

Serum leptin levels and malnutrition in patients with chronic renal failure

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ABSTRACT

Objectives: To investigate the correlation between serum leptin levels, body mass index, and triceps skin fold thickness, which are anthropometric measurements, as well as serum albumin levels in patients with chronic renal failure on hemodialysis.

Methods: We studied 75 patients (48 males, 27 females; ages between 18-82) at the Hemodialysis Unit, Cumhuriyet University Medical School; Private Sivas Dialysis Center; Hemodialysis Unit, Sultan Izzettin Keykavus Hospital; and the Hemodialysis Unit, SSK Sivas Hospital between January 2003 and February 2004. Patients were excluded if they had been on dialysis for less than one year, if they were anuric, or if they had been on dialysis with jugular or subclavian catheter and long-term permanent port catheter. Similarly, patients with diabetes mellitus, chronic pulmonary disorders, and hepatic cirrhosis or hepatitis B, hepatitis C carriers as well as those on active tuberculosis therapy were excluded. C-reactive protein was measured in all patients and those with above normal values were excluded.

Results: While the mean age for the males was 44.52 ± 16.53 years (18-77), it was 48.29 ± 14.32 years (22-82)

for the females. The mean triceps skin fold thickness for males was 6 ± 1.81 mm (3-11.3 mm), and for females, it was 14.07 ± 8.79 mm (4.3-33.3 mm). The mean body mass index for males was 20.77 ± 2.61 kg/m² (14.8-26.6 kg/m²), and for females, it was 25.36 ± 6.47 kg/m² (17.3-42.2 kg/m²). The mean serum leptin level for males was 4.61 ± 4.20 ngr/dl (0.1-18.7 ngr/dl), and for females, it was 52.06 ± 61.67 ngr/dl (0.6-172.5 ngr/dl). A positive correlation was observed between triceps skin fold thickness and leptin, both in the male group ($r=0.478$; $p<0.05$), and in the female group ($r=0.876$; $p<0.05$). Body mass index and leptin were also correlated positively both in the male group ($r=0.502$; $p<0.05$) and in the female group ($r=0.905$; $p<0.05$). No correlation was established between serum albumin levels and leptin. Leptin did not correlate with other measured parameters

Conclusion: Our study demonstrates that serum leptin levels positively correlated with body mass index and triceps skin fold thickness, which are malnutrition parameters. Therefore, the leptin hormone may be utilized in obtaining preliminary information regarding malnutrition.

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Malnutrition is more frequent in patients with chronic renal failure than it is in healthy individuals. Patients with malnutrition have higher mortality, and morbidity rates.^{1,2} Therefore, detecting malnutrition early and providing the required therapy is of vital importance. Various parameters are utilized in detecting malnutrition such as serum albumin,

transferrin level, and prealbumin level, as well as certain anthropometric measurements. However, none of these can provide definite and sufficient information on their own.^{3,4} The hormone called leptin is secreted from the fat tissue. It was first proposed in 1953 that it could be a marker of fat tissue regulation.⁴ Later, Zhang et al⁵ isolated the leptin hormone in 1994. The

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human leptin is localized on chromosome 7q31, and the 16 kilo Dalton leptin is made up of 167 amino acids.^{6,7} Leptin levels are sensitive to gender, active infections or pathologies, which are accompanied with acute phase response, hepatic failure and diabetes. Furthermore, hunger status has an impact on leptin levels. Serum leptin levels can be a clinical marker in the diagnosis and follow up of malnutrition in hemodialysis patients with chronic renal failure. This present study investigates the correlation between serum leptin levels, body mass index (BMI), and triceps skin fold thickness, which are anthropometric measurements, as well as serum albumin levels in hemodialysis patients with chronic renal failure.

