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RESEARCH ARTICLE

ASSOCIATION OF SERUM LEPTIN WITH INFLAMMATION, ANEMIA AND BODY MASS INDEX IN EGYPTIAN CHRONIC HEMODIALYSIS PATIENTS.

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Abstract

Background:- ESRD is a major healthcare problem worldwide, especially in developing countries. Nutrition disorders especial anemia and loss of weight are very common and important risk factors for morbidity and mortality in patients on regular hemodialysis and so We aimed to evaluate the relationship between serum leptin,anemia and nutrition state in patients on regular hemodialysis

Subjects and methods:- A case- control study included 55 Egyptian patients on chronic hemodialysis 34 healthy subjects as control. Each group were stratified according to their body mass index (BMI) to four subgroup, In all studied participants we determined BMI, body surface area (BSA) and waist to hip ratio (WHR), blood urea, serum creatinine, sodium, potassium , calcium, phosphorus , albumin, serum bilirubin. ALT, AST, complete blood count, Lipid profile, HbA1c, fasting blood glucose (FBG), post prandial blood glucose were measured.Also,we estimate serum leptin andCRP levels.

Results:- there were highly statistical significance differences between cases and control in Leptin and CRP with
marked elevated level in hemodialysis group(HD)compared to control group.There was positive correlation between BMI and leptin in cases group with marked elevated level in obese and over- weight compared to under - weight and normal cases but there was no significant correlation in control group. In hemodialysis group,there was non- significant correlation between CRP and leptin level.Linear regression analysis showed that, serum leptin levels were independently correlated with diastolic blood pressure and platelet in hemodialysis group.

Conclusion:- In the present study, serum leptin and CRP levels were higher in Egyptian patients. On regular hemodialysis, there were significant positive correlation between serum leptin levels and BMI. According to the results of this study, serum leptin can be used as diagnostic marker of nutrition disorders especially anemia and weigh changes in patients with ESRD on hemodialysis.

Introduction:-

Chronic kidney disease (CKD), a worldwide problem with a high incidence, is commonly accompanied by inflammation and anemia. Between 6.5 and 10% of the population in developed countries suffer from various renal diseases. CKD is a condition, which is characterized by chronic inflammation and is hypothesized to be promoted by cytokines and oxidation reactions (1).

Leptin is a 16-kDa protein hormone made up of 167 amino acids. It is mainly produced by adipocytes and leptin is confirmed as major regulator of body weight since it decreases food intake and increases energy expenditure (2).Leptin is a pro-inflammatory cytokine. Its synthesis is mostly dependent on the amount of body fat but it is also enhanced during acute infection and inflammation. Secretion of leptin is also regulated by the actions of pro-inflammatory mediators such as tumor necrosis factor (TNF)-α, IL-6, and IL-1 (6). Moreover, leptin itself stimulates the production of pro-inflammatory cytokines from macrophages (4, 5).

Leptin is cleared from the circulation by the kidney through both glomerular filtration and metabolic degradation in the renal tubules. Several studies observed that serum leptin concentrations are increased in patients with chronic kidney disease (CKD) and those on hemodialysis (HD). Results of these studies suggest that elevated leptin levels in patients with damaged kidney function are primarily due to reduced renal filtration and metabolism (3).

CRP is a sensitive but non-specific marker of systemic inflammation synthesized by the liver. Studies conducted so far have shown that increased CRP levels reflect presence of chronic inflammation in HD patients (6). Study by Stenvenkel (7) found that more than 50% of HD patients had increased serum CRP concentration.

Inflammation in HD patients is often associated with malnutrition. Furthermore, numerous studies have demonstrated that HD patients with lower Body Mass Index (BMI) have higher relative mortality risk (8).

Anemia often occurs in CKD patients and is closely associated with a high incidence of cardiovascular disease. Anemia in CKD is associated with cognitive impairment, sleep disturbances, CKD progression, cardiovascular comorbidities, and higher mortality (9).

In the general population, a high body mass index (BMI; in kg/m2) is associated with increased cardiovascular disease and all-cause mortality. However, the effect of overweight (BMI: 25–30) or obesity (BMI: >30) in patients with chronic kidney disease (CKD) undergoing maintenance hemodialysis (MHD) is paradoxically in the opposite direction; as a high BMI is associated with improved survival. Although this "reverse epidemiology" of obesity or dialysis-risk-paradox is relatively consistent in MHD patient's .on the contrary, Kara et al. (10) reported negative correlation between leptin levels and malnutrition inflammation score which remained significant even after adjustments for BMI. However, significance of hyperleptinemia as well as its associations with inflammatory and BMI in HD patients is far from being fully elucidated (10).

In our Egyptian population nutrition disorder especially; anemia, obesity and chronic renal failure are very common and have not been extensively analyzed. leptin hormones in Egyptian hemodialysis patients, and their results are controversial. Therefore, the purpose of current novel study is to investigate serum concentration of leptin , CRP, anemia and BMI values in HD patients. Moreover, we aimed to clarify the possible relationships of serum leptin, biochemical parameters of renal failure,anthropometric parameters; BMI ,BSA and WHR as well as complete blood count in Egyptian hemodialysis patients with different grade of BMI .

