Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 1.6, September 2024, Supplement Issue
Manuscript ID:ZUMJ-2312-3055 (R2) DOI10.21608/ZUMJ.2024.256402.3055

ORIGINAL ARTICLE

Study of Plasma Copeptin as a Diagnostic biomarker for Nephropathy in Type 2 Diabetes

Abdel Monem Fathy Zeid [1],Atef Gouda Hussien [2], Ahmed Mohamed Ramadan Mesalam[*1], Alhoussein Alsayed Abdelaal [1]

[1] Internal Medicine Department, Faculty of Medicine, Zagazig University, Egypt
[2] Medical Biochemistry Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author*
Ahmed Mohamed Ramadan Mesalam

Email:
ahmedramadan1492@gmail.com ,

Submit Date 18-12-2023
Revise Date 16-01-2024
Accept Date: 199-01-2024
Modify Date: 15-07-2024

ABSTRACT

Background: Copeptin, a surrogate marker of the hormone arginine vasopressin (AVP) and the stable C-terminal portion of provasopressin, has been linked to declining kidney function in the general population. AVP testing is therefore helpful, but it is not frequently employed in clinical practice because of its extremely short half-life, which makes quantification challenging. Conversely, copeptin is easily detected immunologically and can be used as a vasopressin surrogate biomarker. This study aimed to investigate plasma copeptin in type 2 diabetic patients and to evaluate its potential utility as a diagnostic biomarker for the development of diabetic nephropathy. **Methods:** A case-control study that involved 52 individuals divided into two groups; 26 patients with type 2 diabetes and 26 normal subjects as a control group. Patients were subdivided into 2 subgroups; 13 patients with nephropathy and 13 patients without nephropathy.Investigations were serum creatinine, plasma copeptin, HbA1C, UACR. **Results:** Plasma copeptin levels were considerably elevated in diabetic patients with nephropathy than in those without (P< 0.001). Additionally, plasma copeptin showed a negative correlation with eGFR (P=0.005) and a positive correlation with serum creatinine, urea, and UACR (P=0.008, 0.014 and 0.005, respectively) in diabetic individuals with nephropathy. ROC curve analysis showed that serum copeptin at a cutoff point of 2pmol/l can be used to distinguish patients with and without diabetic nephropathy with a high sensitivity and a moderate specificity. **Conclusion:** Plasma copeptin levels are higher in diabetic individuals, especially in those who have nephropathy, and may serve as a biomarker for diabetic nephropathy diagnosis.

Keywords: Copeptin, Diabetes mellitus, Nephropathy

INTRODUCTION

Diabetes mellitus (DM) is one of the most common diseases with an increasing incidence worldwide. The Middle East and North Africa region had the highest prevalence of DM in 2019 at 12.2% and it is estimated that DM contributes to about 16.2% of deaths in the same region **[1]**. DM represents the leading cause of both chronic kidney disease and renal failure. Diabetic nephropathy (DN) affects between 20 and 40% of those who suffer from DM. Early detection and treatments are necessary to prevent the development of DN and to maintain proper glycemic control **[2].**

50% of cases of end-stage renal disease (ESRD) are caused by DN. Diminished glomerular filtration rate (GFR), glomerular lesions, and abnormal excretion of albumin in urineare the hallmarks of DN. As DN is a

complex disease, several factors contribute to its development, including inflammation, glycated protein accumulation, hyperglycemia, and genetics. While the diagnosis of DN is still based on the detection of abnormal albuminuria, reduced GFR can occasionally be found in conjunction with normal urine albumin excretion. Furthermore, diabetes may be associated with non-diabetic kidney disease in the absence of or in the presence of DN, which cannot be recognized from DN **[3].**

The GFR cannot be measured directly in a clinical setting. Although it is accepted that exogenous radionuclide clearance more closely reflects GFR, the exorbitant cost of this detection severely restricts its widespread use in clinical practice and large-scale surveys. Finding novel biomarkers is therefore essential for the prompt and precise diagnosis of early DN **[4].**

