| Original Article |

# Correlation of Estimated-Glomerular Filtration Rate (e-GFR) with diabetic nephropathy and non-nephropathy patients in a tertiary care hospital

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## Article Info

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## Abstract

The estimated glomerular filtration (e-GFR) and serum creatinine is the screening methods of reduced renal function in patients with type-II diabetes (T2DM) in both patient with diabetic nephropathy and with no diabetic nephropathy. The objective of this study was to evaluate the clinical significance of e-GFR in type-II diabetes mellitus patients with diabetic nephropathy and without diabetic nephropathy.This cross-sectional study was conducted from March 2020 to February 2021 in the Department of Laboratory Medicine in collaboration with Department of Nephrology, Bangbandhu Sheikh Mujib Medical University (BSMMU), Dhaka involving 60 patients from the department of Nephrology, BSMMU. Among 60 patients, 30 were with diabetic nephropathy and 30 were without nephropathy. Both nephropathy and without nephropathy group were selected according to selection criteria. Random blood sugar (RBS), Glycated hemoglobin (HbA1c), serum creatinine and e-GFR level were measured in all patients. After data collection and processing, all statistical analysis was done by using SPSS Version 26.0. In this study, the mean(±SD) age was 50.5±11.71 in group-I and 45.53±9.97 in group-II. The difference was statistically not significant(p=0.082). It was observed that 20(66.7%) were male and 10(33.3%) were female in group I and 13(43.3%) were male and 17(56.7%) were female in group-II. Age group 51-60 years had highest percentage of nephropathy patients 9(30.0%) and 31-40 years of age group had highest percentage of diabetic patient without nephropathy 13(43.3%). The mean e-GFR in Group I was 47.56±35.48 and in Group II was 93.75±31.29 which was statistically significant (p=0.001). There was a significant negative correlation between serum e-GFR and serum creatinine in between Group I (r=-0.809, p<0.001) and Group II (r=-0.715, p<0.001). In conclusion, serum creatinine was higher in type 2 diabetes mellitus patients with nephropathy group and mean e-GFR was significantly reduced in type 2 diabetes mellitus patients with nephropathy group than without nephropathy.

## Introduction

Assessment of renal function in individuals with diabetes mellitus (DM) is extremely important since diabetic nephropathy (DN) constitutes a major cause of chronic kidney disease in the world, which makes DM the most frequent cause of end-stage renal disease.[1,2] Diabetic nephropathy is the major microvascular complication and the leading cause of end stage renal disease (ESRD) globally.[3] The incidence of diabetic nephropathy (DN) in Bangladesh is 3% per year during the first 10-20 years after onset of diabetes mellitus and the prevalence is 25%.[4] A study found that there was an association of microvascular complication in diabetic nephropathy with low educational status of patients in India.[5] Currently proper screening of diabetic nephropathy is done on the basis of routine measurement of urinary albumin excretion and glomerular filtration rate (GFR).[6] DN is characterized by elevated urine albumin excretion or reduces glomerular filtration rate or both in diabetes mellitus patients.[6] Early identification and appropriate management of chronic kidney disease

(CKD) are important measures to slow its progression. In clinical practice, measurement of plasma creatinine has been the method most often used to assess renal function. However, it has been demonstrated that "apparently normal" serum creatinine levels may be accompanied by loss of renal function, making this a relatively late parameter for lesion detection.[7] Although the measurement of the calculated creatinine clearance is considered the reference standard for determining the glomerular filtration, its methods are laborious, expensive and require specialized equipment and personnel, making them impractical in daily practice.[8] Therefore, some formulas to estimate GFR were developed and the most employed and analyzed equations are Cockcroft and Gault (CG),[9] Modification of Diet in Renal Disease (MDRD)[10] and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).[11] The e-GFR is then calculated by equation of glomerular filtration rate by using age, sex and body weight of individual.[12] Changes in glomerular filtration rate provide a valuable indicator for the progression of diabetic nephropathy.[13] For the assessment of glomerular filtration rate, serum creatinine is the most widely used index.[14] Despite its specificity serum creatinine demonstrates an inadequate sensitivity particularly in the early stage of renal impairment.[14] Creatinine is not an inert substance and is secreted by the proximal tubule. Its level is affected by independent variable.[14]

In this context, aim of this study was to evaluate the clinical significance of e-GFR in type-2 diabetes mellitus patients with diabetic nephropathy and non-nephropathy patients.

