ORIGINAL ARTICLE

The Relation Between Acidosis and Albumin Level in Regular Hemodialysis Patients (Case-Control Study)

MUDHFAR MOHAMMED MEIZEL
Assistant Professor, College of Medicine, University of Al-Qadisiyah, Iraq

ABSTRACT

At the final stage of hemodialysis(HD), the strongest indicator of mortality is hypoalbuminemia. By excluding hypoalbuminemia caused by underlying renal disease or other diseases, the metabolic acidosis causes net negative nitrogen and overall protein balance in the body. Because of insufficient dialysis, some patients going through maintenance dialysis have spuriously low plasma bicarbonate levels. The study aimed to estimate the role of common serum bicarbonate on serum albumin concentration. The case study was performed in Baghdad Educational Hospital/ the Medical City, in the Iraqi Hemodialysis Center. The study group of 100 subjects with ESRD on HD was split up evenly into low albumin levels and control with normal albumin levels before and after HD sessions. VBG was done for every patient in study groups and hco3 to measure the Kt/V and show the adequacy of dialysis and take information about the number and duration of dialysis sessions. (The result shows an important correlation between low albumin levels and low hco3 in patients with HD and between dialysis session with albumin) still unclear to me. Hypoalbuminemia is also substantially correlated with low Kt\V. However, according to the logistic regression model, it tends to be dependent on the existence of other hypoalbuminemia risk factors. Age and sex are not statistically significant with hypoalbuminemia.

Conclusions: A significant amount of evidence indicates that metabolic acidosis that has not been corrected is detrimental to overall health. Independent and significant associated with hypoalbuminemia in maintained hemodialysis (MHD) patients indicate the metabolic acidosis exerts a detrimental effect on the nutritional condition of patients with MHD.

INTRODUCTION

Hypoalbuminemia in hemodialyzed ESRD patients: Malnutrition affects 1/3 of hemodialysis patients and is linked to a higher risk of morbidity and mortality. In patients with end-stage renal disease (ESRD), hypoalbuminemia is the most significant indicator of death, but the cause of hypoalbuminemia in the majority of ESRD patients is unknown. Serum albumin is a nutrient and inflammation marker that predicts mortality. (1) The rate of synthesis and catabolism, external losses, and distribution of any protein in plasma during steady-state conditions are defined by its level of synthesis and catabolism, as well as dialysis patient studies(2), kidney failure per sedoes has not been shown to inhibit albumin synthesis or lead to decreased albumin pools. In fact, the majority of hemodialysis patients have natural albumin concentrations (1). Data suggests that hypoalbuminemia is not a result of kidney failure, but rather the result of a certain process. Among the most essential regulators of albumin synthesis is dietary protein supply. (2.) Protein malnutrition reduces albumin synthesis at the RNA transcription level and by post-transcriptional mechanisms. (3). Reduced albumin production, lower plasma albumin levels, and increased morbidity and mortality are all potential outcomes of protein calorie malnutrition. Reduced synthesis may be caused by a reduction in protein intake, an inflammatory reaction, or a combination of these factors. Both mechanisms that tend to lower albumin levels have the potential to increase morbidity and mortality (4, 5). Since protein deficiency is the only cause of hypoalbuminemia in dialysis patients, a correlation between hypoalbuminemia and the rate of urea formation as a reflection of net protein catabolism can be expected, and nutritional supplementation can effectively restore albumin pools, just as it can in patients with protein malnutrition-induced hypoalbuminemia. These connections were not readily recognizable (6, 7, 8). In addition to being nutritionally modulated, albumin is a negative acute-phase reactive protein (9). During an inflammatory response, plasma concentrations of positive acute-phase reactive proteins such as C-reactive protein, a1-acid glycoprotein, and a2-macroglobulin rise, while albumin levels fall, even in the absence of malnutrition (10). Plasma 2macroglobulin serves as a carrier for IL-6 in humans (11, 12), rises during cuprophane dialyzer hemodialysis (13), and increases after an acute myocardial infarction (20). Thyroid hormone, growth hormone, and cortisol are also needed to maintain the basal rate of albumin synthesis. If hypoalbuminemia is caused by a decrease in albumin synthesis in ESRD patients, this decrease may be caused by protein starvation, hormone deficiency, inflammation, or a combination of these factors (2). Hypoalbuminemia can also occur without a decrease in albumin synthesis rate. Hypoalbuminemia can occur as a result of irregular albumin transfer from the vascular compartment to the extravascular space, which can happen after an injury or during sepsis. (15) In rats with chronic kidney failure, plasma albumin concentrations were found to have decreased in part as a result of plasma failure. Increased extracorporeal losses, such as those seen in nephrotic syndrome, may also cause hypoalbuminemia. Albumin synthesis is usually increased in these conditions. In patients undergoing hemodialysis, some albumin may be lost through the dialysis membrane, leading to hypoalbuminemia (16,17)