Arginine vasopressin (AVP) or antidiuretic hormone is one of the principal hormones of the hypothalamic-pituitary-adrenal axis, which is primarily triggered by hyperosmolarity. AVP has detrimental effects on the kidneys, including glomerular hyperfiltration, albuminuria, glomerulosclerosis, and hypertension. Because of its instability in separated plasma and its bond with platelets, AVP is difficult to quantify directly in humans **[5].**

Copeptin is a readily detectable surrogate marker of vasopressin, as it is the stable portion of the AVP precursor's COOH terminus. Equimolar quantities of copeptin and AVP are secreted into the bloodstream by the posterior pituitary gland. Copeptin mimicked the AVP level and its behavior, which can be altered by stress, plasma osmolality, and different illness states **[5].**

There is a paucity of data in the literature about the correlation between serum copeptin and DN. The present study aimed to investigate plasma copeptin in patients with type 2 DM and to evaluate its potential utility as a prospective biomarker for the development of DN.

PATIENTS AND METHODS

This is a case–control study that was carried out in internal medicine outpatient clinics at Zagazig University Hospitals and the National Institute of Diabetes and Endocrinology between August 2022 and March 2023. It included 52 individuals; aged from 20 to 73 years old and divided into two groups, 26 Patients with type 2 DM and 26 normal subjects who served as the control group. Patients were subdivided into 2 subgroups: 13 patients with nephropathy and 13 patients without nephropathy. Written informed consent was provided by each participant. The study was authorized via the Local Ethics Committee (ZU-IRB # 9263/23-3-2022).

We included patients with type 2 diabetes aged more than 18 years and excluded patients with type 1 diabetes, those with nephropathy due to causes other than type 2 DM and individuals who have recently been exposed to radiocontrast media.

All participants underwent thorough history taking, complete physical examination and laboratory investigations.

Sampling and laboratory investigations:

Blood samples were obtained from each participant by standard venipuncture. Two milliliters of blood were added to two glass tubes containing EDTA, one for complete blood count using the Erma Automated Blood Count Machine (Tokyo, Japan) and the other for glycosylated hemoglobin (HbA1c) using the Shimadzu® (Japan) Spectrophotometer. Serum samples were prepared by allowing them to clot for 10 minutes and then centrifuging them at 3000 rpm for 15 minutes for separation of serum. The separated serum samples were then kept at –80°C until the analysis was done. Serum creatinine and urea were assayed by the Shimadzu® (Japan) Spectrophotometer. Using the CKD-EPI formula, the glomerular filtration rate (GFR) was calculated. Serum copeptin levels (pmol/l) were measured using human copeptin ELISA kits. An early morning spot urine sample was collected for complete urine analysis. Urinary albumin/creatinine ratio (UACR) was measured using the spectrophotometer. Normal reference range of Plasma Copeptin is 1.7- 11.25 pm/l.

Statistical analysis:

All data were gathered, tabulated, and then statistically analyzed using the SPSS 22.0, IBM/SPSS Inc., Chicago, IL. The continuous data were described as mean and standard deviation for data that were normally distributed or median and range for data that were skewed. The method for presenting qualitative data was frequency with percentage (%). To compare two or more groups regarding a single qualitative variable, the Pearson Chi-square ($\chi 2$) test was employed. The Monte Carlo test was used as an alternative when the conditions for a chi squared test weren't met. For continuous data, a one-way ANOVA test was applied to test for significant differences between more than two normally distributed groups. The Shapiro-Wilk test and Levine's test were used to confirm the assumptions of normality and homogeneity of variances, respectively. When comparing more than two groups with skewed data, the Kruskal-Wallis test was employed. Following a significant ANOVA test, Tukey's HSD test was utilized as a post hoc test to identify which significant difference existed between pairs of groups whereas Bonferroni test was employed after a significant Kruskal-Wallis test. We applied the Mann-Whitney U test to compare two groups of continuous non-normally distributed data.All statistical comparisons were two-tailed. P-values ≤ 0.05 were considered statistically significant and P-values < 0.01 were considered highly statistically significant. Spearman's correlation coefficient was used to assess the association that exists between two variables. The receiver operating characteristic (ROC) curves were created to select a cut-off point value for copeptin. The area under the curve (AUC) determines the overall accuracy of a test.

