BMC Neuroscience

RESEARCH **Open Access**

Effects of multisystem exercises on balance, postural stability, mobility, walking speed, and pain in patients with diabetic peripheral neuropathy: a randomized controlled trial

Sidra Khurshid[1], Aruba Saeed[2*], Muhammad Kashif[1], Aniqa Nasreen[1] and Huma Riaz[1]

Abstract

Background Diabetic peripheral neuropathy (DPN), a common complication of diabetes mellitus, is associated with peripheral nerve damage, leading to balance impairments, postural instability, and reduced mobility. Addressing these challenges requires comprehensive interventions that target multiple deficits simultaneously. Evidence suggests that exercise programs combining balance, proprioception, strength, and reaction time training can improve postural stability, enhance mobility, and alleviate pain in individuals with DPN.

Objective The objective of this study was to compare the effects of multisystem exercises and conventional exercises on balance, postural stability, mobility, and walking speed and to reduce pain in patients with diabetic peripheral neuropathy.

Methods This double-blinded, two-arm parallel design randomized controlled trial was conducted at DHQ Hospital, Pakpattan, Pakistan. A total of 50 participants who met the inclusion criteria were recruited using the nonprobability convenience sampling technique. They were randomly assigned to either a multisystem physical exercise (MPE) group ($n = 26$) and a conventional exercise group ($n = 24$). The MPE program included balance, proprioception, strength, and reaction time training, while the control group received conventional exercises, consisted of strength, balance, stretching, and range of motion exercises. Both groups underwent 30 min intervention sessions, 3 times per week, for 8 weeks. The outcome measures used for assessing the balance, postural stability, mobility, and pain included the Berg balance scale (BBS), functional reach test (FRT), time up and go test (TUG), 10 min walk test (10-MWT), and numeric pain rating scale (NPRS). The data was analyzed using SPSS version 26.

Results Significant group and time interactions were observed for all outcome measures including BBS, FRT, TUG, 10-MWT, and NPRS ($p < 0.001$). The between-group analysis also revealed significant differences between the multisystem physical exercise group and the conventional exercise group at both the 4th week and 8th week for BBS, FRT, TUG, 10-MWT, and NPRS ($p < 0.05$).

*Correspondence:
Aruba Saeed
arubasaeedpt@gmail.com

Full list of author information is available at the end of the article

Conclusion The study concluded that multisystem exercises resulted in significant improvement in balance, postural stability, mobility, and walking speed, along with reduction in pain, compared to conventional exercises in patients with diabetic peripheral neuropathy.

Trial registration This randomized controlled study was registered prospectively on November 11th, 2023 with the ClinicalTrials.gov (NCT06130917).

Keywords Postural balance, Diabetic related neuropathy, Exercise therapy, Peripheral neuropathy, Proprioception

Introduction

Diabetic peripheral neuropathy (DPN) is a common complication of type 2 diabetes mellitus [1] and is a highly predominant condition that significantly impacts patients by increasing falls, altering sensation, and reducing quality of life [2, 3]. It manifests as peripheral nerve dysfunction in individuals with diabetes after other potential causes are ruled out [4, 5]. The increasing number of diabetes cases has emerged as a primary health concern in Pakistan [6]. According to the International Diabetes Federation (IDF) 2021, Pakistan has the highest global prevalence of diabetes at 26.3% [7], ranking third in the world in terms of the number of diabetes patients, followed by China (140 million) and India (74 million). In Pakistan, 1 in 4 adults are living with diabetes [8], which is a major contributor to peripheral neuropathy [9, 10]. The literature indicates substantial variation in the prevalence of peripheral neuropathy among people with diabetes in Pakistan, ranging from 16.30 to 79.50% [9, 11].

Approximately one-third of individuals with DPN experience painful sensations such as burning, tingling, shooting, or lancing (stabbing) [12]. These sensations, along with daytime discomfort, often hinder an individual's ability to carry out routine activities [13]. A study highlighted the substantial burden of painful DPN, revealing persistent discomfort despite the use of multiple medications and extensive resources, which results in limitations in daily activities and dissatisfaction with treatments [14–17].

Diabetic peripheral neuropathy significantly contributes to falls, and individuals with DPN show increased postural sway, especially those with closed eyes, due to proprioceptive impairment [18]. Basic protective reflexes and, simultaneously, coordinated movements of the joints, as well as balance and postural control is reduced with a decrease in DPN [19]. Muscle weakness, delayed response to postural adjustment, and the inability to distribute body weight evenly due to poor proprioception result in a balance problem [20]. Furthermore, reduced balance in people with diabetic neuropathy is another key element that leads to more falls and a decrease in quality of life [21]. Hence, addressing balance deficit through exercises in patients with diabetic peripheral neuropathies is essential to reduce the risk of falls and improve the quality of life [21, 22].

