

Postural Control in Diabetic Peripheral Neuropathy: A Narrative Review

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ABSTRACT

Diabetes mellitus is a metabolic disease of chronic hyperglycaemia which leads to neurological complications such as Diabetic Peripheral Neuropathy (DPN). When compared to healthy persons, those with DPN are more likely to fall, especially in geriatric population. Present review aims to provide an insight to the pathophysiology, outcome measures, and physiotherapy treatment of impaired postural control in DPN. Searches for relevant articles were conducted using Google Scholar, PubMed, Ovid, Springerlink, Science Direct (SD), Seniorcare Ageing Growth Engine (SAGE), Elton B. Stephens Company (EBSCO) Discovery Service and Web of Science. Keywords used were diabetes, DPN, diabetic foot, postural control, balance, postural sway, physiotherapy intervention. Irrespective of their year of publication, studies and reports published in English, that provide data of postural control in individuals with DPN and its physiotherapy management were included in the study. The included publications were reviewed and a narrative review was formulated. A total of 35 studies were included in this review. All studies suggest that there is postural instability in people with DPN which increases with age and duration of diabetes. Multidirectional postural sway was observed in most of the studies with medio-lateral instability encountered in more cases. Significant improvement in timed up and go test, single leg stance test, Berg balance scale, and other outcome measures post physiotherapy intervention were reported. Literature suggests that multidirectional postural instability is present in DPN patients. Physiotherapy, offloading devices and diabetic foot care education improve postural stability in individuals with DPN.

Keywords: Balance, Diabetic foot, Diabetes mellitus, Neurological complications, Postural sway, Physiotherapy

INTRODUCTION

Diabetes mellitus is a metabolic disease where chronic hyperglycaemia occurs due to abnormality in insulin secretion, insulin action, or both [1]. The number of people with diabetes in India increased from 26.0 million in 1990 to 65.0 million in 2016 [2]. Diabetes mellitus leads to macrovascular as well as microvascular complications [3]. Because of hyperglycaemia, there is a defect in both nerve function and structure which leads to neurological complications such as diabetic neuropathy [4].

Postural control means controlling the body's position in upright posture for the purpose of stability and orientation [5,6]. The ability to maintain the Centre Of Mass (COM) in relationship to base of support is termed as postural stability. Postural sway is the displacement of centre of gravity within the base of support and with a larger sway path there is greater postural unsteadiness. Postural control for stability and vertical orientation requires a complex interaction of musculoskeletal and neural system [6]. In diabetic neuropathy, there is lack of accurate proprioception, visual and vestibular problems and impaired motor function which leads to postural instability [5]. Impaired postural control in diabetic individuals causes increase postural sway which leads to balance problems and high risk of fall in older DPN patients [3,7].

When compared to healthy persons, those with DPN are more likely to fall, especially in geriatric population [8]. As a result, it is critical to understand the factors that influence falls in DPN patients, such as postural control deficit and available physiotherapy measures to improve postural control in DPN. The present review aimed to study majority of published studies to date on the effects, features, and physiotherapy treatment of abnormalities in postural control in DPN.

LITERATURE SEARCH

The literature was searched using various search engines like Google Scholar, PubMed, Ovid, Springerlink, Science Direct (SD),

SAGE, EBSCO Discovery Service and Web of Science databases, etc., Hand search of articles were also done in the University library. In effort to compile vital information published till date, the articles published in English language and irrespective of the year of publication were screened for inclusion criteria.

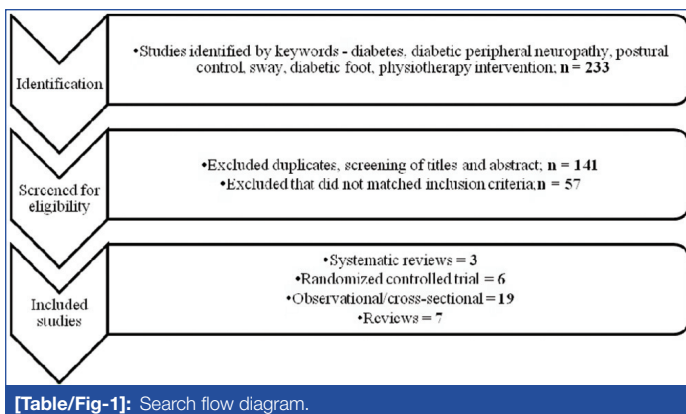
Inclusion criteria: All those studies (systematic review, meta-analysis, randomised control trials, cohort studies, case control studies, narrative reviews and case series) and reports that provided data on the postural control in diabetic neuropathy and its physiotherapy treatment were included for review.

Exclusion criteria: The animal studies and studies done on diabetic patients without diabetic neuropathy were excluded.

The study strategy identified a total of 233 studies, following the removal of duplicates and the screening of titles and abstracts, a total of 141 potentially relevant studies were excluded. Remaining 92 studies were analysed for the inclusion criteria to determine if they should be considered as a part of this study or not, which further excluded 57 articles, and at last 35 studies remained. From these 35 articles, a narrative review on postural control in DPN patients was formulated [Table/Fig-1]. The included articles were critically appraised for appropriateness of the study design for the research question, key methodological features, statistical methods used and their subsequent interpretation, potential conflicts of interest and the relevance of the research to present study aim.

DIABETIC NEUROPATHY

DPN include varying disorders that involve a wide range of abnormalities affecting both peripheral and autonomic nervous systems, leading to significant rise in morbidity and mortality. These neuropathies can be focal or diffuse, proximal or distal, and could also affect somatic and autonomic nerves [Table/Fig-2] [9-12].



