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Original Article

Evaluation some Biochemical Levels in Patients undergoing Hemodialysis in Baghdad Governorate

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Abstract: The objective of investigating some biochemical parameters like urea, creatinine, Hb and other parameters as CRP and leptin in the serum of ESRD patients on hemodialysis pre-dialysis.
Method: Sample of 250 cases which consists of the patient with ESRD, their mean ages were 52.66 ± 12.55 years with ranged from 18-83. Moreover, under hemodialysis treatment not less than three months. Apparently, 20 healthy subjects were selected as (control) for comparison.
Results: The results showed that there was a significant increase ($p<0.01$) in the serum urea, creatinine, CRP, and leptin. While, revealed significant ($p< 0.05$) decrease in the levels of uric acid, serum glucose, albumin, inorganic phosphorus, potassium, Hb and platelet in patients before dialysis compared to the control group. Non-significant ($p>0.05$) is in total cholesterol, calcium and total protein in patients undergoing hemodialysis which was compared to the control group. It is concluded from the findings of the present study, it shows a highly significant increased serum concentration of leptin as well as, elevated serum values of CRP. Whereas a highly significant decrease in GFR and CrCl result from loss of the ability of the kidney to clearance. Also, abnormal mineral parameters and hematological parameters. According to the results of this study, serum total protein and cholesterol cannot be used, as a diagnostic marker of nutrition disorders in patients on regular hemodialysis requires further investigation and clarification.

Keywords: CRP, Hemodialysis, Blood serum, Leptin.

1. Introduction

The condition when the kidneys lose their normal functionality called renal failure [1]. It occurs when the kidneys cannot properly remove wastes that cause a buildup of waste and fluid in the body [2]. Renal impairment continues to be associated with high morbidity and mortality [3]. In the other way, renal failure is characterized by a wide change of biochemical instabilities and many clinical symptoms and signs [4]. Leptin plays a vital role in promoting anorexia and malnutrition in uremic patients [5]. Factors like the decline in renal clearance and erythropoietin level and inflammation have been supposed to raise leptin level in end-stage renal disease (ESRD) patients [6]. The previous study revealed high serum levels of C-reactive protein (CRP) and cytokines elevate leptin gene expression [7,8]. The result of renal failure is usually death unless the blood is filtered by some other means [9]. Dialysis keeps the body in balance [10]. It is a procedure that removes excess fluids and toxic end products of metabolism such as urea from the plasma, when the kidneys fail and correct electrolytes balance by dialyzing the patient's blood against fluid containing no urea but with appropriate concentrations of electrolytes, free-ionized calcium and some other plasma constituents [11]. Hemodialysis (HD) is a medical method that uses a special machine to filter waste products from the blood and to restore normal constituents to it when the kidneys are unable to do so [12]. Hemodialysis is frequently done to treat patients with (ESRD). Under such circumstances, kidney dialysis is typically administered using a fixed schedule usually over four-hour of three times per week [13]. The primary goal of hemodialysis is to restore the intracellular and extracellular fluid environment that is characteristic of normal kidney function [14]. This is accomplished by the transport of solutes such as blood urea and bicarbonate take place down a concentration gradient from the circulation into the dialysate and in the reverse direction [15].

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2. Material and Methods

The condition when the kidneys lose their normal functionality called renal failure. During the time from April 2016 to March 2017, a cross-sectional study was conducted with 250 HD patients (138 males and 112 females). The patients were collected from four different major HD centers in public hospitals in Baghdad capital, their mean age was 52.66 ± 12.55 years with ranged from 18-83. Apparently, 20 healthy subjects were selected to participate as a normal group (control) for comparison. They were collected from medical staff and relatives who were free from signs and symptoms of renal disease. A blood sample was taken from the patients pre-dialysis and healthy subjects to perform the study which included measurement pre-dialysis of the following variable, renal function tests: urea, creatinine, uric acid, glomerular filtration rate (GFR), and creatinine clearance (CrCl). To calculate each one of the (Serum Urea, Creatinine, and Uric acid), used Randox Kit specific for each parameter by Roche Cobas c 111 clinical chemistry analyzer, for assay the glomerular filtration rate (GFR) at baseline and during follow-up was estimated by the following formula: eGFR-EPIcreat = 141 × min (SCr/k, 1) α × max (SCr/k, 1) − 1209 × 0.993 Age [×1.018 female] [×1.159 if black], Where SCr is serum creatinine in mg/dL, k is 0.7 for females and 0.9 for males, α is −0329 for females and −0411 for males, min is the minimum of SCr/k or 1, and max is the maximum of SCr/k or 1 (Levey *et al.*, 2009) [16]. Whereas CrCl estimated by Cockcroft-Gault equation (C-G = [140 – age (years)] × weight (kg) × 1.23 [if male] / sCr (μmol/L) (Pierrat *et al.*, 2003) [17]. Biochemical parameters like albumin, total protein, cholesterol and blood glucose. In addition, electrolytes levels: calcium, phosphorus, potassium, sodium, and chloride, were determined by a Randox kit for each parameter and RX Monza semi-automated clinical chemistry analyzer for analysis. Whereas leptin level and C-reactive protein in serum that they were estimated by Enzyme-Linked ImmunoSorbent Assay (ELISA) method. In the current study, hematological disorder Hb, PCV, lymphocyte, RBC, and platelets were measured by RUBY Hematology Analyzer. All the results are presented as mean ± SE. The Statistical Analysis System- SAS (2012) program was used to effect of different factors in study parameters. The least significant difference – LSD test was used to significant compare between means in this study.

