

Glycaemic status and insulin resistance in diabetic peripheral neuropathy

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Abstract

Background: Complication of diabetes mellitus includes peripheral neuropathy which causes ischemic foot ulceration. Hyperglycemia and insulin resistance may accelerate the development of diabetic peripheral neuropathy. **Objective:** To assess the glycaemic status and insulin resistance for development of peripheral neuropathy in type 2 diabetes mellitus. **Methods:** This control case control study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2014 to June 2015. A total number of 150 Type 2 diabetic patients of both sexes were selected with age ranging 40 to 50 years. Among them, 75 patients with peripheral neuropathy were included in study group and 75 patients without peripheral neuropathy were control. For evaluation of glycaemic status, fasting serum glucose (FSG), Glycosylated hemoglobin (HbA1c) and to calculate insulin resistance by homeostatic model assessment for insulin resistance (HOMA-IR), fasting serum insulin (FSI), were estimated. For statistical analysis, unpaired Student's 't' test was done. **Results:** In this study, significant increase in FSG, HbA1c, FSI, HOMA-IR were found in diabetic subjects with peripheral neuropathy in comparison to control group. **Conclusion:** From the study results, it is concluded that poor glycaemic control and greater insulin resistance may be associated with diabetic peripheral neuropathy.

Key words: Diabetes mellitus, peripheral neuropathy, glycaemic status, insulin resistance.

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Introduction

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia caused by relative or absolute deficiency of insulin in the body¹. According to World Health Organization (WHO 2005) diagnostic criteria of diabetes mellitus are fasting blood glucose ≥ 7.0 mmol/L, 2 hour after glucose ≥ 11.1 mmol/L and HbA_{1c} $\geq 6.5\%$ ². According to International Diabetic Federation (IDF), there were 382 million people had diabetes in 2013 and by the year 2035, this will rise to 592 million, whereas the national prevalence in Bangladesh is about 5.52%³.

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Chronic complications of DM are microvascular complications and macrovascular complications. The microvascular complications are retinopathy, neuropathy and nephropathy. Peripheral neuropathy is one of the most common complication in patients with type 2 diabetes mellitus⁴.

In peripheral neuropathy, damage involves autonomic, motor and sensory nerves in the peripheral nervous system, sparing neurons in the central nervous system⁵. American Diabetes Association (ADA) published a statement on diabetic neuropathies as "the presence of symptoms and/or signs of peripheral nerve

dysfunction in people with diabetes after exclusion of other causes". Diabetic peripheral neuropathy (DPN) can affect 20%-50% of the population with diabetes⁶. A study reported that the prevalence of DPN in Bangladesh is about 19.7%⁷.

Several studies suggested that chronic hyperglycemia is the important risk factor for development of neuropathy. Good glycaemic control can improve the symptoms of neuropathy in type 2 diabetic patients. Some researchers showed that intensified metabolic control can prevent or delay the development of diabetic peripheral neuropathy. Glycosylated hemoglobin act as an index of long term diabetes control and HbA_{1c} > 7.0% is considered as good glycaemic control^{8,9}.

Hyperinsulinemia and insulin resistance is a major feature of type 2 diabetes. Various physiological dysfunctions and several neurological syndromes can occur due to insulin resistance^{10,11}. Neuronally targeted insulin treatment can improve sign of neuropathy without altering blood glucose levels¹³.

Various group of researchers showed the correlation among hyperglycemia, insulin resistance and DPN and they also reported that the prevalence of DPN are increasing. However, very little research work has been conducted to observe the effects of hyperglycemia, insulin resistance on peripheral neuropathy among the diabetic patients. So the aim of this study is to assess the glycaemic status and insulin resistance to find out their association with peripheral neuropathy in type-2 diabetic patients.

Methods

This case control study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2014 to June 2015. Protocol of this study was approved by Ethical review committee of Dhaka Medical College, Dhaka. For this study 75 diagnosed type 2 diabetes mellitus patients with peripheral

neuropathy (DPN) of both sexes with age ranging 40 to 50 years were case. Selection of DPN was based on sign, symptom of PN such as numbness, burning sensation, tingling sensation, fatigue, cramping pain and diagnosis was confirmed by nerve conduction velocity (NCV). They were selected from indoor and outpatients department of BIRDEM general hospital. Diagnosis was done by FSG ≥ 7.0 mmol/L and HbA_{1c} $\geq 6.5\%$ ². 75 age matched type 2 diabetic subjects without peripheral neuropathy were considered as control for comparison. After selection of subjects, the nature, purpose, benefits of the study were explained to each subject in details. Informed written consent was taken from the participants. Before taking blood, detail family and medical history were taken. Anthropometric measurement of the subject was done and blood pressure was measured. All the information were recorded in a prefixed data schedule. With aseptic precaution, 5 ml of venous blood was collected from antecubital vein by a disposable plastic syringe from each subject for estimation of FSG, HbA_{1c}, fasting serum insulin in the Department of Biochemistry of National Institute of ENT, Dhaka. NCV of each subject was determined in Department of Neurology of BIRDEM general hospital. All the parameters were expressed as mean \pm SE. Statistical analysis was done by unpaired Student's 't' test. p value ≤ 0.05 was accepted as level of significance. Statistical analysis were performed by using a computer based statistical program SPSS (version 20).