Aim of Study: This Research's Aim Is To Assess The Role Of Low Serum Bicarbonate In Serum Albumin Concentration.

PATIENTS AND METHODS

The methodology employed in the conduct of this review. It covers methodological problems with regard to the position

of the research, the nature of the study and the statistical analysis used to test the hypotheses of the study.

Study Design: This study carried out at Medical City/ Baghdad Educational Hospital/ Dialysis Center from June 2015 to December 2015 to determine differences in albumin levels in cases with low hco3 and Kt/V and controls with normal hco3 and Kt/V (both cases and controls with ESRD and hemodialysis) and to clarify the differences in hco3 levels before and after hemodialysis.

Study Population: "A total of 100 ESRD patients on regular HD 50 patient as cases and 50 patient as control(duration of hemodialysis range between 3months to 4 years at Dialysis Center ."

Data Collection: A history taken for each patient participate in this case control study regarding his a patient's name, their age, and gender also if there is any other disease for chronic kidney disease, numbers of sessions, duration of each session, duration of dialysis. Serum albumin concentration was calculated every 30 days in all patients (N =100), those with serum albumin concentrations at time of study below 3.5 g/dl consider as a case. And those with serum albumin between 3.5-5.5 g\dl consider as a control, then measure the Kt\V from the hemodialysis machine at the end of the session. VBG for each participant measured before the hemodialysis session and after it and before next session . For all of the participants in this study, the dialysis prescription was the same:

1. "Intermittent conventional Hemodialysis by B Braun Dialysis machine' two-three days a week, for a total of three-four hours.
2. "Low-flux polysulfone hollow fiber dialyzers".
3. The temperature was 36.5c
4. hco3 profile 31.6 mmole/l
5. Na 145 mmole/l with normal profile
6. K^+ 2mmole/l,Ca^{++} =1.5mmole\l
7. UF based on the patient's requirements
8. Blood flow is determined by the patient's needs as well as the forms of vascular access available to him or her.
9. "Dialysate flow" 500ml\min

The criterion for inclusion and exclusion for this study groups were as follows:

Inclusion criteria: Included Participant in this study were any patient of kidney disease end stage who undergo regular hemodialysis 2-3 sessions each week 3-4 hours for each sessions at "Dialysis Center in Baghdad teaching hospital" .

Exclusion criteria: This case-control study groups were all Patient with a suspicious of hyopalbunemia because of the underlying pathology :

1. Patient with "liver cirrhosis".
2. Patient with hepatitis
3. "an active stage of nephrotic syndrome"
4. Patient with "protein losing enteropathy".
5. Patient with "neoplasia", sever systemic illness and chronic D.M.

Study Instruments

hco3: hco3 is calculated by drawing a venous blood sample from the central vein into a syringe containing heparin, putting it in an ice tray, and sending it to the "Respiratory care center at Baghdad Teaching Hospital" and the "blood gas analysis" is performed using a special system (ABL800FLEX) that uses a solution to test the blood gas.

The normal range for venous hco3 is 22-26 mmol/1.