Physical exercise designed to improve balance, muscle force, reaction time, walking speed and similar measures has been recognized as a valuable therapeutic intervention for patients with diabetic peripheral neuropathy [23]. Exercise programs incorporating balance training have shown promising outcomes in improving balance and reducing the risk of falls in patients with DPN [23, 24]. Balance training stands out as a crucial tool in preventing falls and demonstrating notable enhancements across various aspects of postural control, balance, and gait [25]. Balance training engages multisensory systems (visual, vestibular, and proprioceptive) and promotes central nervous system adaptation, thereby improving the integration of sensory inputs essential for postural control [26]. Multiple studies have documented favourable results of balance exercises when performed independently and in conjunction with other interventions in individuals with neuropathy linked with diabetes [25, 27, 28]. Several studies have shown that engaging in strength training exercises can significantly improve muscular strength, contributing to better support for joints, improved mobility and functional abilities in individuals with DPN [29, 30]. Which is reported to be compromised in patients with DPN [31]. Strength training enhances muscle spindle sensitivity and neuromuscular coordination, potentially compensating for the diminished proprioceptive input caused by peripheral neuropathy [32].

Literature already supports that balance exercises with resistance training and other types of exercises leads to significant improvements in balance and functional outcomes for patients with DPN [28, 33]. As DPN has multifactorial nature of impairments like deficits in balance, proprioception, strength and reaction time [29, 30]. Engaging in a multisystem exercise program including balance, strength, proprioception and reaction time exercises designed to improve sensory integration, enhance muscle control, and promote anticipatory and reactive postural control [34]. Although the benefits of balance exercises, strength training, and proprioception exercises have been documented individually in this population, the combined effects of these interventions, particularly when including reaction time exercises, have not been thoroughly explored.

By incorporating combined exercise as a regular component of the treatment regimen for patients with diabetic peripheral neuropathy, may have the potential to mitigate the negative impact of DPN on balance, ultimately promoting greater functional independence and reducing the risk of falls [35, 36]. The choice of a comprehensive multisystem exercise program may lead to synergistic improvements in functional outcomes of patients with DPN. The program ensured that all components were complementary rather than competing. Each exercise targeted interrelated aspects of physical function, contributing collectively to improvements in balance, mobility, and pain reduction. The significant and consistent findings across all measured outcomes support the effectiveness of this integrated approach [35, 36]. By using a comprehensive approach this study aims to determine the effects of multisystem physical exercises for managing the effects of diabetic peripheral neuropathy.

It is hypothesised that a pronounced improvement in functional outcomes in patients with DPN may result with multisystem physical exercises, as all components of these exercises are complementary, and each exercise targeted interrelated aspects of physical function, contributing collectively to improvements in balance, mobility, and pain reduction.

Materials and methods

Design and settings

This double-blinded two-armed parallel design randomized controlled trial was conducted at the District Headquarters Hospital, Pakpattan, Pakistan, from November 2023 to April 2024. This study followed the CONSORT guidelines and was approved by the Riphah International University Research Ethical Review Committee (Riphah/REC/RCR&AHS/23/0242). Interventions aligned with the Helenski Declaration of Ethical Principles for Medical Research and Riphah International University Ethical Standard.

Study participants

Diabetic peripheral neuropathy patients of both genders, age 40–60 years, with a Michigan neuropathy scale score ≥ 7 and moderate balance impairment on the BBS (score 21–40) were included in this study. Those with a history of lower limb surgery in the last 3 months, amputations, Deep venous thrombosis, gangrene, neurological disorders affecting the vestibular systems and CNS, and orthostatic hypotension were excluded. Additionally, DPN patients participants in any other physical activity > 150 min per week were excluded. Informed written consent was obtained from all patients before participation in the study.

A nonprobability convenience sampling technique was used for sample selection to facilitate efficient recruitment while ensuring that sample met the predefined selection criteria. To mitigate the selection bias, random allocation was applied to evenly distribute the potential confounding factors into two intervention groups.

