The relationship between hypoalbuminemia and intradialytic hypotention in hemodialysis patients

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Objective
The aim of this study was to evaluate the relationship between serum albumin and intradialytic hypotension (IDH).

Background
Hypoalbuminemia and IDH are common complications during hemodialysis (HD) session. Hypotension is a risk factor for mortality and morbidity in HD patients.

Patients and methods
We conducted a cross-sectional study on 50 patients with end-stage renal disease who received regular HD session three times weekly for more than 3 months (from April to July 2017) at Ashmoun General Hospital. They were divided into two groups: group 1 included patients who developed recurrent attacks of IDH (24 patients) and group 2 included patients who did not develop IDH (26 patients). Data collected from each patient included the following: (i) demographic features and clinical features (blood pressure (BP) changes during session, ultrafiltration rate, intradialytic weight gain, duration of dialysis, cause of end-stage renal disease, surface area of dialyzer, and blood flow of the machine); (ii) blood chemistry (creatinine level, urea, hemoglobin, hematocrit value, albumin, triglycerides, cholesterol, aspartate aminotransferase, alanine aminotransferase, Na*, K*, and KT/V); (iii) echocardiographic assessment of left ventricular geometry; and (iv) inferior vena cava-guided ultrasonography.

Results
Serum albumin level among group I ranged between 2.4 and 4.7 mg/dl, with mean ± SD of 3.1 + 0.53 mg/dl, whereas in group II, serum albumin level ranged between 2.6 and 4.6 mg/dl with mean ± SD of 3.6 ± 0.48 mg/dl, with *P* value of 0.002, indicating there was a high significant difference between both groups. There was a highly significant positive correlation between delta systolic BP and IVC collapsibility index (IVCC). There was a highly significant negative correlation between serum albumin and IVCC, and there was a highly significant negative correlation between delta systolic BP and IVC diameter.

Conclusion
We concluded that serum albumin is a parameter that is associated with IDH and found that bedside measurements of IVCC and IVC diameter are easy and good markers for prediction of IDH.

Keywords:
hemodialysis, hypoalbuminemia, intradialytic hypotension, inferior vena cava diameter and collapsibility index

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Introduction

Acute complications commonly occur during routine hemodialysis (HD) treatments. They include the following: hypotension, hypertension, cramps, causea and vomiting, arrhythmia, chest pain, sudden death, headache, seizure, and bleeding diathesis [1].

Intradialytic hypotension (IDH) is caused by impaired plasma volume refilling (too high ultrafiltration and autonomic dysfunction), decreased cardiac reserve (diastolic or systolic dysfunction), impaired venous compliance, autonomic dysfunction (diabetes and uremia), arrhythmias, anemia, drug therapy (vasodilators, β-blockers, and calcium channel blockers), alteration of vasoactive substances in blood (low NO and high endothelin-1 and angiotensin-2), eating during treatment (increased splanchnic blood flow), and too low target weight estimation [2]. IDH continues to be a leading problem, especially in elderly and cardiovascular compromised patients [3].

The association between blood pressure (BP) changes and death rate is higher in HD patients, which can be

used as an independent and negative predictor of long-term fistula outcome [4].

The sensitivity of patients for IDH may not be a stable condition. Many patients were found to have large differences in the incidence of IDH over a 24-month period [5]. Hypoalbuminemia is an important risk factor of hypotension during HD [6]. Moreover, hypoalbuminemia was an important risk factor for progressive left ventricular hypertrophy in patients with end-stage renal disease (ESRD) [7].

Hypoalbuminemia and dialysis efficacy have been shown repeatedly to be perhaps the most critical predictors of outcomes in patients with ESRD. The relationship between hypoalbuminemia and mortality was especially present; each 1 g/dl decrease in mean serum albumin is associated with the development of de novo and recurrent cardiac failure, de novo and recurrent ischemic heart disease, cardiac mortality, and overall mortality [8].

The aim of this study was to examine the relationship between hypoalbuminemia and IDH in HD patients.

