Glycemic status with microalbuminuria and peripheral neuropathy in type II diabetes mellitus

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ABSTRACT

Objective: To determine the relationship of glycemic status with microalbuminuria and peripheral neuropathy in type II diabetes mellitus.

Study Design: A cross sectional observational study.

Place and Duration: Al- Tibri Medical College and Hospital Karachi from 1st January 2018 to 30th June 2018.

Methodology: This study comprises of patients of both genders with diagnosis of type II diabetes between 35-75 years of age. Demographic variables such as age, gender, duration of diabetes, hypertension, body mass index and laboratory parameters, i.e. fasting blood sugar, random blood sugar, glycosylated hemoglobin and microalbuminuria were recorded.

Results: Out of 120 patients, there were 55.8% males. Subjects having uncontrolled blood sugar as assessed by glycosylated hemoglobin had microalbuminuria 76.7% (p value <0.001) and peripheral neuropathy 58.1% (p value 0.003). While subjects having uncontrolled random blood sugar, microalbuminuria was present in 90% and peripheral neuropathy in 87.1% (p values of 0.002 and 0.014 respectively). With uncontrolled fasting blood sugar, microalbuminuria was observed in 66.7%, while peripheral neuropathy among in 67.7% with statistically significant p values of 0.003 and 0.001 respectively.

Conclusion: Poor glycemic control in terms of HbA1c, pre-prandial and post prandial hyperglycemia were significantly associated with microalbuminuria and peripheral neuropathy.

Keywords: Diabetes, Peripheral neuropathy, Microalbuminuria, Glycosylated hemoglobin, Fasting blood sugar, Random blood sugar.

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INTRODUCTION

Diabetes Mellitus (DM) is one of the metabolic disorders characterized by hyperglycemia either due to defect in insulin secretion or action. An increase in the estimate number of patients with diabetes by up to 552 million is expected by 2030[1] with largest number of patients from India, China and United States[2,3]. Prevalence of microvascular complications ranges from 36 to 68% for neuropathy,28 to 56% for nephropathy and 12 to 31% for retinopathy reported in hospital based studies in Pakistan[4]. Nephropathy associated with diabetes impacts financial burden on patients of developing countries[5], likewise Diabetic peripheral neuropathy (DPN) is responsible for ulceration and gangrene of the feet, thereby increasing the jeopardies of amputation[6] resulting in poor quality of life and adds a cost of diabetes care[7].

Microalbuminuria characterized by albumin excretion of 30 -300 mg/ 24 hours is the earliest predictor of diabetic nephropathy, incipient nephropathy at a stage where nephropathy is reversible and further progression can be halted. Hence it is very important to screen patients for incipient nephropathy by detecting microalbuminuria to prevent from development of End Stage Renal Disease (ESRD)[8].

Glycated hemoglobin (HbA1c) is benchmark to grade severity and average glycemic control over last 8 to 12 weeks in patients of diabetes[9,10]. A few studies propose counteractive action of neuropathy by tight glycemic control as seen by HbA1c and likewise propose inconsistencies in HbA1c and increment danger of advancement of nephropathy[11,12].

HbA1c has a number of significant limitations in medical conditions such as the presence of various systemic conditions like cirrhosis, anemia and malignancies, medications (aspirin, dapsone, antiretroviral therapy and ribavirin) and pregnancy are associated with variations in the HbA1c and may provide unpredictable information[13]. Because HbA1c does not provide glucose variability in short period of time so other parameters

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like random blood sugar (RBS) and fasting blood sugar (FBS) can be used for safe and timely management and clinical decision making[4]. Diabetes Intervention Study shows that RBS predicts cardiovascular disease in type 2 diabetics[14].

The rationale of the study was to predict the relationship of glycemic status as assessed by FBS, RBS and HbA1c with the common complications like peripheral neuropathy and nephropathy, as the local studies are lacking. Monitoring of RBS and FBS will be more helpful to attain favorable glycemic control and prevent long term diabetes complications in the absence of HbA1c, because of cost effectiveness and availability of test, especially in developing countries. The objective of the study is to determine the relationship of glycemic status with microalbuminuria and peripheral neuropathy in type II diabetes mellitus.

METHODOLOGY

This cross sectional observational study was conducted at Outpatient Department Medicine in Al –Tibri Medical College and Hospital Karachi from 1st January 2018 to 30th June 2018. Patients between 35-75 years of age of either gender of diagnosed case of type II diabetes based on the screening recommendation by American Diabetes Association (ADA)[15] were included in this study. The exclusion criteria were patients with type I diabetes and pregnant females. After taking written consent from the subjects, data was collected on a proforma especially designed for this study, which included age, gender, systolic and diastolic blood pressure (SBP and DBP), duration of diabetes and details of oral hypoglycemic agents (OHA) and /or use of insulin recorded at the baseline.

