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RELATIONSHIP BETWEEN HYPOALBUMINEMIA AND INTRADIALYSIS HYPOTENSION IN HEMODIALYSIS PATIENTS

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Abstract:

Background: *Hypoalbuminemia is an important risk factor for the development of hypotension during hemodialysis and progressive left ventricular hypertrophy in patients with chronic kidney disease (CKD).*

Aim: *The aim of the study was to evaluate the relationship between serum albumin, intradialysis hypotension (IDH) and cardiac function.*

Place and Duration: *In the Nephrology and Cardiology department of Nishtar Hospital Multan for one-year duration from August 2019 to 2020.*

Patients and Methods: *Forty patients undergoing regular hemodialysis (HD) were enrolled in the study. They were divided into two groups; Group 1: Patients in this group had recurrent attacks of IDH and Group 2: Patients in this group did not develop IDH. Patients were reclassified according to their serum albumin level into two groups; Group A: patients with hypoalbuminemia and group B: patients without hypoalbuminemia. Data collected from each patient included: (1) demographic characteristics (age, gender) and clinical characteristics (changes in blood pressure during the session, ultrafiltration index, cardio-thoracic ratio, duration of dialysis and Kt / V); (2) Blood chemistry (creatinine, urea, hemoglobin, hematocrit value, total proteins, albumin, triglycerides, cholesterol, AST, ALT, Kt / V and fasting blood sugar); and (3) Echocardiographic evaluation of left ventricular geometry.*

Results: *There was a significant negative correlation between serum albumin and Delta BP in HD patients. There were also no significant changes in heart function in the various groups studied.*

Conclusion: *We concluded that there is an association between low serum albumin and intradialysis hypotension and cardiac function in patients with CKD undergoing HD. Recommendations: Regular serum albumin testing is mandatory for all HD patients.*

Key words: *hemodialysis, hypoalbuminemia, risk factor, intradialysis hypotension.*

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INTRODUCTION:

The relationship between blood pressure changes and mortality is higher in hemodialysis patients than in the general population. Interdialysis hypotension (IDH) has been found to be an independent and negative prognostic factor for a late fistula outcome.

Intra-dialysis hypotension remains a major problem, especially in elderly patients and patients with cardiovascular disorders. Patients' susceptibility to IDH may not be stable. Many patients had large differences in the incidence of IDH over a 24-month period.

Rapid ultrafiltration, especially in elderly patients, may cause blood pressure to drop prematurely during hemodialysis, before the patient is dry weight. Hypoalbuminaemia is an important risk factor for the development of hypotension during hemodialysis. Hypoalbuminaemia was also an important risk factor for progressive left ventricular hypertrophy in patients with end-stage renal disease (ESRD).

AIM:

The aim of the study is to determine the relationship between serum albumin and intradialysis hypotension and heart function in patients with chronic kidney disease (CKD) undergoing regular hemodialysis.

PATIENTS AND METHODS:

Study groups:

This study was conducted in the Nephrology and Cardiology department of Nishtar Hospital Multan for one-year duration from August 2019 to 2020 on 40 chronic kidney disease patients undergoing regular hemodialysis (HD). They were divided into 2 groups according to the changes in blood pressure during HD:

Group 1:

This group consisted of 20 patients with chronic kidney disease in regular HD for at least 6 months, 3 times a week, duration of each session was 4 hours, 11 of them were men, 9 were women, their age ranged from 17 up to 63 years with an average of 47.1 ± 2.72. Also, their serum albumin ranged between 2.4 and 4.7 g / dL with an average of 3.55 ± 0.15. Access to blood was provided by an arteriovenous fistula. Duration of HD ranged from 1 to 12 years, mean 5.8 ± 0.89. The inclusion criteria for the study was that patients had recurrent episodes of intradialysis hypotension (IDH) and normal interdialysis BP. Of these twenty patients in Group 1, 9 were hypoalbuminemia (<3.5 mg / dL) and 11 were non-hypoalbuminemia (≥3.5 mg / dL). The dialyzer used was the Fresenius Polysulfone F6 and F7 models, intended for single use only, with a surface suitable for each patient. We used a bicarbonate dialysis concentrate with a final dilute solution concentration in mEq / liter as follows:

Na^+ 135 mEq/l	Cl^- 106.5 mEq/l
K + 2.5 mEq/l	Mg 2+ 1.5 mEq/l
Ca 2+ 3.5 mEq/l	CH_3COOH 8.5 mEq/l

During dialysis, the patient received heparinization with a maximum dose of 10,000 units. Erythropoietin was taken from each patient depending on the body weight (100-150 IU / kg / week). The blood flow rate was appropriate for each patient. The dialysate flow rate was 500 ml / min for all patients.