Patients and methods

Study population

This study was done in the dialysis unit at Ashmoun General Hospital on patients with ESRD on regular HD for more than 3 months. All gave informed consent, and the study was approved by ethics committee of Menoufia University.

Study groups

This study was conducted on 50 patients with ESRD who received regular HD session 3 times weekly for more than 3 months at Ashmoun General Hospital. The selected 50 patients were classified into two groups according to presence of IDH: group I included 24 patients who has had IDH and group II included 26 who did not have IDH.

Study design

All patients was examined for history [age in years, sex (male or female), associated comorbidities [diabetes mellitus (DM), hypertension (HTN), and hepatitis C virus (HCV) positive], dietary habits (eating during session), clinical examination, dialysis data, laboratory investigation (serum creatinine, blood urea nitrogen predialysis and blood urea nitrogen postdialysis, complete blood count, serum albumin, serum triglyceride and cholesterol, alanine aminotransferase, aspartate aminotransferase, serum Na^+, and serum K^+), echocardiography, and ultrasound on the inferior vena cava (IVC).

Inclusion criteria

Patients with ESRD maintained on hemodialysis for more than 3 months 3 times weekly, each session for 4 h, were included in the study.

Exclusion criteria

Patients with decompensated chronic liver disease and severe inflammation and/or active infection were excluded from the study.

Statistical analysis

Data were analyzed using the statistical program for the social sciences (SPSS, version 20.0; IBM, Armonk, New York, USA). Quantitative data were expressed as mean ± SD and qualitative data were expressed as frequency and percentage.

The following tests were conducted: independent sample *t*-test of significance was used when comparing between two means; the c^2-test of significance was used to compare proportions between two qualitative parameters; and Pearson's correlation coefficient (*r*) test was used for correlating data. *P* values were interpreted as follows: *P* value less than or equal to 0.05 was considered significant.

Results

Of the 50 patients included, there were 13 (26%) female and 37 (74%) male patients. Group I comprised of 24 patients who had IDH and included nine (18%) female and 15 (30%) male patients. Group II comprised of 26 patients who did not have IDH and included four (8%) female and 22 (44%) male patients. *P* value was 0.07, indicating there were no significant differences between both the groups.

In group II, there were seven (14%) diabetic, 14 (28%) hypertensive, eight (16%) HCV, and three (6%) patients with congestive heart failure (CHF), and in group II, there were five (10%) diabetic, 13 (26%) hypertensive, four (8%) HCV, and one (2%) patient with CHF *P* values were 0.31, 0.38, 0.12, and 0.28, respectively, indicating there were no significant differences between both groups regarding the presence of associated comorbidities (DM, HTN, HCV, and CHF).

There were no significant differences between both groups regarding age (P = 0.06), duration of dialysis (P = 0.76), and BMI (P = 0.683) (Table 1).

There was a highly significant difference between both groups regarding serum albumin level (P = 0.002), IVCD (P = 0.001), and IVCC (P = 0.002) (Table 2).

There were no significant differences between both groups regarding surface area of dialyzer (P = 0.326), blood flow of the machine (P = 0.372), ultrafiltration (UF) (P = 0.187), intradialytic weight gain (IDWG) (P = 0.266), and dialysis adequacy (KT/V) (P = 0.244) (Table 2).

There was a highly significant negative correlation between serum albumin and delta systolic BP or IVC collapsibility index (IVCC) ($P \leq 0.01$) (Figs. 1–3).

There was a highly significant positive correlation between serum albumin and IVC diameter (IVCD) ($P \leq 0.01$) (Fig. 2).

Receiver operator curve was used for studying sensitivity and specificity of serum albumin, IVCD, and IVCC as a predictor for IDH. The curve shows that IVCC is the only predictor for IDH that has a high sensitivity and specificity (area under curve for IVCC = 79%; cutoff point = 52.5%). At this cutoff point, sensitivity of IVCC for detection of IDH is 78%, whereas specificity is 70% (Fig. 4).