Subjects and methods:-

Subjects:-

This study included 89 unrelated subjects;55 patients on Maintenance hemodialysis thrice weekly; 4 hours each session for more than 3 months. Patients recruited from Hemodialysis and Endocrinology units of Internal Medicine Department of Zagazig University Hospitals and 34 healthy controls,were matched to cases by age, gender, and ethnic origin. Subjects were stratified into four groups based on BMI; Under weight <18.5, Normal weight 18.5-25, Overweight 25-30 and Obese>30 .All patients were subjected to thorough history taking and full clinical assessment including blood pressure. Height, waist circumference, and hip circumference circumferences were measured to calculate obesity indices. Anthropometric variables including BMI was calculated as weight in kg/ height in (meters) ^{2}, WHR= waist circumference (cm)/hip circumference (cm), Body surface area (BSA) in square meter (m^2) was calculated from the height and weight using "Dubois" formula.(11) BSA (m^2) = Wt (kg) $^{0.425}$ × Ht (cm) $^{0.725}$ × 0.007184.

Patients suffering from any acute infection, acute renal failure, any endocrine disorder except diabetes mellitus, those who were taking glucocorticoids 8 weeks prior to or during the study, as well as receiving medications for weight reduction or participating in a dietary or exercise programs were excluded from the study. The ethical

committee of Faculty of Medicine, Zagazig University approved our study protocol, and all participants assigned written informed consent.

Blood sampling:-
Blood samples were drawn from all subjects after an overnight fasting and divided into 3 portions: and HbA1c; 1 ml of whole blood was collected into evacuated tubes containing fluoride for fasting blood glucose. Serum was separated immediately from remaining part of the sample and stored at −20 °C until analysis.

Biochemical measurements:-
We determined fasting blood glucose using the glucose oxidase method (Spinreact, Girona, Spain). Total cholesterol and triglycerides were measured by routine enzymatic methods (Spinreact, Girona, Spain). HDL cholesterol was determined after precipitation of the apoB-containing lipoproteins. LDL cholesterol was calculated using the Friedewald formula (12) Biochemical parameters including serum levels of blood urea nitrogen (BUN), uric acid, creatinine, and albumin were measured with standard techniques by an automatic analyzer. Serum CRP concentrations were analyzed through enzyme immuneassay. Serum leptin levels were assessed using commercial ELISA (Enzyme Linked Immunosorbent Assay) kit (Human Leptin ELISA kit, (Biovendor [Cat No: RD191001100], USA). The serum samples were immediately frozen at -70˚C until analysis.

Statistical analysis:-
Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (version 22.0; SPSS Inc., Chicago, IL, USA). Data were expressed using descriptive statistic (mean ± standard deviation) and were analyzed. One-way analysis of variance (ANOVA) test was done to compare different parameters between more than two groups. Pearson correlation coefficient was used to assess the association between leptin, obesity indices, hematological, biochemical tests and other studied metabolic parameters in patients with hemodialysis. A linear regression analysis was performed to detect the main predictors of leptin levels in hemodialysis P-values were considered significant if <0.05.

Results:-
Among case individuals, 34% were male and 66% female, and in control individuals' 44% male and 56% female. The mean age of case group was 35.56±7.48 years and in controls 35.96±5.75years. The case and control individuals were thus balanced in terms of age and Gender (Table 1).

Clinical and Anthropometric characteristics of the studied groups are summarized in Table 1.
Patient on chronic hemodialysis had significantly higher values of systole (115.35 ± 25) ,($p < 0.05$). On the other hand, there were non-significant differences between control and hemodialysis group as regard diastole, Body surface area, BMI, weight, height and Waist-hip ratio, ($p > 0.05$).

Table 1: Clinical and anthropometric parameters of the studied groups.

Variable	Cases (n=55)	Control (n=34)	p
Age (years):	48.35 ± 12.4	43.94 ± 8.06	N.S
Weight(kg)	73.21 ± 16.6	77.07± 12.94	N.S
Height(m)	1.66 ± 0.08	1.65 ± 0.09	N.S
BMI(kg/m²)	26.7 ± 6.18	28.13 ± 4.14	N.S
Body surface area	1.8 ± 0.22	1.84± 0.18	N.S
Waist-hip ratio	0.74 ± 0.07	0.75 ± 0.06	N.S
Diastole(mmHg)	76.4 ± 10.5	72.65 ± 7.51	N.S
systole(mmHg)	127.6 ± 19.9	115.35 ± 25	<0.001*

BMI, body mass index; NS, not significant.