Sample size

The sample size included data from a previous study, which reported an effect size of 0.85 for the Berg balance scale [34]. By using G-Power software (Kiel University, DE), the ANOVA model from the F family test was selected, the level of significance (α) was fixed to 95%, and the study power was 95%. The calculated sample size to detect a statistically significant difference was 42 participants. To account for loss to follow-up, considering the attrition rate of 20%, 50 patients with diabetic peripheral neuropathies were recruited for this study.

Randomization and blinding

The randomization was conducted via the Online Research Randomizer tool (https://www.randomizer.org/). By specifying the group numbers, participants per group, and the total number of participants, unique identification numbers were generated for each participant across two groups. This method ensured a randomized and unbiased distribution of participants across the study groups. Out of total 50 participants, 25 were randomly assigned into a MPE and a control group, with 25 patients in each group. This was a double-blinded study in which the participants and the outcome assessors were blinded to the group allocation. The assessor was a qualified physical therapist with two years of clinical experience in patient assessment.

Interventions

There were two interventional groups in this study. Both the multisystem physical exercise group (MPE) and the conventional exercise group received treatment three days/week for 8 weeks.

Intervention for the Multisystem Physical Exercise (MPE) group

The MPE comprised of four types of exercises including reaction time exercise with auditory cues, proprioceptive, muscle strengthening and balance exercises [34]. These exercises were performed for 8 weeks, three sessions per week, with total of 24 sessions. The training sessions were of 40 min in duration and were supervised to ensure safe and correct execution by the physical therapist. The participants began by learning the four basic components. The program was structured into three levels starting from beginner to intermediate, and advanced levels. All participants started at the beginner level as they had similar baseline abilities, and progressed together through the intermediate and advanced levels. The exercises were designed to enable the participants to advance successfully through each stage. Each component included three sets of 10 repetitions, with a 10-second contraction hold and a 10-second rest interval between the sets. A physiotherapist with 5 years of experience in teaching exercises delivered the 8-week intervention. All exercises were explained below with a week-wise progression in Table 1.

Intervention for the conventional exercise group

Conventional treatment consists of four types of exercise: balance exercise, strength training, stretching, and ROM exercises. The exercise session lasted 40 min and was performed 3 times per week for 8 weeks in total.

Range of Motion (ROM) exercises It includes passive ROM exercises of the hip, knee, and ankle. Progresses to active ROM exercise of the hip, knee, and ankle.

Muscle strengthening It involves alternating double-knee lifts in a seated position with weights and modified chair stands. Progressed to exercises including sit-to-stand with support, knee stands with support and weight, squats to a chair with support, and supported steps back lunges. At the advanced level, the exercises include unsupported sit-to-stand, unsupported knee raises while standing and with weight, unsupported squats to a chair, and unsupported step-back lunges.

Balance It included supported weight shifts, calf and toe raises, heel raises, and crossover exercises on alternate legs in the seated position. Progresses involved heel-to-toe supported standing, side leg raises with support, unsupported heel raises, calf and toe raise without support, and crossover exercises without support. At an advanced level, the patients performed heel-to-toe stand without support, heel walk, toe walk, and 8-shaped walk [34].

Stretching exercises It includes stretching exercises for the hamstring, quadriceps, and calf muscles, beginning with a 15-second hold at the start, progressing to a 20-second hold, and advancing to a 30-second hold [37].

Outcome measures

Berg balance scale: balance

Balance was evaluated with the Berg balance scale [38] with high interrater reliability (0.98) and interrater reliability (0.99) [38, 39]. The participants were assessed for their ability to maintain balance during 14 common balance tasks, and their performance was observed and scored on a 5-point ordinal scale ranging from 0 to 4, where 0 represents an inability to complete the task entirely and 4 represents full completion of the task.

Functional reach test (postural control)

The functional reach test (FRT) is a commonly used clinical tool to assess an individual's stability and postural control [40]. It involves measuring how far a person can reach forward while maintaining a stable base of support in a standing position [41]. The patients were asked

Table 1 Multisystem physical exercise (MPE)

