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SERUM LEPTIN LEVEL AND ITS RELATIONSHIP WITH CONVENTIONAL LABORATORY AND ANTHROPOMETRIC INDICES OF MALNUTRITION IN PATIENTS ON MAINTENANCE DIALYSIS.

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ABSTRACT

Background: Nutrition is one of the key parameters in predicting morbidity and mortality in patients with end stage renal disease (ESRD) on dialysis, Body weight, BMI, visceral protein level (serum protein, albumin, and transferrin) has traditionally been used as markers for nutritional status. Serum leptin has been recently added to the list of markers of nutritional status. It has been reported that serum leptin levels are high in patients with ESRD patients. Objective: The purpose of the present study was to measure serum leptin level and to study the relationship between serum leptin concentration, anthropometric measurements and laboratory markers of malnutrition in patients diagnosed as end stage renal disease on maintenance dialysis (HD/ CAPD). Methods: This cross sectional study was conducted from April 2017 to March 2018 in the Department of Nephrology at Bangabandhu Sheikh Mujib Medical University, Dhaka. Adult patients with chronic kidney disease stage 5 on dialysis (HD and CAPD) for > 3 months were included. Modified SGA was used where score <10 is normal, >10was taken as malnutrition. Skin fold thicknesses, body mass index (BMI) and mid arm muscle circumference (MAMC) were calculated for anthropometry. Laboratory parameter like hemoglobin, serum creatinine, albumin, leptin, lipid profile, iron profile was done. Result: Serum leptin level of CAPD patients was higher when compared with those of HD patients. Serum leptin level significantly correlated positively with duration of dialysis, and serum creatinine in both groups and with age, BMI only in HD group. Conclusion: Based on above observations, we conclude that serum leptin level correlates with several malnutrition markers such as BMI, duration of dialysis, serum creatinine, serum iron.

KEYWORDS: Serum leptin, Anthropometry, Malnutrition, End stage renal disease (ESRD), Maintenance dialysis (HD/ CAPD).

INTRODUCTION

Chronic kidney disease (CKD) is equally affecting the people of developed countries as well as developing countries. The prevalence of CKD is rapidly increasing globally. In developed countries it is 13%;^[1] however, in developing countries, population based studies on the prevalence of CKD are limited.^[2]

Kidney functions can only be partly replaced by maintenance dialysis.^[3] Protein-energy malnutrition is a

common problem in dialysis patients. According to the studies, 40-70% of end-stage renal-disease (ESRD) patients are malnourished.^[4] Malnutrition causes increase morbidity and mortality as a result of accompanying infection and cardiovascular diseases.^[5]

Generally, there are multiple causes contributing to malnutrition in dialysis patients. These include anorexia, restricted diet, metabolic acidosis, gastroparesis, appetite suppression as a side effect of the drugs, chronic volume overload, presence of an acute or chronic systemic diseases which cause inflammatory responses and dialysis itself.^[6]

One of the causes of malnutrition is anorexia which may have different reasons such as inadequate dialysis, medications, gastroparesis, elevated serum leptin level etc.^[7]

Leptin is a 16-kDa protein hormone and a product of obesity gene (ob) which is produced exclusively by adipocytes and its main effect on hypothalamus that decreases appetite, increases energy expenditure, and reduces weight.^[8,9]

The exact reason of serum leptin level elevation in ESRD is not known and factors like decrease in renal clearance, chronic inflammation have been thought to be the contributing factors.^[9] Some studies showed a positive correlation between serum leptin and some malnutrition parameters.^[10,11,12,13] But this correlation was not seen in one of them.^[14] On the contrary, leptin was introduced as a marker of good nutritional status in hemodialysis patients in another study.^[15]

Due to the different results of studies, the definite role of leptin as a marker of malnutrition in dialysis patient is not definite. So this study is designed to investigate the correlation between serum leptin level and malnutrition parameters in dialysis patients.

METHODOLOGY

This cross sectional study was conducted from April 2017 to March 2018 in the Department of Nephrology at Bangabandhu Sheikh Mujib Medical University, Dhaka. A total 70 Adult patients with chronic kidney disease stage 5 on dialysis (HD and CAPD) for > 3 months were included. After getting Institutional review board approval subjects were selected on the basis of enrollment criteria. Written informed consent was taken from all patients.

Procedures

Modified SGA was used where score <10 is normal, >10 was taken as malnutrition. Skin fold thicknesses, body mass index (BMI) and mid arm muscle circumference (MAMC) were calculated for anthropometry. Laboratory parameter like hemoglobin, serum creatinine, albumin, leptin, lipid profile, iron profile was done.