Albumin: In this hemodialysis program, albumin was calculated by drawing venous blood and sent to the laboratory which measured by the "spectrophotometry method"

Kt/V: The amount of early and later dialysate UV absorption mirrors pre and post serum uric acid, and Kt/V is determined directly during hemodialysis sessions by a B Braun hemodialysis system that measures UV light absorbance at a selected wave length, which corresponds to dialysate concentration of uric acid or other molecule weight solute, and the average of early and late dialysate UV absorption mirrors pre and post serum uric acid.

Normal Kt\V =1.2

Data Analysis: SPSS version 20 was used for statistical analysis. The mean and standard ± deviation of continuous variables were presented. Frequency and percentage had been used to present categorical variables. To see the contrast between two continuous variables, and independent sample a t-test was used. The relation between categorical variables was determined using Pearson's chi square (X2) test and the Fisher exact test. Statistical significance was described as a p-value of less than 0.05.

RESULTS

Distribution of Study Groups by Age and Sex: The average age of the cases and controls was 47.50 ± 12.25 and 52.16 ± 13.58, respectively. There was no noticeable age gap between cases and controls (t=1.801, df= 98, p= 0.075)

Figure one: Age gap between the groups

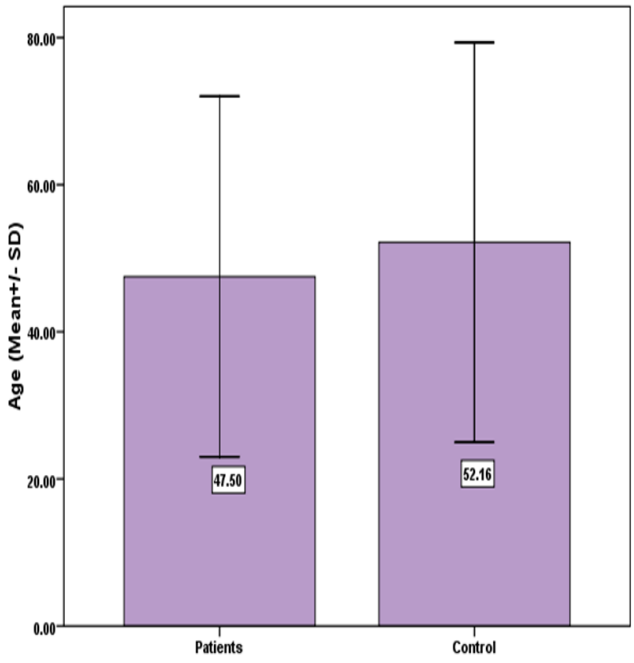

Figure two: the gap in research groups based on gender. P value of 0.15
There's no statistically considerable difference in study groups based on gender**.(I suggest deleting it)**

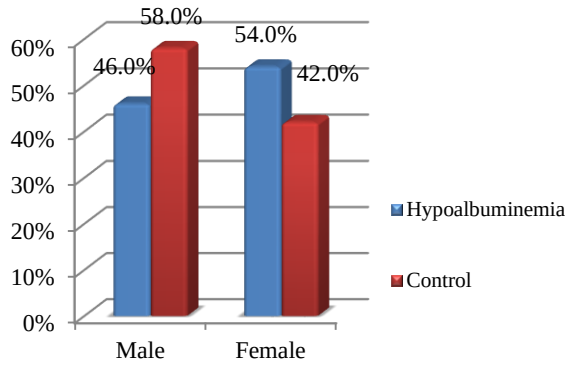

Table one : "Logistic Regression Model" for Patients with Acidosis and Control in "End Stage Renal Failure"

Variable	Wald	P value	Odds Ratio	95% C.I. for Odds Ratio	
				Lower	Upper
hco3 preceding the sessions of haemodialysis Low** Normal	11.255	<0.001*	102.83	6.86	1540.40
hco3 following the sessions of haemodialysis Low** Normal	0.329	0.566	2.39	0.12	47.16
hco3 preceding the next of haemodialysis Low** Normal	4.168	0.041*	7.88	1.08	57.28
Kt/V Low Normal	1.735	0.188	0.11	0.00	2.86
Session of haemodialysis 2 sessions** 3 sessions	4.612	0.032*	20.46	1.30	321.80
time between haemodialysis Three 3 hours ** four hours	5.005	0.025*	15.92	1.40	179.85
Age	0.359	0.549	1.02	0.94	1.11
Sex Male** Female	0.234	0.629	1.59	0.24	10.48
Constant	5.645	0.018	0.00		

