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# The Relationship Study between Uremic Pericardial Effusion and Blood Osmolality, Electrolytes in Patients with End-Stage Renal Failure Disease on Maintenance Hemodialysis.

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# The Relationship Study between Uremic Pericardial Effusion and Blood Osmolality, Electrolytes in Patients with End-Stage Renal Failure Disease on Maintenance Hemodialysis*

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## ABSTRACT

Uremic pericardial effusion is one of important complications of renal failure but its causes and pathogenesis remain obscure to find the association of variable electrolytes, albumin level and blood osmolality to degree of pericardial effusion we did a cross sectional study conducted in Al Sadr Medical city in Al Najaf from June 2021 to April 2022. 35 Uremic patients 22 males and 13 females and age 18-65 mean (40.2±12.5) on maintenance hemodialysis who had pericardial effusion diagnosed by Echocardiography were put into 3 groups (mild, moderate and large pericardial effusion). We calculate serum osmolality, BUN, blood glucose, serum calcium, serum sodium, serum potassium, and also serum albumin. The study showed inverse correlation between serum calcium and size of pericardial effusion p-value< 0.001, correlation coefficient R 0.557 and there is directly proportional relation between serum osmolality and pericardial effusion p value = 0.003, correlation coefficient R 0.493 while the serum albumin showed no significance relation with degree of pericardial effusion p-value=0.716 correlation coefficient R 0.493.

Keywords: Pericardial effusion, ESRD, Osmolality, Hemodialysis Echocardiography.

## 1. Introduction

Pericardial effusion is one of the significant complications in acute and chronic renal failure first described by Richard Bright in 1836[1,2,3]

The prevalence of asymptomatic pericardial effusion found to be70% to 100% of patients with uremia and dialysis [4,5]. The exact etiology of pericardial effusion is not well established. Uremic pericarditis are believed to be caused by accumulation of uremic toxins that may end with initiation or more intensive dialysis [6,7,8]. Volume overload for long period with low serum albumin are additional

possible mechanisms, because not all effusions are inflammatory in nature [9,10,11]. The incidence of uremic pericarditis can be decreased with highly efficient membranes in dialysis, which make better solute clearance, control of volume overload [12]. With more and rapid accumulation of pericardial fluid into a closed pericardial space the pericardial effusion causes increase tin intrapericardial pressure. When the pressure becomes high that causes decrease in cardiac filling, with heart failure and cardiac tamponed can be considered to be present [12]. Pericarditis from untreated uremia is rare today [12]. Intensive dialysis is indicated for uremic pericarditis; the optimal treatment of dialysis-associated pericarditis is much less clear in patients without hemodynamic compromise [12] Echocardiography is both specific and sensitive for the detection of pericardial effusion and can also provide information regarding the hemodynamic significance of the effusion. The Echocardiography can determine the effectiveness of the dialysis procedure [13].

Objective of the study: To assess the association of variable electrolytes, serum albumin level and blood osmolality with the degree of pericardial effusion.

## 2. Materials and Methods

This is a cross sectional study was conducted in Al Sadr teaching hospital in AL-Najaf city from June 2021 to April 2022. We conduct patients in al Sadr hospital diagnosed with end-stage renal failure on maintenance hemodialysis (dialysis dependent) GFR 15ml/min/1.73m2 or less who did hemodialysis for 3 months or more and dividing them into three groups depending on Echocardiographic degree of pericardial effusion. The serum osmolality with serum electrolyte and serum albumin were obtained and the results were correlated with degree of pericardial effusion.

Ethics consideration: After the agreement of the hospital administration and explanation of the study aim to the subjects enrolled in the study, written permission was taken from all the participants in the study.

The exclusion criteria

1. Patients with dialysis less than 3 months and Patients who did dialysis less than 12 hours/week.
2. Patients who had evidence of fluid overload (ascites, pleural effusion which detected by clinical examination and chest x ray and abdominal ultrasound).
3. Any medications that cause pericardial effusion. (hydralazine, amiodaron, warfarin, sulphanamide, phenytoin, mesalamin, minoxidil or chemotherapeutic agent that cause pericardial effusion (cyclophosphamide, 5-fluorouracil).
4. Patient with history of tuberculosis (pericardial TB)

5. Any patient had autoimmune disease (SLE, scleroderma, granulomatosis polyangitis).
6. Left ventricular systolic dysfunction with EF less than 53.

