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Study of prevalence and stages of diabetic nephropathy in a rural tertiary care centre - Southern India

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is an alarming health care concern the world over affecting more-than 220 million people worldwide according to World Health Organization. Kidney disease in diabetic patients is clinically characterized by increasing rates of urinary albumin excretion (UAE), starting from normoalbuminuria, which progresses to microalbuminuria, macroalbuminuria and eventually to End-Stage Renal Disease. Diabetic nephropathy has been categorized into stages based on the values of urinary albumin excretion and estimated glomerular filtration (eGFR). There is accumulating evidence suggesting that the risk for developing diabetes nephropathy and cardiovascular disease starts when UAE values are still within normoalbuminic range. Objective: To study the prevalence and stages of nephropathy in T2DM patients and to compare albumin levels with glycemic control in rural population. Methodology: Cross-sectional study was carried out from January 2011 to April 2012 among diabetic patients attending General Medicine department in RL Jalappa Hospital. Random blood sample and spot urine sample was collected for analysis and the data was collected in a predesigned, pretested semi-structured questionnaire. Results: The prevalence of diabetic nephropathy in our study was 37.02%. The prevalence microalbuminuria was 30.79% in males and 24.46% in females. The prevalence of overt nephropathy was 9.27% in males and 6.73% in females. Around 62.97% were in microalbuminuric range. 75.76% of the patients had poor glycemic control, but among patients with poor glycemic control 79.78% had overt nephropathy and 86.80% had microalbuminuria. Among patients with good glycemic control 20.28% had overt nephropathy and 13.19% had microalbuminuria. Conclusion: Microalbuminuria was earliest sign in Diabetic Nephropathy (DN). Progression of DN can be prevented on early detection. Poor glycemic control and duration of diabetes was associated with increase in UAE level and progression of Chronic Kidney Disease. Screening for DN at the time of diagnosis in T2DM and measures to reduce albuminuria at earliest could prevent further progression of DN in patients with T2DM

Key Words: Type-2 Diabetes mellitus, UAE, eGFR, Diabetic Nephropathy

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Introduction: Type 2 diabetes mellitus (T2DM) is an alarming health care concern the world over.[1] According to the World Health Organization (WHO), T2DM affects more than 220 million people worldwide and is projected to reach 370 million by 2030. India has the largest number of diabetic patients in the world, estimated to be about 40.9 million in the year 2007 and expected to increase to about 69.9 million by the year 2025.[2] About a third of these patients are likely to develop diabetic nephropathy and progressive chronic kidney disease(CKD).[3]

The propensity of development of nephropathy in diabetic patients also depends on other demographic factors and racial differences have been seen to

influence the prevalence of diabetic nephropathy.[4,5] In the United States, the risk of end stage renal disease (ESRD) is reported to be higher among Hispanics and Afro-Americans than among Caucasian subjects even after adjusting confounding factors.[6,7] Asian subject have significantly (P<0.01) higher prevalence (52.6%) of diabetic ESRD when compared with the Caucasians (36.2%).[8]

Kidney disease in diabetic patients is clinically characterized by increasing rates of urinary albumin excretion (UAE), starting from normoalbuminuria, which progresses to microalbuminuria, macroalbuminuria, and eventually to ESRD.[9] Microalbuminuria is the earliest clinically detectable stage of diabetic kidney disease at which appropriate interventions can retard or reverse the progression of the disease.[10]

Diabetic nephropathy (DN) has been categorized into stages based on the values of UAE (ADA, 2004) and estimated glomerular filteration rate (eGFR).[11,12] There is a accumulating evidence suggesting that the risk for developing DN and cardiovascular disease starts when UAE values are still within normoalbuminic range.[13,14,15,16]

In this regard, the study was designed to assess the prevalence and stages of nephropathy in T2DM patients and to compare albumin levels with glycemic control in a rural population thereby the progression of T2DM patients to DN can be constrained early through screening them for UAE and eGFR.

