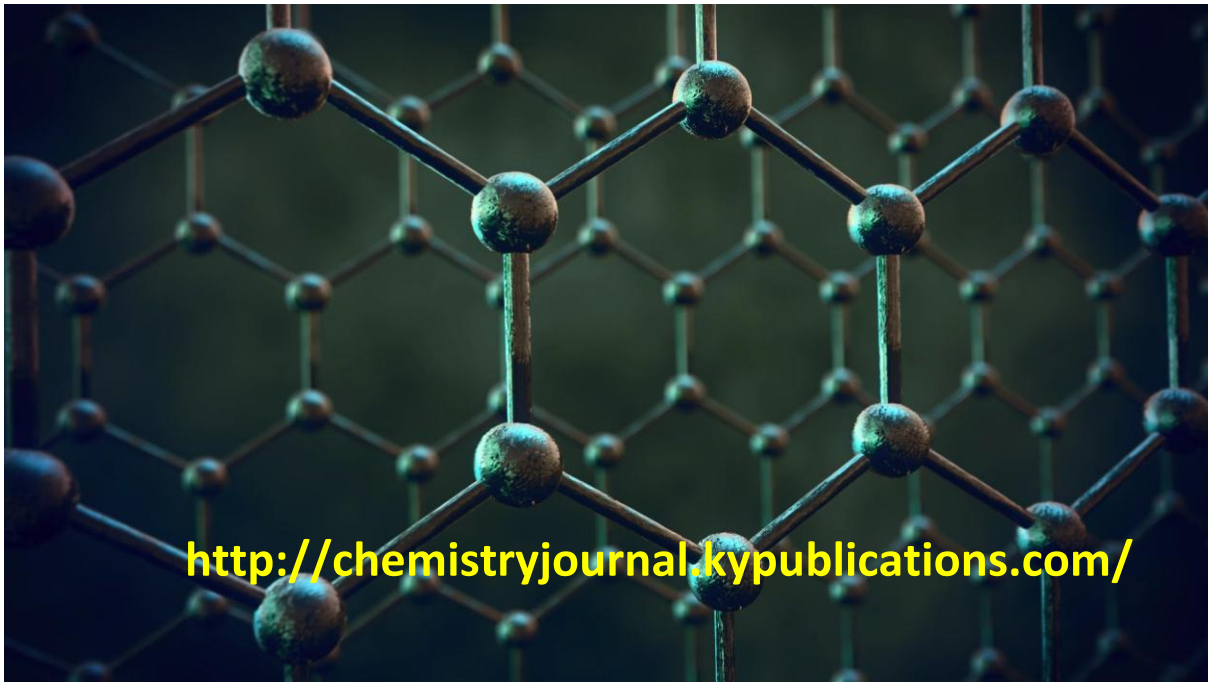

International Journal of Chemistry and Aquatic Sciences (IJCA)

http://www.chemistryjournal.kypublications.com/

e-ISSN: 2355-033X

Editor-in-Chief
Dr.Y.H.Rao
Email:submitijca@gmail.com

©KY PUBLICATIONS
International Journal of Chemistry and Aquatic Sciences(IJCA)
Volume: 3, Issue 4, 2017 (July-August); Page 1-10
e-ISSN: 2355-033X
Research Article

EFFECT OF PRE-ALBUMIN AND ITS RELATION TO LIVER DISEASE IN DIALYSIS PATIENT

Prof. Dr. Fadhil Jawad Al-Tu'ma, Mohammed Abdulridha Wadi, Assist.Prof. Dr.Ali abdulmajid Allawi
Ministry of Higher Education and Scientific Research
University of Kerbala, College of Medicine, Department of Biochemistry
Republic of Iraq

