Research Article
ISSN (Print): 0971-913X
ISSN (Online): 2455-1244
J Endocrinol Reprod. *Vol 28(3), 203-213, September 2024, DOI: 10.18311/jer/2024/45389*

Effect of Structured Exercise Program and Pain Neuroscience Education on Glycated Haemoglobin in Type 2 Diabetes with Painful Diabetic Neuropathy: A Pilot Randomised Controlled Trial

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Abstract

Aims: To describe the sequential development of a structured exercise program for painful diabetic neuropathy in Type 2 diabetes and to determine the effect of structured exercise on neuropathic pain, nerve function, and glycosylated haemoglobin in Type 2 diabetes individuals with painful diabetic peripheral neuropathy. **Methods:** The development of the exercise regimen was supported by evidence-based research, which included a thorough evaluation of the literature, expert advice, and the most recent standard exercise recommendations for people with Type 2 Diabetes. Twenty sedentary diabetics were divided into experimental and control groups, with ten subjects in each group. At baseline and after 12 weeks, the following measures were taken: HbA1c, Pain Catastrophizing Score, Tampa Scale of Kinesiophobia Score, and Visual Analog Scale. **Results:** The baseline VAS scores for the control and experimental groups were 7.5±0.05 and 7.54±0.843, respectively, with corresponding mean and standard deviations of 8.19±1.05 and 9.53±0.68 for HbA1c. Following twelve weeks, the control and experimental groups' mean VAS ratings were 6.40±0.516, 3.30±0.676, and HbA1c were 8.15±1.04 and 6.99±0.199, respectively. **Conclusion:** The developed exercise program is found to be effective in improving glycosylated haemoglobin and should further be evaluated using large randomised clinical trials.

Keywords: Comprehensive Structured Exercise Program, Glycosylated Haemoglobin, Neuropathic Pain, Pilot Study, Type 2 Diabetes, Visual Analog Scale

Highlights

- There is still a lack of consensus regarding exercise prescription guidelines for Type 2 diabetes with painful diabetic neuropathy.
- The developed comprehensive structured exercise program was found to be effective in reducing HbA1c significantly.
- Other possible mechanisms of exercise for relieving neuropathic pain need to be explored.

Abbreviations: MHR: Maximum Heart Rate, RM: Repetition Maximum, FITT: Frequency, Intensity, Type, Time, P: Progression, HR max: Maximum Heart rate, ADA: American Diabetes Association, ACSM: American College of Sports Medicine, SD: Standard deviation, miR: microRNA, CSEP: Comprehensive Structured Exercise Program, VAS: Visual Analog Scale, CSEP: Comprehensive Structured Exercise Program; SR: Systematic review; MA: Meta-analysis; RCT: Randomised controlled trial; HbA1c: Glycosylated haemoglobin, CSEP: Comprehensive Structured Exercise Program

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Article Received: 11.08.2024 Revised on: 23.03.2025 Accepted on: 09.05.2025

1. Introduction

Diabetes is the most debilitating chronic metabolic disease, where about 828 million adults have diabetes worldwide, with age-standardised gender prevalence of 13.9% in females and 14.3% in males[1]. Further, India occupies first place in diabetes prevalence, with 212 million adults population, affecting individuals' function and quality of life[1]. The total number of people living with diabetes in urban areas is expected to rise from 360.0 million to 596.5 million by 2045[2]. According to IDF 2021 global estimates, approximately one in two adults, i.e., 239.7 million people (44.7%), between the age group of 20–79 years with diabetes were unaware of their diabetes status[3]. Not only this, India ranks second with 39.4 million people undiagnosed with diabetes mellitus[3]. In India, according to estimates based on the National Survey on people aged 18 to 69, the prevalence of diabetes and impaired glucose tolerance is 9.3% and 24.5%, respectively[4]. Diabetic neuropathy is a type of microvascular complication with a prevalence of 51% when evaluated objectively using the Michigan Neuropathy Screening Instrument (MNSI) in India[5]. The most common form of peripheral neuropathy is distal symmetric polyneuropathy, usually involving both small and large diameter nervefibres[6]. Often, the patients become symptomatic after experiencing many years of poorly controlled diabetes, whereas on the contrary, it may also develop in a short time after the diagnosis of Type 2 diabetes if increased blood glucose levels were undetected for years before confirmed diagnosis by the physician[6].

