

PREVALENCE OF SUBCLINICAL PERIPHERAL NEUROPATHY BY NERVE CONDUCTION STUDY IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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ABSTRACT

BACKGROUND

The most important and hidden microvascular complication of diabetes mellitus is diabetic neuropathy. Uncontrolled and prolonged hyperglycaemia is associated with subclinical neuropathy in type 1 diabetes mellitus. Assessment of this complication early will be important in prevention of foot complications that occur due to subclinical peripheral neuropathy. The aim of the study is to evaluate the prevalence of subclinical peripheral neuropathy in patients with type 1 diabetes.

METHODS

75 patients who were diagnosed and treated as type 1 diabetes attending the OP of Department of Diabetology- Govt. Mohan Kumaramangalam Medical College and Hospital, Salem, were included in this study during the period of January 2018 to August 2018. The study was conducted after getting ethical committee approval of our institution. The study group consists of 43 males and 32 females. The age at onset, duration of diabetes mellitus, anthropometric measurements, clinical neurological examination and glycaemic assessment were done and recorded. Subclinical peripheral neuropathy was assessed using nerve conduction study at the Department of Neurology at GMKMC, Salem.

RESULTS

Abnormal nerve conduction was found in 20 patients with 2 patients of diabetes duration less than 5 years, 18 patients had duration more than 5 years. Subclinical Peripheral neuropathy has been found in 20 patients out of 75 type 1 DM study population (26%).

CONCLUSIONS

Peripheral neuropathy is a major disabling and reversible complication of diabetes mellitus. Neurological assessment is recommended to detect subclinical neuropathy in asymptomatic type 1 diabetes mellitus. Nerve conduction study which is considered as the gold standard method is helpful for early detection of peripheral neuropathy.

KEYWORDS

Type 1 Diabetes mellitus, Nerve Conduction Study, Peripheral Neuropathy

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BACKGROUND

Diabetic neuropathy is a heterogeneous group of disorders with varied clinical manifestations. Early recognition and

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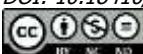
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appropriate management is essential because peripheral neuropathy is a frequent and disabling complication of diabetes mellitus. The incidence of peripheral neuropathy occurring type 1 & Type2 diabetes mellitus at younger age of onset is increasing globally.¹ The Incidence of New case of peripheral neuropathy in type 1 diabetes mellitus was 6.1 per 100 person years.²

Diabetic polyneuropathy constitutes abnormalities of sensory, motor, and autonomic nerve fibers.³ The most common type of diabetic polyneuropathy is symmetrical distal sensory polyneuropathy.⁴ The persistent and longer duration of hyperglycaemia causes alteration in sorbitol

pathway. This leads to increased formation of Advanced Glycosylated End products (AGE), activation of Protein kinase C and increased oxidative stress. This all causes axonal atrophy, degeneration, Conduction abnormalities which leads structural and functional nerve abnormality. The micro vascular insufficiency that occurs due to autonomic dysfunction results in damage to nerves. The neurotropic factors like NGF, Neurotrophin 3, Neurotropic 4/5 and Insulin like growth factors-IGF1 are essential for viability of the neurons. These neurotropic factors are found to be deficient in hyperglycaemic individuals. Hyperglycaemia leads to increased free radical formation which causes endothelial cell dysfunction and is toxic to nerve fibers leading to nerve damage.

Longer axons of lower limbs are more vulnerable for damage due to hyperglycaemia induced lesions (Length related distribution). This is being correlated between the presence of diabetic peripheral neuropathy and height. The most important factors that are associated with DPN are hypoinsulinaemia, poor glycaemic control, longer duration of diabetes mellitus, height hypertension, age, smoking, visceral adiposity and Dyslipidemia. The neurological assessment in a patient with diabetes comprises of comprehensive neurological history besides diabetes, neurological examination and foot examination. The clinical examination of peripheral neuropathy has less specificity and sensitivity. The Michigan neuropathy screening instruments describes the following positive and negative symptoms for detection of peripheral neuropathy. The negative symptoms are numbness over legs and feet, inability to distinguish between hot and cold water, loss of foot sensation. The positive symptoms includes burning sensation over feet, hypersensitivity for normal sensory stimuli like contact with clothes, pricking pain with more of nocturnal symptoms.⁵