Level -I (Beginner)	Level -II (Intermediate)	Level-III Advanced
(Weeks 1 to 3)	**(Weeks 4 to 6)**	**Weeks (6 to 8)**
Proprioception	**Proprioception**	**Proprioception**
Performed seated ankle exercises on a ball, focusing on single-leg stance with hip flexion, using support as needed, and incorporating knee flexion and extension on the other leg. Performed single-leg stance with hip extension, with or without support, and integrated knee flexion and extension on the other leg.	Performed standing ankle exercises with a ball, maintaining a single-leg stance with hip flexion while keeping eyes closed, and practiced knee flexion and extension with support. Practiced the same with hip extension, support, and knee movements.	Progressed to unsupported standing ankle exercises, in single-leg stance position with hip flexion, and incorporating knee flexion and extension. Practiced single-leg stance with hip extension, without support, and included knee movements.
Muscle strengthening	**Muscle strengthening**	**Muscle strengthening**
Performed alternate double knee lifts along with weights, modified chair stand, alternate kicks with weights in the seated position, and hip extensions while standing with support and using weights.	Performed sit-to-stand with support, knee raises with support and weights, squats to a chair with support, and practiced lunges in step-back position with support.	Progressed to unsupported sit-to-stand exercises, unsupported knee raises and weights, unsupported squats to a chair, and unsupported lunges in a step-back position.
Balance	**Balance**	**Balance**
Performed alternate weight shifts, calf raises in the seated position, toe raises, and heel raises with support. Practiced crossover movements with support.	Perform supported heel-to-toe standing, supported side leg raises, unsupported heel raises, unsupported calf and toe raise, and unsupported crossover movements.	Progressed to heel-to-toe standing without support, heel walking, toe walking, and walking on a figure-8-shaped flex mat.
Reaction time	**Reaction time**	**Reaction time**
Performed alternate touching movements to the front, back, and side, as well as 3-step sequences (forward, side, backward) while seated.	Practiced step-up with support, performed step-forward, step-backward, and step-to-side movements with support, and 3-step sequences with support.	Progressed to stepping exercises without support, including forward, backward, and sideward steps, and 3-step sequences without support. (34)

