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PREVALENCE OF DIABETIC NEPHROPATHY AND RETINOPATHY IN INDIAN TYPE 2 DIABETIC SUBJECTS ATTENDING TERTIARY DIABETES INSTITUTE

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ABSTRACT

Objective—the aim of this study was to determine the prevalence of diabetic nephropathy and retinopathy among Indian type 2 diabetic subjects attending a tertiary diabetic institute. **Research Design and Methods**—Type 2 diabetic subjects 500 in number were randomly selected from patients attending Karnataka institute of endocrinology and research over 6 months. Microalbuminuria was estimated by immunoturbidometric assay and diagnosed if albumin excretion was between 30 and 299 µg/mg of creatinine, and overt nephropathy was diagnosed if albumin excretion was ≥300 µg/mg of creatinine in the presence of diabetic retinopathy, which was assessed by stereoscopic retinal color photography. **Results**—the prevalence of overt nephropathy was 6%. Microalbuminuria was present in 22.2%. Duration of diabetes, systolic blood pressure, FPG,PPPG,HBA1C, serum creatinine and e GFR levels had correlations with prevalence of diabetic nephropathy. Chronic kidney disease distribution was stage 1-65.8%, stage2-28%, stage3-5.4%, stage4-0.6% and stage5-0.2%. Prevalence of diabetic retinopathy was 33.2%. Duration of diabetes, systolic blood pressure, FPG, PPPG, albuminuria, serum creatinine and e GFR levels had correlations with diabetic retinopathy. **Conclusions** - the results of the study suggest that in Asian Indians, the prevalence of overt nephropathy and microalbuminuria was 6 and 22.2% respectively; prevalence of diabetic retinopathy was 33.2%. Achieving HBA1c and blood pressure target are main factors in the prevention of diabetic nephropathy and retinopathy. Microalbuminuria was present in 22.2% of diabetes subjects; by suitable intervention at this stage we can prevent development of overt nephropathy.

KEYWORDS: Nephropathy, Retinopathy, Microalbuminuria.

INTRODUCTION

According to the most recent estimates published in the IDF 2019.[1] India has 77 million diabetics and expected to increase to 134.2 million by the year 2045.

The chronic complications of diabetes mellitus affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease.[2] Chronic complications can be divided into vascular and nonvascular complications. The vascular complications of DM are further subdivided into microvascular (retinopathy, neuropathy, and nephropathy) and macrovascular complications [coronary artery disease (CAD), peripheral arterial disease (PAD), cerebrovascular disease]. Both microalbuminuria and macroalbuminuria in individuals with DM are associated with increased risk of cardiovascular disease. Individuals with diabetic nephropathy commonly have diabetic retinopathy.[3] So this study was done to find out prevalence rate of diabetic nephropathy (DN), diabetic retinopathy and its associated risk factors.

Kidney disease in diabetic patients is clinically characterized by increasing rates of urinary albumin excretion, starting from normoalbuminuria, which progresses to microalbuminuria, macroalbuminuria, and eventually to ESRD. Microalbuminuria is the earliest clinically detectable stage of diabetic kidney disease at which appropriate interventions can retard, or reverse, the progress of the disease. Diabetic nephropathy (Kimmelstiel-Wilson syndrome) is the leading cause of end-stage renal disease (ESRD) worldwide, and it is estimated that 20% of type 2 diabetic patients reach ESRD during their lifetime.[4]

Type 2 diabetes in Asian Indians differs from that in Europeans in several aspects: the onset is at a younger age, obesity is less common, and genetic factors appear to be more common.[5] Some studies.[6-8] conducted in migrant Asian Indians in the U.K. and Europe has reported increased prevalence of diabetic nephropathy compared with white Caucasians.

MATERIAL AND METHODS

Type 2 diabetic subjects 500 in number were randomly selected from patients attending Karnataka institute of endocrinology and research over 6 months.

Clinical and biochemical studies

Measurements of weight, height, and waist circumference were obtained using standardized techniques. The BMI was calculated using the following formula: weight (kg)/height (m^2). Blood pressure was recorded in the sitting position in the right arm. Two readings were taken 5 min apart, and the mean of the two was taken as the final blood pressure reading. The study was approved and informed consent was obtained from all the participants.