RESULTS

Table 1; demonstrates the demographic characteristics of the studied groups.

Table 2; demonstrates that when comparing diabetic patients with nephropathy to those without, the disease duration in the former group was statistically substantially longer (P=0.001).

Table 3; shows that in the diabetic patients with nephropathy, serum urea, serum creatinine and UACR were significantly higher and eGFR was significantly lower compared to the diabetic patients without nephropathy & the control group (P<0.001 for all) with no statistically significant difference between the two latter groups. HbA1c and the mean plasma copeptin levels were statistically significantly higher in the diabetic patients with and without nephropathy compared to

the control group (P<0.001 for HbA1c and <0.001 & =0.002 for copeptin, respectively). Moreover, HbA1c and the mean plasma copeptin levels were significantly higher in diabetic patients with nephropathy as compared to diabetic patients without nephropathy (P=0.034 for HbA1c and <0.001 for copeptin).

Table 4; shows that in diabetic patients with nephropathy, plasma copeptin was positively correlated with serum creatinine, serum urea level and UACR (P=0.008, 0.014 and 0.005, respectively) and negatively correlated with eGFR (P=0.005). A statistically significant positive correlation was also found between copeptin with UACR in the other two groups (P=0.027 for the control group and 0.017 for diabetics without nephropathy).

Table 5; shows that the best cutoff point of Copeptin level to differentiate between group 2 A (Diabetic without nephropathy) and group 2 B (Diabetic with nephropathy) was > 2 pmol/l, with high sensitivity (92.3%) and moderate specificity (76.9%) (P<0.001).

Figure 1; shows the ROC curve of Copeptin level (pmol/L) to differentiate between Group 2 A (Diabetic without nephropathy) and Group 2 B (Diabetic with nephropathy)

Table 6; shows that with univariate regression analysis, higher age, female gender, increased disease duration, increased serum creatinine, increased serum urea, increased UACR , decreased eGFR and increased copeptin level were shown as risk predictors for diabetic nephropathy. However, with multivariate regression analysis, female gender, increased disease duration, increased serum urea, increased UACR and decreased eGFR were shown as independent risk predictors for diabetic nephropathy.

Table (1): The demographic characteristics of the studied groups

Variables	Group 1 (Control group) (n=26)	Group 2 A (Diabetic without nephropathy) (n=13)	Group 2 B (Diabetic with nephropathy) (n=13)	Test of significance	Multiple comparisons
Age (years) [Mean ± SD]	39.42 ±12.51	52.54 ±11.42	61.31 ±8.46	F = 14.276 P **<0.001** *	P_1= **0.009*** P_2 **<0.001** * P_3= 0.185
Gender [n (%)]				MC = 6.655 P= **0.036***	P_1=0.828 P_2 = **0.015*** P_3= **0.022***
Male	15 (57.7%)	7 (53.8%)	2 (15.4%)		
Female	11 (42.3%)	6 (46.2%)	11 (84.6%)		

MC: Monte Carlo test KW: Kruskal Wallis test F: One-way ANOVA test

P: General intergroup significance

P1: Comparison between Group 1 (Control group) and Group 2 A (Diabetic without nephropathy)

P2: Comparison between Group 1 (Control group) and Group 2 B (Diabetic with nephropathy)

P3: Comparison between Group 2 A (Diabetic without nephropathy) and Group 2 B (Diabetic with nephropathy)

*: Statistically significant ($p \leq 0.05$)

Table (2): Comparison of the clinical history in the diabetic groups

Variables	Group 2 A (Diabetic without nephropathy) (n=13)	Group 2 B (Diabetic with nephropathy) (n=13)	Test of significance
Disease duration (years) [Median (Range)]	5 (1-15)	20 (2-25)	z = 6.481 P = **0.001***
Diabetic treatment [n (%)]			c^2 = 1.764 P= 0.283
Insulin	4 (30.8%)	5 (38.5%)	
Oral antidiabetic	9 (69.2%)	8 (61.5%)	

c^2: Pearson Chi-square test
z: Mann Whitney U-test
P: General intergroup significance
*: Statistically significant (p≤ 0.05)