## 3. Methods

Formal medical history and general examination was performed for every participant. Fasting blood sample was taken using aseptic techniques for blood sugar, serum electrolytes sodium, potassium, ionized calcium, serum albumin and BUN were measured before dialysis session using standardized protocols. calculation of serum osmolality by the equation:

Serum osmolality mosm/L= 2(Na)+ BUN/2.8 + Glucose/18 [7] ECG and CXR: was done in suspected pericardial effusion patient and suspected fluid over loaded.

Transthoracic Echocardiography was performed using a commercially available system (Vivid GE 9) by a trained physician following a standardized protocol. The patients were divided into 3 groups according to degree of pericardial effusion According to guidelines of American's society of echocardiography 2013 [13]

Group1: mild pericardial effusion group if less than 0.5cm from left ventricular wall

Group2: moderate if between 0.5 -2.0 cm from left ventricular wall

Group3: large if more than 2.0 cm from left ventricular wall

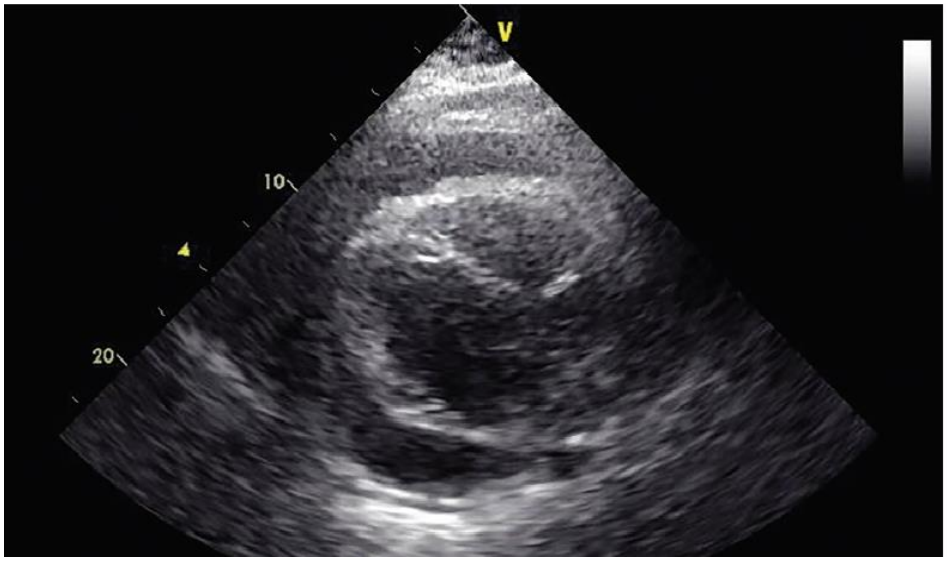



**Figure [1] Echocardiographic examination of the heart in the parasternal long axis position showing pericardial effusion.**

**Statistical Analysis:** We used SPSS® Software (version 23.0 for Linux®) to do analysis. Qualitative data are presented as numbers and percentages, the continuous numerical data are presented as mean

± standard deviation. Comparisons of different study groups were performed using chi-square test for categorical data, and using Student's t-test for continuous data. While the Correlations were established using Pearson's product-moment correlation coefficient for continuous variables and Spearman's rank-order correlation coefficient for discrete variables. The P value of < 0.05 was considered statistically significant.

## 4. Results

This study included a total of (35) patients with renal failure on maintenance hemodialysis. Age of participants ranged from (18) years to (65) years, with a mean age of (40.2 ± 12.5) years and a median of (40) years. Figure (2) illustrates the age group distribution of the study participants. Demographic characteristics of the study participants are detailed in Table (1).