S. No.	Author/ Year	Type of the article	Conclusion	Remark
1	Vinik AI, 1999 [9]	Review	Immune mechanisms and microvascular insufficiency are the causative factors for the development of diabetic neuropathy.	Chronic hyperglycaemia causes increase in polyol pathway activity resulting in nerve damage.
2	Cancelliere P, 2016 [10]	Review	DPN is classified as sensory neuropathy, motor neuropathy and autonomic neuropathy.	Tingling and burning, hypoesthesia, loss of vibration and proprioception, loss of ankle reflex, and reduced muscle strength, dry scaly skin are commonly seen in individuals having diabetic peripheral neuropathy.
3	Volmer-Thole M and Lobmann R, 2016 [12]	Review	In autonomic peripheral neuropathy, there is disturbance in sweat glands. As a result, foot skin dries and there is reduced protective skin function, increasing the risk of injury.	Chronic hyperglycaemia leads to deal in healing resulting in diabetic foot ulcers.
4	Sytze van Dam P 2002 [11]	Review	Oxidative stress is considered a major factor contributing to the development of the microvascular diabetic complications.	Oxidative stress is responsible for the development of DPN.

[Table/Fig-2]: Pathophysiology of Diabetic Peripheral Neuropathy (DPN) [9-12].

Clinical Presentation of Diabetic Peripheral Neuropathy (DPN)

[Table/Fig-2] depicts the comparative analysis of various clinical signs and symptoms and pathophysiologies associated with them [9-12].

DPN is progressive, degenerative and is classified into three main types:

- Sensory neuropathy
- Motor neuropathy
- Autonomic neuropathy

The classical feature observed in DPN is of "gloves and stockings" distribution. The symptoms frequently worsen throughout the night and create sleep problems, lowering one's quality of life. During the initial phase of the disease patients usually complain of allodynia which is characterised as alteration in perception of pain and temperature, tingling, and burning sensation. This occurs because of active degenerative of nerve fibres or due to compromised regeneration process [10, 11]. As the condition progresses, symptoms also increase and gradually there is complete loss of sensation, called as anaesthesia along with progression of symptoms from distal to proximal portion.

Vibration sensation is typically the first sensation that is found to be lost in DPN [10]. The presence of neuropathy is associated with increased body sway and foot ulceration. Foot instability increases in foot ulcer patients due to defects in proprioception. Thus, diabetic patients with a history of foot ulceration have significantly increased body sway with increase in vibration perception threshold

[13]. Pain or paraesthesia is also a clinical feature seen in patients with DPN which occurs because of active degeneration of nerve fibres or due to compromised regeneration process [11]. As the disease progresses, there is complete loss of pain sensation which increases the risk of trauma and causes serious ulceration [12].

If no strict action is taken to control blood glucose level and the sensory symptoms being ignored, it would further damage motor and autonomic nerve fibres and will lead to motor and autonomic dysfunctions. Motor neuropathy causes a variety of foot abnormalities (deformities) because of intrinsic muscle weakness. Foot abnormalities can be as simple as hammer toe deformity or as severe as Charcot Arthropathy, which affects the anatomic architecture of the foot [10]. Hence, both sensory and motor impairments in DPN will result into unequal foot loading resulting to abnormal gait and history of frequent falling with higher chances of foot ulceration [12,13] and in later stages limb amputation is done [10].

Autonomic neuropathy will lead to alteration in the integrity of skin because of disturbance in cutaneous blood flow, loss of normal perspiration and activity of oil glands [10]. This results in dry and fragile skin vulnerable to injury. Clinically, diabetic foot ulcers are presented in circular shape surrounded by hyperkeratotic borders which are usually developed at the area of constant high pressure [12].

Beside this, there are few recent studies that have stated that the central nervous system is also involved. Presynaptic inhibition either inhibitory or excitatory spinal reflex, helps in maintaining balance and postural stability. A study done by Chun J and Hong J aimed to find out the relationship between presynaptic inhibition and DPN in ability to control postural stability [14]. He found out that people with DPN had reduced presynaptic inhibition and also had decreased balance leading to increased postural sway. The possible reason could be that presynaptic inhibition is responsible for fine motor control and so, people with less presynaptic inhibition tends to have less fine motor control followed by instability [14].

Postural Control in Diabetic Peripheral Neuropathy (DPN)

Posture is a complex task which demands the gathering and integration of sensory (afferent) information to coordinate effectively with the neuromusculoskeletal system in order to maintain balance. The peripheral sensory systems involved are the vestibular apparatus, the visual system, and the kinesthetic and proprioceptive receptors which are widely distributed throughout the body [15]. Apart from this, body alignment, muscle tone and postural tone contributes in maintaining postural stability. They help in maintaining the effect of gravitational force acting upon the body and help in preventing the body from collapsing due to the pull of gravity [6]. Afferent fibres of lower limbs play an important function in reflex control of the body during a quiet upright stance [16].

Alteration in any of these systems leads to increased body sway leading to postural control disturbances. It could be because of failure of the lower extremities and postural muscles to generate an adequate amount of activity. Strength of lower extremity muscles decreases in neuropathy especially of ankle flexor and extensor muscles of DPN patients [17]. This reduction in muscle strength is found to be linked with higher glucose concentrations [18,19]. In addition, there is compromised reflex activity of lower extremity muscles [20]. Along with reduction in muscle strength and deterioration in reflex response, the spinal sensation of muscles i.e., position, velocity, and force sensation components are also compromised. Thus, DPN degrades the motor and sensory function which causes poor balance in DPN patients [21,22].

