ORIGINAL ARTICLE

The value of Copeptin and Lung Ultrasound in Assessment of Volume Status in Chronic Regular Hemodialysis Patients

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Abstract

Background: ***Research indicates that copeptin levels are raised in cases with end-stage kidney disease (ESKD) and may serve as an alternate biomarker to vasopressin for predicting cardiovascular illnesses and death in end-stage kidney disease cases.***

Aim: ***To assess the role of lung ultrasound and Copeptin in the assessment of volume status before and after a dialysis session in hemodialysis cases.***

Patients and methods: ***The cross-sectional investigation comprised ninety cases of patients who had been diagnosed with chronic renal failure on regular dialysis and fulfilled the selection criteria from the Nephrology Unit, Al Hussein University Hospital. This was a prospective observational investigation performed at the Department of Internal Medicine, Faculty of Medicine, Al-Azhar University.***

Results: ***A significant reduction has been observed in copeptin level post-hemodialysis than pre-hemodialysis (p<0.001). There was a significant positive association among copeptin, SBP, DBP, body weight, B-line score, and IVC diameter (p <0.001). There was a significant negative association between copeptin and IVC Collapsibility (p <0.001).***

Conclusion: ***In summary, Copeptin and lung ultrasonography can evaluate fluid volume status. This provides an effective approach for assessing fluid status in cases with volume overload. Future directions could involve the expansion and application of lung ultrasonography and Copeptin for the quantitative assessment of volume status in additional volume-sensitive populations, like cases with heart failure.***

Keywords: Copeptin; Lung Ultrasound; Hemodialysis; ESKD

1. Introduction

Chronic kidney disease (CKD) is a gradual deterioration of renal function occurring over months or years. Cases with a glomerular filtration rate under fifteen ml/min/1.73 m² for a duration of three months are categorized as having end-stage renal disease (ESRD). The global prevalence rates of chronic kidney disease are significant, having risen in recent years to approximately thirteen to fifteen percent, coinciding with a heightened occurrence of hypertension and diabetes.[1]

In cases with end-stage renal disease undergoing intermittent hemodialysis, it is essential to regulate fluid status within an ideal range to prevent circulatory problems. The adequacy of dialysis solute removal is assessed by evaluating the case's dry weight.[2]

Dry weight is established through clinical assessment and often represents the minimum post-dialysis weight that the cases can tolerate without suffering intradialytic symptoms, hypotension, or excessive fluid intake. The clinical assessment of dry weight lacks consideration of nutritional status alterations and fat-free body mass, complicating the determination of whether the case is hyper- or hypovolemic, potentially leading to increased morbidity and death.[3]

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If a case hasn't reached its dry weight, it will suffer from the difficulties associated with insufficient dialysis. Physical examination serves as the primary method for assessing hemodialysis cases due to the restricted availability of alternative diagnostic technologies. A diagnostic test comprising chest ultrasound, physical examination, and inferior vena cava diameter measurement is necessary to evaluate volume status and identify lung congestion in hemodialysis cases .[4]

Copeptin is a 35-amino acid glycopeptide derived from the C-terminal of the arginine vasopressin precursor, exhibiting stability for 7 days at ambient temperature and 14 days at four degrees Celsius. It is a stable molecule with a prolonged half-life of eighty-six minutes in comparison to AVP, and it is readily measurable. Research indicates that copeptin levels rise in cases with ESKD and may serve as an alternate biomarker to vasopressin for predicting cardiovascular illnesses and death in this population. Additional research has indicated that copeptin is associated with renal cystic disease, chronic kidney disease, diabetes mellitus, diabetes insipidus, as well as cardiovascular and metabolic diseases.[5]

The research aimed to evaluate the usefulness of lung ultrasonography and Copeptin in assessing volume status prior to and following dialysis sessions in hemodialysis cases.

2. Patients and methods

The cross-sectional investigation comprised ninety cases diagnosed with chronic renal failure undergoing regular dialysis, who met the selection criteria, from the Nephrology Unit at Al Hussein University Hospital. This was a prospective observational investigation carried out in the Department of Internal Medicine, Faculty of Medicine, Al-Azhar University.

Inclusion criteria: Cases aged eighteen to sixty years, undergoing hemodialysis for over six months, utilizing arteriovenous fistulas.

Exclusion criteria: Myocardial infarction (MI), pregnancy, corpulmonale, or stroke throughout the past six months. Cases with a prior or present diagnosis of clinically documented left ventricular dysfunction and an ejection fraction of under fifty percent. Cases with interstitial lung disease, malignancy, active infection, debilitating diseases, low serum albumin, deep vein thrombosis (DVT), ascites, or a history of psychiatric disorders.