A fasting and post prandial blood sample was taken for estimation of plasma glucose by hexokinase method and serum lipids using a Hitachi C 311 autoanalyser (Roche Diagnostics, Mannheim, Germany). A1C was measured by the high-performance liquid chromatography method using the Bio-rad Variant 2 turbo analyser.

Estimation of microalbuminuria

Microalbumin concentration was measured in a fasting urine sample using immunoturbidometric assay (Hitachi C311 autoanalyser; Roche Diagnostics).

Retinopathy

The ocular fundi were photographed using four-field stereo color retinal photography by Kowa fundus camera. Photographs were graded by an ophthalmologist (Vitreoretinal specialist). The minimum criterion for diagnosis of diabetic retinopathy was the presence of at least one definite microaneurysm in any field photographed. Photographs were assessed and assigned a retinopathy level, and the final diagnosis for each patient was determined from the grading of the worse eye according to the Early Treatment Diabetic Retinopathy Study criteria for severity of an individual eye.[9]

Definitions

Hypertension

Subjects with self-reported hypertension and those who had a systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg,[10] were considered to have hypertension.

Smoking

Individuals were classified as nonsmokers and current smokers.

Microalbuminuria

Microalbuminuria was diagnosed if the albumin excretion was between 30 and 299 μg/mg of creatinine (**3**).

Overt nephropathy was diagnosed if albumin excretion was ≥300 μg/mg of creatinine in the presence of diabetic retinopathy.

International classification of diabetic retinopathy

Diabetic Retinopathy	Findings Observable on Dilated Ophthalmoscopy
No apparent DR	No abnormalities
Mild nonproliferative DR	Microaneurysms only
Moderate nonproliferative DR	Microaneurysms and other signs (e.g., dot and blot hemorrhages, hard exudates, cotton wool spots), But less than severe non proliferative DR
Severe nonproliferative DR	Moderate nonproliferative DR with any of the following: Intraretinalhemorrhages (≥20 in each quadrant) Definite venous beading (in 2 quadrants) Intraretinalmicrovascular abnormalities (in 1 quadrant); No signs of proliferative retinopathy
Proliferative DR	Severe nonproliferative DR and 1 or more of the following: Neovascularization Vitreous/preretinalhemorrhage

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1. Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent.

The one-way analysis of variance (ANOVA) is employed to determine whether there are any statistically significant differences between the means of three or more independent (unrelated) groups.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. A t-test is a statistical test that is used to compare the means of two groups. Chi-square/ Fisher

Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis.

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01)

Statistical software: The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

The age distribution of diabetes subjects range from20 to >60 years. The percentage of Male diabetes subjects were 58.8%. the duration of diabetes range from <1 to >10 years. Family history of diabetes was present in 53.2%. History of smoking was present in only 3% of subjects. The BMI of diabetes subjects range from <18.5 to >30 kg/square meters. Hypertension was present in 35.4% of patients.

The prevalence of overt nephropathy was 6%. Microalbuminuria was present in 22.2%. (Table 1) The distribution of chronic kidney disease was stage 1-65.8%, stage 2-28%, stage3-5.4%, stage-4-0.6% and stage-5-0.2%. (Table 2).

Table 1: Prevalence of Diabetic nephropathy.

Albumin	No. of patients	%
<29	349	69.8
30-299	111	22.2
>300	40	8.0
Total	500	100.0

Table 2: Stages of chronic kidney disease.

eGFR	No. of patients	%
<15	1	0.2
15-29	3	0.6
30-59	27	5.4
60-89	140	28.0
>90	329	65.8
Total	500	100.0

Table 3: Comparison of study variables according to Albuminuria levels of diabetes subjects studied.