**reference group
*p value ≤ 0.05 is substantial

DISCUSSION

In this study, 100 patient with ESRD on regular hemodialysis were inculded in Baghdad teaching hospital in the dialysis center. 50 participant consider normal according to normal albumin level and 50 participant consider cases according to abnormal albumin level .

The mean age in cases were (47.50 ± 12.25) years old and the mean age of control (52.16 ± 13.58) years old. There was no significant mean difference of age by cases and control where the p value = 0.075.The association of hypoalbuminemia and age has been the focus of many studies. Previous studies by George A. Kayse*etal* show that albumin synthesis hasn't been noticed to vary with age. On the other hand others mentioned that there is a strong relationship with age from the age of 60 years and up [18] .Our patient was 65 years old at the most. Figure two shows the gender is not significant in our study with p value =0.15 .There were 23(46%) male and 27(54%) female in cases and there were 29 (58%) male and 21(42%) female in control group. There was no significant correlation between serum albumin and gender [19] also There is no evidence of a connection between gender and low albumin levels. 64% of cases have two sessions per week, 36% of cases have three sessions per week. Just 16% of the control group had two sessions per week, while 84% had three sessions per week. The time of each session were three hours in 44% of cases and four hour in 56% of cases while the control group there were only two which is 4% three hours a session and 96% with 4 hour per session. Cases were nine to eighteen times more possible to have two of hemodialysis sessions for three hours duration, sequentially. The reason is that patients who had two weekly sessions and those who had a three-hour session received less dialysis and were considered to have

insufficient dialysis in comparison to those who had three weekly sessions and four-hour sessions, which limited proper acidosis correction and resulted in low albumin levels, as previously stated. Inadequate dialysis can also cause uremia, which results in anemia, anorexia, nausea, vomiting, and inadequate food consumption, all of which contribute to a low albumin level. This relationship of hypoalbuminemia with dialysis adequacy has been identified by Wapenskeyet al. and Laville and Fouqueetal. as a significant correlation. Ali J. H. AL-Saedyetal found a connection between dialysis adequacy and undernourishment, as evidenced by low albumin and cholestrol levels. A strong association "between hco3 and albumin level was detected where the acidosis associated with hypoalbuminemia and it significant when measured hco3 before dialysis session p-value <0.001, after dialysis session p-value <0.001 and before next session p-value= 0.014. The number of cases had low hco3 level before dialysis session was 45(90%) compare with 6(12%) of control and had normal hco3 level in 5(10%) of cases in comparison with 44(88%) of control. While after HD session the cases had normal hco3 in 40 (80%) compare with 48(96%) of control and only 10 (20%) of cases had low hco3 level compare with only 2(4%) of control. The hco3 level in cases before the next session was normal in 6(12%) of cases compared with 36(72%)of control and low in 44(88%) of cases and 14(28%) of control".

The mechanisms whereby acidosis causes hypoalbumenmia was explained in the introduction.

Based on the study results, These explanations are introduced by author

1. A dialysis that is inadequate.

A. As previously mentioned, the duration of dialysis and the number of sessions.

B. Despite the fact that we did not include in our research the number of participants who rely on temporal double lumen dialysis, poor blood flow and a high incidence of inflammation and infection are still significant causes of inefficient dialysis in our participants.

2. Infection: A rise in infection average leads to acidosis, and a lot of ESRD patients have low immunity, are poorly informed about infections avoidance, and have inadequate nourishment.

3. Nutritional causes, with the majority of our patients were unable to follow the diet prescribed by their doctor or dialysis center.

