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Investigating Nutritional Status of Hemodialysis Patients and Its Relationship with Serum Leptin, Adiponectin and CRP in Patients Undergoing Hemodialysis Treatment

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Abstract: *Introduction: Some ailments and restrictions in the diet of patients undergoing hemodialysis can lead to undesirable changes in the nutritional status, a decrease in quality of life, and an increase in disease and mortality. The purpose of this study was to evaluate the nutritional status of these patients and its relationship with the level of leptin and adiponectin and CRP in patients under hemodialysis treatment. Materials and Methods: This was a cross-sectional study with the participation of 42 hemodialysis patients who have been undergoing dialysis for at least 6 months. To assess the nutritional status of the patients, the score of malnutrition-inflammation was used. Leptin, adiponectin and serum level were measured by ELISA method. The level of significance was considered as 0/05. To compare the means, the independent t-test and Mann-Whitney test were used for the nonparametric data and also the relationship between variables was investigated by the Pearson correlation test. Findings: The results of this study showed that there was a positive correlation between serum leptin level and body mass index in the patients, which was statistically significant (P = 0.036). Serum adiponectin in patients was negatively associated with their body mass index, nutritional status and serum level. There was a positive and significant correlation between the serum level of the patients and BMI, but this variable was not significantly correlated with the nutritional status of the patients. Leptin, adiponectin and serum levels did not correlate with the nutritional status of the patients, and there was no significant difference in patients with an optimal nutritional status and malnutrition. After assessing the nutritional status of patients using the malnutrition-inflammation score, 24 people were in favorable condition (0-7), 18 were in moderate (8-18) and none of the patients were nutritionally under the Undesirable situation (score above 18). Discussion and Conclusion: The results of this study showed that leptin, adiponectin and serum levels of patients had a reverse relationship with their score of malnutrition-inflammation. This indicated that these variables were good indicators for the nutritional status of patients undergoing hemodialysis.*

Keywords: *Hemodialysis, Leptin, Adiponectin, CRP concentration, Malnutrition, Inflammation.*

INTRODUCTION

In the hemodialysis patients, the constraint of receiving certain food groups, anorexia, loss of water-soluble nutrients during hemodialysis and, on the other hand, high catabolism due to an increase in the production of inflammatory cytokines can easily lead to undesirable nutritional status (Ashabi et al., 2010; Morais et al., 2005). However, malnutrition is complicated in the hemodialysis patients and is not fully understood. Several indices, such as albumin and creatinine, cholesterol, and some body composition measurements have been used to evaluate nutritional status (Blumenkrantz et al., 1980). Important factors in malnutrition in the dialysis patients include inadequate food intake, chronic inflammation, endocrine gland disruption, and protein loss (Laville and Fouque, 2000). Malnutrition in the hemodialysis patients can reduce the quality of life and increase the incidence of disease and mortality (Morais et al., 2005; Kopple, 1997; Kalantar-Zadeh, 2001).

Various studies in the countries of the world have reported the prevalence of malnutrition in the hemodialysis patients (16-90%) (Morais et al., 2005; Aparicio et al., 1999). Some studies have also shown that 51-70% of hemodialysis patients have a lack of energy or received protein (Jacob et al., 1990; Bossola et al., 2005). So far, there has been no comprehensive study on the prevalence of malnutrition in the hemodialysis patients in Iran. In a limited number of studies, the nutritional status of hemodialysis patients referring to one or maximum of two hospitals has been investigated. These limited studies have shown that the prevalence of malnutrition in the hemodialysis patients referring to hospitals in Tehran, Kerman and Zanjan is between 38 and 75% (Din Mohammadi and Poormemari, 2002; Razeghi, 2006; Arjmandi, 1996).