ABSTRACT
In spite of the fact that not broadly valued, the revealed convergence of serum pre-albumin, similar to that of serum cholesterol, has a tendency to be higher in patients on peritoneal dialysis (PD) than on hemodialysis (HD), regardless of the generous loss of protein amid PD. Determination of the level of prealbumin, a hepatic protein, is a sensitive and practical strategy for evaluating the seriousness of sickness coming about because of lack of healthy sustenance in patients who are fundamentally sick or have a constant ailment. Prealbumin levels have been appeared to relate with understanding results and are an exact indicator of patient recuperation. In high-hazard patients, prealbumin levels decided twice week after week amid hospitalization can alarm the doctor to declining healthful status, enhance tolerant result, and abbreviate hospitalization in an inexorably cost-cognizant economy.
In the present study, prealbumin levels estimated in selected Kidney patients and compared PAB levels various nutritional markers, also it is not significantly correlated with any of the investigated parameters. Moreover, further analysis showed that patients are malnourished independently whether they have inflammation or not.

1.0 Introduction

Pre-albumin (PAB), is an instinctive protein, goes about as a transport protein for thyroxine and as a bearer for retinal binding protein. Because of the short half-life of pre-albumin (2-3 days), it is thought to be a superior indicator of dietary repletion. In any case, it is influenced by an indistinguishable incendiary process from albumin and reductions amid the intense stage reaction. A pre-albumin level decreases with contamination, hyperglycemia, dialysis, liver malady, and surgery. Pre-albumin might be raised with corticosteroids and intense renal disappointment, as it is debased by the kidneys.

PAB is degraded by the kidneys, and consequently any renal dysfunction causes an increase in its serum levels. Furthermore, one of the functions of PAB is to act as a transport protein for thyroxine. In hyperthyroid states, the molecules of prealbumin are saturated with thyroxine, and hence the measured serum levels of PAB are low. Similarly, PAB levels are high in hypothyroid states[1].

Prealbumin response correlates with patient outcome. Among 102 patients whose average daily in-hospital intake was less than 50 percent of calculated maintenance requirements, persons who developed low prealbumin levels had a higher rate of mortality[2].

In a study[3] of patients on hemodialysis, the serum prealbumin level correlated with other measures of nutrition, including serum albumin, but appeared to be the single best nutritional predictor of survival. Patients at severe risk (i.e., prealbumin levels below 10 mg per dL [100 mg per L]) averaged hospital stays of 22 days compared with an average of six days in patients at moderate risk (prealbumin levels between 10 and 17 mg per dL [100 and 170 mg per L])[4].

In a study in Spain,[5] patients in an intensive care unit who were receiving formulas rich in branch chain amino acids recovered more rapidly from sepsis. Their recovery was associated with a rise in prealbumin levels.

In spite of the fact that the prealbumin level is a sensitive indicator of insufficient supplement admission, it ought to be utilized just as an indispensable piece of a general appraisal program. Such factors as intense alcoholism, steroid utilize, and zinc hardship may influence the prealbumin level. In patients at healthful hazard, prealbumin levels evaluated twice week after week amid hospitalization can effectively sharpen the doctor to the patient's nutritional status.[6]

The aim of this study is to evaluate serum prealbumin as an inflammatory and nutritional marker and determine whether there is an association between prealbumin and other anthropometric and biochemical markers. Furthermore, this study will compare the nutritional and inflammatory status between dialysis patients, through prealbumin and other indices

Experimental

2.1 Subjects and Study protocol

This study was carried out at Medical City Complex, Baghdad Teaching Hospital, Iraqi Center of Kidney Dialysis under the supervision of consultant nephrologist from December 2016 to August 2017 One hundred and four subjects were selected to participate in this study. Only (90) subjects completed the courses of the study successfully. All patients (49 male & 41 female) . Mean age of the subjects was 53.2 ± 13.5 years. These subjects were recruited into the following groups. It classified in to two groups.