Low hco3 and albumin levels were also found to have an important relationship, with a p value of 0.019. Grahametal also found a connection between acidosis and low albumin in MHD patients, and that treating acidosis reduces body protein degradation. Lofberg*etal*[52] also correspond to our result and the treatment of acidosis lead toincreased intracellular concentrations of branched-chain amino acids . Metch *etal* which shown that Metabolic acidosis stimulate hypoalbuminemia through upregulating "the adenosine triphosphate (ATP)-dependent ubiquitin proteasome pathway and increasing proteolysis" Verove et al shown considerable rise in serum albumin and prealbumin levels on treatment of acidosis

We have 36(72%) of cases have low Kt\V and 14(28%) have normal Kt\V. While control have 3(6%)and 47(97%) with low and normal Kt\V respectively .The association between efficiency of dialysis and albumin level discussed above in discussion the correlation also is mentioned by many studies .Teixeira Nunes*etal* stated that there is strong correlation between low Kt\V and low albumin level . Azar A.T*etal* Blake *et al* and Yang *et al* also reported relation of Kt\V and dialysis adequacy with the albumin level with increase the dialysis dose improve the albumin level.

CONCLUSIONS

1. Our results show that age and sex are not significantly associated with albumin level.
2. There is significant relation between numbers of hemodialysis sessions per week and duration of dialysis sessions and albumin level where the cases appear more to have two dialysis sessions per week and three hours duration which also demonstrated by logistic regression model.
3. These data demonstrate that patients onMHD with metabolic acidosis had a lower serumalbumin concentration. The inverse effect on serum albumin concentration in MHD patients also demonstrated by logistic regression model.
4. There is relationship between adequacy of hemodialysis in form of Kt\V and occurrence of hypoalbumenimia but logistic regression model it appear not significantly associated due to it depend on the presence of other factors like acidosis.

Recommendations:

According to result of this thesis we recommended the following:1. Improve the efficacy of dialysis and reach the target kt\v by:

A. Early diagnosis of CKD and preparation of the patient for RRT by HD with creation of AV fistula in stage 5 CKD for usage during emergency or when the nephrologist decide to start the dialysis .WhereAV fistula need at least 6 week for maturation and given adequate blood flow instead of use the temporarily double lumen which deliver inadequate blood flow lead to decrease HD efficiency and also expose the patient to risk of infection which lead to acidosis.

B. Increase the dialysis time to at least 4 hour per session, 3times per week to improve the dialysis adequacy and hco3 level and according to residual renal function of patient. This can be achieved by increase the numbers of dialysis machines per each dialysis center or increase the numbers of dialysis centers per each area to match the need for adequate dialysis.

2. Improve the hco3 level by increase the dialysis efficacy as mentioned above and adjust the bicarbonate dosesin dialysate according to patients bicarbonate levels.
3. Give attention to the protein intake and nutrition of hemodialysis patients to improve the albumin level . So we need a team work consist of nursing staff, nephrologist and dietitian for education about the amount and type of food which must be taken by those patients.