Material and Methods: Cross-sectional study was conducted in the department of General Medicine, RL Jalappa Hospital and Research Center, attached to Sri Deveraj Urs Medical College, Kolar. The diabetic patients attending medicine out-patient department, from January 2011 to April 2012 were included. All the patients were interviewed with pre-designed, pre-tested, semi-structured questionnaire. Patients with known renal failure, urinary tract infection, hematuria, acute febrile illness, vigorous exercise and short term pronounced hyperglycemia, uncontrolled hypertension and heart failure were excluded from the study. Informed consent was obtained by the subjects and Institutional Ethical Clearance was obtained for the study.

Random blood sample was taken for estimation of serum creatinine using a Hitachi 912 auto-analyzer (Roche Diagnostics, Mannheim, Germany) for calculation of Glomerular Filtration Rate (GFR). GFR is estimated by prediction equation that is taken into account serum creatinine concentration and age, sex, race and body size. The recommended equation by the national kidney foundation is that of the modified diet in renal disease (MDRD), which estimates the GFR as follows.[17]

GFR (ml/min/1.73 m^2) = 186*[serum creatinine (mg/dl) - 1.154*age(yr) - 0.203*(0.742, if female)*(1.210, if African American)] and later eGFR were classified into stages.[18]

Glycosylated hemoglobin HbA1C was analyzed by the high-performance liquid chromatography method using the Variant machine (Bio-red, Hercules and California). Glycemic control was considered as good in patients with HbA1c< 7 and poor in patients with HbA1c ≥ 7.[19] Albuminuria concentration was measured in a spot urine sample using immunoturbidometric assay (Hitachi 902 auto-analyzer; Roche Diagnostics). Micro-albuminuria was diagnosed if the albumin excretion was between 30 and 299 mcg/mg creatinine. Overt nephropathy was diagnosed if albumin excretion was ± 300mcg/mg creatinine.[20] The report obtained from the sample on analysis was scrutinized by the NABL trained technician and a qualified biochemist before it is being dispatched from the laboratory as a data quality control procedure.

Statistical analysis was performed by SPSS software. Qualitative data was expressed in proportions and quantitative data in mean and standard deviation. Test of significance was done with chi-square and student t-test. Correlation analysis was carried out and correlation coefficient was calculated. P value <0.05 was considered statistically significant.

Results: A total of 821 T2DM patients (539 males and 282 females) were studied. The mean age in the study group was 54.75 years, mean serum creatinine was 0.98, mean eGFR was 91.75, mean UAE was 95.21 and mean HbA1c was 9.06 [Table-1].

Table-1: Clinical characteristics of Type-2 diabetic patients

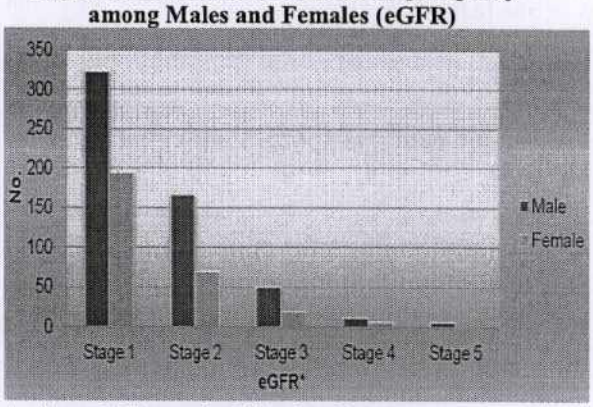
Parameter	Figures (Mean±SD)
Age	54.75 ±11.98
Serum creatinine	0.9755 ± 0.62
eGFR*	91.7524 ± 32.11
UAE**	95.2096 ± 318.41
HbA1c***	9.0627 ± 2.40

*estimated Glomerular Filtration Rate, **Urinary Albumin Excretion, ***Glycosylated Haemoglobin

The most common stage of DN as per eGFR was in stage-1 (51.64%), followed by 33.86%, 11.57%, 2.07% and 0.85% patients in stage 2,3,4 and 5 respectively [Table-2]. The prevalence of DN was more among

males compared to females among all the stages as per eGFR [Figure-1].