## Methods

This was a cross-sectional study of 60 patients, 30 were with nephropathy and 30 were without nephropathy attending the Department of Nephrology, BSMMU, Dhaka from March 2020 to February 2021. Patients attended sequentially, consented for study participation and were recruited at first visit. Consent was taken regarding participation in the study. Data collection was accomplished by maintaining adequate privacy and confidentiality and without any physical harm. Patients were evaluated by history and clinical examination. The inclusion criteria were: 1) Patients of type-2 diabetes mellitus defined according to American diabetic association[15], 2) Age-18 years or above, 3) Sex-both male and female, 4) Oedema, 5) Microalbuminuria. The exclusion criteria were: 1) Hypertension, 2) Urinary tract infection, 3) Pregnancy, 4) Leukemia, 5) Multiple myeloma, 6) Collagen diseases: Systemic lupus erythematosus 7) Viral disease. The study subjects were divided into two groups, Group I: type-2 diabetes mellitus patients with nephropathy, Group II: type-2 diabetes mellitus patients without nephropathy. Blood samples was collected from ante cubital vein after aseptic precaution with 0.5% chlorhexidine gluconate. About 6.0 ml venous blood was collected into plastic tube. Two ml blood was drawn and labeled with the patient's identification number and kept it for 30 minutes and centrifuged for fasting blood sugar. For glycated hemoglobin 2 ml blood whole blood taken in EDTA tube. For serum creatinine, e-GFR 2 ml of random blood was taken in plastic red screw capped plain tube without anticoagulant. For e-GFR MDRD formula: e-GFR = 184 x (SCr)-1.154 x (age)-0.203 x 0.742 [if female] was used. Statistical analysis was done by SPSS (Statistical package for social science) version 26.0. The anthropometric and biochemical parameters were compared were between the two groups by Student's t-test and Chi-square test. Statistical significance was defined as $p \leq 0.05$.

## Results

In this study, out of 60 patients, the mean(±SD) age was 50.5±11.71 in group-I and 45.53±9.97 in group-II. The difference was statistically not significant. It was observed that 20(66.7%) were male and 10(33.3%) were female in group I and 13(43.3%) were male and 17(56.7%) were female in group-II. The males were predominant in group I and females were predominant in group II. The difference was statistically not significant (p=0.069). The study showed, in Group-I, 7(23.3%) belonged to age group 31-40 years , 8(26.7%) belonged to 41-50 years, 9(30.0%) belonged to age group 51 -60 years and 6(20.0%) belonged to age group 61-70 years. In group-II, highest percentage of the of patients (43.3%) belonged to age group of 31-40 years followed by 11(36.7%) belonged to 41-50 years and 3(10.0%) belonged to both age group 51-60 years and 61-70 years. Age group 51 -60 years had highest percentage of nephropathy patients 9(30.0%) and 31-40 years of age group had highest percentage of patients without nephropathy 13(43.3%) (Table-I & Table-II).

It was observed that mean(±SD) differences of serum creatinine and e-GFR levels between two groups were statistically significant ($p<0.001$). There was a significant negative correlation between serum e-GFR and serum creatinine in between Group I ($r=-0.809$, $p<0.001$) and Group II ($r=-0.715$, $p<0.001$) (Figure-1).

