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Original Article

Alterations in Renal Function and Serum Electrolytes in Diabetic Patients

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Abstract

Diabetic kidney disease (DKD) is becoming a significant cause of morbidity and mortality, and its incidence is rising globally. Early diagnosis of DKD may prevent the progression of renal disease. Both functional and structural markers are used to diagnose and classify DKD. In this study, we investigated the effect of diabetes mellitus on kidney function and electrolytes. A total of 120 subjects were enrolled in the study and classified into three groups: (Group I) 40 normal healthy subjects, (Group II) 40 DKD patients without end-stage renal disease (ESRD), and (Group IIII) 40 DKD patients with ESRD. There was a significant increase in the results of random blood glucose, Hemoglobin A1C (HbA1C), serum urea, and creatinine in patients (Group II and Group III) than in controls (Group I). Estimated glomerular filtration rate (eGFR) and hemoglobin levels were significantly lowered in Group III and Group II compared to Group I. Electrolyte levels, mainly sodium, potassium, and ionized calcium, were significantly deranged in DKD patients with or without ESRD.

Keywords: Diabetic kidney disease (DKD), kidney, Estimated glomerular filtration rate (eGFR), End-stage renal disease (ESRD), Electrolytes

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Introduction

Diabetic kidney disease is a serious complication of type 1 and type 2 diabetes mellitus. DKD occurs in approximately 40% of diabetic patients and is the principal cause of chronic kidney disease worldwide **(Alicic et al., 2017)**. Through its progressive nature to end-stage renal disease (ESRD), DKD is becoming a major morbidity and mortality concern worldwide **(Selby & Taal, 2020)**. The incidence of DKD is on the rise globally by 2045, it's predicted to increase to 783 million (12%) **(Hoogeveen, 2022)**.

The classical phenotype DKD is characterized by major structural changes in the kidney, including hyperfiltration, thickening of glomerular basement membrane, mesangial expansion, podocyte injury, along with tubular damage, all of which lead to glomerular sclerosis and renal fibrosis **(Raval et al., 2020)**. It can be defined clinically as a progressive deterioration of renal function measured as glomerular filtration rate (GFR) **(Lin et al., 2018)**.

The glomerular filtration rate is demarcated as the amount of fluid, which is filtered by all nephrons of both kidneys/ min, which is normally equal to 125 ml/min or 180 L/day **(Provenzano et al., 2024).** It can be measured using clearance of exogenous filtration markers, which is called measured GFR or using endogenous filtration markers, which is called estimated GFR **(Tuttle & Levey, 2024)**.

The gold standard for assessing kidney function is still the indirect measurement of GFR by clearance of exogenous filtration markers. But because of its complexity, time, expense, and invasiveness, this method isn't the best for normal practice or research **(Lopez-Giacoman & Madero, 2015)**. Therefore, in clinical practice, endogenous markers like cystatin C and serum creatinine are used to assess eGFR and kidney function. Yet, variables unrelated to glomerular filtration, like muscle mass, age, gender, and race, can influence serum creatinine levels. In contrast, measuring cystatin C is difficult, costly, and lacks standardization **(Inker et al., 2021)**.

Early diagnosis of DKD may prevent the progression of renal disease **(Nascimento & Domingueti, 2019)**. Both functional and structural markers are used to diagnose and classify DKD, with eGFR being used for functional assessment, as stated by the Kidney Diseases: Improving Global Outcomes (KDIGO) guideline **(Jung & Yoo, 2022)**.

Materials and methods

A case-control study was performed in the Nephrology Department at Ain Shams University Hospitals. Informed consent was obtained in writing from all subjects before taking

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part in the study. They were allocated into three groups (40 individuals in each group) as follows:

Group I: 40 normal healthy subjects (control).

Group II: 40 DKD patients without ESRD.

Group III: 40 DKD patients with ESRD.

The estimated Glomerular filtration rate was calculated using the Modification Diet in Renal Disease (MDRD) Equation. This calculator uses the 4-variable equation from **Levey et al. (2005):** sex, age, race, and serum creatinine in mg/dL (SCr):

GFR = 175 × (SCr)-1.154 × (age)-0.203 × (0.742 if female) × (1.212 if Black).