Group 2:

This group consisted of 20 patients with chronic kidney disease in normal HD, undeveloped IDH (as a control group), for at least 6 months, 3 times a week, duration of each session was 4 hours, 12 of them were male, 8 were women, their age ranged from 22 to 62 years, mean 45 ± 3.01, and serum albumin from 3.3 to 4.9 g / dl with an average of 4.03 ± 0.088. Access to blood was provided by an arteriovenous fistula. Duration of HD ranged from 1 to 11 years, mean 4.37 ± 0.68. The inclusion criterion for the study was the absence of IDH episodes in patients. The dialyzer, dialysate solution, heparinization and erythropoietin doses were the same as for patients in Group 1.

Patients were reclassified according to their serum albumin level into two groups:

Group A: A Patients with hypoalbuminemia, the number was 11 patients.

Group B: Patients without hypoalbuminemia, their number was 9 patients.

All patients underwent: (1) history taking and clinical examination; (2) Blood biochemical tests (serum creatinine, serum urea, hemoglobin, hematocrit value, total proteins, serum albumin, serum triglycerides, serum cholesterol, AST, ALT, Kt / v and fasting blood sugar); and (3) Echocardiographic evaluation of left ventricular geometry.

(1) Clinical and dialysis criteria: age (years); gender (male or female); weight (kg); body mass index (kg / m2); ultrafiltration rate (ml / hour); simple x-ray of the chest and heart to calculate the cardiovascular ratio (CTR); duration of dialysis (years); blood flow rate

(BFR); dialyzer surface (DSA); blood pressure changes during the session [Pre-session systolic blood pressure (SBPBS), pre-session diastolic blood pressure (DBPBS); lowest systolic blood pressure (LSBP); and lowest diastolic blood pressure (LDBP)]. Systolic blood pressure delta (SBP delta) was calculated as: Systolic blood pressure delta = Pre-dialysis systolic blood pressure - Lowest systolic blood pressure during the session. The increase in Delta SBP indicates a greater decrease in systolic BP which may predispose to IDH.

(2) Blood biochemistry tests: Sampling: After an overnight fast, ten CC venous blood samples were taken from each patient and divided into test tubes as follows: 1) Regular test tubes in which blood samples were centrifuged and divided into equal portions of serum for routine testing . 2) EDTA tubes for blood imaging. Biochemical tests: total proteins and serum albumin, serum creatinine and blood urea, serum hemoglobin (Hb) and hematocrit (hct), serum triglycerides (TG) and serum cholesterol, aspartate transaminase (AST) and alanine transaminase (ALT) enzymes), fasting blood sugar (FBS), determination of serum sodium (Na) and potassium (K) and Kt / V:
The HD dose can be expressed as (Kurea × td) / Vurea (abbreviated Kt / V), where Kurea is the effective (delivered) clearance of urea by the dialyzer in milliliters per minute integrated into the total dialysis, Td is the time in minutes measured from start to finish dialysis, and urea is the patient's volume of urea distribution in milliliters.
Kt / V is a good indicator of the adequacy of dialysis, it should be greater than 1.4.

(3) Echocardiographic assessment of left ventricular geometry and systolic function: M-mode echocardiography was performed by one experienced echocardiograph unaware of the results of other study parameters, all patients were examined in the left-sided position. M-mode measurements included: ventricular septal thickness (IVST), left ventricular posterior wall thickness (PWT), left ventricular end systolic diameter (LVESD), left ventricular end diastolic diameter (LVEDD), left ventricular mass (LVM), left ventricular fraction contraction (FS) and ejection fraction (EF).

Left ventricular hypertrophy (LVH) was defined as: LVMI> 131 g / m2 in men and> 100 g / m2 in women. Systolic dysfunction was defined as: Ejection fraction less than 50.0%.

