

## A study of estimated glomerular filtration rate in diabetic patients in an Indian metro city



### Medical Science

**KEYWORDS:** Diabetes mellitus, creatinine, eGFR

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### ABSTRACT

#### Background

End stage renal disease is very common in diabetic patients. Early diagnosis using estimated glomerular filtration rate (eGFR) is helpful in management.

#### Objective

To assess eGFR associated with diabetes at a private clinic in an Indian metro city.

#### Methods

Patients attending a private clinic in Chennai were enrolled. Prevalence of diabetes was assessed by using fasting and postprandial blood sugar levels. eGFR values were calculated using formula provided by Modification of Diet in Renal Disease (MDRD) study group. Data was analyzed using appropriate statistical tests.

#### Results

Out of the 274 patients in whom further analysis was done, 62 patients had blood sugar levels higher than those required for diagnosis of diabetes. About 23 percent of the enrolled patients were diagnosed to be suffering from diabetes. Mean serum levels of creatinine in the diabetic patients was found to be  $1.04 \pm 0.26$  mg%. Mean serum creatinine concentration in diabetic males was  $1.05 \pm 0.46$  mg%, while mean creatinine concentration in females was found to be  $0.95 \pm 0.42$  mg%. However, creatinine values were in the normal range in majority of the patients i.e. diabetics as well as non-diabetics. On estimation of GFR in the diabetic patients it was found that mean GFR was  $73.14 \pm 27.04$  ml/min/1.73sq.m. Mean GFR level in the diabetic males was  $78.15 \pm 16.8$  ml/min/1.73sq.m while mean GFR levels in the diabetic females was  $68.08 \pm 18.9$  ml/min/1.73sq.m. Difference was found to be statistically significant on comparing the two genders for serum creatinine as well as eGFR ( $p < 0.05$ ). 50 patients had stage 1 or 2 renal disease.

### Introduction

Prevalence of type 2 diabetes mellitus continues to rise within India and around the world. Diabetes is a growing epidemic in all parts of the world. About 62 million people diagnosed with diabetes currently live in India. India topped the world with number of people diagnosed with diabetes in 2000.<sup>1,2</sup> Wild et al predicted that the global prevalence of diabetes will double in 2030 as compared to 2000 with maximum impact of increase in India i.e. in the year 2000 about 31.7 million people were afflicted with type 2 diabetes and this number is expected to go up to 79.4 million in 2030.<sup>3,4</sup> Pattern of diabetes is related to geographic distribution in India. Prevalence of diabetes in rural India is about one-fourth as compared to urban India.<sup>5,6</sup> The dramatic rise in prevalence of diabetes could be attributed to rapid lifestyle changes brought about by rapid urbanization in last 50 years.<sup>5,6</sup> Reasons for the growth in type 2 diabetes in India include an ageing population, increasing obesity rates, increasing population of affluence in middle class and a shift towards sedentary lifestyle. Diabetes among children and youth is also increasing.

Diabetes mellitus induces micro as well as macro-vascular changes in the body including diabetic nephropathy. Mechanism includes hyperglycemia induced increased glomerular filtration rate<sup>8,9</sup>. This may later progress to end stage renal disease. Diabetic kidney disease is also the leading cause of end stage kidney disease around the world<sup>9</sup>. Hence, it is important to monitor glomerular function in diabetic patients to prevent development of end stage renal disease. Diabetic nephropathy imposes significant socioeconomic burden in the form of hospitalizations, cardiovascular disease, and mortality. Hence, it is important to identify at-risk individuals and manage them aggressively. Definitive diagnosis of diabetic glomerulopathy can only be done based on histology from a kidney biopsy, while clinical diagnosis requires history of diabetes mellitus along with elevated albuminuria and or progressive decline<sup>10</sup> in kidney function (glomerular filtration rate). It is important to assess renal function of these patients using the most important test i.e. GFR because

