Effect of Hemodialysis on Some Biochemical Parameters in Diabetic Nephropathy Patients

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Abstract

Diabetes mellitus is a worldwide epidemic and is associated with long-term damage and causes dysfunction of several organs like kidney leading to diabetic nephropathy. This study was designed to evaluate some biochemical aspects. This study was conducted on 95 patients which included (35) HD patients with diabetes and (35) HD patients without diabetes and (25) Type 2 diabetes mellitus patients, who attended at Ramadi General Hospital. For the purpose of comparison, (25) samples as control. Several tests were performed such as FSB, urea, creatinine, glomerular filtration rate (GFR), albumin, sodium ion, calcium ion, Phosphorus ion, potassium ion and magnesium ion were calculated. This study showed the level of urea and creatinine were a significant increase in HD patients with diabetes(128.29±22.59 and 7.1±1.76) mg/dl respectively, and HD patients without diabetes were (125.74±23.28 and 6.80±2.71) mg/dl respectively. The levels of Na^+ and Ca^{++} were decrease in HD patients with diabetes (137.6±4.8 mmol/L and 6.72±1.76mg/dl) respectively. The levels of P, K^+ and Mg^{++} were a significant increase in HD patients without diabetes(6.26±0.84 mg/dl, 5.52±0.61 mmol/L and 2.2±0.13mg/dl) respectively. The urea, creatinine and GFR are simple and useful biomarkers which can serve as predictor tests for assessing kidney functions in diabetic patients.

Key words: *Chronic kidney disease (CKD), Diabetes mellitus (DM), Hemodialysis (HD), Sodium ion, Urea.*

Introduction

Diabetes mellitus (DM) is a metabolic disorder of carbohydrate leading persistent high level of blood glucose due to factors that oppose the action of insulin. Presently, DM is a worldwide epidemic and a great challenge to health care systems everywhere [1]. Chronic kidney disease (CKD) is a progressive loss of kidney function over a period of months or years through five stages or defined as decreased GFR and increased urinary albumin excretion. Each stage is a progression through a low and deteriorating glomerular filtration rate (GFR) [2]. Therefore, CKD a major global public health problem. Urea and creatinine are renal function markers indicating normal functioning of the kidney and increase of these substances in the serum indicate kidney dysfunction [3]. Patients with CKD have marked disruption in bone and mineral metabolism resulting in a complex disorder. The biochemical alterations of CKD-mineral bone disorder include elevated serum phosphate and decreased serum calcium [4]. The kidney is the route of potassium and sodium excretion from the body. Advanced renal failure typically results in potassium and sodium retention [5]. The tissue sodium accumulation has different pathophysiologic that may be amenable to therapeutic strategies in CKD patients. While low serum magnesium levels are associated with vascular calcification and increased cardiovascular mortality in CKD patients [6]. Aims of the study to measure and compare the levels of urea, creatinine, albumin, and GFR in study groups and to assess serum electrolytes levels in HD patients and T2DM patients.

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Materials and Methods

The samples collection were started from April,

2019 till end of June 2019. The study is designed on 95 patients and (25) samples Control group. Patients divided into (35) hemodialytic patients with diabetes and (35) hemodialytic patients without diabetes and (25) T2DM patients. HD patient with diabetes and HD patient without diabetes samples were collected from the Industrial Renal department and T2DM patients from Diabetes Center at Ramadi General Hospital.

Blood Samples Collection:

Before the collection of samples, a careful history was taken from each patient according to a questionnaire and all patients provided written informed consent before participation in this study. From each patient and control, 5 ml of blood were obtained by venipuncture, the blood was dispensed in a gel plain tube and left for 30 minutes to clot at room temperature (18-25°C). Then, it was centrifuged at 3000 r.p.m for 10 minutes to collect serum, the serum were used in the estimation of FBS, Urea, Creatinine, Albumin, Na, Ca++, P, K, and Mg++.

Biochemical tests:

Determination of urea, creatinine, albumin, Na, Ca, P, K, and Mg as cited by manufacturing company kits which provided from human company / Germany. FBS determination according to [7] method, which provided with kit from linear company/ Spain.

GFR Calculated: According to [8] equation which is:

GFR= 141× min (Scr\k,1) α × max (Scr\K,1)-1.209 × 0.993 Age ×1.018 [if women] ×1.159 [if black]. **Scr:** Serum creatinine mg/dl, **K:** is 0.9 man and 0.7 woman, **α:** -0.411 man and -0.329 women, **Min:** minimum of Scr/k and max indicates the maximum of Scr/ k.

Statistical Methods:

The data were translated into a computerized database structure, and the statistical analyses were carried out SPSS version 25. One way ANOVA test was used to find means and standard deviation (SD) for all variables of the study. The difference significances in proportions analyzed by LSD test, P-value less than 0.05 were considered to be significant.