Table(3): Comparison of the laboratory data in the studied groups

Variables	Group 1 (Control group) (n=26)	Group 2 A (Diabetic without nephropathy) (n=13)	Group 2 B (Diabetic with nephropathy) (n=13)	Significance test	Intergroup Significance
Creatinine (mg/dL) [Median (range)]	0.9 (0.6- 1.2)	0.9 (0.6 - 1.3)	1.8 (1.23 – 5.5)	KW = 11.123 P = **0.001** *	P_1= 0.994 **P_2<0.001** * P_3**<0.001** *
Urea (mg/dL) [Median (range)]	26 (18 - 45)	24 (15 - 43)	70 (16 - 160)	KW = 6.345 P = **0.012** *	P_1= 0.999 P_2**<0.001** * P_3**<0.001** *
HbA1c (%) [Mean ± SD]	5.23 ± 0.20	8.23 ± 1.69	9.57 ± 2.05	F = 53.077 P **<0.001** *	P_1**<0.001*** **P_2<0.001*** P_3**= 0.034***
eGFR (ml/min/1.73m^2) [Median (range)]	99 (71– 133)	81 (61 – 114)	33 (9 – 59)	KW = 18.112 P **<0.001** *	P_1 = 0.116 **P_2<0.001*** P_3**<0.001***
UACR [Mean ± SD]	9.45 ± 3.07	16.92 ± 5.94	71.46 ± 20.39	F = 151.885 P **<0.001** *	P_1= 0.112 **P_2<0.001*** P_3**<0.001***
Copeptin level (pmol/L) [Mean ± SD]	0.98± 0.31	1.66 ± 0.51	3.37 ± 0.84	F =103.08 P **<0.001** *	P_1**= 0.002*** **P_2<0.001*** P_3**<0.001***

KW: Kruskal Wallis test
F: One-way ANOVA test
P: General intergroup significance
P1: Comparison between Group 1 (Control group) and Group 2 A (Diabetic without nephropathy)
P2: Comparison between Group 1 (Control group) and Group 2 B (Diabetic with nephropathy)
P3: Comparison between Group 2 A (Diabetic without nephropathy) and Group 2 B (Diabetic with nephropathy)
A1C: glycosylated hemoglobin, eGFR: estimated glomerular filtration rate,
UACR: urine albumin- creatinine ratio
*: Statistically significant (p≤ 0.05)

Table (4): Correlations between copeptin level with other variables in the studied groups

Variable		Copeptin		
		Group 1 (Control group)	**Group 2 A (Diabetic without nephropathy)**	**Group 2 B (Diabetic with nephropathy)**
Age	r_s	0.079	0.170	-0.384
	P	0.702	0.578	0.195
Duration of diabetes	r_s	-	-0.104	0.280
	P	-	0.735	0.355
Creatinine	r_s	-0.132	-0.287	**0.694**
	P	0.519	0.342	**0.008***
Urea	r_s	0.301	0.003	**0.661**
	P	0.135	0.993	**0.014***
A1C	r_s	0.137	-0.039	0.345
	P	0.506	0.899	0.248
eGFR	r_s	-0.017	0.025	**-0.722**
	P	0.935	0.936	**0.005***
UACR	r_s	**0.432**	**0.642**	**0.724**
	P	**0.027***	**0.017***	**0.005***

*: Statistically significant ($p \leq 0.05$)

A1C: glycosylated hemoglobin, eGFR: estimated glomerular filtration rate,

UACR: urine albumin- creatinine ratio

Table (5): Predictive value of Copeptin level (pmol/L) to differentiate between Group 2 A (Diabetic without nephropathy) and Group 2 B (Diabetic with nephropathy)

	Copeptin level (pmol/L)
AUC	0.962
Cut off point	**> 2**
Sensitivity	**92.3%**
Specificity	**76.9 %**
PPV	**84.6%**
NPV	**89.2%**
Accuracy	**90.8%**
P	< 0.001*

