Correlation of Diabetic Nephropathy and HbA1C in Newly Diagnosed Type 2 Diabetic Patients of Western UP

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Abstract- Insulin resistance is characterized by a subnormal response to a given concentration of insulin and can be measured indirectly by a fasting insulin level. The prevalence of diabetes continues to grow worldwide, disease-related morbidity and mortality is emerging as major healthcare problems. Clearly, type 2 diabetes has a strong genetic component. Diabetic–nephropathy is the leading cause of end stage renal disease (ESRD) in US and a leading cause of diabetes mellitus related morbidity and mortality. Nephropathy complicates approximately 30% of type 2 diabetic patients. However no study has been performed that compared the HbA1c in type II diabetes mellitus with nephropathy to without nephropathy. Therefore aim of this study was to evaluate the glycosylated hemoglobin and their association with diabetic nephropathy in a western Uttar Pradesh. The body mass index (BMI) was calculated as weight (Kg) divided by height (m) squared. Venous blood was collected after 12 hours fasting into two test tubes; with no anticoagulant for serum creatinine, and with Ethylene Diamine Tetra Acetic Acid (EDTA) for HbA1c.we observed that Incidence of microalbuminuria increases with age as well as with increased duration of diabetes mellitus. Our study also evaluated relationship between diabetic retinopathy and nephropathy and found a significant correlation.

Index Terms- insulin resistance Hb A1c Microalbuminuria Nephropathy

I. Introduction

Diabetes mellitus (Type- 2 diabetes), the common endocrine disorder, is characterized by persistent hyperglycaemia due to lack of insulin and/or insulin resistance[1]. Insulin resistance is characterized by a subnormal response to a given concentration of insulin and can be measured indirectly by a fasting insulin level[2]: higher levels of insulin correspond to higher degrees of insulin resistance. Factors that contribute to insulin resistance include obesity[3], aging, and a sedentary lifestyle[4]. The prevalence of diabetes continues to grow worldwide, disease-related morbidity and mortality is emerging as major healthcare problems[5]. Clearly, type 2 diabetes has a strong genetic component[6,7] and is found more frequently in certain families and ethnic minority groups, such as Hispanics, African Americans, Pacific Islanders, and American Indians. Patients with Type- 2 diabetes may be asymptomatic[8] and may have complications at the time of diagnosis. Diabetic–nephropathy is the leading cause of end stage renal disease (ESRD) in US[9] and a leading cause of diabetes mellitus related morbidity and mortality. Nephropathy complicates approximately 30% of type 2 diabetic patients[10]. The laboratory test for early detection of diabetic nephropathy is the measurement of microalbumin in urine (Microalbuminuria). Microalbuminuria predicts progression to diabetic nephropathy and cardiovascular diseases.[11] HbA1c is a measure of erythrocyte haemoglobin glycation, since erythrocytes have about 120 days life span, HbA1c reflects mean glycaemic value for the previous 3 months (weighted to the most recent months).[12] It provides no information about the immediate blood glucose concentration. Blood samples for HbA1c can be drawn whether or not the patient is fasting, as it does not reflect the patterns of glycaemia, the effects of food or exercise.[13,14], However no study has been performed that compared the HbA1c in type II diabetes mellitus with nephropathy to without nephropathy. Therefore aim of this study was to evaluate the glycosylated hemoglobin and their association with diabetic nephropathy in a western Uttar Pradesh.

II. Material and Methods

This was a cross sectional study conducted at the L.L.R.M. Medical College, Meerut (western UP) during January 2014to July 2014. One hundred known Type 2 diabetic patients (55 males and 45 females), with age range 30–70 were included in the study. Purposive non-probability sampling technique was used for data collection. Informed consent was obtained. A structured questionnaire regarding the demographic data such as age, sex, duration of diabetes, height and body weight were measured while wearing light weight clothing, but not shoes. Blood pressure, smoking habit, family history of diabetes, renal disease and hypertension was recorded for each patient.

Inclusion Criteria:

1. Age > 30 years & < 60 years
2. Patient who gave written informed consent.
3. Mentally and physically fit up to a minimum level required to participate in study.

4. Patients with newly diagnosed type 2 diabetes mellitus (with in 1 month) according to WHO criteria and ADA recommendations for diabetes mellitus

Exclusion criteria:

1. Not interested/unable to provide informed consent.
2. Any substance abuse, mental illness or medical condition that in opinion of investigator would make it difficult for potential participant to participate in intervention.
3. Patient of known hypertension with or without treatment, ischemic heart disease, cardiomyopathy, valvular heart disease, heart failure, chronic pulmonary illness, severe anaemia, hemoglobinopathies.
4. Known case of diabetes mellitus type 1 and type 2 who are already diagnosed or on antidiabetic treatment.

