Independent Association Between Malnutrition Inflammation Score And C Reactive Protein/Albumin Ratio In Hemodialysis Patients

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Research Article

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Abstract

Objective

At this study we aimed to investigate relationship between Malnutrition Inflammation Score (MIS), C reactive protein /albumin ratio (CAR), albumin, CRP and other biochemical parameters at hemodialysis patients.

Design and Methods

66 ESRD patients on maintenance hemodialysis has been recruited to the study. MIS, biochemical parameters and CAR were analyzed.

Results

Statistically significant positive correlation was found between CAR and MIS≥7 (r=0.413, p=0.026), with CRP and MIS≥7 (r=0.388, p=0.038) and negative correlation was found with albumin and MIS (r=-0.511, p=0.005). For MIS, CAR, albumin and CRP a multiple regression ANOVA model was conducted to examine that relation of CAR, CRP, albumin on MIS (F=6.432, p=0.002). ANOVA model was found statistically significant (r=0.660, p=0.002). Variables CAR (p=0.003), albumin (p=0.008) and CRP(p=0.003) was found significant in the ANOVA model.

Conclusion

Our study showed first time in the literature that CAR is independently associated with MIS in HD patients.

Introduction

End stage renal disease (ESRD) and hemodialysis (HD) patients are characterized with chronic inflammatory status (1). Malnutrition is a common problem for HD patients, which its prevalence is reported between 28–54% globally (2). Inflammation and malnutrition are both concurrent and clinically important conditions at HD patients. Systemic inflammation may contribute to deterioration of nutritional status of HD patients by cytokine induced poor appetite, endotoxine and reactive oxygen species (ROS) production and metabolic derangements, leading to malnutrition and protein energy wasting (PEW). (3). PEW and inflammation are both associated with disease severity and mortality at HD patients. (4). Seemingly intertwined relationship between malnutrition and inflammation at ESRD has led to naming of malnutrition inflammatory complex syndrome at literature (5). However further evidence needed in regard to association between inflammation and malnutrition at HD patients.

Malnutrition Inflammation Score (MIS) is a validated nutritional assessment tool for chronic kidney disease (CKD). MIS components incorporates anthropometric measurements, biochemical data including albumin, serum total iron binding capacity (TIBC) and components of Subjective Global Assessment (SGA).

C reactive protein (CRP) is an acute phase protein that has a role in inflammatory processes. Albumin is an important plasma protein with anti inflammatory features. C reactive protein /albumin ratio (CAR) is a novel inflammation marker which is reported to associated with various conditions such as sepsis, nasopharyngeal carcinoma and non small cell lung cancer (6–8).

At this study we aimed to investigate relationship between MIS and inflammatory markers CAR, albumin and CRP at hemodialysis patients.

Material And Methods

Study was conducted at Ahi Evran University Faculty of Medicine Hemodialysis Unit Kirsehir, Turkey. 66 ESRD patients on maintenance hemodialysis three times a week for at least 3 months has been recruited to the study. All patients were receiving standard 4-hour hemodialysis with standard bicarbonate dialysate. Informed consent was obtained from all of the participants. Patients with malignancy, active infection, connective tissue disease, sepsis, hepatic insufficiency and other inflammatory diseases were excluded from the study. Study has been approved from Ahi Evran University Faculty of Medicine Research Ethics Committee (Decision Number 2020-19/145). The procedures followed were in accord with the Declaration of Helsinki. All participants signed an informed consent form approved by the Ahi Evran University Faculty of Medicine. All serum blood samples were obtained before beginning of the HD session and blood sample analysis was carried out with standard techniques. Anthropometric measurements were performed before the HD session. Body mass index (BMI) was calculated as body weight (kg)/body height squared (m2).

Malnutrition inflammation score criteria was based on Kalantar Zadeh et al. (9). MIS is consisted with 10 components including patient’s medical history, change in end dialysis dry weight, dietary intake, gastrointestinal symptoms, functional capacity, comorbid diseases, dialysis years, physical examination, assessment of patient’s fat store and muscle mass loss, BMI, laboratory parameters, serum albumin and serum total iron binding capacity measurement. Each component is evaluated with four severity levels ranging from 0 (normal) to 3 (very severe). Total score is sum of these 10 components ranging between 0 to 30. At present study malnutrition is defined with MIS $\geq$ 7 (10).

Statistical Analysis

Normally distributed numerical data are expressed as a mean ± standard deviation, appropriate statistical tests used to find correlations between variables, for nonparametric variables Spearman's Correlation Test was used, and for continuous variables Pearson's Correlations Test was used. Categorical data were analyzed with the chi-square test. The receiver operating characteristic (ROC) curve was used to calculate the area under the curve (AUC) and thereby identify a suitable cutoff value for MIS. For normality tests, standardized skewness and Shapiro-Wilk tests used before multivariate analysis. Multivariate ANOVA regression analysis was used to test the independent effects of said variables on MIS, according to the

constructed linear model. All statistical analysis performed using SPSS for Windows (version 25.0; SPSS Inc, USA). A P-value of < 0.05 was considered statistically significant.

