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Analysis of the Relationship Between Urea and Creatinine Levels in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia, which may lead to microvascular complications such as diabetic nephropathy. Prolonged elevated blood glucose can damage renal structures, including the glomerular membrane, and may progress to renal failure. **Materials & Methods:** A descriptive–correlative study was conducted to analyze the association between urea and creatinine levels in type 2 DM patients. Seventy patients with fasting blood glucose ≥ 126 mg/dL were included. Urea levels were measured using an enzymatic UV method, and creatinine levels were assessed using the Jaffe method. Statistical analysis utilized the Spearman correlation test. **Results:** Participants had a mean age of 52 years (range: 46–69 years), and all were female. Mean urea and creatinine concentrations were 37 mg/dL (15–108 mg/dL) and 1,08 mg/dL (0,7–2,3 mg/dL), respectively. The data were not normally distributed. A significant correlation was observed between urea and creatinine levels ($p < 0.05$). **Conclusion:** There is a significant association between urea and creatinine levels in patients with type 2 DM, suggesting concurrent elevations may reflect early renal impairment.

Keywords : Type 2 DM, Urea, Creatinine, Renal Function, Diabetic Nephropathy

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INTRODUCTION

The Diabetes melitus (DM) is a chronic metabolic disorder of carbohydrate metabolism characterized by persistent hyperglicemia, Poor glycemic control in DM can result in multiple systemic complications involving the eyes, kidneys, nerves, cardiovascular system, reproductive organs, and extreities (1).

One of the most important chronic micro-vascular complications of DM is diabetic nephropathy (also called diabetic kidney disease, in which sustained hyperglycemia damages glomerular and tubular structures, leading to progressiveness impairment and potentially end-stage renal failure [2].

Hyperglycemia promotes endothelial dysfunction and accelerates arteriosclerosis, narrowing the lumen of small a blood vessels. This reduces renal perfusion, impairs glomerular filtration, and ultimately elevates nitrogenous waste products such as blood urea nitrogen (BUN/urea) and creatinine [2]. Clinically, serum urea and creatinine are routinely measured to elevated kidney function. Urea from dietary protein metabolisms and tissue protein turnover, whereas creatinine derives from creatine and phosphocreatine catabolism in muscle. Increased levels of these parameters reflect impaired renal clearance, which can be caused by diabetic nephropathy among other factors [3].

Assessing the relationship between urea and creatinine in patient with type 2 DM is important to understand disease progression and guide timely intervention. Local studies support this association. Rachmad and Setyawati (2023) reported that serum creatinine levels were highest inpatient aged 61-70 years (56%) and more common among women (52%) [4]. Putri, et al., (2025) found that among Dm patient with diabetic nephropathy, women predominated (62%) and individuals (means 7.65 mg/dL) [5]. Purwati et al., (2023), studying 134 patient with type 2 DM at Budi Kemuliaan Hospital, Batam City, demonstrated a significant relationship between serum urea, creatinine, and blood pressure. These finding underscore the importance of regular renal function monitoring in DM to slow progression toward kidney failure [6].

MATERIALS AND METHODS

Jaffe Method for Creatinine Testing

Creatinine reacts with picric acid in an alkaline environment to form an orange-colored complex. The intensity of the color formed is proportional to the creatinine concentration in the sample and is measured using a photometer at a wavelength of 510 nm. Serum was used as the specimen for analysis. The creatinine testing procedure is presented in Table 1. All reagents were shaken until homogeneous, and the absorbance was subsequently measured using a photometer at a wavelength of 510 nm.

Table 1. Creatinine Testing Procedure

Component	Creatinine reagent (µL)	Standard (µL)	Serum (µL)
Blank	500	-	-
Standard	500	50	-
Serum	500	-	50

UV-Method for Urea Testing

In the UV method for urea testing, the enzymatic urease–GLDH principle was applied. Urea present in the sample was initially hydrolyzed by the enzyme urease to produce ammonia and bicarbonate. The liberated ammonia then reacts with α-ketoglutarate (oxoglutarate) and NADH in a reaction catalyzed by Glutamate dehydrogenase (GLDH), producing glutamate NAD^+, and water. The consumption of NADH leads to a decrease in absorbance, which is measured photo-metrically at 340 nm. The rate of thus decrease is directly proportional to the urea concentration in the sample [7].