**Table (1): demographic characteristics of study participant by grade of effusion.**

| Demographic characteristics | | Gender of pericardial effusion | | | Total | P-value |
|---|---|---|---|---|---|---|
| | | Mild | Moderate | Server | | |
| Gender | Male | 9 (40.91%) | 10 (45.45%) | 3 (13.64%) | 22 (62.86%) | 0.238 |
| | Female | 4 30.77% | 4 30.77% | 5 38.46% | 13 37.14% | |
| Diabetes mellitus | Yes | 5 (41.37%) | 4 (33.33%) | 3 (25.00%) | 12 (34.29) | 0.844 |
| | No | 8 (34.78%) | 10 (43.48%) | 5 (21.74%) | 23 (65.71%) | |
| Duration of dialysis | 3-6 months | 4 (23.53%) | 8 (47.06%) | 5 (29.41%) | 17 (48.57%) | 0.262 |
| | >6 months | 9 (50.00%) | 6 (33.33%) | 3 (16.67%) | 18 (51.43%) | |

Correlation between serum calcium level and degree of pericardial effusion was assessed by calculating Spearman's rank-order correlation coefficient. There was a highly significant strong correlation in the negative direction between serum level of calcium and the degree of pericardial effusion (mild, moderate, or large). Spearman's correlation coefficient (R) = -0.557, degrees of freedom (d.f.) = 33, P-value < 0.001.A scatter plot diagram in Figure (3) illustrates the finding.

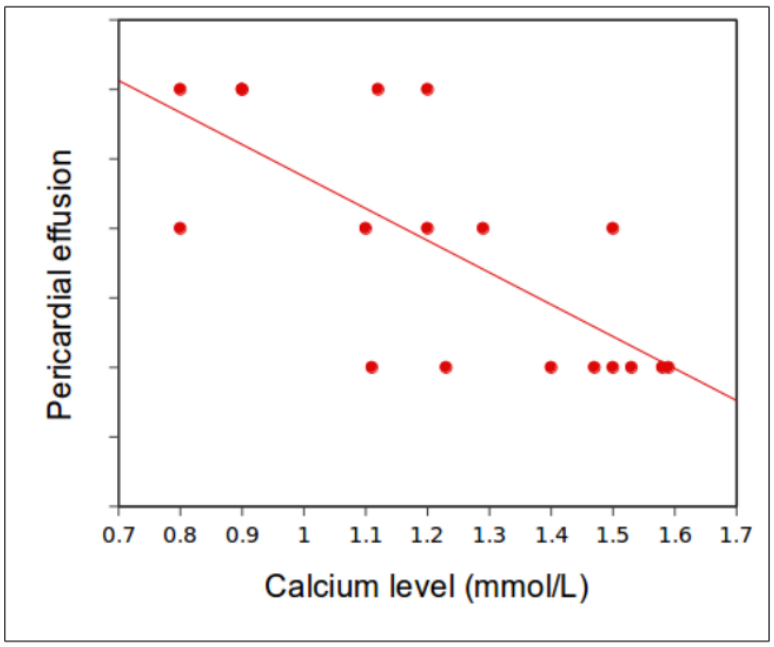



**Figure (3): Scatterplot diagram showing the correlation between serum calcium level (mmol/L) and the degree of pericardial effusion. P-value <0.001**

Similarly, correlation between serum osmolarity and the degree of pericardial effusion was also assessed using Spearman's rank-order correlation coefficient. There was a statistically significant positive correlation of medium strength between serum osmolarity and the degree of pericardial effusion, (R) = 0.493, d.f. = 33, P-value=0.003. Figure (4) illustrates the finding.