Dixit S et al., and Boucher P et al., found that individuals with neuropathy had significantly raised sway speed, velocity moment and mediolateral and anteroposterior displacements under four conditions- eye open, eye close, eye open on foam and eye close on foam [23,24]. Standing with eyes closed worsens their postural

Serial No.	Author/Year	Type of the article	Methodology	Result	Remark
1	Mustapa A et al., 2016 [7]	Systematic review	38 published articles were included regarding postural control impairment and alteration in gait performance in DPN patients. Keywords used- diabetes mellitus, DPN, postural control, gait performance, and balance.	Most of the studies had strong correlation of DPN with postural control deficits.	Postural instability and gait impairment creates high risk of falling.
2	Chun J and Hong J 2015 [14]	Observational study	Subjects: 8 DPN, 8 healthy age and gender matched. Neuropathy and its tests: Double leg static balance with eyes open was measured using the Biodex Balance System. Postural sway measured using Stability index. Muscle response recorded with surface electrodes at soleus belly and ground electrode over lateral malleolus	DPN patients had significantly lower presynaptic inhibition (p-value <0.05) and less balance p-value <0.05) than normal subjects. No correlation between balance and presynaptic inhibition (p-value=0.15)	Postural instability is a significant indicator of fine motor control and so with decreased levels of presynaptic modulation, there is decreased fine motor control and balance.
3	Timar B et al., 2016 [15]	Cross-sectional study	Subjects: 198 (57 DPN). Presence of diabetic Neuropathy and its tests: Michigan Neuropathy Screening Instrument (MNSI). Balance impairment and risk of falls was evaluated using four validated tools: Berg Balance Scale (BBS), single leg stand test (SLS), Fall Efficacy Scale (FES-I), and Timed up and go test (TUG)	The presence of DN was linked to lower BBS and SLS scores, as well as higher TUG time and FES-I scores. BBS: p-value <0.0001 SLS: p-value=0.003 TUG: p-value=0.002 FES-I score: p-value=0.034 Correlation between severity of neuropathy (MNSI) and balance- BBS: p-value <0.001, SLS: p-value=0.017	The presence of DN is linked to impaired balance which further increases the risk of falling.
4	Nardone A and Schieppati M, 2004 [16]	Observational study	Subjects: 22 DPN, 13 normal body sway area, stretch responses of postural muscles on the force platform was assessed. Neuropathy and testing: The tibial, deep peroneal, and sural nerve conduction velocities, as well as vibration threshold detection, cooling, warming, and heat-pain, were all measured.	Body sway area was increased in patients. Toe up rotation produced short and medium latency responses in distal muscles, which were found to be diminished or absent in DPN patients. CV was also reduced.	Diabetes-related neuropathy is characterised by changes in medium-sized myelinated afferent fibres.
5	Toosizadeh N et al., 2015 [21]	Observational study	Subjects: 18 DPN and 18 healthy age matched adults (>55 years) Neuropathy and its testing: 10-g Semmes- Weinstein monofilament, vibration perception threshold. Balance- 2-15 sec Romberg balance test. Sensors-triaxial accelerometer and gyroscope. Local and central control strategies- Stabilogram diffusion analysis.	Local control sway was significantly higher in the DPN group (p<0.01), indicating that local control is compromised in DPN. With central control- sway was 60% less- Adaptation mechanism responsible. Lack of sensory feedback cuing leads to high instability in DPN patients.	Local control- postural muscle control, central control- higher central nervous sensory feedback cues.
6	Lim KB et al., 2014 [22]	Cross-sectional study	Subjects: Total 60 subjects; DPN=17, diabetic control group=25, and subjects without diabetes=18. Neuropathy and its testing: nerve conduction studies and MNSI. Balance stability evaluation: Balance Master System. All patients underwent Sensory Impairment Assessment (SIA), Motor Impairment Assessment (MIA), and Functional Limitation Assessment (FLA).	SIA=no significant difference MIA=left to right directional control in the rhythmic weight shifts was significantly poor in diabetic subjects. (p-value=0.027 for slow movement and p-value=0.022 for fast movement). FLA- Sit to stand and Step-quick turn - no significant difference. Unilateral stance mean cognitive (COG) velocity was significantly higher in DPN group [p-value=0.11 (LT) and p-value=0.008 (RT)] Significant slower walking speed in tandem walk for DPN group (p-value=0.033). Higher end sway in DPN group (p-value=0.020)	Dynamic balance stability decreased and Functional limitation was more in patients with diabetes and peripheral neuropathy.
7	Dixit S et al., 2015 [23]	Cross-sectional study	Subjects: 61 diabetic patients with clinical neuropathy. Neuropathy and its testing: MNSI Postural stability measured: Metitur good balance system. Static posturography (force platform) was measured in four conditions- eyes open, eyes close, eyes open on foam and eyes close on foam. Variable used: Sway velocity, velocity moment, antero-posterior and Medio-Lateral (ML) displacement.	Increase in sway speed, velocity moment and antero-posterior and medio-lateral displacement was observed from eyes open (EO) to eyes closed (EC), eyes open on a foam surface (EOF) and eyes closed on a foam surface (ECF) respectively with greater sway amplitude. Participants with neuropathy had - Sway velocity- p-value <0.05 for firm and foam surface (X-axis) Velocity moment- p-value <0.05 for firm and foam surface. Medio-lateral displacement- significant increase with firm and foam surface (p-value <0.05)	DPN patients rely more on hip strategy as peripheral sensation is affected. Hence, more ML displacement. Age, duration of diabetes and MNSI also affects postural stability.
8	Boucher P et al., 1995 [24]	Observational study	Subjects: 17 diabetic, 12 control individuals. Neuropathy and its testing: sensory and motor examination. Nerve conduction velocity (NCV)- motor: tibial and peroneal nerve, sensory: sural nerve. Kistler Force platform used to measure displacement of the Centre of foot pressure (CoP) with upright posture- eyes open and close. Variables measured: Antero-Posterior and Medio-Lateral sway, scalar range, sway speed and dispersion.	DPN patients showed larger sway in all four directions but Medio-lateral sway had greater sway range (p-value <0.001) without vision. Faster sway speed in neuropathic people (p-value <0.05) with greater sway dispersion (p-value <0.001). Postural instability increased with severity of neuropathy (p-value<0.05).	Even with vision, postural stability of DPN patients is impaired. Higher risk of fall.
9	Vaz MM et al., 2013 [26]	Cross-sectional study	Subjects: 19 with Diabetes Mellitus type 2 (DM2) without DN, 13 with DM2 with Peripheral neuropathy and 30 without DM2. Neuropathy and its testing: sensory and motor examination, nerve conduction study Balance and functional strength evaluation- Polhemus device Upright balance evaluated in 4 conditions- fixed platform, unstable platform, eye open, and eye close. Functional strength- 5 times sit to stand test. Functional balance- BBS Functional mobility- Time Up and Go (TUG)	Greater AP displacement (p-value<.05) in unstable platforms with Eyes Closed (EC). Also, DM type 2 with/without neuropathy had greater trunk displacement. Sit to stand- time spent by DM type 2 and DPN was more than the control group (p-value <0.05). BBS- lower score in DM type 2 than control group (p-value <0.05) TUG- more time taken	DM type 2 and diabetic neuropathy patients have impaired postural control and altered functional strength.