Biochemical characteristics of the studied groups are summarized in Table 2.
Patient on chronic hemodialysis had significantly higher values of PPBS (177.13 ± 70) , HbA1c(6.69 ± 0.42) , Urea(157.8 ± 42.69) ,S. Creatinine(10.7 ± 2.95) ,($p < 0.05$). On the contrary, Patient on chronic hemodialysis had significantly lower values of Albumin (3.25 ± 0.6) .On the other hand, there were non significant differences between control and hemodialysis group as regard WBCS, Platelets ,LDL ,HDL, Cholesterol ,Triglyceride ,FBS ,bilirubin ,ALT ,AST,Serum Ca and Po4 , ($p > 0.05$).

Table 2: Biochemical parameters of the studied groups.

Variable	Cases (n=55)	Control (n=34)	p
WBCS*1000	6.15 ± 2.15	6.58 ± 1.94	N.S
Platelets*1000	266.45 ± 90.56	256.18 ± 67.11	NS
LDL(mg/dL)	77.75 ± 27.42	67.9 ± 25.95	N.S
HDL(mg/dL)	52.84 ± 15.52	52.8 ± 15.61	N.S
Cholesterol (mg/dL)	158.16 ± 27.26	147.5 ± 26.3	N.S
Triglyceride (mg/dL)	132.27 ± 30.29	135.6 ±11.6	NS
PPBS(mg/dL)	177.13 ± 70	117.9 ± 9.7	<0.001*
FBS(mg/dL)	99.92 ± 84.83	80.82 ± 7.42	N.S
HbA1c	6.69 ± 0.42	6.38 ± 0.3	<0.001*
Albumin (g/dL)	3.25 ± 0.6	3.69± 0.24	<0.001*
Bilirubin	0.84± 0.07	0.86± 0.06	N.S
ALT(u/l)	35.57 ± 17.63	28.59 ± 5.83	< 0.05
AST(u/l)	28.07 ± 19.51	26.39 ± 7.1	NS
S. Creatinin (mg/dL)	10.7 ± 2.95	0.83 ± 0.21	<0.001*
Urea (mg/dL)	157.8 ± 42.69	34.12 ± 6.85	<0.001*
Serum Ca (mg/dl)	8.11 ± 1.59	8.59 ± 0.53	N.S
Po4 (mg/dl)	4.11 ± 1.64	3.49 ± 1.67	N.S

BUN, blood urea nitrogen; CRP, C-reactive protein; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; PPBS, post prandial blood glucose; FBG, fasting blood glucose;HbA1c,hemoglobin A1c. * $P < 0.05$ when compared with control group

Table 3: Comparison of body weight of the two studied groups according to Body mass index: There were non - significant differences between control and hemodialysis group as regard BMI, ($p > 0.05$).

Table 3: Comparison of body weight of the two studied groups according to Body mass index.

Variable	Cases (n=55)	Control (n=34)	χ^2	P
BMI:				
Under –weight N (%)	2 (3.6%)	0 (0%)		
Normal weight N (%)	18 (32.7%)	9 (26.5%)	2.83	N.S
Over weight N (%)	24 (43.6%)	14 (41.2%)		
Obese N (%)	11 (20%)	11 (32.4%)		

BMI, body mass index,* $P < 0.05$ when compared with control group.

Pearson correlations between serum Leptin(ng/ml) and other parameters (Table 4)

In patients on chronic regular hemodialysis, serum leptin level was positively correlated with body mass index,age, weight, body surface area and waist/hip ratio. On the contrary, there were significant negative correlations between serum leptin level and diastolic blood pressure and systolic blood pressure in control group, there were non-significant correlation between leptin and other clinical and biochemical characters.

Table 4: Pearson correlations between serum Leptin (ng/ml) and clinical ,anthropometric parameters and biochemical tests in the two studied groups.

Variable	Cases (N=55)		Control (n=34)	
	r	P		r
Age	0.38	<0.01	-0.18	NS
Weight	0.57	<0.001	0.09	NS
Height	0.06	NS	-0.34	N.S
Body mass index(BMI)	0.61	<0.001	-0.11	NS
Body surface area(BSA)	0.46	<0.001	-0.11	NS
Waist/hip ratio	0.53	<0.001	0.2	NS
Diastolic blood pressure	-0.35	<0.01	-0.22	NS
Systolic Blood Pressure	-0.28	<0.05	-0.19	NS
Albumin	0.22	NS	-0.14	NS
Bilirubin	0.15	NS	0.16	NS
ALT	-0.04	NS	0.14	NS
AST	-0.05	NS	-0.31	NS
Sca	0.23	NS	-0.16	NS
Po4	0.005	NS	0.02	NS
Na	-0.03	NS	0.34	NS
K	0.25	NS	-0.27	NS
S Creatinin	0.11	NS	-0.11	NS
Urea	-0.09	NS	0.25	NS
CRP	0.04	NS	-0.13	NS
WBCS	0.07	NS	0.05	NS
HB	0.07	NS	-0.12	NS
Platelets	0.04	NS	0.14	NS
LDL	0.12	NS	0.16	NS
HDL	0.17	NS	-0.17	NS
Cholesterol	0.2	NS	0.05	NS
Triglyceride	-0.1	NS	-0.07	NS
PPBS	0.07	NS	-0.15	NS
FBS	-0.03	NS	-0.003	NS
HbA1c	-0.08	NS	0.12	NS
Age	0.38	<0.001	-0.18	NS
Weight	0.57	<0.001	0.09	NS

BUN, blood urea nitrogen; CRP, C-reactive protein; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; PPBS, post prandial blood glucose; FBG, fasting blood glucose;HbA1c,hemoglobin A1c. * $P < 0.05$ when compared with control group

Linear regression analyses in hemodialysis patients to test the influence of the main independent variables against serum leptin levels (dependent variable).

