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Correlation of Leptin Levels and Total Body Fat in Patients with Chronic Kidney Disease on Hemodialysis.

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ABSTRACT

Anorexia is a known complication of uraemia which worsens with the progress of renal failure. Malnutrition and reduction in lean body mass is seen in patients undergoing dialysis. Serum leptin levels are elevated in patients with chronic kidney disease (CKD). Serum leptin level is suggested to control appetite and metabolism. The aim of the study is to establish a relationship between serum leptin levels and total body fat in normal subjects and patients undergoing hemodialysis for chronic kidney disease. Serum leptin levels were measured in 25 patients undergoing hemodialysis and 25 anthropometrically matched control subjects. Body mass index (BMI) and total body fat percentage were measured. The correlation between serum leptin levels, BMI and total body fat percentage was evaluated. Serum leptin levels in cases and controls were 16.38 ± 31.59 ng/ml and 3.91 ± 4.15 ng/ml respectively. Total body fat percentage in cases and controls were 25.76 ±7.22 and 19.42 ± 6.0 respectively. Serum leptin levels were higher in cases when compared to controls. Positive correlation was found between serum leptin levels and total body fat percentage.

Keywords: chronic renal failure, hemodialysis, leptin, malnutrition

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INTRODUCTION

Chronic renal failure also known as chronic kidney disease (CKD) is the slow progressive loss of kidney function over the span of years, resulting in irreversible kidney damage. It is common in recent times because of increased risk factors like diabetes, high blood pressure and increased usage of analgesics [1]. Chronic kidney disease may go undiagnosed until the process is far advanced. The symptoms of worsening kidney function are not specific and might include feeling of general unwell and experiencing a decreased appetite. Confirmation can be done by investigation like serum creatinine levels. People with permanent kidney failure need dialysis or renal transplant.

Leptin is a protein produced by adipocytes and acts as an adipostatic hormone, regulating the fat-mass by controlling food intake and energy expenditure [1]. Leptin is cleared from circulation by the kidney. Its level is altered in patients with chronic renal failure with or without dialysis [2]. Following release into the circulation, leptin crosses the blood-brain barrier and binds to leptin receptors in the hypothalamus, influencing the activity of various hypothalamic neurons as well as the expression of various genes, encoding orexigenic and anorexigenic neuropeptides [3]. Leptin levels are influenced by the amount of body fat, as they are found high in obese and low in lean individuals

Malnutrition is a common clinical problem in CKD patients. According to the literatures the increase of serum leptin levels in patients on hemodialysis may cause anorexia and malnutrion. In the present study, efforts were made to evaluate the serum leptin levels with respect to body fat using bioelectrical impedance method in patients with CKD undergoing hemodialysis.

MATERIALS AND METHODS

The study was carried out in M.S.Ramaiah teaching hospital. Ethical clearance was obtained from the institutional ethical review board. The subjects participated in this study by giving written informed consent. It was a case controlled study. Baseline information and relevant clinical history was taken from all cases and controls. Twenty five patients in the age group of 15 to 55 years with chronic kidney disease undergoing maintenance hemodialysis were recruited as subjects. Patients on steroids, infection with HIV, malignancy, bacterial infection requiring IV antibiotics were excluded from the study. Twenty five anthropometrically matched healthy subjects attending the OPD for master health check up were recruited as controls. Anthropometric measurements height and weight was taken and BMI was calculated for all subjects. The total body fat was measured using the bioelectrical impedance technique by body composition analyzer (Omron body composition analyser) for all cases and controls. Blood sample for leptin was collected from the subjects after an overnight fast and serum from the samples were separated and stored at -20^0C. Serum leptin levels were estimated by ELISA method using DRG Human Leptin Enzyme-Linked Immunosorbent (ELISA, EIA-2395) Kit, Germany. The findings were recorded on a pre-designed proforma.

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Statistical Analysis Of The Data

All the quantitative parameters such as age, leptin levels, anthropometric measurements and total body fat were summarized in terms of descriptive statistics such as mean, standard deviation (SD), median, inter quartile range (IQR). Data was entered in M S excel and was analyzed using the SPSS version 20 software. $p < 0.05$ was considered statistically significant.

The differences in the leptin levels and total body fat between hemodialysis patients and controls were tested employing independent t-test and Mann Whitney test (where the parameter did not follow normal distribution). To evaluate the correlation between leptin levels and total body fat, Spearman's correlation coefficient was computed.