Participants with the following criteria were excluded from the study: Pregnant females, chronic kidney disease patients due to obstructive uropathy, Polycystic kidney disease, or autoimmune diseases like systemic lupus erythematosus, rheumatoid arthritis, and individuals with a history of drug addiction / NSAIDs. Other exclusion criteria are: thyroid disorders and active urinary tract infection.

Sampling

Five milliliters of venous blood were taken and stored from each patient for the biochemical tests. Samples were left at room temperature for 30-min clotting for 10-min then centrifuged at 3000 g to separate the serum. Then the top yellow serum layer was pipetted off and carefully collected into a new tube.

Chemicals

Serum sodium, ionized calcium, and potassium levels were measured using an ion-selective electrode (ISE) method with the RAPIDLab 348EX analyzer (Siemens Healthcare Diagnostics Manufacturing Ltd, UK) **(Fonseca et al., 2016)**. Random blood glucose was measured using glucometer kits **(Trinder, 1969)**. Glycosylated hemoglobin A1c was measured using the Human Hemoglobin A1c (HbA1c) Assay Kit **(Jeppsson et al., 2002)**. Serum urea was measured by using the enzymatic colorimetric method (BIO-MED Kit) **(Fawcett & Scott, 1960)**. Serum creatinine was measured by using the Jaffe colorimetric method (kit from Reactivos GPL, Barcelona, Españ) **(Jaffé, 1886)**.

Statistical analysis:

It was performed using IBM-SPSS 21**(IBM_SPSS. Statistical Package for Social Science. Ver. 21. Standard version. Copyright © SPSS Inc., NY, USA. 2012)**. Descriptive statistics: Means, standard errors were calculated. One-way ANOVA was carried out to compare the means of the groups. $P \leq 0.05$ was considered significant.

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Results

Socio-demographic characteristics of the study participants

There was no statistically significant difference between groups concerning age and gender (*P*= 0.322, 0.171, respectively) (**Figures 1 and 2)**.

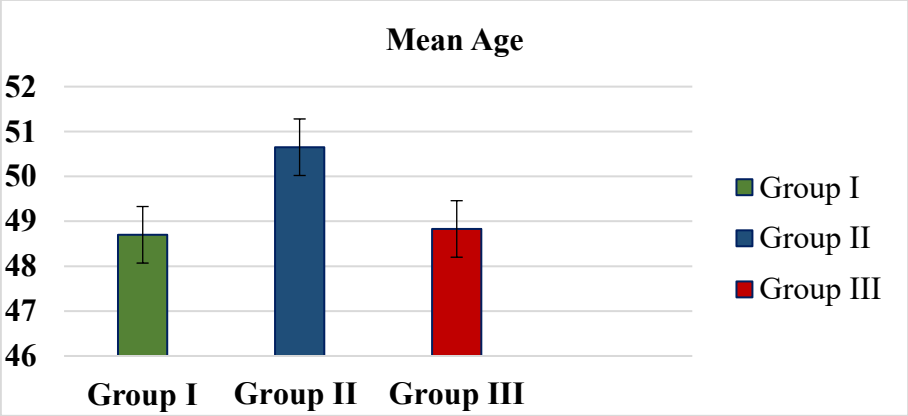

Figure 1: Mean age (years) in different groups

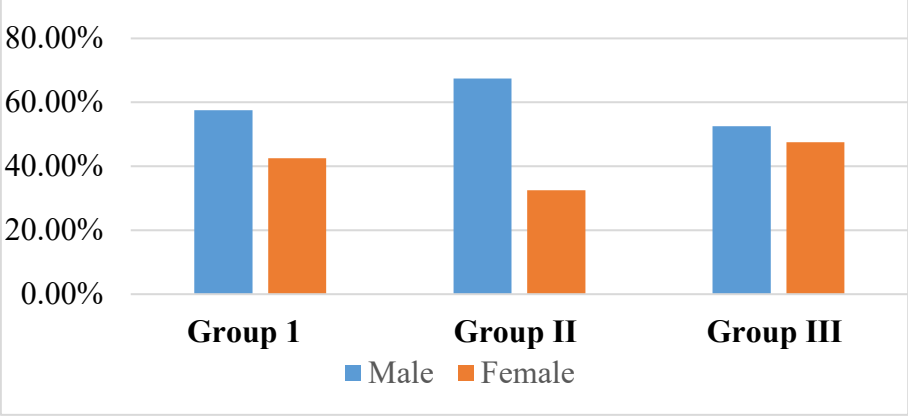

Figure 2: Gender differentiation between different groups

Glucose levels and HbA1C between different groups

There are significant differences in the results of random blood glucose (RBG) and HbA1C between controls (Group I) and patients (Group II and Group III) ($p < 0.001$) (**Figures 3 and 4)**.