Diabetic neuropathy was assessed by symptoms of numbness, tingling, burning pain in the feet and signs were examined by reduced or absent ankle reflexes (using an appropriate reflex hammer), reduced or absent vibration perception (using a 128-Hz tuning fork) and touch sensation (using a 10-g monofilament). After exclusion of factors like fever, infection, congestive heart failure, menstruation, marked hypertension and exercise that can elevate urinary albumin excretion above baseline values as indicated by recommendation of recent ADA guidelines to screen for increased urinary albumin excretion, a random spot collection was performed for the measurement of the albumin-to-creatinine ratio (ACR). On at least two consecutive occasions of more than 30-300 mg is considered as positive for microalbuminuria.

Fasting blood sugar (FBS), random blood sugar [2 hours postprandial] (RBS), glycosylated hemoglobin (HbA1c) were send to the laboratory. Poor glycemic status was considered if FBS> 130mg/dl, RBS >180mg/dl and HbA1c ≥7%.

Data Analysis: The analyses were performed by using Statistical Packages for Social Sciences (SPSS 22). Chi-square Test of independence and Z Test were used for data analysis. For categorical variables frequency and percentage was used. P value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 120 patients were fulfilled with inclusion criteria. The mean ± SD of age was 52.58± 9.71. There were 67(55.8%) males and 53 (44.2%) were females. Hypertension was present in 72(60%) of the subjects of which 50(83.3%) had microalbuminuria and 46(74.2%) had peripheral neuropathy.

Subjects having uncontrolled blood sugar as assessed by HbA1c had microalbuminuria 46 (76.7%) with p value <0.001 and peripheral neuropathy 36(58.1%) and that relation was statistically significant (p value 0.003).

While subjects having uncontrolled RBS, microalbuminuria was present in 54(90%) and peripheral neuropathy was present in 54(87.1%) with statistically significant p values of 0.002 and 0.014 respectively.

With uncontrolled FBS, microalbuminuria was present in 40(66.7%) while peripheral neuropathy was present in 42(67.7%) with statistically significant p values of 0.003 and 0.001 respectively.

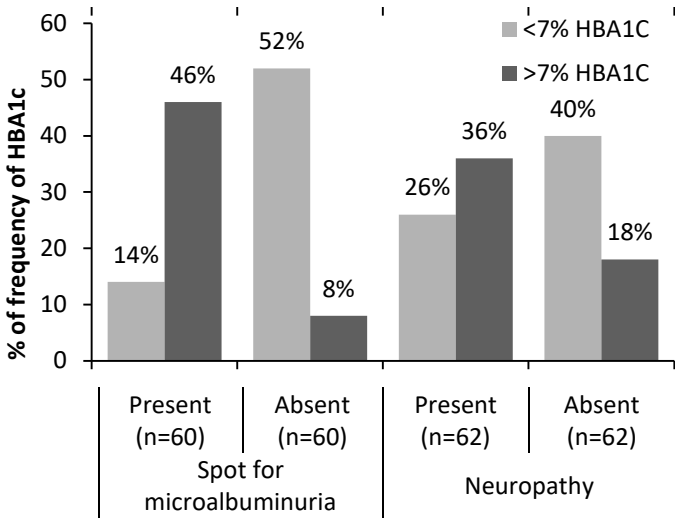

Figure-1: Frequency of HBA1c with spot for microalbuminuria and neuropathy (N=120)

DISCUSSION

In type II diabetes, there is a well-documented role of hyperglycemia in the development of microvascular complications[16,17], and it is recognized by the *United Kingdom Prospective Diabetes Study (*UKPDS) that therapies intended for achieving glycemic control are valuable in reducing the advancement and also delaying the evolution of long-term microvascular diabetic complications[18]. A disparity had been observed in different studies about assessment tools of glycemic status(FBS, RBS and HbA1c) and their role as a predictor of microvascular complications like Kumamoto study reported a curvilinear association between retinopathy and microalbuminuria with both fasting and 2-h postmeal plasma glucose control[19]. While Baig MA had found in his study that HbA1c is a strong predictor of diabetes complications and is widely recognizable to clinicians as a marker of glycemic control than FBS and RBS[1]. An acceptable control of RBS is required for an easier accomplishment of HbA1c goals[18,20].

Table-I: Comparison of demographic and clinical characteristics of diabetics in outpatient department (N=120)