RESULTS

Study population consisted of 25 subjects as controls and 25 patients undergoing dialysis for CKD as cases. The median age of cases 47 (42-54) years and controls 34 (19-45) years. The mean BMI of cases was found to be 21.55 ± 2.51 as compared to controls being 20.98 ± 4.41 (Table.1). The median (IQR) of total body fat percentage of cases was 23.59 (18.75-32.55) compared to controls being 19.22 (14.33-24.73) Table1. The median value of the total body fat was higher in cases as compared to controls. This difference was found to be statistically significant (p=0.004) Figure 1. Median (IQR) serum leptin levels in cases was 2.30(0.85-14.15) ng/ml compared to controls 2.10 (0.50- 6.50) ng/ml. However this difference was not statistically significant (p=0.394) Figure 2.

Figure 1: Mean body fat percentage in cases and controls

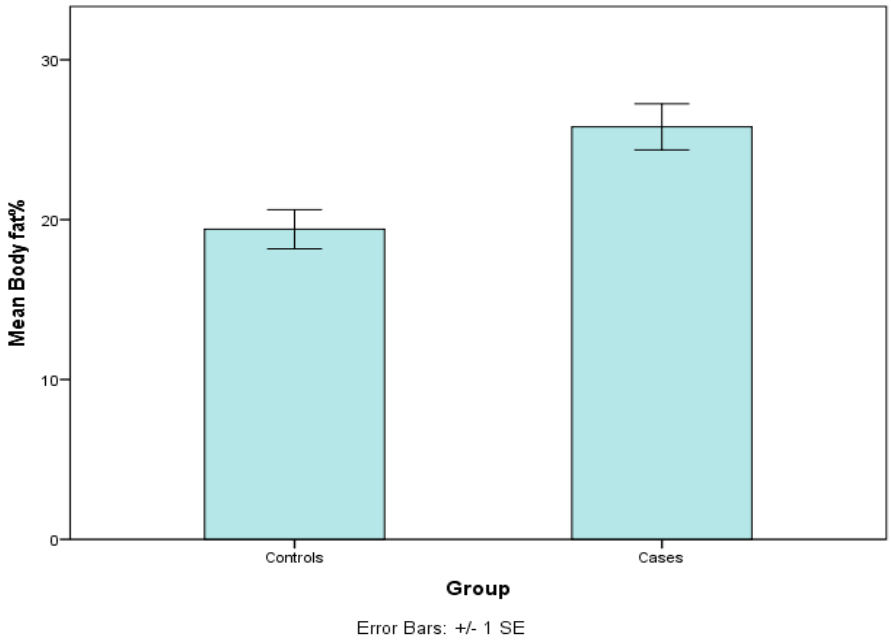

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Figure 2: Mean serum leptin levels in cases and controls