•Group A : included 45 persons as diabetic nephropathy

•Group B : included 45 persons non diabetic nephropathy

The study protocol was approved by the local ethical committee of the college of medicine Karbala University, with verbal informed consent from patients

2.1.1 Inclusion Criteria: The primary inclusion criteria involved patients with chronic renal failure on maintenance hemodialysis for at least six months, Secondary inclusion criteria involved patients diabetic nephropathy and non diabetic nephropathy

2.1.2. Exclusion Criteria

- Acute renal failure.
- Patients with hepatitis B virus
- Patients with hepatitis C virus
- Inadequate data.
- Patients with arthritis and Rheumatoid
- Peritoneal dialysis
- Renal carcinoma.
- Heart disease and bone disease

2.2 Data Collection

Information on demographic characteristics (such as age, weight, height, occupation, handedness, consanguinity and current smoking and alcoholic status) were obtained through patient interview at baseline (Appendix A). Causes and family history of CKD and the presence of co morbidities including coronary artery disease, hypertension, diabetes mellitus and congestive heart failure, as well as the medication history, duration of dialysis and dialysis treatment, were reported by the patients' nephrologists. Blood pressure, mean arterial blood pressure (MABP), and

pulse rate were recorded from the dialysis machine directly when the patient in a supine position during a dialysis session. Body mass index (BMI) was calculated as weight in kilogram divided by height in meter squared

2.3 Sample Collection and Preparation

Five to eight milliliters of venous blood were obtained from patients and control group, Blood samples were collected in the morning by venipuncture using 10 mls disposable syringes. Blood was divided into 2 parts

First part: 6ml was put in the plain tube and left to clot for 30 minin room temperature and then separated by centrifugation at (3000 rpm) for (10 min), then the serum was divided into three parts, and put into three eppendorff tubes then stored in the freezer at -70˚C until use then collected in tubes without anticoagulants.

Second part: 3ml blood was put into EDTA tube, tube with anticoagulants blood group mixed gently and put on shaker for measurements HbA1C.

2.3.1 Chemicals: All chemicals and reagents were of the highest available purity and needed no more purification. Specific diagnostic kits and chemicals used in this study are listed in table 2-1 with their suppliers.

2.3. Methods

2.3.1. Determination of pre-albumin

Principle: This kit uses enzyme-linked immune sorbent assay (ELISA) based on biotin double antibody sandwich technology to assay Human prealbumin(PA). Add prealbumin(PA) to wells that are pre-coated with prealbumin(PA) monoclonal antibody and then incubate. After incubation, add anti PA antibodies labeled with biotin to unite with streptavidin-HRP, which forms the immune complex. Remove unbound enzymes after incubation and washing, then add substrate A and B. The solution will turn blue and change to yellow with the effect of acid. The shades of solution and the concentration of Human prealbumin(PA) are positively correlated

Washing method

A. Washing by hand:Shake off liquids in the wells of the ELISA plate. Lay several bibulous papers on the test bed and pat the ELISA plate hard several times downward. Then inject at least 0.35ml of diluted washing concentrate and soak for 1-2 minutes. Repeat as needed.
B. Washing by automatic plate washer: If an automatic plate washer is available, it should only be used in the test by those proficient with its function

Assay procedure

A. Dilution of standard solutions: This kit provides one standard original concentration. Users may independently dilute in small tubes following the chart below:

Standard solution **No.5** **No.4** **No.3** **No.2** **No.1**

B. The number of stripes needed is determined by that of samples to be tested added by the standards. It is recommended that each standard solution and each blank well be arranged with multiple wells as much as possible.

C. Sample injection: 1) Blank well: Do not add sample, anti PA antibody labeled with biotin and streptavidin-HRP; add chromogen reagent A & B and stop solution, each other step operation is the same. 2) Standard solution well: Add 50µl standard and streptomycin-HRP 50µl (biotin antibodies have united in advance in the standard so no biotin antibodies are added). 3) Sample well to be tested: Add 40µl sample and then 10µl PA antibodies, 50µl streptavidin-HRP. Then cover it with seal plate membrane. Shake gently to mix. Incubate at 37°C for 60 minutes.
D. Preparation of washing solution: Dilute the washing concentration (30X) with distilled water for later use.
E. Washing: carefully remove the seal plate membrane, drain liquid and shake off the remainder. Fill each well with washing solution, let stand for 30 seconds, then drain. Repeat this procedure five times then blot the plate.
F. Color development: First add 50µl chromogen reagent A to each well, and then add 50µl chromogen reagent B to each well. Shake gently to mix. Incubate for 10 minutes at 37°C away from light for color development.
G. Stop: Add 50µl Stop Solution to each well to stop the reaction (color changes from blue to yellow immediately at that moment).
H. Assay: Take blank well as zero, measure the absorbance (OD) of each well one by one under 450 nm wavelength, which should be conducted within10 minutes after having added stop solution.