Figure-1: Prevalence of Diabetic Nephropathy among Males and Females (eGFR)



*estimated Glomerular Filtration Rate

In Table-3, the prevalence of diabetic nephropathy was 37.02% (8.40% was overt nephropathy and 28.62% was microalbuminuria) and 62.97% were in normoalbuminuric range. 75.76% of the patients had poor glycemic control and 24.33% had good glycemic control. A statistically significant association was observed between UAE and glycosylated haemoglobin. The prevalence microalbuminuria was 30.79% in males and 24.46% in females and the prevalence of overt nephropathy was 9.27% in males and 6.73% in females [Figure-2]. Table-4 depicts maximum subjects i.e., 52.25% had T2DM since five years. The prevalence of overt nephropathy increased with the duration of diabetes and a significant association was observed between duration of diabetes and UAE.

Table-2: Stages of Diabetic Nephropathy in Males and Females

Stages of nephropathy	eGFR* ml/min/1.73m^2	Males	Females	Total
Stage 1	≥90	278 (51.57)	146(51.77)	424(51.64)
Stage 2	60-89	192(35.62)	86 (30.49)	278(33.86)
Stage 3	30-59	52(9.64)	43(15.24)	95(11.57)
Stage 4	15-29	11(2.04)	6(2.12)	17(2.07)
Stage 5	<15	6(1.11)	1(.35)	7(0.85)
Total		539(99.98)	282(99.97)	821(99.99)

Figures in parenthesis indicates percentages, *estimated Glomerular Filtration Rate

Table-3: Urine Albumin Excretion of type 2 diabetes mellitus subjects in relation to glycemic status

UAE* (mcg/mg of creatinine)	HbA1c**<7 n=199	HbA1c**≥7 n=622	Total
<30	154 (29.78)	363(70.20)	517(62.97)
30-299	31(13.19)	204(86.80)	235(28.62)
>300	14(20.28)	55(79.78)	69(8.40)

Figures in parenthesis indicates percentages, * Urinary Albumin Excretion,** Glycosylated Haemoglobin

X^2= 24.87, df =2, P< 0.001The relationship between HbA1C with eGFR and UAE level of the T2DM are revealed in Figure-3 & 4 respectively. There was statistically significant correlation observed between HbA1C with eGFR and UAE levels. As HbA1c values increased a rise in the UAE values was observed, whereas eGFR values decreased.

Discussion: The fact that there is a relationship between nephropathy and diabetes has been established.[11] From the results obtained in this study, 28.62% and 8.40% of the diabetic subjects have albumin levels greater than the acceptable upper limit of normal (30 mg/l). This implies that microalbuminuria and macro albuminuria is prevalent amongst the diabetes. In this study, we observed 8.40% had overt nephropathy.

Table-4: Duration of diabetes and urine albumin levels

Diabetes Duration in Years	UAE* (mcg/mg creatinine)			Total
	<30	30-299	±300	
<5	312 (60.23)	114 (48.31)	3 (4.48)	429 (52.25)
5-10	182 (35.14)	107 (45.34)	13 (19.40)	302 (36.78)
>10	24 (4.63)	15 (6.36)	51 (76.12)	90 (10.96)
Total	518 (100.00)	236 (100.00)	67 (100.00)	821 (100.00)

Figures in parenthesis indicates percentages,*Urinary Albumin Excretion, $X^2 = 329.325$, df= 4, $p<0.001$

Figure-2: Prevalence of Diabetic Nephropathy among Males and Females (UAE)

