The predominance of chronic kidney disease (CKD) is expanding around the world. The identification of variables contributing to its movement is critical for planning preventive measures. Past ponders have proposed that chronically high vasopressin is pernicious to renal function. Here, we assessed the affiliation of plasma copeptin, a surrogate of vasopressin, with the rate of CKD within the common populace. CPP increased in CRF, and more deterioration directly related to the degree of renal failure. Conclusions: rise copeptin levels are connected with the development and the progression of CKD in the general population. Interferences studies are needed to assess the potential beneficial effect on kidney health in the general population of decrease vasopressin secretion or action.

**Keywords:** CKD (chronic kidney disease), CPP (copeptin)

**Material and Methods**

The study was case–controlled in design. We selected the patients as they presented 176 patients with undergoing chronic kidney disease mean age of the sample was 64.86 (±14.89) years with minimum and maximum values of 30 and 60 years.

Stage I: 20 patients (7 male, 13 female), Stage II: 32 patients (21 male, 11 female), Stage III: 32 patients (20 male, 12 female), Stage IV: 32 patients (20 male, 12 female), Dialysis: 44 patients (30 male, 14 female), Control: 16 patients (10 male, 6 female)
Compared with 16 healthy subjects (10 male and 6 female) as control group. Were all admitted to the Ibn Sina center for dialysis in Baquba teaching hospital for the period. Fully informed consent was obtained from patients and controls. Copeptin was determined in serum of all subjects by using a commercially ELISA Micro wells kit (from LDN, Germany).

**Statistical analysis**

Analysis of data was carried out using the available statistical package of SPSS-25 (Statistical Packages for Social Sciences-version 25). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). The significance of difference of different means (quantitative data) were tested using Students-t-test for difference between two independent means or Duncan test for difference of any two independent means, or ANOVA test for difference among more than two independent means. The significance of difference of different percentages (qualitative data)

**Results**

The study showed that the stage III was the highest range compared to the rest of the stages (61.85±41.09 pg /ml).

**Table 1: Comparison between difference groups in copeptin and kidney function**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Copeptin (pg/ml)</td>
</tr>
<tr>
<td>Stage I</td>
<td>30.70±12.65 bc</td>
</tr>
<tr>
<td>Stage II</td>
<td>26.83±3.00 c</td>
</tr>
<tr>
<td>Stage III</td>
<td>61.85±41.09 a</td>
</tr>
<tr>
<td>Stage IV</td>
<td>30.67±12.51 bc</td>
</tr>
<tr>
<td>Dialysis</td>
<td>37.38±14.23 b</td>
</tr>
<tr>
<td>Controls</td>
<td>30.59±9.81 bc</td>
</tr>
<tr>
<td>LSD value</td>
<td>9.291 **</td>
</tr>
</tbody>
</table>

Means having with the different letters in same column differed significantly. ***(P<0.01).***

Urea level was higher in dialysis (22.57±9.73 mMol/L), than in control group (3.87±1.23 mMol/L) but it was higher than the control group in stage IV and III, II (18.60±9.70 mMol/L), (10.27±4.08 mMol/L), (7.27±2.95 mMol/L), Urea levels showed significant difference (p<0.01) amid two groups. The levels of Urea are shown in Fig. 1

![Fig. 1: Urea levels in all subgroups](image)

Creatinine level was higher in dialysis (547.44±105.50 mMol/L), than in control group(43.37±13.37 mMol/L ) but it was higher than the control group in stage IV and III, II (263.80±48.77 mMol/L), (157.56 ± 25.60 mMol/L), (92.55±15.28 mMol/L). Creatinine levels showed significant difference (p< 0.01) amid two groups. The levels of Creatinine are shown in Fig. 2

![Fig. 2: Creatinine levels in all subgroups](image)

The glomerular filtration rate GFR was the lowest in the dialysis group (9.83±2.43 mMol/L), and in the stage IV( 22.15 ± 4.21 mMol/L ) compared to the control group (210.58 ± 121.06 mMol/L) GFR levels showed significant difference (p< 0.01) amid two groups. The levels of GFR are shown in Fig. 3

![Fig. 3: GFR levels in all subgroups](image)
Evaluation of copeptin hormone function in chronic renal failure stages and dialysis

**Discussion**

Our current data extend our previous finding that increased levels of copeptin independently predict decline in eGFR (Tasevka et al., 2016) and suggest that copeptin can be used to identify individuals at higher risk for development of CKD. Whether the relationship between VP (measured as copeptin) and disease development is causal or due to covariation is unknown. Together with previous experiments in humans and animals, showing progressive renal function decline during VP exposure (Bouby et al., 1999) as well as beneficial effects on kidney function as a result of genetic lack of VP (Bardoux P et al., 1999), VP receptor antagonism, and increased water intake (Perico et al., 2009), our current data point at a possible causal role of elevated VP in the progression of CKD. Assuming causality between VP and CKD development, lowering of circulating VP level, for example by increased water intake or pharmacological manipulation, would represent a promising treatment target.