Variables	Number of patients (n=120)	Microalbuminuria		Neuropathy	
		Yes	No	Yes	No
Age					
35-45yrs	19(15.8%)	05(8.3%)	14(23.3%)	5(8.1%)	15(25.9%)
46-55yrs	54(45%)	26(43.3%)	28(46.6%)	34(54.8%)	20(34.9%)
56-65yrs	35(29.1%)	23(38.3%)	12(20%)	15(24.2%)	19(32.8%)
66-75yrs	12(10.1%)	06(10.1%)	06(10.1%)	8(12.9%)	4(6.9%)
Gender					
Male	67(55.8%)	29(48.3%)	38(63.3%)	34(54.8%)	26(44.8%)
Female	53(44.2%)	31(51.7%)	22(36.7%)	28(45.2%)	32(55.2%)
Diabetes duration					
<1yr	12(10%)	04(6.7%)	08(13.3%)	0(0.0%)	12(20.7%)
1-10yrs	68(56.7%)	28(46.7%)	40(66.7%)	38(61.3%)	30(51.7%)
11-20yrs	34(28.3%)	24(40%)	10(16.7%)	20(32.3%)	14(24.1%)
21-30yrs	06(5%)	04(6.7%)	02((3.3%)	4(6.5%)	2(3.4%)
Hypertension					
Yes	72(60%)	50(83.3%)	22(36.7%)	46(74.2%)	26(44.8%)
No	48(40%)	10(16.7%)	38(63.3%)	16(25.8%)	32(55.2%)
Use of Hypoglycemic Agents					
Only OHA	88(73.3%)	44(73.3%)	44(73.3%)	44(71.0%)	44(75.9%)
Only Insulin	18(15%)	10(16.7%)	08(13.3%)	10(16.1%)	8(13.8%)
Insulin and OHA	14(11.7%)	06(10%)	08(13.3%)	8(12.9%)	6(10.3%)

Table II: Relationship of FBS, RBS and glycosylated hemoglobin with microalbuminuria (N=120)

Glycemic control		Microalbuminuria present (n=60)	Microalbuminuria absent (n=60)	P values
Fasting blood sugar(FBS)mg/dl	≤130 >130	20(33.3%) 40(66.7%)	36(60%) 24(40%)	0.003
Random blood sugar(RBS) mg/dl	≤180 >180	06(10%) 54(90%)	20(33.3%) 40(66.7%)	0.002
Glycosylated hemoglobin (HbA1c) %	<7% ≥7%	14(23.3%) 46(76.7%)	52(86.7%) 08(13.3%)	<0.001

Table III: Relationship of FBS, RBS and glycosylated hemoglobin with peripheral neuropathy (N=120)

Glycemic control		Peripheral neuropathy present (n=62)	Peripheral neuropathy absent (n=58)	P values
Fasting blood sugar(FBS) mg/dl	≤130 >130	20(33.3%) 42(67.7%)	36(60%) 22(37.9%)	0.001
Random blood sugar(RBS) mg/dl	≤180 >180	8(12.9%) 54(87.1%)	18(31.0%) 40(69.0%)	0.014
Glycosylated hemoglobin (HbA1c) %	<7% ≥7%	26(41.9%) 36(58.1%)	40(69%) 18(31.0%)	0.003

The relation of microalbuminuria with glycemic status as assessed by different level of HbA1c has been reported by certain studies. In this study the relation of microalbuminuria with HbA1c ≥ 7% was found to be 46(76.7%). This was much higher reported than in previous study by Aziz who found that 38% of subjects had both micro and macroalbuminuria with HbA1c 8.2±1.5[21]. This variation could be attributed to ethnicity of population, huge sample size, different methods for doing HbA1c, and level of glycemia.

Our study results shown a significant relation between HbA1c and neuropathy that 58.1% of subjects had neuropathy with HbA1c ≥ 7% (p value0.003). The Jawed also showed a statistical significant results with HbA1c >8% with neuropathy (44.75%)[22]. Another study by Nisar et al. reported bit higher frequency of neuropathy (88.6%)[23]. This disparity in results of different studies was might be due to different populations, sample sizes, methods of neuropathy assessment and different cutoff values of HbA1c.

Another tool of glycemic status of assessment is RBS has been well studied for its role in prediction of microalbuminuria. In this study, microalbuminuria appeared in 90% of the subjects who had uncontrolled RBS as opposed to 10% of subjects with controlled RBS with statistically significant p value 0. 002.While to our knowledge no studies had been found with same objectives for comparison of findings in relation to RBS with microalbuminuria.

Moreover, postprandial hyperglycemia was statistically significant (p value 0.014) associated with peripheral neuropathy (87.1% vs 12.9%). This was in contrast to Nisar et al., neuropathy was statistically significant with p value <0.001 [23] and the variation probably caused by the level of glycemic control.

Our study also showed a statistical significant results of FBS with microalbuminuria (p value 0.003) in 66.7% vs 33.3%. No studies to our information had been found the relation of FBS with microalbuminuria.

FBS was also being significantly associated with peripheral neuropathy (67.7% vs 32.3%) and (p value 0.001) in our study. This was in agreement to Nisar et al. (p value <0.001) [23].

Limitations of this study include that other microvascular complication like retinopathy is not included and the studies regarding glycemic control especially with pre-prandial and postprandial hyperglycemia is not available so future studies are required to analyze the relationship with microvascular complications.

CONCLUSION

Poor glycemic control in terms of HbA1c, pre-prandial and post prandial hyperglycemia were significantly associated with microalbuminuria and peripheral neuropathy.

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CONTRIBUTION OF AUTHORS

Rafi S: Conceived idea, Designed research methodology, Literature review, Manuscript writing, Data collection
Tasleem S: Literature review, Manuscript writing, Data collection
Rabb A: Literature review

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