GFR is the most widely used and acceptable measure of renal function<sup>11</sup>. GFR is the volume of fluid filtered from the renal glomerular capillaries into the Bowman's capsule in unit time. GFR can be estimated using creatinine clearance rate (Ccr). Ccr is calculated using creatinine concentration in the collected urine sample (Ucr), urine flow rate (v), plasma concentration of creatinine (Pcr)<sup>12</sup>. Most recently advocated formula for calculating the GFR is the one developed by the Modification of Diet in Renal Disease (MDRD) study group which estimates GFR using four variables: serum creatinine, age, race and gender<sup>13</sup>. Kidney disease can be classified according to estimated GFR (eGFR) as<sup>14</sup>: (Table 1)

**Table 1. Classification of renal disease based on eGFR**

Stage	Description	GFR(ml/min/1.73sq.m)
0	Normal	$\geq 90$
1	Kidney damage with normal or raised GFR	$\geq 90$
2	Kidney damage with mild reduce GFR	60-89
3	Moderately reduced GFR	30-59
4	Severely reduced GFR	15-29
5	Kidney failure	$< 15$

This may allow early detection in abnormalities of renal function and allow institution of more rigorous management. This may also provide advance warning of progression to end stage renal disease. Reduced glomerular filtration rate (GFR) is also associated with an increased risk of cardiovascular events and mortality in diabetic patients<sup>15</sup>. Pathophysiologic mechanisms have been proposed explaining the association between reduced eGFR and increase in cardiovascular risk. A decreased eGFR is associated with increase oxidative stress, increase C-reactive protein, homocysteine, abnormal level of lipoprotein (a), hyperinsulinaemia and increased coagulability leading to endothelial dysfunction and development of atherosclerosis<sup>16-20</sup>. Studies relating early renal changes with the risk factors for diabetic renal disease have been few. Hyperfiltration and renomegaly are not commonly used in the clinical evaluation of diabetics as these procedures are technically complex. The following study was

conducted to find out the earliest stage of diabetic renal disease in the enrolled patients by measuring GFR using simpler and non-invasive methods at a private clinic in Chennai.

**Methods**

The following study was conducted in out-patient set up in a private clinic in urban area of Chennai city. After informing the patient written consent was obtained for the study, Patients of both genders were enrolled in the study. Patients attended the outpatient department of the private clinic. Blood glucose i.e. fasting and postprandial levels were estimated, while in other patients random blood sugar (RBS) was estimated. As per WHO 2006 recommendations, patients having fasting blood glucose levels more than 126 mg/dl or postprandial levels higher than 200 mg/dl were diagnosed to be suffering diabetes, while those having fasting blood glucose less than 126 mg/dl and postprandial blood glucose between 110 mg/dl and 200 mg/dl were said to be having impaired glucose tolerance. A patient having apparent symptoms of diabetes and RBS value more than 200 mg/dl was also diagnosed to be suffering from diabetes. Serum creatinine levels were also estimated using appropriate tests. All the parameters were recorded in Microsoft excel worksheet version 2007. Unpaired *t* test was used for intergroup comparisons while qualitative was compared using Fisher's exact test. Graph pad demo version 3.0 was used for detailed analysis of the obtained data.

**Results**

**Demographic details**

A total of 305 patients were enrolled in the study. Out of the enrolled patients, about 152 were males and 153 were females. Mean age of the study population was 43.17 ± 14.5 years. Mean age of females was 46.11 ± 28.18 years while mean age of the males was 42.59 ± 16.12 years. Minimum age of the enrolled patients was 21 years and maximum was 69 years.

**Laboratory parameters**

**Blood glucose**

Blood glucose values were available for 274 patients. Out of 274 patients, data was available for 138 females and 136 males. Remaining 26 patients were excluded from further analysis. Mean fasting glucose level was found to be 114 ± 76 mg/dl while mean postprandial glucose levels was 156 ± 79 mg/dl. Mean RBS value of 10 patients was 109 mg/dl. In males, mean fasting blood sugar levels were found to be 113 ± 74 mg/dl, while mean postprandial blood sugar level was found to be 159 ± 64 mg/dl. In females, mean fasting blood sugar value was 114 ± 49 mg/dl while, mean postprandial level was 155 ± 49 mg/dl. On comparison, there was no statistical difference between the two genders, neither for fasting blood glucose nor for postprandial blood glucose levels.