Results

General characteristics are presented in table I. There were no significant differences in any parameter between case and control.

Mean FSG, HbA_{1c}, FSI and HOMA-IR were significantly ($P < 0.001$) higher in case compared to control (Table II).

Among the cases 58.7% had FSG > 7 , 84% had HbA_{1c} > 6.5 and 88% had HOMA-IR > 2.5 . Similarly in the control subjects 10.7% had FSG > 7 , 50.7% had HbA_{1c} > 6.5 and 8% had HOMA-IR > 2.5 (Table III).

Table I: General characteristics of the subjects in both groups (n=150)

Parameters	Control (n=75)	Case (n=75)
Age (years) mean±SE	43.69±0.715	45.87±0.729 ^{ns}
Male no (%)	38 (50.7%)	41 (54.7%)
Female no (%)	37 (49.3%)	34 (45.3%)
Systolic blood pressure (mmHg) mean±SE	117.53±0.653	120.67±0.761
Diastolic blood pressure (mmHg) mean± SE	78.13±0.401	80.13±0.401

Unpaired Student's 't' test and Chi square test were performed for statistical analysis.

Table II: FSG, HbA_{1c}, FSI, HOMA-IR parameters in two groups (n=150)

Parameters	Control (n=75)	Case (n=75)
FSG (mmol/L)	5.31±0.167	8.09±0.315 ^{***}
HbA _{1c} (%)	6.25±0.101	7.93±0.192 ^{***}
FSI (μIU/ml)	6.94±0.419	29.03±1.181 ^{***}
HOMA IR	1.29±0.064	4.13±0.235 ^{***}

Data were expressed as mean ± SE. Statistical analysis was done by Unpaired Student's 't' test. FSG=Fasting serum glucose; FSI=Fasting serum insulin; HOMA IR=Homeostatic model assessment for Insulin resistance. *** p value <0.001

Table III: Distribution of the subjects by different parameters in both groups (n=150)

Parameters	Case (n=50) No (%)	Control (n=50) No (%)
Fasting serum glucose (mmol/L)		
≥ 7 HbA _{1c} (%)	44 (88.0)	8 (16.0)
≥ 6.5 HOMA IR	63 (126.0)	38 (76.0)
≥ 2.5	66 (132.0)	6 (12.0)

n = number of subjects

Discussion

In the present study, higher FSG and HbA_{1c} levels in diabetic patients with peripheral neuropathy compared to diabetic patients without peripheral neuropathy were observed. This finding agrees to others^{7,16-20}. But Ashok et al. found lower FSG and HbA_{1c}²¹. In DPN patients, Morkrid, Ali and Hussain found borderline HbA_{1c} in them⁷. In addition, observed higher HOMA-IR in DPN

patients in this study is consistent with others observations^{10, 22,23}.

In this study abnormally elevated FSG, HbA_{1c} and HOMA-IR was found with higher frequency of DPN than without DPN. Similar observations are reported by others^{7,16-20}.

Suggested that chronic hyperglycaemia activate variety of mechanisms that are likely to be

involved in the development of diabetic peripheral neuropathy such as activation of polyol pathway, deposition of advanced glycation end products (AGE), depletion of myoinositol, protein kinase C. In polyol pathway, the excess glucose are converted to sorbitol by aldose reductase. Elevated intracellular sorbitol level results in increase in intracellular osmotic pressure, cell lysis and neuropathy²⁴.

In insulin resistance, the activity of hormone sensitive lipase in adipose tissue is increased resulting in increased levels of circulating fatty acids. Excess accumulation of lipids can trigger an increase in ROS generated by mitochondrial α oxidation that causes peripheral neuropathy²⁵.

In this study, higher levels of FSG, HbA1c and insulin resistance (HOMA-IR) levels in diabetic patients with peripheral neuropathy are suggestive of risk factors for development of peripheral neuropathy.

Conclusion

This study included that, poor glycaemic control and insulin resistance may be the potent risk factors for the development of peripheral neuropathy in type 2 diabetes mellitus. Therefore, early detection and proper management of these factors can reduce the development of peripheral neuropathy and can also reduce morbidity and mortality associated with peripheral neuropathy in type 2 diabetic subjects.

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Conflict of interest

None

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