In chronic hemodialysis patients (n=55), stepwise linear regression analysis showed that, serum leptin levels were independently correlated with diastolic blood pressure, ($p < 0.001$) (**Table 5**).

Table 5: Linear regression analyses in hemodialysis patients to test the influence of the main independent variables against serum leptin levels (dependent variable).

Model		Unstandardized Coefficients		Standardized Coefficients	T	P	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	229.952	173.140		-1.328-	.195	-585.205-	125.301
	Weight	.340	1.307	.426	.260	.797	-2.341-	3.021
	Height	42.850	106.778	.270	.401	.691	-176.240-	261.941
	BMI	.087	2.638	.041	.033	.974	-5.326-	5.500
	Body surface area	-32.346-	67.520	-.534-	-.479-	.636	-170.885-	106.193
	Waist /height	40.723	46.315	.223	.879	.387	-54.307-	135.753
	Diastole	1.148	.401	.884	2.865	.008	.326	1.970
	Systole	-.321-	.183	-.477-	1.756-	.090	-.696-	.054
	Albumin	-.693-	4.679	-.032-	-.148-	.883	-10.294-	8.909
	Total bilirubin	-4.946-	39.336	-.025-	-.126-	.901	-85.657-	75.764
	ALT	-.105-	.105	-.157-	-.996-	.328	-.321-	.111
	AST	-.076-	.196	-.076-	-.385-	.704	-.479-	.328
	Serum calcium	-2.965-	3.869	-.124-	-.766-	.450	-10.904-	4.973
	Serum phosphorus	.369	2.664	.025	.138	.891	-5.098-	5.836
	Creatinine	.413	.715	.103	.578	.568	-1.054-	1.881
	Urea	-.063-	.055	-.219-	-1.146-	.262	-.175-	.049
	WBC	-.936-	1.186	-.154-	-.789-	.437	-3.369-	1.498
	Hemoglobin	-.422-	1.236	-.060-	-.341-	.736	-2.957-	2.113
	Platelet	.057	.024	.393	2.325	.028	.007	.107
	Ldl	-.082-	.227	-.127-	-.362-	.720	-.548-	.384
	Hdl	-.135-	.205	-.161-	-.660-	.515	-.556-	.285
	Tc	.147	.181	.303	.811	.425	-.225-	.518
	Tg	.045	.084	.106	.539	.594	-.128-	.219
	Na	.535	.314	.289	1.706	.100	-.109-	1.179
	K	6.185	2.333	.380	2.652	.013	1.399	10.971
	PPBG	-.032-	.033	-.169-	-.963-	.344	-.099-	.036
	FBG	-.011-	.029	-.070-	-.372-	.713	-.070-	.048
	Hba1c	7.165	5.882	.226	1.218	.234	-4.903-	19.234

Comparison of Leptin level of the studied groups (Fig.1 and 2):

Patient on chronic hemodialysis had significantly higher values of serum leptin (17.05 ± 13.24) more than controls (8.43 ± 7.84) moreover, Patient on chronic hemodialysis stratified according to BMI to four group; under-weight(n=2) ,(**2.52±3.54**), normal weight (n=18) , (**9.65±7.05**) over weight (n=24) ,(16.84±10.24) and obese group (n=11),(25.27± 15.080),there were high significant different among these groups.

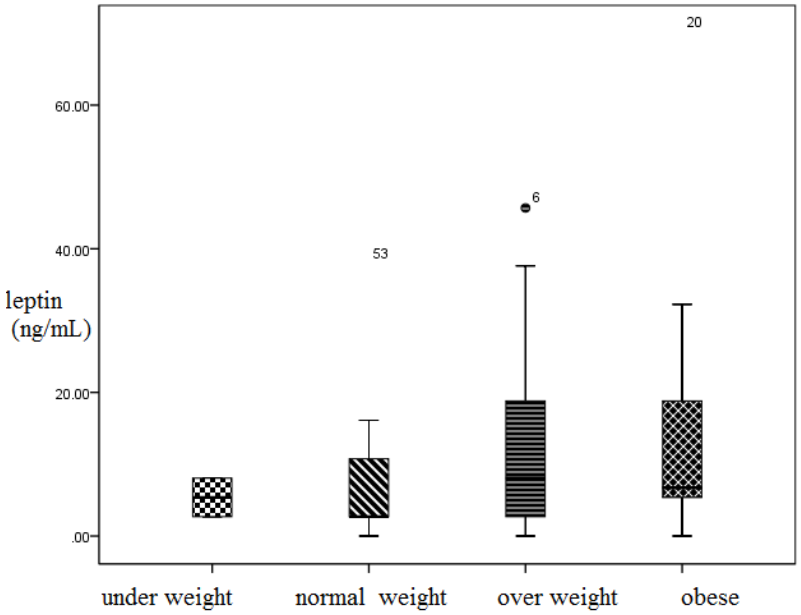

Figure 1: serum leptin levels in studied groups stratified according to BMI.