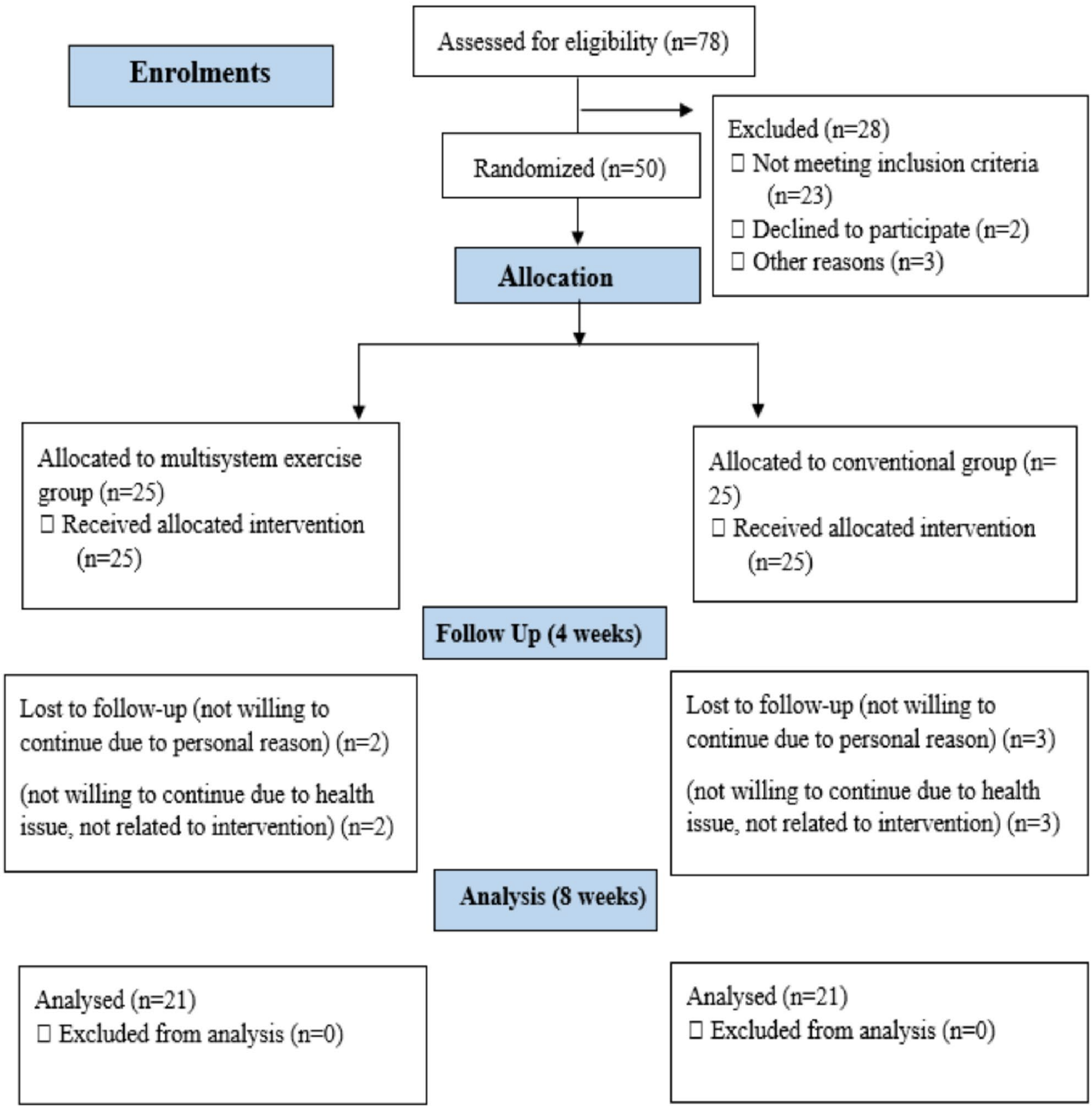

Fig. 1 CONSORT diagram

to extend their reach as far forward as possible without moving their feet. The distance reached was recorded. FRT exhibits high reliability, with an intraclass correlation coefficient ranging from 0.90–0.97 [42].

Time up and go test: (mobility)

This test is a valid tool for examining balance and functional mobility [43]. The participants were instructed to walk a distance of 3 m, turn around, walk back to the chair, and sit down while wearing their regular footwear. The time to complete the task was measured in seconds by using a stopwatch.

10 m walk test: walking speed

The 10-meter walk test is a performance measure used to assess walking speed over a 10-meter distance in seconds. The ICC for test-retest reliability (95% CI) is 0.712 [44].

Numeric pain rating scale: (pain)

The NRS is a reliable and valid tool [46] for assessing pain levels [45]. Subjects were instructed to rate their pain intensity from the feet and lower legs on a scale from 0 to 10, where 0 indicates no pain and 10 represents the worst pain imaginable. The participants were asked to verbally provide the numerical value that best represents their current level of pain.

Data analysis procedure

The data was analysed with IBM SPSS Statistics for Windows, version. 26 (IBM Corp., Armonk, NY, USA) software. The normality of the data was evaluated via the Shapiro−Wilk test and the data were normally distributed for all outcome measures. The within-subject factor comprised three levels (baseline, 3rd week, and 6th week), whereas the between-subject factors encompassed two independent groups (multisensory exercise group and conventional exercise group). Mixed model ANOVA tests were applied on all outcome measures with time (baseline, 3rd week, and 6th week) as the within-subject factor and group as the between-subject factor; one-way ANOVA was used for between-group comparisons at three different levels, and repeated measure ANOVA was used for determining within-group improvement.

Results

Baseline characteristics

A total of 78 patients were assessed for eligibility among whom 28 were excluded because they did not meet the inclusion criteria. The remaining 50 participants were allocated to multisensory exercise groups or conventional exercise groups. There were four dropouts from the multisensory exercise group and four in the conventional training group because of non-compliance. Analysis was performed on 42 DPN patients, with 21 patients in each group **(Fig. 1).** The demographic characteristics of the participants are presented in Table 2.

Table 2 Demographic characteristics of the participants

Characteristics		MPE group ($n=21$)	Conventional exercises group ($n=21$)	*P*-value
		Mean ± SD	**Mean ± SD**	
Age (years)		53.76 ± 4.63	54.61 ± 5.90	0.404
Michigan neuropathy scale		9.00 ± 1.63	8.30 ± 1.33	0.30
BBS		43.57 ± 1.56	42.57 ± 1.53	0.07
Duration of Diabetes (years)		7.63 ± 2.07	8.35 ± 1.52	0.200
		Number (%)	**Number (%)**	**Chi-Square**
Hypertension	**Yes**	14 (66.7%)	12 (57.1%)	0.107
	No	7 (33.3%)	9 (42.9%)	
Diabetic Medication	**Yes**	17 (81%)	18 (86%)	0.652
	No	4 (19%)	3 (14%)	
Gender	**Male**	8 (38.1%)	7 (33.3%)	0.500
	Female	13 (61.9%)	14 (66.7%)	
Marital Status	**Married**	21 (100%)	21 (100%)	1.000
	Unmarried	0 (0%)	0 (0%)	
Employment status	**Employed**	5 (23.8%)	4 (19%)	0.500
	Unemployed	16 (76.2%)	17 (81%)	

MPE; Multisystem physical exercise

Mixed ANOVA test (group and time interaction)