Statistical analysis:
Data were analyzed using SPSS version 21. Results are expressed as mean ± standard deviation (SD) for normally distributed data and percentages for categorical data. The comparison of the means was performed with the student's t-test, and the comparisons between the groups with the chi-square test (χ 2). In the correlation study, data were analyzed using Pearson's correlation; the degree of association is expressed as (r) (correlation coefficient). The significance level for t, χ 2, the correlation was assumed with a value of p <0.05.

RESULTS:
Regarding age and gender, Table (1) compares Group 1 (patients with IDH) and Group 2 (patients with undeveloped IDH), there was no significant difference between the two groups.

Table (1): Demographic characteristics of patients in group 1 (patients with IDH) and group 2 (patients not developed IDH) as regard age and gender

Variables	Group 1 (n=20)		Group 2 (n=20)		t*-value χ^2-value	P- value
	No.	%	No.	%		
Age (year): Mean± SD	47.1±2.72		45.0±3.01		0.570*	0.576
Gender:						
Male	11	55.0	12	60.0		
Female	9	45.0	8	40.0	0.1	0.749

For mean changes in blood pressure (Table 2); before the dialysis session there was no significant difference between the two groups in terms of diastolic pressure, but there was a significant difference in terms of systolic pressure; mean systolic blood pressure was lower in group 1. Meanwhile, there were significant differences between the two groups in the lowest systolic and diastolic blood pressure during dialysis; patients in group 1 were more hypotensive than patients in group 2 for both the lowest SBP and DBP. Finally, Delta SBP was significantly higher among patients in group 1. As for the ultrafiltration index (UFR), it was significantly higher among patients in group 2. Meanwhile, mean cardio-thoracic ratio

(CTR) was significantly higher among patients in group 1.

Table (2): Mean± standard deviation (SD) of the studied patients in group 1 and 2 according to blood pressure, ultrafilteration rate, cardiothoracic ratio, and duration of hemodialysis

Variables	Group 1 (n=20) patients with IDH	Group 2 (n=20) patients with no IDH	t-value	P- value
	Mean± SD	Mean± SD		
Blood pressure before the dialysis session				
Systolic	123.5±2.43	132.0±1.86	-12.422	0.007*
Diastolic	80.0±1.62	83.0±1.63	-5.838	0.186
Lowest blood pressure during the dialysis session				
Systolic	78.0±2.47	119.5±1.23	-67.261	0.0001*
Diastolic	47.0±1.93	77.0±1.05	-61.063	0.0001*
Delta systolic blood pressure (SBP)				
Delta SBP	45.5±2.45	13.0±1.93	-46.6	0.0001*
Ultrafiltration rate (UFR)				
UFR	456.25±26.08	606.25±26.9	-17.9	0.0001*
Cardiothoracic ratio (CTR)				
CTR	55.85 ±0.68	48.5 ±0.43	-40.85	0.0001*
Duration of hemodialysis (years)				
Duration (year)	5.8±0.89	4.37±0.68	1.16	0.257

As for the duration of hemodialysis, it was slightly longer in patients from group 1. In terms of laboratory data of the studied groups (Table 3); there were no significant differences between the 2 groups, with the exception of mean serum albumin which was significantly lower in group 1 than in group 2.

Table (3): Mean± standard deviation (SD) of the studied patients in group 1 and 2 according to laboratory results

Variables	Group 1 (n=20) patients with IDH	Group 2 (n=20) patients with no IDH	t-value	P- value
	Mean± SD	Mean± SD		
Kt/V	1.03±0.08	1.16±0.1	-1.168	0.257
Urea	112.4±12.18	117.45±10.46	-0.367	0.718
Creatinine	6.37±0.95	5.86±0.40	0.954	0.352
Hematocrit	29.42±1.32	29.99±1.24	-0.328	0.746
Hemoglobin	8.98±0.45	8.96±0.38	0.037	0.970
Triglycerides	185.15±24.27	173.9±16.33	0.348	0.731
Cholesterol	123.1±5.19	111.05±2.31	1.956	0.065
FBS	130.65±9.37	113.85±4.24	1.686	0.108
AST	28.8±2.32	29.5±2.96	-0.225	0.824
ALT	31.55±3.23	34.4±3.96	-0.615	0.546
Albumin	3.55±0.15	4.03±0.088	-2.218	0.039*
Total proteins	5.29±0.09	5.4±0.1	0.438	0.667

Regarding the echocardiographic parameters of the studied groups (Table 4); there were no significant differences between the 2 groups.

