Evaluation of estimated glomerular filtration rate (eGFR), serum creatinine, urea and electrolytes profile levels in diabetic patients attending medical outpatient clinic in Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria

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Abstract

This case control study was aimed at evaluating the estimated glomerular filtration rate (eGFR), serum creatinine, urea and electrolytes profile levels in diabetic subjects attending medical outpatient clinic, Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Nigeria. The protocol for the study was explained to the prospective subjects and those who gave informed consent were recruited. . A total of 114 subjects comprising of 57 diabetic subjects and 57 controls aged between 40 and 73 years were recruited for the study. The patients and controls were aged and sex matched. Thereafter, 5mls of blood sample was collected from each subject into plain container for estimation of biochemical parameters. Serum creatinine and urea were assayed by colorimetric method. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) formula while serum electrolytes (Na^+, K^+, Cl^- and $HCO3^-$) were determined using Ion Selective Electrode (ISE). Statistical Package for the Social Sciences (SPSS) version 21.0 was used for the analysis of the data obtained using Students't-test and pearson correlation and presented as mean ± standard deviation (SD). The results revealed a significant decreases in the mean serum levels of eGFR, Creatinine and bicarbonate in diabetic subjects than in the control ($p<0.05$). However, no significant differences were observed in the mean serum concentrations of urea, sodium, potassium and chloride in the diabetic subjects compared with control ($p>0.05$) respectively. Also, no significant differences were observed between both male and female subjects in the parameters studied ($p>0.05$). There was also a strong negative correlation between serum sodium and eGFR, as well as between creatinine and eGFR in the diabetic subjects ($r = -0.016$, -0.930 respectively), ($P<0.05$). In conclusion, the decline in the eGFR coupled with a lower creatinine level in diabetic subjects compared with control could be an indication of a progressive renal disease.

Keywords: Diabetes mellitus, Kidney disease, Estimated Glomerular Filtration (eGFR), Creatinine, Urea, Electrolytes.

Introduction

Diabetes mellitus is a metabolic disorder of multiple etiologies which is characterized by hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both (WHO, 1999). Diabetes mellitus has become an issue of great public health importance globally, accounting for a prevalence of 8.5% in 2014 (Sarwar et al., 2010). According to World Health Organization, in 2016, diabetes was the direct cause of 1.6million deaths word wide (WHO, 2016). It is a leading cause of kidney failure (USRDS, 2014). Therefore, the assessment of renal function in individuals with diabetes mellitus (DM) is of utmost importance 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 (Zhang and Rothenbacher, 2008; Atkins and Zimmet, 2010). Diabetic nephropathy (DN) is the progression to end-stage renal disease (ESRD) independently of traditional cardiovascular

risk factors (CVRF). Chronic kidney disease (CKD) is considered an important public health problem (Levey et al., 2007), as it increases the mortality risk for any cause, which increases the frequency of cardiovascular disease episodes. Approximately 40% of all diabetic patients develop DN (Murussi et al., 2007), which is the most common diagnosis among individuals in renal replacement programs, accounting for up to 44% of cases (USRDS, 2010). Also, diabetes has been reported to have a prevalence of 1% and 5% to 7% in rural areas and urban sub-saharan Africa respectively (Kengne et al., 2005). The number of people with diabetes has been reported to increase over time due to population growth, aging, increased obesity, physical inactivity and urbanization especially in developing countries of the world including Nigeria (Wild et al., 2004). Furthermore, the prevalence of DM has been estimated to increase to as much as 37% by 2030 (Wild et al., 2004), with Nigeria having a total of 1,702,900 recorded cases of diabetes in 2015 and a high prevalence of 2% among the adult population which

calls for concern (IDF, 2015). Therefore, this case control study was designed to evaluate the estimated glomerular filtration rate (eGFR), serum creatinine, urea and electrolytes profile levels in diabetic patients attending Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria.

Materials and Methods

Study Site
This study was carried out at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, South Eastern Nigeria.