10	Fortaleza AC et al., 2013 [28]	Observational study	Subjects: 30 women (55-70 year) divided in 2 groups: 17 non diabetic and 13 with DPN. Neuropathy and its testing: postprandial glycaemia and MNSI respectively. Postural control and functional balance assessment-kinematics system, Anterior-Posterior and Medial-Lateral sway measured under three conditions – eyes open, eyes close and semi-tandem position on floor. Dynamic functional balance- Tug up and go test (TUGT)	Neuropathic individuals fluctuate more in both AP and ML directions, but ML displacement was more significant (p-value=<0.005). Persons with neuropathy were more unstable in ML direction in case of Semi-Tandem (ST) condition. (p-value=<0.005) Time taken by neuropathic group was more for TUG (p-value=0.001)	A significant and positive relationship between medial-lateral instability and functional balance was discovered.
11	Turcot K et al., 2009 [29]	Observational study	Subjects: 12 control, 12 diabetic type 2 patients and 12 DPN patients included. Neuropathy and its testing: fasting blood sugar level and Vibration perception threshold (VPT) respectively. Variables measured: Performance-oriented assessment of balance (POMA-B) was performed with eyes open and eyes closed conditions and acceleration signals were measured by accelerometer.	Eye open- AP range of lumbar acceleration was significantly higher in DPN group (p-value=0.017) Eye close- significantly higher AP range of lumbar acceleration in DPN group (p-value=0.005) Lower score in POMA-B test for DPN group (p-value=0.007)	Suggests greater instability with higher acceleration during standing tasks in DPN individuals.
12	Lafond D et al., 2004 [31]	Observational study	Subjects: 11 elderly patients with type 2 diabetes with Diabetes Sensory Neuropathy (DSN) and 20 healthy age matched subjects included. Neuropathy and its testing: Subjects were tested in quiet standing on a dual force platform with their eyes open and closed to assess postural mechanisms and motor strategies of the ankle and hip joints.	Even with vision postural control mechanisms at ankle joints are impaired in DSN patients especially in ML direction.	It is important to focus on postural control instability in ML of DSN patients.
13	Brown SJ et al., 2015 [33]	Observational study	Subjects: 89; DPN=22, DM2=22, healthy control=28 Neuropathy and its testing: modified Neuropathy Disability Score (mNDS) and Vibration Perception Threshold (VPT) Variables measured: Gait analysis during walking, stair climbing and descending was done using a motion analysis system and force plate embedded on stairs and level pathway. The separation between Centre Of Mass (COM) and Centre Of Pressure (COP) was measured during level walking, as well as stair climbing and descending.	DPN patients had greater range of separation of COM and COP in ML plane in level walking, stair climbing and descending. (p-value<0.05) During stair climbing – greater anterior separation found (p-value<0.05)	Higher medial-lateral separations in DPN necessitate more muscular effort to maintain upright posture.
14	Turcot K et al., 2012 [34]	Observational study	Postural stability and instability evaluated in 25 diabetes patients with PN under two standing tasks. Angular velocity signals from trunk and ankle levels were analysed in both POMA-B test and Biodex-Balance system. Angular velocities were also analysed in terms of CCF in order to estimate the degree of synergy between different levels and sides.	Postural strategies are affected by challenging standing tasks and are also linked with the level of PN and strength of muscles in diabetes patients.	There is a correlation between postural strategies and balance instability with the level of peripheral neuropathy and with hip and ankle strength.
15	Ghanavati T et al., 2012 [36]	Observational study	Subjects: 14 older adults with DPN, 14 age matched healthy adults. Neuropathy and its testing: Diabetic Neuropathy Examination (DNE) Functional balance evaluation- Berg Balance Scale (BBS).	BBS total score significantly lower p<0.001 in DPN individuals. Out of 15 tasks, 8 tasks had significantly lower scores in BBS.	DPN individuals are more unsteady while performing daily activities.

[Table/Fig-3]: Postural control in Diabetic Peripheral Neuropathy (DPN) patients [7,14-16,21-24,26,28,29,31,33,34,36].

stability in individuals with diabetic neuropathy. Also, with increase in duration of diabetes, postural stability was more affected. The postural stability in DPN individuals is affected even in quiet stance and could increase the risk of fall when on foam or deformable surface [7,23,24].

Mustapa A et al., performed a systematic review which revealed, DPN contributes to abnormal postural control by causing impairments in proprioceptive and tactile sensation (somatosensory input) and reduction in reaction time and muscle strength (motor output) [7]. Reduction in ankle strategy was present and if combined with visual defect was resulting in greater postural sway in DPN [25]. The review also reported lower equilibrium score, lower balance score in berg balance scale, larger trace surface area, with faster mean velocity of body sway in eye open and closes condition in patients with DPN [7].