variables	Albumin Levels			Total	P value
	≤29	30-299	≥300		
Age in years	52.13±10.72	54.33±12.39	52.18±10.35	52.62±11.10	0.184
Duration of Disease yrs	7.28±5.54	9.35±5.83	10.87±6.13	8.02±5.77	<0.001**
BMI (kg/m^2)	26.96±4.85	26.32±4.72	26.48±4.41	26.78±4.79	0.439
WCR	94.26±10.32	93.52±13.67	94.41±10.93	94.11±11.18	0.818
SBP (mm Hg)	136.89±17.47	138.64±20.47	146.85±23.84	138.07±18.89	0.006**
DBP (mm Hg)	83.25±10.44	83.6±12.51	86.83±11.91	83.62±11.07	0.155
FPG	157.22±60.16	192.43±85.18	186.38±87.34	167.37±70.43	<0.001**
PPPG	237.54±95.64	288.83±106.49	274.10±127.83	251.85±103.17	<0.001**
HbA1c	8.28±1.85	10.28±8.04	9.33±2.39	8.81±4.22	<0.001**
Creatinine (mg/dl)	0.81±0.16	0.93±0.46	1.38±1.51	0.88±0.52	<0.001**
eGFR	96.8±14.17	89.68±23	74.74±28.02	93.45±18.89	<0.001**

The study variables duration of diabetes, systolic blood pressure, FPG, PPPG, HBA1C, serum creatinine and e-GFR levels had significant correlations with prevalence of diabetic nephropathy. (Table 3)

Prevalence of diabetic retinopathy was 33.2% with mild NPDR in 19.6%, moderate NPDR in 4.8% severe NPDR in 2.4% and proliferative diabetic retinopathy in 6.4% of diabetes subjects. (Table 4)

Table 4: Prevalence of diabetic retinopathy.

Retinopathy	No. of patients	%
No DR	334	66.8
Mild NPDR	98	19.6
Moderate NPDR	24	4.8
Severe NPDR	12	2.4
PDR	32	6.4
Total	500	100.0

Table 5: Comparison of clinical variables according to Retinopathy of diabetes subjects studied.

variables	Retinopathy					Total	P value
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR		
Age in years	51.96±11.46	53.11±10.51	53.08±10.40	53.75±9.73	57.28±9.29	52.62±11.10	0.126
Duration Disease yrs	6.28±4.96	10.87±5.46	12.40±6.42	11.33±6.73	13.00±5.40	8.02±5.77	<0.001**
BMI (kg/m^2)	27.05±4.57	26.49±5.89	25.93±3.85	27.37±4.98	25.18±3.38	26.78±4.79	0.202
WCR	94.62±11.76	93.44±9.97	92.72±8.07	94.75±11.95	91.63±10.17	94.11±11.18	0.552
SBP (mm Hg)	136.46±18.53	139.18±17.03	153.96±22.74	145.17±24.58	136.94±17.4	138.07±18.89	<0.001**
DBP (mm Hg)	83.19±11.62	84.41±8.60	88.13±12.4	87.08±12.03	81.03±9.67	83.62±11.07	0.094+

The clinical variables studied duration of diabetes mellitus and systolic blood pressure had significant correlations with diabetic retinopathy. (Table 5)

Table 6: Comparison of Study outcome variables according to retinopathy of diabetes subjects studied.

variables	Retinopathy					Total	P value
	No DR	Mild NPDR	Moderate NPDR	Severe NPDR	PDR		
FPG	157.99±66.04	181.91±72.46	210.29±86.23	196.08±90.05	177.81±68.60	167.37±70.43	<0.001**
PPPG	238.19±95.22	271.31±109.87	306.96±116.62	298.83±121.13	275.94±117.70	251.85±103.17	<0.001**
HbA1c	8.62±4.92	8.94±2.03	9.66±2.22	9.83±2.70	9.31±2.34	8.81±4.22	0.580
Albumin	40.47±89.91	75.59±140.55	175.18±199.95	148.75±218.96	193.06±215.73	66.18±131.35	<0.001**
Creatinine (mg/dl)	0.82±0.20	0.90±0.42	1.27±1.89	0.95±0.25	1.16±0.64	0.88±0.52	<0.001**
eGFR	96.22±16.63	91.92±19.76	85.54±22.62	84.23±20.22	78.70±25.14	93.45±18.89	<0.001**

The study outcome variables, FPG, PPPG, Albumin, Creatinine (mg/dl) and e-GFR had significant correlations with diabetic retinopathy. (Table 6)