A significant time × group interaction was revealed for all the outcome variables. The experimental group's mean BBS score increased from 43.57 to 51.04, while the control group's score increased from 42.57 to 47.09 ($F = 288.79$, $p < 0.001$). The FRT of the experimental group improved to 13.18, whereas that of the control group was 10.78 ($F = 200.41$, $p < 0.001$). Compared with that of the control group, the TUG score of the experimental group improved to 10.07, whereas that of the control group was 12.23 ($F = 214.18$, $p < 0.001$). In the 10MWT, the experimental group improved to 1.12, whereas the control group increased to 0.75 ($F = 254.81$, $p < 0.001$). Finally, the NPRS score was 5.66 lower in the experimental group than in the control group ($F = 175.00$, $p < 0.001$). These results revealed significant differences between the groups across different time points in terms of balance, postural stability, mobility, walking speed, and pain, with the experimental group showing significant improvement in the MPE group compared with the conventional exercise group. (Table 3)

Repeated-measures ANOVA (between- and within-group differences)

The results revealed a significant improvement in the MPE and conventional exercise groups from baseline to the 8th week. A significant improvement in BBS was observed in the MPE and conventional exercise groups ($P < 0.001$). Similarly, significant improvements in postural control ($P < 0.001$), mobility ($P < 0.001$), walking speed ($P < 0.001$), and significant reductions in pain in the MPE and conventional exercise groups ($P < 0.001$) were observed in both groups. (Table 4).

One-way ANOVA (between-group differences)

While assessing between-group differences at different time points via ANOVA, no significant results were observed for balance, postural stability, or mobility. Walking speed and pain at baseline were significantly different at the 4th week ($P = 0.03$) and 8th week ($P < 0.001$), with greater improvement in the MPE group; however, postural stability at the 4th week ($P = 0.02$) and 8th week ($P < 0.001$), with greater improvement in the MPE group; mobility at the 4th week ($P = 0.04$) and 8th week ($P < 0.001$), with more pronounced improvement in the MPE group; and walking speed at the 4th week ($P = 0.03$)

Table 3 Group and time interaction (mixed ANOVA)

Outcome Measure	Outcomes	MPE Group			Conventional Exercises Group			F Value	*p*-value	η^2
		Mean ± SD			Mean ± SD					
		Baseline	At 4th Week	At 8th weeks	Baseline	At 4th Week	At 8th week			
BBS	Balance	43.57 ± 1.56	45.42 ± 1.46	51.04 ± 1.59	42.57 ± 1.53	44.52 ± 1.56	47.09 ± 1.99	288.79	< 0.001***	0.88
FRT	Postural stability	9.42 ± 1.18	10.48 ± 1.13	13.18 ± 0.76	9.38 ± 0.93	10.07 ± 0.77	10.78 ± 0.77	200.41	< 0.001***	0.83
TUG	Mobility	15.19 ± 1.50	12.71 ± 1.34	10.07 ± 0.88	15.66 ± 2.15	14.04 ± 1.90	12.23 ± 1.70	214.18	< 0.001***	0.84
10MWT	Gait speed	0.65 ± 0.04	0.05 ± 0.01	1.12 ± 0.11	0.64 ± 0.04	0.69 ± 0.04	0.75 ± 0.04	254.81	< 0.001***	0.86
NPRS	Pain	8.04 ± 0.92	7.00 ± 0.94	5.66 ± 0.91	8.28 ± 1.00	7.42 ± 1.07	6.66 ± 0.97	175	< 0.001***	0.81

BBS = Berg balance scale, FRT = functional reach test, TUG = time up and go, 10MWT = 10-meter walk test, NPRS = numeric pain rating scale Significance level **=P < 0.001

Table 4 Between- and within-group differences (one-way & repeated-measures ANOVA)

