# The Biochemical Changes in Patients with Chronic Renal Failure

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***Abstract*—This study was conducted in AL-Zahraa general hospital in Al-kut city/ Iraq. To assess serum urea, creatinine, lipid profile (cholesterol, TG, DHL and LDL) and thyroid hormones (FT3, FT4 and TSH) in chronic renal failure (CRF) patients it included 50 patients, 29 were males and 21 were females and their age range from 20 to 60 years. The control groups were 30; who were free from signs and symptoms of renal disease, lipid disorders, and thyroid hormones disorders, 20 were males and 10 were females, and their ages range from22 to 66 years. The study shows that the Serum urea and creatinine concentrations in CRF patients were found to be significantly high compared with control group (P<0.001), Serum triglycerides concentrations in CRF patients were found to be normal or no significantly increase compared with control group (P> 0.05), Serum cholesterol, HDL and LDL concentrations in CRF patients were found to be no significantly lower compared with control group, Serum FT3, FT4 and TSH concentrations in CRF patients were found to be no significantly lower compared with control group and No significant relationship between lipid profiles concentrations changes and thyroid hormones concentrations changes were found.**

***Index Terms*—renal failure, lipid profiles, thyroid hormones**

## I. Introduction

Renal failure refers to a condition where the kidneys lose their normal functionality, which may be due to various factors including infections, auto immune diseases, diabetes and other endocrine disorders, cancer, and toxic chemicals. It is characterized by the reduction in the excretory and regulatory functions of the kidney; it is the ninth leading cause of death in United States as well as most industrialized nation throughout the world [1], [2].

Abnormalities in lipid metabolism and dyslipidemia are known to contribute to glomerulo-sclerosis and are common in renal disease [3]. In addition, post-transplant dyslipidemias have been associated with an increased risk of ischemic heart disease and have been shown to increase risk of chronic rejection, altered graft function and mortality [4].

Manuscript received January 20, 2015; revised March 25, 2015.

The impact of lipid abnormalities on renal function has been evaluated in various studies [5]. In these studies, unfavorable lipoprotein profiles interacted as risk factors for progressive renal decline. Abnormal lipid profiles start to appear soon after renal function begins to deteriorate [6].

Thyroid hormones (TH) are necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of TH. From a clinical practice viewpoint, it should be mentioned that both hypothyroidism and hyperthyroidism are accompanied by remarkable alterations in the metabolism of water and electrolyte, as well as in cardiovascular function. All these effects generate changes in water and electrolyte kidney management [7]. Moreover, the decline of kidney function is accompanied by changes in the synthesis, secretion, metabolism, and elimination of TH. Thyroid dysfunction acquires special characteristics in those patients with advanced kidney disease [8]. On the other hand, the different treatments used in the management of patients with kidney and thyroid diseases may be accompanied by changes or adverse events that affect thyroid and kidney function respectively.

TH plays an important role in growth, development, and physiology of the kidney [9], [10]. It is known that hypothyroidism reduces and hyperthyroidism increases the kidney-to-body weight ratio by a not fully understood mechanism [11]. On the other hand, children with congenital hypothyroidism have an increased prevalence of congenital renal anomalies. These findings support an important role of TH during early embryogenesis [12].

Thyroid function also influences water and electrolyte balance on different compartments of the body [13]. The kidney also plays a role on the regulation of metabolism and elimination of TH and is an important target organ for TH actions [14]. The decrease in the activity of TH is accompanied by an inability to excrete an oral water overload [15]. This effect is not due to an incomplete suppression of vasopressin production, or a decrease in the reabsorptive ability in the dilutor segment of the kidney tubule, but rather to a reduction in the glomerular filtration rate (GFR) [16].

Thyroid dysfunction causes significant changes in kidney function. Both hypothyroidism and hyperthyroidism affect renal blood flow, GFR, tubular function, electrolytes homeostasis, electrolyte pump functions, and kidney structure [17].

Chronic renal failure is often associated with dyslipoproteinemia, high levels of cholesterol and triglycerides, as well as a decrease in the polyunsaturated fatty acids. Each of these abnormalities has been identified as an independent risk factor for atherosclerosis [18]. Some of them persisting and becoming worse during dialysis treatment [19]. On the other hand, an increment of plasma homocysteine concentration is highly prevalent among patients under hemodialysis [20], [21], and it is considered an independent risk factor for atherosclerotic complications of end-stage renal disease [22].

The objective of this study is to find out the biochemical changes (urea, creatinine, lipid profile, thyroid hormones) in patients with chronic renal failure and compare the obtained results with the results of healthy individuals as control groups.