REFERENCES

1. El-Sheikh, M., & El-Ghazaly, G. (2016). Assessment of

hemodialysis adequacy in patients with chronic kidney disease in the hemodialysis unit at Tanta University Hospital in Egypt. *Indian Journal of Nephrology, 26*(6), 398-404. https//doi.org/10.4103/0971-4065.168141.
2. Gama-Axelsson, T., Heimburger, O., Stenvinkel, P., Bárány, P., Lindholm, B., Qureshi, A.R. (2012). Serum albumin as predictor of nutritional status in patients with ESRD. *Clin J Am Soc Nephrol, 7*(9), 1446-1453. https://doi.org/10.2215/CJN.10251011.
3. George, A. K. (1998). Biological Basis of Hypoalbuminemia in ESRD. *J AmSoc Nephrol, 9*, 2368-2376.
4. Hemayati, R., Lesanpezeshki, M., & Seifi, S. (2015). Association of dialysis adequacy with nutritional and inflammatory status in patients with chronic kidney failure. *Saudi J Kidney Dis Transpl, 26*(6), 1154-60.
5. Ikuko, G., Hideki, F., Makoto, S., Yoshiyuki, M., Takashi, A. T., & Hisataka, M. (2007). Relationship between serum albumin level and aging in community-dwelling self-supported elderly population. *J Nutr Sci Vitaminol, 53,* 37-42.
6. Kalantar-Zadeh, K. (2016). Moderator's view: Higher serum bicarbonate in dialysis patients is protective.
a. *Nephrology Dialysis Transplantation, 31*(8), 1231-1234. https//doi.org/10.1093/ndt/gfw258
7. Kalender, N., & Tosun, N. (2014). Determination of the relationship between adequacy of dialysis and quality of life and self-care agency. *J Clin Nurs, 23*(5-6), 820-8. https://doi.org/10.1111/jocn.12208
8. Kapl, A. A., Halley, S. E., Lance, R.A., & Graeber, C. W. (1995). Dialysate protein losses with bleach processed polysulphone dialyzers. *Kidney Int, 47,* 573-578.
9. Kovesdy, C. P. (2012). Metabolic acidosis and kidney disease: does bicarbonate therapy slow the progression of CKD? *Nephrol Dial Transplant, 27*(8), 3056-62. https://doi.org/10.1093/ndt/gfs291
10. Lecker, S. H., Goldberg, A. L., & Mitch, W. E. (2006). Protein Degradation by the Ubiquitin–Proteasome Pathway in Normal and Disease States. *JASN, 17*(7), 1807-1819. https://doi.org/10.1681/ASN.2006010038
11. Lofberg, E., Wernerman, J., Anderstam, B., & Bergstrom, J. (1997). Correction of acidosis in dialysis patient's increases branched-chain and total essential amino acid levels in muscle. *Clin Nephrol, 48*(4), 230-237.
12. Mirsa, S. (2016). Pro: Higher serum bicarbonate in dialysis patients is protective. *Nephrology Dialysis Transplantation, 31*(8), 1220-1224. https://doi.org/10.1093/ndt/gfw259
13. NKF-DOQI. National Kidney Foundation. (2002). Clinical practice guidelines for chronic kidney disease: Evaluation, classification and stratification: Guideline 4: Estimation of GFR. *Am J Kid Dis*, *39* (1), 83-86.
14. *NFK-DOQI .* National Kidney Foundation. (2015). *Clinical Practice Guideline for Hemodialysis: 2015 Update.*Retrieved from https://www.kidney.org/professionals/guidelines/hemodialysis.
15. Pathology Harmony Group. (2013). *Harmonization of Reference Intervals. Pathology harmony.co.uk.* Retrieved from http://www.acb.org.uk/docs/default-source/committees/scientific/guidelines/acb/pathology-harmony-ii-bioc hemistry.pdf? sfvrsn=2
16. Pickering, W. P., Price, S. R., Bircher, G., Marinovic, A.C., Mitch, W.E., & Walls, J. (2002). Nutrition in CAPD: Serum bicarbonate and the ubiquitin proteasome system in muscle. *Kidney Int, 61*(4), 1286-1292. https://doi.org/:10.1046/j.1523-1755.2002. 00276.x
17. Pourafshar, N., Pourafshar, S., & Soleimani, M. (2018). Urine Ammonium, Metabolic Acidosis and Progression of Chronic Kidney Disease. *Nephron, 138*, 222-228. https://doi.org/10.1159/000481892
18. GREENBLATT DJ. Reduced serum albumin concentration in the elderly: a report from the Boston Collaborative Drug Surveillance Program. Journal of the American geriatrics society. 1979 Jan;27(1):20-2.
19. Soleymanian T, Hamid G, Arefi M, Najafi I, Ganji MR, Amini M, Hakemi M, Tehrani MR, Larijani B. Non-diabetic renal disease with or without diabetic nephropathy in type 2 diabetes: clinical predictors and outcome. Renal failure. 2015 Apr 21;37(4):572-5.