3. Results and Discussion

3.1 Evaluate the changes in renal function tests

In the Table (1) from current study, the urea and creatinine high significant (P<0.01) increased in patients when compared with control group, this is due to a decline in the number of nephrons [18]. This increase in urea and creatinine level occurs because in CRF the kidney loses its ability to eliminate nitrogenous wastes from the blood results in accumulation of these substances in the blood [19]. This result agrees with [20,21,22,23], they showed a highly significant increase in urea and creatinine concentrations in chronic kidney disease. Uric acid levels were normal range in both groups with a significant (p<0.05) increase in patients group, this result of the present study agreed with those obtained by [20,24]. Elevated serum uric acid levels as observed in current study may result secondary to decreased glomerular filtration, decreased tubular secretion or enhanced tubular reabsorption. Decreased urate filtration can contribute to the increase in a uric acid of renal insufficiency [25], which in turn the fall in the glomerular filtration rate (GFR) in CRF patients [26]. The value of urea as a test of the renal function depends on the observation that serum/plasma urea concentration reflects GFR: our study demonstrated that the GFR level significant (p<0.01) decrease in the patients when compared with control subject and this result agree with [27,28]. However, as the GFR falls, the creatinine clearance increases because of an increased tubular secretion of creatinine [29], as GFR declines, plasma/serum urea rises [30]. To determine the GFR for clarifying the stage of renal disease uses the level of creatinine in the blood. These results are supported by findings of other workers Abdul Wahid *et al*., who reported that as a result, this leads to loss of the ability of the kidney to clearance which can explain the decline of creatinine clearance level [31].

Table 1. Renal function tests in HD patients and healthy individuals.

Parameters	Groups		P-value
	Control	Patients	
Urea mg/dl	18.60 ± 0.80	129.27 ± 12.78	0.0001 **
Cr mg/dl	0.620 ± 0.02	6.96 ± 0.76	0.0001 **
Uric Acid mg/dl	5.42 ± 0.20	7.00 ± 0.63	0.0448 *
GFR mL/min per 1.73 m^2	122.40 ± 1.88	8.69 ± 1.02	0.0001 **
CrCl mL/minute	109.20 ± 4.23	13.74 ± 0.96	0.0001 **

- Mean ± SE
- NS: Non-Significant.
- ** Significant difference at (p< 0.01).
- Significant difference at (p< 0.05).

3.2 Evaluate the changes in some biochemical parameters tests

In the present study, we showed, in the Table (2). There was non-significant difference (P>0.05) between patient and control in level of serum total protein, these results were accordance to that found by [32,20]. The results of normal total protein concentration were not inconsistency to those results obtained by other studies [33,34], they found that there was a non-significant difference when protein and albumin were reduced in their levels in the serum of patients with renal failure. Otherwise, serum albumin concentration is significantly lower (p<0.05) in renal failure patients when compared

with those of the control group. A reduction in the rate of albumin synthesis which may be caused by metabolic acidosis, impaired protein intake, and inflammation show a significant decrease in albumin level in HD patients [35,36]. Changes in the structure of basement membrane of glomeruli which consequent lead to the leakage of albumin and some low molecular weight proteins [37]. Proteinuria is considered as a marker of renal disease progression [38]. Restriction of protein intake [39] and protein malnutrition may attribute to such decrease in albumin and total protein of the serum of the corresponding patients [40]. This result is similar to the previous studies done by [31,41,23], they suggested that proinflammatory cytokines (TNF-a and interleukins) induce an acute phase response decreases hepatic synthesis of albumin and increases its catabolism the degradation of albumin. Thus, much of the observed association of albumin level with outcomes may be attributed to inflammation rather than malnutrition in the ESRD population [42].