Table (4): Mean± standard deviation (SD) of the studied patients in group 1 and 2 according to echocardiographic parameters

Variables	Group 1 (n=20) patients with IDH	Group 2 (n=20) patients with no IDH	tvalue	Pvalue
	Mean± SD	Mean± SD		
Left ventricular mass index (LVMI)	152.45±6.15	150.28±8	0.198	0.848
Left ventricular ejection fraction (LVEF)	52.32±1.82	58±2.56	-1.931	0.069
Left ventricular fractional shortening (LVFS)	27.62±0.98	30.45±1.45	-1.819	0.085
Left ventricular end-diastolic diameter (LVEDD)	5.0±0.08	5.02±0.13	0.237	0.815
Left ventricular end-systolic diameter (LVESD)	3.66±0.09	3.36±0.18	1.340	0.196
Interventricular septal thickness (IVST)	1.21±0.03	1.13±0.04	1.461	0.160
Left ventricular posterior wall thickness (LVPWT)	1.22±0.044	1.09±0.04	1.868	0.077

Considering the changes in mean blood pressure in patients with hypoalbuminemia (Group A) and without hypoalbuminemia (Group B) (Table 5), there was no significant difference between the two groups in diastolic BP before dialysis, but there was a significant difference to consider mean systolic blood pressure; it was higher in group A. During dialysis, significant differences were found between the 2 groups in terms of the lowest systolic and diastolic pressure; patients from group A were more hypotensive than patients from group B for both the lowest SBP and DBP. Delta SBP was also significantly higher among patients from group A. Meanwhile, mean CTR was significantly lower among patients from group A.

Table (5): Mean± standard deviation (SD) of the studied patients in group A and B (with- and without hypoalbuminemia) according to blood pressure and cardiothoracic ratio

Variables	Group 2 patients with no IDH (n=20)		t-value	P- value
	Group A Hypoalbuminemia (n=11)	Group B No hypoalbuminemia (n=9)		
	Mean± SD	Mean± SD		
Blood pressure before the dialysis session				
Systolic	130.0±3.3	126.89±1.93	-2.625	0.04*
Diastolic	82.72±2.37	81.0±1.34	2.041	0.276
Lowest blood pressure during the dialysis session				
Systolic	79.08±5.63	105.5±3.56	-12.756	0.005*
Diastolic	50.9±4.75	65.86±2.78	-8.77	0.005*

Delta systolic blood pressure (SBP)				
Delta SBP	41.5±1.95	13.5±2.43	-27.97	0.001*
Cardiothoracic ratio (CTR)				
CTR	3.55±0.15	4.03±0.08	-2.22	0.039*

In terms of echocardiographic parameters of the studied groups (Table 6); there was a significant difference between the two groups in the mean values of LVMI, LVEDD and LVPWT as they are higher in group A than in group B. Meanwhile, other echocardiographic parameters were statistically insignificant between the two groups.

Table (6): Mean± standard deviation (SD) of the studied patients in groups A and B (with- and without hypoalbuminemia) according to echocardiographic parameters

Variables	Group 2 patients with no IDH (n=20)		t-value	P- value
	Group A Hypoalbuminemia (n=11)	Group B No hypoalbuminemia (n=9)		
	Mean± SD	Mean± SD		
Left ventricular mass index (LVMI)	176.63±9.91	141.81±4.73	3.321	0.008*
Left ventricular ejection fraction (LVEF)	51.13±2.32	56.72±2.0	-0.563	0.586
Left ventricular fractional shortening (LVFS)	26.95±1.31	29.82±1.11	-0.545	0.598
Left ventricular end-diastolic diameter (LVEDD)	5.3±0.1	4.94±0.09	2.620	0.026*
Left ventricular end-systolic diameter (LVESD)	3.87±0.08	3.37±0.13	2.166	0.056
Inter ventricular septal thickness (IVST)	1.26±0.06	1.13±0.02	2.058	0.067
Left ventricular posterior wall thickness (LVPWT)	1.18±0.31	1.02±0.01	3.068	0.044*