The serum samples and all required reagents were prepared in accordance with the established protocol and allowed to reach room temperature prior to use. The required test tubes or cuvettes were arranged according to the number of samples and standards to be analyzed. Reagents were then combined with the samples and standards as specified in the assay instructions, and the mixtures were mixed thoroughly to ensure complete homogeneity. The resulting solutions were incubated at 25°C for 30 seconds. Prior to measurement, the UV spectrophotometer was properly calibrated, and the specified wavelength (e.g., 340 nm) was selected. A blank reading was performed using distilled water or a blank reagent to zero the instrument. The absorbance of each sample and standard was subsequently measured at the specified wavelength. Urea concentrations in the samples were determined by applying the appropriate calculation through comparison of sample absorbance with that of the standard [7]. The detailed procedure for urea level determination is presented in Table 2. All reagents were shaken until homogeneous, and the absorbance was subsequently measured using a photometer at a wavelength of 340 nm.

Table 2. Urea Testing Procedure

Component	R1 (µL)	R2 (µL)	Standard (µL)	Serum (µL)
Blank	400	100	-	-
Standard	400	100	10	-
Serum	400	100	-	10

RESULTS AND DISCUSSION

Results

This section The study involved 70 female patient with diabetes mellitus, ranging in age from 41 to 69 years, with a mean age of 52 years. The majority of participants were in the pre-elderly age group (45-59 years), comprising 46 patients (66%) (Figure 1). Urea levels varied from 15 mg/dL to 108 mg/dL, with an average concentration of 37 mg/dL (Figure 2). Serum creatinine levels ranged from 0,7 mg/dL to 2,3 mg/dL, with a mean of 1,08 mg/dL (Figure

3). Analysis of the relationship between urea and creatinine demonstrated a moderate positive correlation, with a correlation coefficient of 0,530 an a significance level pf p<0,000.

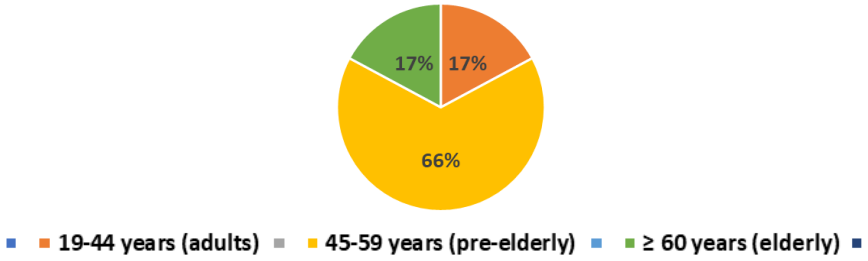

Figure 1. Graph of number of respondent by age group

Table 3. Distribution of respondents' age classification with urea, creatinine, and fasting blood glucose levels

	19-44 years (adults)		45-59 years (pre-elderly)		≥ 60 years (elderly)	
	n	%	n	%	n	%
Urea (normal)	2	3%	39	56%	12	17%
Urea (abnormal)	10	14%	7	10%	0	0%
Creatinine (normal)	10	14%	39	56%	9	13%
Creatinine (abnormal)	2	3%	7	10%	3	4%
Fasting blood glucose (normal)	0	0%	0	0%	0	0%
Fasting blood glucose (abnormal)	12	17%	46	66%	12	17%

Table 4. Urea and creatinine levels (mg/dL) and the percentage of patients with normal and abnormal levels (%)

Parameters	Ranged levels (mg/dL)	Mean (mg/dL)	Normal (%)	Abnormal (%)
Urea	15-108	37	76	24
Creatinin	0.7 - 2.3	1.08	87	13
Glucose (nuchter)	128-324	197	0	70

Seventy female patient with diabetes mellitus participated in this study. Ages ranged from 41 to 69 years, with a mean age of 52 years. The largest proportion belonged to the pre-elderly age group (45-59 years), comprising 46 individuals (66%) (Figure 1).

Serum urea concentrations ranged from 15-108 mg/dL, with a mean value of 37 mg/dL. 17 patient (24%) showed levels above the normal reference range (Table 4). Serum creatinine levels varied from 0.7 -2.3 mg/dL, with a mean of 1.08 mg/dL. 9 patient (13%) had values exceeding the normal range (Table 4). Of all the DM patients studied, 70 patients had fasting glucose levels above 126 mg/dL with a range of 128-324 mg/dL and an average of 197 mg/dL (Table 4).