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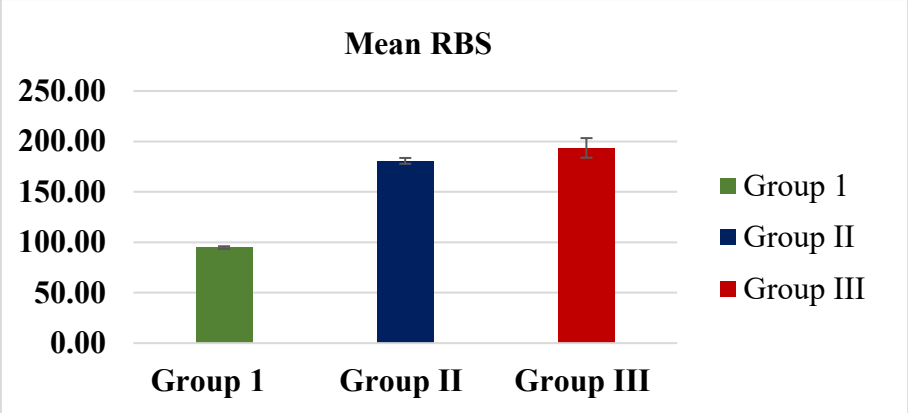

Figure3: Mean RBS (mg/dL) in different groups

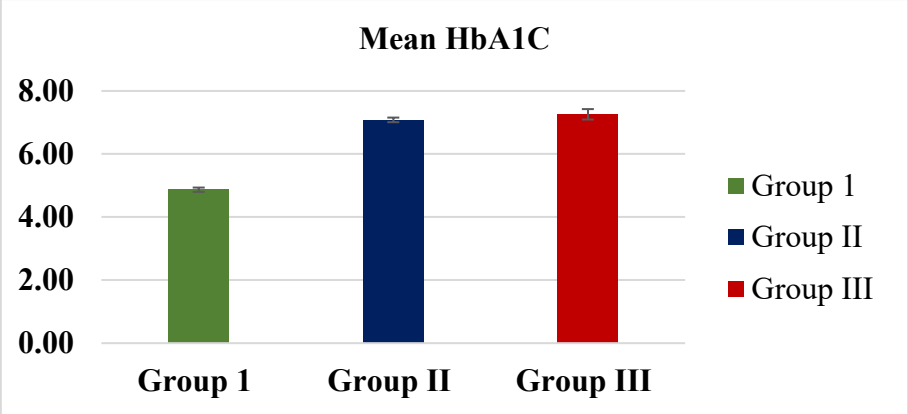

Figure 4: Mean HbA1C in different groups

Renal function and electrolytes between different groups

Regarding kidney function, Serum urea in DKD patients was significantly high (Group III: 143.05±5.821; Group II: 81.53 ± 3.857) compared to the control population (Group I: 23.63 ±0.566, p **< 0.001**) (**Figure 5)**. Serum creatinine in Group III (7.61± 0.3865) and Group II (1.99± 0.0486) was markedly elevated in comparison to the control population (Group I: 0.79±0.0146, p **< 0.001**) (**Figure 6)**. Accordingly, eGFR was significantly lowered in Group III: (7.57± 0.4812) and Group II (33.97 ± 1.288) compared to the control population (Group I: 93.21 ±0.7306, p**< 0.001**) (**Figure 7)**.