Out of the 274 patients in whom further analysis was done, 62 patients had blood sugar levels higher than those required for diagnosis of diabetes. Hence, about 23 percent of the enrolled patients were diagnosed to be suffering from diabetes. Out of the 62 diabetic patients, 34 (54%) were males and 28 (46%) were females. Mean age of patients diagnosed with diabetes was 48.84 years. The mean age amongst diabetics was comparable in both genders (49.6 vs. 48.2). Percentage prevalence was 25 percent in males and 20 percent in females. Percentage prevalence was also high among males in our study. However, the difference in diabetes prevalence was not statistically significant on comparing the two genders.

**Table 2. Demographic details and blood glucose characteristics of the enrolled patients**

Parameter	Males	Females	Total
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Number of enrolled patients	138	136	274
Mean fasting blood glucose levels (Mean ± SD)	113 ± 74 mg/dl	114 ± 49 mg/dl	114 ± 76 mg/dl
Mean postprandial blood glucose levels (Mean ± SD)	159 ± 64 mg/dl	155 ± 49 mg/dl	156 ± 79 mg/dl
Number of diabetic patients	34 (54%)	28 (46%)	62
Mean age of diabetic patients	48.6	47.4	47.54

**Serum Creatinine assessment**

Serum creatinine levels were estimated in the enrolled patients (table 3). Mean serum creatinine concentration of the entire enrolled patients was 1.02 ± 0.49 mg%. Mean serum creatinine concentration in males was 1.08 ± 0.76 mg%, while mean serum creatinine concentration in the enrolled females was found to be 0.96 ± 0.44 mg%. The difference was found to be statistically significant on comparing the two genders (p<0.05). Similar assessment was done in the diabetic patients enrolled in the study. Mean serum levels of creatinine in the diabetic patients was found to be 1.04 ± 0.26 mg%. Mean serum creatinine concentration in diabetic males was 1.05 ± 0.46 mg%, while mean serum creatinine concentration in females was found to be 0.95 ± 0.42 mg%. Here too the difference was found to be statistically significant on comparing the two genders (p<0.05). However, creatinine values were in the normal range in majority of the patients i.e. diabetics as well as non-diabetics.

**Estimation of GFR levels**

GFR was estimated using the formula developed by the Modification of Diet in Renal Disease (MDRD) study group which estimates GFR using four variables: serum creatinine, age, race and gender (GFR3 5) (table 2).

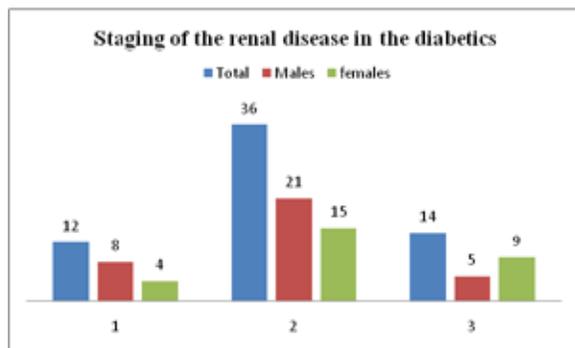
Mean GFR of the enrolled patients was found to be 76.48 ± 24.48 ml/ min/1.73sq.m. Mean GFR values of the enrolled females was found to be 73.32 ± 18.76 ml/ min/1.73sq.m while mean GFR values of the enrolled males was 80.50 ± 25.07 ml/ min/1.73sq.m. This difference was found to be statistically significant on comparison (p<0.05). On estimation of GFR in the diabetic patients it was found that mean GFR was 73.14 ± 27.04 ml/ min/1.73sq.m. Mean GFR level in the diabetic males was 78.15 ± 16.8 ml/ min/1.73sq.m while mean GFR levels in the diabetic females was 68.08 ± 18.9 ml/ min/1.73sq.m. On observation it is found that the level of GFR is reduced in all the categories as compared to overall patients. GFR levels were significantly lower in the diabetic females as compared to the males and this difference was statistically significant.

