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END STAGE RENAL DISEASE (ESRD) PATIENT'S ASSESSMENT AND EVALUATION OF PRE AND POST DIALYSIS LEVELS OF INTERLEUKIN-6 (IL – 6) AND LEPTIN

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Abstract:

Objective*: Appetite can be controlled through "Leptin" which is the obese gene product. Our research aim was the pre and post level of leptin determination in the ESRD cases experiencing hemodialysis, in order to compare the level of pre serum leptin ESRD cases and healthy normal controls. Our research also determines the level of serum "IL – 6" before and after the experience of hemodialysis in ESRD cases.*

Methodology: *Pre and post dialysis level of leptin was measured in 78 patients who underwent hemodialysis with ESRD to normal healthy volunteers at Services Hospital, Lahore (February, 2016 to December, 2016). We also measured the level of "IL – 6" in ESRD cases pre and post dialysis.*

Results*: Significant high level of mean leptin serum was observed in ESRD cases in comparison to the normal healthy controls with respective mean and SD values as (38.22 ± 6.25) and (7.1 ± 4.38) ng/ml, with a significant P-value as (< 0.01). Post dialysis level of leptin serum was more than the pre dialysis level of leptin serum level with respective mean and SD values as (44.78 ± 5.85) and (38.22 ± 6.25) ng/ml, with a significant P-value as (< 0.05). IL – 6 post dialysis level was more than the pre dialysis level respectively as (14.7 ± 4.6) and (9 ± 4.9) pg/ml, with respective P-value as (< 0.01).*

Conclusion: *Circulating leptin is cleared by kidneys in the human body. However, evaluation may be standardized through more research work in order to evaluate the increased leptin significance in the ESRD patients.*

Keywords: *Interleukin-6 (IL – 6), Leptin and End Stage Renal Disease (ESRD).*

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INTRODUCTION:

Appetite can be controlled through "Leptin" which is the obese gene product [1 – 3]. Secretion of Leptin is exclusively done by adipocytes and in human body; concentrations of plasma are directly linked with adipocytes [4 – 5]. No information is available about the route and physiological activity in human body [6]. Numerous evidences suggest major route as the renal clearance for metabolism of the leptin.

Its presence and short half-life is also reported in the kidneys; it is also considered that kidneys are the clearance site for the leptin through its circulation [7]. If the clearance of leptin is made through kidney; a net leptin uptake is expected to reduce the patient's renal uptake including insufficiency of renal and across renal vascular bed.

Moreover, level of leptin is expected to increase in the patients of chronic hemodialysis. Increased level of leptin is influential in the decreased appetite which is a feature of ESRD patients. In a recent research it was observed that increase in the level of leptin serum in the course of peritoneal dialysis has an association with the lean body mass loss and inflammation [8].

Appetite can be controlled through "Leptin" which is the obese gene product. Our research aim was the pre and post level of leptin determination in the ESRD cases experiencing hemodialysis, in order to compare the level of pre serum leptin ESRD cases and healthy normal controls. Our research also determines the level of serum "IL – 6" before and after the experience of hemodialysis in ESRD cases.

METHODOLOGY:

Pre and post dialysis level of leptin was measured in 78 patients who underwent hemodialysis with ESRD to normal healthy volunteers at Services Hospital, Lahore (February, 2016 to December, 2016). We also measured the level of "IL – 6" in ESRD cases pre and post dialysis. Informed consent was taken before the enrolment of the patients in the research. Total population had a male to female proportion such as 48 males (61%) and 30 females (38%) as shown in Table – I. The cases under one year of experience of dialysis were not included in the research paper because of a possible corticosteroids interaction with the production of leptin [9]. We also enrolled healthy normal controls (78) with a male to female proportion respectively 45 and 33 for comparison.

All unwilling and above seventy years' patients were not included in the research. We used dialysis filter with these specifications (modified cellulose membrane composition also called "Hemophane" with 11,000 Daltons as pore size).

ESRD cases plasma samples (Aliquots) was taken before and after dialysis and it was stored at a temperature of seventy degrees centigrade which was used at a later stage for the IL – 6 and leptin measurements. Collections of dialysis samples was made in the regular working hours. All the patients were given routine medicines and diet. ELISA Kit was used for the determination of the level of leptin plasma. Leptin concentration was also measured along with the measurement of IL – 6 with a technique known as "Quantitative Sandwich Immune Assay".
SPSS was used for the performance of statistical analysis and outcomes were shown in mean and SD for the comparison of the pre and post dialysis IL – 6 and leptin levels in the ESRD patients.

RESULTS:

Significant high level of mean leptin serum was observed in ESRD cases in comparison to the normal healthy controls with respective mean and SD values as (38.22 ± 6.25) and (7.1 ± 4.38) ng/ml, with a significant P-value as (< 0.01). Post dialysis level of leptin serum was more than the pre dialysis level of leptin serum level with respective mean and SD values as (44.78 ± 5.85) and (38.22 ± 6.25) ng/ml, with a significant P-value as (< 0.05). IL – 6 post dialysis level was more than the pre dialysis level respectively as (14.7 ± 4.6) and (9 ± 4.9) pg/ml, with respective P-value as (< 0.01) as shown in Table – II.