Diabetic neuropathy is characterised by tingling, numbness, altered sensation, hyperalgesia symptoms like burning pain, throbbing pain, cramping pain, electric shock-like sensation, or allodynia[7]. Painful diabetic neuropathy imposes a tremendous challenge to the healthcare system, affecting an individual's quality of life with the continuous growth in the prevalence of diabetes[8]. Of these, 10-26% of the diabetics present with symptoms such as neuropathic pain and decreased sensory input, leading to hindrance in activities of daily living, have shown involvement of both central and peripheral mechanisms[9]. Such sensory information processing helps to protect the tissues, provide position sense and proprioception, which, when disrupted, can cause profound physical consequences and may lead to loss of balance and postural control, increasing the risk of falls[10].

Exercise and physical activity per se are proven to be very helpful for individuals with painful diabetic neuropathy[11]. The physiological benefits demonstrate widespread effects on all the systems in the body, including cardiovascular, respiratory, endocrine, musculoskeletal, and neurological systems[12]. Exercise is shown to augment sensory input in the lower limb and may help prevent the progression of peripheral neuropathy and reduce the risk and fear of falls[11].

Maintaining good glycaemic control is the mainstay for the prevention of diabetes complications[13]. Therefore, effective therapeutic strategies are needed to manage problems in people with diabetes with active participation in society, and provide support for better self-management and self-care. Exercise, along with dietary management, is considered one of the best, cost-effective, feasible, and conservative treatment options in the management of painful diabetic neuropathy[14]. Pain Neuroscience Education (PNE) has emerged as a teaching strategy to alter a patient's understanding of pain and diminish its threat by using simple metaphors, examples, and images to explain these intricate biological processes to patients. However, PNE by itself produces beneficial effects in reducing fear of movement and pain catastrophizing that are clinically significant, and hence recommended to be used as an adjunct to physiotherapy[15].

To be able to provide a simple, safe, easy, and feasible exercise program for painful diabetic neuropathy, it is crucial to develop, describe, and test the efficacy of a comprehensive, structured exercise prescription in this group of diabetic patients with neuropathic pain. Literature suggests integration of psychological intervention along with exercise programs in the management of painful diabetic neuropathy. The present pilot RCT evaluates the feasibility of a structured exercise program and psychological approaches like pain neuroscience education on glycosylated haemoglobin and psychosocial variables in painful diabetic neuropathy.

2. Methodology

2.1 Development of CSEP

The development of a comprehensive, structured exercise program was based on synthesised evidence from three important sources,

(i) Evidence from the research literature review–January 2011-2023

(ii) Professional clinical expertise/ experts' opinion
(iii) Clients' progress/patient satisfaction

This study addresses the research question in the framework of 5 steps

Step 1: Initially, a systematic review and meta-analysis were performed to understand the different exercise protocols followed for neuropathic pain in diabetic peripheral neuropathy. The standard exercise guidelines used are those of the American College of Sports Medicine (ACSM), the American Diabetes Association (ADA), and the American Heart Association (AHA) for Type 2 diabetes. Moreover, strength and balance exercises were recommended by ACSM and ADA in a joint consensus for neuropathy[16]. However, there was no defined specific exercise prescription for painful diabetic neuropathy, and there is a need to develop an exercise program for a 12-week duration. A detailed review process description is explained and published elsewhere[17].

Step 2: The research literature on exercise prescription for painful diabetic neuropathy is limited. Hence, a survey was conducted to obtain expert recommendations on the ideal exercise program for painful diabetic neuropathy. A 35-item questionnaire was validated and circulated to diabetes researchers and clinicians worldwide to get expert opinion on exercise prescription for painful diabetic neuropathy. Experts recommended the Michigan neuropathy screening instrument as the commonly used assessment tool for diabetic peripheral neuropathy. Further, an aerobic exercise of 150 min/week for 3-5 times per week was suggested, at an intensity of 50-80% maximum heart rate for 8 to 12 weeks. The maximum heart rate is calculated by 220 minus age and is tailored for each individual. Resistance exercise intensity to be 50-60% of 1 Repetition Maximum (RM) with at least 8-10 exercise for 10-15 repetitions and at least eight balance exercises for 12 weeks along with 2 to 4 flexibility exercises with each stretch for 2-4 repetitions, held for 10-30 s. Overall, 12 weeks was considered as the optimum duration for the exercise program by the experts in the present survey and from the literature review[18,19].