**Table 3. Serum Creatinine and Glomerular filtration rate in the enrolled patients**

Parameter	Observed Value
Serum Creatinine (Total patients n=274)	
• Total	1.02 ± 0.49 mg%
• Males	1.08 ± 0.76 mg%
• Females	0.96 ± 0.44 mg% *
Diabetic patients (n=62)	
• Total	1.04 ± 0.26 mg%
• Males	1.05 ± 0.46 mg%
• Females	0.95 ± 0.42 mg% #
Glomerular filtration rate (Total patients n=274)	
• Total	76.48 ± 24.48 ml/ min/1.73sq.m.
• Males	80.50 ± 25.07 ml/ min/1.73sq.m.
• Females	73.32 ± 18.76 ml/ min/1.73sq.m*
Diabetic patients (n=62)	
• Total	73.14 ± 27.04 ml/ min/1.73sq.m.
• Males	78.15 ± 16.8 ml/ min/1.73sq.m.
• Females	68.08 ± 18.9 ml/ min/1.73sq.m#

\*, # =p<0.05 as compared to the females in the group

Renal disease was also staged in the diabetics using the classification mentioned above (figure 1). It was found that the 12 patients had normal or stage 1 renal disease, 36 patients had stage 2 renal disease while 14 patients had stage 3 renal disease. In the diabetic males, 8 patients had stage 1 renal disease, 21 patients had stage 2 renal disease while 5 patients belonged to stage 3. Similarly, in the enrolled females, 4 patients had stage 1 renal disease, 15 patients had stage 2 renal disease while 9 patients had stage 3 renal disease.



**Figure 1.** Staging of the renal disease in the enrolled diabetics.

#### Discussion

Diabetes is a disease caused by absolute or relative deficiency of insulin. It is a non-communicable disease which has assumed epidemic proportions. Prevalence of the disease is increasing day by day and it is one of the most important causes of end stage renal disease. Our study was conducted at a private clinic in Chennai city to know about estimated glomerular filtration rate (eGFR) in the diabetics. Our study had 274 patients, out of which 62 patients were diabetic. Out of 62 diabetics 34 were males and 28 were females. Prevalence of diabetes was 23%. Serum creatinine values were significantly lower in the females as compared to males. Estimated GFR values were also found to be significantly lower in the females as compared to males. Based on classification mentioned above, majority of diabetics in our

study had stage 2 or stage 3 of renal disease.

Glomerular function changes during the course of renal disease in type-2 diabetics are difficult to evaluate because the exact onset of diabetes is uncertain and it has a protracted course. Also, in some populations prevalence of non-diabetic renal disease is high<sup>21</sup>. Previous studies in type-2 diabetics have stated that proteinuria and renal failure are common<sup>22</sup>. Several pathways have been implicated in diabetic kidney disease. In hyperglycemia, glucose is metabolized through the polyol pathway, which decreases the amount of NADPH, leading to lower levels of glutathione which can lead to oxidative damage<sup>23</sup>. Increased Protein Kinase C activity and Advanced glycation end products (AGE) are also implicated in the pathogenesis of renal disease in the diabetics<sup>24,25</sup>. RAAS system has also been implicated in the same<sup>26</sup>. Our study revealed that serum creatinine values were normal in majority of the diabetic and non diabetic patients; however, eGFR values were abnormal in majority of diabetics. Our findings is similar to the findings of Segura et al. which suggests that serum creatinine is less sensitive than eGFR to detect small differences in kidney function<sup>27</sup>.

The seventh report of Joint National Committee (JNC-7) recognized eGFR (<60 ml/min) as one of the major risk factors for cardiovascular disease<sup>27</sup>. Our study also had 14 patients who had eGFR levels less than 60. Several large scale population based studies like the Hope Study, Cardiovascular Health Study (CHS), Hypertension optimal treatment (HOT) study, Atherosclerosis risk in communities (ARIC) study have shown that occurrence of ischemic heart disease is higher in diabetic subjects who have reduced eGFR<sup>27</sup>.

#### Conclusion

Our study has suggested that eGFR is a significant predictor of renal function in diabetic patients as compared to serum creatinine. Significant difference was observed in the eGFR values between males and females with the latter having significantly lower values. Our study reemphasizes the need for early diagnosis and management of renal disease in diabetic patients. However, the sample size of our study was small and it was a cross sectional study. Keeping the results in mind it needs to be confirmed on large scale population based studies.

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