i) According to standards concentrations and corresponding OD values, calculate the linear regression equation of the standard curve. Then according to the OD value of samples, calculate the concentration of the corresponding sample. Statistical software could also be employed

Determination of Serum Albumin

Principle:

Albumin in the presence of bromocresol green at a slightly acid pH, produce a color change of the indicator from yellow-green to green-blue. The intensity of the color formed is proportional to the albumin concentration in the sample **(Gendler,1984)**.After reading absorbance at 630 nm, results were expressed as g/dl and the reference range was 3.5 – 5.0 g/dl in serum.

Reagent 1	**Citrate buffer**	**95 mmol/l, PH 4.1**
Reagent 2	**Bromcresol**	**0.66 mmol/l**

Procedure: Serum sample was introduced into micro-sampler tube , 60 µL was taken by micro-sampler tube and after about 50 second the result was appeared and printed on micro-printer automatically.

Statistical analysis

Anderson darling test was done to asses if continuous variables follow normal distribution, if follow normal distribution than mean and standard deviation used, if did not follow normal distribution than median and interquartile range (25% to 75% percentile range) will be used to present the data (boxplot and whisker used to present them graphically).

Discrete variables presented using there number and percentage used to present the data, chi square test used to analyze the discrete variable or Fisher exact test used to analyze the distribution between 2 groups (used instead of chi square for 2x2 table, if total sample <20 and if 2 or more with expected frequency less than 5).

Two samples t test used to analyzed the differences in means between two groups (if both follow normal distribution with no significant outlier), while one way ANOVA used to analyzed the differences between more than two groups (if they follow normal distribution with no significant outlier), trend ANOVA used the differences in mean between the same group over 3 time periods.

Mann Whitney U test used to analyzed the differences in median of two groups (if they do not follow normal distribution), while for more than two groups Kruskal Wallis test was performed, if the same group over 3 consecutive time periods Friedman ANOVA used then

Linear regression analysis performed to assess the relationship between different variables, if one or both of them follow normal distribution person regression used but if both did not follow normal distribution spearman correlation will used. Scatter plot used to present the regression analysis, r (correlation coefficient or standardized beta is a representative of magnitude and direction of the relationship), r<0.25 weak, 0.25 – 0.5 mild, 0.5 – 0.75 moderate, >0.75 strong correlation. Negative sign indicate inverse relationship, but positive sign represent direct relationship. SPSS 20.0.0, Minitab 17.1.0, MedClac 14.8.1, GraphPad Prism 7.0 software package used to make the statistical analysis, p value considered when appropriate to be significant if less than 0.05.

3.0 Results

3.1 Demographic and disease characteristics

Mean age (Table 3.1) of the subjects was 53.2 ± 13.5 years, with mean BMI of 26.6 ± 5.3 Kg/m^2, female and male had similar distribution (49; 54.4% female and 41; 45.6% males), mean duration of ESRD was 9.9 ± 4.7 years, 50 patients (55.6%) had fistula access and 40 patients (44.4%) had graft catheter access, mean arterial blood pressure was 107.6 ± 18.5

Table 3-1: Demographic and disease characteristics

	Non diabetic	Diabetic	All	P value
Number	45	45	90	-
Gender, number (%)				0.672
Female	22 (48.9%)	19(42.2%)	41 (45.6%)	
Male	23 (51.1%)	26(57.8%)	49 (54.4%)	
Disease duration, mean± SD	10.9 ± 5.0	8.9 ± 4.1	9.9 ± 4.7	0.046 [Sig.]