Our data further implicate beneficial effects of lower circulating VP concentrations/ increased hydration in the progression of specific other renal diseases. The exact mechanisms regarding the relationship between copeptin, albuminuria and GFR are not known but two mechanisms were suggested. First, as copeptin is cleared by kidney excretion, copeptin levels would tend to increase as kidney function decreases. Second, in patients with lower kidney function, more copeptin is released, because the AVP system is activated due impaired urine concentrating capacity to maintain water homeostasis (Zittema et al., 2012). Longitudinal studies in humans have shown that plasma copeptin levels increase before eGFR decreases (Ponte et al., 2015). Studies in the 5/6 nephrectomized rat model suggested that increased water intake decreases circulating AVP levels and slows down the progression of kidney disease (Bouby et al., 1990). The relationship between copeptin and hypertension is also worth to mention. Most of the studies have shown a positive association with copeptin and hypertension recent evidence suggests that elevated blood pressure is associated with increased copeptin levels. For example, in hypertensive adolescents, copeptin levels were higher in normotensive adulterants. Not only office blood pressure but ambulatory blood pressures (both systolic and diastolic) were associated with copeptin levels (Tenderenda-Banasiuk et al., 2014). In another recent study, the relationship between copeptin and resistant hypertension were investigated. Baseline plasma copeptin concentration was positively associated with male sex, plasma osmolality, BP, and negatively with glomerular filtration rate. It was higher in the resistant hypertension than in the controlled blood pressure group [geometric mean 5.7 (confidence interval 95% 5.1–6.4) vs. 2.9 (2.3–3.9) fmol/ml, adjusted P < 0.0001] (Mendes et al., 2016) In fact older studies have already suggested that AVP may have a role in development of hypertension (Bakris et al., 1997). Several lines of evidence suggest a role of copeptin in hypertension. One of the suggested mechanisms is the local tissue Renin Angiotensin Aldosterone System (RAAS) activation in supraoptic and paraventricular nuclei which stimulates the production and release of arginine vasopressin. Second mechanisms involve the vasocostriction. This vasoconstriction is due to both direct effects on smooth muscle cells and by indirectly increasing renin secretion (Tenderenda-Banasiuk et al., 2014). Third mechanism is the effect of copeptin on increased tubular sodium retention (Perucca et al., 2008) Thus copeptin may be common marker for essential hypertension and kidney disease. In conclusion, our study demonstrates that high copeptin levels are associated with the development and the progression of CKD in the general population. Our results argue for the relevance in human pathology of the experimental data obtained in animal models, suggesting a causal link between vasopressin and kidney disease. Together, they provide a strong basis to design future intervention studies that assess the effect of reducing vasopressin secretion, and the potential role of high water intake, in the prevention of kidney disease in the general population. Our study demonstrates that high copeptin levels are associated with the development and the progression of CKD in the general population. A few studies investigated the impact of high copeptin levels on renal function in people with diabetes (Velho et al., 2016), (Boertien et al., 2013), and co-workers analysed data from 1328 patients with type 2 diabetes of relatively recent onset (4 years of median duration of diabetes) from the Dutch ZODIAC prospective study (Boertien et al., 2013).

They reported the higher quartile of baseline plasma copeptin to be associated with a faster decline in eGFR during a follow-up of 6.5 years. In a Swedish study of people with newly diagnosed type 2 diabetes from the Skaraborg Diabetes Register, plasma copeptin was positively associated with eGFR decline at re-examination after 12 years of follow-up (Pikkemaat et al., 2015). So It has been suggested that high copeptin levels observed in people with CKD might merely reflect a decline in GFR. Both vasopressin and copeptin are small-sized molecules and thus could be subjected to renal clearance. However, results from a recent investigation suggest that renal clearance is not the predominant factor in the degradation of circulating copeptin (43). Moreover, strong experimental data have been accumulated in the last decades supporting a direct causal role for vasopressin in the pathogenesis of CKD (Bankir et al., 2013). Moreover, copeptin is also known as a stress hormone and may serve as a marker of individual stress. Copeptin is even more reliable for the stress level determination than cortisol, due to its higher stability (Katan et al., 2008). In one of the largest studies conducted by (Enho¨ rning et al., 2010) copeptin was the independent predictor for future risk of diabetes mellitus (DM). In conclusion the authors also suggest that their findings may be relevant for risk evaluation and contribute to a new
therapeutic approach in the prevention and treatment of diabetes. Similar results were also reported with respect to metabolic syndrome (MetS), where elevated plasma copeptin concentration have significantly correlated with MetS independently, as well as with high fat intake and low physical activity (Enhörning et al., 2011). Several publications have appeared in recent years documenting the relation between copeptin and renal outcomes in patients with type 2 diabetes. As reported by (Boertien et al., 2013), baseline copeptin levels have correlated with albumin/creatinine ratio and eGFR in patients with type 2 diabetes mellitus. This relation was only observed among patients not treated with renin–angiotensin–aldosterone system inhibitors. Similar results have been also revealed by (Velho et al., 2016), in the long term follow-up study concerning patients with type 2 diabetes. In this cohort plasma copeptin was significantly associated with severe renal outcome and albuminuria, independently of age, duration of diabetes, hypertension and baseline levels of eGFR.

**Conclusion**

In this study CPP hormone was increased in chronic renal failure disease and more elevation was seen at the end stage of renal disease and

**References**


Perucca, J.; Bichet, D.G.; Bardoux, P.; Bouby, N. and Bankir, L. (2008). Sodium excretion in response to vasopressin and selective vasopressin receptor