Vaz MM et al., and Melo TA et al., reported Type 2 Diabetic Mellitus (Type 2 DM) patients took more time to complete Five-Times-Sit-to-Stand Test (FTSST) compared to non diabetic people, suggesting that those with Type 2 DM have higher risk of falls during dynamic situations in which integration of several body components, such as sensory system, motor coordination, mobility and muscle strength are required [26,27].

In order to maintain Antero-Posterior (AP) stability, the ankle strategy is normally used, which is often affected in individuals with DPN [25]. On the other hand, the hip joints have a greater impact on Medio-Lateral (ML) stability, with alternating action of the abductor and adductor muscles [23,28]. Because of reduction

in ankle strategy, a compensatory greater use of hip strategy is seen in DPN [23,29]. Lim KB et al., reported that while testing static and dynamic balance abilities with Modified Clinical Test Sensory Interaction on Balance (mCTSIB), individuals with DPN showed more balance instability than both diabetic control and non diabetic control patients [22]. Fortaleza AC et al., found that DPN group had worse ML instability during semi-tandem stand [28]. ML stability is more affected even with vision in DPN patients [28,30,31]. Dixit S et al., reported multidirectional postural instability in DPN individuals. Hence, management should not only direct towards one strategy [23].

During gait activities like ground level walking, stair ascent and descent; balance is greatly impaired in patients with DPN [32]. This is because while walking an individual transfers his/her weight from one limb to another causing brief periods of large separation between centre of mass and the centre of pressure [33]. To maintain balance during these period, high levels of muscular strength is required which is compromised in DPN patients [33,34]. Thus, they have higher risk of falling during gait activities than during quiet standing. A study done by Brown SJ et al., concluded that balance impairment with DPN is predominantly in the ML plane and was greatest during stair descent [33]. Also, shortening step length is a common strategy used among those who are at higher risk of falling [35]. This maintains a closer control of the centre of mass above the centre of pressure, thereby reducing muscular demands and the risk of falling [33]. Individuals with DPN tend to have temporal-spatial

parameters of the gait affected, and have greater gait variability. Impaired perturbation response also potentially increases the risk of falling [7].

Ghanavati T et al., reported that elderly individuals with DPN had a considerably lower total score of Berg Balance Scale (p-value <0.001) in comparison to healthy age matched individuals [36]. DPN patients had significantly lower scores in tasks like standing on one leg, standing unsupported with one foot in front, reaching forward without stretched arm while standing, standing independently in narrow Base of Support (BOS), stand to sit, sit to stand, transfer activities, turning, standing independently with eyes close and stepping on stool while standing unsupported. [Table/Fig-3] depicts the comparative analysis of postural control impairment and alteration in gait performance in DPN patients and various inferences drawn from them. Thus, elderly with DPN are more unstable while performing their activities of daily living [Table/Fig-3] [7,14-16,21-24,26,28,29,31,33,34,36].

Assessment of postural control in diabetic patients: There are several outcomes measures ranging from advance technology to clinical tests and functional scales by which we can assess the postural stability in diabetic neuropathy patients. Static, dynamic and functional balance tests like One Leg Stance (OLS), Functional Reach (FR) test and TUG are been developed and have shown to have good reliability, validity and responsiveness in older population and people with balance impairment [37-40]. Dominguez-Muñoz FJ et al., reported the reliability of TUG in diabetic neuropathy patients [41]. Intraclass Correlation Coefficient (ICC) was higher than 0.90 (excellent) in individuals having moderate neuropathy and individuals with normal foot vibration perception. Whereas, it was found just good in individuals with severe neuropathy with ICC as 0.70-0.90. He also found that time required to complete TUG was more in individuals with severe DPN [41].

The Wii Balance Board (WBB) and Pedalo®-Sensomove balance device have also demonstrated to be a highly valid and reliable method for assessing the COP range and COP displacement (sway) during different balance tests in older adults with Type 2 DM and in individuals with DPN [40,42].

A systematic literature review carried by Dixon CJ et al., found that commonly used clinical balance measures for people with Type 2 DM and DPN do not assess all systems of balance, and most of them have not yet been validated in a Type 2 DM and DPN population [43]. Therefore in future, studies are required to establish reliability and validity of these tests in patients with Type 2 DM and DPN [Table/Fig-4] [38,40-43].

Physiotherapy Management

The sensory-motor deficits in patients with DPN leads to balance problems, risk of falling and further alteration in motor programming. Therefore, it is important to focus on sensorimotor training (balance training). Sensorimotor training helps in adequate recruitment of various muscles responsible for maintaining stability of the body [44]. Ahmad I et al., found that sensorimotor and gait training was an effective treatment protocol in order to achieve improvement in proprioception and nerve function [44]. Exercise was conducted on alternate days, thrice a week for 8 weeks. Each session consisted of 10 minutes of warm-up (treadmill/cycle ergometer), followed by 50-60 min of exercise (wall slides, bridging exercises, prone plank, sit to stand, wobble board exercise, one leg stand, heel to toe raise, tandem stance, walking on line, tandem walk, high march tandem walk and high arch tandem backward walk) and ended with cool down (deep breathing exercise, abdominal breathing and mild stretching) for 5-10 minutes. Progression was done by incorporating unstable surfaces. Positive effect was observed in proprioception in all directions, nerve conduction velocity and in electromyographic activities recruiting tibialis anterior, medial gastrocnemius and multifidus. Also, sensorimotor and gait training was found feasible