Results

Mean age of the participants was 56.47 ± 17,3. %42 of the patients was male. %50 of the patients had malnutrition. 34% of the study group had heart failure, 33% had hypertension, 17% had diabetes mellitus, %24 had coronary artery disease. Descriptive characteristics of the patients has been shown at the Table 1.

Table 1
Descriptive characteristics of the study group (N = 66)

	Mean ± Std. Deviation		**Mean ± Std. Deviation**
Age	56.47 ± 17.3	BMI	24 ± 5
MIS	7.8 ± 0.4	Total Protein	6.9 ± 0.6
CAR	4.21 ± 9	Ferritin	270 ± 235
Albumin	3.5 ± 0.3	Uric Acid	6.6 ± 1
CRP	13.4 ± 24.2	Serum Iron	47 ± 21
Urea	151.1 ± 36.9	TIBC	232 ± 36
Creatinine	8.59 ± 2.85	Total Cholesterol	173 ± 62
White Blood Cell	6.8 ± 1.9	LDL	110 ± 60
Hemoglobin	10.54 ± 1.57	Triglyceride	177 ± 142
Platelet	208 ± 62	HDL	38 ± 9
Lymphocyte Count	1.5 ± 0.5	ALT	9.9 ± 6.8
Neutrophile Count	4.5 ± 1.5	AST	12 ± 6
RDW	14 ± 1.4	ALP	167 ± 117
RBC	3.7 ± 0.6	GGT	37 ± 55
MCV	90 ± 5.8	Calcium	9 ± 0.8
MPV	10 ± 1	Phosphorus	5.1 ± 1.6
Eosinophile	0.24 ± 0,2	Glucose	116 ± 60
Sodium	138 ± 3.8	Chloride	102 ± 4.3
Potassium	5.5 ± 0.8	Sedimentation	28 ± 29

Statistically significant positive correlation was found between CAR and MIS ≥ 7 (r = 0.413, p = 0.026), with CRP and MIS ≥ 7 (r = 0.388, p = 0.038) and negative correlation was found with albumin and MIS (r=-0.511, p = 0.005). MIS and hemoglobin were found negative correlated for MIS ≥ 7 (r=-0.412, p = 0.026). There was a negative correlation between creatinine (r=-0.568, p = 0.001) and positive correlation with ferritin (r = 0.584, p = 0.001) for MIS ≥ 7. Table 2 shows all said correlations.

Table 2
Correlations between Malnutrition Inflammation Score, CRP/Albumin Ratio and biochemistry parameters

MIS x VARIABLE	MIS < 7		MIS ≥ 7	
	R	p	R	p
CAR	.080	.664	.413	.026
Albumin	− .507	.003	− .511	.005
Total Protein	− .430	.014	.156	.393
CRP	.047	.798	.388	.038
Total Cholesterol	− .376	.036	− .220	.219
Serum Iron	− .393	.026	− .173	.337
MCH	.358	.030	.164	.232
Urea	− .287	.112	− .376	.044
Creatinine	− .164	.369	− .568	.001
RBC	− .310	.084	− .459	.012
Hemoglobin	− .296	.100	− .412	.026
MCV	.108	.557	.458	.012
Sodium	− .122	.508	.372	.047
Potassium	− .385	.018	− .520	.004
Triglyceride	− .069	.729	− .467	.011
Uric Acid	− .215	.238	− .372	.047
Ferritin	.072	.697	.584	.001

For testing the normality, standardized skewness and Shapiro-Wilk test indicated that data were statistically normal. For MIS, CAR, albumin and CRP a multiple regression ANOVA model was conducted to examine that relation of CAR, CRP, albumin on MIS (F = 6.432, p = 0.002). ANOVA revealed that there was a statistically significant relation between dependent and independent groups (for CRP p = 0.003, for

albumin p = 0.008, for CAR p = 0.003). Model summary, ANOVA results of the model and coefficients of the model are shown at Table 3,4,5 respectively.

Table 3
Model Summary

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.660[a]	.436	.368	2.68869
a. Predictors: (Constant), CRP/Albumin Ratio, Albumin, CRP				

Table 4
ANOVA results of the model

ANOVA[a]						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	139.481	3	46.494	6.432	.002[b]
	Residual	180.726	25	7.229		
	Total	320.207	28			
a. Dependent Variable: MIS						
b. Predictors: (Constant), CRP/Albumin Ratio, Albumin, CRP						

Table 5
Coefficients of the model, CAR (CRP/Albumin Ratio)

Coefficients[a]						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	31.537	7.315		4.311	.000
	CRP	.378	.117	3.891	3.237	.003
	Albumin	-5.813	2.014	− .624	-2.886	.008
	CAR	-1.051	.315	-4.091	-3.337	.003
a. Dependent Variable: MIS						

Discussion

At current study we found that there was a statistically significant correlation between CAR, CRP and albumin and MIS ($r = 0.413$ $p = 0.026$, $r = 0.388$ $p = 0.038$ and $r=-0.511$ $p = 0.005$ respectively). ANOVA showed that was a statistically significant independent correlation between MIS, CRP, albumin and CAR (for CRP $p = 0.003$, for albumin $p = 0.008$, for CAR $p = 0.003$). Lower albumin values, higher CRP and CAR values were found strong indicators for malnutrition in HD patients.