Methods. The 75 patients enrolled in the study were on hemodialysis at the Cumhuriyet University Medical School Hemodialysis Unit, Private Divas Dialysis Center, Sultan Izzettin Keykavus Hospital Hemodialysis Unit, and the SSK Sivas Hospital Hemodialysis Unit. In these 3 hemodialysis units, the same dialysis membrane (hemaphrein dialyzer membranes) was used. Patients who were on hemodialysis for less than a year were excluded. All patients who were included in this study were anuric, to rule out the possibility of protein loss in urine. The exclusion criteria included patients who could pass urine, patients who had been on dialysis with jugular or subclavian catheter and long-term permanent port catheter, and patients with diabetes mellitus, severe infections, malignancy or major surgery in 6 months prior to the study, chronic pulmonary disorders, and hepatic cirrhosis or hepatitis B, hepatitis C carriers as well as those who were on active tuberculosis therapy. The C-reactive protein (CRP) was measured in all the patients and those with values above normal were excluded. After obtaining a detailed anamnesis on each patient enrolled, they were informed regarding the study. The patients were told that their blood samples were going to be taken and, therefore, not to exercise heavily, smoke or consume alcohol on the preceding day, fast overnight, and carry on taking their routine medicines, to keep their blood test results accurate. The patients' height, weight, BMI, and triceps skin fold thickness were established. A total of 10 cc venous fasting blood sample was drawn between 8:00 and 9:00 am, before going into dialysis from all the patients to establish serum leptin levels and other parameters. The blood were set aside for serum leptin levels was centrifuged within an hour, and was kept deep-frozen at -20°C. The other parameters were also established within the same day by using the blood samples set aside for that purpose. The BMI was calculated by dividing

weight in kilograms by height square in meters. Triceps skin fold thickness measurement was taken from the arm's dorsal surface at halfway between the acromion process and olecranon process by utilizing a Harpenden Skin-fold Caliper of 1/10 sensitivity by taking the mean value of at least 3 measurements of 15 second-intervals. The arm without fistula was chosen for this measurement. Serum leptin level was measured by radioimmunoassay through employing a DPC Gambyt-CR (Japan) gamma counter at the Department of Nuclear Medicine. The DSL-23100 RCA (Diagnostic systems Lab, USA) kit was used for serum leptin levels.

The SPSS statistics software was utilized to assess the results. Quantitative results were reported as the mean \pm SD. Pearson's correlation coefficients were used in comparing the parameters.

Results. Of the 75 enrolled patients who had been diagnosed with chronic renal failure, 48 (64%) were male and 27 (36%) were female. The age range for the male patients was 18-77 years, and the mean age was 44.52 ± 16.53 years. The female patients' age range was 22-82 years, and the mean age was 48.29 ± 14.32 . **Table 1** summarizes the leptin and anthropometric values for all patients. The biochemical parameters and mean values are shown in **Tables 2 & 3**. Both mean hemoglobin, and hematocrit values were found to be low in both male and female groups. However, platelet values were within normal limits in both groups. Hemoglobin and hematocrit values were not correlated significantly with triceps skin fold thickness, BMI and leptin values. Total protein and albumin values were not significantly correlated with leptin values. Duration of dialysis ranged from 1-17 years, and the mean score was 6.37 ± 3.97 years for the male group. The range in the female group was from 1-13 years, and their mean score was 5.11 ± 3.71 years. Duration of dialysis was not found to be correlated with leptin values. As shown in **Figures 1 & 2**, both triceps skin fold thickness and BMI correlated positively with serum leptin levels both in the male group and in the female group, and the correlation was observed to be stronger in the female group. However, there was a weak correlation between serum leptin levels and albumin values in the female group ($r=0.288$; $p<0.05$). However, the same value was $r=0.244$ ($p<0.05$) in the male group, therefore, the correlation was not significant.

Discussion. Malnutrition is a major co-morbid condition in people with chronic renal failure. Malnutrition rates are very high despite efforts to provide nutritional support for chronic renal failure

Table 1 - Leptin and anthropometric values.

Parameters	Female	Male	Mean score (female)	Mean score (male)
Triceps skin fold thickness (mm)	4.3 – 33.3	3 – 11.3	14.07 ± 8.79	6 ± 1.81
Body mass index (kg/m ²)	17.3 – 42.2	14.8 – 26.6	25.36 ± 6.47	20.77 ± 2.61
Leptin (ngr/dl)	0.6 – 172.5	0.1 – 18.70	52.06 ± 61.67	4.61 ± 4.20

Table 2 - Biochemical parameters and mean values in the male group.

Parameters	Borderline values	Mean value	Normal value
Hemoglobin (gr/dl)	5.3 - 13.6	10.62 ± 1.96	12 - 16
Hematocrit (%)	15.6 - 45.4	32.33 ± 6.41	37 - 47
Platelet (x10 ³ /mm ³)	66 - 431	182.56 ± 69.53	150 - 400
blood urea nitrogen (mgr/dl)	16 - 148	70.12 ± 25.43	7 - 21
Creatinine (ngr/dl)	3.6 - 17.3	9.82 ± 2.88	0.5 - 1
Potassium (mmol/l)	3.4 - 7.9	5.41 ± 1.07	3.5 - 5
Calcium (mgr/dl)	7 - 11.9	8.96 ± 0.95	8.4 - 10.8
Phosphorus (mgr/dl)	2.1 - 9	4.96 ± 1.6	3 - 4.5
Total protein (gr/dl)	4.8 - 9.4	6.57 ± 0.71	6.3 - 8.4
Albumin (gr/dl)	2.9 - 4.7	3.66 ± 0.35	3.5 - 5.5

Table 3 - Biochemical parameters and their mean values in the female group.