Outcome measures	Outcomes	Assessment	MPE Group	Conventional exercise group	F value	*P* value
			Mean ± SD	Mean ± SD		
BBS	Balance	**Baseline**	43.57 ± 1.56	42.57 ± 1.53	17.45	0.07
		4th week	45.42 ± 1.46	44.52 ± 1.56	20.22	0.03
		8th week	51.04 ± 1.59	47.09 ± 1.99	22.88	< 0.001***
		Within group *p*-value	< 0.001***	< 0.001***		
FRT	Postural stability	**Baseline**	9.42 ± 1.18	9.38 ± 0.93	10.98	0.06
		4th week	10.48 ± 1.13	10.07 ± 0.77	12.03	0.02
		8th week	13.18 ± 0.76	10.78 ± 0.77	14.52	< 0.001***
		Within group *p*-value	< 0.001***	< 0.001***		
TUG	Mobility	**Baseline**	15.19 ± 1.50	15.66 ± 2.15	8.8	0.05
		4th week	12.71 ± 1.34	14.04 ± 1.90	7.89	0.04
		8th week	10.07 ± 0.88	12.23 ± 1.70	8.89	< 0.001***
		Within group *p*-value	< 0.001***	< 0.001***		
10MWT	Walking Speed	**Baseline**	0.65 ± 0.04	0.64 ± 0.04	129.9	0.06
		4th week	0.05 ± 0.01	0.69 ± 0.04	231	0.03
		8th week	1.12 ± 0.11	0.75 ± 0.04	155.26	< 0.001***
		Within group *p*-value	< 0.001***	< 0.001***		
NPRS	Pain	**Baseline**	8.04 ± 0.92	8.28 ± 1.00	2.03	0.05
		4th week	7.00 ± 0.94	7.42 ± 1.07	4.83	0.02
		8th week	5.66 ± 0.91	6.66 ± 0.97	3.91	< 0.001***
		Within group *p*-value	< 0.001***	< 0.001***		

BBS = Berg balance scale, FRT = functional reach test, TUG = time up and go, 10MWT = 10-meter walk test, NPRS = numeric pain rating scale

Significance level ***=P < 0.001

and 8th week ($P < 0.001$), with distinct enhancement in the MPE group; and pain at the 4th week ($P = 0.02$) and 8th week ($P < 0.001$), with a marked reduction in the MPE group (Table 4).

Discussion

In this study, a multisystem exercise program implemented a carefully designed exercise protocol, incorporating strength training, reaction time, proprioceptive training, and balance training. The results revealed that there was a statistically significant difference in the improvement of balance, postural stability, mobility, walking speed, and pain in patients with diabetic peripheral neuropathy following multisystem exercise compared with conventional exercise.

Balance exercises improves postural stability, and strengthening exercises increase the muscle endurance and mass, both of these reduce the strain on the musculoskeletal system and improve overall stability [46]. Additionally, proprioceptive and reaction time exercises are useful to enhance the the speed of sensory feedback and motor responses needed for maintaining balance and postural control [46, 47]. These exercises are considered to facilitate sensory re-education and result in faster reflex activity in DPN patients, which enables them to walk more efficiently [47].

In the present study, multisystem exercise programs, which include balance training, proprioception exercises, reaction time, and strength exercises, provide comprehensive interventions and allow balance and functional mobility improvement, not only in walking speed but also in balance, postural stability, mobility, and pain reduction. The results of this study are supported by a study focused primarily on proprioceptive and balance exercises, resulting in improved walking speed and sensitivity in patients with DPN [48–50]. Another study explored the effects of a 16-week exercise-training program, on balance, stretching, strengthening, and locomotion [51], and reported a reduction in postural sway and improved performance in the timed up-and-go (TUG) test [51]. The current study, with its multisystem approach, revealed significant improvements not only in balance and postural stability but also in functional reach, walking speed, and pain reduction. The diversity of exercises in our protocol contributes to a more comprehensive enhancement of various functional mobility outcomes. Another study conducted in South Africa specifically targeted ankle mobility, balance, and muscle strength [52] and revealed significant improvements in all parameters of the lower extremities [52]. Another study reported the similar findings [28]. These findings are consistent with the findings of the current study that the multisystem exercise program resulted in improvements across various measures, revealing a more comprehensive impact on functional outcomes.

Additionally, a study conducted by Kavita Venkataraman et al.'s RCT focused on a 2-month organized strength and balance training. This study concluded a notable enhancement in functional tests, knee range, ankle muscle strength, and balance [30]. The finding of the current study aligns with the previous study findings, which revealed that multisystem exercises have positive effects on a broader range of outcomes, including balance, postural stability, mobility, walking speed, and pain reduction. Additionally, another study conducted by Irshad et al. (2020) investigated the impact of sensorimotor and gait training on proprioception, nerve function, and muscle activation and had similar findings [53]. The multisystem exercises may have improved neuromuscular coordination and reduced mechanical strain on affected structures, leading to pain relief. Additionally, regular physical activity is known to stimulate the release of endogenous endorphins and enhance overall blood circulation, potentially alleviating pain [54]. These indirect effects of exercise might explain the observed changes in pain scores, even though pain was not the primary focus of the interventions.