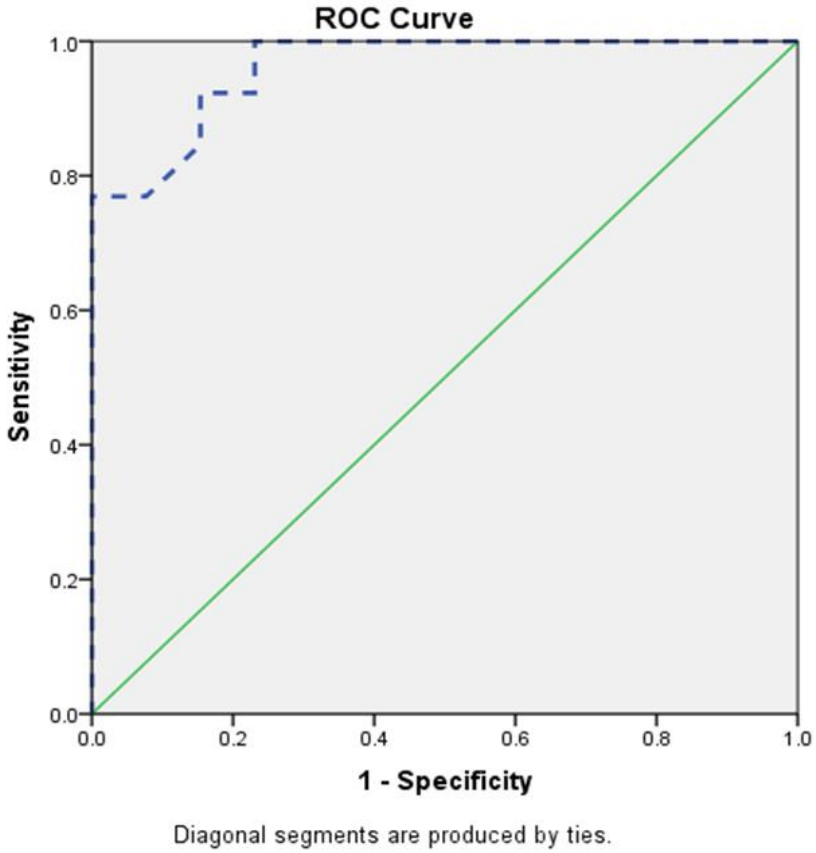
AUC: Area under curve, PPV: positive predictive value, NPV: Negative predictive value

Table (6): Univariate and multivariate regression analysis for prediction of diabetic nephropathy (n= 13)

Predictors	Univariate regression				Multivariate regression			
	P value	Odds ratio	95% C.I. for odds ratio		P value	Odds ratio	95% C.I. for odds ratio	
			Lower	Upper			Lower	Upper
Age	**0.049***	**1.079**	**1.036**	**1.123**	0.096	1.215	0.687	1.422
Male gender	R							
Female gender	**0.001***	0.092	0.022	0.379	**0.005***	0.483	0.230	0.846
Disease duration	**<0.001***	1.570	1.264	2.117	**<0.001***	2.364	1.11	3.78
Insulin therapy	R							
Oral antidiabetic	0.225	0.609	0.274	1.357				
Serum creatinine	**0.036***	1.466	1.225	1.868	0.062	1.046	0.738	1.262
Serum urea	**0.012***	1.030	1.087	1.257	**0.045***	1.347	1.179	1.636
HBA1C	0.088	1.240	0.823	1.636				
UACR	**<0.001***	2.692	1.584	3.172	**0.001***	1.702	1.342	2.109
eGFR	**<0.001***	0.648	0.255	0.487	**<0.001***	0.740	0.425	0.907
Serum Na	0.345	1.184	0.716	1.693				
Copeptin level	**0.011***	1.443	1.240	1.822	0.130	1.019	0.839	1.376

CI: Confidence interval
OR: Odd's ratio

Figure (1): ROC curve of Copeptin level (pmol/L) to differentiate between Group 2 A (Diabetic without nephropathy) and Group 2 B (Diabetic with nephropathy)



DISCUSSION

Diabetic nephropathy, the primary cause of renal failure in Middle Eastern populations, is among the most common microvascular complications of diabetes mellitus **[6]**. The main reason for increased albumin excretion in urine is protein glycosylation by advanced glycated end products, which results in glomerular hypertrophy. The persistent leak of albumin with other proteins into urine then leads to diabetic nephropathy **[7]**.

