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Correlation of Estimated Glomerular Filtration Rate with Microvascular Complications in Type - 2 Diabetes Mellitus Patients

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Abstract: ***Background: Diabetes mellitus (DM) is a global health problem which carries a risk for a myriad of microvascular and macrovascular complications, including retinopathy, nephropathy, and neuropathy (microvascular) and ischemic heart disease, peripheral vascular disease, and cerebrovascular disease (macrovascular). GFR is the best measure of kidney function. Changes in GFR appear earlier than microalbuminuria in diabetic patients. The present study was conducted to investigate the potential association of estimated glomerular filtration rate with prevalence of microvascular complications as well as to evaluate the effect of decline in estimated glomerular filtration rate with severity of microvascular complications of diabetes. Materials & Methods: This was conducted on 100 patients in the department of Medicine, Government Medical College, Amritsar. The study protocol was approved by the institutional ethics committee. The patients were enrolled in the study after obtaining written informed consent. The urine microalbumin excretion test and serum creatinine test were performed. Serum creatinine test was done to calculate the eGFR by modification of diet in renal disease (MDRD) formula. The results were then analysed. Results: Out of 100 patients, eGFR was <15 mL/min in 30% patients, 15 - 30 mL/min in 35% patients, 30 - 60 mL/min in 33% patients, 60 - 90 mL/min in 4% patients and >90 mL/min in 1% patient. There was a negative correlation between eGFR and systolic blood pressure which was statistically significant (p=0.01). However, there was no correlation between eGFR and diastolic blood pressure. Though a downward trend in eGFR change was demonstrated alongside an HbA1C reduction, however, no statistically significant correlation between HbA1C and eGFR was found. There was a negative correlation between eGFR with Urinary Albumin Creatinine Ratio (Pearson Coefficient - 0.39), implied that more was the Urinary Albumin Creatinine Ratio, less was the eGFR. Similarly, there was also a negative correlation between eGFR with Serum Creatinine, and Systolic BP (Pearson Coefficient - 0.48 and - 0.30, respectively). Conclusion: eGFR estimation is an indicator of kidney function which enables the identification and classification of the level of renal impairment in diabetic nephropathy. Retinopathy, neuropathy, and nephropathy are the microvascular complications of diabetes that are strongly and substantially correlated with a reduction in eGFR. The worsening severity of microvascular consequences of diabetes are related to lower levels of eGFR. Controlling the pace of eGFR drop will lessen the likelihood of complications, which will lower the burden of the condition and enhance patient quality of life. Therefore, new treatment approaches should focus on maintaining steady renal function in diabetics.***

Keywords: Diabetes mellitus, Diabetic neuropathy, Diabetic nephropathy, Estimated glomerular filtration rate

1. Introduction

Diabetes mellitus (DM) is increasing globally at an alarming rate. Approximately 80% cases of diabetesarefrom developing countries. [1]Diabetic mellitus carries a risk for a myriad of complications which can be microvascular and macrovascular in origin, including retinopathy, nephropathy, and neuropathy (microvascular) and ischemic heart disease, peripheral vascular disease, and cerebrovascular disease (macrovascular). [2, 3]GFR is the best measure of kidney function since it accounts for age, BMI and sex. [4]Changes in GFR appear earlier than microalbuminuria in diabetic patients. Past studies have reported that GFR is one of the variables that affects the likelihood of developing diabetic retinopathy and other complications of DM. [5, 6]The American Diabetes Association recommends estimation of glomerular filtration rate by eGFR (in ml per min per 1.73 m2), which is calculated by the Cockcroft - Gault (CG) formula, corrected for Body Surface Area (BSA), and the Modification of Diet in Renal Disease (MDRD) equation in all patients with diabetes. [7, 8]The present study was conducted to investigate the potential association of estimated glomerular filtration rate with prevalence of microvascular complications as well as to evaluate the effect of decline in estimated glomerular filtration rate with severity of microvascular complications of diabetes.

