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Glomerular Dysfunction in Type 2 Diabetes Mellitus-A Comparison of Early Onset with Late Onset Type 2 Diabetes Mellitus

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Abstract

The India State-Level Disease Burden Initiative Diabetes study collaborators reported that Tamil Nadu had the highest the prevalence of Diabetes in 2016. CURES Study done in Urban South Indian (Chennai) Population reported prevalence of overt nephropathy was 2.2% and microalbuminuria was 26.9%. A higher prevalence of hyperfiltration has been reported in certain ethnic groups, such as Pima Indians, African Americans, Asians and Polynesians, than in Caucasians. The prevalance and complication of early onset type 2 diabetes is understudied in South India. Our aim was to assess the glomerular function of the kidneys in Early Onset Type 2 Diabetes Mellitus. Diabetics attending the NCD outpatient for routine check - up were included in this study. The biochemical parameters were analysed in automated autoanalysers photometrically. Glomerular Filtration was estimated using Modification of Diet in Renal Disease equation (MDRD). The mean e GFR was increased and the percentage of mild to moderate damage of kidney was more indicating renal damage in early onset diabetes. Lower creatinine levels were noted in early onset diabetics indicating glomerular hyperfunctioning of the kidneys which precedes renal damage. The eGFR was increased considerably in obesity category 2. Glomerular hyperfiltration was considerably more in early onset diabetics. Liu *et al* found in an Asian T2DM cohort, with 1189 patients with early-onset DM had higher risk of progressive CKD and had both albuminuria and renal function deterioration. The decreasing trend of eGFR is a better marker and indicator of the Diabetic Nephropathy.

Keywords

Diabetic Nephropathy, Glomerular Hyperfiltration, eGFR, MDRD equation, early onset type 2 diabetes

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INTRODUCTION

The India State-Level Disease Burden Initiative Diabetes study collaborators [1] reported that Tamil Nadu had the highest the prevalence of Diabetes in 2016. As the prevalence of Type 2 Diabetes is increasing, the incidence of Diabetic Nephropathy is also increasing. CURES Study done in Urban South Indian (Chennai) Population reported prevalence of overt nephropathy was 2.2% and microalbuminuria was 26.9% [2] Diabetic Nephropathy (DN) is the leading cause of End Stage Renal Disease (ESRD) in developed countries as well as in some developing

countries [3, 4].The age of patients with Type 2 Diabetes Mellitus (T2DM) is declining and the incidence of early-onset T2DM has been rising rapidly in recent years [5] TODAY Study had indicated, patients with early-onset T2DM had accelerated decline of β-cell function than those with later-onset T2DM [6]. Druet *et al* [7] found that second phase of nutrient-induced insulin secretion might reduce faster in early-onset T2DM than elder, which might be related to abnormal tubular-glomerular feedback and cause Diabetic nephropathy. Renal Biopsy study done in 89 subjects with early-onset T2DM showed higher glomerular grades and arteriolar hyalinosis scores than those with late onset of age above 40 years [8]. A higher prevalence of hyperfiltration has been reported in certain ethnic groups, such as Pima Indians, African Americans, Asians, and Polynesians, than in Caucasians [9, 10]. Adolescents and young adults with diabetes, have renal hyperfiltration in approximately 50% of individuals and which may lead to renal injury [11, 12]. There are not many studies about the renal function in early onset. The prevalance and complication of early onset type 2 diabetes is understudied in South India. The decreasing trend of eGFR is said to be a better marker and indicator of the Diabetic Nephropathy. Our aim is to assess glomerular function of the kidneys in Early Onset Type 2 Diabetes Mellitus. Measure the renal parameters and calculate the estimated Glomerular Filtration Rate eGFR using Modification of Diet in Renal Disease equation (MDRD) in diabetics whose age of onset of diabetes is less than 40 (group 1) with that of the diabetics whose age of diabetes onset is more than 40 years (group 2)

MATERIALS AND METHODS

Sampling

Diabetics attending the Non-Communicable Diseases Outpatient Department in Mahatma Gandhi Memorial Government Hospital, Trichy for routine follow-up were included in this study. The diagnosis of diabetes type II was made according to ADA criteria based on Fasting and Postprandial blood sugar. History of microvascular complications of diabetes (nephropathy, neuropathy, and retinopathy) was not noted in any of the patients. Subjects without history of ketoacidosis and on oral hypoglycaemics only were involved in the study. Patients with type 1 or other special type of diabetes were excluded. Pregnancy and lactating mothers were excluded.