Study Design
This is a case control study aimed at determining the estimated glomerular filtration rate (eGFR), serum creatinine, urea and electrolytes profile levels in diabetic patients attending the Nephrology Unit in Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria. The protocol was explained to the subjects and those who gave their informed consent were recruited for the study. A total of 114 subjects comprising of 57 diabetic subjects and 57 controls aged between 40 and 73 years were recruited for the study. The patients and controls were aged and sex matched. Subsequently, structured questionnaire were used to obtain patients' biodata and thereafter, 5mls of blood sample was collected from each patient into plain container and used for the estimation of biochemical parameters (serum creatinine, urea and electrolytes-sodium, potassium, chloride and bicarbonate).

Inclusion and Exclusion Criteria
Known diabetic subjects aged between 40 and 73 years were recruited for the study, whereas those younger than 40 or older than 73 years and non-diabetic subjects were excluded from the study.

Ethical Consideration
The ethical approval for this study was sought and obtained from the Ethics Committee of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria.

Estimated Glomerular Filtration Rate (eGFR)
The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease (MDRD) formula as described by Levey *et al.,* (1999).

Estimation of Serum Creatinine Level
Serum creatinine level was assayed using Jaffe-Slot Alkaline Picric Acid Method as described by Ochei and Kolhatkar, (2007).

Estimation of Serum Urea
Estimation of serum urea level was done using Berthlot Method as described by Ochei and Kolhatkar, (2007).

Determination of Electrolyte Profile Levels
Estimation of electrolytes (sodium, potassium, chloride and bicarbonate) profile levels was done using Ion Selective Electrode (ISE) Method.

Statistical Analysis
Statistical Package for Social Sciences (SPSS) version 21.0 was used for the analysis of the results. Data was presented as mean ± standard deviation (SD). Students't-test and pearson correlation was used to compare biochemical parameters of the test subjects with control subjects. The level of significance was tested at $P < 0.05$.

Results
There was a statistical significant difference in the mean serum levels of Creatinine (75.02±2.34), bicarbonate (21.81±2.10) and eGFR (82.24±8.67) of the diabetic subjects when compared with control subjects (118.33±9.38, 24.49±1.77, 110.71±4.20) ($p < 0.05$); while mean serum level of sodium (143.85±2.14), potassium (5.61±1.27), chloride (102.40±4.89) and Urea (6.35±5.80), showed no statistical significant difference between the diabetic and control subjects (141.69±2.33, 4.54±0.76, 101.97±2.68)($p < 0.05$). Also, serum level of bicarbonate in test subjects (21.81±2.10) was significantly lower when compared with the control subjects (24.49±1.77), ($p < 0.05$). The mean serum level of creatinine in diabetic subjects (75.02±2.34) was significantly lower when compared with the control subjects (118.33±9.38), ($p < 0.05$). Also, the mean serum eGFR of diabetic subjects (82.24±8.67) was significantly lower when compared with the control subjects (110.71±4.27), ($p < 0.05$). See table 1.

Table 1: The mean levels of serum eGFR, creatinine, urea and electrolyte profile levels in diabetic and control subjects

Parameters	Control	Diabetic Subject	p-value	t-value
Sodium (mmol/L)	141.69±2.33	143.85±2.14	0.167	1.397
Potassium (mmol/L)	4.54±0.76	5.61±1.27	0.640	−0.255
Chloride (mmol/L)	101.97±2.68	102.40±4.89	0.640	−0.470
Bicarbonate (mmol/L)	24.49±1.77	21.81±2.10	*0.000	5.843
Urea (mmol/L)	4.65±4.27	6.35±5.80	0.159	1.424
Creatinine (µmol/L)	118.33±9.38	75.02±2.34	*0.000	−4.479
eGFR(ml/min/1.73m^2)	110.71±4.20	82.24±8.67	*0.005	2.945
*Statistically significant at ($p < 0.05$)				

Table 2: The mean serum levels of eGFR, serum creatinine, urea and electrolyte in male and female test subjects