Adipose tissue plays an important role in regulating metabolism and energy homeostasis. Several cytokines and hormones called adipokines are secreted from adipose tissue, which include leptin, adiponectin, resistin, and visfatin. Leptin and adiponectin are two of the adipokines that are considered. In the kidney failure, levels of leptin rises. The reason for this increase is unclear, but it is likely that factors such as reduced kidney function, dialysis membranes and type of dialysis (Zbroch et al., 1999; Coyne et al., 1998), low level of plasma erythropoietin (Axelsson et al., 2005), chronic inflammation, and increased serum insulin (Zoccali et al., 2005) may have contributed to this increase. A number of studies have reported a positive correlation between the serum leptin and a number of malnutrition parameters (Svobodova et al., 2001; Yilmaz et al., 2005), while in another studies, this association was not observed. On the other hand, in a study, leptin has been mentioned as a good parameter in assessing the nutritional status of patients (Koo et al., 1999). Studies have shown that the increased serum leptin in hemodialysis patients may cause anorexia and malnutrition (Ahmadi et al., 2009).

Adiponectin is an important regulator of lipid and carbohydrate metabolism, by increasing the production of glucose in the liver, reducing fat in the liver, controlling homeostasis in fat-sensitive tissues (Oh and Ciaraldi, Henry, 2007), and it may be associated with weight loss through an increase in the energy intake (Qi et al., 2004). Studies have shown that there is a negative correlation between adiponectin and body mass index in the dialysis patients (Stenvinkel et al., 1999). Adiponectin levels in patients with malnutrition are higher than dialysis patients without malnutrition (Lee et al., 2011). Adiponectin plays an important role in regulating body weight, appetite, fat metabolism, insulin sensitivity, and cardiovascular complications (Ouchi et al., 2003; Ouchi and Shibata, Walsh, 2006; Cnop et al., 2003; Tschritter and Fritsche, Thamer). Few studies have been done on the relationship between adiponectin and the nutritional status of dialysis patients. Studies have shown the role of anti-atherosclerotic and anti-inflammatory drugs of adiponectin (Malgorzewicz et al., 2010; Dervisoglu et al., 2008).

CRP, or C-reactive protein, is an appropriate marker for the evaluation of inflammation and malnutrition in patients with renal problems (Stenvinkel et al., 1999). Protein-energy malnutrition and reduced body mass have been associated with elevated CRP level in the cardiovascular disease and cancer (Lee et al., 2011).

The results of studies on the relationship between leptin and adiponectin and serum CRP concentrations on the one hand, and the nutritional status of hemodialysis patients on the other hand, have been controversial.

Therefore, this study was designed to determine the relation of leptin and adiponectin and serum CRP concentrations with the nutritional status and inflammation in hemodialysis patients.

Materials and Methods

- **Population under study**

This survey was performed as a cross-sectional study in patients referring to hemodialysis centers of Yazd hospitals in 2014. Patients who were over the age of 21 years and were under dialysis for at least 6 months were participated in the study.

- **• Measurements**

To assess the nutritional status of patients, the malnutrition inflammation score was used having ten components. The first part of the form, which is about the patient's medical history, includes weight changes, dietary intake, gastrointestinal symptoms, patient's practical capacity, and the presence of hypercatabolic underlying diseases. The second part of this form is a physical examination that involves subcutaneous fat analysis and muscle analysis. In addition, this form includes three other components including body mass index, serum albumin concentration, and total serum iron bonding capacity. In this form, each of the components are scored 0 to 3. If any of the components be perfectly normal, the score would be zero and if they have worst case, then the score would be 3, so the score of each hemodialysis patient would range from 0 to 30, which are used as the final score earned by each individual for determining the severity of malnutrition. If the score be between 0 and 7, the nutritional status of the patient would be normal. If the score be between 8 and 18, the patient would have a mild to moderate malnutrition, and if the score ranges between 19-30, the patient would be suffering from severe malnutrition.

To calculate the body mass after measuring their weight and height, BMI formula was used based on weight / kg / cm2. The necessary tests for the study, such as measurements of leptin, adiponectin, serum inflammation of patients, serum albumin concentration and total serum bonding capacity, were performed using 5 ml blood samples taken at the beginning of dialysis. Measurements were carried out through ELISA method using a German-made radial strip device. Leptin measurement was performed using the Dia Source-k and Adiponectin plasma using the Nediagnost kit.