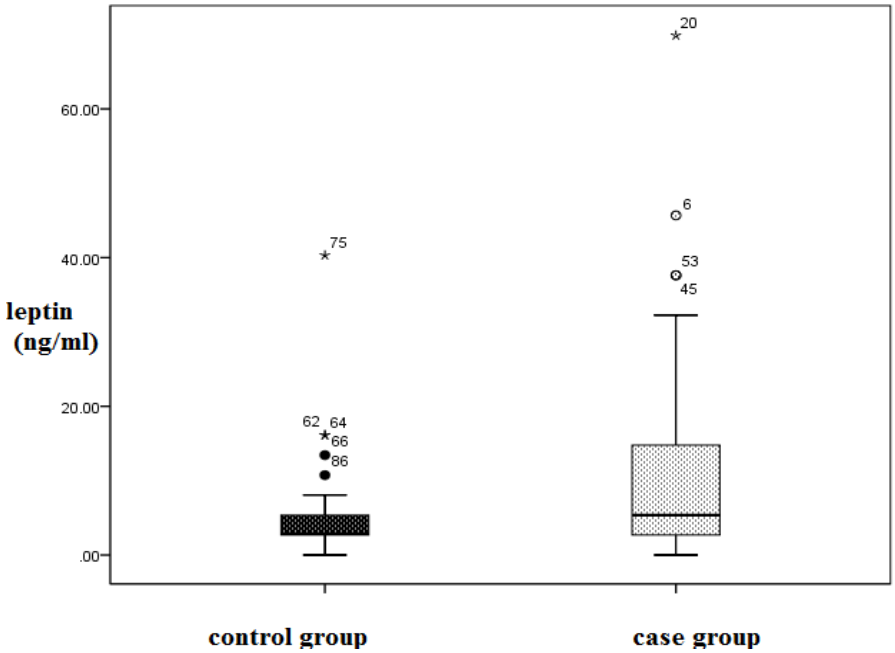

Figure 2: serum leptin levels in studied groups.

Comparison of CRP level of the studied groups (Fig.3and 4):

Patient on chronic hemodialysis had significantly higher values of CRP (11.1 ± 13.02) more than controls (5.19 ± 7.44).moreover, Patient on chronic hemodialysis stratified according to BMI to four group; under -weight (n=2) ,(5.37±3.8), normal weight (n=18) , (7.33±8.97) over weight (n=24) ,(12.54 ±11.34) and obese group (n=11),(15.15± 20.65), there were high significant different among these groups

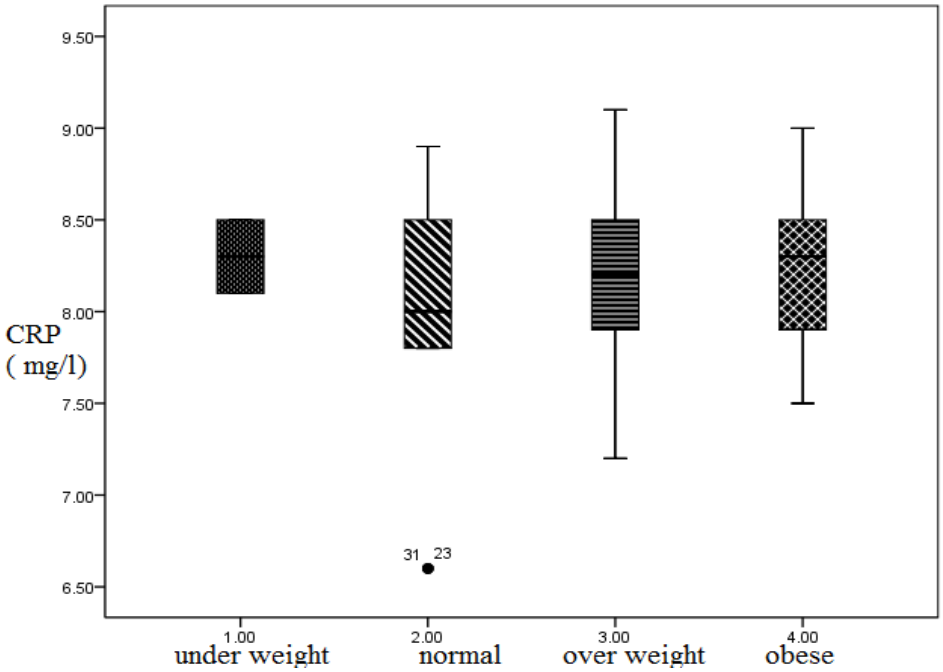

Figure 3: CRP levels in studied groups stratified according to BMI.