Diabetic patients suffering from any other medical problems were excluded from the study. The body mass index (BMI) was calculated as weight (Kg) divided by height (m) squared. Venous blood was collected after 12 hours fasting into two test tubes; with no anticoagulant for serum creatinine, and with Ethylene Diamine Tetra Acetic Acid (EDTA) for HbA1c. Morning urine sample was collected in a container (without preservative) for analysis of creatinine and microalbumin. HbA1c was estimated by Boronate affinity chromatography (HPLC) which separates total glycated haemoglobin by binding to solid–phase dihydroxyborate using Nycocard immunoassay kit (USA). Serum creatinine was analysed by alkaline picrate, Jaffe‘s Method (Erba Kit).Urinary creatinine was estimated by Jaffe‘s Method (Erba kit). Urinary microalbumin was estimated by Sandwich Format Immunometric Assay method. Fasting & Post prandial plasma glucose (glucose–oxidase peroxidise method),

III. DIAGNOSTIC CRITERIA

A) Criteria for the diagnosis of diabetes :

1. FPG ≥126 mg/dl (7.0 mmol/l). (Fasting is defined as no caloric intake for at least 8 h.) OR
2. 2-h plasma glucose ≥ 200 mg/dl (11.1mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. OR
3. In a patient with classic symptoms of hyperglycemia or hyperglycaemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l). OR
4. Hb**A1C ≥ 6.5%.** The test should be performed in a laboratory using a method that is NGSP (National Glycohemoglobin Standardisation Program) certified and standardized to the DCCT (Diabetes Control & Complication Trial) assay.

IV. DIABETIC NEPHROPATHY

Presence of diabetic nephropathy has been assessed by measuring urinary excretion of albumin in a morning urine sample & GFR

Measurement of Albuminuria: Significant albuminuria is defined as urinary excretion of albumin ≥30mg/dl albumin in 24 hr collection or ≥30 mcg/mg of creatinin in spot urine collection (morning urine sample).

Microalbuminuria: urinary excretion of 30-299 mg/dl albumin in 24 hr collection or 30-299 mcg/mg of creatinin in spot urine collection

Macroalbuminuria: urinary excretion of ≥300 mg/dl urinary albumin in 24 hr collection or ≥ 300mcg/mg of creatinine in spot urine sample.

Calculation of GFR: calculated by MDRD(MODIFIED DIET FOR RENAL DISEASE) formula using software

Statistical analysis: Data were analysed for mean, percentage, standard deviation, Student_t‘ test, Fisher‘s exact test, by using SPSS-16(Statistical Package for the Social Sciences) for Windows (SPSS, Chicago, IL). The t‘-test and Fisher‘s exact tests were applied to study quantitative and qualitative data, respectively with P‘value < 0.05 was considered statistically significant.

V. OBSERVATION AND RESULTS

Table 1: Age and Sex wise distribution of cases

Age group (yrs)	Male		Female		Total	
	No.	%	No.	%	No.	%
30-39	03	03	03	03	06	06
40-49	21	21	16	16	37	37
50-60	41	41	16	16	57	57
Total	55	55	45	45	100	100

Hundred newly diagnosed type 2 diabetes mellitus patients age between30-60 years were selected for this cross sectional study. Out of which 55 (55%) were males and 45 (45%) females.

Table-2: Frequency of Diabetic nephropathy

	Microalbuminuria	**Macroalbuminuria**	**Total**
Male	14	01	**15**
Female	02	02	**04**
Total	**16**	**03**	**19**

Out of 100 patients of newly diagnosed type 2 DM ; 19 % patients were found to have diabetic nephropathy. Out of this 19 % cases, 16 cases (84.21%) were of microalbuminuria and 03 cases (18.75%) were of macroalbuminuria Out of 19 cases 15 were male and 04 were females.

Table 3: Distribution of diabetic nephropathy according to sex

Sex	**Diabetic nephropathy**		**Total**
	Present	**Absent**	
Male	15	50	65
Female	04	31	35
Total	19	81	100

P=0.1896 Relative risk = 2.019 95% CI =0.7254 to 5.621

Table-3 showed that male and female populations were compared for frequency of Diabetic nephropathy applying Fisher's exact test but no significant difference was found (p=0.1896) regarding the incidence of diabetic retinopathy between the two populations.