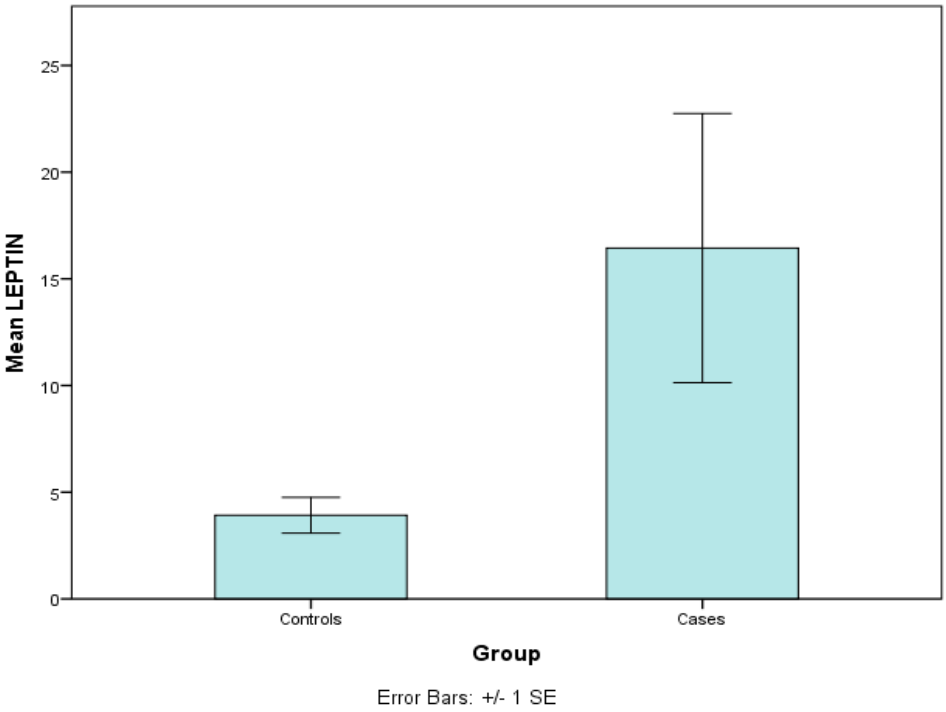

Figure 3

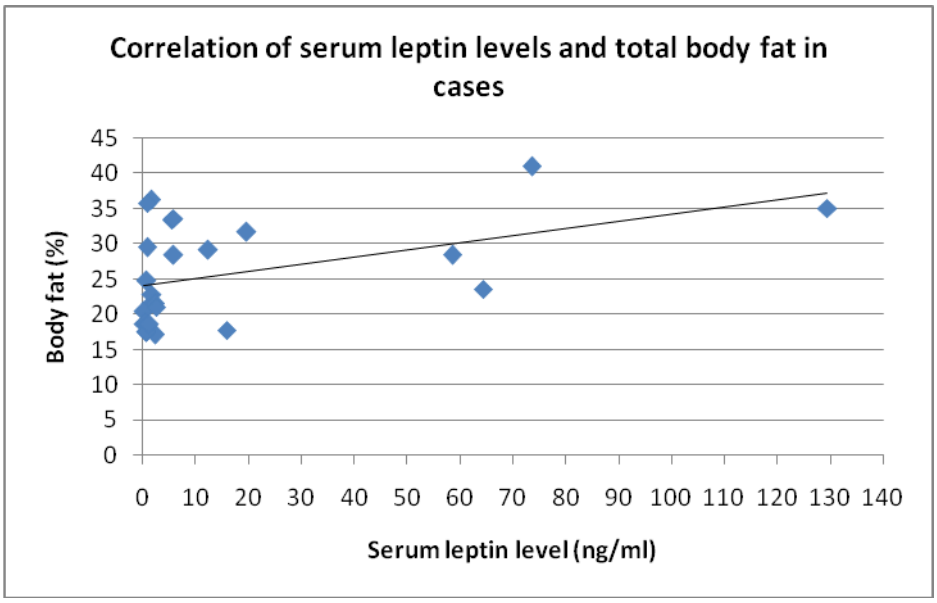

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Figure 4

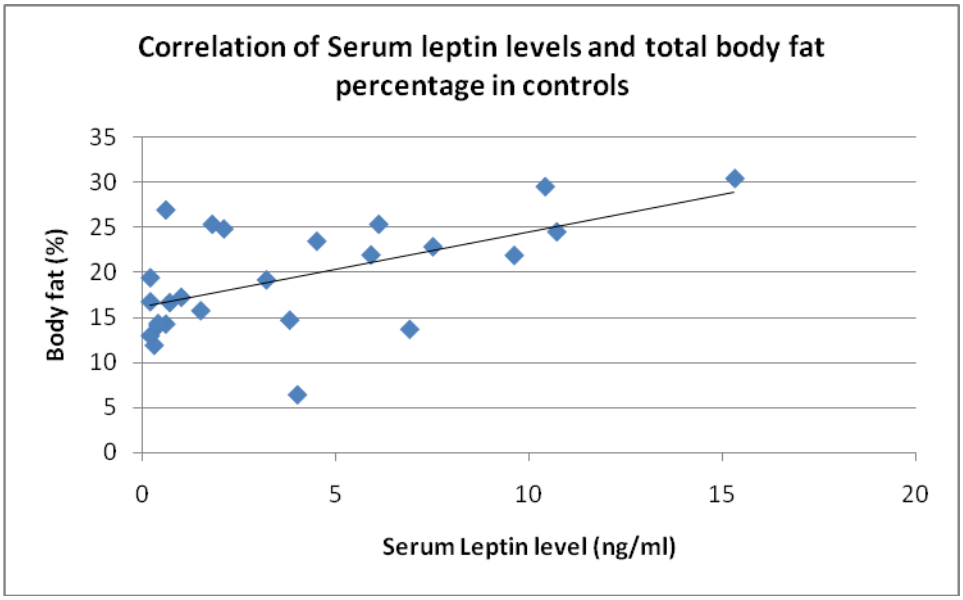

Table 1: Comparison of Cases and Controls based on Mean±SD / Median (IQR)