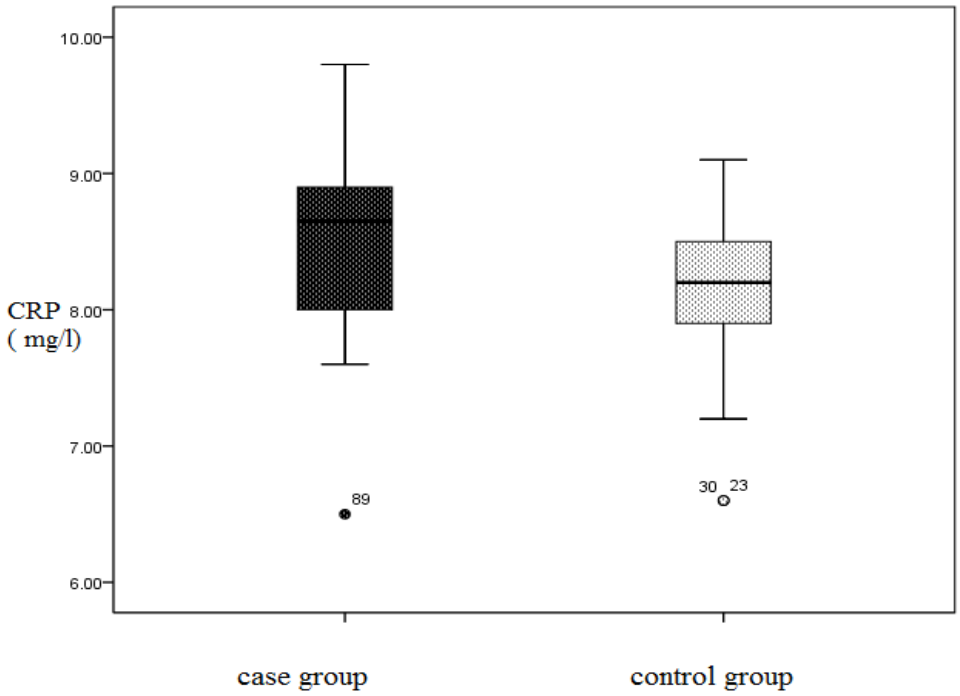

Figure 4: CRP levels in studied groups.

Comparison of hemoglobin level of the studied groups (Fig.5 and 6):
Patient on chronic hemodialysis had significantly lower values of hemoglobin (9.95 ± 1.86) more than controls (12.12 ± 1.1).moreover, Patient on chronic hemodialysis stratified according to BMI to four group; under -weight (n=2) ,(9.2±0.63), normal weight (n=18) , (9.5±1.68) over weight (n=24) ,(10.16 ±1.62) and obese group (n=11),(10.48± 2.07), there were high significant different among these groups.

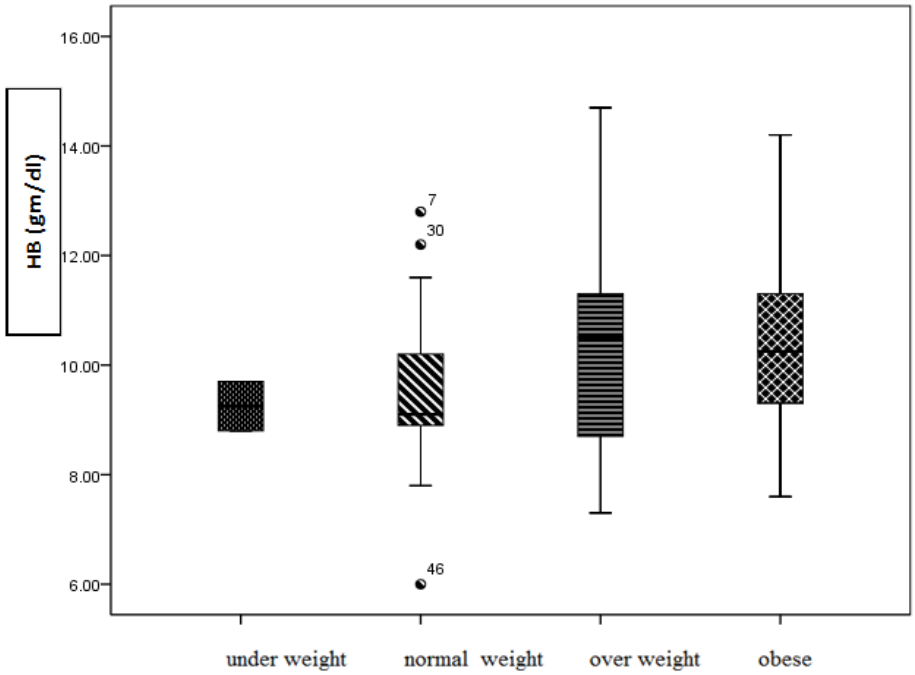

Figure 5: hemoglobin levels in studied groups stratified according to BMI.