PARAMETERS	WITH MICRO/MACRO ALBUMINURIA	WITHOUT MICRO/MACRO ALBUMINURIA	p VALUE ('t' -test)
No. of Patients	19	81	--
Fasting Plasma Glucose (mg/dl)	211.52 ± 27.85	173.55 ± 27.24	<0.0001
HbA1C (%)	8.37 ± 0.83	7.19 ±0.58	< 0.0001
Age (year)	53.78 +4.28	49.20 + 6.31	0.0035
BMI (kg/m²)	26.93 + 2.31	24.92 + 2.45	0.0015
S. CREATININE (mg/dl)	1.76 +0.59	1.12 + 0.52	< 0.0001
S. CHOLESTEROL (mg/dl)	199.13± 23.23	184.02 ± 19.56	0.0043

Mean fasting plasma glucose levels of population with nephropathy were 211.52 ± 27.85 mg/dl and that of population without nephropathy was 173.55 ± 27.24 mg/dl .This shows that FPG is positively associated with the incidence of diabetic nephropathy in population as mean of FPG of population with nephropathy was higher as compare to population without nephropathy and correlation was found extremely significant (p<0.0001) Mean HbA1C of population with nephropathy was 8.37 + 0.83 %and that of population without nephropathy was7.19 + 0.58 %.HbA1C is positively associated with the incidence of diabetic nephropathy in population as mean of HbA1C of population with nephropathy was higher as compare to population without nephropathy and correlation was found extremely significant (p<0.0001). Mean age of population with nephropathy was 53.78 +4.28 yrs and that of population without nephropathy was 49.20 + 6.31 yrs.Age is positively associated with the incidence of diabetic nephropathy in population as mean of age of population with nephropathy was higher as compare to population without nephropathy and correlation was found very significant (p<0.0035)

Mean body mass index of population with nephropathy was 26.93+ 2.31 kg/m² and that of population without nephropathy was 24.92 + 2.45 kg/m² .BMI is positively associated with the incidence of diabetic nephropathy in population as mean of BMI of population with nephropathy was higher as compare to population without nephropathy and correlation was found very significant (p=0.0015) . Mean serum chloesterol of population with nephropathy was 199.13 ± 23.23mg/dl and that of population without nephropathy was 184.02 ± 19.56 mg/dl. serum cholesterol is found positively associated with the incidence of diabetic nephropathy in population as mean of serum cholesterol of population with nephropathy was higher as compare to population without nephropathy and correlation was found very significant (p=0.0043) Mean serum creatinine of population with nephropathy was 1.76 ± 0.59mg/dl and that of population without nephropathy was 1.12 ± 0.52mg/dl. Serum creatinine is found positively associated with the incidence of diabetic nephropathy in population as mean of serum creatinine of population with nephropathy was higher as compare to population without nephropathy and correlation was found extremely significant (p<0.0001)

VI. DISCUSSION

Diabetes Mellitus is a multifactorial disease, associated with a number of microvascular (neuropathy and nephropathy) and macrovascular (ischemic heart disease, cerebrovascular disease and peripheral vascular diseases) complications. The gap between the onset of the disease and clinical diagnosis of diabetes leads to the development of these chronic complications, which are the leading causes of premature mortality among diabetic patients. In this study, which is one of the first studies in this regards in western U.P., we assessed the incidence of nephropathy and their correlation with various parameters like glycosylated haemoglobin (HbA1C), body mass index (BMI).Present study has also shown incidence of diabetic nephropathy 19% (in form of microalbuminuria 16% as well as macroalbuminuria 03% in newly diagnosed diabetic patient which is lesser when compared to the study by Ghai et al[15]. **Unuigbe et al[16]** observed microalbuminuria in 50% and **Khan et al [17]** showed prevalence of 30%, of newly diabetic cases. Method of estimation of microalbuminuria as well as ethnical differences would have played a role in giving lower prevalence in the present study. The level of glycemic control seems to be the strongest factor influencing transition from normoalbuminuria to microalbuminuria. As reported in many studies our study also showed significant correlation between FBS, BMI ,s. creatinine, s. cholesterol and microalbuminuria. No sex preponderance has been seen in this study. Diabetic nephropathy can conveniently be categorized into different stages with respect to renal hemodynamic, systemic blood pressure, urinary findings, and susceptibility to therapeutic interventions. In the initial renal hyperperfusion stage, glomerular filtration is elevated with absent albuminuria. In the second stage (clinical latency) glomerular filtration will be high normal with absent albuminuria. Next stage is incipient nephropathy, wherein glomerular filtration will be normal with presence of microalbuminuria. It usually appears 5-15 years after the diagnosis of diabetes mellitus. In the subsequent stage, glomerular filtration decreases with appearance of macroproteinuria and clinical manifestations of nephropathy. Finally ends up in end stage renal disease with massive

albuminuria and diminished glomerular filtration. Hence microalbuminuria may not be associated with abnormal serum creatinine, but can be an important warning signal which if ignored can result in irreversible renal damage. Incidence of microalbuminuria increases with age as well as with increased duration of diabetes mellitus. Our study also evaluated relationship between diabetic retinopathy and nephropathy and found a significant correlation. **Anila Chandy et al**[21] from Christian Medical College and Hospital, Ludhiana, Punjab, and Nader Baharivand,[22] in Iran also found similar correlation between these two microvascular complications. This correlation can be explained by the common mechanism involved in tissue damage by all those factors.

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