Results and Discussion

Determination of serum Urea, Creatinine, GFR and albumin in four study groups:

This study showed that the FBS was a significant increase in diabetic group (215±11.1)mg/dl, followed by HD patients with diabetes (188.7±18.39)mg/dl. These findings showed mean of urea and creatinine were a significant increase in HD patients with diabetes (128.29±22.59, 7.1±1.76) mg/dl respectively and in HD patients without diabetes (125.74±23.28, 6.80±2.71) mg/dl respectively. While level of GFR was a significant decreased in HD patients with diabetes and HD patients without diabetes (8.22±1.69 and 9.93±1.47) mL/ min/1.73m^2 respectively compared with control and diabetic patients (115.56±4.39 and 113.92±3.14) mL/ min/1.73m^2 respectively. This study indicates the no significant difference in mean of the albumin in groups of the study, as shown in the **Table (1)**.

Table (1): The difference in mean of FBS, urea, creatinine, GFR and albumin among four study groups.

Groups	N.	Mean±SD of FBS NV(70-100) mg/dl	Mean±SD of Urea NV(10-50) mg /dl	Mean±SD of Creatinine NV(0.6-1.1)mg/dl	Mean±SD of GFR NV(120) mL/ min/1.73m2	Mean±SD of Albumin NV(3.81-4.65) g/dl
Control	25	88.5 ± 4.88a	25.42±5.56a	0.76±0.14a	115.56±4.39a	4.2±1.76a
Diabetes	25	215 ± 11.1b	30.8±3.33b	0.98±0.34b	113.92±3.14a	4±1.14a

Cont... **Table (1): The difference in mean of FBS, urea, creatinine, GFR and albumin among four study groups.**

HD patients with diabetes	35	188.7±18.3c	128.29±22.5c	7.1±1.76c	8.22±1.69b	3.96±1.72a
HD patients without diabetes	35	92.2 ± 2.7a	125.7±23. 8c	6.80±2.71c	9.93±1.47b	3.92±1.11a
Total	120	146.1 ±26.3	78.57±78.54	4.1±3.22	58.44±45.81	3.952±2.18
*Different Letters (a, b, c): Means significant difference at P ≤0.05. *Similar Letters: Means no significant difference at P ≤0.05.						

These results agreed with [9; 10; 3; 11] who recorded that urea and creatinine levels increased in diabetic patients compared with control.

An increase in urea and creatinine levels and decreased GFR is seen when the kidney is not functioning properly. GFR is the best measure of kidney function since it accounts for age, BMI, and sex. Irrespective of its cause, kidney disease is associated with a decrease in GFR, and the severity of kidney disease correlates closely but inversely with GFR [3]. In this study, the HD patients showed higher levels of both urea and Cr compared to controls, as clear evidence for the microvascular abnormalities in the renal system. Elevations in urea occur as the number of functional nephrons decreases[12]. Creatinine is separated by the glomerulus; in this way, the creatinine level is an indirect measure of glomerular filtration. As GFR reduces, there is an ascent in the concentration of urea and creatinine[13]. In this study diabetic patients showed a significantly increase in urea and creatinine compared with control due to hyperglycemia in T2DM starts after the age of forty usually when the kidneys have already suffered the long-term consequences of aging and other promoters of chronic renal injury such as arterial hypertension, dyslipidemia, obesity. This probably might be a cause for increased levels of serum creatinine and urea in T2DM [9]. The inflammatory process is the most widely recognized cause of decreased concentration of albumin, and since DM was known to be an express provocative, this may be one reason that causes the observed decline in Albumin concentration to occur [14].

Determination of serum Na, Ca^{++}, P, K and Mg^{++} among four study groups:

This study indicates that mean of Na was a significant decrease in HD patients with diabetes and HD patients without diabetes (137.6±4.8 and 136.6 ±5.1) mmol/L respectively compared with control (140.75±1.84) mmol/L. The results indicate that mean of Ca++ is a significant decrease in HD patients with diabetes (6.72±1.76) mg/dl and HD patients without diabetes (6.88±1.59)mg/dl compared with control (9.72±0.63) mg/dl. Where P level was a significant increase in HD patients without diabetes and HD patients with diabetes (6.26±0.84 and 6.11±0.75) mg/dl respectively compared with control (4.22±0.67) mg/dl. While K level was a significant increase in HD patients with diabetes and HD patients without diabetes(5.59±0.7 and 5.52±0.61) mmol/L respectively. These results indicate Mg^{++} level was a significant increase in HD patients without diabetes and HD patients with diabetes (2.2±0.13 and 2.18±0.27) mg/dl respectively compared with diabetic patients and control, as shown in the **Table (2).**

Table (2): The difference in mean of Na, Ca^{++}, P, K and Mg^{++} among four study groups.