Serial No.	Author/Year	Type of the article	Methodology	Result	Remark
1	Ahmad I et al., 2019 [40]	Observational study	20 subjects with DPN Validity assessed by correlating Centre of Pressure (COP) range and sway, using Pedalo®-Sensomove Balance device with Functional Reach Test (FRT), Time Up and Go (TUG), Online Linguistic Support (OLS)	Significant correlation between COP range (p-value=0.001) and COP sway {Antero-Posterior – p-value=0.022, Medio-Lateral – p-value=0.047}	COP range and sway for balance assessment were valid using Pedalo®-Sensomove Balance device.
2	Dominguez-Muñoz FJ et al., 2019 [41]	Observational study	Subjects- 56 participants divided in three groups – severe, moderate neuropathy and normal perception TUG performed using force platform	Intraclass Correlation Coefficient (ICC)=0.90 (excellent) – moderate neuropathy ICC=0.70-0.90 (good) – severe neuropathy.	TUG is a reliable tool in DPN for balance measures.
3	Álvarez-Barbosa F et al., 2020 [42]	Observational study	43 adults with T2DM (age 62.1 ± 12.1 yrs) in the validity trial and 27 (age 63.5 ± 10.8 yrs) in the reliability study. Total COP area and range of antero- posterior (AP) and medio-lateral (ML) COP sway was collected simultaneously on a Force Platform and a Wii Balance Board.	Mean CoP sway path values are similar in all conditions for Force Platform when compared with the Wii Balance Board (WBB). Test-retest reliability for WBB – excellent. ICC value for AP (0.73-0.90) and the ML (0.77-0.91) directions.	WBB has been a validated and accurate method of quantifying COP displacement during various balance tests in older people with T2DM.
4	Duncan PW et al., 1990 [38]	Observational Study	The study was conducted to assess the predictive validity of functional reach in identifying elderly subjects at risk for recurrent falls. 217 elderly, community-dwelling male veterans (aged 70-104) underwent baseline screening including functional reach test and were followed for six months to monitor falls.	Functional reach test and Tinetti balance measure are reliable and valid balance measures for assessing balance in elderly individuals aged 65 or above. Have shown excellent test-retest reliability.	Functional Reach (FR) may be useful for detecting balance impairment, change in balance performance over time, and in the design of modified environments for impaired older persons.
5	Dixon CJ et al., 2017 [43]	Systematic review	Studies included=8 Keywords used- diabetes, balance, validity, outcome Measure Studies included dynamic balance test, balance walk, tandem and single leg stance, functional reach test, clinical test of sensory interaction, berg balance scale, Tinetti performance oriented mobility assessment, activity specific balance confidence scale, time up and go and dynamic gait index as the assessment tool for balance.	Several studies have reported that balance measures fail to assess all the systems responsible for balance and most of them are not validated.	Future studies should focus on validity and reliability of balance outcome measures in diabetic/DPN patients.

[Table/Fig-4]: Outcome measures for Diabetic Peripheral Neuropathy (DPN) [38,40-43].

and easy to be used in the clinical set-up as well as home exercise, protocol in patients with DPN due to lesser risk [44]. It is believed that with balance exercise, there is stimulation of mechanoreceptors present in muscle spindle, Golgi tendon organ and joint capsule leading to improvement inputs of proprioception from foot, ankle and trunk. Repetitive ankle and foot movement while performing exercise also improves proprioception [44,45].

In an Randomised Clinical Trial (RCT) by Ahmed I et al., effect of eight weeks of sensorimotor (balance) training and diabetes and foot care education on postural control was evaluated using Functional Reach Test (FRT), TUG, OLS and Pedalo®- Sensomove balance Test Pro [46]. There was significant improvement found in FRT, TUG, COP range, OLS and proprioception. The improvement was greater in the middle-age group compared to older adults with DPN possibly because of aging and longer duration of DPN [46].

In elderly with DPN, resisted training of lower limb along with ankle strategy training helps in enhancing muscle strength of foot and ankle improves the ability to walk and balance [45-48]. Allet L et al., conducted an RCT on diabetic patients with minimal neuropathy [47]. Experimental group received exercise sessions twice a week for 60 minutes for 12 weeks. Starting with warm up for 5 minutes followed by circuit training for 40 minutes which involved gait and balance exercise (stance on heel/toe, tandem stance, OLS, functional strength training, endurance exercise, walking up and down a slope, sit to stand, mini hops, stair climbing and interactive games like obstacle race and badminton). Tasks were performed twice for one minute and then challenges were added by changing to unstable surfaces, increasing step height. Postintervention, there was improvement in patients' habitual walking speed by 0.149 m/s (0.54 km/h; $p < 0.001$) compared to control group. Also, clinically significant improvement in static and dynamic balance was noted ($p < 0.0026$) [40]. Increased strength of hip and ankle musculature and its mobility could be possible reason for this improvement [45,47]. Similar findings were reported by Pan X and Bai JJ, [48] who reported that weight training for 12 weeks could significantly improve the lower limbs strength and thereby walking ability in patients with DPN [45,48].

Elderly having DPN often suffer with vestibular dysfunction. The sensitivity levels of the vestibular system are attributable to high blood glucose and insulin level, which leads to impaired balance by large anterior translation of the body [7,48]. It also leads to disturbance in integrating information to the brain leading to difficulty in maintaining balance resulting in increased risk of falling. Thus, it is important to train vestibular functions in the form of rotational movement, posture reactive movement etc. It aids in the rapid processing of sensory signals, as well as making the correct judgment motion response through sensory reorganisation [48].

Najafi B et al., used plantar electrical stimulation for improving postural balance and plantar sensation in DPN patients [49]. Transcutaneous Electrical Nerve Stimulation (TENS) (SENSUS®) with duration of 60 minutes with the placement of electrodes in hind and midfoot area was applied daily for six weeks. The post-treatment results were significant and there was improvement in plantar sensation by 27% in the intervention group. These findings were similar to previous studies which stated that following electrical stimulation treatment, there is reduction in vibration perception threshold which further leads to increase chances of monofilament detection in people with DPN [49].