- Nutritional status was assessed by using a modified quantitative subjective global assessment of nutrition for dialysis patients (Malnutrition score)
- The demographic information (age, sex, duration of dialysis, h/o drugs, etc) clinical examination findings and investigations reports were recorded in the preformed data collection sheet.
- Anthropometry in maintenance dialysis patients were assessed between 10- 20 mins after termination

of dialysis session. According to National Health and Nutrition Examination Survey 3 anthropometry of Mid Arm Circumference (MAC) and skin fold thickness was done by the following way. Mid Arm Muscle Circumference (MAMC), Biceps skin fold and Triceps skin fold thickness was measured on non fistula arm. Mid point between upper edge of posterior border of acromion process and tip of olecranon process were marked. This was the site for measuring mid arm circumference (MAC) and triceps skin fold thickness (TSF). All skinfold were measured with the skinfold caliper. Mid Arm Muscle Circumference (MAMC) was calculated from the equation-

 $MAMC = MAC - (3.1415 \times TSF).$

- 10 ml of blood was taken from maintenance dialysis patients at the starting of dialysis from arterial line for biochemical parameter.
- Serum leptin was measured by using enzyme linked immunosorbent assay method by human leptin ELISA Kit (YL biont, Shanghai, China)
- After the measurement of leptin, adjusted leptin was calculated by dividing serum leptin by body mass index (BMI).

Statistical analysis: Computer based statistical analysis was carried out with appropriate techniques and systems. All data were recorded systematically in preformed data collection form. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. Statistical analyses were performed by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-21) (SPSS Inc, Chicago, IL, USA). To evaluate the correlation of variables considering whether they are quantitative or qualitative and type of their correlation parametric statistical tests (analysis of variance, ANOVA, T-test, and pearson's test) and nonparametric statistical tests (Mann- Whitney and Spearmans test) was used. For all statistical tests, we were considered p value <0.05 as statistically significant.

Ethical implication

Prior to the commencement of this study, the research protocol was approved by the Institutional review board (IRB) of BSMMU, Dhaka. The aims and objectives of the study along with its procedure, risks and benefits of this study will be explained to the patients in easily understandable local language and then informed consent (appendix) will be taken from each patient. It will be assured that all information and records will be kept confidential and the procedure will be helpful for both the physician and the patients in making rational approach of the case management. The data collected will be solely used for the research purpose. Patient has the right to withdraw from the research at any time without explanation or prejudice and to withdraw any unprocessed data previously supplied.

RESULTS

Table I: Comparison of serum leptin and adjusted serum leptin level between normal nutrition and malnutrition (n=70).

	Normal nutrition (n=39)	Malnutrition (n=31)	p-
	[Median (min-max)]	[Median (min-max)]	value
Serum Leptin (ng/ml)	5.56 (2.70-24.45)	6.41 (3.87-58.72)	0.083
Adjusted Serum Leptin	0.23 (0.13-0.99)	0.30 (0.10-2.20)	0.020

Mann-Whitney U test was done to measure the level of significance.

Table I shows comparison of serum leptin level and adjusted serum leptin level between normal nutrition and

malnutrition. Both serum leptin level and adjusted leptin level were increased in malnourished group.



Figure 1: Bar diagram showing distribution of study population according to BMI in different dialysis groups.

Figure 1 shows that among the patients with low BMI, more patients are in CAPD group and among the patients with over nutrition more patients are in HD group.

Nutritional status	HD (n=55) [n(%)]	CAPD (n=15) [n(%)]	p-value
Normal (MS 7 - 10)	34 (61.8)	5 (33.3)	0.049
Malnutrition (MS 11 - 35)	21 (38.2)	10 (66.7)	

Chi-square test was done to measure the level of significance MS – Malnutrition score.

Table II shows comparison of nutritional status in different dialysis group. Malnourished patients were

significantly higher in CAPD group (66.7%) compared to HD group (38.2%).

Table III: Anth	ropometric	parameters	of malno	urished g	roups of n	naintenance	dialysis	patients (n=31)
		363							

	Malnourished patients on HD (n=21) [mean±SD]	Malnourished patients on CAPD (n=10) [mean±SD]	P value
BMI (kg/m2)	22.96 ± 5.02	22.78 ± 2.65	0.916
BSF (mm)	13.95 ± 6.17	11.60 ± 2.46	0.258
TSF (mm)	17.38 ± 7.34	19.20 ± 4.34	0.476
MAC (cm)	26.79 ± 4.73	26.00 ± 4.57	0.665
MAMC (cm)	20.92 ± 3.01	19.96 ± 3.93	0.474

Unpaired student's t-test was done to measure the level of significance.

Table III shows anthropometric parameters of malnourished groups of maintenance dialysis patients. BMI, BSF, MAC, MAMC were higher in malnourished

HD group and TSF was higher in malnourished CAPD group. But the results were not statistically significant.