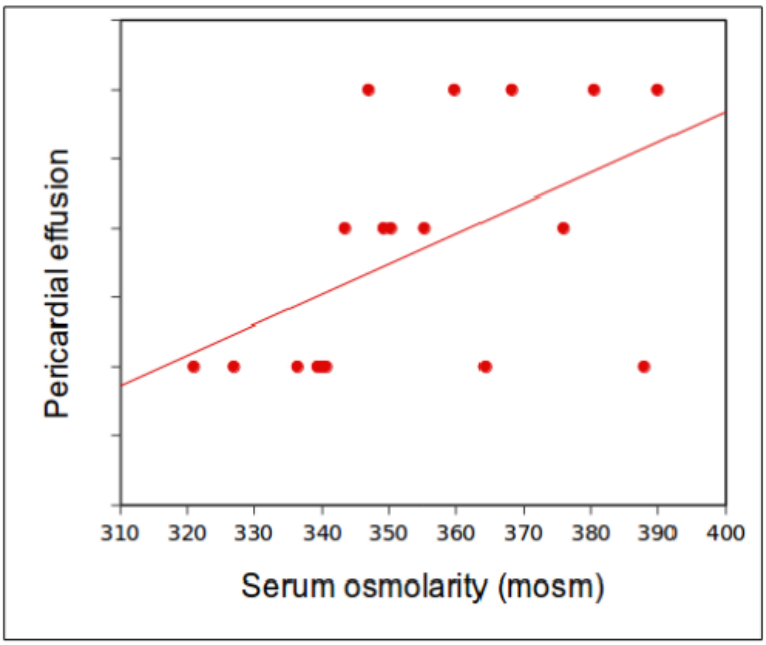
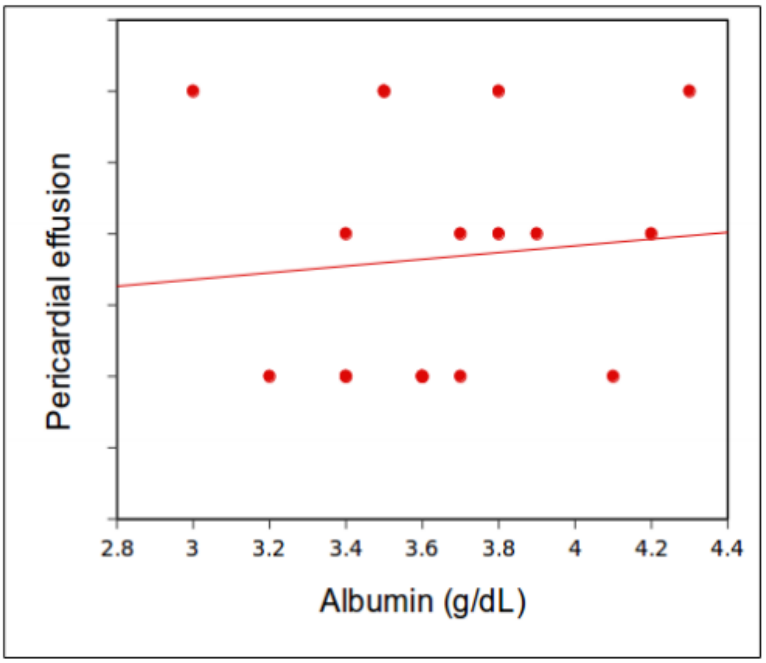



**Figure (4): Scatterplot diagram showing the correlation between serum osmolarity (mosm) and the degree of pericardial effusion. P-value =0.003.**

Serum albumin level correlation with the degree of pericardial effusion was also assessed using Spearman's coefficient. No significant correlation was observed between the two variables, (R) = 0.064, d.f. = 33. P-value = 0.716, Figure (5).




**Figure(5): Scatterplot diagram showing comparison between serum albumin level (g/dL) and the degree of pericardial effusion. P-value = 0.716.**

## 5. Discussion

More than half of the study participants were in age group 30-49 of the study population. No relationship was found between the degree of pericardial effusion and gender. This is consistent with the finding of Santas et al. in their study conducted from 2004 to 2013 which observed no significant relationship between gender and pericardial effusion degree[14] Significant negative correlation was observed in the current study between serum calcium level and the grade of pericardial effusion, i.e. the lower calcium levels in ESRD was associated with higher grade of pericardial effusion. This finding is consistent with the finding by Ravi et al. in their case-control study conducted from 2004 through 2011, which included 84 patients of chronic kidney disease with pericardial effusion, this study concluded that low serum calcium level was associated with pericardial effusion, and the calcium level below 8 mg/dL is considered as a predictor with 95% specificity for moderate and large pericardial effusion [15]. This relationship could be a reflection of the effects of renal dysfunction whether compensated or non-compensated on the occurrence of lower calcium level which in turn is also associated with more advanced grade of pericardial effusion[16].Another significant finding among the study participants in the present study was the positive correlation between serum