Independent t test and chi square was used

Serum prealbumin was higher in male compared to female 36.8 vs. 29.3 mg/dL, but it was statistically not significant, while serum albumin was similar between genders, as illustrated in table 3-1a.

Table 3-1a: Comparison of some marker according to the gender

	Female	Male	P value
	41	49	-
Pre-albumin	29.3 ± 20.6	36.8 ± 25.4	0.133
Albumin	3.5 ± 0.6	3.5 ± 0.6	0.945
Independent t test			

3.2. Relationship between pre-albumin and various variables

There was direct and significant relationship between disease duration and pre-albumin, and also significant and inverse relationship with protein in diabetic patients only as illustrated in table 3-2

Table 3-2: Correlation between pre-albumin and various variables in both groups

	r	P value	r	P value
Variables	Non DM		DM	
Age	0.038	0.806	0.029	0.846
BMI	-0.047	0.760	0.007	0.965
Disease Duration	0.280	0.063	0.308	0.035 [Sig]
MABP	0.141	0.356	0.081	0.587
Albumin	-0.113	0.459	-0.067	0.655
Vitamin D	-0.074	0.628	0.003	0.986
Protein	-0.048	0.755	-0.297	0.043 [Sig]

Globulin	-0.014	0.928	-0.280	0.057
HsCRP	0.176	0.248	-0.042	0.778
HbA1c	0.062	0.687	0.048	0.750
FBS	0.093	0.545	-0.043	0.775
PTH	-0.035	0.818	-0.096	0.522
Calcium corrected	0.177	0.245	0.231	0.118
PO_4	-0.086	0.574	0.015	0.922
CaxPO4	-0.043	0.779	0.112	0.454
Urea	-0.128	0.402	0.268	0.069
Creatinine	-0.073	0.633	0.106	0.477
GFR	0.006	0.969	-0.029	0.847

Table 3-3: Correlation between prealbumin and various variables in all subjects

Variables	r	P value
Age	0.046	0.665
BMI	-0.012	0.910
Disease duration	0.228	0.031 [Sig.]
MABP	0.098	0.356
Albumin	-0.124	0.244
Vitamin D	-0.042	0.694
Protein	-0.129	0.226
Globulin	-0.093	0.386
HsCRP	0.029	0.783
HbA1c	0.111	0.297
FBS	0.075	0.481
PTH	-0.095	0.372
Ca corrected	0.248	0.018 [Sig.]
PO4	-0.036	0.737
CaxPO4 product	0.048	0.651
Urea	0.022	0.836
Creatinine	-0.098	0.358
GFR	0.082	0.445
r: correlation coefficient		

3.7. Relationship between pre-albumin and liver enzyme

There is an inverse significant logarithmic relationship between ALT and AST with prealbumin while no such relationship was found with albumin as illustrate in table 3-4 and 3-5 and figure 3-2 and 3-3

Table 3-4: Logarithmic correlation between liver enzyme and prealbumin

Variables	r	R^2	P value
ALT	0.228	0.052	0.031
AST	0.218	0.048	0.039
Logarithmic regression			