Parameters	Borderline values	Mean value	Normal value
Hemoglobin (gr/dl)	6 - 14.1	10.21 ± 1.92	12 - 16
Hematocrit (%)	17.2 - 44.3	32.33 ± 6.41	37 - 47
Platelet (x10 ³ /mm ³)	72 - 396	180.66 ± 67.42	150 - 400
BUN (mgr/dl)	17 - 156	71.02 ± 23.39	7 - 21
Creatinine (ngr/dl)	3.5 - 18.1	9.92 ± 2.70	0.5 - 1
Potassium (mmol/l)	4.1 - 7	5.17 ± 0.77	3.5 - 5
Calcium (mgr/dl)	7.1 - 13.4	9.15 ± 1.48	8.4 - 10.8
Phosphorus (mgr/dl)	2.2 - 7.7	4.08 ± 1.32	3 - 4.5
Total protein (gr/dl)	5.9 - 8.8	6.85 ± 0.61	6.3 - 8.4
Albumin (gr/dl)	2.9 - 4.9	3.62 ± 0.36	3.5 - 5.5

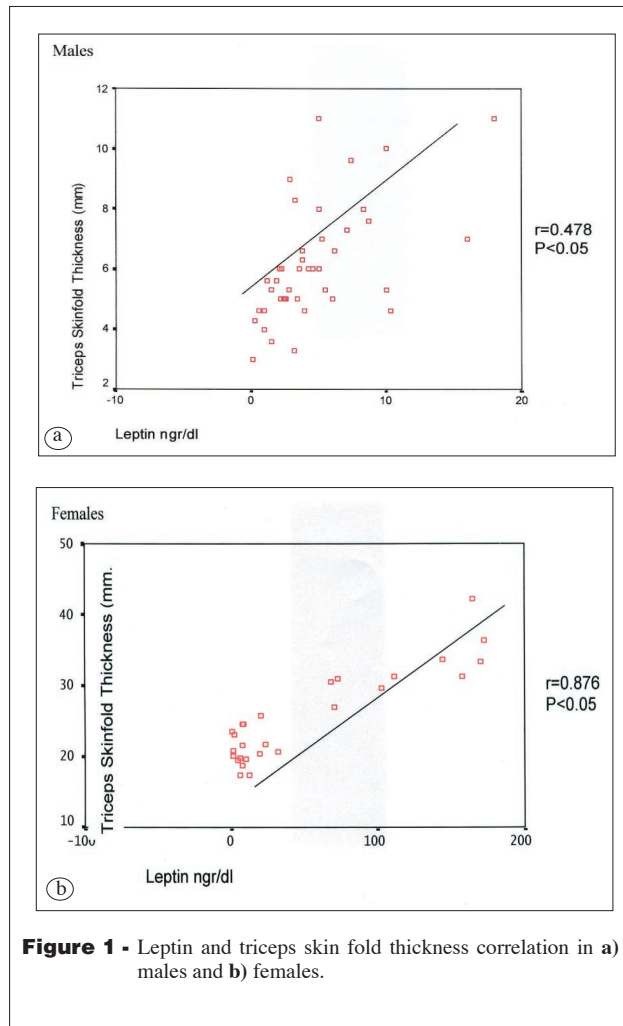


Figure 1 - Leptin and triceps skin fold thickness correlation in a) males and b) females.