Table IV: Con	parison of laboratory para	ameters of	malnourishe	d HD and	CAPD	patient	ts (n=31)
		363		3.6.1	• 1	1	

	Malnourished patients on HD (n=21) [mean±SD]	Malnourished patients on CAPD (n=10) [mean±SD]	p-value
Hb (gm/dl)	9.51 ± 1.48	10.05 ± 1.26	0.357
Serum creatinine (mg/dl)	9.15 ± 2.50	12.80 ± 9.14	0.110
Serum albumin (gm/L)	35.16 ± 5.43	24.20 ± 9.39	<0.001
Serum ferritin (ng/ml)	1334.08 ± 844.10	870.80 ± 361.87	0.123
Serum iron (µg/dl)	81.38 ± 66.96	96.00 ± 50.03	0.571
TIBC (µg/dl)	184.83 ± 38.71	150.70 ± 61.39	0.128
Choleterol (mg/dl)	161.44 ± 42.50	145.00 ± 30.58	0.282
LDL (mg/dl)	98.78 ± 30.22	100.60 ± 26.75	0.875
HDL (mg/dl)	45.39 ± 10.53	40.40 ± 3.37	0.160
TG (mg/dl)	142.00 ± 81.34	81.00 ± 13.22	0.028

Unpaired student's t- test was done to measure the level of significance.

Table IV shows comparison of laboratory parameters of malnourished HD and CAPD patients. Serum albumin and serum triglyceride were significantly lower in malnourished patients on CAPD group compared to malnourished patient on HD group.

Table	V:	Correlation	of sei	rum l	leptin	with	demographic,	anthropometric	and	laboratory	parameters	of	the
malno	uris	hed HD pati	ients (r	n=21).	•								

	Malnutrition			
	r value	p value		
Age	0.549	0.018		
BMI	0.809	<0.001		
Duration of dialysis	0.711	0.001		
BSF	0.548	0.019		
TSF	-0.125	0.620		
MAC	0.322	0.193		
MAMC	0.285	0.303		
Hb	0.586	0.035		
Serum creatinine	0.658	0.003		
Serum Albumin	0.266	0.287		
Serum Ferritin	-0.020	0.955		
Serum Iron	0.094	0.773		
TIBC	0.507	0.111		
Choleterol	-0.256	0.305		
LDL	-0.128	0.613		
HDL	-0.066	0.796		
TG	-0.214	0.393		

Pearson's correlation was done to measure the level of significance.

Table V shows correlation of serum leptin with demographic, anthropometric and laboratory parameters of the malnourished HD patients. Serum leptin level was positively correlated with age, duration of dialysis, BMI, BSF and serum creatinine.

	Malnutrition				
	r value	p value			
Age	0.495	0.146			
BMI	-0.034	0.926			
Duration of dialysis	0.992	<0.001			
BSF	-0.023	0.950			
TSF	-0.347	0.326			
MAC	-0.160	0.658			
MAMC	-0.062	0.865			
Hb	-0.800	0.005			
Serum creatinine	0.882	<0.001			
Serum Albumin	-0.344	0.330			
Serum Ferritin	0.016	0.965			
Serum Iron	0.652	0.041			
TIBC	0.272	0.448			
Choleterol	-0.418	0.230			
LDL	-0.626	0.053			
HDL	-0.536	0.110			
TG	-0.322	0.365			

Table VI: Correlation of serum leptin with demographic, anthropometric and laboratory parameters of the malnourished CAPD patients (n=10).

Pearson's correlation was done to measure the level of significance.

Table VI shows correlation of serum leptin with demographic, anthropometric and laboratory parameters of the malnourished CAPD patients. Serum leptin level was positively correlated with duration of dialysis, serum creatinine and serum iron.

DISCUSSION

This cross sectional study was carried out with an aim to measure serum leptin level and to study the relationship between serum leptin concentration, anthropometric measurement and laboratory markers of malnutrition in patients diagnosed as end stage renal disease treated with dialysis (HD/ CAPD).

A total 70 patients were included in this study, out of which 55 patients were in the maintenance hemodialysis (HD) group and 15 patients were in the continuous ambulatory peritoneal dialysis (CAPD) group. The study was carried out in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka from April 2017 to March 2018.

The present study demonstrated that malnutrition status was higher in CAPD group (66.7%) than HD group (38.2%). Cianciaruso B et al.^[16] showed significantly greater proportion of malnourished CAPD patients than MHD patients (42.3 % vs.30.8 %).

In this study, serum leptin concentration was significantly higher in CAPD group than HD group. Johansen K L et al.^[17] found that mean serum leptin concentration was significantly higher in CAPD group than HD group.

In this study, anthropometric parameters like BMI, BSF, MAC, MAMC were higher in malnourished HD group

and TSF was higher in malnourished CAPD group. But the results were not statistically significant. On the other hand laboratory parameters like serum albumin and serum triglyceride were significantly lower in malnourished patients on CAPD group compared to malnourished patient on HD group.

In this study, serum leptin had statistically significant positive correlation with age, BMI, duration of dialysis, BSF, serum Hb, serum creatinine in malnourished HD patients. On the other hand , in CAPD group, Serum leptin had statistically significant positive correlation with duration of dialysis, serum creatinine, serum iron, serum hemoglobin and negative correlation with serum LDL in malnutrition patients. Bossola et al.^[10], Kayardi et al.^[11] had found almost same correlation with serum lobansen K.L et al.^[17] showed no correlation with serum leptin level.

CONCLUSION

This cross sectional study demonstrated that serum leptin levels are greater in CAPD patients than patients on HD. Significant correlations were found between serum leptin and age, duration of dialysis, BMI, serum creatinine and serum iron.

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