Parameters	Male	Female	P-Value	t-Value
Sodium (mmol/L)	140.78±2.34	141.11±1.96	0.654	0.453
Potassium (mmol/L)	4.67±1.36	4.53±1.20	0.744	0.329
Chloride (mmol/L)	101.63±3.38	103.22±6.10	0.339	0.973
Bicarbonate (mmol/L)	21.84±1.95	21.78±2.31	0.928	0.091
Urea (mmol/L)	6.74±5.34	5.93±6.38	0.676	0.422
Creatinine (µmol/L)	115.25±13.32	121.57±13.54	0.741	0.333
egfr(ml/min/1.73m2)	96.34±13.52	67.34±9.86	0.093	1.732
*Statistically significant at (p<0.05)				

There was no significant difference in the mean serum levels of eGFR (96.34±13.52, 67.34±9.86), serum creatinine (115.25±13.32, 121.57±13.54), urea (6.47±5.34, 5.93±6.08) and electrolyte (sodium: 140.78±2.34, 141.11±1.96, potassium: 4.67±1.36, 4.53±1.20, chloride: 101.63±3.38, 103.22±6.10, bicarbonate: 21.84±1.95, 21.78±2.31) observed between the male and female diabetic subjects. See table 2.

There was a significant strong negative correlation with serum creatinine and eGFR in the test subjects (r = -0.794, p<0.05,). There was also a significant strong negative correlation with serum sodium and eGFR in the test subjects (r = -0.93, p<0.05). On the other hand, serum levels of potassium, chloride, bicarbonate and urea showed no significant correlation with eGFR in the diabetic subjects (P >0.05). See table 3.

The mean serum level of bicarbonate (24.38±1.85) in the male diabetic subject was significantly higher when compared with the control (21.84±1.95)(p<0.05), while there were no significant differences in the mean serum levels of sodium (141.22±2.36), potassium (4.87±0.76), chloride (101.28±2.42), urea (4.55±4.57) and eGFR (119.36±5.85) in male diabetic subjects when compared with control (P >0.05) respectively. See table 4.

The mean serum level of bicarbonate (24.59±1.75) in female diabetic subjects was significantly higher when compared with control subjects (21.78±2.31)(p<0.05) The

Table 3: The mean serum level of eGFR and creatinine, urea and electrolyte respectively in diabetic subjects.

Parameters	R-Value	P-Value
sodium Vs. eGFR	−0.93	*0.016
Potassium Vs. eGFR	−0.198	0.274
Chloride Vs. eGFR	−0.216	0.198
Bicarbonate Vs. eGFR	0.017	0.918
Urea Vs. eGFR	−0.244	0.1454
Creatinine Vs. eGFR	−0.794	*0.000
*Statistically significant at (p<0.05)		

mean serum level of creatinine in female diabetic subjects (72.02±3.53) was significantly lower when compared with the control subjects (121.57±13.54). While the mean serum eGFR (101.33±13.54)(p<0.05) was significantly lower in female when compared with control subjects (101.55±5.59) (p<0.05). While there was no significant difference in the mean serum levels of sodium (142.17±2.27), potassium (4.61±0.78), chloride (102.59±2.87) and urea (4.73±4.07) in female diabetic subjects when compared with control (P >0.05) respectively. See table 5.

Table 4: Levels of eGFR, serum creatinine, urea and electrolyte in the males diabetic and male control Subjects

Parameters	Control	Diabetic Subject	p-value	t-value
Sodium (mmol/L)	140.79±2.34	141.22±2.36	0.58	0.558
Potassium (mmol/L)	4.67±1.36	4.87±0.76	0.598	0.533
Chloride (mmol/L)	101.63±3.38	101.38±2.42	0.803	0.251
Bicarbonate (mmol/L)	21.84±1.95	24.38±1.85	*0.000	4.074
Urea (mmol/L)	6.75±5.34	4.55±4.57	0.187	1.345
Creatinine (µmol/L)	15.25±13.32	77.85±3.04	*0.013	2.736
eGFR(ml/min/1.73m²)	96.35±13.52	119.36±5.85	0.131	1.561
*Statistically significant at (p<0.05)				

Table 5: The mean serum levels of eGFR, creatinine, urea and electrolyte in female diabetic and female control subjects