- **Statistical analysis**

Data were analyzed using SPSS, version 16, software. The results of the data has been expressed as six standard deviations from the mean. The mean, standard deviation and percentage were used to describe the data. The significance level was considered to be 0.05. To compare the means, the independent t-test and Mann-Whitney test were used for nonparametric data; also the Pearson correlation test was utilized for investigating the relationship between variables.

Findings

- **Basic features of hemodialysis patients**

These features have been shown in Table 1. A total of 42 (13 females and 29 males) hemodialysis patients of the hospitals of Yazd province were participated in the study. The mean age of patients was 62.6 ± 1.73 years. 27 patients (64.3%) had diabetes mellitus. Also, 27 patients (64.3%) were reported having a history of high blood pressure. The mean body mass index was 24.5 ± 0.49 kg / m2 and on average the mean duration of the disease was 3.4 ± 0.31 years.

- **Relationship between serum features and nutritional status**

These data have been shown in Table 2. There was a positive correlation between serum leptin level and body mass index, which was statistically significant (P = 0.036). Also, leptin had a negative correlation with the nutritional status and serum inflammatory concentration of the patients, which was not statistically significant. Serum adiponectin showed a negative correlation with their body mass index, nutritional status

and serum inflammatory concentration in hemodialysis patients, which was not statistically significant. There was a positive and significant correlation between the serum inflammatory concentration and body mass index, but this variable was not significantly correlated with the nutritional status of the patients.

- **Comparing nutrition status in patients**

Table 3 shows that after assessing the nutritional status of patients using the malnutrition-inflammation score, 24 patients were of a desirable nutrition (0-7 scores), 18 patients were in moderate status (8-18 scores) and none of the patients were under an undesirable situation (score above 18) in terms of nutrition. Individuals with a normal nutritional status had higher BMI; on the other hand, those with a moderate nutritional status had higher levels of leptin and adiponectin, but none of these differences were statistically significant.

Discussion and Conclusion

According to the results of the study, 43% of the participants in the study had mild to moderate malnutrition and none of the patients had severe malnutrition. Studies done in Spain (Marcén et al., 1997), Sweden (Qureshi et al., 1998), Jordan (Tayyem et al., 2008) and Brazil (Morais et al., 2005) reported 48, 51, 62 and 90 percent, respectively, in the incidence of malnutrition in hemodialysis patients. The difference in the prevalence of malnutrition in different studies can be due to the different ways of assessing nutritional status, age, duration of disease and underlying diseases, drug use and supplements and other factors that can affect the nutritional status of individuals.

In this study, malnutrition-inflammation score was used to determine the nutritional status of hemodialysis patients. Considering the fact that this index had positive predictive value and a higher likelihood compared to other indices, it acted strictly in diagnosing hemodialysis patients with malnutrition, and therefore perhaps some patients with malnutrition in the borderline range were not placed in the malnutrition group. This index used criteria such as BMI, albumin concentration, and total serum iron bonding capacity and had a stronger relationship with the risk of death (Tabibi et al., 2010).

The results of the study indicated that the average age of patients with mild to moderate malnutrition was higher than those with a favorable nutritional status. This can be due to the underlying diseases in this group. Also, the physical or economic disadvantage of providing food can be effective (Bossola et al., 2005).

The results of this study showed a positive and significant correlation between serum leptin and body mass index. There was a reverse relationship between leptin and score of malnutrition-inflammation, which was not statistically significant. It was also shown that the mean serum leptin level was higher in a moderate to mildly nutritional group, which was not significant with the group that had good nutrition. Different studies have been carried out about the relationship between leptin and nutritional status of hemodialysis patients, the results showed a positive relation (Koo et al., 1999; Malgorzewicz et al., 2010). Leptin also showed a direct correlation with the body mass index of hemodialysis patients (Małgorzewicz et al., 2010). In one study, there was a negative relationship between leptin level and malnutrition-inflammation score in hemodialysis patients, which was not statistically significant (Dervisoglu et al., 2008); it was consistent with the results of this study. The reason for the difference in the results of various studies regarding the relationship between leptin and nutritional status can be due to how nutritional status and the sample size were calculated.