Respecting the correlation between the serum albumin level and test parameters (Table 7); there were significant positive correlations between serum albumin and ultrafiltration rate, BMI, Kt / V, hematocrit and hemoglobin. Meanwhile, there were significant negative correlations between serum albumin and Delta BP, CTR, LVMI, IVST, LVPWT, LVEDD, and LVESD. On the other hand, there were non-significant negative correlations between serum albumin and age, LVEF and LVFS.

Table (7): Correlation co-efficient between serum albumin level and the study parameters among the studied patients

Variables	r	P
Age	-0.099	0.273
Delta blood pressure (BP)	-0.670	0.0001*
Ultrafiltration rate (UFR)	0.361	0.011*
Cardiothoracic ratio (CTR)	-0.618	0.0001*
Body mass index (BMI)	0.323	0.042*
Kt\V	0.402	0.005*

Hematocrit (Hct)	0.283	0.038*
Hemoglobin (Hb)	0.320	0.022*
Left ventricular mass index (LVMI)	-0.555	0.0001*
Left ventricular ejection fraction (LVEF)	0.266	0.97
Left ventricular fractional shortening (LVFS)	0.259	0.107
Left ventricular end-diastolic diameter (LVEDD)	-0.341	0.031*
Left ventricular end-systolic diameter (LVESD)	-0.344	0.030*
Inter ventricular septal thickness (IVST)	-0.435	0.005*
Left ventricular posterior wall thickness (LVPWT)	-0.435	0.003*

Regarding the correlation between serum albumin and LVMI (Fig. 1), a significant negative correlation was found. As for the correlation between serum albumin and Kt / V (Fig. 2), a significant positive correlation was found.