Tai Chi exercise and Thai foot massage are also effective in glucose control, neuropathy score, balance control, improving protective sensation and in improving quality of life in patients with DPN [47]. A systematic review done by Gu Y and Dennis SM included two studies regarding Tai-Chi as an intervention [45]. After Tai-Chi intervention there was significant improvement in single leg stance (baseline 32.5 ± 3.3 seconds to postintervention 34.6 ± 2.4 seconds (6.46%), $p = 0.004$) and reduction in time required for performing 8-foot up and go test (baseline 9.2 ± 3.3 seconds to postintervention

8.3 ± 2.0 seconds, $p = 0.02$). This led to improvement in gait measures like stride length and time spent in single leg support aiding their participation in social life [45].

Balance training can also be given with Biodex Balance System (BBS). BBS is considered to be an effective tool for training balance and postural stability. Eftekhari-Sadat B et al., measured diabetic and peripheral neuropathy subject's ability to maintain balance performing functional tasks using BBS [30]. For balance training, subjects were asked to touch target points using an on-screen cursor with subjects legs placed on the platform. Both static and dynamic balances were assessed by using usual tasks such as reach, standing position and transferences. There was significant reduction observed in TUG, fall risk index with higher changes in berg balance scale. Thus, its result proved that balance training was effective in gaining postural stability and balance in elderly patients with DN [30].

Exercising in people with diabetes is limited in some older people with DPN because they have high risk for falls. So, an alternative intervention is required which effectively addresses the loss of plantar sensation and helps in improving balance, reduces fear of fall and increases participation. Conventional training is not always appropriate for all DPN patients as it decreases the accuracy of exercise performance and has higher risk of excessive plantar loading which could lead to foot ulcers [50]. Grewal G et al., used sensor-based interactive balance training including visual joint movement feedback for enhancing postural stability in patients in DPN [51]. There was significant reduction in centre of mass sway area for intervention group by 53.81% with eyes open. Also, their quality of life and performance of daily physical activities showed improvement [51]. Rao N and Aruin AS used auxiliary sensory clues as a balance prosthesis to improve balance and postural stability in individuals with sensory neuropathy [52]. Sensory clues were provided to the calf with the help of a device similar to Ankle Foot Orthosis (AFO) with no additional stabilisation of the ankle joint. However, no significant improvement in static balance was found [52].

While training elderly population, it is important to start with lower intensity resistance training using major muscle groups. The progression is done gradually by increasing the intensity [53]. A minimum duration of 40 minutes is necessary to have the best effect with strict adherence to exercise protocol [54]. Groups or music mediated sports training and campaign training can help in motivating and encouraging elderly population with DPN to adhere to their exercises [48].

Foot care education, techniques to reduce pressure over diabetic foot and glycaemic control are also important part of management. Offloading plays an important component of treatment in order to prevent or heal foot ulcers [52,55]. Offloading devices of numerous types (soft and shock absorbing materials, custom moulding, forefoot offloading devices and rocker-bottom shoes, total contact casts, walkers and braces) have shown significant improvement [55-57]. When Sorbothane and calcaneal heel pad were used together as an insole material, the shock attenuation was found to be only 18%. However, standing on soft materials further disturbs postural stability [58]. So, while choosing insole material it is important to keep in mind both the offloading effect and its effect on postural stability. High resilience material tends to give more bouncy effects whereas low resilience material has more dampening effects. Thus, low resilience materials offer more stability. Increased plantar contact area leads to improved cutaneous feedback from the plantar surface thus, enhancing inputs for postural control [57]. Wear and tear of shoes could also affect postural stability and could lead to fall [59]. A custom-molded insole fitted inside a fixable shoe gives 20% of offloading in the forefoot but a cast shoe with molded rigid sole gives 48% offloading [Table/Fig-5] [30,44-49,51,52,55,57,60].