Table 5. Spearman's rho correlation test

Correlation					
			Urea	Creatinine	FBG
Spearman's rho	Urea (mg/dL)	Correlation coefficient	1.000	0.531**	0.056
		Sig. (2-tailed)	0.000	.000	.644
		N	70	70	70
	Creatinine (mg/dL)	Correlation coefficient	0.531**	1.000	-0.047
		Sig. (2-tailed)	0.000	0.000	0.700
		N	70	70	70
	FBG (mg/dL)	Correlation coefficient	0.056	-0.047	1.000
		Sig. (2-tailed)	0.644	0.700	0.000
		N	70	70	70

The sign (**) indicates that the relationship is considered significant at the 0.01 level (2-tailed).

Correlation analysis revealed a moderate positive association between urea and creatinine levels (r = 0.530; p < 0.000), indicating that an increase in one parameter is accompanied by a corresponding rise in the other. The findings also suggest that after the age of 40, degenerative processes contribute to gradual anatomical, physiological, and biochemical changes, including a decline in renal function and overall quality of life at an estimated rate of about 1% per year [8, 9, 10].

Elevated creatinine levels indicate the onset of nephron injury, resulting in reduced filtration efficiency and increased concentrations of creatinine in the bloodstream. In cases of chronic or poorly controlled diabetes mellitus, persistent hyperglycemia can damage small blood vessels and the millions of nephrons within the kidneys, leading to impaired filtration and progressive renal dysfunction that may eventually result in kidney failure.

A decline in glomerular filtration capacity causes the accumulation of metabolic waste products, which explains the elevated urea and creatinine levels observed in these patients.

Discussion

Most diabetes mellitus cases in this study were found in the pre-elderly age group (45–59 years), consistent with previous findings reported by Putri et al. [5, 11, 12]. This distribution may be attributed to the onset of age-related degenerative changes that typically begin after the age of 40. During this period, gradual anatomical, physiological, and biochemical alterations contribute to a steady decline in renal function and overall health, estimated at approximately 1 mL/min/1.73 m^2 per year (or ~1%) [12].

The moderate correlation observed between urea and creatinine levels is physiologically reasonable, as both serve as indicators of glomerular filtration efficiency. Elevated creatinine levels often signal early nephron impairment, resulting in suboptimal filtration and increased serum creatinine concentrations. In individuals with long-standing or poorly controlled diabetes, chronic hyperglycemia may damage the micro-vascular, injuring large numbers of nephrons and reducing the kidney's ability to filter metabolic waste effectively. Over time, this progressive decline can culminate in significant renal dysfunction or even end-stage kidney failure. Consequently, metabolic waste products such as urea and creatinine accumulate, explaining the elevated levels observed in some study participants [13, 14].

These findings underscore the importance of routine monitoring of both urea and creatinine in patients with diabetes mellitus. Early detection of alterations in these parameters is essential for preventing or slowing further renal deterioration [15, 16].

Although urea and creatinine levels demonstrated a significant and moderately strong correlation, no association was found between either marker and fasting blood glucose levels. This suggests that, in the Type 2 Diabetes Mellitus population examined in this study, renal dysfunction may not yet have progressed substantially, or that other physiological or clinical factors influence these biochemical parameters independently of glycemic status [17, 18].

An increase in creatinine levels typically reflects the early stages of declining renal function due to nephron loss and reduced filtration efficiency, leading to creatinine accumulation in the bloodstream. In chronic diabetes, micro-vascular complications such as diabetic micro-angiopathy can contribute to ongoing renal injury, eventually resulting in advanced kidney disease or failure when left unaddressed.

To obtain a more comprehensive understanding of the interplay between these biochemical parameters, future research should incorporate larger sample sizes and consider additional variables, including blood pressure, duration of diabetes, and more detailed assessments of renal function—such as glomerular filtration rate measurements [19, 20].

CONCLUSIONS

Analysis showed no significant correlation between urea levels and fasting blood glucose (p=0,644 > 0.05) and no significant correlation between creatinine levels and fasting blood glucose (p=0.700 > 0.05). In contrast, a significant correlation was observed between urea and creatinine levels (p=0.000 , 0.05), with a moderate strength of association (r=0,530).

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