Evaluation of the level of Leptin was made at pre and post dialysis with the help of dialysis filter with these specifications (modified cellulose membrane composition also called "Hemophane" with 11,000 Daltons as pore size). A positive association was observed in the ESRD patients in terms of IL – 6 and leptin (P < 0.05). Distribution of the gender has been displayed in the tabular form in Table – I.

Table – I: Gender distribution

Gender	Number	Percentage
Male	48	61
Female	30	38

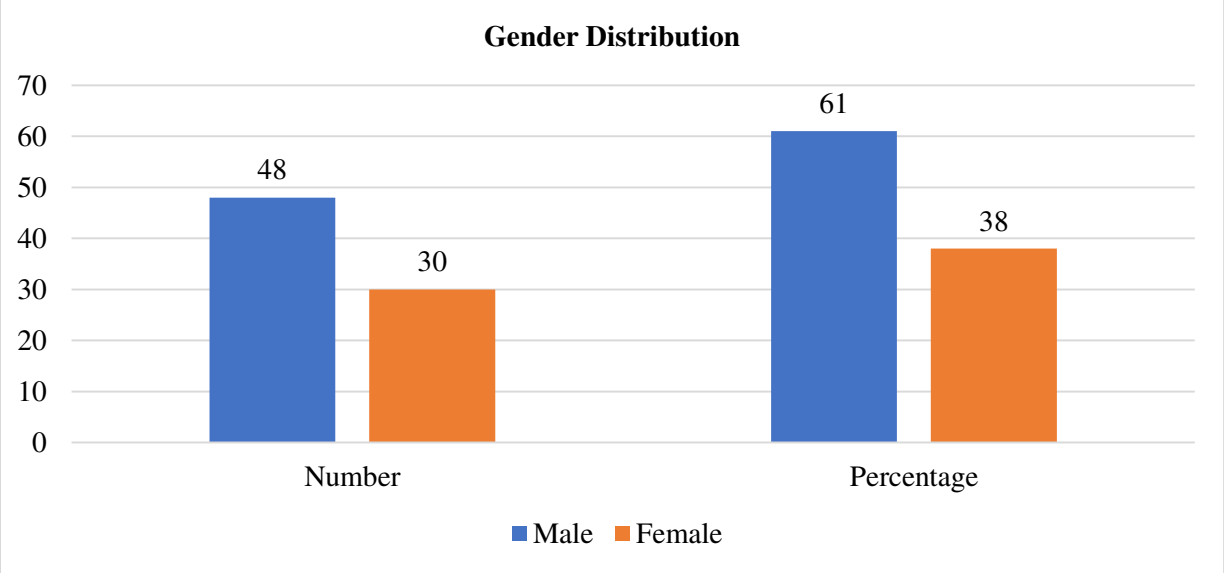
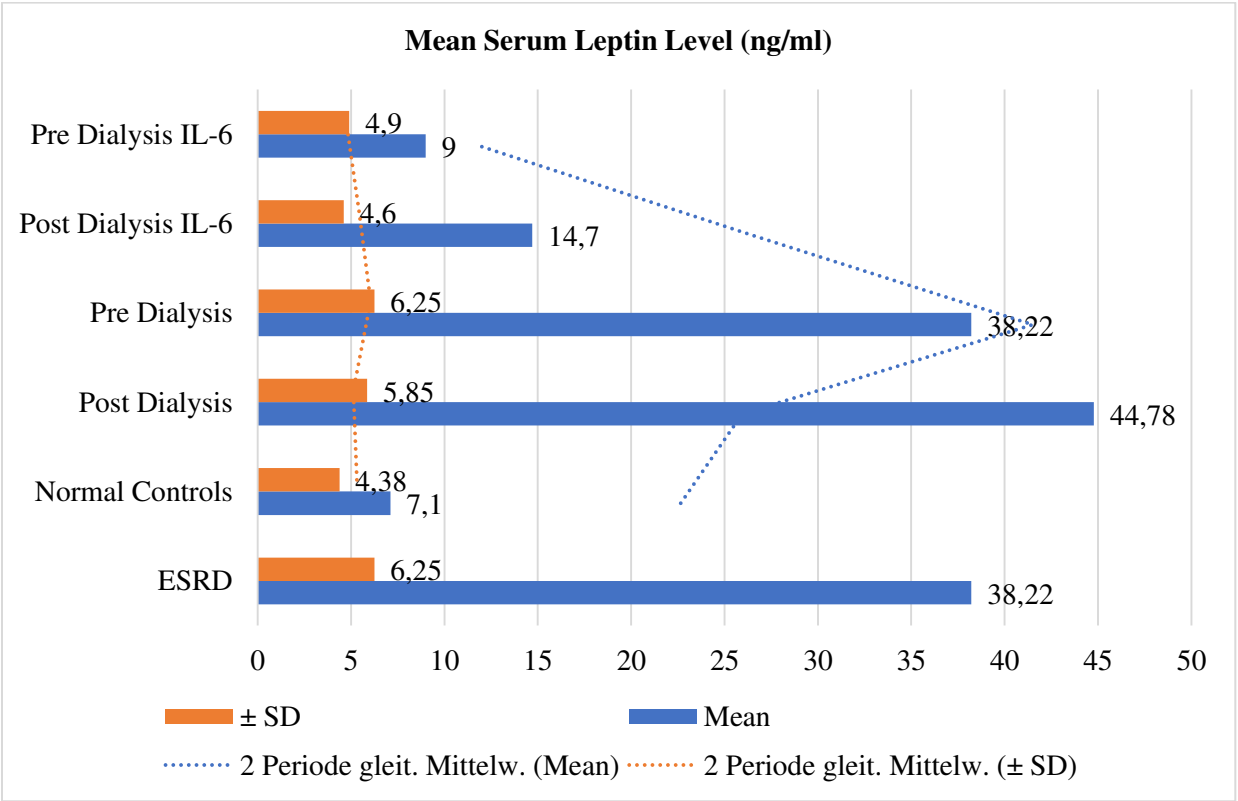


