which participants were blinded to group allocation, while the treating therapists were aware of the intervention being delivered. Outcome assessment focused on the severity of diabetic peripheral neuropathy and was performed using the Michigan Neuropathy Screening Instrument, a validated and widely used tool that combines a self-reported symptom questionnaire with a structured clinical examination. Data were collected at baseline and after completion of the eight-week intervention period. Statistical analysis was carried out using SPSS version 24 for Windows. Data normality was assessed using the Shapiro–Wilk test, which confirmed a normal distribution and justified the use of parametric statistical methods. Descriptive statistics were used to summarize participant characteristics and outcome measures. Within-group comparisons were analyzed using paired sample t-tests, while independent sample t-tests were applied to compare post-intervention outcomes between the two groups. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 41 participants completed the study, with 21 individuals in the therapeutic ultrasound plus routine physiotherapy group and 20 individuals in the high-intensity laser therapy plus routine physiotherapy group. The mean age of participants was comparable between groups, measured at 63.52 ± 6.72 years in the therapeutic ultrasound group and 63.40 ± 7.14 years in the high-intensity laser therapy group. Mean body weight was 73.71 ± 12.96 kg in the therapeutic ultrasound group and 82.90 ± 12.88 kg in the high-intensity laser therapy group, while mean height was 161.28 ± 12.95 cm and 163.10 ± 11.88 cm, respectively. Gender distribution showed a predominance of female participants in the therapeutic ultrasound group (57.1%) and a slightly higher proportion of male participants in the high-intensity laser therapy group (55.0%). Baseline demographic characteristics were generally comparable across groups. At baseline, no statistically significant difference was observed between the two groups in Michigan Neuropathy Screening Instrument scores, with mean values of 4.71 ± 1.10 in the therapeutic ultrasound group and 4.95 ± 1.31 in the high-intensity laser therapy group ($p = 0.53$). Following the intervention period, a statistically significant between-group difference was observed, with post-intervention scores of 5.85 ± 1.49 in the therapeutic ultrasound group and 9.10 ± 1.71 in the high-intensity laser therapy group ($p < 0.001$). Within-group analysis demonstrated significant changes from baseline in both groups, with a mean change of −1.14 in the therapeutic ultrasound

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group and −4.15 in the high-intensity laser therapy group ($p < 0.001$ for both). Functional outcomes assessed using the Foot and Ankle Disability Index showed no significant difference between groups at baseline, with mean scores of 43.42 ± 5.03 in the therapeutic ultrasound group and 43.10 ± 5.23 in the high-intensity laser therapy group ($p = 0.83$). Post-intervention scores increased to 55.52 ± 7.34 and 68.80 ± 8.37, respectively, demonstrating a statistically significant between-group difference in favor of the high-intensity laser therapy group ($p < 0.001$).

Within-group comparisons revealed significant improvements in both groups, with mean changes of −12.09 in the therapeutic ultrasound group and −25.70 in the high-intensity laser therapy group ($p < 0.001$). Muscle strength assessed using pressure biofeedback on the left side showed comparable baseline values between groups (43.94 ± 6.28 vs 43.15 ± 8.17; $p = 0.72$). Post-intervention measurements demonstrated higher strength gains in the high-intensity laser therapy group (66.75 ± 13.25) compared to the therapeutic ultrasound group (51.28 ± 6.85), with a statistically significant between-group difference ($p = 0.02$). Within-group analysis indicated significant improvements in both groups, with mean changes of −7.33 and −23.60, respectively ($p < 0.001$). Similarly, pressure biofeedback measurements on the right side showed no significant baseline difference between groups (51.71 ± 6.50 vs 52.20 ± 7.23; $p = 0.82$). Post-intervention scores increased to 69.71 ± 9.11 in the therapeutic ultrasound group and 81.25 ± 13.28 in the high-intensity laser therapy group, demonstrating a statistically significant between-group difference ($p < 0.001$). Within-group changes were significant in both groups, with mean differences of −18.00 and −29.05, respectively ($p < 0.001$).

Table 1: Descriptive statistics of demographics in both groups

Age in years			
Groups	N		Mean ± S.D
Therapeutic Ultrasound+ Routine Physiotherapy	21		63.52±6.72
High intensity laser therapy+ Routine Physiotherapy	20		63.40±7.14
Weight in KGs			
Therapeutic Ultrasound+ Routine Physiotherapy	21		73.71±12.96
High intensity laser therapy+ Routine Physiotherapy	20		82.90±12.88
Height in cm			
Therapeutic Ultrasound+ Routine Physiotherapy	21		161.28±12.95
High intensity laser therapy+ Routine Physiotherapy	20		163.10±11.88
Gender			
Therapeutic Ultrasound+ Routine Physiotherapy	Male	Frequency	Percentage
		9	42.9%
	Female	12	57.1%
High intensity laser therapy+ Routine Physiotherapy	Male	11	55.0%
	Female	9	45.0%