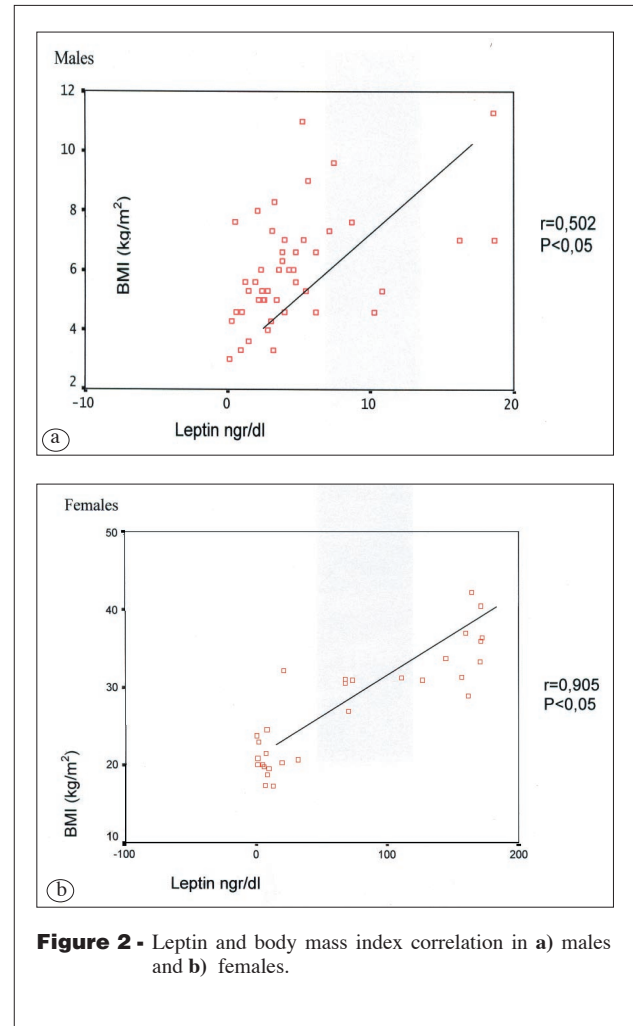


Figure 2 - Leptin and body mass index correlation in a) males and b) females.

patients with malnutrition.⁸ Approximately 40% of dialysis patients suffer from varying degrees of malnutrition, which is a problem of vital importance. In fact, many studies assessing nutritional status associate increased morbidity and mortality with malnutrition.^{9,10} Protein limitation recommended to curb the reduction in glomerular filtration rate in the final step before end-stage renal failure also contributes to the decline in nutritional status. The studies on leptin have shown that it is not only a food intake regulator or satiety hormone, but it also has certain other functions in the body.^{11,12} Study results proposed that leptin might play a role on loss of appetite and cachexia, induced by chronic or malign diseases and infections.

A previous study failed to establish a correlation between serum leptin levels and metabolic alterations, such as anemia, metabolic acidosis, and uremia observed in chronic renal failure.¹³ Likewise, our study did not establish a correlation between

serum leptin levels and hemoglobin, hematocrit, and platelet levels. In addition, no correlation was observed between serum leptin levels and blood urea nitrogen (BUN), creatinine, phosphorus, potassium and depressed calcium levels, which are predicted laboratory results in patients with chronic renal failure. Studies investigating the correlation between serum levels and total protein and albumin levels proposed that increased serum leptin level was associated with elevated albumin levels, and that the correlation was stronger in peritoneal dialysis patients.^{14,15} Our study did not reveal a correlation between serum leptin levels, and albumin and total protein levels. Only hemodialysis patients were enrolled in the study. Peritoneal dialysis patients might reveal a correlation. The main reason could be the fact that means dialysis period of the patients in our study was 5-6 years, whereas half-life of albumin is only 20 days. Albumin could be of use in assessing short-term malnutrition. Considine et al¹¹ demonstrated that serum leptin

concentrations were correlated with BMI as well as body fat percentage. The correlation between leptin and body fat mass is stronger in patients with chronic renal failure when compared with those with normal renal functions.¹⁴ Triceps skin fold thickness was regarded as an indicator of body fat mass and a positive correlation was observed between serum leptin levels and triceps skin fold thickness, with a stronger positive correlation in the female group. A study carried out on rats demonstrated that plasma leptin clearance was primarily by the kidney.¹⁵ The fact that leptin did not exist in normal urine in this study indicated that leptin was completely catabolized in the kidney. Small and varying amounts of leptin present in the patients' urine may be a predictor of low molecular weight proteinuria that can be observed in potential renal failure. Since, the patients enrolled in the present study had renal damage, presence of leptin in their urine was predicted. Therefore, only anuric patients were enrolled. Previous study discovered significantly higher serum leptin levels in patients with chronic renal failure when compared with the controls. Although western blot analysis helped them to differentiate active and inactive leptin forms, they demonstrated that leptin accumulated in chronic renal failure patients was as natural protein.¹⁶ Many studies compared serum leptin levels in hemodialysis patients with those of healthy individuals, higher leptin levels in hemodialysis patients.^{14,16,17} Merabet et al¹⁸ proposed that impaired renal elimination alone could not be accountable for elevated leptin levels in patients with chronic renal failure as their study demonstrated low leptin levels in 2 surgically anephric individuals. We demonstrated a significant positive correlation between serum leptin level and BMI, as well as with triceps skin fold thickness. However, the correlation was stronger in the female group in both cases. This could be as mean BMI and triceps skin fold thickness values were higher in the female group. Alternatively, a higher incidence of smoking in the male group could also have led to this result.