Measurement of Parameters

Height and weight were recorded for calculating Body Mass Index (BMI). Using BMI, the subjects were classified into the obesity categories. Blood samples were collected in appropriate vacutainers for the estimation of Fasting Blood Glucose, Post Prandial Blood Glucose, Serum Urea and Serum Creatinine. The biochemical parameters were analysed in automated autoanalyzer's photometrically using respective reagents. For all the subjects the urine was tested for urine sugar and protein which was negative at the time of examination. Glomerular Filtration was estimated using Modification of Diet in Renal Disease equation (MDRD) and CKD staging was applied. Glomerular Hyperfiltration was defined as estimated glomerular filtration rate (eGFR) above the age- and sex-specific 95thpercentile, while hypofiltration was defined as eGFR below the 5th percentile [12]

Statistical analysis

Data analysis was carried out using the Statistical Package for Social Sciences (SPSS) program and the results were tabulated as descriptive information (i.e., frequency, percentage, mean and standard deviation) and comparison of continuous variables between groups are shown as box plots.

RESULTS

In this study 114 subjects were included in which group 1 or early onset diabetics were 53 and the late onset-group 2 were 61. The duration of diabetes in late onset was very short of less than 5 years. There was not much difference in the mean BMI between the groups though the BMI was lower in group 1. The mean arterial pressure was increased in early onset diabetics (Table 1). There was not much difference in the BMI between the groups, but there were subjects with obesity category 3 in group 1 (Figure 1). In early onset diabetics the Mean arterial pressure increased proportionally to the obesity category, but the variation was most in normal BMI category (Figure 2). eGFR varied in all the BMI categories with no consistent increase or decrease trend.

The mean eGFR was increased in group 1 but the percentage of mild to moderate damage of kidney was more. Lower creatinine levels were noted in early onset diabetics as compared to late onset diabetics. Mild to moderate reduction in renal function was seen in significant number of subjects in group 1 indicating renal damage in early onset diabetes (Table 2). The eGFR was increased considerably in obesity category 2 in group 1. Glomerular hyperfiltration was considerably more in early onset diabetics. (Figure 3)

Table 1: Mean of the Demographics

		Mean
AGE	Late onset	46.3607
	Early onset	41.0755
DM DURATION	Late onset	2.1746
	Early onset	5.4458
BMI	Late onset	27.0955
	Early onset	27.1019
MEAN ARTERIAL PRESSURE	Late onset	95.5574
	Early onset	96.9057
e GFR	Late onset	93.2907
	Early onset	98.9491

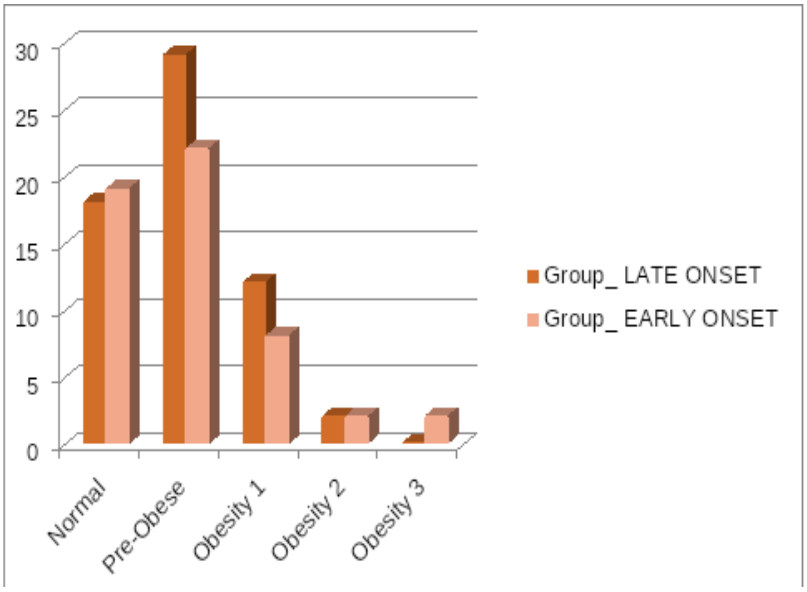

Figure 1: Distribution of subjects according to BMI

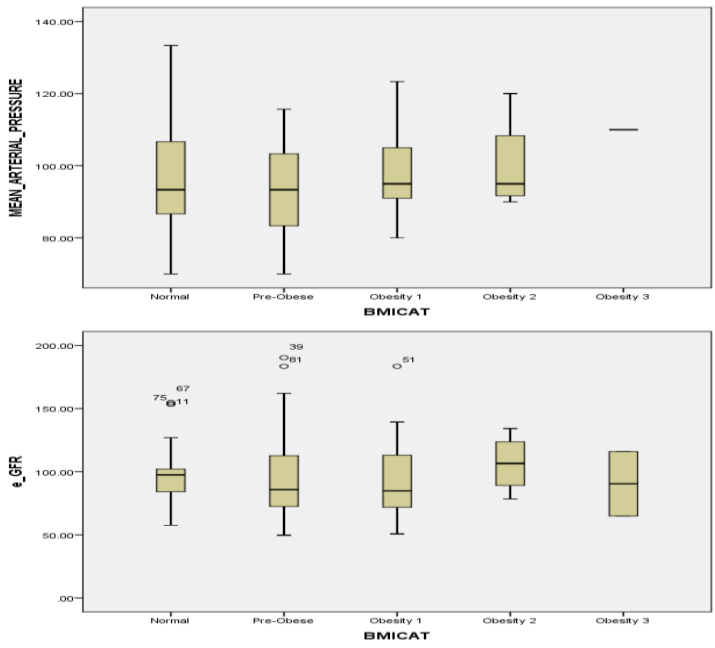

Figure 2: Relation of obesity categories with Mean Artery Pressure and eGFR

Table 2: Distribution of subjects based on eGFR.