The electrophysiological study has advantage of being the most objective specific sensitive and reproducible. Hence nerve conduction studies serve as a gold standard to detect subclinical neuropathy in diabetic patients.⁶ Diabetes affects both peripheral and autonomic nervous system. Diabetic neuropathy can also be classified as subclinical and clinical neuropathy. The subclinical neuropathy implies electrophysiological abnormalities of nerve function without clinical symptoms of peripheral nerve disease. Clinical neuropathy is defined as signs of abnormal neurological examination consistent with peripheral sensorimotor polyneuropathy plus abnormal nerve conduction study in at least 2 peripheral nerves.⁷ 50% of diabetic peripheral polyneuropathy may be asymptomatic. Foot complications occur mostly due to insensate foot caused by diabetic peripheral neuropathy. In such patients if preventive foot care is not implemented, patients are at risk for injuries to their insensitive foot.⁸ There are certain simple clinical tests which may be used to assess small and large fiber function and protective sensation- i. small fiber function- pinprick and temperature sensation. ii. large fiber function- vibration perception and iii. 10 g monofilament test- Protective sensation (LOPS – Loss of Protective Sensation)

The Electrophysiological profile obtained from patients with diabetic peripheral neuropathy constitutes following a) Axonal sensory poly neuropathy b) Axonal motor sensory poly neuropathy) Demyelinating sensorimotor poly neuropathy d) Carpel Tunnel Syndrome e) Normal nerve conduction study.

The prevalence of peripheral neuropathy increases with increase in duration of diabetes mellitus. Most of the type 1 diabetes patients have subclinical neuropathy because of poor glycemic control and younger age of onset with prolonged duration of diabetes. Hence the study was conducted to assess the prevalence of subclinical neuropathy in type 1 diabetic patients.

METHODS

75 patients who were diagnosed as type 1 diabetes and who were on insulin therapy from the onset of diabetes mellitus attending Department of Diabetology. Outpatient services at Government Mohan Kumaramangalam Hospital, Salem, and Tamil Nadu were included for the study during the period of January 2018 to August 2018. The study was conducted after getting Ethical committee approval of our Institution Age, sex, duration of diabetes mellitus, anthropometry measurements and clinical neurological examination were done and recorded. Glycaemic assessment was also recorded. Nerve conduction study in median, Ulnar, Peroneal, Tibial and Sural nerves were done was done in all type 1 diabetic patients enrolled in the study in department of Neurology, GMKMCH, and Salem. Both Motor and sensory nerve conduction in both orthodromic and antidromic stimulation was done. All participants were informed consent was obtained.

Exclusion Criteria

Type 2 diabetes and other types of diabetes mellitus, diabetic patients with symptomatic DN, anaemia, chronic renal failure, liver disease, thyroid disease, and chronic alcoholism were excluded.

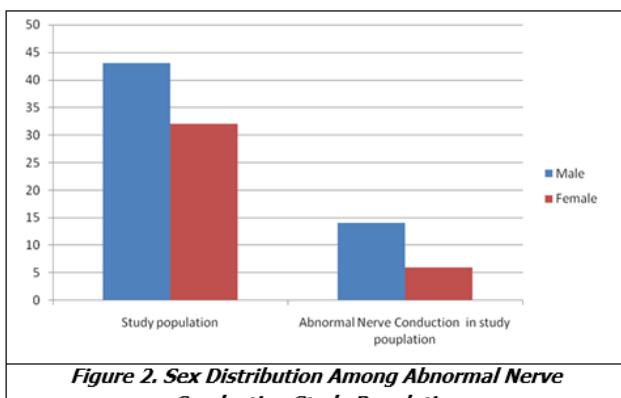
RESULTS

Statistical analysis was done with SPSS Version 16. The total number of patients enrolled in the study is 75. Out of 75, Males are 43, Female are 32. This is depicted in Figure 1. All the patients in the study group were asymptomatic and found negative on clinical examination for peripheral neuropathy. The nerve conduction study found to be abnormal in 20(26%) of the study population which is shown in Table 1. (10 patients found to have sensory demyelinating polyneuropathy, 9 patients were Axonal sensory Polyneuropathy and 1 was sensory motor demyelinating polyneuropathy. The study population comprises of predominantly males and subclinical peripheral neuropathy detected by nerve conduction study also male predominance shown in Figure 2.

Results of Nerve Conduction Study	No's
Normal	55 (74%)
Abnormal	20 (26%)

Table 1. Results of Nerve Conduction Study

Abnormal Nerve Conduction Study According to Age		Total- 20
<25 Years		3(15%)
>25		17(85%)

Table 2. Age & Abnormal Nerve Conduction Study**Figure 2. Sex Distribution Among Abnormal Nerve Conduction Study Population**

Abnormal Nerve Conduction Study and Duration of diabetes		Number
<5 yrs.		2(10%)
>5 yrs.		18(90%)