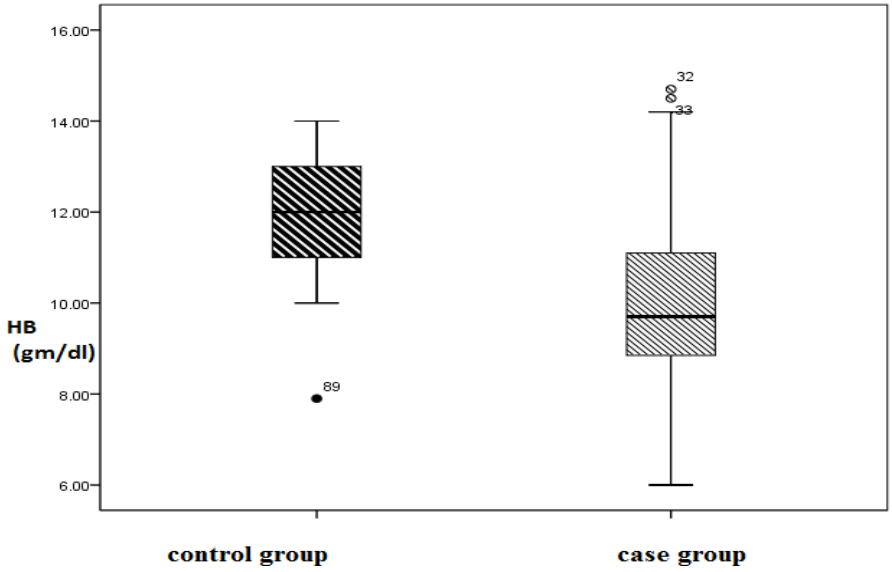

Figure 6: hemoglobin levels in studied groups.

Discussion:-

Leptin, "a negative acute phase protein," is secreted by adipose tissue and acts on the hypothalamus in order to regulate food intake and energy expenditure (13, 14, 15). Leptin reduces body weight via neuronal activity modulation within the hypothalamus (16). It has been postulated that leptin plays an important role in inducing anorexia and malnutrition in uremic patients (13), but the mechanisms by which it affects progressive malnutrition

in kidney failure and its clinical significance are not clearly understood (14). Conflicting results have been published about the relationship between serum leptin level and ESRD.

Leptin is considered to be a pro-inflammatory cytokine. Its synthesis is mostly dependent on the amount of body fat but it is also enhanced during acute infection and inflammation. Production of leptin is also regulated by the actions of pro-inflammatory mediators such as tumor necrosis factor (TNF)-α, IL-6, and IL-1 (17)Moreover, leptin itself stimulates the production of pro-inflammatory cytokines from macrophages (18)

Inflammation mediated by pro-inflammatory cytokines is very common in patients with CKD and HD patients, and contributes to mortality of these patients alongside with other mortality risk factors, such as malnutrition, anemia, vascular disease, and left ventricular hypertrophy. Studies have shown that in patients with chronic renal failure TNF–α and IL-1 are major pro-inflammatory cytokines, whereas interleukin IL-6 appears to be key mediator of acute phase reactant synthesis, including C-reactive protein (CRP) (19).

C-reactive protein (CRP) is a positive acute phase protein and can be increased with any kind of infection/inflammation (20) Since increased serum CRP inhibits the serum albumin generation in hemodialysis patients (20) it may be a powerful determinant for anorexia, hypoalbuminemia, and the diagnosis of malnutrition in renal failure patients (21).

Patients on hemodialysis are exposed to persistent low-grade inflammation which is often accompanied with malnutrition. (22)Some studies suggested that protein malnutrition is both a cause and a consequence of inflammation and related comorbidities in HD patients., adipose tissue is the key regulator of serum CRP concentration, as one of the best studied markers of micro inflammation (22) Moreover, many studies have shown that serum CRP levels are significantly associated with different dietary patters and nutritional status (20).

Obesity is a risk factor for progressive decline in renal function in patients with known renal disease (23). BMI is an appropriate, simple, and cheap measurement, and a low BMI value is closely associated with mortality in HD patients (24). Also, BMI is a simple method and reliable indicator to estimate fat mass in dialysis patients (25) .and a positive correlation between BMI and risk for CKD has been reported (26,27) . Furthermore, a high BMI is associated with glomerular hyperperfusion and hyperfiltration, resulting in renal injury with proteinuria obesity-related glomerulopathy (28,29) . BMI has been considered as a common, strong, and potentially modifiable independent risk factor for CKD (27). .
Anemia, a well-known complication in CKD patients, is associated with various poor clinical outcomes such as left ventricular hypertrophy, cardiovascular morbidity, more rapid loss of kidney function, increased hospitalization, and poor quality of life (30).Anemia develops early in the course of CKD and is almost universal in patients with CKD stage 5 (31); erythropoietin insensitivity in addition to reduced erythropoietin production in renal failure patients (32).Other possible causes of anemia in CKD include iron deficiency, inflammation, and the accumulation of uremic toxins (33)

Obesity is a risk factor for ESRD in patients with known renal disease .In our study, we adjust BMI between case and control group in order to assess the role of hemodialysis alone between case and control. But for further analysis the impact of body weight changes on anemia , CRP and leptin we stratified both case and control groups into four groups according to BMI; underweight, normal weight ,over weight and obese

Our study found that, in Patient on chronic hemodialysis when stratified according to BMI to four group ;under-weight ,normal ,over weight and obese to assess the role of leptin on body weight we found that ,serum leptin levels were higher in obese group, moreover the levels of serum leptin were positively correlated with BMI. This agrees with the result of Kaur et al., who stated that serum leptin levels found to be significantly higher in hemodialysis group than that of the control group(34)..