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Table 2: Michigan Neuropathy Screening Instrument Scores: Between- and Within-Group Comparisons

Variable	Group A (Therapeutic Ultrasound + Routine Physiotherapy)	Group B (High-Intensity Laser Therapy + Routine Physiotherapy)	Significance (Between Groups)
Pre-intervention score (Mean ± SD)	4.71 ± 1.10	4.95 ± 1.31	0.53
Post-intervention score (Mean ± SD)	5.85 ± 1.49	9.10 ± 1.71	0.00
Within-group change (Pre–Post)	−1.14	−4.15	—
Within-group significance (p-value)	0.00	0.00	—

Table 3: Between group studies of foot ankle and disability index

Variables	Group A	Group B	Sig.
Pre-intervention score	43.42±5.03	43.10±5.23	0.83
Post-intervention score	55.52± 7.34	68.80± 8.37	0.00

Table 4: within group studies of foot ankle and disability index

Within Group Change	Group A	Sig.
Pre-training	-12.09	0.00
Post-training		
	Group B	
	-25.70	.00

Table 5: Left-Side Muscle Strength Assessed by Pressure Biofeedback: Between- and Within-Group Comparisons

Variable	Group A (Therapeutic Ultrasound + Routine Physiotherapy)	Group B (High-Intensity Laser Therapy + Routine Physiotherapy)	Significance (Between Groups)
Pre-intervention score (Mean ± SD)	43.94 ± 6.28	43.15 ± 8.17	0.72
Post-intervention score (Mean ± SD)	51.28 ± 6.85	66.75 ± 13.25	0.02
Within-group change (Pre–Post)	−7.33	−23.60	—
Within-group significance (p-value)	0.00	0.00	—

Table 6: Between group studies of pressure biofeedback for strength on the right side

Variables	Group A	Group B	Sig.
Pre-intervention score	51.71±6.50	52.20±7.23	0.82
Post-intervention score	69.71±9.11	81.25±13.28	0.00

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Table 7: Within group studies of pressure biofeedback for strength on the right side

Within Group Change	Group A	Sig.
Pre-intervention	-18.00	0.00
Post-intervention		
	Group B	
	-29.05	.00