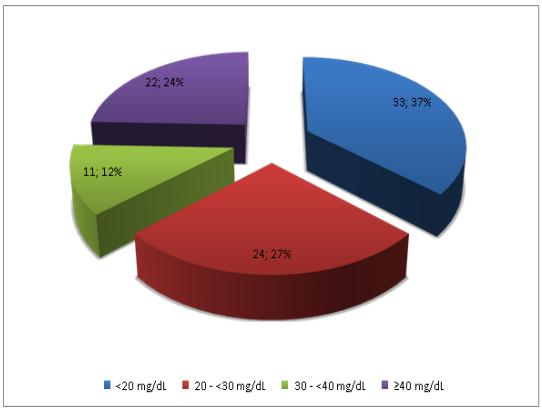

Figure 3-2: Serum prealbumin divided as risk of mortality

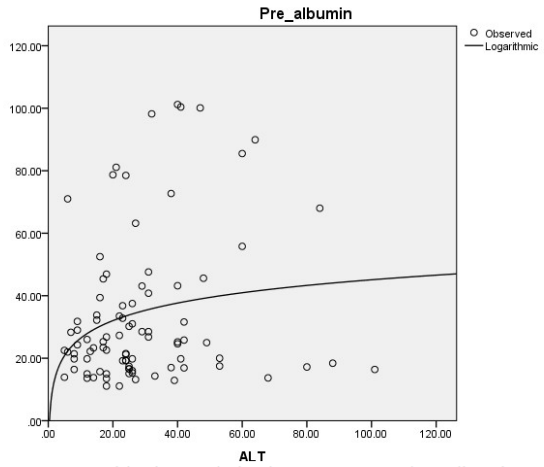

Figure 3-5: Logarithmic correlation between ALT and prealbumin

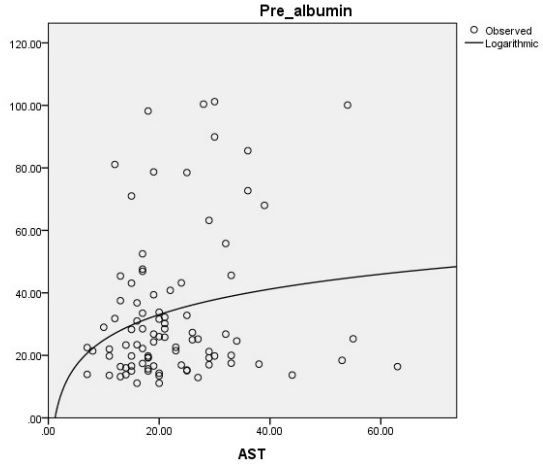

Figure 3-6: Logarithmic correlation between AST and prealbumin

Table 3-5: Linear correlation between liver enzyme and prealbumin

Variables	r	R^2	P value
ALT	0.017	<0.001	0.872
AST	0.010	<0.001	0.928
Linear regression			

Discussion

In the current study serum prealbumin was higher in male compared to female (36.8 ± 25.4 vs. 29.3 ± 20.6 mg/dL) however it was not statistically significant (Chertow *et al.*, 2005). found a similar finding (32.9 vs. 31.1 mg/dL for male and female respectively) and similar to (Chertow *et al.*, 2000). in which (27.9 vs. 26.0 mg/dL respectively, all these indicate male have higher prealbumin compared to female which can be related to difference in protein component of the body.

In the present investigation pre-albumin was 26.6 ± 6.4 mg/dL, also higher than (Rambod *et al.*, 2009). with 28.3 ± 9.6 mg/dL serum pre-albumin.and similar to Chertow *et al.*, 2005 with serum pre-albumin 32.0 ± 8.8 mg/dL, however all these prealbumin remain normal acceptable range of 20 – 40 mg/dL.

In the current study prealbumin was not statistically different between diabetic patients compared to non-diabetic (35.2 ± 26.1 vs. 30.3 ± 20.5 mg/Dl, p =0.319) which is in contrary to **(Chertow *et al.*, 2000)**[7] in which concentration of prealbumin were 25.5 vs. 27.3 mg/dL (diabetic vs. not) and to **(Chertow *et al.*, 2005)**[8]. with serum prealbumin (30.5 vs. 33.3 mg/dL) this difference can be caused by profile of diabetic in our patients is less severe than in the previous studies and since we

do not the duration nor the severity of their patients we cannot exclude nor confirmed this explanation, another possible explanation is the lower sample size in our study (n=90) while in **(Chertow *et al.*, 2005).** the sample was 7519 patients, and in **(Chertow *et al.*, 2000).** it was 3009 patients.