Variables	Cases	Controls	P value
Height [Mean±SD]	161.8 ± 10.35	165.8 ± 6.32	0.09
Weight [Mean±SD]	56.64 ± 10.04	57.72 ±12.11	0.72
BMI [Mean±SD]	21.55 ± 2.51	20.98 ± 4.41	0.57
Leptin [Median (IQR)]	2.30 (0.85-14.15)	2.10 (0.5-6.5)	0.39
Body fat [Median (IQR)]	23.59(18.72-32.55)	19.22(14.33-24.73)	0.004*

*P value significant at 0.05(Mann Whitney Test), IQR – Inter quartile range,
SD – Standard deviation

There was a positive correlation between total body fat and leptin levels in both cases (r = 0.548) and controls (r = 0.47) which was statistically significant (p= 0.016 in cases and p =0.005 in controls) Figure 3 and 4.

DISCUSSION

The major problem in patients on hemodialysis with chronic kidney disease is malnutrition. The causes for malnutrition is multifactorial, number of studies done earlier have attempted to identify probable cause for the same in patients undergoing dialysis. Earlier study has compared the serum leptin levels in patients on hemodialysis, peritoneal dialysis and subjects with normal renal function after adjustment for age, gender and percentage of body fat. Mean serum leptin concentration was significantly higher in patients on peritoneal dialysis than other two groups. Body fat had a strong influence on leptin levels in both dialysis groups compared to control subjects [4].

Leptin circulates in the blood partly in free form and rest bound to proteins. It crosses the blood brain barrier to act on the hypothalamus causing decreased appetite and increased metabolism [5-7]. Leptin signals the brain about the quantity of stored body fat to regulate food intake [8].

Increased serum leptin levels have been reported in patients with morbid obesity. It has been proposed that in such obese patients there is a defective transport of leptin across the blood brain barrier or receptor insensitivity to the action of leptin [9].

Serum leptin levels were increased in patients with chronic renal failure mainly due to decreased clearance by kidneys. As leptin is a 16 Kda protein, it is also not cleared by dialysis using conventional dialysers. However elevated serum leptin is not universally present in severe renal failure [10,11].

Markedly elevated serum leptin concentrations without any increased body fat mass has been demonstrated in chronic kidney disease patients with and without ongoing dialysis. Hyperleptinemia in patients with renal disease may be responsible for the decreased appetite. Earlier studies have reported that increased leptin causes decreased food intake and malnutrition[12,13]. in renal failure patients on conservative therapy and those on dialysis , whereas other studies have not observed such relationship [14,15].

Although hyperleptinemia is postulated to play a role in anorexia and malnutrition associated with renal disease its clinical significance is unclear. It has been reported higher leptin level is associated with anorexia, less protein intake and malnutrition [13]. Further, increase in duration of dialysis is associated with higher leptin levels and decreased BMI[12]. The mean serum leptin levels were found to be significantly elevated in haemodialysis patients when compared to matched controls. Higher leptin levels were found in patients with increase in body mass index suggesting good nutrition is associated with higher leptin levels. A positive correlation was found between serum leptin and insulin levels [5].

Abdulkarim Yilmaz et al have found the gender difference serum leptin levels in hemodialysis patients. It was twice as high in woman as in men [1]. Fat mass but not the lean body mass related to serum leptin concentration [16]. Chronic inflammation and endotoxins present in CKD patients have been shown to increase leptin gene expressions [17,18].

Dae Joong Kim et al showed that serum leptin levels are inappropriately higher than in increase of body weight and BMI in patients on peritoneal dialysis [19].

Kayardi et al have shown positive correlation between serum leptin levels and body mass index or body fat [3].

In patients with chronic kidney disease on dialysis, free leptin levels are increased in serum and bound for remains stable without influencing the body weight [20].

In our study, serum leptin levels were higher in patients on hemodialysis. Mean leptin levels were higher in patients with higher BMI and total body fat. It could be attributed that in such obese patients there is a defective transport of leptin across the blood brain barrier or receptor insensitivity to the action of leptin.

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