2. Materials and methods

This study was conducted on 100 diabetic patients admitted in the department of Medicine, Guru Nanak Dev Hospital, Government Medical College, Amritsar (Punjab). The study protocol was approved by the institutional ethics committeeand written informed consentwas obtained from the patients enrolled in the study.

Inclusion criteria -

- Patients who are known cases of type 2 diabetes mellitus with duration of more than or equal to 5 years.

Exclusion criteria -

- Recent Febrile Illness
- Recent Vigorous exercise
- Recent Urinary tract infection
- Recent Hematuria
- Recent Congestive heart failure
- Recent Smoking
- Recent uncontrolled Hypertension

All the patients were examined and detailed history regarding the duration of diabetes mellitus was noted, and clinical investigations were performed according to a predesigned and pretested proforma. Specific investigations such as urine microalbumin excretion test and serum

creatinine test were also performed. Serum creatinine test was done to calculate the eGFR by modification of diet in renal disease (MDRD) formula. All the type 2 diabetes mellitus patients were divided into various stages of kidney disease by calculating the eGFR by MDRD. The results of observations of individual patients were tabulated and analysed using appropriate statistical software.

3. Results

Baseline data of patients: Majority of the patients (32%) were in 51 - 60 years, followed by 19% patients in 61 - 70 years, 18% patients in <40 years, 17% patients in 41 - 50 years, and 14% patients in >70 years. There was a slight male preponderance (51% male vs 49% female patients). Most of the patients (59%) were from rural background and remaining 41% were from urban background. Neuropathy, retinopathy, and hypertension were present in 62%, 65%, and 71% patients, respectively. Proliferative Diabetic Retinopathy and Non - Proliferative Diabetic Retinopathy were present in 23% and 43% patients, respectively. Body mass index (BMI) grading showed 20% patients were overweight, 9% patients were underweight, and rest had normal BMI. Upon ultrasound, renal size was contracted in 12% patients, borderline in 58% patients, and normal in remaining 30% patients. Out of all the 100 patients, 86 patients had diabetes for 5 - 10 years constituting the maximum proportion of the study group, 12 patients had diabetes for 11 - 15 years and 2patients had diabetes for 16 - 20 years (Table 1).

Comparison of eGFR with various parameters: Out of 100 patients, eGFR was <15 mL/min in 30% patients, 15 - 30 mL/min in 35% patients, 30 - 60 mL/min in 33% patients, 60 - 90 mL/min in 4% patients and >90 mL/min in 1% patient. The mean (±SD) systolic blood pressure (SBP) and diastolic blood pressure (DBP) of patients with eGFR more than 90 ml/min was 122/60 mm Hg. The mean (±SD) SBP and DBP of patients with eGFR 60 - 90 ml/min was 135±18.94 mm Hg and 69.5±7.37mm Hg, respectively. The mean (±SD) SBP and DBP of patients with eGFR 30 - 60 ml/min was 134.55±18.7 mm Hg and 72.18±11.07 mm Hg, respectively. The mean (±SD) SBP and DBP of patients with eGFR 15 - 30 ml/min was 140.06±15.35 mm Hg and 78±11.04 mm Hg, respectively. The mean (±SD) systolic blood pressure of patients with eGFR <15 ml/min was 150.30±18.36 mm Hg and 109.48±175.89 mm Hg, respectively. There was a negative correlation between eGFR and systolic blood pressure which was statistically significant (p=0.01). However, there was no correlation between eGFR and diastolic blood pressure. The mean (±SD) HbA1C of patients with eGFR more than 90 mL/min was 6.8%, mean (±SD) HbA1C of patients with mean (±SD) 60 - 90ml/min was9.95 ±1.48%, mean (±SD) HbA1C of patients with mean (±SD) 30 - 60 ml/min was 8.47 ± 1.29%, mean ± SD HbA1C of patients with eGFR 15 - 30 ml/min was 8.99 ± 1.59%, mean (±SD) HbA1C of patients with eGFR <15ml/min was 8.05± 2.02%. Though a downward trend in eGFR change was demonstrated alongside an HbA1C reduction, however, no statistically significant correlation between HbA1C and eGFR was found (p value=0.66). Out of 100 patients, patients eGFR >90 had mean (±SD) creatinine 0.9 mg/dL. Patients with eGFR 60 - 90 ml/min had mean (±SD) creatinine 1.2±0.23 mg/dL. Patients with eGFR 30 - 60 ml/min had mean (±SD) creatinine 1.99±0.55 mg/dL. Patients with eGFR 15 - 30 ml/min had mean (±SD) creatinine 3.57±3.28 mg/dL, and patients with eGFR <15 ml/min had mean (±SD) creatinine 5.22±1.82 mg/dL. There was rise in serum creatinine with decline in eGFR which was statistically significant p<0.0001 (Table 2).