Step 3: Based on the results of the systematic review with meta-analysis and experts' recommendations from the survey, a comprehensive structured exercise prescription for painful diabetic neuropathy was developed and included in the patient's education manual. The results of the survey and content validation are published elsewhere[19].

Step 4: The barriers and facilitators were identified among Type 2 diabetes individuals with the help of the Exercise Benefits and Barriers Scale and were also screened for symptoms of diabetic neuropathy using the MNSI subjective tool.

Step 5: The developed structured exercise program was then implemented in Type 2 diabetes individuals diagnosed with painful diabetic neuropathy in a pilot study. An exercise activity log sheet was given to improve the adherence rate.

Step 6: The efficacy of the exercise program is being recently investigated in a randomised controlled trial (CTRI/2022/02/039990).

The flow chart of CSEP development is explained in Figure 1.

The brief description of the exercise program from the patient education manual and exercise log sheet (checklist) can be found in supplementary material S1. The exercise program is designed for 12 weeks with an alteration in parameters every four weeks.

Research Questions

- A pilot study was conducted to answer the following questions
- What is the type of study design, methodology, and statistical procedures that will be used in the subsequent randomised controlled trial?
- What novel information is required?
- To elucidate the development of structured exercise prescription for painful diabetic neuropathy.
- What is the feasibility and effectiveness of the newly developed exercise program?
- Any modifications to be made to the exercise program?
- Any precautions to follow while implementing the exercise program for patient safety?

2.2 Participants and Outcomes

This experimental study was conducted for a period of nine months from February 2022 to October 2022 in the Apollo College of Physiotherapy, Physical Medicine and Rehabilitation Department, Apollo Hospitals, Hyderabad, Telangana, India. Ethical committee approval was taken from Apollo Institute of Medical Sciences and Research (AIMSR) (EC no. EC/AIMSR/1527/2021/08/010), Hyderabad. Informed consent was taken from all the participants included in the study. The study included 20 participants with ten in control and ten subjects in the experimental