Our findings were also similar to those detected by Dervisevic et al., as they observed that serum leptin levels were higher in HD patients compared to healthy subjects of the control group (35). These findings are in a close agreement with results reported by Beberashvili et al., (11) who have also determined increased leptin levels in HD patients. They suggested that, Hyperleptinemia observed in their studies might be result of decreased renal clearance and consequent leptin retention in HD patients (36).

On the contrary, Montazerifar et al found that,the mean serum leptin level was significantly decreased in HD patients, particularly in subjects with BMI < 18.5 kg/m² and serum albumin level < 3.5 g/dL. Additionally, serum leptin levels were found to positively correlate with BMI and serum albumin levels They explained their results as HD patients consumed the lower daily servings of the food groups compared to the control subjects (37).

Our study demonstrated that,in patients on chronic regular hemodialysis, serum leptin level was positively correlated with body mass index, age, weight, body surface area and waist/hip ratio. On the contrary, there were non-significant correlations between leptin and CRP levels. Similar results observed by Montazerifar et al., (37).

Kaur et al., also observed a positive correlation between serum leptin and BMI. (34). Similar studies reported by Iglesias et al.,38) Nizhizawa et al.,(41) and Lonnqvist et al.(38) had shown a strong direct correlation between serum leptin levels and BMI. This could be attributed to leptin's direct action on hypothalamus (40).

Nevertheless, some studies had shown that there was no correlation between plasma leptin levels and history of weight change during dialysis (41), also, a study reported by Pecoits et al., on hemodialysis patients suggested a paradoxically inverse association between higher serum leptin levels and markers of nutritional status (41), a finding that was consistent with the theory of reverse epidemiology given by Kalantar et al. in the same year (42).

Dervisevic et al., demonstrated significant positive correlation of elevated serum leptin levels with BMI values but not with values of CRP and ESR, suggest that leptin is more valuable indicator of nutritional status in HD patients than markers of micro inflammation (35).

Montazerifar et al., found no correlation was found between serum levels of CRP with leptin and other nutritional factors, suggesting that CRP is a poor predictor of malnutrition in dialysis patients (37).

Our study found that , in Patient on chronic hemodialysis when stratified according to BMI to four group ;under-weight ,normal ,over weight and obese group ,as we know that obesity is a state of inflammation and so to explore the association of CRP with BMI we found that ,serum CRPlevels were higher in obese group, moreover the levels of serum CRP were positively correlated with BMI

Kaur et al., found that the study group had a significantly higher value of CRP than the control group. However, in patients with ESRD on hemodialysis (34)CRP and BMI did not show a significant correlation.
Malnutrition in hemodialysis patients is very common, the most important nutrition disorders are anemia and weight changes To assess anemia in patients with ESRD on regular hemodialysis.our study revealed that Patient on chronic hemodialysis had significantly lower values of hemoglobin more than controls .moreover, when Patient on chronic hemodialysis stratified according to BMI there were high significant lower levels in under–nutrition,also there were positive correlation between anemia and body weight these finding may due to good appetite and consume healthy diets in obese patients with ESRD.

A similar results had been detected by other authors **Moossavi S, et al**., (44) **and Robinson B , et al**.,(45) ,they explained that due to decrease erythropoietin production in ESRD.

Our study demonstrated that , Patient on chronic hemodialysis had significantly lower levels of albumin more than controls .Moreover, when Patient on chronic hemodialysis stratified according to BMI there were high significant lower levels in under –nutrition ,also there were positive correlation between albumin and body weight these finding may due toassociation between malnutrition , hypoalbuminemia and inflammation in ESRD.

Similar results by Montazerifar et al., they found that, albumin level was markedly lower in HD patients than controls(37). Other studies in HD patients have demonstrated a potential relationship between malnutrition and hypoalbuminemia, which depends on both nutrition and inflammation (46,47,48).

Conclusion:-

In the present study, increased serum concentration of leptin as pro-inflammatory cytokine as well as elevated serum values of CRP indicates presence of systemic micro inflammation in HD patients. In HD patients there were significant positive correlation between serum leptin concentrations and BMI values. However, absence of

significant association between serum leptin and CRP levels and different clinical and biochemical parameters in HD patients requires further investigation and clarification .According to the results of this study; serum leptin can be used as diagnostic marker of nutrition disorders in patients on regular hemodialysis.

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