It is well established that AVP levels in the blood are elevated in patients with type 1 and type 2diabetes **[8]**. Although the exact reason for the elevated vasopressin in diabetic mellitus is unknown, it may be due to either a relative extracellular volume contraction brought on by glycosuria or increased hypothalamic osmoreceptors' sensitivity to plasma osmolarity **[9]**.

High levels of AVP may be helpful in the short run by reducing the amount of water lost in urine caused by glycosuria. But, in the long term, consistently high levels of AVP could be detrimental to the kidneys **[10]**.

To our knowledge, only a few studies investigate serum copeptin in diabetic nephropathy, so, the current study was designed to investigate the plasma copeptin in type 2 diabetic patients and to evaluate its potential value as a prospective biomarker for the onset of DN.

The results of this work revealed that plasma copeptin is positively correlated with serum creatinine, serum urea and UACR in patients with diabetic nephropathy and it can be used as an early diagnostic biomarker to predict the development of diabetic nephropathy.

The current study showed no significant difference in mean age between diabetic patients with nephropathy and diabetic patients without nephropathy. In concordance with this finding, the Third National Health and Nutrition Examination Survey (NHANES) study highlighted that diabetes has a higher impact on kidney function than aging does. It revealed that the rising incidence of renal dysfunction in the US population between 2005 and 2008 was related to rising diabetes trends, while the population's age distribution remained constant during the observation period **[11]**.

On the other hand, **Couser et al [12]** reported that kidney dysfunction is rising along with population ageing affecting approximately 25% of individuals aged 65–74 years and more than 50% of those above 75 years.

This discrepancy in the impact of ageing on kidney function may be ascribed to variations in patient characteristics, sample size, and management of risk factors of kidney damage other than ageing.

The current study's findings indicate that patients with diabetic nephropathy had considerably longer diabetes durations than people without nephropathy. This aligns with **Inassi and Vijayalakshmy [13]** who observed an association between the development of proteinuria and the duration of diabetes.

Moreover, **Ali et al [14] and Badawy Othman et al [15]** observed that the longer a patient has had diabetes, the higher their mean blood urea and serum creatinine levels. Additionally, they observed that the duration of their diabetes is positively correlated with the presence of proteinuria negatively correlated with the estimated glomerular filtration rate (eGFR).

In agreement with **El-Soudany et al [16]** and **Norris et al [17]**, the current study revealed that patients suffering from diabetic nephropathy showed higher levels of blood urea and serum creatinine and lower levels of eGFR when compared to both the control group and diabetics without nephropathy.

Clinical research has consistently shown an association between DN and inadequate glycemic management **[18]**. On the other hand, optimal glycemic management (HbA1c level < 7%) was linked to a decrease in microvascular damage **[19]**. The group receiving rigorous treatment in the UKPDS demonstrated a 30% decrease in the likelihood of developing microalbuminuria **[20]**. Consistent with these results, the present work showed that HbA1c levels were higher in patients with DN than in patients without.

In a study conducted by **Wang et al [21]**, although no significant difference was found between patients with DN and patients without DN in HbA1c levels, the incidence of

DN was found to be higher in patients with HbA1c ≥ 7% compared to patients with HbA1c levels < 7% (39.7% versus 25.6%, P< 0.001).

In line with **Ali et al [14]**, the levels of serum copeptin in the present study were higher in patients with and without DN than in healthy controls.