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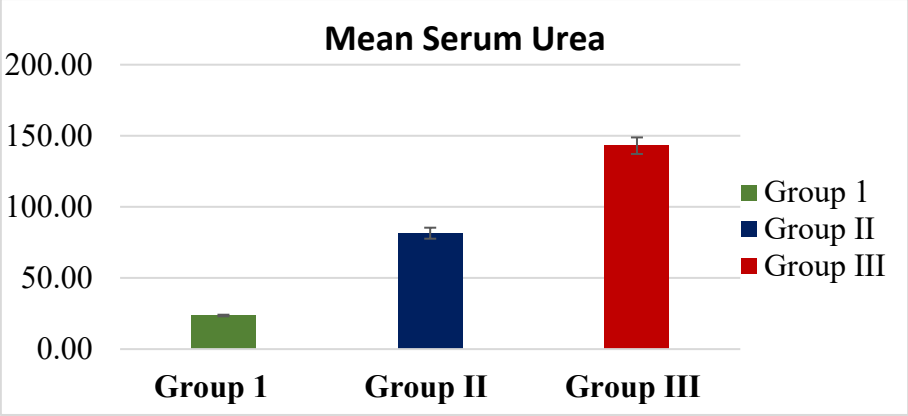

Figure 5: Mean serum Urea (mg/dL) in different groups

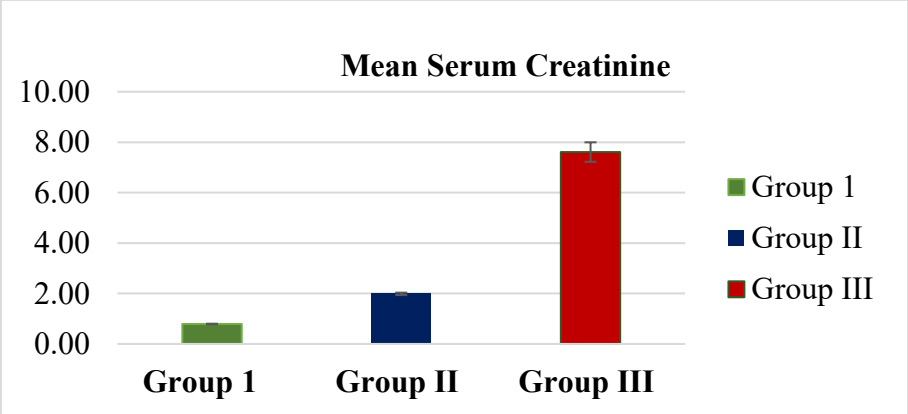

Figure 6: Mean serum Creatinine (mg/dL) level in different groups

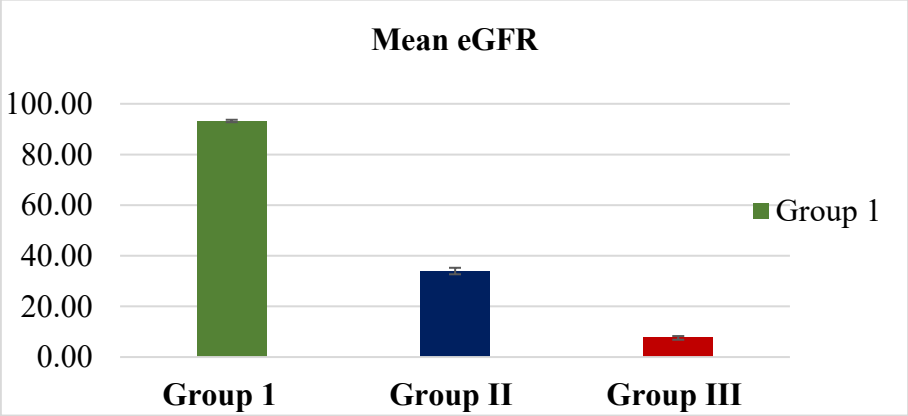

Figure 7: Mean eGFR in different groups

Serum sodium levels in DKD patients were significantly lowered (Group III: 134.05 ± 0.586) compared to the control population (Group I: 141.65 ±0.652) and Group II (140.68± 0.412, p **< 0.001**) (**Figure 8)**. Serum potassium in Group III was significantly higher (5.07 ± 0.1515) compared to that of the control population (Group I: 4.25± 0.0653) and Group II (4.09 ± 0.043, p **< 0.001**) (**Figure 9)**. Serum ionized calcium in Group III (1.16 ± 0.0114) was lower

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compared to that of the control group (Group I: 1.18± 0.0076) and Group II (1.20 ± 0.095, *p*=**0.013**) (**Figure 10)**.