Table 2. Biochemical parameters tests in HD patients and healthy individuals.

Parameters	Groups		P-value
	Control	Patients	
Total Protein g/dl	6.18 ± 0.05	6.50 ± 0.17	0.1983 NS
Albumin g/dl	5.36 ± 0.04	3.61 ± 0.04	0.0412 *
Cholesterol mg/dl	171.20 ± 5.22	170.89 ± 9.51	0.675 NS
FBS mg/dl	104.20 ± 7.66	122.19 ± 11.47	0.0382 *

- Mean ± SE
- NS: Non-Significant.
- ** Significant difference at ($p < 0.01$).
- Significant difference at ($p < 0.05$).

In addition, The result demonstrated non-significant ($P>0.05$) difference in serum cholesterol in chronic renal failure patients when compared with those of the control group, and this result is consent with [43,21,23]. Also, with study by Vazir, who stated that plasma Cholesterol concentration is normal or even reduced in ESRD [44]. Whereas these results were not like that found [45]. It is thought that malnutrition is a factor contributing to both the low lipid values and the high mortality in the dialysis patients [46]. On the other hand, the result demonstrated a significant ($P<0.05$) increase in serum glucose, elevated in FBS due to most of the patients have diabetes which causes damage to the kidneys, and this condition can lead to kidney failure [47]. The similar result has been reported by [48,43,49]. Several factors, including uremic toxins, may increase insulin resistance in ESRD, leading to a blunted ability to suppress hepatic gluconeogenesis and regulate peripheral glucose utilization [50].

3.3 Evaluate the changes in some Minerals levels tests

From Table (3) in the present analysis a non-significant decrease in calcium (Ca) ($P>0.05$) in ESRD patients as compared with their control groups. Decreased Ca level found when the kidneys fail, decreasing its ability to reabsorb calcium and leading to loss of calcium in the urine [47,51] and Patients with chronic renal failure tend to ingest less calcium in their diets than normal subjects. This result is compatible with [52,23]. In the current study, the patient takes exogenous sources of excess Ca include dietary Ca, Calcium supplements, Calcium-containing phosphate binders, and dialysate solutions that may be avoided the decline of calcium level. On the other hand, the table (3) shown a significant ($p<0.05$) increase in electrolytes levels phosphorus (PO_4) and potassium (K) in patients when compared with control. Among mineral abnormalities, the most prevalent is hyperphosphatemia, which is a common problem among patients with ESRD [53,54]. Several studies have found a significant increase in serum phosphorus levels in patients in CKD [55,56,48]. These findings are similar to our study. We observed a statistically significant increase in serum PO_4 levels in cases as compared to controls. The previous study reported a significant increase in PO_4 levels and concluded that high levels of PO_4 as a significant risk factor for mortality in CKD [57]. Raised serum (PO_4) can result in renal mineralization, secondary hyperparathyroidism and potentially (not conclusive), to the progression of renal damage [58]. Medications and special diets can be used to help keep (PO_4) levels down [59]. Potassium homeostasis is largely regulated by the kidney accounting for excretion of 90% of daily K loss [60]. Patients with renal failure, acute or chronic, have impaired regulatory mechanisms and are prone to hyperkalemia [61]. The results revealed a significant ($p<0.05$) increase in the levels of K in patients with CRF when compared with control, thought to result from the failure to follow dietary K restrictions and ingestion of medications that contain K, or from an endogenous release of K, as in case of trauma or infection [19]. In the present study, serum sodium (Na) level non-significant ($p>0.05$) change in ESRD patients as compared with control group. The similar result has been reported by [43,26]. However, these results disagree with a previous study done by Williams, who related that to a major inability of the kidney to respond normally to change in Na concentration [62]. Probably the explained the normal level of serum Na due to reducing Na intake and humoral natriuretic factor in CRF that helps to increase sodium excretion and maintain normal Na balance. In addition, do not forget the effect of permanent hemodialysis on maintenance of normal Na concentration [63]. On the other hand, salt wasting is a common problem in advanced renal failure because of impaired tubular reabsorption of sodium [19], which may support our results. Also from data in the same table, found level of chloride (Cl) non-significant ($p> 0.05$) difference with slightly higher in patients and this result conflict with study done by [64].

Table 3. Minerals levels tests in HD patients and healthy individuals.

Parameters	Groups		P-value
	Control	Patients	
Ca mg/dl	7.70 ± 0.04	7.77 ± 0.10	0.894 NS
P mg/dl	3.08 ± 0.03	8.07 ± 1.08	0.0241 *
K meq/l	3.86 ± 0.03	5.32 ± 0.06	0.0238 *
Na meq/l	139.80 ± 0.30	139.27 ± 0.61	0.873 NS
Cl meq/l	100.00 ± 0.29	105.94 ± 0.62	0.779 NS

- Mean ± SE
- NS: Non-Significant.
- ** Significant difference at (p< 0.01).
- Significant difference at (p< 0.05).