In this study, patients with DN showed a correlation between their serum copeptin level and a decline in kidney function. This result is consistent with that obtained by **Velho et al [22]** who noted an association between plasma copeptin and the deterioration in renal function in populations with chronic kidney disease (CKD) or in those at risk of developing CKD, such as individuals with DM. Additionally, **Butler-Dawson et al [23]** found that lower serum copeptin concentration was associated with an improvement in serum creatinine and eGFR and that greater copeptin concentration was linked to worsened renal function. Furthermore, the plasma copeptin level may be predictive of a decline in renal function over several months.

This is also supported by **El Soudany et al [16]** who stated that copeptin has a high sensitivity and specificity for recognizing nephropathic consequences of type 2diabetes.

Conversely, in a study conducted by **Noor et al[24]**,the copeptin levels were not significantly increased in diabetic patients with and without nephropathy when compared to the healthy controls.

The discrepancy in results could be explained by the different sample sizes in each study. Variations in the disease severity, glycemic management, and diabetes duration could also account for this difference in results. In the same setting, **Noor et al [24] and Villela-Torres et al [25]** revealed a negative correlation of copeptin with eGFR, albumin, and hemoglobin, and a positive correlation with diabetes duration, and serum glucose.

According to ROC curve analysis in the current study, copeptin has a high sensitivity and a moderate specificity to distinguish patients with and without DN at a cutoff point of 2 pmol/l.

The current study had some limitations. All patients included in the study had type 2 diabetes; therefore, these results cannot be generalized to type 1 diabetes. Additionally, blood glucose level was not checked at the time of measurement of copeptin, which if high can increase plasma osmolarity and further increase the copeptin level.

These results need to be confirmed with larger studies. Also, long-term follow-up is required to study the effect of treatment of diabetic nephropathy on the plasma copeptin level.

CONCLUSION

Patients with type 2 diabetes, particularly those who have nephropathy, have higher levels of plasma copeptin, which may serve as a biomarker for diabetic nephropathy diagnosis. Further multicenter studies on different ethnic groups are required for more evaluation.

Declaration of interest

The authors report no conflicts of interest.

The authors along are responsible for the content and writing of the paper.

REFERENCES

1-Saeedi P, Salpea P, Karuranga S, Petersohn I, Malanda B, Gregg EW et al. Mortality attributable to diabetes in 20-79 years old adults, 2019 estimates: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2020; **162:108086**.

2- Tuttle KR, Bakris GL, Bilous RW, Chiang JL, De Boer IH, Goldstein-Fuchs J et al. Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes care. 2014 Oct 1; 37(10):2864-83.

3- Zhao L, Liu F, Li L, Zhang J, Wang T, Zhang R et al. Solidified glomerulosclerosis, identified using single glomerular proteomics, predicts end-stage renal disease in Chinese patients with type 2 diabetes. *Sci Rep*. 2021; 25;11(1):4658.

4- Then C, Kowall B, Lechner A, Meisinger C, Heier M, Koenig W, et al. Plasma copeptin is associated with type 2 diabetes in men but not in women in the population-based KORA F4 study.Acta Diabetol. 2015 Feb;52:103-12.

5- Lacquaniti A, Chirico V, Cernaro V, Lupica R, David A, Buemi M. Apelin and Copeptin as Biomarkers of Kidney Disease. In: Patel V., Preedy V. (eds) Biomarkers in Kidney Disease. Biomarkers in Disease: Methods, Discoveries and Applications. Springer. Dordrecht. 2016.

6-Tervaert TW, Mooyaart AL, Amann K, Cohen AH, Cook HT, Drachenberg CB, et al. Pathologic classification of diabetic nephropathy. J Am Soc Nephrol. 2010;21(4), 556–563.

7- Kondaveeti SB, D K, Mishra S, Kumar RA,

Shaker IA. Evaluation of glycated albumin and microalbuminuria as early risk markers of nephropathy in type 2 diabetes mellitus. J Clin Diagn Res.. 2013;7(7), 1280–1283.

8- Bankir L, Bardoux P, Ahloulay M. Vasopressin and diabetes mellitus. Nephron. 2001;87(1), 8–18.

9-Zerbe RL, Vinicor F, Robertson GL. Regulation of plasma vasopressin in insulin-dependent diabetes mellitus. Am J Physiol. 1985;249 (3 Pt 1), E317–E 25.