Methods:

All cases included in the research have been exposed to the following: Personal history, along with present history covering the cause of ESRD, onset, and hemodialysis period. A thorough medical history was taken. Clinical investigation included body weight measurement prior to and following dialysis and assessment for signs of hypervolemia. Weight was measured using a digital scale. Supine blood pressure, involving diastolic, systolic, and mean arterial pressure, was determined using a mercury sphygmomanometer before and after dialysis. Blood samples were taken after an 8-hour fasting period for routine investigations, including CBC, iron profile, urea, creatinine, albumin, Calcium, Phosphorus, and PTH, conducted once before dialysis. Hemodialysis was performed using a low-flux polysulfone dialyzer with bicarbonate dialysis and constant ultrafiltration. The dialysate contained sodium (105 millimoles per liter), potassium (2 millimoles per liter), chloride (111.5 millimoles per liter), Calcium (1.75 millimoles per liter), magnesium (0.5 millimoles per liter), bicarbonate (34 millimoles per liter), and acetate (3 millimoles per liter), with a blood flow rate of 250 to 350 milliliters per minute and a dialysate flow rate of five hundred milliliters per minute. All cases had dialysis in a supine position to reduce posture-related fluctuations in blood volume. Two blood samples have been obtained prior to and following dialysis to assess copeptin levels (Enzyme Linked Immunosorbent Assay Kit assay, Bioassay Technology Laboratory, China), hematocrit, sodium (Na), blood urea nitrogen (BUN), and hemoglobin. The volume assessment encompassed a lung examination for B-lines and pleural effusion, as well as a subcostal evaluation of the inferior vena cava diameter and its collapsibility. An ultrasound examination was conducted with a Clarius HD scanner (Clarius Mobile Health, Canada, 2020), which was linked via Bluetooth to an iOS 15 iPad for image transfer. The extravascular volume has been evaluated utilizing lung ultrasonography with a Clarius C3 HD curvilinear probe set to five megahertz, utilizing a four-zone lung protocol to examine both lung bases for pleural effusion. B-lines are characterized as hyperechoic, distinctly defined comet-tail artifacts originating from the pleural line, exhibiting movement in conjunction with lung sliding when present. Over 3 B-lines in one lung zone indicated extravascular lung water (EVLW), with B-line numbers categorized into three groups (0-<3, ≥3-<10, and ≥10). Pleural effusion was visually assessed using a curvilinear probe in the midaxillary line. Intravascular volume evaluation used a 2.5-megahertz curvilinear probe in a cardiac setting, with the inferior vena cava viewed in the anterior sub-sternal window. The Inferior vena cava diameter was measured using the leading-edge method at the hepatic vein-inferior vena cava junction, 3–4 cm from the inferior vena cava-right atrial confluence. Maximum inferior vena cava diameter (IVCdmax) was recorded at end-expiration, and minimum inferior vena cava diameter (IVCdmin) at end-inspiration. The inferior vena cava collapsibility index was calculated as ([IVCdmax – IVCdmin] / IVCdmax × 100%). Normal inferior vena cava collapsibility exceeds 50% with normal breathing or sniffing. A collapsibility index <20% suggests hypervolemia, while a collapsibility below 50% with IVCdmax ≥2.1 cm also indicates hypervolemia. A collapsibility index >50% without a sniff or Valsalva, with IVCdmax <1.2 centimeters, suggests hypovolemia. Statistical analysis was conducted using SPSS version 20.0 (SPSS Inc., Chicago, Illinois, United States of America). Quantitative data have been expressed as mean ± SD, whilst qualitative data have been shown as frequency and percentage. A p-value of ≤0.05 was deemed significant, ≤0.001 highly significant, and >0.05 insignificant.

Ethical consideration

The Local Ethics Committee permitted the research protocol, and written informed consent has been obtained from all participants.

Informed written consent has been acquired from each case for all procedures conducted.

3. Results

Table 1 represents the baseline demographic characteristics of the study group. The mean age of studied cases was 46.68 ± 14.57, 74.4% were male, 25.6% were female with mean BMI was 25.51 ± 6.25 kg/m2

Table 1. Distribution of examined cases regarding baseline characteristics

VARIABLES		
AGE, YEARS		
MEAN ± SD	46.68 ± 14.57	
GENDER	N	%
MALE	67	74.4%
FEMALE	23	25.6%
BMI, KG/M^2		
MEAN ± SD	25.51 ± 6.25	

Table (2): shows that mean of HD duration was 3.44 + 0.26 hours, mean of Known dry weight (kg) was 75.12 ± 16.77 and mean of Inter dialytic weight gain (Kg) was 2.79 ± 1.23.