Table – II: Mean Serum Leptin Level (ng/ml)

Serum Leptin Level	Mean	± SD	P-Value
ESRD	38.22	6.25	< 0.01
Normal Controls	7.1	4.38	
Post Dialysis	44.78	5.85	< 0.05
Pre Dialysis	38.22	6.25	
Post Dialysis IL – 6	14.7	4.6	< 0.01
Pre Dialysis IL – 6	9	4.9	



DISCUSSION:

Clearance of Leptin is made through kidney; therefore, level of leptin increases in the ESRD patients [7, 10, 11]. There is a negative correlation of level of leptin serum with GFR (Glomerular Filtration Rate) in patients having different level of chronic renal inadequacy. Healthy controls have less accumulation of leptin than ESRD cases [7, 12, 13]. Leptin accumulation is also linked with decreased GFR [7, 12].

In the patients of dialysis lower level of leptin and high-flux membranes are almost (30 %); whereas, no molecular elimination has been observed in the low-flux membranes [7, 13, 14]. Increased level of leptin has been observed in the peritoneal dialysis patients as with peritoneal clearance measurement as (0.7 – 1.7) ml/min [15, 16]. Kidney is among various peripheral tissues exhibiting reception of the leptin and leptin size permits to cross basement of glomerular capillary membrane, with a hypothesis of kidney as primary organ that accounts for the leptin removal through circulation. It is demonstrated in our research net renal leptin extraction in normal renal function patients; whereas, in the mild or moderate renal insufficiency cases renal extraction is reduced. Modified cellulose dialysis membrane removes the leptin circulation because of the size of the membrane pore.

Sharma et al. and our outcomes can be compared which reflects leptin plasma partially cleared by the kidney which increased in the patients of hemodialysis [7]. Inflammatory mediators are increased in the maintenance and peritoneal hemodialysis patients as suggested by numerous authors [11, 17, 18].

Feeding behavior is reduced through pro-inflammatory cytokines in animals including leptin that is implicated in malnutrition development in the patients of ESRD [10]. We observed that there is a positive association between IL – 6 and level of serum leptin which suggests contribution of the inflammation in the hyper leptinemia in ESRD cases. There is no originality in the hypothesis of leptin production due to inflammation stimulation. Numerous evidences are available in the literature about the acute phase response suggestion for the production of leptin stimulation.

Increased level of (mRNA) leptin was found in ESRD cases having an inflammatory response and Fouque is of the view that there is a positive association between leptin serum and IL – 6 in the patients of hemodialysis group [19, 20]. Numerous studies also report increase in the leptin cytokines [21 – 23]. Moreover, research studies conducted on humans, pro-inflammatory cytokines administration has been reflected to enhance the level of leptin serum in the patients whose level of sepsis leptin is increased [23 – 25]. Finally, there are common functional and structural similarities in the family of cytokine family. There may be a reaction between leptin and IL – 6.

Furthermore, relation of IL – 6 is to (20KDa) polypeptide cytokines family, which is an inflammation indicator in ESRD cases. There is no clarity about the precise mechanisms, responsible for ESRD patient's inflammation, dialysis filters repeated exposure, low grade infection and auto-oxidation products as factors that excite [26]. Arterial damage is primarily caused due to inflammation. Mortality has a strong association with increased IL – 6 serum concentrations in the patients undergoing dialysis. Moreover, it has been recently shown that enhanced atherosclerosis can be predicted through increased traditional risk [27].

CONCLUSION:

Circulating leptin is cleared by kidneys in the human body. However, evaluation may be standardized through more research work in order to evaluate the increased leptin significance in the ESRD patients.

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