CKD STAGING BASED ON eGFR	EARLY ONSET	LATE ONSET
GLOMERULAR HYPERFILTRATION (eGFR 121 - 150)	9	7
STAGE 1 (eGFR 90 - 120) NORMAL FUNCTION	24	22
STAGE 2 (eGFR 60 – 89) MILD REDUCTION	15	30
STAGE 3a (eGFR 45 – 59) MILD TO MODERATE REDUCTION	5	2
STAGE 3b (eGFR 30 – 44) MODERATE TO SEVERE REDUCTION	--	--
STAGE 4 (eGFR 15 – 29) SEVERE LOSS OF KIDNEY FUNCTION	--	--
STAGE 5 (eGFR < 15) KIDNEY FAILURE/ END STAGE RENAL DISEASE	--	--

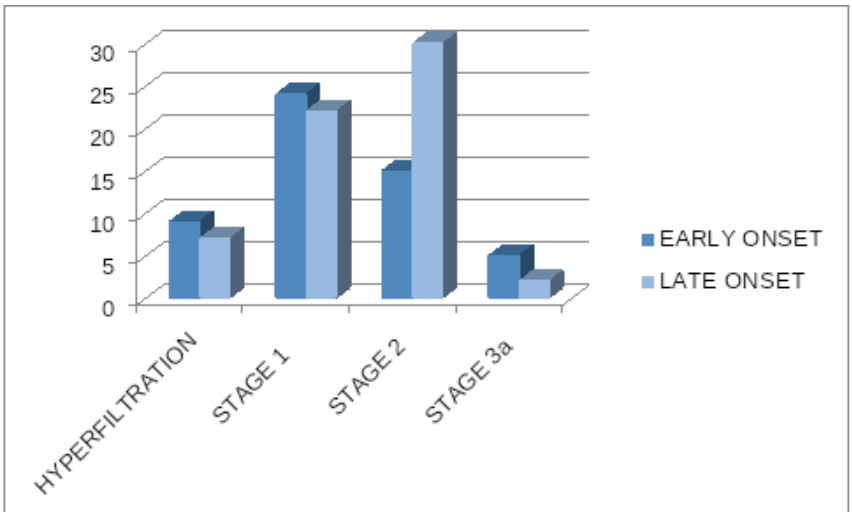

Figure 3: CKD staging comparison between the groups.

DISCUSSION

We have seen that the glomerular function is reducing in the early onset diabetics and most of them are in glomerular hyperfiltration stage which is said to be an indicator of early renal damage. The glomerular function in the late onset with short duration of diabetes was decreased probably due to increased age. The creatinine levels were low in early diabetics, probably indicating hyperfiltration and renal damage. Hyper perfusion was also noted in early diabetics as the mean arterial pressure was high as compared to controls.

A retrospective renal biopsy-based study showed that, those with early-onset T2DM had more severe glomerular and vascular pathological lesions, higher risk of ESRD than later-onset ones though their renal function and proteinuria were similar at the time of renal biopsy [8]. Renal hyperfiltration seems to represent the earliest hemodynamic abnormality seen in diabetes [13]

Liu *et al* [14] found in an Asian T2DM cohort, with 1189 patients with early-onset DM had higher risk of progressive CKD and had both albuminuria and renal function deterioration. Another study on T2DM and clinical diagnosed DN in 1111 individuals indicated that patients with early-onset had higher prevalence of ESRD and early-onset was an independent risk for ESRD after adjusted for traditional risk factors [15]. American Diabetes Association recommends routine screening of GFR in adults and now in adolescents with diabetes [16]. Lower serum creatinine is considered a risk factor for type 2 diabetes. A lower volume of skeletal muscle associated with lower serum creatine would mean fewer target sites for insulin which is the pathogenesis of type 2 diabetes. [17]

CONCLUSION

In this study we found a decrease in eGFR in early onset Type 2 Diabetics. Low creatinine levels were seen and hence there is glomerular hyperfunctioning of the kidneys which precedes renal damage. The eGFR is a better marker and indicator of the Diabetic Nephropathy. In our study the study population was very small and follow up could not be done this is a major limitation. Larger population-based cohorts are required with inclusion of confounding factors with follow up to analyse and shed some light on the Early Onset Type 2 Diabetes and the complications associated.

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