Table 2. Distribution of studied cases according to dialysis data

VARIABLES	
HD DURATION, HOURS	
MEAN ± SD	3.44 + 0.26
KNOWN DRY WEIGHT (KG)	
MEAN ± SD	75.12 ± 16.77
INTER-DIALYTIC WEIGHT GAIN (KG)	
MEAN ± SD	2.79 ± 1.23

Table (3): shows that mean of HB (g/dl) was 10.70 ± 1.77, mean of Alb (g/dl) was 3.32±0.45, mean of BUN (mg/dL) was 67.2±22.5, mean of Cr (mg/dL) was 9.04 ± 2.76, mean of Na+ was 132.23 ± 4.24 mmol/L, mean of K+ was 5.53 ± 1.05 mmol/L, mean of Ferritin was 650.48±87.23 μg/L, mean of PTH was 217.3±52.2 nanograms per milliliter, mean of Calcium was 8.68 ± 0.83 milligrams per deciliter and mean of Phosphorus was 5.23 ± 1.83 mg/dL.

Table 3. Distribution of studied cases according to laboratory data

VARIABLES	
HB (G/DL)	
MEAN ± STANDARD DEVIATION	10.70 ± 1.77
ALB (G/DL)	
MEAN ± STANDARD DEVIATION	3.32±0.45
BUN (MG/DL)	
MEAN ± STANDARD DEVIATION	67.2±22.5
CR (MG/DL)	
MEAN ± STANDARD DEVIATION	9.04 ± 2.76
NA+ (MMOL/L)	
MEAN ± STANDARD DEVIATION	132.23 ± 4.24
K+ (MMOL/L)	
MEAN ± STANDARD DEVIATION	5.53 ± 1.05
FERRITIN, MG/L	
MEAN ± STANDARD DEVIATION	650.48±87.23
PTH, NG/ML	
MEAN ± STANDARD DEVIATION	217.3±52.2
CALCIUM (MG/DL)	
MEAN ± STANDARD DEVIATION	8.68 ± 0.83
PHOSPHORUS (MG/DL)	
MEAN ± STANDARD DEVIATION	5.23 ± 1.83

Table (4): shows that there was a significant decline in systolic blood pressure and diastolic blood pressure post hemodialysis compared to pre hemodialysis (p<0.001).

Table 4. Comparative analysis among pre hemodialysis and post hemodialysis as regards Blood pressure

VARIABLES	PRE-HEMODIALYSIS	POST-HEMODIALYSIS	TEST	P-VALUE
SBP (MMHG)			5.32	0.002*
MEAN ± SD	132.5±10.5	119.5±8.0		
DBP (MMHG)			6.98	0.001*
MEAN ± SD	88.5±11.0	76.0±9.5		
MAP (MMHG)			4.22	0.04*
MEAN ± SD	115.0±5.6	102.5±7.0		

Table (5): shows that there was a significant decrease in B line score and IVC diameter post hemodialysis compared to pre hemodialysis (p-value below 0.001). while there was a significant rise in IVC Collapsibility post hemodialysis compared to pre hemodialysis (p<0.001).

Table 5. Comparative analysis among pre hemodialysis and post hemodialysis as regards Lung ultrasound findings

VARIABLES	PRE-HEMODIALYSIS	POST-HEMODIALYSIS	TEST	P-VALUE
B LINE SCORE			6.87	0.001*
MEAN ± SD	12.1±2.8	4.7±1.6		
IVC DIAMETER, CM			4.32	0.004*
MEAN ± SD	1.95 ± 0.85	1.3± 0.54		
IVC COLLAPSIBILITY, %			5.32	0.032*
MEAN ± SD	35.60 ± 11.63	40.08 ± 12.46		

Table (6): shows that there was a significant decline in copeptin level post hemodialysis than pre hemodialysis (p<0.001).

Table 6. Comparative analysis among pre hemodialysis and post hemodialysis as regards copeptin

VARIABLES	PRE-HEMODIALYSIS	POST-HEMODIALYSIS	TEST	P-VALUE
COPEPTIN			6.49	0.001*
MEAN ± SD	763 ± 206.11	325.9 ± 119.6		

Table (7): shows that there was significant positive association among copeptin, SBP, DBP, body weight, B line score and IVC diameter (p <0.001). There was significant negative association among copeptin and IVC Collapsibility (p <0.001).