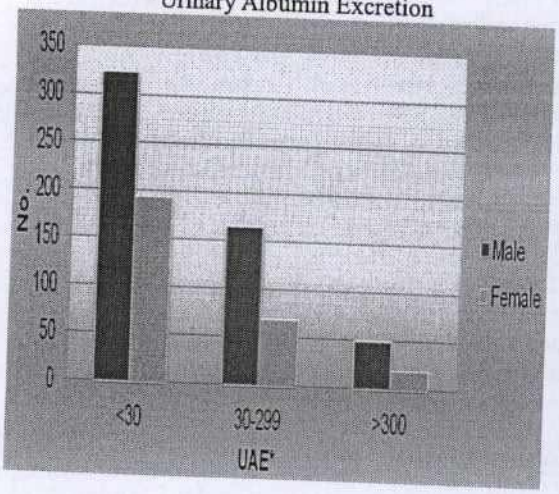
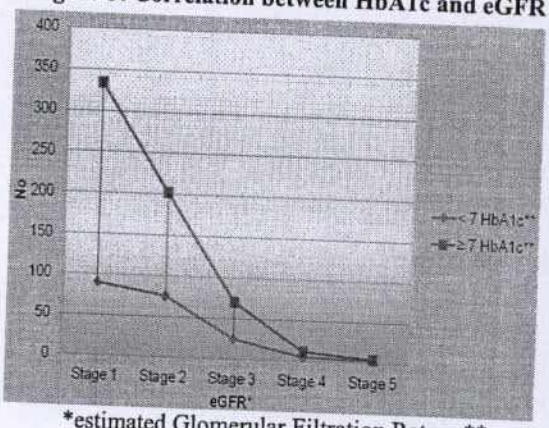


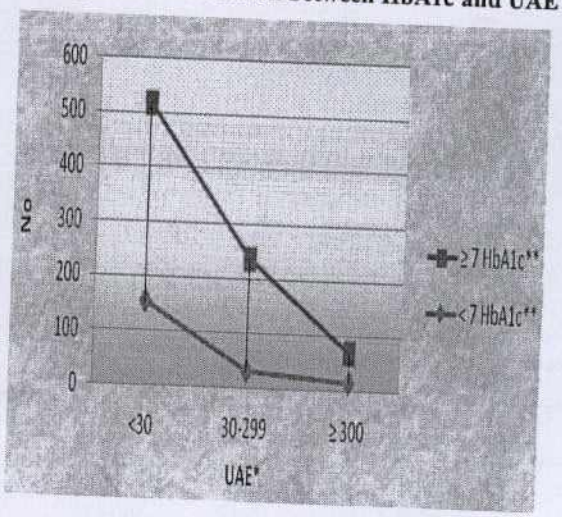
Figure-3: Correlation between HbA1c and eGFR



*estimated Glomerular Filtration Rate, , ** Glycosylated Haemoglobin

This finding agrees with the prevalence report of diabetic nephropathy in type 2 diabetic subjects, reported to be 5-9% in data analyzed from various Indian studies.[21-24] However, this value is much less when compared with the prevalence of the same in Asian-Indians in the UK (22.3%) in a study conducted by Samanta et al. [25] Once overt nephropathy occurs without specific interventions, the glomerular filtration rate (GFR) gradually falls over a period of several years at a rate that is highly variable from individual to individual (2-20ml/min/year). [26] In addition to its being the earlier manifestation of nephropathy, albuminuria is marker of greatly increased cardiovascular morbidity and mortality for patients with T2DM. [27] As a result, diabetic patients should be screened and monitored regularly for microalbuminuria to avoid the risk of diabetic nephropathy complications. The relationship between HbA1c with eGFR and UAE as in figure-3 & 4 respectively showed statistically significance. This implies that urine albumin levels increased with HbA1c level.

Figure-4: Correlation between HbA1c and UAE



*Urinary Albumin Excretion, ** Glycosylated Haemoglobin

The confounding factors for microalbuminuria like renal failure, urinary tract infection, hematuria, acute febrile illness, vigorous exercise, short term pronounced hyperglycemia, uncontrolled hypertension and heart failure were excluded from the study. The study results are limited to cross-sectional hospital based study and for multiple risk factor analysis a community based study needs to be undertaken with a larger sample size.

Conclusion: Diabetic Nephropathy was common in south Indian type 2 DM and microalbuminuria was earliest clinical sign. Progression of DN can be prevented if detected early. Poor glycemic control and duration of diabetes was associated with increase in UAE level and progression of CKD. Hence screening for DN at the time of diagnosis in T2DM and measures to reduce albuminuria at earliest can prevent further progression. Although the renal risk in diabetic nephropathy can be reduced by 20 to 40%, the fact remains that 70% still progress, justifying the attempts to develop novel approaches. It is important to understand the epidemiological aspects of the conditions and demographic pattern of the population along with the pathophysiology and comprehensive management steps that need to be taken to prevent the progression of diabetic kidney disease.

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