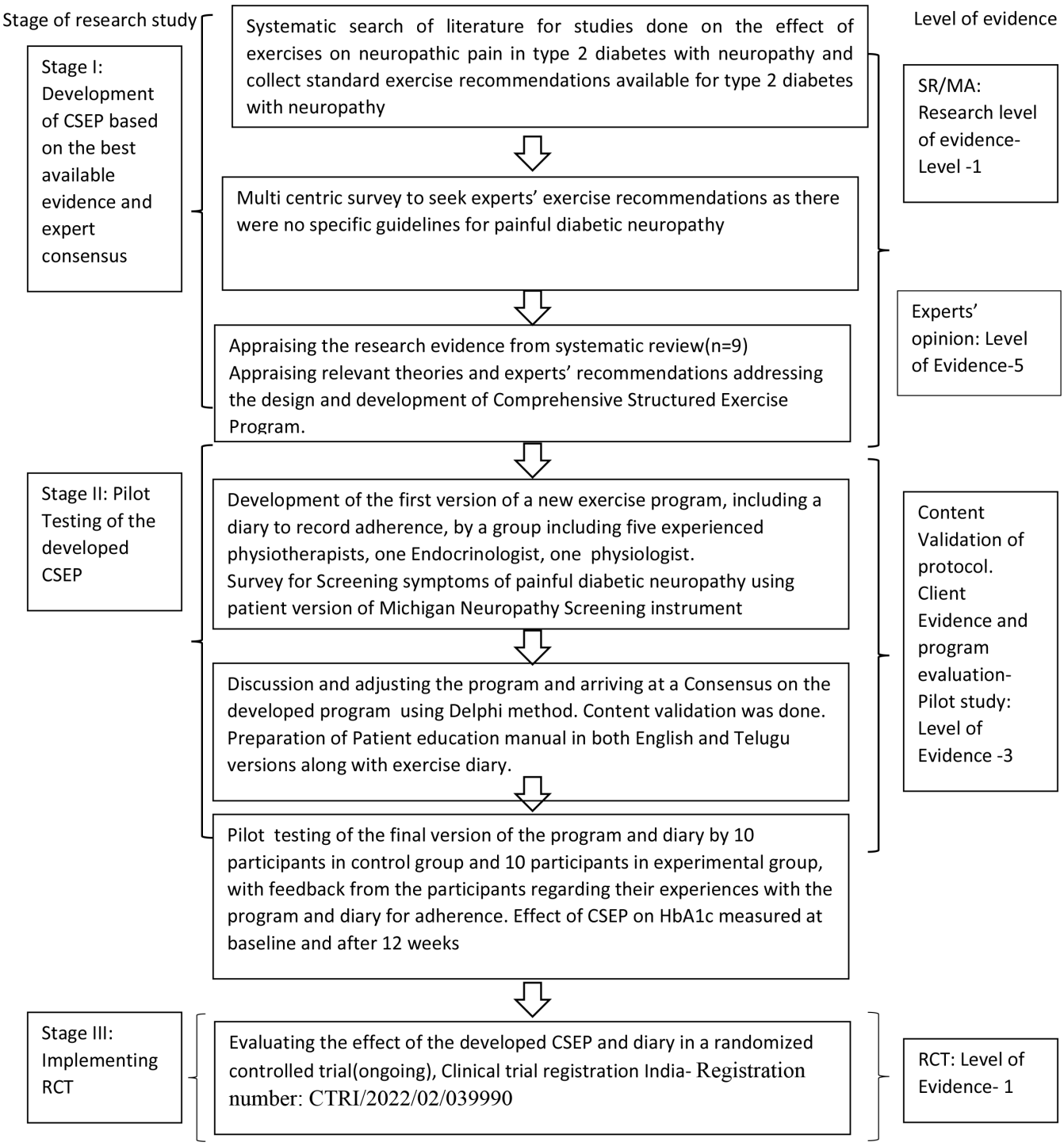


Figure 1: Flow chart explaining the process of development of Comprehensive Structured Exercise Program for Painful Diabetic Neuropathy in Type 2 Diabetes and testing its efficacy for Evidence based practice

group, aged between 30-70 years, both males and females, who had Type 2 diabetes with painful diabetic peripheral neuropathy, neuropathy severity ≥7 on MNSI symptom score and ≥2 on MNSI clinical examination score, symmetric neuropathy, Average Vibration Perception Threshold (VPT) ≥15 as recorded by biothesiometer, a validated portable device to measure severity and prognosis of peripheral neuropathy, Neuropathic pain measured with Visual Analog Scale (VAS) ≥5, Glycosylated haemoglobin (HbA1c) ≥6.5 were taken into the study. Subjects were recruited using a

purposive sampling method and consisted of patients on oral antidiabetic medications with or without insulin therapy. Glycosylated haemoglobin was analysed in the hospital laboratory using high performance liquid chromatography method. The exclusion criteria were participants with Type 1 diabetes, history of cardio-respiratory problems, pregnancy, or musculoskeletal problems interfering with the exercise program. The study objectives were explained, and informed consent was obtained. A Pre-participation Readiness Questionnaire (PARQ) was used to assess the risk level, and risk stratification was performed before recruitment into the study. The evaluator analysing the blood samples was blinded and was not aware of the group being analysed at baseline and the end of 12 weeks. The patient flow process was explained in Figure 2.

Before enrollment, each participant was explained the purpose of the study and underwent a graded maximal exercise test on a treadmill to determine the exercise intensity of a moderate level individualised for each patient under the supervision of an experienced physiotherapist trained in Basic Life Support. Any symptoms for termination of the test were noted. Each exercise session started with warm-up exercises and ended with a cool-down period. Rating of perceived exertion, blood sugars, blood pressure, and other vitals were monitored regularly, and special attention was given to foot examination and foot care to prevent the development of foot ulcers.

Twenty participants were enrolled in the research study, with ten participants in the control group and ten participants in the experimental group. Fasting blood glucose, post-prandial blood glucose, VAS, MNSI, Average Vibration perception threshold, and HbA1c were recorded at baseline and also after 12 weeks. The control group was given standard of care, including dietary advice and foot care, whereas the experimental group received a comprehensive, structured exercise program for 12 weeks, along with pain neuroscience education.