Table 7. Comparative analysis among copeptin and different variables

VARIABLES	R	P-VALUE
SYSTOLIC BLOOD PRESSURE	0.36	0.001*
DIASTOLIC BLOOD PRESSURE	0.47	0.02*
BODY WEIGHT	0.18	0.003*
B LINE SCORE	0.61	0.001*
IVC DIAMETER	0.15	0.04*
IVC COLLAPSIBILITY	-0.61	0.02*

Table (8): shows the diagnostic accuracythe lung ultrasound findings and copeptin levels as discriminatory markers prior to and following hemodialysis in ESKD cases was evaluated utilizing a receiver operating characteristic curve analysis, revealing a 89.3 percent sensitivity and a 90.7 percent specificity at a cutoff value of >425.48 pg/ml, demonstrating an acceptable discriminative accuracy of 89.3 percent .The diagnostic accuracy of the B line score as a distinguishing marker prior to and following hemodialysis in cases suffering from ESKD has been evaluated utilizing the ROC curve, which demonstrated a 91.2 percent sensitivity and a specificity of 89.3 percent at a cutoff value greater than 9, yielding an adequate discriminative accuracy of 90.6 percent.

The diagnostic accuracy of the IVC diameter score for predicting volume overload in hemodialysis cases has been evaluated utilizing the receiver operating characteristic curve, which demonstrated a sensitivity of 92.3% and an 88.7 percent specificity at a cutoff value greater than 1.6, yielding an adequate discriminative accuracy of 91.3 percent.

The diagnostic accuracy of the IVC Collapsibility score for predicting volume overload in hemodialysis patients was evaluated utilizing the receiver operating characteristic curve, which demonstrated a sensitivity of 90.8 percent and a specificity of 91.2 percent at a cutoff value greater than 37.6, yielding an adequate discriminative accuracy of 92.4 percent.

Table 8. ROC curve analysis of Lung ultrasound findings and copeptin levels for predicting volume overload in hemodialysis cases.

VARIABLES	CUT-OFF	AUC (95% CI)	SENSITIVITY (%)	SPECIFICITY (%)	ACCURACY (%)	P-VALUE
B LINE SCORE	>9	0.872 (0.700 to 0.965)	91.2	89.3	90.6	0.001*
IVC DIAMETER	> 1.6	0.713 (0.520 to 0.862)	92.3	88.7	91.3	0.002*
IVC COLLAPSIBILITY	> 37.6	1 (0.884 to 1.000)	90.8	91.2	92.4	0.001*
COPEPTIN	> 425.48	0.873 (0.700 to 0.966)	89.3	90.7	89.3	0.003*

4. Discussion

Our study represents the baseline demographic characteristics of the study group. The mean age of studied cases was 46.68 ± 14.57, 74.4% were male, 25.6% were female with mean BMI was 25.51 ± 6.25 kg/m2.

Our study shows that mean of HD duration was 3.44 + 0.26 hours, mean of Known dry weight (kg) was 75.12 ± 16.77 and mean of Inter dialytic weight gain (Kg) was 2.79 ± 1.23.

Our study shows that mean of HB (g/dl) was 10.70 ± 1.77, mean of Alb (g/dl) was 3.32±0.45, mean of BUN (mg/dL) was 67.2±22.5, mean of Cr (mg/dL) was 9.04 ± 2.76, mean of Na+ was 132.23 ± 4.24 mmol/L, mean of K+ was 5.53 ± 1.05 mmol/L, mean of Ferritin was 650.48±87.23 µg/L, mean of PTH was 217.3±52.2 nanograms per milliliter, mean of Calcium was 8.68 ± 0.83 milligrams per deciliter and mean of Phosphorus was 5.23 ± 1.83 mg/dL.

In this study, we demonstrated that there was a significant reduction in systolic blood pressure and diastolic blood pressure post-hemodialysis compared to pre-hemodialysis (p<0.001).

Mohammad et al.[6] found a statistically significant decrease in systolic blood pressure (P = 0.001), diastolic blood pressure (P = 0.039) after the HD sessions.

Eseroglu et al.[7] found that after the sessions of HD, there was a significant decline in patients' average arterial pressure (p<0.01).

In this study, we illustrated that there was a significant decline in B-line score post-hemodialysis compared to pre-hemodialysis (p<0.001).

Abdelbaset et al.[8] observed a statistically significant decline in the mean B-line scores after the HD sessions. Prior to dialysis, the average total number of B-lines was (22±14.59); after dialysis, it was (11.1±10.22).