The mean (±SD) eGFR of the study group was 28.45±17.37mL/min. Out of 100 patients, 58% patients had borderline renal dimensions with mean (±SD) eGFR 28.87±14.50mL/min, 12% patients had contracted kidneys with mean (±SD) eGFR13.07±11.42mL/min. Thirty (30%) patients had normal kidneys with mean (±SD) eGFR33.80±20.95mL/min. The patients with neuropathy had eGFR 23.18±11.88 mL/min, and those without neuropathy had eGFR 37.05±21.27 mL/min. The patients with retinopathy had eGFR 23.45±13.42 mL/min, and those without retinopathy had eGFR 37.73±20.06 mL/min. Mean (±SD) eGFR of patients with normoalbuminuria was 51.32±35.22 mL/min while patients with microalbuminuria had mean (±SD) eGFR34.16±12.90 mL/min and patients with macroalbuminuria had mean (±SD) eGFR23.96±14.56 mL/min. There was a strong association between urinary albumin creatinine ratio and eGFR which was statistically significant p=0.000 (Table 3).

Correlation of eGFR with Urinary Albumin Creatinine Ratio, S. Creatinine, and Systolic BP: There was a negative correlation between eGFR with Urinary Albumin Creatinine Ratio (Pearson Coefficient - 0.39), this implied that more was the Urinary Albumin Creatinine Ratio, less was the eGFR. Similarly, there was also a negative correlation between eGFR with S. Creatinine, and Systolic BP (Pearson Coefficient - 0.48 and - 0.30, respectively) (Table 4).

Table 1: Baseline parameters of patients

Parameters	Variables	Number of patients
Age (years)	≤40	18
	41 - 50	17
	51 - 60	32
	61 - 70	19
	>70	14
Gender distribution	Males	51
	Females	49
Household	Rural	59
	Urban	41
Hypertension	Absent	29
	Present	71
Neuropathy	Absent	38
	Present	62
Retinopathy	Absent	35
	Present	65
Proliferative Diabetic Retinopathy	Absent	77
	Present	23
Non - Proliferative Diabetic Retinopathy	Absent	57
	Present	43
Body Mass Index Grading	Normal	71
	Overweight	20
	Underweight	9
Renal size (ultrasound)	Normal	30
	Borderline	58
	Contracted	12
Duration of diabetes (years)	5-10	86
	11-15	12
	16 - 20	2

Table 2A: Comparison of eGFR with blood pressure and biochemical parameters

Range of eGFR (mL/min)	No. of patients	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	HbA1C	S. Creatinine (mg/dL)
<15	30	150.30±18.36	109.48±175.89	8.05± 2.02	5.22±1.82
15 - 30	35	140.06±15.35	78±11.04	8.99 ± 1.59	1.99±0.55
30 - 60	33	135±18.94	72.18±11.07	8.47 ± 1.29	1.99±0.55
60 - 90	4	135±18.94	69.5±7.37	9.95 ±1.48	1.2±0.23
>90	1	122	60	6.8%	0.9