2.3 Exercise Recommendations for Diabetic Peripheral Neuropathy ADA 2022, 2013[20,21]

(i) Most adults with diabetes should engage in 150 min or more of moderate-to-vigorous intensity activity

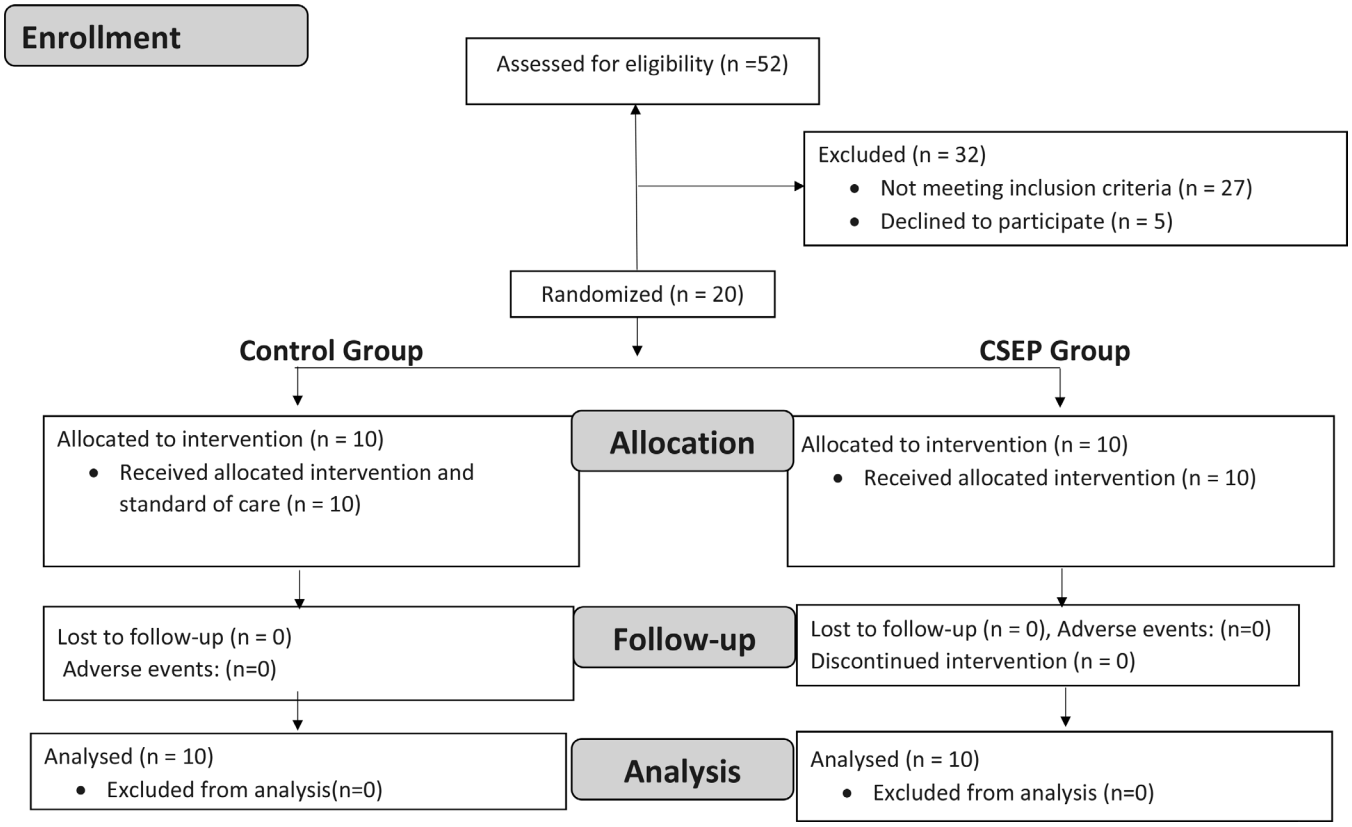


Figure 2: Patient flow diagram in the pilot study.
Abbreviations: CSEP: Comprehensive Structured Exercise Program

weekly, spread over at least 3 days/week, with no more than 2 consecutive days without activity.

(ii) Range of motion exercises are performed daily

(iii)People without any acute foot ulcers can perform mild to moderate weight-bearing exercise through low-impact activities like swimming, cycling, chair exercises, *etc*.

