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A CASE STUDY ON GLYCEMIC INDEX AND DIABETIC PERIPHERAL NEUROPATHY

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ABSTRACT: The term HbA1c refers to glycated haemoglobin. By measuring glycated haemoglobin (HbA1c), clinicians are able to get an overall picture of what our average blood sugar levels have been over a period of weeks/months. Diabetic neuropathy is generally assessed in clinical practice by a combination of objective and subjective measures. Nerve conduction studies, the distal sural sensory nerves and the bilateral common peroneal and posterior tibial motor nerve was performed in lower limb in female patient of 20-years old suffering from type-I diabetes from past 10-yeras and had poor glycemic control (haemoglobin [HbA1c] 9.56%). Studies showed motor conduction studies (MNCV) and sensory conduction studies (SNCV) of the lower extremities, revealed borderline- prolonged distal latencies, evoked CMAPs of reduced amplitude of common peroneal, posterior tibial (right and left) with reduced conduction velocity was observed and however sural SNAP amplitude recordings in lower limb was normal. F response latencies were markedly prolonged in patient. Electro-diagnostic techniques play an important role in the prognosis of diabetic neuropathy because timely intervention reduces disability and morbidity.

INTRODUCTION: Diabetic neuropathies are a disabling complication of diabetes mellitus. Clinical sign and symptom of neuropathy are seen in approximately 20% of the diabetic patient. Diabetic neuropathy is one of the most common complications of diabetes mellitus (DM). Approximately 10-50% of diabetic patients have some degree of diabetic neuropathy [1], independent of the type of DM (45% with type 2 and 54% with type- 1, according to the Rochester Diabetic Neuropathy Study) [2]. Diabetes is major risk factor for all entrapment neuropathies. Symmetric polyneuropathies start with paresthesias of feet and legs in typical length related pattern, the upper limb is rarely affected affected [3].

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This is a length-dependent process, with the most distal portions of the longest nerves affected earliest. Thus, the earliest symptoms typically involve the toes, and then ascend. The arms are involved later, less often and less severely, also in a distal-to-proximal pattern. The term HbA1c refers to glycated haemoglobin. It develops when haemoglobin, a protein within red blood cells that carries oxygen throughout our body, joins with glucose in the blood, becoming 'glycated'. By measuring glycated haemoglobin (HbA1c), clinicians are able to get an overall picture of what our average blood sugar levels have been over a period of weeks/months. For people with diabetes this is important as the higher the HbA1c, the greater the risk of developing diabetes-related complications. Nerve conduction studies (NCS) are the most sensitive and specific DPN detection method [4], their use is recommended for quantitative confirmation DPN in clinical practice [5]. Expanded access to NCS has the potential for early diagnosis and improved outcomes [6].

Case study:

The patient was 20-years old female. She had type-I diabetes from past 10-yeras. She went for cataract surgery in both eyes five years back. She had no previous evidence of diabetic retinopathy. According to patient she was apparently alright 2-month back then she felt progressive weakness in lower limb and which start distally later on, not able to perform her daily routine work comfortably. Upper limb was normal and there was no report of felling of dizziness and vomiting. She had good appetite, usual sleep and abdomen was distended with normal bowel sound. She doesn't visit physician regularly and had poor glycemic control (haemoglobin [HbA1C] 9.56%). Patient appears unwell.

Physical examination:

Revealed the following: normal weight, blood pressure (110/70), heart rate (100-betas/min), respiratory rate (30-breath/min) and body temperature (38.4^0c). Family history includes, the patient's mother, father and one brother was alive and well without any medical illness. She had no habit of smoking and drinking alcohol. The chest was normal along with normal heart and breathes sound.

Laboratory evaluation:

The patient liver function test: SGOT (AST) - 24.0 (0 to 45 U/L, SGPT (ALT) - 15.0 (0 to 45 U/L), renal function test: Na^+ - 128 mEq/L (132-144), K^+- 4.3mEq/L(3.5-5.5), Urea-32.0(20-40 mg/dl), BUN-13.33(8-25mg/dl), creatinine- 0.73(0.6-1.3 mg/dl), uric acid-2.60(2.4-7.0mg/dl), urine volume was normal and acidic(ph-6.6), spgravity-1.020.urine protein -0.20, albumin-nil, ketone bodies-nil, epithelial cell, WBC cell and RBC cell-nil and the patient blood report: haemoglobin - 9.9g/dl(9-12), ESR-13mm/hr(0-5), MCV-85fl(80-95), WBC- 4.2×10^3(4-11), platelets-180×10^3µl(150-400). On clinical examination we found that, there was diffuse weakness in lower limb (**Fig.1**), distal was greater (grade 3**)** than proximal (grade 4). Muscle tone was decreased. Muscle stretch reflexes were absent. No pathologic reflexes were present. On neurological examination, the patient was alert and oriented with intact speech and memory, pupils equally reactive to light. His cranial nerve exam was intact. His sensation was intact on both upper and lower extremities.