**Table-I**

**Distribution of the study subjects by age (N=60)**

| Age (years) | Group I (n=30) | | Group II (n=30) | | p-value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 31-40 | 7 | 23.3 | 13 | 43.3 | |
| 41-50 | 8 | 26.7 | 11 | 36.7 | 0.082ns |
| 51-60 | 9 | 30.0 | 3 | 10.0 | |
| 60-70 | 6 | 20.0 | 3 | 10.0 | |
| Mean±SD | 50.5±11.71 | | 45.53±9.97 | | |
| Range (min to max) | 30 – 70 | | 30 – 70 | | |

Results were expressed as mean±SD
ns=not significant,
P value reached from Unpaired t-test)

**Table-II**

**Distribution of the study subjects by gender (N=60)**

| Gender | Group I (n=30) | | Group II (n=30) | | p-value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Male | 20 | 66.7 | 13 | 43.3 | .069ns |
| Female | 10 | 33.3 | 17 | 56.7 | |

ns =not significant,

P value reached from Chi-square test

**Table-III**

**Comparison of study subjects by biochemical parameters (N=60)**

| Biochemical parameters | Group I (n=30) | Group II (n=30) | p-value |
|---|---|---|---|
| *S. creatinine (mg/dl) | 2.51±1.50 | 0.91±0.32 | <0.001s |
| **e-GFR (ml/min) | 47.56±35.48 | 93.75±31.29 | <0.001s |

Results were expressed as mean ± SD.

Unpaired t-test was done as a test of significance

p<0.05 is considered as significant;

s = significant

*S creatinine: Male: 0.7-1.2 mg/dl (60-110µml/l)

*Female: 0.5-1.0 mg/dl (45-90 µml/l)

**GFR: 125ml/min or 180L/day.

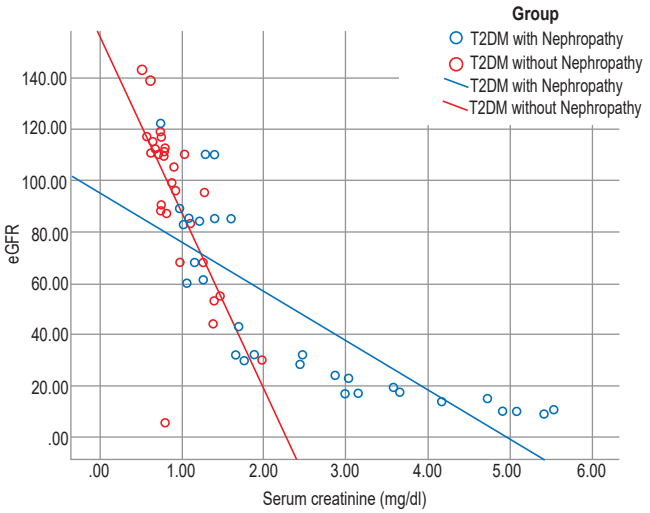


**Figure-1:** Scatter diagram showing the Pearson's correlation of serum creatinine with e-GFR in two groups

## Discussion

Diabetic nephropathy is a serious long-term major microvascular complication. It is recorded in approximately one third of patients with diabetes. Diabetic nephropathy is the main cause of end stage renal diseases (ESRD) and 30-50% of ESRD developed from type 2 Diabetes mellitus. Several biomarkers associated with diabetic nephropathy have been the subject of research in last few decades. In this study significance of the e-GFR in type 2 diabetes mellitus patients with nephropathy and non-nephropathy groups was done. Patients diagnosed to have type 2 diabetes mellitus (n=60) from the department of nephrology, BSMMU were enrolled in this study and analysis was done accordingly.