(iv)Individuals with foot injury or open ulcers should avoid or limit weight-bearing activities

(v)Balance training exercises, along with core strength training and lower body exercises, are suggested for diabetics with insensate feet

(vi)Chair exercises for people with limited mobility to improve strength and flexibility

(vii)Advised to use proper footwear and inspect feet regularly before and after physical activity to detect injuries early and prevent blisters

(viii)People with diabetes should avoid jogging as it can place a threefold increase in pressure when compared with walking

(ix)Individuals with hypertension should avoid the Valsalva manoeuvre during strength training

2.4 Statistical Analysis

It was performed using SPSS version 21 and Microsoft Excel 2019 for graph representation. The pvalue was set at 0.05. The categorical variables were expressed as percentages, whereas continuous variables were expressed as mean ± standard deviation. Independent-samples t tests are used to compare the same variable but for two different groups of cases, for calculating the pvalue (pvalue<0.05 significant).

3. Results

Table 1 shows demographic characteristics of the study participants (Mean±SD).

Out of 20 study participants in both groups together, 70% are female participants and 30% are male. The average age of the experimental group (N=10) is 56 years (SD=8.125), and the control group (N=10) is 54 years (SD=4.254), and were diagnosed with diabetes an average of 10.4 ± 4.69 years in the experimental group and 8.6 ± 2.54

Table 1. Prevalence of demographic characteristics

Demographic Characteristics		Experiment (N=10)	Control (N=10)
Age		55.7 ± 8.125	54.1 ± 4.254
Gender	**Female**	8 (80%)	6 (60%)
	Male	2 (20%)	4 (40%)
Height (cm)		154.1 ± 11.761	155.5 ± 10.512
Weight (kg)		72.4 ± 7.706	68.9 ± 7.430
Body Mass Index (Kg/m$^{2)}$		30.95 ± 5.369	28.98 ± 4.470
Duration of diabetes (years)		10.4 ± 4.695	8.60 ± 2.547
Duration of hypertension (years)		6.6 ± 7.367	6.4 ± 5.680
Waist-hip ratio		0.94 ±0.011	0.93 ±0.012

cm – centimeters, kg - kilogram

Table 2. Medication History

Drug		Experiment (N=10)	Control (N=10)
Anti Hypertensives	**Yes**	5 (50%)	6 (60%)
	No	5 (50%)	4 (40%)
Pain Medications	**Yes**	6 (60%)	5 (50%)
	No	4 (40%)	5 (50%)
OHA	**Yes**	9 (90%)	8 (80%)
	No	1 (10%)	2 (20%)
Insulin	**Yes**	3 (30%)	3 (30%)
	No	7 (70%)	7 (70%)
OHA + Insulin	**Yes**	2 (20%)	1 (10%)
	No	8 (80%)	9 (90)

OHA: Oral Hyperglycemic Agents

Table 3. Mean and standard deviation of MNSI, FBG, PPBG, VPT

	Experiment (N=10)		Control (N=10)	
	Pre-test	**Post-test**	**Pre-test**	**Post-test**
MNSI symptoms score	8.2 ± 1.22	5 ± 0.66	8.60 ± 1.43	6.00 ± 0.81
MNSI examination score	2.75 ± 0.42	1.55 ± 0.43	2.70 ± 0.48	2.45 ± 0.49
VPT	26.30±1.05	17.00±1.15	25.60±1.51	23.30±1.82
FBG (mg/dl)	194.6 ± 59.74	140.7 ± 35.29	140.94 ± 32.72	167 ± 61.93
PPBG (mg/dl)	292.2 ± 86.00	182.5 ± 56.33	223.26 ± 41.57	241.5 ± 87.41

Abbreviations: MNSI: Michigan Neuropathy Screening Instrument, VPT: Vibration Perception Threshold; FBG: Fasting Blood Glucose, PPBG: Post Prandial Blood Glucose

Table 4. Mean, SD, MD, and pvalue of VAS, PCS, TSK, and HbA1c

Variable	Control Pre Mean± SD	Control Post Mean±SD	Experimental Pre Mean±SD	Experimental Post Mean ±SD	Post-intervention MD	Post-intervention pvalue
VAS	7.5±0.050	6.40±0.516	7.54±0.843	3.30±0.676	3.10	<0.001
PCS	39.80±1.98	38.80±20.98	40.80±1.39	24.50±1.26	14.3	<0.001
TSK	50.60±2.01	50.30±2.21	48.80±2.15	34.60±5.60	14.20	<0.001
HbA1c	8.19±1.05	8.15±1.04	9.53±0.68	6.99±0.199	1.160	<0.003
FC	427±44.51	468.10±42.13	414.10±24.16	536.1±21.88	68.00	<0.001