Groups	N.	Mean±SD Na (135-155) mmol/L	Mean±SD Ca++ (8.1-10.4) mg/dl	Mean±SD P (2.5-5) mg/dl	Mean±SD K (3.6-5.5) mmol/L	Mean±SD Mg++ (1.9-2.5) mg/dl
Control	25	140.75±1.84a	9.72±0.63a	4.22±0.67a	4.31±0.8a	1.93±0.15a
Diabetic patients	25	139.8±1.15a	9.04±0. 5b	4. 5±0.41a	4.12±0.79a	1.99±0.14a
HD patients with diabetes	35	137.6±4.8b	6.72±1.76c	6.11±0.75b	5.59±0.7b	2.18±0.27b
HD patients without diabetes	35	136.6 ±5.1b	6.88±1.59c	6.26±0.84b	5.52±0.61b	2.2±0.13b
Total	120	138.37±4.62	7.89±4	5.42±4.20	4.29±0.83	2.01±0.67
*Different Letters (a, b, c): Mean significant difference at P ≤0.05.						

These results correspond with [15; 16] who recorded sodium level was decreased in HD patients compared with control. These findings agreed with [11; 17; 18] who recorded that the Ca^{++} showed significant decrease in HD patients, while phosphorus and K were increased in HD patients compared to control. These results no correspond with [6] who found that the mean Na^{+} was increased, while mean of phosphorus, Mg and potassium were decreased in HD patients compared with control.

CKD is a catabolic state and is associated with progressive nephron destruction and miss of renal function decreases the body ability to release a sodium load, which causes extracellular volume enlargement and sodium retention, and as such, the restoration of sodium balance is one of the key objectives of HD treatments [19]. Where in chronic HD patients, Na+ balance largely depends on interdialytic dietary salt intake and intradialytic Na+ removal[5].

Moreover, it is now recognized that increased sodium intake does not necessarily result in increased urinary sodium excretion and that sodium can exchange for intracellular potassium and accumulate in tissue matrix without any corresponding fluid status changes, the so-called non-osmotic sodium balance [20]. Ca++ plays an important role in the regulation of glucose level in the blood particularly postprandial glucose level, hence Ca++ should be measured in patients with T2DM who have uncontrolled hyperglycemia. There is evidence to suggest that altered Vit D and Ca++ homeostasis may play a role in the development of T2DM [11]. The reduction in serum Ca^{++} levels were most likely due to several factors: Reduction in insulin levels that impair bone formation due to stimulation of osteoblast proliferation and impairment of Ca^{++} homeostasis; Hyperglycemia, which increases the excretion of Ca^{++} and phosphorus in urine [21]. In this study, the serum Ca++ levels decreased in HD patients with/ without diabetes because the serum Ca□□ at dialysis initiation to be associated with all-cause mortality after dialysis initiation. Severe hypocalcemia is highly likely to occur during the early period after dialysis initiation [17].

In our results, we observed that the mean of phosphorus was increased in HD patients with/ without diabetes compared with control and diabetic patients the usual cause is a decrease in renal excretion of phosphate. Advanced renal insufficiency reduces excretion sufficiently to increase serum phosphor [18]. At later CKD stages, the hyperphosphatemia occurs either by increasing bone reabsorption and phosphate release or by reducing the bone formation and phosphate uptake[22].

HD patients present with hyperkalemia, which reduces the resting membrane potential, slows the conduction velocity and increases the rate of repolarization [23]. All these changes are the signs of membrane instability and cardiac arrest or ventricular fibrillation may follow and thus this situation usually requires careful and prompt management [24]. During hemodialysis, there is a quick shift of serum K+ which leads to hypokalemia after HD sessions[25]. This study did not show an association between serum Mg++ levels and a risk of incident T2DM in patients with T2DM, compared to controls these slight differences may be supplements drugs or maybe a compensatory state [11]. The young erythrocytes have a higher Mg++ concentration than older cells for this reason in patients undergoing HD have a higher Mg++ concentrations and have been shown to be dependent on residual renal function [26].

Conclusion

GFR, urea and creatinine are simple and useful biomarkers which can serve as predictor tests for assessing kidney functions in diabetic patients. The serum Mg, P and K were increased in HD patients, these a worthwhile tool in assessing duration of disease, morbidity and mortality in HD patients. They estimation may help in evaluating conservative treatment and dialysis in CKD .Decreased levels of Na and Ca in HD patients compared with control group.

Conflict of Issue - Nil

Ethical Clearance – Obtained.

Fund – Self.

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