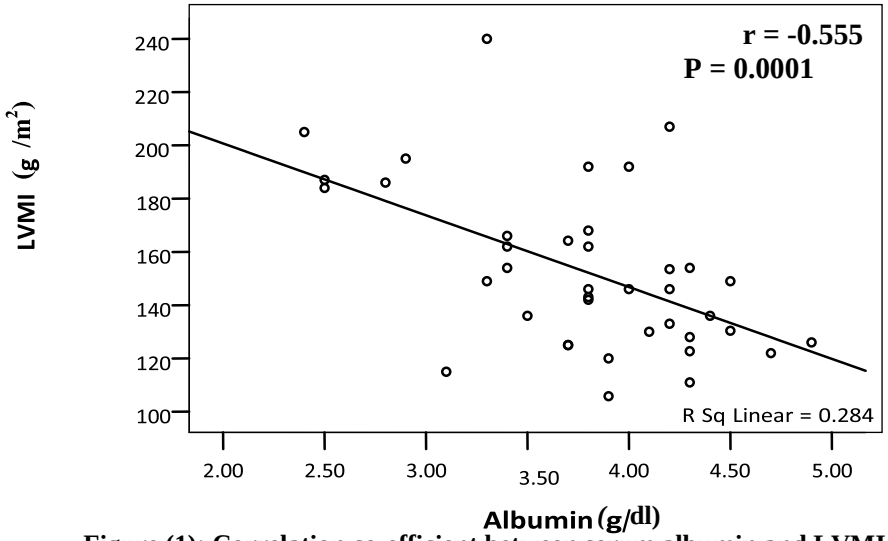

Figure (1): Correlation co-efficient between serum albumin and LVMI

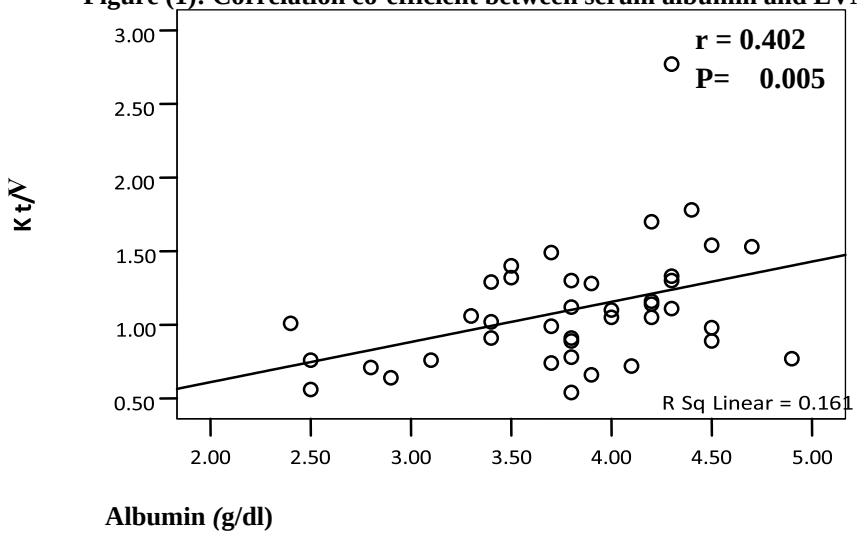

Figure (2): Correlation co-efficient between serum albumin and Kt/V

DISCUSSION:

Given the possibility that changes in serum albumin in HD patients may contribute to cardiac dysfunction as well as the development of IDH and deterioration of residual renal function and inadequate dialysis, we investigated serum albumin and cardiac function as

potential risk factors in hypoalbuminemia and - hypoalbuminemia and normotensive HD patients with recurrent episodes of IDH who were well maintained on regular HD and did not develop IDH.
It has been repeatedly shown that hypoalbuminemia and the effectiveness of dialysis are probably the most important prognostic factors of treatment outcomes in patients with end-stage renal disease. The relationship between hypoalbuminemia and mortality was particularly strong; each 1 g / dl reduction in mean serum albumin is associated with de novo development and recurrent heart failure, de novo and recurrent ischemic heart disease, cardiac mortality and overall mortality.

In this study, the mean CTR of hemodialysis patients who developed IDH (group 1) was significantly higher than that of hemodialysis patients without IDH (group 2). The difference was statistically significant and it was found that CTR was higher in hemodialysis patients with hypoalbuminemia (group A) than in patients without hypoalbuminemia (group B) who developed IDH. This can be attributed to volume overload and / or anemia-induced LV dilation and compensatory LV hypertrophy. Thus, hypoalbuminemia may contribute to the pathogenesis of hypervolemia and the enlargement of the heart size. This result was also in agreement with Parfrey and Foley who found that CTR was significantly increased in hypotensive patients than in patients with normal blood pressure. They suggested that there is a pathophysiological role for hypervolemia in increased heart size.

In this study, a significant negative correlation was found between serum albumin and BMI. Hypoalbuminemia was also evident in group 1 (hypotension). The explanation for these findings is that recurrent hypotensive episodes lead to insufficient dialysis, which in turn increases the likelihood of malnutrition, so that hypoalbuminemia is not only a cause but may also be a consequence of IDH. These results correspond to Bergstrom, who found that inadequate dialysis leads to anorexia and poor nutrition, and then to the development of hypoalbuminemia. Therefore, adequate dialysis is a very important determinant of dialysis outcome and can be assessed by calculating the Kt / V. In this study, we found a significant positive correlation between serum albumin and hematocrit. Our result is in line with Sean et al. who found a significant positive correlation between serum albumin and hematocrit value. In addition, lower levels of hematocrit and albumin may be correlated with inflammatory mechanisms that contribute to erythropoietin resistance and decreased albumin synthesis, respectively. Anemia, which has many complications, is a common complication in HD patients. Left ventricular hypertrophy is one of the complications of anemia. In the present study, we showed a significant positive correlation between serum albumin and hemoglobin. Our result is consistent with Locatelli et al.

CONCLUSIONS:

A significant positive correlation was found between serum albumin and Kt / V, ultrafiltration rate, hemoglobin, hematocrit value and BMI. Meanwhile, there were significant negative correlations between serum albumin and Delta BP, CTR, LVMI, LVPWT, IVST, LVESD, and LVEDD. Moreover, patients with recurrent episodes of IDH had increased CTR and Delta systolic BP than patients without IDH. Thus, we conclude that there was a relationship between serum albumin and intradialysis hypotension and cardiac function.

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