In the current study prealbumin was correlated significantly with disease duration (r = 0.228) and with calcium (r = 0.248) while no significant correlation with nutritional variables was found (Age , BMI, albumin, vitamin D, Creatinine**,** GFR) this results was in disagreement with In **(Chertow *etal.*, 2000)** . which prealbumin correlated with albumin (r =-0.124), with Creatinine (r = -0.098), with body weight (r = -0.012), Vitamin D (r =-0.042), with age (r = 0.046) in which 22.1% of the variability of prealbumin was explained by albumin (which in our study 1.5% explained by albumin), this disagreement can caused by low sample size of our study leading to under power of detection.

Prealbumin which is known as "transthyretin" a 54 KD protein produced by the liver, its primary function thyroxin transporter and indirectly vitamin A, since it serves as a carrier for retinol-binding protein **(Spiekerman, 1993)**[9]. It has been shown that, prealbumin to increase with increases in protein and calorie intake and also to decrease as protein intakes become inadequate **(Spiekerman, 1993)**. Also, both albumin and prealbumin considered as Negative acute-phase reactant proteins. In which serum level of albumin and prealbumin decline in response to inflammation in the form of decreased synthesis **(Kaysen *et al.*, 2004)**[10] in addition to altered vascular permeability which affect the concentrations of these proteins. An advantage of prealbumin is its half-life as it is relatively short compared to albumin (approximately 2–3 days vs. 14–21 days) **(Chertow *et al.*, 2000)**. That's lead prealbumin to be more sensitive indicator of nutritional status than albumin **(Ingenbleek *et al.*, 1994)**[11].

Several studies shown that there is association between prealbumin and mortality **(Cano et al, 2002)**[12]**.** In which they found that a serum prealbumin with concentration <30 mg/dL at the initiation of dialysis increased risk of mortality in 258 dialysis patients (half of them on peritoneal, the rest on hemodialysis) as they follow them over 10 years, even after adjustment for multiple confounders. In an earlier study, prealbumin concentration <25 mg/dL were associated with mortality and after performing multivariable analysis it was significant only with prealbumin concentrations <20 mg/dL **(Chertow *et al.*, 2000)**.

A later study demonstrated a graded increase in the mortality risk at different level of prealbumin serum concentrations, however the risk started at serum prealbumin <40 mg/dL (however it was <30 mg/dL with multivariable adjustment), suggesting that optimal values are in excess of 30–40 mg/dL **(Chertow *et al.*, 2005)**. In the current study only 24% of our patients serum prealbumin above 40 mg/dL indicating 76% at increased risk of death unless it is corrected.

The lack of relationship between prealbumin and HsCRP (r = 0.029) which is in disagreement with previous studies like**, (Chertow *et al.*, 2005)** and **(Chertow *et al.*, 2000)**. a possible explanation that in our patients only 12.2% had low levels of HsCRP and state of high inflammatory status in evident that will lead to prolong reduction of prealbumin production **(Kaysen *etal.*,2004)**. so we hypnotized that in prolong inflammation status there is a loss of the relationship between prealbumin with HsCRP and this explain our contradictory findings.

In the current study the relationship between prealbumin and liver function (presented here as the liver enzyme ALT and AST) was direct and significant with both ALT (r = 0.228, p = 0.031) and AST (r = 0.218, p = 0.039) while no such relationship between albumin and liver enzyme was observed this indicate that prealbumin is better predictor and more sensitive indicator of hepatic dysfunction than albumin, this was in agreement with **(Chertow *et al.*, 2005)**. in which they pound prealbumin correlated with AST.

Moreover, further analysis showed that patients are malnourished independently whether they have inflammation or not. None of the patients have inflammation without being malnourished at the same time.