Table 1 Comparison between both groups as regard age, BMI, and duration of dialysis

	Group I (n=24)	Group II (n=26)	U-test	P
Age (mean±SD)	57.3±12.90	50.0±16.17	1.86	0.06
Duration of dialysis (mean±SD)	26.2±22.47	33.4±34.79	0.30	0.76
BMI (mean±SD)	28.8±8.95	27.6±6.50	0.408	0.683

U-test, Mann-Whitney U-test.

Table 2 Comparison between both groups regarding serum albumin, surface area of dialyzer, blood flow of machine, ultrafiltration during dialysis session, intradialytic weight gain, KT/V, IVCC, and IVCD

	Group I (n=24)	Group II (n=26)	U-test	P
Albumin (mean±SD)	3.1±0.53	3.6±0.48	3.231[a]	0.002[b]
SA (mean±SD)	1.59±0.21	1.65±0.19	0.982	0.326
QB (mean±SD)	271.6±34.59	263.4±35.77	0.892	0.372
UF (mean±SD)	2.5±0.98	2.1±0.94	1.3	0.187
IDWG (mean±SD)	2.6±1.19	2.2±0.98	1.11	0.266
KT/V (mean±SD)	1.2±0.35	1.1±0.35	1.16	0.244
IVCD (mean±SD)	7.5±1.14	8.5±0.73	3.4	0.001[b]
IVCC (mean±SD)	57.8±7.18	51.5±4.83	3.1	0.002[b]

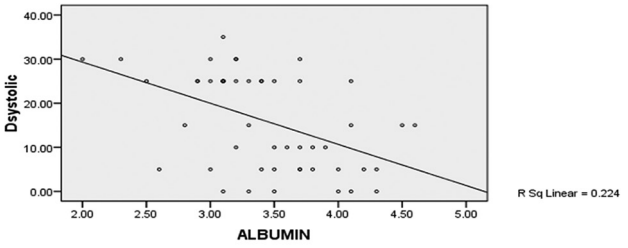
U-test, Mann-Whitney U-test. IDWG, intradialytic weight gain; IVCC, inferior vena cava collapsibility index; IVCD, inferior vena cava diameter; KT/V, dialysis adequacy; QB, blood flow of the machine; SA, surface area of dialyzer; UF, ultrafiltration. [a]Student's t-test. [b]High significant test.

Discussion

IDH is a frequent complication of HD as a result of imbalance of intravascular volume removal and the inadequacy of hemodynamic compensatory mechanisms such as vascular shunting to the central circulation, increased vascular resistance in the splanchnic and cutaneous beds, increasing arterial tone, and increasing cardiac output [9].

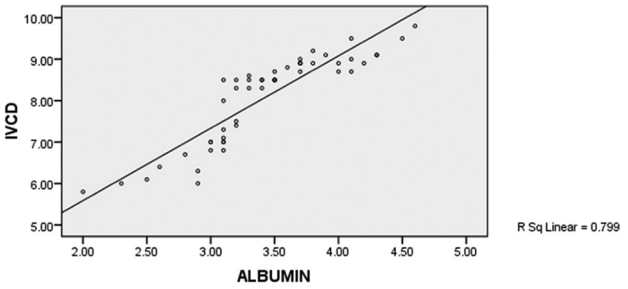
Hypoalbuminemia and dialysis intensity have been shown repeatedly to be perhaps the most critical predictors of outcomes in patients with ESRD. The relationship between hypoalbuminemia and mortality was especially strong. In the Canadian study, each 1 g/dl decrease in mean serum albumin

Figure 1



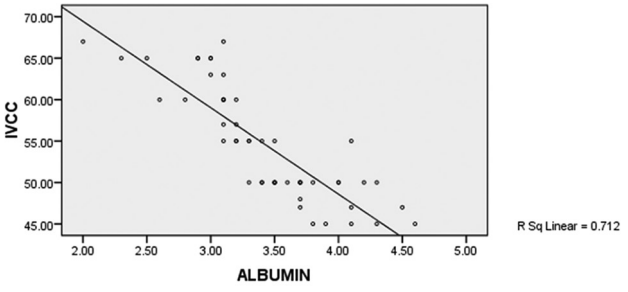
There was a highly significant negative correlation between serum albumin and delta systolic blood pressure (r=–0.47, $P \leq 0.01$).