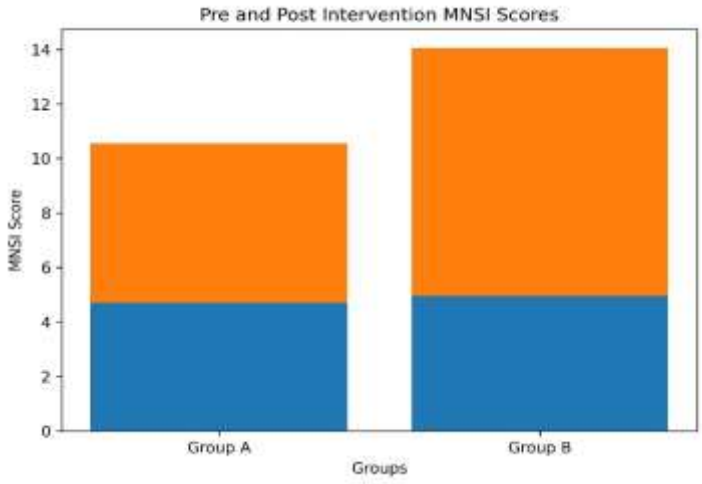

Figure 2 Pre and Post Intervention MNSI Scores

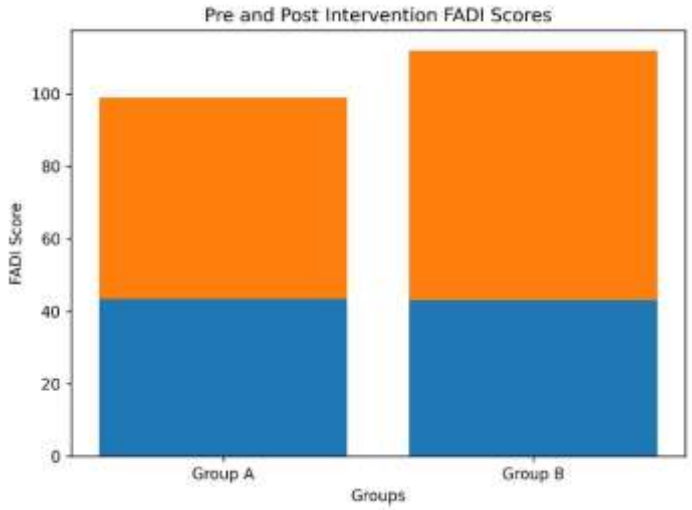

Figure 2 Pre and Post Intervention FADI Scores

DISCUSSION

The findings of this randomized clinical trial demonstrated that an eight-week intervention combining high-intensity laser therapy with routine physical therapy was effective in reducing the severity of diabetic neuropathic symptoms, improving lower-limb muscle strength, and enhancing functional status in individuals with diabetic foot involvement. Although both intervention approaches produced statistically significant improvements within groups, the magnitude of change was consistently greater in the group receiving high-intensity laser therapy alongside conventional physiotherapy. These results suggest that adjunctive physical modalities can meaningfully augment standard rehabilitation strategies in the management of diabetic peripheral neuropathy. The observed superiority of high-intensity laser therapy in reducing neuropathic symptom burden aligns with prior clinical investigations that have reported enhanced pain relief and functional recovery when laser-based modalities were integrated with conventional physiotherapy for neuropathic and musculoskeletal pain conditions (18). The present findings extend this evidence by specifically addressing diabetic neuropathic pain, a population in which therapeutic options are often limited by comorbidities and medication-related adverse effects. In contrast, some earlier studies have reported comparable efficacy between therapeutic ultrasound and high-intensity laser therapy when used as adjuncts to routine care. Variability in outcomes across studies may be attributable to differences in participant characteristics, disease duration, severity of neuropathy, treatment dosimetry, and outcome measures employed, all of which are known to influence treatment responsiveness (19).

Differences in laser parameters represent an important consideration when interpreting the present findings. Existing literature indicates substantial heterogeneity in the application of high-intensity laser therapy, including variation in wavelength, energy density, pulse frequency, session duration, and total delivered energy. Previous studies have reported wavelengths around 750 nm with total energy

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delivery ranging from 1250 to 3000 joules per session, whereas the present trial utilized a wavelength of 905 nm with a total energy delivery of approximately 125 joules per session (20). Despite the lower energy dosage, clinically meaningful improvements were observed, suggesting that therapeutic effects may not be solely dose-dependent but may also relate to tissue-specific absorption, depth of penetration, and cumulative neuromodulatory effects over repeated sessions. The beneficial effects observed in muscle strength and functional outcomes further support the role of high-intensity laser therapy in neuromuscular rehabilitation. Laser-induced photobiomodulation has been proposed to enhance mitochondrial activity, improve microcirculation, and reduce inflammatory mediators, mechanisms that may collectively contribute to improved neuromuscular performance and reduced pain perception. While much of the existing evidence has focused on musculoskeletal pain conditions, such as cervical or lumbar disorders, the present study adds to the growing body of evidence suggesting that similar mechanisms may be relevant in neuropathic pain states associated with diabetes (21).

Several strengths of this study merit consideration. The randomized design, use of validated outcome measures, and standardized intervention protocols enhance internal validity. The inclusion of both symptom-based and functional assessments allowed for a more comprehensive evaluation of treatment effects. However, certain limitations should also be acknowledged. The use of non-probability convenience sampling and a single-center design may limit generalizability. The relatively small sample size and single-blinded methodology may increase the risk of bias, and the absence of long-term follow-up restricts conclusions regarding the durability of treatment effects. Additionally, biochemical markers of neuropathy and objective electrophysiological assessments were not included, which could have provided further insight into underlying neural changes. Future research should consider larger, multicenter trials with double-blinded designs and longer follow-up periods to confirm and extend these findings. Standardization of laser therapy parameters would facilitate comparison across studies and aid in establishing optimal treatment protocols (22). Incorporating patient-reported quality of life measures alongside objective neurophysiological outcomes may further clarify the clinical relevance of high-intensity laser therapy in diabetic peripheral neuropathy. Collectively, the present findings support the potential role of high-intensity laser therapy as a valuable adjunct to conventional physiotherapy in the multidisciplinary management of diabetic neuropathic pain, while underscoring the need for continued investigation to refine and optimize its clinical application.

CONCLUSION

This study concludes that both therapeutic ultrasound and high-intensity laser therapy, when combined with routine physical therapy, are effective interventions for managing diabetic foot–related neuropathic complications. However, high-intensity laser therapy demonstrated a more pronounced clinical benefit, particularly in alleviating neuropathic pain, enhancing lower-limb strength, and improving overall quality of life. These findings highlight the practical value of integrating advanced electro-physical modalities into conventional rehabilitation programs for individuals with diabetic peripheral neuropathy and support high-intensity laser therapy as a promising adjunctive option in clinical practice aimed at improving functional outcomes and patient well-being.

AUTHOR CONTRIBUTIONS

Author	Contribution
Zara Tariq*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Siddra Yasir	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sonia Gul	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published

Author	Contribution
Javeria Sana	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Aqsa Rana	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Balaj Khan	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Elsa Junaid	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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