A review highlighted the positive effects of different physical exercises on foot sensation in type 2 diabetes patients with peripheral neuropathy [55]. Their focus was broader, covering aerobic exercise, resistance exercise, balance exercise, and flexibility exercise [55]. The results of this study align with the overall findings, emphasizing the effectiveness of targeted exercise programs. Similarly, the current study demonstrated improved outcomes in balance, postural stability, and gait in the MPE group, aligning with their emphasis on sensorimotor aspects. The multisystem approach in our study complements their findings, suggesting that diverse exercises can positively affect various dimensions of neuropathy.

In summary, while previous studies have offered valuable insights into different interventions individually, this study uniquely emphasizes the effectiveness of multisystem exercises, providing comprehensive evidence of their benefits in improving various aspects of DPN. By incorporating reaction time and proprioceptive exercises alongside balance and strengthening exercises, this study adds to the existing knowledge base and highlights the significant impact of tailored multisystem exercises on functional outcomes. The consistently positive results across diverse measures demonstrate that integrating these innovative multisystem exercises can offer multiple benefits in healthcare and rehabilitation settings, leading to improvement in functional outcomes, pain reduction, and overall quality of life enhancement in patients with DPN.

This research has the following limitations. First, the sampling approach used in the study may limit the generalizability of the findings to other regions or populations within Pakistan where variations in disease severity, comorbidities, or access to healthcare may exist. Second, the lack of objective tools for assessing balance, proprioception and postural stability. Moreover, the 8-week treatment duration of research was too short, which may not fully capture long-term effects; extending the follow-up period could provide more comprehensive insights into the intervention's benefits Third, the sample was not homogenous with respect to their initial fitness level as it was not assessed. insights into the sustained impacts of observed improvements such as additional neuromuscular adaptation, enhanced proprioceptive integration, and even greater physical conditioning.

Future studies with larger, multi-center samples, involving probability sampling technique reflecting the broader demographic and clinical diversity of DPN patients in Pakistan could strengthen the applicability of these results to the national context. Use of advanced objective tools to assess balance, proprioception and reaction time will provide a detailed understanding of balance and postural control improvements with the MPE program.

Conclusion

This study concluded that multisystem exercises improve balance, postural stability, mobility, walking speed, and reduce the pain as compared to conventional exercises in patients with DPN.

This study suggests the potential benefits of incorporating proprioception, muscle strengthening, balance, and reaction time exercises into the treatment plans of patients with DPN. These interventions could be effectively used in clinical and rehabilitation settings to enhance functional outcomes, improve quality of life, and reduce the risk of falls in this population.

Abbreviations

DPN	Diabetic Peripheral Neuropathy
DM	Diabetes Mellitus
MPE	Multisystem Physical Exercise
FRT	Functional Reach Test
TUG	Time Up and Go Test
BBS	Berg Balance Scale
10MWT	10 Meter Walk Test
QOL	Quality of Life
FST	Functional Strength Training
NPRS	Numeric Pain Rating Scale
ADLs	Activities of daily living
PEG	Proprioception exercise group

Acknowledgements
The authors would like to express gratitude to the participants in this study for their cooperation and valuable contributions. Special thanks to the ethical review board of RCRAHS for providing approval and DHQ Pakpattan for permission to collect the data.

Author contributions
AS: conceptualization, AS, SK: formal analysis. SK, AN: investigation. AS, MK: methodology. SK, AN: project administration. AS, MK, HR: resources. SK, AN: writing—original draft preparation. AS, MK, HR: critical review and editing. All authors participated in the interpretation of the data and in the editing, critical revision, and approval of the final manuscript and were accountable for accuracy of work.

Funding
None to declare.

Data availability
Data used in this study will be made available upon reasonable demand.

Declarations

Ethics approval and consent to participate
The study protocols were approved by the Research Ethics Committee of Riphah International University Lahore Ref no: REC/RCR& AHS/23/0242. All participants provided informed consent to participate in the study. The trial was registered prospectively with registration number NCT06130917, registered on 9 November 2023. The trial started on November 5, 2023, and was completed on April 10, 2024 is available at https://clinicaltrials.gov/study/NCT06130917.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Riphah College of Rehabilitation and Allied Health Sciences, Riphah International University, Lahore Campus, Islamabad, Pakistan
[2]Faculty of Rehabilitation Sciences, Lahore University of Biological and Applied Sciences, Lahore, Pakistan

Received: 31 August 2024 / Accepted: 31 December 2024
Published online: 27 February 2025

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