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Relationship between Diabetes Mellitus and Peripheral Neuropathy

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ABSTRACT

Diabetes mellitus is a public health problem worldwide, with diabetic neuropathy (DN) being a common complication. Studies indicate that, neurons can develop insulin resistance (IR) and cannot respond to the neurotrophic properties of insulin. Although studies exist on the relation between DN and glycemic exposure index (GEi), papers about correlation of DN with IR is rare. This study focused on the prevalence of neuropathies in DM patients.

INTRODUCTION

Diabetes mellitus is a major public health problem both in developing and developed world. There is an alarming increase in the incidence and prevalence of diabetes mellitus particularly in Asian Indians [1], due to increased predilection for them to develop the disease. There is evidence showing that South Asians have greater insulin resistance even at comparable levels of total body fat percent and BMI, India (31.7 million) had the highest number of people with diabetes mellitus in world followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively[2].

Diabetes is a complex metabolic disorder characterized by hyperglycemia and associated microvascular and macrovascular complications. Though macrovascular complications like cardiovascular diseases are major contributors to mortality, microvascular complications lead to prolonged morbidity, functional impairment and economic burden. Among microvascular complications, Diabetic neuropathy is a common and costly

complication of both Type 1 and Type 2 Diabetes as well as the leading cause of non-traumatic lower limb amputations[3].

Risk factors for development of diabetic neuropathy and it's types

The exact cause of each type of neuropathy is unknown and any patient with diabetes can develop neuropathy but these risk factors makes it more likely to get nerve damage:

1-**Poor blood sugar control**

2-Diabetes history

3-Kidney disease

4-Being overweight

5-Smoking

Types of diabetic neuropathy include

1-Peripheral Neuropathy

Peripheral diabetic neuropathy goes by various names: peripheral diabetic nerve pain and distal polyneuropathy, Peripheral neuropathy is the most common form of neuropathy caused by diabetes[4]. It affects nerves leading to extremities—to the feet, legs, hands, and arms. This nerve damage can lead to the foot problems often associated with diabetes, including foot deformities, infections, ulcers, and amputations.

2-Proximal Neuropathy

Proximal neuropathy can also be called diabetic amyotrophy. That *myo* in the word means muscle, so this is a form of neuropathy that can cause

muscle weakness. It specifically affects the muscles in the upper part of the leg(s), buttocks, and hips.

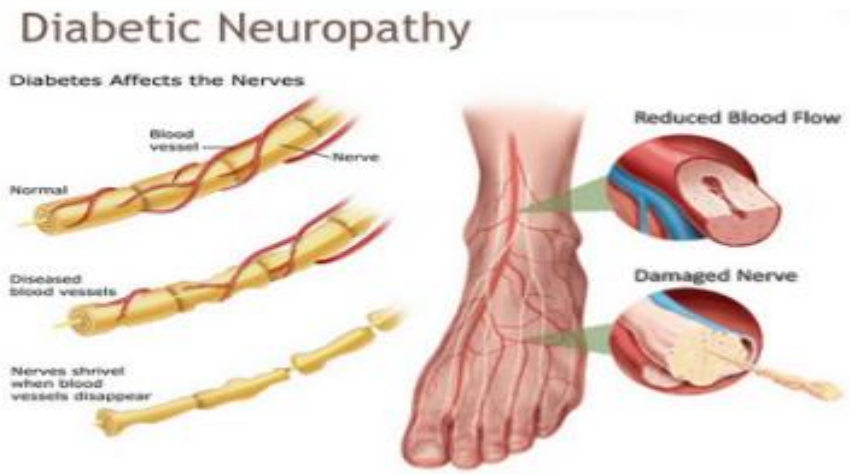
Proximal neuropathy is the second most common type of diabetic neuropathy (second only to peripheral diabetic neuropathy). It usually affects elderly people with diabetes; as opposed to peripheral neuropathy, it usually resolves with time or treatment.

3-Autonomic Neuropathy

Autonomic neuropathy is a group of symptoms that occur when there is damage to the nerves that manage every day body functions. These functions include blood pressure, heart rate, sweating, bowel and bladder emptying, and digestion.