Electro diagnostic investigation:

Nerve conduction study (NCS) was carried out in a quiet room of neurophysiology laboratory at a temperature of 26^0 to 30^0C by using Neuroperfect-2000. Skin temperatures were recorded and maintained above 32°C for all recordings. Nerve conduction studies were performed using standard techniques of supramaximal percutaneous stimulation and surface recording. The nerves (Common peroneal, posterior tibial for motor and sural for sensory) in lower limb were stimulated sub-cutaneous along their course where they are relatively superficial. The skin resistance was reduced by rubbing with spirit swab; the active electrode was placed over muscle belly and reference electrode over tendon. Amplitudes of compound muscle action potentials (CMAPs) were measured from baseline to negative peak and were reported for stimulation at distal and proximal sites; conduction velocity was measured in the lower limb.

Evidence of abnormal temporal dispersion was estimated by comparing proximal and distal CMAP amplitudes, F response latencies were measured as the minimal latency in a series of F responses following distal (wrist or ankle) motor nerve stimulation. Sensory nerve action potential (SNAP) amplitudes were measured peak to peak.

Nerve Conduction Studies showed motor conduction studies (MNCV) and sensory conduction studies (SNCV) of the lower extremities, revealed borderline- prolonged distal latencies, evoked CMAPs of reduced amplitude of common peroneal, posterior tibial (right and left) with reduced conduction velocity was observed and however sural SNAP amplitude recordings in lower limb (**Table 1, 2, Fig. 2**) was normal. F wave studies have been established as a valuable tool in clinical neuro-physiology [7]. F wave studies included F wave conduction velocity and F wave latency. F wave is a late response resulting from antidromic activation of motor neurons involving conduction to and from spinal cord. F response latencies were markedly prolonged in patient (**Table 3**).

TABLE 1: MNCV (LOWER LIMB)

Nerve	Rec – Stim Site	Distance (mm)	Latency difference(ms)	NCV(m/s)
Rt. CPN	EDB- ANKLE	75	6.38	11.75
	EDB-FIB.HEAD	410	9.54	42.97
Lt. CPN	EDB- ANKLE	80	5.88	13.60
	EDB-FIB.HEAD	415	8.40	49.40
Rt. PTN	Abd. Halls- ANKLE	105	7.85	13.37
	Abd. Halls- POP. FOSSA	420	11.63	36.11
Lt. PTN	Abd. Halls- ANKLE	105	6.50	16.15
	Abd. Halls- POP. FOSSA	425	10.50	40.47

TABLE 2: SNCV (LOWER LIMB)

Nerve	Rec – Stim Site	Distance (mm)	Latency difference (ms)	NCV (m/s)
Rt. SURAL	Laterals Malls-MID CALF	165	2.75	60.00
Lt. SURAL	Laterals Malls- MID CALF	170	2.80	60.71

TABLE 3: F WAVE (LOWER LIMB)

Nerve	Distance (mm)	Latency difference (ms)	Velocity (m/s)
Rt. CPN	92	25.23	3.64
Lt. CPN	85	24.25	3.50
Rt. PTN	100	25.50	3.93
Lt. PTN	105	22.26	4.71