The results of this study showed that serum adiponectin had an inverse correlation with BMI and malnutrition-inflammation score, which was not statistically significant. Also, the mean of this variable was higher in subjects with moderate to mild nutritional status, although this difference was not significant. Results were different in different studies. Some studies have shown a positive correlation between adiponectin and nutritional status and a negative correlation with body mass. Indeed, these results indicated that adiponectin was associated with a worse nutritional status (Lee et al., 2011; Akhoondzadeh and Jalalmanesh, Hojjati, 2014). In contrast, some studies have shown an inverse relationship between this variable and the nutritional status and have shown that adiponectin was a good indicator for evaluating

nutritional status in hemodialysis patients (Małgorzewicz et al., 2010), and some studies have shown that serum adiponectin didn`t have a significant relationship with Malnutrition-inflammation score and body mass (Dervisoglu et al., 2008).

Current study showed that leptin and CRP concentration had an inverse relationship. The levels of leptin, adiponectin, and CRP concentration in patients did not correlate with their nutritional status score. In the chronic kidney patients, especially hemodialysis patients, the inflammatory reactions, atherosclerosis, infections and malnutrition were commonly associated with an increase in CRP concentration (Heidari et al., 2013; Heidari et al., 2015). Studies have shown that the rate of this variable in the hemodialysis patients increased by about 35% (Antonio and Elena, 2002).

Strengths and weaknesses of the study: One of the strengths of this study was the use of the malnutrition-inflammation score to assess the nutritional status of hemodialysis patients. Some of the weak points of this study were the low sample size, the absence of patients with the severe malnutrition status in the study to better compare all the groups together, the absence of a control group with normal kidney function.

Conclusion

Regarding the fact that malnutrition in the hemodialysis patients decreases the quality of life and increases the incidence of diseases and deaths, the diagnosis of hemodialysis patients with malnutrition is very important. Since the prevalence of malnutrition in this study was lower compared to other studies, it can be concluded that the nutritional status of hemodialysis patients in this study can be influenced by the lifestyle and socioeconomic level of society. On the other hand, in order to reduce malnutrition in these patients, the nutritional status of these individuals should be investigated and nutritional counseling should be considered as part of their therapeutic program.

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Table 1. Basic characteristics of hemodialysis patients

Variables / Gender	Number	Percentage
Male	29	69
Female	13	31
Diabetes Mellitus	27	64/3
Hypertension	27	64/3
Hyperlipidemia	4	9/5

Table 2. Relationship between patients' serum parameters and nutritional status

Variables		Body mass index	Malnutrition Score - Inflammation	CRP concentration
Leptin (mg / dl)	correlation coefficient	0/324	- 0/017	- 0/022
	significance level	0/036	0/915	0/891
Adiponectin (mmol / mg)	correlation coefficient	- 0/011	- 0/002	- 0/077
	significance level	0/946	0/989	0/626
CRP concentration (µg / l)	correlation coefficient	0/381	- 0/027	-
	significance level	0/013	0/864	-

Table 3. Comparison of mean quantitative attributes in terms of nutritional status

Variables	Optimal nutritional status (n = 24)	Mild or moderate nutritional status (n = 18)	significance level
Average age (years)	60/54 ± 11/44	65/44 ± 10/69	0/160
BMI	25/22 ± 3/20	23/54 ± 2/98	0/090
Leptin	12/26 ± 12/77	14/53 ± 18/58	0/640
Adiponectin (mmol / mg)	5/46 ± 9/67	5/87 ± 2/67	0/620
CRP concentration (µg / l)	5/46 ± 7/13	6/30 ± 9/84	0/740