Independent t-test, 95% Confidence Interval, pvalue<0.05;
Abbreviations: VAS: Visual Analog Scale, PCS: Pain Catastrophizing Scale, TSK: Tampa Scale of Kinesiophobia, FC: Functional capacity, SD: Standard Deviation, MD: Mean Difference

years in the control group, respectively. An average number of participants in the control group were overweight, while in the experimental group, they were obese.

Table 2 shows the medication history of the study participants; yes indicates the number of participants taking specific medication (%).

Table 3 depicts the sample's means and standard deviations of the MNSI history score, MNSI physical examination score, VPT, FBG, and PPBG.

The mean, SD, MD, and pvalue of VAS, PCS, TSK, HbA1c and Functional Capacity are shown in Table 4. The means and standard deviation for scores of VAS at baseline for control and experimental groups were 7.5±0.05 and 7.54±0.843. HbA1c values were 8.19±1.05 and 9.53±0.68. Post twelve weeks, the mean scores for the control and experimental group for VAS were 6.40±0.516, 3.30±0.676, and HbA1c were 8.15±1.04, 6.99±0.199, respectively. The outcomes VAS, PCS, TSK, and HbA1c have shown a significant difference with a pvalue of <0.05 with a 12-week structured exercise intervention program in the experimental group.

4. Discussion

This study reports on the pilot testing of the developed evidence-based structured exercise prescription for people with painful diabetic neuropathy in Type 2 diabetes. It provides an extensive description of the exercise program. An exercise activity log diary was also included, along with a patient education manual to monitor patients' exercise adherence. The exercise program development was based on a systematic review of literature, input from experts, followed by the implementation of a pilot study. The exercise program adheres to the guidelines put forward by ADA, ACSM, and recommendations given by experts in the field. Overall, this entire process represents the stepwise sequential development of a comprehensive exercise program for painful diabetic neuropathy.

The objective of the pilot study was to examine the effect of CSEP on neuropathic pain and glycosylated haemoglobin, which were measured by VAS, MNSI, and HbA1c levels at the baseline and the end of 12 weeks of the intervention in the control and experimental groups. The significant results shown in the CSEP group can be attributed to the structured program designed according to the recommendations of ACSM, ADA, synthesis of evidence from the literature review, and experts' opinions along with pain neuroscience education. The adherence rate is high, which clearly illustrates that if patients were given clear and consistent education with proper follow-up, they were more likely to be compliant with the exercise program with less number of dropouts.

There are 80% females and 20% males in the experimental group, whereas 60% females and 40% males are in the control group. Females were more in the study (70%). The results of this study are in line with other research that found neuropathic symptoms are more noticeable in women[22,23]. This could be because of various biological and hormonal variables and greater susceptibility to nerve damage in females[24].

In the present study, CSEP group has shown significant improvement in HbA1c with a significant difference in mean of VAS and Glycosylated haemoglobin (HbA1c) between experimental and control group of post-test ($p<0.05$), which may be because exercise was shown to have anti glycation effect with 14% and 21% reduced incidence risk with acute myocardial infarction and diabetes related deaths with every one percent HbA1c value reduction[13]. Further, it was noted that glucose uptake remains elevated for up to 120 min after physical activity