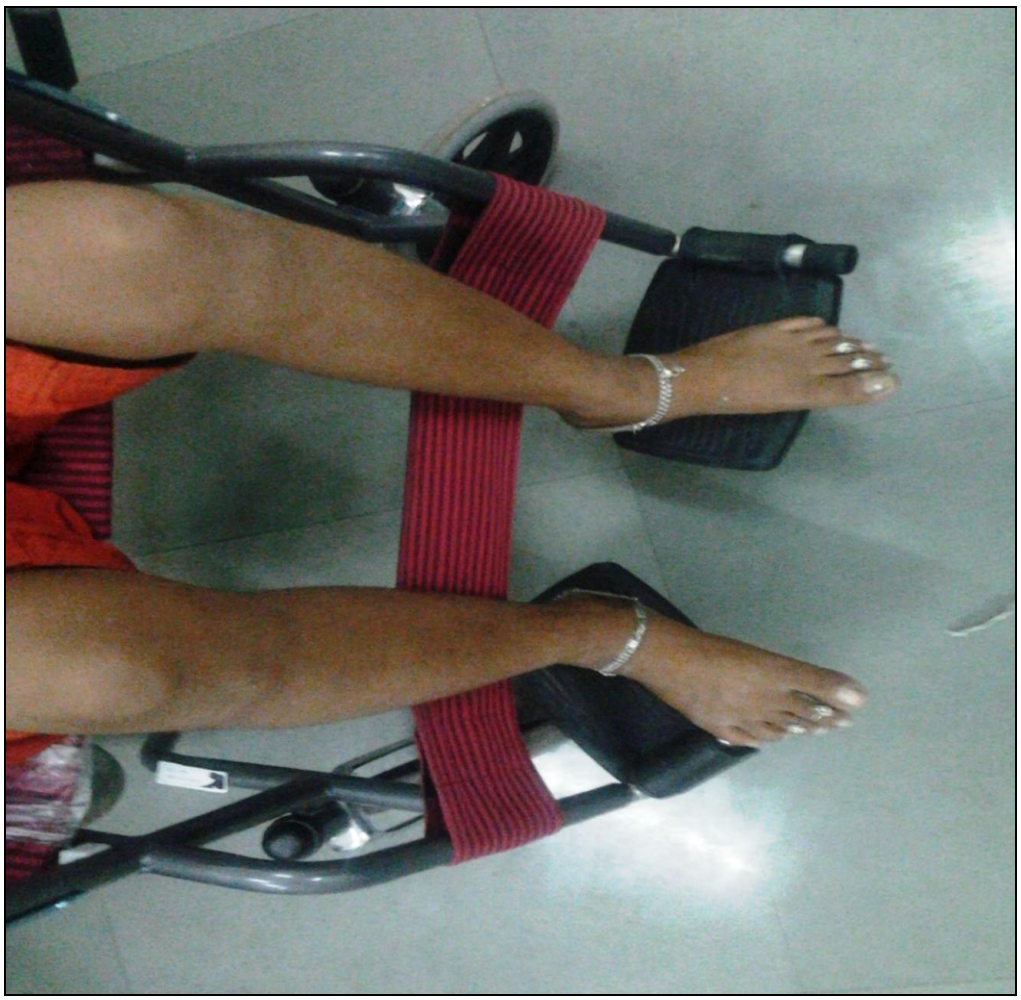

FIG.1: BILATERAL MUSCLE ATROPHY IN LOWER LIMB.