In this study, it was observed that majority 9 (30%) patients belonged to 51-60 years in Group I and majority 13 (43.3%) patients belonged to 31-40 years in Group II (Table-I). The mean±SD age was 50.5±11.71 years in group I and 45.53±9.97 years in group II. No statistically significant difference was observed between two groups (p=0.082). Similar study was done by Elsebai et al. [15] where mean±SD age was 51±5 years in diabetic nephropathy group and without diabetic nephropathy group it was 48.1±6 years. The difference was not statistically significant (p>0.05). Another study was conducted by Aksun et al.[14], they reported that mean±SD age of diabetic nephropathy group was 56.8±9.4 years and without nephropathy group was 48.1±9.3 years. The difference was not statistically significant (p>0.05). Findings of this study consistent with these previous studies. Kim et al.[16] found that the mean±SD age of nephropathy patients was 61.3±12.7 years and without nephropathy patients was 51.4±13.8 years. The difference was statistically significant (p<.0001). This dissimilarity from the current study may be due to large sample size (n=366) of their study.

In this study, it was found that out of 60 patients, majority 20(66.7%) of the participants were male in Group I and 17 (56.7%) of study population were female in Group II (Table-II). Mohiuddin[34] found that in Bangladesh prevalence of nephropathy was higher in male compared to female which is consistent with this study in nephropathy group. In a study by Foster et al. found female was predominant 57.3% then male which was consistent with this study in without nephropathy group.[17] Aksun et al. found that female respondents (22%) were more affected in nephropathy group than male (17%) in Turkey. Which is not consistent with this study.[14] It may be due to small sample size, lifestyle, environmental factor, genetic factors or ethnicity.

This study found mean serum creatinine level in Group I was 2.51±1.50 mg/dl and in Group II was 0.91±0.32mg/dl and this differences were statistically significant ($p<0.001$) and serum creatinine levels was elevated in Group I than Group II. Mean e-GFR in Group I was 47.56±35.48 mg/dl and in Group II was 93.75±31.29 mg/dl which was statistically significant ($p<0.001$). e-GFR was reduced in Group I than Group II. Kim et al. also found patient with nephropathy group had low e-GFR compared to control group (93.8±17.8 vs 78.4±14.0) which was statistically significant ($p<0.001$).[16] Fontela PC et al also found the same results that were consistent with this study.[18] The current study was supported by the previous studies. Scatter diagram showed in this study that there was a significant negative correlation between serum eGFR and serum creatinine in Group I ($r=-0.809$, $p<0.001$) and Group II ($r=-0.715$, $p<0.001$) (Figure-1).

After analyzing the results, we concluded that the prevalence of individuals with reduced renal function based on serum creatinine was lower, reinforcing the need to follow the recommendations of estimating the value of glomerular filtration as a complement to the results of serum creatinine to better assess the patients' renal function. Though it is already established that creatinine is a sensitive marker for predicting renal damage in Type 2 DM cases, but in our study e-GFR, not creatinine was found to be significantly reduced in type 2 DM cases with nephropathy group. Therefore according to our study, e- GFR, not creatinine can serve as a reliable indicator for predicting renal impairment in an early stage in Type 2 Diabetes Mellitus cases.

## Limitations

The study had some limitations. It was a single center study with relatively small sample size. Samples were not collected from patients receiving dialysis or renal replacement therapy. The study population was selected from only one tertiary level hospitals in Dhaka city. Therefore, sample may not be representative of the selected wholepopulation of the country. Patients with exclusion criteria were excluded on the basis of history and clinical feature. No confirmatory tests were carried out to exclude these patients due to lack of financial source and time constraint.

## Conclusion

Majority of the subjects were male in nephropathy group. Serum creatinine were higher in type 2 diabetes mellitus patients with nephropathy group and mean e-GFR were significantly reduced in type 2 diabetes mellitus patients with nephropathy group than without nephropathy group.

## Funding Support

Self-funded.

## Ethical Issue

The protocol for this study was approved by the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University.

## Author contribution

MK and MSY constructed idea of this research and prepared the manuscript. Other authors have analyzed and finally reviewed the manuscript before the submission.

## Conflict of Interest

Authors declare no conflict of interest.

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