In conclusion, there is a strong correlation between serum leptin levels and BMI and triceps skinfold thickness, markers of malnutrition, in patients on long-term hemodialysis. No significant correlation was observed between serum leptin levels and serum albumin levels. Serum leptin levels could be utilized as a malnutrition marker in evaluating malnutrition in hemodialysis patients. However, serum albumin levels may not provide adequate information in evaluating long-term malnutrition.

References

1. Naber THJ, Schermer T, de Bree A. Prevalence of malnutrition in nonsurgical hospitalized patients and its association with disease complications. *Am J Clin Nutr* 1997; 1232-1239.
2. Halsted HC. Malnutrition and nutritional assessment in Harrison's principles of internal medicine. In: Braunwald E, Fauci SA, Hauser SL, Longo LD, editors. USA: McGraw-Hill Comp; 2001. p. 455-478.
3. Aktüel Tıp Dergisi: Nütrisyon sayısı 1 ve 2; 1998.
4. Kennedy GC. The role of depot fat in the hypothalamic control of food intake in the rat. *Proc R Soc Lond B Biol Sci* 1953; 140: 578-596.
5. Zhang F, Basinski MB, Beals JM, Briggs SL, Churgary LM, Clawson DK, et al. Crystal structure of the obese protein leptin -E100. *Nature* 1997; 387: 206-209.
6. Caro JF, Sinha MK, Kolaczynski JN, Zhang PL, Considine RV. Leptin: The tale of an obesity gene. *Diabetes* 1996; 45: 1455-1462.
7. Tritos NA, Mantzoros CS. Leptin; its role in obesity and beyond. *Diabetologia* 1997; 40: 1371-1379.
8. Norton PA. Affect of serum leptin on nutritional status in renal disease. *J Am Diet Assoc* 2002; 102: 1119-1125.
9. Mehrotra R, Kopple JD. Nutritional management of maintenance dialysis patients: why aren't we doing better? *Annu Rev Nutr* 2001; 21: 343-379.
10. Jerin L, Ladavac R, Kuzmanovic G, Dodic D, Griparic D. Subjective general assessment of nutritional status in patient with chronic renal failure and regular hemodialysis. *Acta Med Croatica* 2003; 57: 23-28.
11. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephenes TW, Nyce MR, et al. Serum immunoreactive leptin concentrations, in normal weight and obese humans. *N Engl J Med* 1996; 334: 292-295.
12. Grunfeld C, Pang M, Shimizu L, Shigenaga JK, Jensen P, Feingold KR. Resting energy expenditure caloric in take and short-term weight change in human. *Am J Clin Nutr* 1999; 55: 455-460.
13. Kokot F, Chudek J, Adamczak M, Wiecek A. Interrelationship between plasma leptin concentration and severity of metabolic acidosis in hemodialysed patients with chronic renal failure. *Exp Clin Endocrinol Diabetes* 2001; 109: 370-373.
14. Young GA, Woodrow G, Kendall S, Oldroyd B, Turney JH, Brownjohn AM, et al. Increased plasma leptin/fat ratio in patients with chronic renal failure: a cause of malnutrition? *Nephrol Dial Transplant* 1997; 12: 2318-2323.
15. Cumin F, Baum HP, Levens N. Leptin is cleared from the circulation primarily by the kidney. *Int J Obes Relat Metab Disord* 1996; 20:1120-1126.
16. Coyne DW, Dagogo-Jack S, Klein S, Merabet E, Audrain J, Landt M. High-flux dialysis lowers plasma leptin concentration in chronic dialysis patients. *Am J Kidney Dis* 1998; 32: 1031-1035.
17. Nishizawa Y, Shoji T, Tanaka S, Yamashita M, Morita A, Emoto M, et al. Plasma leptin level and its relationship with body composition in hemodialysis patients. *Am J Kidney Dis* 1998;31: 655-661.
18. Merabet E, Dagogo-Jack S, Coyne DW, Klein S, Santiago JV, Hmiel SP, et al. Increased plasma leptin concentration in end-stage renal disease. *J Clin Endocrinol Metab* 1997; 83: 847-850.