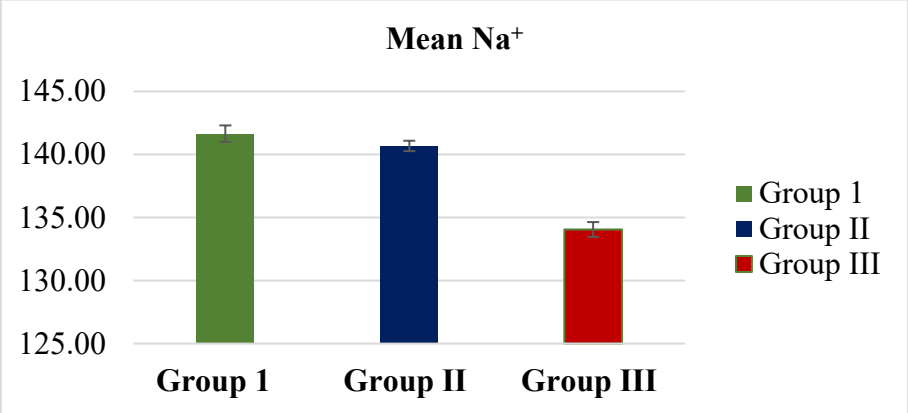

Figure 8: Mean Na^+ level (mEq/L) in different groups

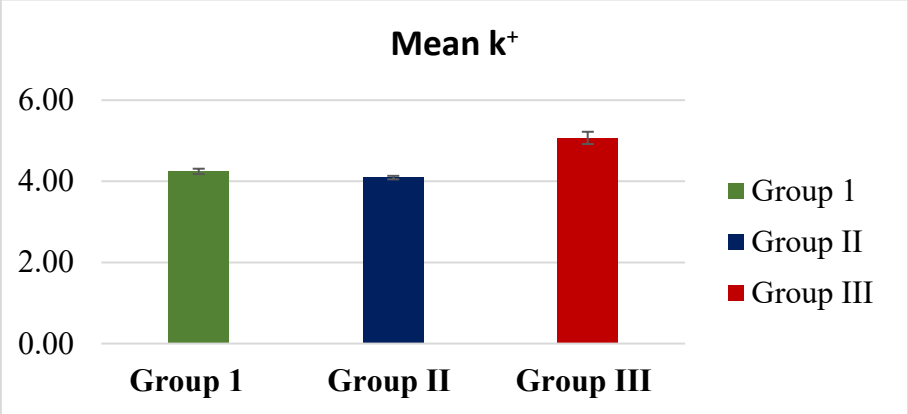

Figure 9: Mean serum K^+ level (mEq/L) in different groups

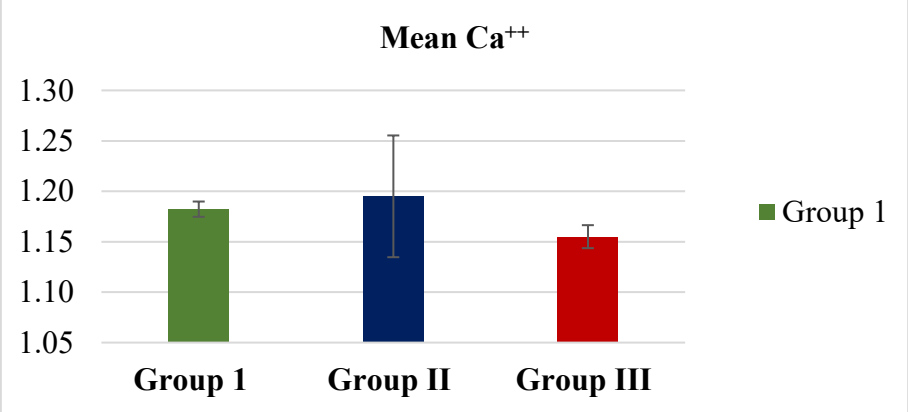

Figure 10: Mean ionized Calcium (mmol/L) level in different groups

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Hemoglobin levels between different groups

Mean hemoglobin (Hb) levels in Group III (9.13 ± 0.2046) and Group II (11.95 ± 0.157) were significantly lower in comparison to the control population (Group I: 13.01 ± 0.1249) ($p < 0.001$) (**Figure 11**).