This research demonstrated a significant decline in inferior vena cava diameter following hemodialysis than prior to hemodialysis (p-value below 0.001). There was a significant rise in inferior vena cava collapsibility following hemodialysis than prior to hemodialysis (p-value below 0.001).

Al-Zahraa et al.[9] discovered that ultrasound assessment of the diameter of the inferior vena cava and its respiratory variability indicated a mean inferior vena cava minimal diameter of 1.33 ± 0.36 centimeters pre-dialysis and 1.05 ± 0.35 centimeters following dialysis, while the mean inferior vena cava maximal diameter was 2.07 ± 0.48 centimeters before-dialysis and 1.75 ± 0.49 cm post-dialysis, demonstrating a statistically significant decrease in both inferior vena cava minimal and maximal diameters following dialysis. A highly significant rise in the inferior vena cava collapse index was observed during dialysis, rising from 35.60 ± 11.63 to 40.08 ± 12.46.

This research indicated a substantial reduction in copeptin levels post-hemodialysis compared to pre-hemodialysis (p-value below 0.001).

Kim et al.[10] performed an investigation to evaluate the levels of copeptin in forty-one hemodialysis cases. The copeptin level (171.4 pg/mL) was shown to rise prior to hemodialysis and subsequently diminish post-dialysis. Their findings indicate an association between copeptin levels and total body volume before and after dialysis. Moreover, copeptin levels were significantly elevated in cases exhibiting dysfunction of the left ventricular function compared to those with normal LV function. They suggested copeptin as an effective biomarker for diagnosing LV failure in cases with end-stage kidney disease.

In cohort research in Sweden by Enhörning et al.[11], which included two independent groups, a significant correlation has been identified among elevated copeptin levels and a higher probability of kidney illness.

In this study, we illustrated that there was a significant positive association among copeptin, SBP, DBP, body weight, B-line score, and IVC diameter ($p < 0.001$). There was a significant negative correlation between copeptin and IVC Collapsibility ($p < 0.001$).

Abdelhamid et al.[12] found that the strong association among copeptin levels and markers of fluid overload, such as extracellular water (ECW) and extracellular water-to-total body water (TBW) ratio, underscores the potential utility of copeptin in objectively quantifying volume status. This is particularly relevant in hemodialysis patients, where accurate assessment of fluid balance is critical to preventing complications such as hypertension, pulmonary edema, and cardiovascular events.

This investigation established that the diagnostic accuracy of the B-line score as a differentiating marker prior to and following hemodialysis in ESKD cases has been evaluated utilizing the receiver operating characteristic curve, which demonstrated a 91.2 percent sensitivity and a specificity of 89.3 percent at a cutoff value above nine, yielding an acceptable discriminative 90.6 percent accuracy. The diagnostic accuracy of the IVC diameter score for predicting volume overload in hemodialysis has been evaluated using the receiver operating characteristic curve, which demonstrated a 92.3 percent sensitivity and a specificity of 88.7 percent at a cutoff value greater than 1.6, yielding an adequate discriminative accuracy of 91.3 percent. The diagnostic accuracy of the IVC Collapsibility score for predicting volume overload in hemodialysis cases has been evaluated utilizing the ROC curve, which indicated a 90.8 percent sensitivity and a 91.2 percent specificity at a cutoff value greater than 37.6, yielding an adequate discriminative 92.4 percent accuracy.

Zheng et al.[13] reported that the area under the receiver operating characteristic curve was 0.840 (ninety-five percent confidence range, 0.735–0.945; $P < 0.001$). The B-line threshold value on lung ultrasound for predicting overload in hemodialysis cases was 11.5 lines, demonstrating optimal specificity (76.5%) and sensitivity (76.5%).

Facchini et al.[14] investigated heart failure patients, revealing that B-lines exhibited an AUC of 0.72, with a cutoff value of fifteen or greater, yielding sensitivities and specificities of eighty-five percent and eighty-four percent, respectively.

Recommendations: Additional research with bigger sample sizes and extended monitoring durations is necessary to validate the present findings. Future research should employ well-structured randomized controlled trials or extensive comparative observational research, ensuring an adequate sample size to yield significant conclusions and mitigate confounding variables. Furthermore, multiple-center research had to be incorporated to corroborate the results.

4. Conclusion

In summary, Copeptin and lung ultrasonography can evaluate fluid volume status. This offers an effective approach for assessing fluid status in cases with volume overload. Future directions could involve the expansion and application of lung ultrasonography and Copeptin in the quantitative assessment of volume status in additional volume-sensitive populations, like cases with heart failure.

Disclosure

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