Table 3. Duration of diabetes & Abnormal Nerve Conduction Study

Chi Square Test				
NCS- n-75				
Duration of diabetes	Abnormal (20)	Normal (55)	ODDs Ratio 95% CI	p-Value
>5 years	18(29.03%)	44(70.97%)	2.25	
<5 Years	2(15.38%)	11(84.62%)	0.45 -11.18	0.31

Table 4. Association Between Duration of diabetes and Nerve Conduction Status (n-75)

Not Significant at p <0.05

DISCUSSION

The diagnosis of subclinical Diabetic Peripheral neuropathy is difficult on clinical grounds because of asymptomatic in nature. In subclinical Diabetic Peripheral neuropathy there is small alteration in nerve dysfunction. Hence nerve conduction study was useful to detect subclinical Diabetic Peripheral neuropathy. The incidence and prevalence of Diabetic Peripheral neuropathy is higher in patients with type 1 diabetes mellitus compare to Type 2 diabetes mellitus. A The population-based study done in Mayo Clinic reveals Type I diabetes mellitus (66%) developing Diabetic Peripheral neuropathy more than Type 2 diabetes mellitus(59%). In a German's population survey study 77% of case with Diabetic peripheral neuropathy found to have unaware of having the deficit in sensory function of lower limbs. Hence true prevalence will still be higher if proper foot examination and nerve conduction study done in all patients with long duration of diabetes. Attention to diabetic foot preventive practice is essential for all patients with longer duration of diabetes.

Hyllienmark et al, in his study group reported, subclinical neuropathy in type 1 diabetes predates clinical neuropathy many years later which was confirmed by pathological finding in distal nerves in one fourth of patients.⁹ Few follow up studies showed significant association between abnormalities that is detected early by electrophysiological studies ahead of clinical neuropathy.¹⁰ Diabetic neuropathy ranges from asymptomatic to

symptomatic but once established as neuropathy, it becomes irreversible resulting in disability.¹¹ Hence diagnosis of DPN (Diabetic Peripheral Neuropathy) early is important for intervention to decrease this complication and disability.¹² It is difficult to diagnose DPN early by clinical methods because of the minor alteration in nerve function. Hence, NCS (Nerve Conduction Study) is being used widely for evaluation and prediction of DPN.¹³ The present study revealed 26% of type 1 diabetes who were free from symptoms and signs of DPN had subclinical neuropathy. The frequency of DPN was higher in patients with duration of diabetes more than 5 years in our study also. This highlights Global recommendations of screening of neuropathy in all type 1 DM of more than 5 years duration of disease. The prevalence of DPN is low in study conducted at the time of diagnosis of DM. Poor glycaemic control as suggested as strongest predictor of development and progression of clinical and subclinical neuropathy.¹⁴ Some study reported high prevalence of 80% to 87% of subclinical neuropathy in type 1 diabetes mellitus and this could be due to different diagnostic methods, onset and duration of diabetes mellitus.

The development and progression of neuropathy could be prevented by good glycaemic control during first 5 years of onset of diabetes.¹⁵ Aberg ML study demonstrates that Males developed neuropathy earlier than females and early intervention in males improve disease outcome. In our study there is higher predominance of males having abnormalities in Nerve conduction.¹⁶ As diabetes sensory peripheral neuropathy is important complication to foot ulcer and lower limb amputation, an early detection of diabetes sensory peripheral neuropathy is of paramount importance. Nerve conduction velocity and vibration perception threshold which measures neuropathy predicts mortality in patients with diabetes. The corneal confocal microscopy (CCM) is emerging as non-invasive modality for early detection of small fiber neuropathy in diabetes mellitus. The genomic predisposition for developing Diabetic Peripheral Neuropathy in diabetes mellitus has proven in several studies. When family history of Diabetic peripheral neuropathy present they should screened early for subclinical peripheral neuropathy to prevent complications like injuries, foot ulcers.

CONCLUSIONS

Peripheral Neuropathy in diabetes mellitus is the most important dreadful and preventable micro vascular complication. There are no useful prophylaxis and treatment for the common sensory motor polyneuropathy occurring in diabetes mellitus despite decades of basic and clinical research in this field. Early screening and good glycaemic control will be helpful in preventing this complication. The results of current study highlight the importance of screening for subclinical neuropathy in all type 1 diabetes mellitus patients of duration of more than 5 years. This has been recommended in various global guidelines. The symptoms of Diabetic Peripheral Neuropathy are variable. Subclinical neuropathy predicts clinical neuropathy later in diabetic individuals. Nerve Conduction Study is the gold standard for the detection of subclinical neuropathy. Hence

neurological assessment has to be done in all type 1 diabetes of more than 5 years duration to detect subclinical neuropathy.

Limitations

HbA1c was not done in our study hence the Glycaemic state of patient could not be correlated with nerve conduction abnormality.

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