Malnutrition is an important phenomenon in HD patients which is responsible for adverse outcomes. Quality of life impairment, infection risk, progressive loss of body muscle and fat mass and mortality are associated with malnutrition (2,3,11). The etiology of malnutrition in ESRD is multifactorial, comprised by declining appetite, impairment of glucose and amino acid transport and metabolism, low diet quality, uremia, cytokine production, comorbidities and the dialysis procedure itself (3).

Low grade chronic systemic inflammation in which CKD patients are characterized by, is also a potential contributor to malnutrition development and progression. In HD patients, the development of inflammation is caused by various factors, including oxidative stress, uremic milieu, increased cytokine production and decrease of clearance of cytokines, dialysis procedure and infection frequency (4,12). The coexistence of malnutrition and inflammation suggests the potential relationship between these two aspects of ESRD, However the precise role of inflammation in the physiopathology of malnutrition and PEW is not totally elucidated (13). There several hypotheses regarding role of inflammation at malnutrition development in ESRD. Cytokine production affects the regulation of appetite resulting anorexia (14). Inflammation may enhance insulin resistance and impair glucose and amino acid transport metabolism (3). Resting energy expenditure is reported to be raised because of inflammatory status, contributing to muscle mass loss (13). Anabolic hormone resistance caused by inflammation also prompts catabolism (15).

While there are studies to show the relationship between SGA and inflammatory markers such as CRP, adinopectine, IL-6 in HD patients (16–18), studies about the association between MIS and CAR in HD patients are lacking. Our study is the first study in the literature to show an independent association between CAR and MIS in HD patients.

Association between CRP, albumin and MIS in CKD has been reported by number of studies. Aggarwal et al. has found an association between MIS and inflammatory markers CRP and albumin, negative correlation for albumin ($p < 0.01$) and positive correlation for CRP ($p < 0.01$) in CKD stage 3 to 5 (19). At a study conducted at pre-dialysis CKD patients, it has been reported that patients with MIS ≥ 7 had significant increase in Hs-CRP levels ($p < 0.001$), albumin was negative correlated with MIS in the same research (20).

Considering the studies on the HD patient group, Ashabi et al. has found positive correlation between serum CRP and MIS ($p < 0.01$) and negative correlation between albumin and MIS ($p < 0.01$) (21). Another study has reported that CRP level ($\beta = 3.33$, $P < 0.001$), and albumin level ($\beta = -1.95$, $P = 0.008$) were factors independently associated with MIS at HD patients (22) Martins et al. has found that higher CRP (OR 1.01 $p < 0,001$) were independently associated with a higher risk of MIS > 5 (23). Similar results have

been reported by another study, CRP levels had an association with MIS (B = -0.56; P = 0.0001) (24). In our study we found that CRP and CAR are positive correlated and alb is negative correlated with MIS in HD patients.

Literature also comprises conflicting results regarding relation of MIS, CRP and albumin in HD patients. Pisetkul et al. did not found a correlation between hs-CRP and MIS at hemodialysis patients (r = 0.08, p 0.44) (25). Different study has reported that albumin was not significantly correlated statistically with MIS in HD patients. (-0.189 p = 0.345) (26). At the research of Ekremzadeh et al, albumin was not statistically significant between two MIS groups ≥ 10 and < 10, in HD patients (15). Another study conducted in HD patients has found that while albumin level was lower when MIS ≥ 8 (p < 0.001), CRP levels did not differ between two MIS groups (27).

CAR is a novel inflammation index that has been emerged in recent years and it has been reported recently that it can better reflect the inflammation status compared to other markers (28). In current study, multiregression analysis showed that CRP, CAR, ALB were independently associated with MIS. Our research demonstrates statistically significant independent positive correlation between CAR and MIS, CRP and MIS and negative correlation between MIS and albumin. Interesting feature of our study is this is the first time in the literature that shows a strong relation between CAR and MIS in HD patients. Our findings indicate that CAR can be reliable and practical measurement for assessing nutritional status of HD patients.

Precise nutritional status assessment and to be able to detect PEW before related complications emerge are two crucial aims for management of malnutrition in maintenance HD patients. CAR can be used as valuable tool for predicting and screening of PEW and malnutrition risk in HD patients.

Sample size was a possible limitiation in our research. More studies with wider sample size are needed for this topic. At present study, we investigated the relationship between MIS and inflammation markers CAR, CRP, albumin and other biochemistry parameters at HD patients. Interesting feature of our research is that our study showed first time in the literature that CAR is independently associated with MIS in HD patients.

Conclusion

At present study, we investigated the relationship between MIS and inflammation markers CAR, CRP, albumin and other biochemistry parameters at HD patients. Interesting feature of our research is that our study showed first time in the literature that CAR is independently associated with MIS in HD patients.

Declarations

Conflict Of Interest Statement: The authors declared that they have no conflicts of interest to this work. We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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