

## Original Research Article

# Diabetic nephropathy: early markers for monitoring and prevention

Vijayashree S. Gokhale\*, Kshithija R. Sajjan, Rupesh Parati, Keyuri Mehta

Department of Medicine, Dr. D. Y. Patil Medical College, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India

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**\*Correspondence:**

Dr. Vijayashree S. Gokhale,

E-mail: Gokhale.vijayashree@gmail.com

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### ABSTRACT

**Background:** Type 2 diabetes, with its complications is perpetually on the rise more so in India. Diabetic Nephropathy progresses silently, and manifests at a stage where, patient can be offered only renal replacement. This study was undertaken to detect early markers of Diabetic Nephropathy. Aims and objective of the study was to study early nephropathy by UACR (urinary albumin/creatinine ratio), RFT (renal function test) and e-GFR in Type 2 diabetic patients of more than 2 years duration, with and without hypertension.

**Methods:** A hospital based cross-sectional observational study, of 100 patients, 18-60 years of age, of type 2 Diabetes of 2 year duration and above, of which 50 were only diabetic and 50 had diabetes and hypertension. Patients who had an established renal disease were excluded from study.

**Results:** Our study of 100 patients, 18-60 years of age, had 23 male and 77 female patients. Maximum patients were in age group 41-50 years, and 52% had diabetes of 2-4 years duration. Of the renal parameters studied, BUN was normal in 72% and S. Creatinine normal in 67%. UACR was normal in only 38%, and e-GFR was normal in 49%.

**Conclusions:** In our study age and sex, duration of Diabetes and HbA1c did not have any bearing on renal parameters. UACR followed by e-GFR, were deranged early. UACR was more deranged in diabetics with hypertension.

**Keywords:** Diabetic nephropathy, e-GFR, Hypertension, UACR

### INTRODUCTION

According to the international diabetes federation, 592 million (1 in 10 persons) worldwide will have DM by 2035. The macrovascular and microvascular complications of diabetes are the culprits of high mortality and morbidity of diabetes. They include coronary artery disease, hypertension, retinopathy, end-stage renal disease, peripheral vascular disease and neuropathy. In India, there are about 69.2 million people with diabetes and are expected to cross 123.5 million by 2040. Epidemiologic studies have shown that a fifth of all diabetes patients suffer from two or more micro vascular complications.

Diabetic kidney disease (DKD) is diagnosed when there is persistent albuminuria, increasing serum creatinine and a progressive decline in estimated GFR (eGFR) glomerular filtration rate. 20-40% of diabetic nephropathy patients will progress to End stage renal disease. Early diagnosis, treatment of modifiable risk factors, optimum glycemic control and renoprotective anti-diabetic and anti-hypertensive medications may help prevent or at least postpone chronic kidney disease and renal replacement therapy.<sup>1</sup>

Aims and objectives of the study were to study Early Nephropathy by UACR (urinary albumin/creatinine ratio), RFT (renal function test) and e-GFR in Type 2

diabetic patients of more than 2 years duration, with and without hypertension.

**METHODS**

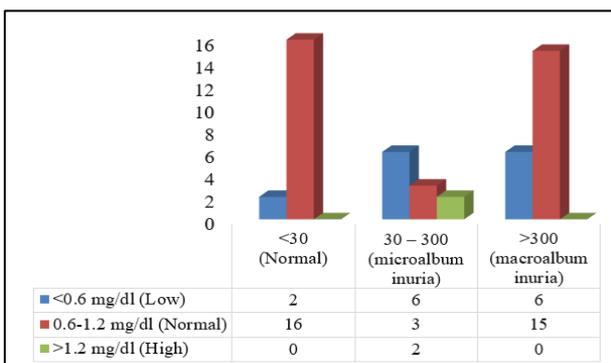
A cross sectional observational study conducted over a period of 3 years in a semi-urban Medical college Hospital of Western Maharashtra, India.

Sample size of 100 patients included diabetic patients aged between 18-60 years, of 2 or more years of duration of diabetes. Of these, 50 also had hypertension. Patients with established renal disease, obstructive uropathy and those with structural kidney disease on ultrasound were excluded from study. All study participants who consented to participate, were clinically examined. Routine and specific investigations done hemogram, BSL F, PP, HbA1c, lipid profile, X-ray chest, ECG, USG abdomen for kidneys. RFT: BUN, S. creatinine, urine routine and microscopy, UACR (urinary albumin/Creatinine ratio) urine albumin was estimated in fresh urine while the creatinine sample was stored at -20°C for a maximum of 24 hours. e-GFR was calculated by the abbreviated MDRD equation:  $186 \times (\text{Creatinine}/88.4) - 1.154 \times (\text{Age}) - 0.203 \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$ .

All data thus collected and tabulated was subjected to statistical analysis. Qualitative data presented as Mean and Standard deviation. Association among the study groups assessed with the help of Fisher test, student 't' test and Chi-Square test. 'p' value less than 0.05 was taken as significant.

**RESULTS**

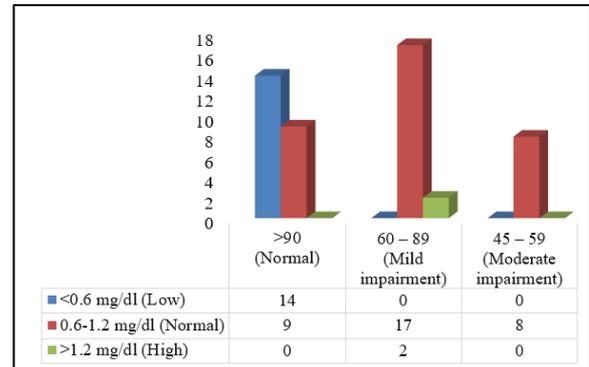
Our study of 100 patients, 18-60 years of age, had 23 male and 77 female patients. Maximum patients were in age group 41-50 years, and 52% had diabetes of 2-4 years duration. Of the renal parameters studied, BUN was normal in 72%, S. Creatinine normal in 67%. UACR was normal in only 38%, and severely deranged in 42%. e-GFR was normal in 49% and moderately deranged in 16%.