3.4 Evaluate the changes in serum Leptin and CRP concentrations

The results showed in the Table (4) serum leptin level is highly significant (p< 0.01) increase in CRF patients as compared to control group, which is similar to the findings of the previous studies [43,65,23] but different with [66]. The difference could be due to discrepancies in numbers of patients in these studies. Hyperleptinemia observed might be the result of decreased renal clearance and consequent leptin retention in HD patients [67]. It is cleared from the circulation by the process of glomerular filtration followed by metabolic degradation in renal tubules [68]. The findings of the present study demonstrated that the patients with elevated CRP levels had markedly increased leptin concentration compared to control subjects. No mechanism has been proven to explain the relationship between CRP and leptin [69]. However, other factors such as hyperinsulinemia [70] and inflammation [71] have been implicated in augmenting leptin secretion in renal failure. The mean levels of CRP in this study were significantly and markedly higher in patients with CKD compared with that in controls, and this is due to the presence of infections among chronic kidney disease patients, as it is a strong predictor of mortality due to heart and blood vessels diseases among hemodialysis patients [72]. This finding is in close agreement with those reported by [43,22,28].

Table 4. Leptin and CRP tests in HD patients and healthy individuals.

Parameters	Groups		P-value
	Control	Patients	
Leptin ng/mL	11.58 ± 1.07	24.50 ± 1.76	0.0001 **
CRP mg/L	1.13 ± 0.28	41.11 ± 1.70	0.0001 **

- Mean ± SE
- NS: Non-Significant.
- ** Significant difference at (p< 0.01).
- Significant difference at (p< 0.05).

3.5 Evaluate the changes in Hematological parameters tests

The results in the Table (5) shows a significant decrease (p< 0.05) in RBCs, Hb and platelet count in all patients group compared with control group. This finding is in accordance with previous studies that have been done by [73,74]. In addition, Han and Kishimoto concluded that the RBCs count, Hb, and PCV level in ESRD patients were significantly lower before HD when compared to healthy subjects [75]. The decrease in RBCs count in CRF patients may be due to the fact that patients with impaired kidney function have diminished erythropoietin (EPO) production in bone marrow, which leads to anemia [76,77]. In addition, CRF patients also show low erythrocyte half-life resulting from a small degree of hemolysis [78]. Such dysfunction can be partially corrected by supplementation with exogenous erythropoietin [79]. Also, erythropoietin potentiates the effect of megakaryocyte colony stimulating factors, acetylhydrolase (PAF-AH) and paraoxonase (PON1). In chronic renal disease, impaired erythropoietin secretion leads to a decrease in platelet count [80,81]. Moreover, showed that PCV and lymphocyte count was highly significant decrease (p<0.01) in HD patients as compared to the control group. In another study by Wasti *et al*., reported similar observations though [82]. While our results in contrast to the finding of the study done by [83], where a majority of the patients had a normal lymphocyte count. The decreased in lymphocytes count may be due to chronic infections, severe stress, kidney failure, or prolonged use of Cortisone injections [82].

Table 5. Hematological parameters tests in HD patients and healthy individuals.

Parameters	Groups		P-value
	Control	Patients	
Hb	14.10 ± 0.21	9.01 ± 0.11	0.0361 *
PCV	43.38 ± 1.03	27.37 ± 0.33	0.0001 **
Lymphocyte	31.92 ± 0.76	22.66 ± 0.55	0.0026 **
RBC	4.86 ± 0.12	3.30 ± 0.04	0.0443 *
PLT	215.20 ± 7.41	176.65 ± 4.52	0.02117 *

- Mean ± SE
- NS: Non-Significant.
- ** Significant difference at (p< 0.01).
- Significant difference at (p< 0.05).

3. Conclusion

From the findings of the present study, it shows highly significant increased serum concentration of leptin may be due to decreased renal clearance as well as elevated serum values of CRP indicates presence of systemic microinflammation in HD patients. Whereas a highly significant decrease in GFR and CrCl result from loss of the ability of the kidney to clearance. Also, abnormal mineral parameters and hematological parameters may be due to that patient with renal failure have no committed to restriction diet and reduced erythropoietin (EPO) production in bone marrow respectively. According to the results of this study, serum total protein and cholesterol cannot be used as diagnostic marker of nutrition disorders in patients on regular hemodialysis requires further investigation and clarification.

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