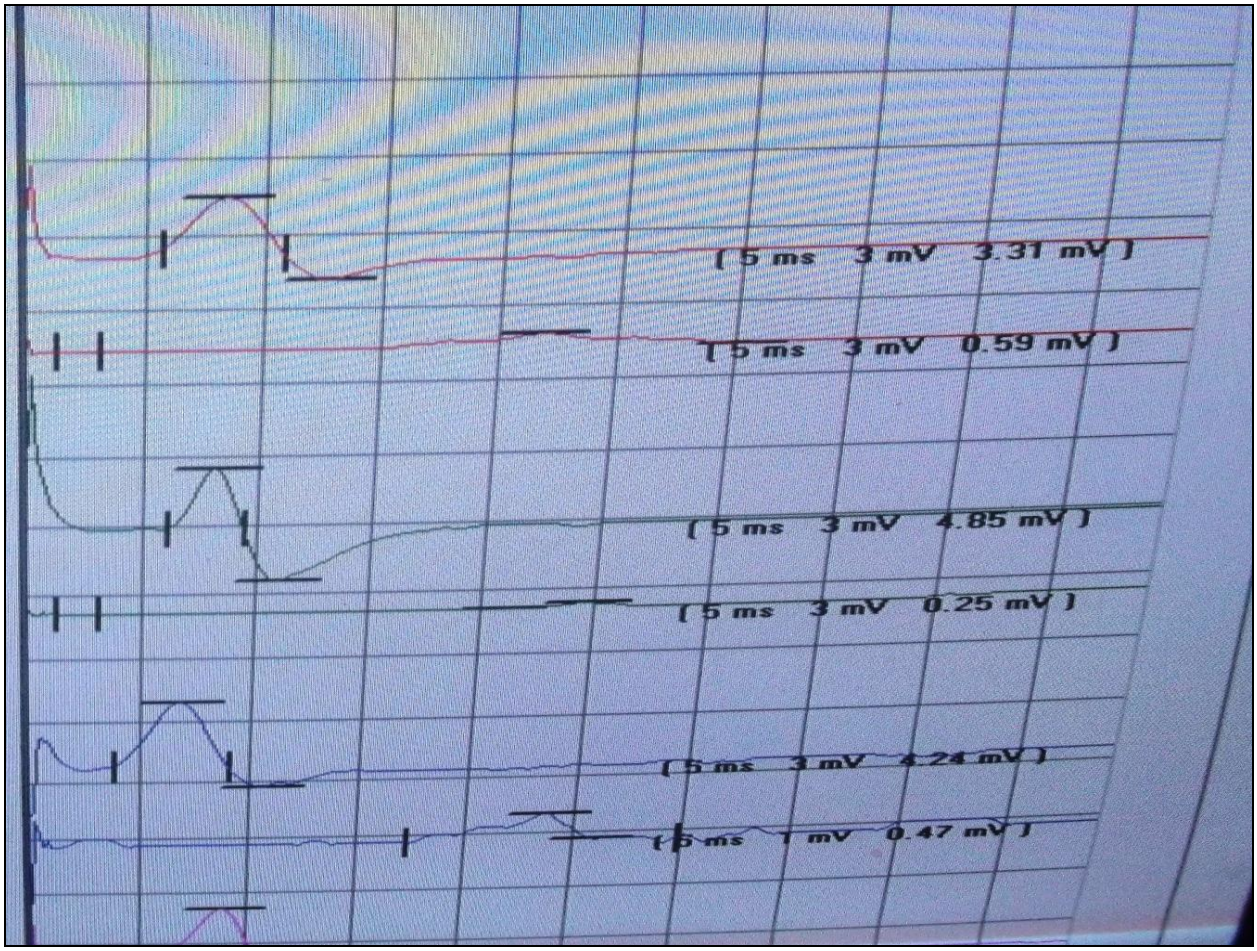

FIG.2: MNCV AND SNCV RECORDING OF LOWER LIMB.

DISCUSSION: In Electrodiagnostic Studies (EMG/NCS), neuropathy is usually classified as both axonal and demyelinating [8]. Metabolic and vascular/hypoxic factors appear to be involved in diabetic polyneuropathy [9]. Advanced glycosylation end products may damage capillaries, inhibit axonal transport, Na+/K+-ATPase activity and cause axonal degeneration. Hyperglycemia and increased intracellular glucose may saturate normal glycolysis. Extra glucose may enter the polyol pathway and activates aldose, which converts it to fructose and sorbitol. Their accumulation results in reduced nerve myoinositol and membrane Na^+/K^+-ATPase activity, impaired axonal transport, and structural damage. Nerve ischemia may result from increased endoneurial vascular resistance to hyperglycemic blood. Control of hyperglycemia delays the appearance of neuropathy and slows progression.

The Diabetes Control and Complications Trial found that intensive IDDM therapy reduced the frequency of neuropathy by 60% over 5 years [10]. Aldose reductase inhibitors (ARIs) such as sorbinil, alrestatin and tolrestat have been studied as a means to prevent or improve polyneuropathy. They act by reducing the flux of glucose through the polyol pathway [1, 11]. Glycation of hemoglobin has been associated with cardiovascular disease, nephropathy and retinopathy in diabetes mellitus[12]. The Diabetes Control and Complications Trial (DCCT) established a clear link between impaired glycemic control and neuropathy [13]. The longer duration and more poorly controlled diabetic may increase risk of neuropathy. Distal painful extremity parenthesias may occur after initiation of insulin therapy and achievement of normoglycemic state axonal nerve injury occurs as glucose is not available for nerve metabolism. However with normalization of blood glucose with insulin symptoms resolves. Intensive glycemic control slows the progression of DPN but does not prevent or arrest its development [14].

CONCLUSION: Electro-diagnostic techniques play an important role in the prognosis of diabetic

neuropathy because timely intervention reduces disability and morbidity. The care of a diabetic neuropathy patient is challenging for the health care team. The acute progression of motor weakness and fatigue makes a profound effect on the patient's healthy life. Intensive glycemic control slows the progression of DPN but does not prevent or arrest its development.

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CONFLICT OF INTEREST: The authors declared no conflict of interest.

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