10-Roussel R, Velho G, Bankir L. Vasopressin and diabetic nephropathy. Current opinion in nephrology and hypertension. 2017;26(4):311–318

11- de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. Jama. 2011 Jun 22; 305(24):2532-9.

12- Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. Kidney Int. 2011 Dec 2;80(12):1258-70.

13- Inassi J, Vujayalakshmy R. Role of duration of diabetes in the development of nephropathy in type 2 diabetic patients. Nat J Med Rese. 2013 Mar 31; 3(01):5-8.

14- Ali DA, Al-Ashmawy GM, Aboelnasr SM, El-Feky OA. Copeptin: Promising Biomarker for Nephropathy in Type II Diabetes. J Adv Med Pharmaceutical Res.2020 Oct 13;2(1):1-7.

15- Badawy Othman AI, Elalem A, Mohamed S, Elsherbini D, Riad NA. Association Between Diabetic Nephropathy Grade and Quality of Life among Type II Diabetic Patients. Tanta Scientif Nurs J. 2021 Nov 1;23(4):268-94.

16- El-Soudany NN, Bessa SS, Morad HA, Selim AA. Plasma copeptin level in type 2 diabetic patients and its role in diabetic nephropathy. Egypt J Inter Med. 2023 Dec;35(1):1-8.

17- Norris KC, Smoyer KE, Rolland C, Van der Vaart J, Grubb EB. Albuminuria, serum creatinine, and estimated glomerular filtration rate as predictors of cardio-renal outcomes in patients with type 2 diabetes mellitus and kidney disease: a systematic literature review. BMC Nephrol. 2018 Dec;19(1):1-3.

18- Fineberg D, Jandeleit-Dahm KA, Cooper ME. Diabetic nephropathy: diagnosis and treatment. Nat Rev Endocrinol. 2013; 9:713–23.

19- The Diabetes Control and Complications (DCCT). Research Group Effect of intensive therapy on the development and progression of diabetic nephropathy in the Diabetes Control and Complications Trial.1995: Kidney Int. 47:1703–20.

20- UK Prospective Diabetes Study (UKPDS). Group Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. Lancet. 1998;352:837–53.

21- Wang G, Ouyang J, Li S, Wang H, Lian B, Liu Z et al. The analysis of risk factors for diabetic nephropathy progression and the construction of a prognostic database for chronic kidney diseases. J Transl Med. 2019 Dec; 17(1):1-2.

22- Velho G, El Boustany R, Lefèvre G, Mohammedi K, Fumeron F, Potier L. et al. Plasma copeptin, kidney outcomes, ischemic heart disease, and all-cause mortality in people with long-standing type 1 diabetes. Diabetes Care. 2016 Dec 1; 39(12):2288-95.

23- Butler-Dawson J, Dally M, Johnson RJ, Johnson EC, Krisher L, Sánchez-Lozada LG, et al. Association of Copeptin, a Surrogate Marker of Arginine Vasopressin, with Decreased Kidney Function in Sugarcane Workers in Guatemala. Ann Nutr Metab. 2020; 76(1), 30–36.

24- Noor T, Hanif F, Kiran Z, Rehman R, Khan MT, Haque Z, et al. Relation of Copeptin with Diabetic and Renal Function Markers Among Patients with Diabetes Mellitus Progressing Towards Diabetic Nephropathy. Arch Med Res. 2020; 51(6), 548–555.

25-Villela-Torres ML, Higareda-Mendoza AE, Gómez-García A, Alvarez-Paredes AR, García-López E, Stenvikel P et al. Copeptin Plasma Levels are Associated with Decline of Renal Function in Patients with Type 2 Diabetes Mellitus. Arch Med Res. 2018; 49(1), 36–43.

Citation:

Fathy Zeid, A., Hussien, A., Ramadan Mesalam, A., Abdelaal, A. Study of Plasma Copeptin as a Diagnostic biomarker for Nephropathy in Type 2 Diabetes. ***Zagazig University Medical Journal*****, 2024; (2984-2993): -. doi: 10.21608/zumj.2024.256402.3055**