DISCUSSION

The criteria used for the diagnosis of overt nephropathy in this study included retinopathy, as it makes the diagnosis of diabetic nephropathy more specific. Poor glycemic control, long duration of diabetes, and systolic blood pressure were the risk factors for overt nephropathy. This is similar to results reported in several other studies.[11]

In a hospital based study by Vimalkumar.V.K.etal prevalence rate of overt nephropathy was 2.5% and microalbuminuria was 13%, Using Binary logistic regression analysis, woman gender, Duration of diabetes, family history of kidney disease, Hypertension, high BMI, low e-GFR, retinopathy were found to be significantly associated with diabetic nephropathy.[12]

Abdulhakeem Hamood Alrawahietal showed total prevalence of diabetic nephropathy of 42.5% (with 95% confidence interval as 38.83% - 46.15%). The two polyclinic catchment areas were found to be similar in respect of diabetic nephropathy prevalence (Sumail-43.2%, Nizwa- 42.2%). The prevalence was significantly higher among males (51.6%) compared to females (36.5%).[13]

Susan Savage et al in their study that included 947 NIDDM patients have noted an association between Urinary albumin and increased prevalence of diabetic retinopathy.[14]

WisitKaewput et al in their multi centric cross sectional nationwide study that included 13192 T2DM patients found decreased GFR was independently associated with increased DR.[15]

Salil S Gadkari et all in their study of 6218 known diabetics, they found the DR prevalence was 21.7%. Prevalence was more in males (P = 0.007), diabetics more than 5 years (P = 0.001), those above 40 years (P = 0.01), insulin users (P = 0.001), and history of vascular accidents (P = 0.0014).[16]

The results of our study are comparable to other clinic based studies in other parts of India. There are few variations. These variations in the prevalence rate of

proteinuria can be attributed to differences in several factors such as; study design, source of study population, sample selection, race, age, sex structure of the study population, diagnostic criteria, as well as the methods of measurement of proteinuria and urine collection, diabetic duration, diabetic treatment, and presence of hypertension.

The Centers for Disease Control and Prevention recommended early detection of microalbuminuria in diabetic patients. Fortunately, the early detection of microalbuminuria and good control of diabetes delay the development of diabetic nephropathy. The causal risk factors for microalbuminuria are hypertension and poor glycemic control. Furthermore, the association between increased blood pressure and diabetic nephropathy was recognized by most of the studies.

The prevalence of DN in Type 2 diabetic patients was found to be high, alarming the health workers and decision makers to face this problem by developing strategies for prevention, detection, and treatment of DN. Therefore, there is an urgent need for annual screening for MA that is recommended by the ADA for all patients with Type 2 DM, which is highly cost-effective. The presence of MA is an indication to the physician to take steps to prevent further renal damage by correction of risk factors, such as control of diabetes and hypertension.

The prevalence of diabetic retinopathy is high in our study as it is a tertiary institute which treats patients referred from different primary and secondary centers with uncontrolled diabetes. It is very much essential to diagnose diabetic retinopathy in the stage of mild NPDR, achieve glycemic and blood pressure targets to prevent progression of retinopathy.

CONCLUSIONS

The results of the study suggest that in Asian Indians, the prevalence of overt nephropathy and microalbuminuria was 6 and 22.2% respectively; prevalence of diabetic retinopathy was 33.2%. Achieving HBA1c and blood pressure target are main factors in the prevention of diabetic nephropathy and retinopathy. Microalbuminuria is present in 22.2% of diabetes subjects; by suitable intervention at this stage we can prevent development of overt nephropathy.

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ABBREVIATIONS

DM-Diabetes mellitus.
BMI-Body mass index.
e-GFR-estimated glomerular filtration rate.
FPG-Fasting plasma glucose.
PPPG-Post prandial plasma glucose.
HBA1C-Glycosylated haemoglobin.
DR-Diabetic retinopathy.
DN-Diabetic nephropathy.
MA-Microalbuminuria.
NPDR-Non proliferative diabetic retinopathy.
PDR-Proliferative diabetic retnopathy.

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