Table 2 (B): Comparison of eGFR with various parameters

Parameters	Variables	Mean eGFR±SD (mL/min)
Duration of diabetes (years)	5 - 10	28.46
	11 - 15	23.26
	16 - 20	16
Renal size (ultrasound)	Normal	33.80± 20.95
	Borderline	28.87± 14.50
	Contracted	13.07± 11.42
Neuropathy	Absent	37.05± 21.27
	Present	23.18± 11.88
Retinopathy	Absent	37.73± 20.06
	Present	23.45± 13.42
Proliferative Diabetic Retinopathy		17.30±12.98
Non - Proliferative Diabetic Retinopathy		26.64±13.43
Urinary albumin creatinine ratio (mg/g)	<30 (Normoalbuminuria)	51.32± 35.22
	30 - 300 (Microalbuminuria)	34.16± 12.90
	>300 (Macroalbuminuria)	23.96± 14.56

Table 4: Correlation of eGFR with S. Creatinine, Systolic BP and Urinary Albumin Creatinine Ratio

Parameters	Pearson Correlation Coefficient	Correlation
S. Creatinine	-0.48	Negative
Systolic blood pressure	-0.3	Negative
Urinary albumin creatinine ratio	-0.39	Negative

4. Discussion

Comparison and Correlation of eGFR with various parameters: A total of 86 patients had diabetes for 5 - 10 years, their mean (±SD) eGFR value was 28.46 mL/min. The mean (±SD) eGFR in 14 patients (having duration of diabetes between 11 - 15 years) was 23.26 mL/min. Two patients had diabetes for 15 - 20 years, their mean (±SD) eGFR was 16 mL/min. It was observed that eGFR decreased with increase in the duration of diabetes which showed a statistically significant association (p=0.004). Rosdiana d et al (2020) in a similar study also observed a decline in eGFR with increase in duration of diabetes (p=0.02). [9]

A total of 65 patients (65%) had retinopathy out of which 23 patients had proliferative retinopathy. The mean eGFR of patients with retinopathy was 23.458±13.43 mL/min while eGFR of patients without retinopathy was mean (±SD) 37.73±20.05 mL/min. The mean (±SD) eGFR of patients with Proliferative retinopathy was 17.30±12.98 ml/min while mean± SD eGFR of patients with non - proliferative retinopathy was 26.64±13.43 ml/min. Lower eGFR was associated with increased risk of retinopathy p=0.0001. It was observed that severe decline in eGFR was associated with severe forms of retinopathy. Rajalakshmi et al (2020) observed that eGFR <30 ml/min was associated with increased risk of progression to diabetic retinopathy (p=0.001). Also, eGFR<30 ml/min/1.73m2 was associated with increased risk of progression to severe threatening diabetic retinopathy. [10]

Among 100 patients, maximum number of patients i. e.35 % had eGFR in the range of 15 - 30 ml/min while only 1% patients had eGFR >90 ml/min. Alongside, 28% patients of our study group had microalbuminuria and 66% patients of our study group had macroalbuminuria when only 6% of patients had normoalbuminuria. Mean (±SD) eGFR of patients with normoalbuminuria was 51.32±35.22 while patients with microalbuminuria hadmean (±SD) eGFR 34.16±12.90 mL/min and patients with macroalbuminuria had mean (±SD) eGFR 23.96±14.56 mL/min. There was a strong correlation between urinary albumin creatinine ratio and eGFR which was statistically significant p=0.0001. Saha et al (2015) found a strong correlation between urinary albumin creatinine ratio and eGFR which was statistically significant with p=0.0063. [11]Rosdiana d et al (2020) also observed increase in urinary albumin creatinine ratio with declining eGFR (p=0.016). [9]