Figure 2



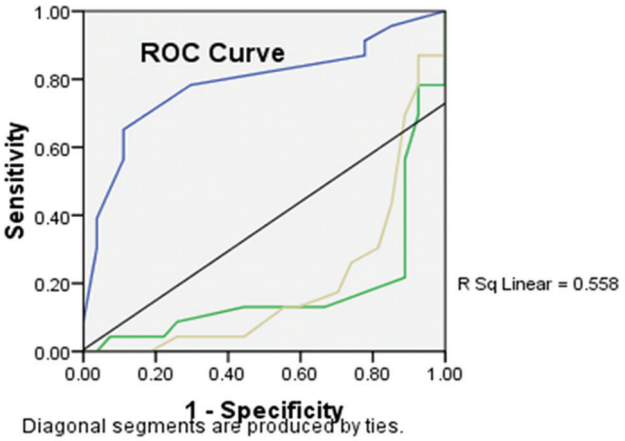
There was a highly significant positive correlation between serum albumin and inferior vena cava diameter (r = 0.894, $P \leq 0.01$).

Figure 3



There was a highly significant negative correlation between serum albumin and inferior vena cava collapsibility index (r=–0.844, $P \leq 0.01$).

Figure 4



Shows receiver operator curve (ROC) for studying sensitivity and specificity of serum albumin, inferior vena cava diameter (IVCD) and inferior vena cava collapsibility index (IVCC) as a predictor for intradialytic hypotension (IDH). The curve shows that IVCC is the only predictor for IDH which has a high sensitivity and specificity (area under curve for IVCC = 79%). Cutoff point = 52.5%. At this cutoff point, sensitivity of IVCC for detection of IDH = 78%, while specificity is 70%.

was independently associated with the development of de novo and recurrent cardiac failure, de novo and recurrent ischemic heart disease, cardiac mortality, and overall mortality [8].

Hypoalbuminemia is a major risk factor of hypotension during HD in patients on HD. One possibility of hypotension during HD is hypovolemia in blood vessels because of low osmolality [6].

Hypoalbuminemia leads to hypovolemia owing to decreased oncotic pressure. This leads to decreased plasma refill and causes premature drop in BP leading to IDH (6).

In the current study, there was no significant difference between the both groups regarding sex. This was in agreement with Locatelli *et al.* [10] who found that there was no significant difference between both groups regarding sex. However, there was disagreement with Tisler *et al.* [11] who found that IDH is more common in female patients. Moreover, Stefánsson *et al.* [12] found that female patients are at a high risk for IDH. The incidence of IDH is higher in old age. Hypotensive episodes occurred frequently in 44% of dialysis patients of 65 years and in 32% of younger dialysis patients (age <45 years).

There was no significant difference between both groups regarding age of the patients. This result is in agreement with the study by Tayyebi *et al.* [13] that found that there was no significant difference between age of patients and incidence of IDH. Long duration of HD might be associated with endothelial dysfunction. Moreover, vascular calcification, which increases with the duration of dialysis, might be responsible for the impairment of vasoconstriction and for arterial stiffness resulting in IDH [14]. In addition, we found that there was no significant difference between the two groups regarding duration of dialysis. This result is in an agreement with Tayyebi *et al.* [13] who found no significant effect between duration of dialysis and IDH. DM is a risk factor for IDH (especially if there is autonomic neuropathy) [2].

In our study, we found no significant correlation between blood flow and IDH. This result is in an agreement with McCausland *et al.* [15] who found no significant effect of increasing blood flow on BP changes during HD session.