4-Focal Neuropathy

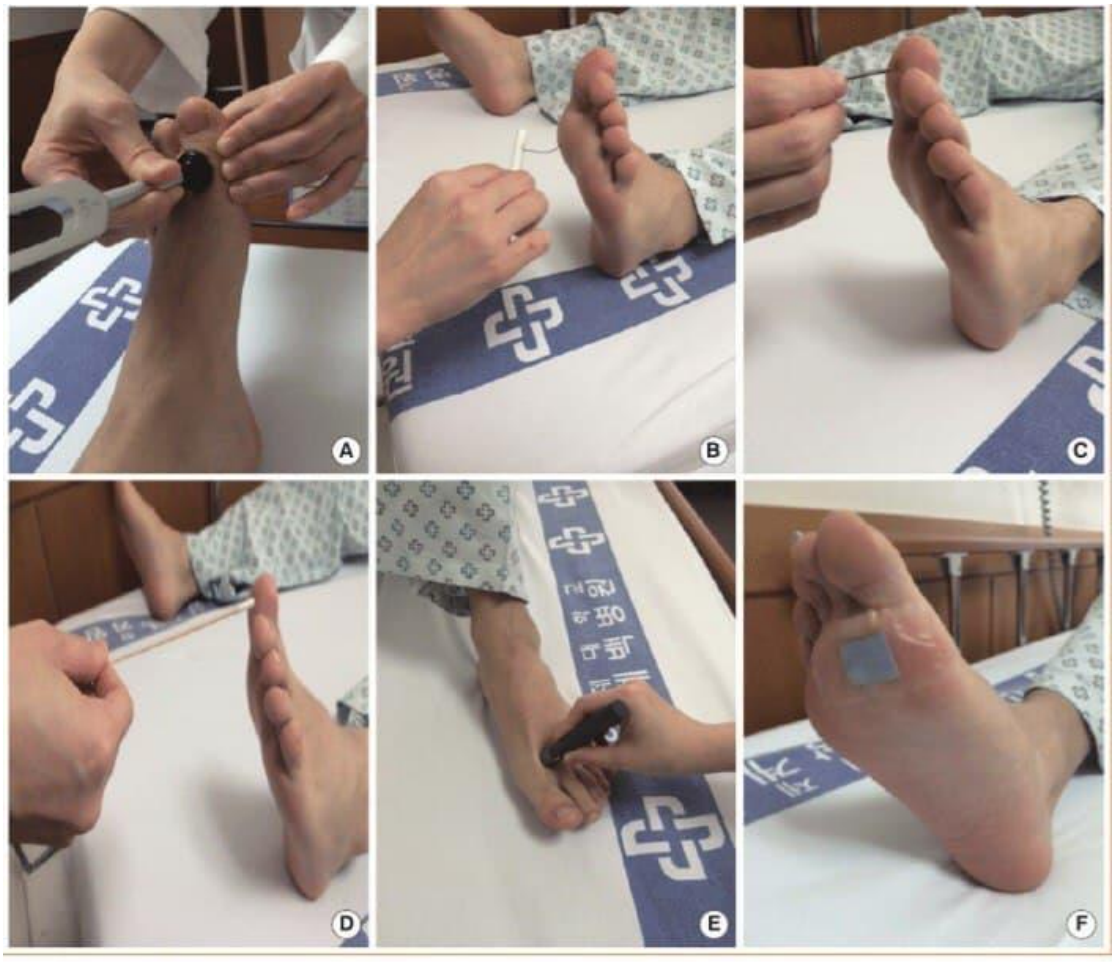
All of the types of diabetic neuropathy above—peripheral, autonomic, and proximal—are examples of polyneuropathy. *Poly* means that they affect many nerves. Focal neuropathy, by contrast, affects one specific nerve; it's *focused* neuropathy. Focal neuropathy, which comes on suddenly, most often affects nerves in the head. It can also affect the torso and legs[5]. Focal neuropathy, causes pain in very specific locations on the legs.



CREENING AND DIAGNOSTIC

MODALITIES FOR DPN

Assessments of pressure sensation, vibration, thermal, and pain thresholds are used as screening tools for patients “at risk” for foot ulcerations [6]. Although there is a lack of uniform guidelines on diagnosis and interpretation of the results from a neurological examination, it is generally accepted that DPN should be diagnosed based on more than one diagnostic test rather than on one symptom, sign, or test alone [7].