Serial No.	Author/Year	Type of the article	Methodology	Result	Remark
1	Eftekhar-Sadat B et al., 2015 [30]	Randomised Controlled Trial (RCT)	Subjects- 44 elderly Diabetic Peripheral Neuropathy (DPN) patients were randomly assigned to one of two groups: intervention (17) or control (17). At the beginning and end of the trial, the Time Up and Go (TUG) test, the Berg balance scale, postural stability tests and the risk of falling were used to assess outcomes. Control group- infrared and TENS: 30 minutes, 3 times/week, 10 sessions Intervention group- same as control group+balance (postural stability) training program using the Biodes Balance System (BBS)- 10 sessions. Balance training: touch targets nine times using an onscreen cursor.	Medial-Lateral index (p=0.04), Anterior-posterior index (p=0.01), fall risk index (p=0.002), TUG (p=0.01), Berg balance scale score (p=0.04), and final stability index (p=0.01) all improved significantly following therapy.	Balance training may improve postural stability and balance in elderly patients with DPN.
2	Ahmad I et al., 2020 [44]	RCT	Subjects- 45-75 years. Total=44, intervention group=22, control group=22. Outcome measure-proprioception- Pedalo@- Sensomove Balance test Pro, nerve conduction test of tibial and peroneal nerve and Electromyography (EMG) to record muscle activity. Control group- diabetic and foot care. Intervention group sensorimotor and gait training+diabetic and foot care. 50-60 minutes of exercise was conducted three times/week for eight weeks.	Intervention group- significant improvement in front, back, left and right proprioception. Nerve Conduction Velocity (NCV)- significant difference in conduction velocity of peroneal nerve p-value=0.007 and for tibial nerve p-value <0.001. EMG- significant changes after intervention observed in tibialis anterior, medial gastrocnemius and multifidus muscle.	Progressive sensorimotor and gait training improved proprioception, nerve and muscle activity function. Due to improvement in proprioception, change in activity of muscle around the ankle and multifidus was found during postural control and walking activity.
3	Gu Y and Dennis SM 2017 [45]	Systematic review	Studies included 10. The evaluation included studies that looked at the effect of exercise training on the risk of falling in adults with Type 2 Diabetes Mellitus (T2DM) and DPN. Lower limb strengthening, balance practice, aerobic exercise, walking programmes, and Tai Chi were all included as interventions in all of the articles.	Balance and walking abilities after a targeted multicomponent program can be improved in people with T2DM and DPN.	People with T2DM and DPN can improve their balance and walking after a targeted multicomponent program without risk of serious adverse events.
4	Ahmad I et al., 2019 [46]	RCT	Subject- Total 37 participation, <60 years- intervention group (n=8) and control group (n=8) ≥60 years- intervention group (n=12) and control group (n=9) Outcome measures- Functional Reach Test (FRT), timed up and go test (TUG), One Leg Stance (OLS), postural assessment and proprioception assessed by Pedalo@- Sensomove balance test. Control group: diabetic and foot care. Intervention group: sensorimotor training+diabetic and foot care eight weeks, with total 24 sessions of 50-60 min exercise each day	Significant improvement in FRT, TUG, Centre of Pressure (COP) range, proprioception. For OLS Eyes Open (EO) and Eyes Closed (EC)- older adults showed smaller changes compared to middle age DPN adults. For FRT and TUG=p-value <0.001 COP range=p-value ≤0.002 Proprioception=p-value ≤0.021	Sensorimotor training improves static as well as dynamic balance measures after eight weeks of treatment. Improvement greater in middle age individuals.
5	Allet L et al., 2010 [47]	RCT	Subjects- 71; intervention group: 35 and control group: 36 Outcome measures- Vibration Perception Threshold (VPT), maximum isometric strength and joint mobility of lower limb, Functional Electrical Stimulation (FES) FES-I Functional test: Performance-Oriented Mobility Assessment (POMA), Outdoor gait assessment with Physiolog system, static and dynamic balance test Intervention group- circuit training involving gait and balance exercises followed by interactive games and home advice. Twice a week, 60 minute for 12 weeks Control group- no treatment, continue usual activities.	Significant improvement in walking speed, balance, risk of falling and performance-oriented mobility was found. There was increased hip flexion range and strength, as well as ankle plantar flexor strength. Walking speed=p-value <0.001 Other outcome measures were significant with p-value <0.0026.	Specific gait and balance exercise improves postural stability in DPN individuals.
6	Pan X and Bai JJ, 2014 [48]	Review	Not mentioned	Proprioception training, vestibular training, lower limb strength training and mixed sports training could enhance balance and reduce its risk of falling in elderly with DPN	To enhance the effectiveness of balance training the form of exercise, duration and its adherence is necessary.
7	Najafi B et al., 2017 [49]	RCT	Subjects- 28 total; IG: 17 and CG: 11. Severity of neuropathy- VPT Validated wearable sensors were used to quantify hip and ankle COM sway, stride length, stride velocity and stride duration, and cadence. Both groups delivered the same plantar electrical stimulation (TENS) devices for 60 minutes. Subjects were instructed to use the device daily for six weeks at home and the device was set to deliver stimulation only to the individuals present in Interrupted Galvanic (IG) Group.	Post therapy, COM and ankle sway with eyes open were significantly improved (p-value <0.05) in the IG group. Gait parameters also showed significant improvement (p-value=0.000). Improvement in VPT (p-value=0.004)	Daily home use of plantar stimulation improves muscle performance and plantar sensation in DPN individuals.
8	Grewal GS et al., 2015 [51]	RCT	Subjects- 20 in control group and 19 in experimental group. Body worn sensor technology used for balance assessment and training. Variables measured were change in hip joint, ankle joint, and CoM sway respectively, while performing a balance test with eyes open and closed. Standard care given to both groups. Intervention group: body worn sensor balance training exercise-ankle reaching task and virtual obstacle crossing task.	Intervention group showed significant differences in COM sway, ankle and hip sway with eyes open. Reduction in ankle sway was observed with eyes closed following treatment (p=0.037)	Sensor-based balance training is effective in improving postural balance. Thus, promotes use of wearable technology during exercise training.
9	Rao N and Aruin AS 2011 [52]	Observational study	Subjects- 12 with diabetic sensory. Computerised Dynamic Posturography (CDP) technique used. Outcome measure: equilibrium score and latency of postural responses. Static and dynamic balance test with or without auxiliary sensory cues given to lower limbs with the subject standing on the force platform.	Group receiving auxiliary sensory cues had significantly higher equilibrium score and less latency score. Improvement followed by auxiliary sensory cues was significant, p-value <0.025	Improves automatic postural responses in standing.

10	Lim JZ et al., 2017 [55]	Review	Search engines: PubMed, MEDLINE, OvidSP and Cochrane Collaboration Database. Keywords: Diabetic foot ulcer, diabetic foot care, neuropathy, management of diabetic foot ulcer, wound dressing and multidisciplinary team. Articles included: Prospective study, RCT and systematic review published up to 11 February 2016.	Persistent hyperglycaemic states result in oxidative stress on nerve cells resulting in motor, autonomic and sensory neuropathy, leading to neuropathic foot ulcers.	Glycaemic control, diabetes and foot care education, medications, and offloading devices helps in preventing further severity of neuropathy and heals ulcers.
11	van Deursen R 2008 [57]	Review	Not mentioned	Thick and soft insoles have been shown to have a negative effect on stability. Low resilience materials seem to provide more stability than high resiliency materials.	Offloading devices creates postural instability so balance training should be incorporated with it.

[Table/Fig-5]: Physiotherapy for improving postural control in DPN [30,44-49,51,52,55,57,60].

CONCLUSION(S)

This review highlights the evidence that reduced sensation including proprioception and muscle strength of distal lower limb lead to multidirectional postural instability in patients with DPN. Early integration of sensory-motor training, balance training and gait training are beneficial in improving postural control in individuals with DPN. In elderly with DPN, vestibular rehabilitation, resistance training of lower limb muscles and ankle strategies training are effective in improving postural control. Foot care education and offloading devices with low resilience materials, helps in improving postural control and reducing risk of foot injury in individuals with DPN.

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