osmolality and the degree of pericardial effusion; suggesting that higher grade of pericardial effusion is linked to higher osmolality of the serum .Osmolality of the serum depend on sodium and potassium BUN and glucose Arevalo-lorido et al studied 316 patients at ESRD with GFR <30 and concluded that The accumulation of toxic metabolites and nitrogenous waste products in the blood.at ESRD raise the osmolality and provide its effect on pericardium resulting in the release of pro-inflammatory markers such as interleukin 1, interleukin 6, and tumor necrosis factor (TNF), leading to inflammation and fibrin deposition and that damage the pericardium .They also found that the higher osmolality associated with more comorbidities especially diabetes mellitus and chronic kidney disease with p-value in the study was=0.001[17] Uremic patients found to have more free radicles considering uremia as pro-oxidant condition [18] .Some researches believed that many metabolites like hyperuricemia, hypocalcemia, hyperparathyroidism, and accumulation of other toxic metabolites may exacerbate endothelial permeability [19] Therapy of the pericarditis and pericardial effusion is mainly by intensive hemodialysis [20,21]

In many conditions in CRF there is water homeostasis instability which, manifested as low- and/or high sodium blood level, and are associated with bad clinical outcomes. The cause of abnormal serum sodium in ESRD is multifactorial. Low serum sodium in dialysis patients is associated with increase weight or increase in extracellular volume, it may be potentially due to increase free water intake, low serum sodium may be exacerbated by thirst, or not enough ultrafiltration. Although rarely seen in uremic patients on dialysis, if low serum sodium is accompanied by decrease in extracellular volume, this may be due to a loss of sodium and potassium salts resulting from poor intake or excess losses [22]

Patients with CKD can be affected by abnormal serum sodium because of the presence of comorbidities that can result in abnormal sodium level in them and also by decrease ability of the kidneys at ESRD to keep and establish normal water homeostasis. Recent studies have suggested that the incidence and prevalence of abnormal sodium level. Low serum sodium appears to affect results equally in patients with different stages of CKD, while high sodium level was found to cause less severe results in those with more advanced stages of CKD [22]. High serum sodium appears to occur in advance renal failure Development of hypernatremia in patients with CKD usually results from water depletion as a result of failure to ingest water in the face of a concomitant inability to concentrate urine. Management of this condition is to keep stable water level by more water intake. [23,24,25]. At ESRD the serum potassium increases and hyperkalemia occurs. The level of serum potassium in total serum osmolality is of little effect. The present study did not find any significant relationship between the presence of diabetes mellitus and the grade of pericardial effusion, despite the fact that diabetes

mellitus is an important risk factor for both of cardiovascular disease and end-stage renal disease. This may be attributed to the relatively small number of patients with both renal failure and diabetes mellitus (12 patients) which may justify the need for further studies with larger proportion of diabetic patients to allow for accurate and reliable analysis for the role of diabetes in the development and extension of pericardial effusion in patients with end-stage renal failure.

Most cases of pericardial effusions are caused by inflammation associated with acute pericarditis. However, any changes in the localized Starling forces within pericardial vasculature can also cause effusion [26]. For example, this may result from decrease in capillary oncotic pressure due to low albumin or an increased in the capillary hydrostatic pressure due to left heart failure. In the current study we found. no significant correlation between serum albumin level and the grade of pericardial effusion, with P-value of 0.716. This observation is closely similar to the observation by Ravi et al. who found a similar non-significant result among their study population, with P-value of 0.425, Serum albumin level on another hand was found to predict the need for the pericardial effusion aspiration [27].

## 6. Conclusions and Recommendations

In patients with end stage renal disease on hemodialysis the severity of hypocalcaemia can predict the degree of pericardial effusion, while the increment of serum osmolality can predict a larger pericardial effusion.

Further study is needed to compare between pre dialysis patients and patients on maintenance hemodialysis in larger study.

Include more patients with diabetes mellitus to see the effect of osmolality in these patients.

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