**Figure 1: Association of creatinine and UACR in diabetic group.**

Creatinine values Chi-square = 14.28, p=0.03;

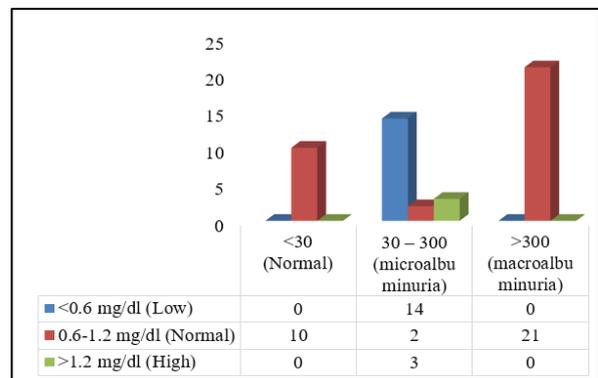
Observation: 9 out of 50 patients who had low to normal creatinine values, had moderately deranged UACR, and 21 had severely deranged UACR.



**Figure 2: Association of Creatinine and eGFR in diabetic group.**

Creatinine values, Chi-square=17.39, p=0.002;

Observation: 25 out of 50 patients had mild to moderate impairment of e-GFR, yet creatinine values were normal.



**Figure 3: Association of Creatinine and UACR in diabetic+hypertension group.**

For Creatinine values Chi-square = 17.57, p=0.002;

Observation: 37 out of 50 patients had deranged UACR.

**DISCUSSION**

Diabetic Nephropathy has been extensively studied over the years and especially so after UKPDS trial. Jorge et al put forward stages of diabetic nephropathy, by microalbuminuria and e-GFR calculated by Cockcroft-Gault equation.<sup>1</sup>

Claude et al studied gene and protein markers, but could not find definitive genetic markers.<sup>2</sup> Nielsen et al, studied impact of ACE inhibitors, and concluded that they do reduce tubular and glomerular injury.

Haque et al in their study concluded that there is no difference between UACR and eGFR in diabetics with and without Hypertension. In our study we found more derangement of UACR in diabetics with hypertension.<sup>4</sup> Vupputuri et al in their population based study concluded that eGFR and albuminuria do correlate with progress of nephropathy.<sup>5</sup>

Around 2015, Klein et al, Fiseha et al, Colombo et al, Chawla et al, Jaggi et al and Gluhovschi et al studied more and more Biomarkers of Diabetic Kidney disease. Of all these UACR and eGFR emerged as reliable markers, similar to our study.<sup>6,9,10,12,13</sup>

At the same time, Stephanie et al, Allison et al and Sydney et al studied pathophysiology and management of Diabetic Kidney disease.<sup>7,8,11</sup> Of the drugs possibly reducing kidney damage, Thiazolidinediones, Gliptins and SGLT-2 inhibitors were studied. But ACE-I and ARB's showed benefit. Radica et al also studied management of diabetic kidney disease, with similar conclusions.<sup>14</sup>

In the years 2017 and 2018 many more investigators studied an array of biomarkers, both glomerular, tubular and interstitial. They were Al-Rubeaan et al, Siddiqui et al, Nektaria et al and Uwaezuoke, Satirapoj et al, Marcovecchio et al and Rolland et al.<sup>16-21</sup> All concluded that eGFR and albuminuria were the best to predict risk of decline of kidney function over time.

Idowu et al in their study concluded that a duration of Diabetes of more than 10 years corresponded to high systolic blood pressure, dyslipidemia and increased microalbuminuria.<sup>18</sup> However in our study, early derangement of UACR and eGFR was seen. In 2019 and 2020 Zhang et al studied serum and urinary biomarkers, as indicators of diabetic nephropathy.<sup>23</sup>

Kopel et al, Elena et al studied various aspects of Diabetic Kidney disease and looked at ADMA and SDMA, dimethylarginines in chronic kidney disease, but yet to arrive at definitive conclusions.<sup>22,24</sup> Xie et al studied and found association between UACR and left ventricular hypertrophy in Type 2 diabetes patients.<sup>26</sup>

Lo et al studied and found beneficial effects of SGLT-2 inhibitor Empagliflozin on cardiovascular and Renal outcomes in Diabetic patients.<sup>25</sup> Our study compared Diabetic patients with and without Hypertension for UACR and eGFR. Bhisare et al study of UACR as an early predictor of diabetic nephropathy, matched our study closely except that their study subjects had slightly longer duration of diabetes.<sup>27</sup>

### **Limitations**

Small sample size.

### **CONCLUSION**

Our study had maximum patients in a relatively young age group of 40-50 years with maximum patients having a duration of diabetes of 2- 4 years. Comparison of BUN, S. Creatinine with UACR showed early derangement of UACR and e-GFR. UACR was more deranged in the Diabetes plus hypertension group. Thus UACR and eGFR did emerge as early markers of diabetic nephropathy and that hypertension if present along with Diabetes, UACR derangement is more severe.

### **Clinical implications**

UACR and e-GFR besides other renal parameters should be a part of regular monitoring of patients of Diabetes and diabetes with hypertension and this monitoring should start at the very onset of diabetes.

So that ACE-inhibitors and ARB drugs can be a part of the treatment regimen and then hopefully Diabetic nephropathy could be prevented or at least postponed.

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