Parameters	Control	Diabetic subjects	p-value	t-value
Sodium (mmol/L)	141.11±1.96	142.17±2.27	0.149	1.48
Potassium (mmol/L)	4.53±1.20	4.61±0.78	0.829	0.218
Chloride (mmol/L)	103.22±6.10	102.59±2.87	0.695	0.397
Bicarbonate (mmol/L)	21.78±2.31	24.59±1.73	*0.000	4.079
Urea (mmol/L)	5.93±6.38	4.75±4.07	0.515	0.659
Creatinine (µmol/L)	121.57±13.54	72.02±3.53	0.002	3.541
eGFR(ml/min/1.73m^2)	101.55±5.59	67.34±9.86	*0.006	3.016
*Statistically significant at (p<0.05)				

Discussion

In this study, the mean serum level of eGFR in test subjects was significantly lower when compared with control. The estimated glomerular filtration rate (eGFR) is an estimation of the capacity of the kidney to filter waste materials from the body. Thus, the decrease of eGFR in the subjects in the present study suggests an increased risk of kidney disease in the diabetic subjects. This result is in agreement with Skupien *et al*., (2016) who reported a significant linear decline pattern in the eGFR level in type 2 diabetes. Also, our finding is in consonance with the report of Belguith, (2012) who had earlier found decreased eGFR among patients with diabetes mellitus. It is necessary to sustain the disease process that underlies progressive eGFR decline once it is initiated as linearity of eGFR decline is associated with increased risk of End Stage Kidney Disease (ESKD).

This research work also found a significantly lower mean serum level of serum creatinine in test subjects when compared with control subjects. This agrees with the result of Harita *et al*.,(2010) who found out an association between lower serum creatinine with an increased risk of type 2 diabetes, which might reflect a lower volume of skeletal muscle. Skeletal muscle is a major target tissue of insulin and a lower volume of skeletal muscle would mean fewer target sites for insulin which lead to increase in insulin resistance, hence, the development of type 2 diabetes. This may explain in part the pathogenesis of type 2 diabetes associated with lower serum creatinine. However, our finding is in contrast with some other previous similar studies (Singh *et al*., 2014; Kanwar *et al*., 2015; Amartey *et al*., 2015).

Furthermore, the present study revealed no significant difference in the mean serum level of urea in diabetic subjects than in control. This is in line with the previous finding of Amartey *et al*., (2015) who recorded no significant difference in the mean serum urea level in diabetic and control subjects.

In the present study, the mean serum concentrations of sodium, potassium and chloride did not differ significantly in diabetic patients when compared with the control (p>0.05). This is in keeping with the report of Deepti *et al.,* (2017) whose work had earlier showed no significant variation in the mean serum levels of sodium, potassium and chloride in diabetes mellitus patients.

However, there was a significant decrease in the mean serum bicarbonate concentration in the diabetic subjects compared with non-diabetic control. This result is in agreement with Enrst *et al*., (2012) who reported a significantly decline in the mean plasma bicarbonate level among those in whom diabetes subsequently developed. Lower serum bicarbonate is a risk factor to type 2 diabetes owing to metabolic acidosis and insulin resistance which is associated with lower serum bicarbonate. Our finding is however in contrast with the finding of Jha, (2017) who reported a significant increase in the mean bicarbonate level in diabetic patients.

Interestingly, no significant differences were observed in the parameters studied between the male and female diabetic subjects. Also, there was a significant strong negative correlation with serum creatinine and eGFR as well as between serum sodium and eGFR in the diabetic subjects (r =-0.930; -0.794, p<0.05).

Conclusion

In conclusion, the mean serum levels of eGFR, creatinine and bicarbonate were significantly reduced in the diabetic subjects compared to the control. However, no significant alterations were observed in urea, sodium, potassium and chloride levels in the studied subjects. The decline in the eGFR coupled with a lower creatinine level in diabetic subjects compared with control could be an indication of a progressive renal disease or susceptibility of diabetic subjects to Chronic Kidney Disease (CKD). Thus, regular monitoring of kidney function in diabetic patients is necessary to monitor kidney function and prevent onset of End Stage Kidney Disease (ESKD).

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