KT/V is an important indicator of dialysis adequacy [15]. In our study, we found no significant effect of IDH on KT/V. This finding was in agreement with Tayyebi *et al.* [13] who found no significant correlation between IDH and KT/V. In another study, KT/V was taken as a target regardless of the time of HD session, and patients who could get the optimal KT/V have been reported to have many hypotensive episodes during HD session [16].

In this study, we found a significant positive correlation between IDWG and delta systolic BP. This result is in agreement with Rocha *et al.* [17] who found a significant correlation between IDWG and changes in BP during session. Ultrafiltration is part of the HD procedure and can also be used exclusively to remove additional fluid in patients with fluid overload. Ultrafiltration that is too aggressive can result in hypotension, cramping, or other untoward effects [16].

Our study revealed a significant positive correlation between UF and delta systolic BP. This result is in agreement with Koomans *et al.* [18], in which there was a significant correlation between UF and changes in BP during session.

In our study, we found there was no significant difference between both groups regarding hemoglobin and hematocrit value. This result is in agreement with McCausland *et al.* [15] who found no effect of hemoglobin and hematocrit value on IDH. Moreover, Tisler *et al.* [11] found no effect of anemia on IDH.

We found no significant difference between both groups regarding cholesterol and triglyceride. This result was in agreement with Kraemer *et al.* [19] who found no effect of dyslipidemia on IDH. Low serum potassium can have a direct vasoconstrictor effect [20]. In our study, there is no significant association between potassium level and IDH.

In our study, we found no significant difference between both groups regarding sodium level. This is in agreement with Kraemer *et al.* [19] who found no effect of sodium level on IDH. On the contrary, the use of a higher dialysate sodium concentration (>140 mEq/l) is an effective means to ensure adequate vascular refilling and has proved to be among the most efficacious and best tolerated therapies for episodic hypotension [21].

In our study, we found significant difference between both groups regarding echocardiographic parameter. This finding was in disagreement with the results obtained by Ritz *et al.* [22], who found that left ventricular hypertrophy predisposes patients to IHD.

Delta BP is a very important indicator of change of systolic BP during dialysis session [6]. The increase of delta systolic BP indicates more declines in BP and consequently increase incidence of IHD. In the present work, we found a significant negative correlation between serum albumin and delta BP.

Malnutrition, which is a common finding in patients with ESRD, is a potential cause of reduced albumin synthesis and decreased albumin levels**.** Serum albumin is the strongest predictor of death in dialysis patients, and even in patients at baseline who are starting dialysis therapy.

Hypoalbuminemia is a major risk factor of hypotension during HD in patients on HD. One possibility of hypotension during HD is hypovolemia in blood vessels because of low osmolality [6].

Hypoalbuminemia is a nontraditional risk factor for cardiovascular diseases in HD patients [23]. So, hypoalbuminemia could be a factor, which accelerates IHD in those patients. In our study, we found a highly significant negative correlation between albumin and IDH. This result is in agreement with Jason *et al.* [24] who found a highly significant negative correlation between hypoabuminemia and changes in BP during session. Moreover, Ezzat *et al.* [25] found an association between hypoalbuminemia and IDH.

IVCD and IVCC were found to be correlated significantly with hypervolemia in HD patient [26]. As serum albumin is a strong predictor of intravascular volume status, we tried to study the correlation between serum albumin and both of IVCC and IVCD. In our study, we found a highly significant positive correlation between serum albumin and IVCD; however, there was a highly significant negative correlation between serum albumin and IVCC.

The incidence of hypoalbuminemia increases with aging [27]. As the number of aged people has increased among HD patients, the incidence of IDH has increased as well [27].

Conclusion

We concluded that serum albumin is a parameter that is associated with IDH. Moreover, we found that IDWG is a risk factor for IDH. In addition, we found that bedside measurements of IVCC and IVCD are easy and good markers for prediction of IDH. We also predict that cutoff point for IVCC is 52.5%.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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