The mean (±SD) HbA1C of patients with eGFR more than 90 mL/min was 6.8%, mean (±SD) HbA1C of patients with mean (±SD) 60 - 90ml/min was 9.95 ±1.48%, mean (±SD) HbA1C of patients with mean (±SD) 30 - 60ml/min was 8.47 ± 1.29%, mean ± SD HbA1C of patients with eGFR 15 - 30ml/min was 8.99 ± 1.59%, mean (±SD) HbA1C of patients with eGFR <15ml/min was 8.05± 2.02%. Though a downward trend in eGFR change was demonstrated alongside an HbA1C reduction, however no statistically significant correlation between HbA1C and eGFR was found (p value= 0.66). Rosdiana D et al (2020) did not find any statistically significant association between HbA1C and decline in eGFR (p=0.15). [9]

Out of 100 patients, patients eGFR >90 had mean (±SD) creatinine 0.9 mg/dL. Patients with eGFR 60 - 90 ml/min had mean (±SD) creatinine 1.2±0.23 mg/dL. Patients with eGFR 30 - 60ml/min had mean (±SD) creatinine 1.99±0.55 mg/dL. Patients with eGFR 15 - 30 ml/min had mean (±SD) creatinine 3.57±3.28 mg/dL, and patients with eGFR <15 ml/min had mean (±SD) creatinine 5.22±1.82 mg/dL. There was rise in serum creatinine with decline in eGFR which was statistically significant p<0.0001. Rosdiana D et al (2020) also observed that serum creatinine increased with decline in eGFR (p=0.001). [9]

In our study patients with neuropathy had mean (±SD) GFR value of 23.18±17.37 ml/min and patients with no neuropathy had mean (±SD) GFR value of 37.06±21.26 ml/min. It was observed that neuropathy increases with declining eGFR which was statistically significant (p=0.000). Babaliche et al in their similar study found that eGFR was associated significantly with neuropathy (p=0.007). [12]

The mean (±SD) systolic blood pressure (SBP) and diastolic blood pressure (DBP) of patients with eGFRmore than 90 ml/min was 122/60 mm Hg. The mean (±SD) SBP and DBP of patients with eGFR60 - 90 ml/min was 135±18.94 mm Hg and 69.5±7.37mm Hg, respectively. The mean (±SD) SBP and DBP of patients with eGFR30 - 60ml/min was 134.55±18.7 mm Hg and 72.18±11.07 mm Hg, respectively. The mean (±SD) SBP and DBP of patients with eGFR15 - 30 ml/min was 140.06±15.35 mm Hg and 78±11.04mm Hg, respectively. The mean (±SD) systolic blood pressure of patients with eGFR <15 ml/min was 150.30±18.36 mm Hg and 109.48±175.89 mm Hg, respectively. There was a negative correlation between eGFR and systolic blood pressure which was statistically significant (p=0.01). However, there was no correlation between eGFR and diastolic blood pressure. Rossing k et al also found negative correlation between eGFR and systolic blood pressure (p=0.01) and no correlation between eGFR and diastolic blood pressure. [13]This was likely due to the fact that type 2 diabetic patients primarily suffered from Isolated systolic hypertension.

5. Conclusion

The present study found that estimation of eGFR is an indicator of kidney function which enables the identification and classification of the level of renal impairment in diabetic nephropathy. Retinopathy, neuropathy, and nephropathy are the microvascular complications of diabetes that are strongly and substantially correlated with a reduction in eGFR. The existence and worsening severity of microvascular consequences of diabetes are related to lower levels of eGFR. Diabetes duration and the ratio of urinary albumin to creatinine can serve as early warning signs of the development of severe diabetic retinopathy and peripheral neuropathy. Controlling the pace of eGFR drop will lessen the likelihood of complications, which will lower the burden of the condition and enhance patient quality of life. Therefore, new treatment approaches should focus on helping type 2 diabetics maintain steady renal function.

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Declaration of Conflicting Interests: The author (s) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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