Correlation Study

In the current study prealbumin was correlateed significantly with disease duration (r = 0.228) and with calcium (r = 0.248) while no significant correlation with nutritional variables was found (Age , BMI, albumin, vitamin D, Creatinine, GFR). In the current study the relationship between prealbumin and liver function (presented here as the liver enzyme ALT and AST) was direct and significant with both ALT (r = 0.228, p = 0.031) and AST (r = 0.218, p = 0.039) while no such relationship between albumin and liver enzyme was observed this indicate that prealbumin is better predictor and more sensitive indicator of hepatic dysfunction than albumin.

The results of the current study show no significant relationship between vitamin D with pre-albumin in all the patients (r=0.044, p=0.677), in diabetic patients (r=0.137, p=0.358) and in non-diabetic patients (r=-0.007, p=0.962), also in the current study no significant correlation observed between vitamin D with serum albumin in all the patients (r=0.015, p=0.883), with diabetic patients only (r=-0.126, p=0.400) and in non-diabetic patients (r=0.071, p=0.643)[13]

Conclusion

Serum prealbumin was higher in male compared to female 36.8 vs. 29.3 mg/dl, but it was statistically not significant, while serum albumin was similar between genders

There was direct and significant relationship between disease duration and pre-albumin, and also significant and inverse relationship with protein in diabetic patients only.

There is an inverse significant logarithmic relationship between ALT and AST with prealbumin while no such relationship was found with albumin.

References

1 Raguso CA, Dupertuis YM, Pichard C, The role of visceral proteins in the nutritional assessment of intensive care unit patients. Curr Opin Clin Nutr Metab Care. 2003 Mar; 6(2):211-6.

2 Sullivan DH, Sun S, Walls RC. Protein-energy undernutrition among elderly hospitalized patients: a prospective study. JAMA. 1999;281:2013–9.

3 Sreedhara R, Avram MM, Blanco M, Batish R, Avram MM, Mittman N. Prealbumin is the best nutritional predictor of survival in hemodialysis and peritoneal dialysis. Am J Kidney Dis. 1996;28:937–42.

4 Mears E. Outcomes of continuous process improvement of a nutritional care program incorporating serum prealbumin measurements. *Nutrition*. 1996;12:479–84.

5 Garcia-de-Lorenzo A, Ortiz-Leyba C, Planas M, Montejo JC, Nunez R, Ordonez FJ, et al. Parenteral administration of different amounts of branch-chain amino acids in septic patients: clinical and metabolic aspects. *Crit Care Med*. 1997;25:418–24.

6 Mears E. Outcomes of continuous process improvement of a nutritional care program incorporating serum prealbumin measurements. Nutrition. 1996;12:479–84.

7. GM Chertow, K ACKERT, N L. LEW, et al. Prealbumin is as important as albumin in the nutritional assessment of hemodialysis patients. Kidney International, Vol. 58 (2000), pp. 2512–2517.

8 GM Chertow, DJ Goldstein-Fuchs, JM Lazarus, et al. Prealbumin, mortality, and cause-specific hospitalization in hemodialysis patients. sKidney International, Vol. 68 (2005), pp. 2794–2800.

9 SPIEKERMAN AM: Proteins used in nutritional assessment. Clin Lab Med 13:353–369, 1993

10 KAYSEN GA, DUBIN JA, MULLER HG, et al, FOR THE HEMO STUDY GROUP: Inflammation and reduced albumin synthesis associated with stable decline in serum albumin in hemodialysis patients. Kidney Int 65:1408–1415, 2004

11 INGENBLEEK Y, YOUNG V: Transthyretin (prealbumin) in health and disease: nutritional implications. Ann Rev Nutr 14:495–533, 1994

12 CANO NJ, ROTH H, APARICIO M, et al: for the French Study Group for Nutrition in Dialysis. Malnutrition in hemodialysis diabetic patients: Evaluation and prognostic influence. Kidney Int 62:593–601, 2002

13 Iguacel.G C et al,Vitamin D deficiency in dialysis patients: effect of dialysis modality and implications on outcome, J Ren Nutr. 2010 Nov;20(6):359-67. doi: 10.1053/j.jrn.2010.03.005. Epub 2010 May 26.