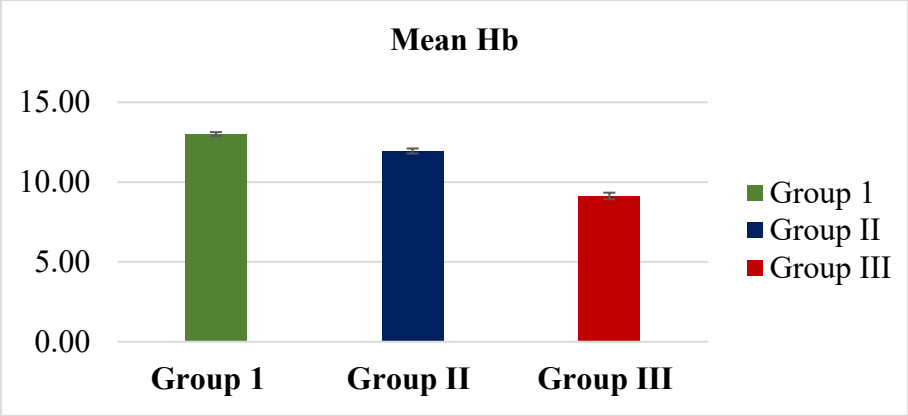

Figure 11: Mean Hb (g/dl) in different groups

Discussion

The study indicated higher serum urea and creatinine levels and accordingly lowered eGFR in DKD without ESRD and DKD with ESRD groups than the control group. This outcome stems from the fact that serum urea and creatinine are common indicators of GFR **(Ebert et al., 2021)**. This result is consistent with the findings of earlier investigations **(Coca et al., 2017; Lalla et al., 2020)**.

Mean hemoglobin level was significantly lower in the DKD without ESRD and DKD with ESRD groups than in the control group. These results are supported **by Mohanram et al. (2004)**, who reported that among type 2 diabetics with nephropathy, anemia is an independent predictor of the development of ESRD. Anemia occurs earlier and more severely in DKD patients than in others due to more complex mechanisms, such as increased bleeding tendency linked to antiplatelet effect, reduced oxygen sensing from autonomic neuropathy, or using inhibitors of renin-angiotensin-aldosterone system, inflammatory cytokines, urinary loss of erythropoietin, and low response to erythropoietin **(Tsai & Tarng, 2019)**.

In the present study, serum sodium level was decreased significantly, while potassium level was elevated significantly in diabetics with the ERD group compared to the control group and the group with other stages of DKD. This result is supported by the results found in a previous study of **Rao and Kuldeep (2022)**. In addition, **Loutradis et al. (2015)** reported hyperkalemia in late stages of DKD patients. The plausible explanation could be that abnormal glucose metabolism and high glucose levels, in consort with Renin-Angiotensin mechanism

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alteration in DKD, resulting in an increase in osmotic force that transports water from the intracellular space to the extracellular space. Consequently, this leads to lowering plasma sodium levels by diluting extracellular sodium and producing hyperkalemia by refluxing potassium into the extracellular space **(Rao & Kuldeep, 2022)**.

Serum ionized calcium levels were significantly lower in diabetics with ERD group in comparison to the control group. These findings were in agreement with the results of **(Kavuparambil et al., 2021)**. Hypocalcemia may be linked to advanced chronic renal insufficiency because of concomitant low vitamin D levels and hyperphosphatemia **(Liamis et al., 2014)**.

Conclusions

The present study indicated higher serum urea and creatinine levels and accordingly lowered eGFR in DKD without ESRD and DKD with ESRD than in the control group. Electrolyte levels, mainly sodium, potassium, and ionized calcium, were significantly deranged in DKD patients with or without ESRD. So, this study revealed the significance of monitoring serum electrolyte levels and kidney function tests in type 2 diabetic patients.

Competing interests

The authors declare no competing interests.

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Ethics approval:

This study was approved by the Medical Research Ethics Committee, National Research Centre, Egypt, through a grant project (approval number: 13060121-2).

Author contribution

Weaam Gouda and Mohamed D. E. Abdelmaksoud developed the design methodology, contributed to data collection, and analysis of the study. Amira Elsawy contributed to data collection, interpretation of the results, and writing up of this manuscript. Naglaa S El-Deen and Samir Azazy assisted in data collection and reviewing the manuscript.

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