due to an increased number of glucose transporter 4 in the muscle membranes, thus increasing insulin sensitivity[25]. The present research findings are similar to a study by Dixit *et al.*[13], where eight weeks of regular moderate intensity aerobic exercise reduced HbA1c levels in elderly people with diabetes. But a study by Yoo *et al.*[26] found no significant improvement in pain intensity with exercise and commented that improvement in hyperglycemia may not be the only mechanism responsible for pain in diabetes. In the present pilot study, the symptoms of pain, neuropathic symptoms, and decreased vibration perception threshold might have improved due to the improvement in oxygenation and blood circulation to nerves and glycemic control. A significant difference in the mean of Neuropathic pain, glycosylated haemoglobin was observed in the experimental group compared to the control group after a 12-week duration (Table 4). The results were in line with Kluding *et al.*[27] 2012 study, who speculated through the research findings that exercise benefits may even extend to the nerve fibres with increased intraepidermal nerve fibre branching, which tend to produce structural improvements, ultimately enhancing neural function. The reduction in neuropathic pain with exercise can be attributed to modulation of proinflammatory factor signalling pathways reducing the levels of Interleukin-6, Interleukin-1 Beta, Tumour necrosis factor alpha thatmight have improved paw withdrawal thresholds and also by altering gene expression miR-21 and miR96 which in turn could have affected sodium channels Nav 1.3 was demonstrated in a rat model[28,29]. Recently, in 2022 a study bySumizono et al on description of mechanisms for neuropathic pain with exercise reported the suppression of microglial activation in the dorsal horn of spinal cord with expression of spinal glial cell markers like Chemokine Receptor 2 (CCR2), Tumour necrosis factor Receptor-Associated Superfamily signalling (TRAF6) and also changes in the dynamics of hippocampal dentate gyrus[30]. The pain might also have reduced as it is subjective and is shown to have a biopsychosocial component, and needs to be focused on this aspect[31]. On the other hand, resistance and balance exercises were found to improve strength, balance, speed of reaction time, and risk of falls with better postural dynamics, indicating that exercise can lead to reasonably rapid positive prognosis of neuropathy[32]. The high adherence rate can be attributed to referral from physicians, positive interactions with other participants, and staff supervising the exercises and providing patient education were found to be some of the factors to increase exercise adherence, similar to other studies[33]. In the present study, significant effects in the glycosylated haemoglobin in the experimental group can be credited to the detailed patient education manual, supervised structured exercise, exercise log sheet for adherence with regular follow-up.

The confounding variables age, gender, BMI, comorbidities, duration of diabetes, hypertension, and medication history could have influenced the results, as evidenced by previous literature[34,35]. Julius etal noted that antihypertensive medications like central imidazoline binding agents and α-adrenergic blockers improve insulin sensitivity, whereas β-blockers and diuretics exacerbate insulin resistance. Angiotensin blockers and ACE inhibitors might also have a beneficial effect on insulin resistance, however, the outcomes are not always favourable[36].

Exercise is shown to have beneficial effects on the AGE pathway and improve metabolic function, thus preventing nerve damage and enhancing vascularity[37].

4.1 Limitation

Though it is called a structured exercise program, the exercise needs to be tailored according to the ability of patient. This study did not address the underlying physiological and biochemical mechanisms associated with hyperglycemia, like the Advanced Glycation End products pathway, the Protein kinase B pathway, Nuclear factor Kappa B inflammatory pathway, Mitogen Activated protein kinase pathway, central mechanisms involving brain-derived growth factor which might have influenced the findings.

4.2 Strength

A major strength of the study is that this comprehensive exercise program integrated with biopsychosocial approach like pain neuroscience education was developed with detailed review of literature, consensus from the experts and therapists with different clinical, research and academic background from primary health care to tertiary care hospitals and research set ups, which ensured that the exercise program is feasible and acceptable in different settings. The exercise manual with pain education and log diary helped to increase the adherence rate.

Exercise was an easy and effective form of intervention and could be performed anywhere possible because of the

simple equipment used, such as therabands, water bottles as a substitute for dumb bells, and weight cuffs.

4.3 Future Recommendation

A randomised clinical trial on a large sample is recommended to strengthen the evidence.

4.4 Clinical Implications

Nevertheless, the findings of the present pilot study are meaningful, encouraging physical activity because mere pain as such can interfere with mobility and quality of life. This developed exercise prescription can form the basis for evidence-based exercise recommendations for painful diabetic neuropathy in Type 2 diabetes with an integrated psychological approach, such as pain neuroscience education, which could have beneficial effects on psychosocial outcomes like pain catastrophizing and kinesiophobia.

5. Conclusion

The preliminary results of this pilot study suggest that neuropathic pain and symptoms may be improved with CSEP in Type 2 diabetes people with painful diabetic neuropathy. A combination of moderate intensity aerobic, resistance, balance, and flexibility exercises for twelve weeks has been shown to produce beneficial physiological, psychological and biochemical changes in painful diabetic neuropathy. The promising findings of this study support the need for future research to explore other possible mechanisms underlying painful diabetic neuropathy using large clinical trials.

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