Figuer2: Bedside neurological and sensory nerve testing. (A) Vibration. Patients are notified when they cannot feel the vibrations from a

-128Hz tuning fork (first interphalangeal joint of the great toe) when the toes are extended, and the investigator feels the vibration and

measures the time when the feeling disappeared. A time difference ≥10 seconds between the investigator and the patient is considered

abnormal [8]. (B) Pressure: 10-g monofilaments are pressed on 10 points on the sole and dorsum of the feet until the monofilament be-

gins to bend (100 mN). If the patient has sensation in fewer than seven points, the results is considered abnormal [9]. Four sites per foot ,

such as the hallux and metatarsal heads 1, 3, and 5, should be screened [10]. (C) Noxious stimuli and (D) light touch. The patient is

touched on the foot using a sterile pin, toothpick, and cotton wisp and asked to identify a “sharp or dull” or “light touch” with their eyes

closed [11]. (E) Warm/cold. Tip-therm (temperature discriminator; AXON GmbH) is a pen-like device with a plastic cylinder on one end

and a metal cylinder on the other end, which is applied to the dorsum of each foot at irregular intervals so patients can identify the sensa-

tion as cold or not with their eyes closed [12]. (F) Sudomotor function. Indicator tests (Neuropad, miro Verbandstoffe) are applied to both

soles at the level of the first and second metatarsal heads. The time to color change from blue to pink is more than 10 seconds; the result.

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METHODS A cross sectional observational study was done .All patients satisfying American Diabetes Association criteria and none of the exclusion criteria were included. Total sample size was 142. Main parameters studied were glycemic status, neurological examination and nerve conduction study findings. Dyck grading was used for severity of distal symmetric polyneuropathy (DSPN). For statistical analysis, logistic and ordinal logistic regressions were used as appropriate.

Results

34.5% of the sample had DN, the commonest type being DSPN (72.9%). The study population
was equally divided in terms of gender and 88.7% were type 2 diabetic. About 62.5% neuropathic cases were asymptomatic. Occurrence of DN correlated significantly with duration
of diabetes, FBS and IR. Age, when adjusted for other risk factors was not significantly correlated to neuropathy.
There was no significant difference in neuropathy occurrence between males and females unlike some studies which show
male propensity to develop microvascular complications.

potentially modifiable risk factors that could be addressed early to manage

DPN effectively:

1) Hyperglycaemia

Chronic hyperglycaemia plays a key role in the pathogenesis of DPN [13,14]. Through several disturbances in the metabolic pathways, hyperglycaemia leads to abnormalities in nerve polyol, hexosamine and protein kinase C pathways [15]. This triggers the release of

proinflammatory cytokines [poly ADP-ribose polymerase (PARP)], the accumulation of advanced glycation end products (AGEs) and generation of reactive oxygen species [16]

Simultaneously, microangiopathic changes of the vasa nervorum result in neuroischaemia [17]. In the Diabetes Control and Complications Trial (DCCT) intensive insulin treatment in T1DM reduced the risk of DPN (78% relative risk reduction) [18,19].

2) Dyslipidaemia

Observational and cross-sectional studies have demonstrated, to varying degrees, an association between hyperlipidaemia and DPN [20]. The strongest evidence, however, is for the association of elevated levels of triglycerides and DPN [21]. In a study of patients with

T2DM there was a graded relationship between triglyceride levels and the risk of lower-limb amputations [22]. In addition to hypertriglyceridemia, low-level of HDL cholesterol has beenreported as an independent risk factor for DPN [23]. Two subsequent, relatively small, randomised clinical studies have reported improvements in nerve conduction parameters of DPN following 6 to 12 weeks of statin treatment [24,25].

3) Hypertension

An association between hypertension and DPN has been demonstrated in several observational studies in both T2DM [26,27] and T1DM [28]. There is some preliminary evidence from relatively small randomised control trials with improvements in DPN based on

clinical and nerve conduction parameters following antihypertensive treatment with angiotensin converting enzyme (ACE) inhibitors [29] and calcium channel blockers [30].

4) Lifestyle

Several studies have revealed an association between obesity and DPN even in the presence of normoglycaemia [31-32]. Not surprisingly, DPN prevalence increases in obese patients with prediabetes and diabetes [33]. Subsequent studies appear to demonstrate that adopting a healthy lifestyle incorporating a balanced diet, regular aerobic
and weight-resistance physical activities may reverse the process, particularly if they are undertaken at an early stage of DPN [34-35].

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