## II. Materials and Methods

The control groups consisted of 30 non-hospitalized adults with no history of systemic disease (matched for age and sex).

A total of 50 diagnosed adult chronic kidney failure patients. The patient was diagnosed as renal failure for both sexes based on the history, clinical examination and taking renal function test. Subject was fasting 12-14 hr. at the time of blood withdrawal. Their age range between 18-60 years where included in this study.

The chemicals and kits that were used in this study were of the highest purity.

The determination of serum creatinine, urea, total cholesterol, triglyceride, high density lipoprotein (HDL), low density lipoprotein (LDL), free Triiodothyronine (FT3), free Thyroxine (FT4) and serum Thyroid stimulating hormone (TSH) concentration were performed by approved methods.

### A. Creatinine Assay

Creatinine is generated from creatine by nonenzymatic dehydration. Creatinine is produced at a constant rate and is excreted from the body through kidney glomerular filtration. Decreased kidney function can affect the rate at which creatinine is filtered by the kidneys and can be used as a measure of kidney function. Decreased kidney function can result in increased serum creatinine levels due to the inability to clear creatinine through urine excretion. Creatinine levels can be affected by changes in muscle mass, pregnancy, or the use of angiotensin inhibitors or angiotensin receptor antagonists. In this assay, Creatinine concentration is determined by a coupled enzyme reaction, which results in a colorimetric (570 nm)/fluorometric (λex = 535/λem = 587 nm) product, proportional to the creatinine present.

### B. Urea Assay

Urea is the major end product of nitrogen metabolism in most animals and is produced in a series of reactions in the liver called the urea cycle. In the urea cycle, ammonia is converted to urea, which is carried by blood to the kidneys for elimination from the body. High levels of urea in the blood may indicate renal failure. Urea levels may also be elevated in response to treatment with certain drugs such as corticosteroids or in response to decreased kidney filtration due to dehydration or congestive heart failure. Decreased blood urea levels can occur in response to liver disease or malnutrition.

In this assay, Urea concentration is determined by a coupled enzyme reaction, which results in a colorimetric (570 nm) product, proportional to the Urea present.

### C. Cholesterol Assay

Cholesterol is an important component of mammalian cell membranes where it functions in intracellular transport, cell signaling, and maintaining membrane fluidity. Within the blood, cholesterol circulates as both the free acid and as cholesterol esters. Controlling serum cholesterol has an important therapeutic role as elevated cholesterol levels are associated with the development of atherosclerosis and cardiovascular pathologies. Recent evidence suggests a disturbance of cholesterol homeostasis contributes to the development of a chronic inflammatory state.

Total cholesterol concentration is determined by a coupled enzyme assay, which results in a colorimetric (570 nm)/fluorometric ($\lambda_{ex}$ = 535/$\lambda_{em}$ = 587 nm) product, proportional to the cholesterol present. This kit is suitable for use with cell and tissue culture samples, urine, plasma, serum, and other biological samples.

### D. Triglyceride Assay

The Serum Triglyceride Determination Kit can be used for the measurement of glycerol, true triglycerides, or total triglycerides in serum or plasma. The procedure involves enzymatic hydrolysis by lipase of the triglycerides to glycerol and free fatty acids. The glycerol produced is then measured by coupled enzyme reactions. Many of the triglyceride reagents which are commercially available do not differentiate between endogenous glycerol and glycerol derived by hydrolytic action of lipase on glycerides.

### E. HDL and LDL Assay

In the assay, cholesterol oxidase specifically recognizes free cholesterol and produces products which react with probe to generate color (570 nm) and fluorescence (Ex/Em = 538/587 nm). Cholesterol esterase hydrolizes cholesteryl ester into free cholesterol, therefore, cholesterol ester and free cholesterol can be detected separately in the presence and absence of cholesterol esterase in the reactions.

### F. FT3 Assay

The fT3 test is a solid phase competitive enzyme immunoassay. Patient serum samples, standards, and T3-Enzyme Conjugate Working Reagent are added to wells coated with monoclonal T3 antibody. fT3 in the patient

specimen and the T3 labeled conjugate compete for available binding sites on the antibody. After 60 minutes incubation at room temperature, the wells are washed with water to remove unbound T3 conjugate. A solution of $H_2O_2$/TMB is then added and incubated for 20 minutes, resulting in the development of blue color. The color development is stopped with the addition of 3N HCl, and the absorbance is measured spectrophotometrically at 450 nm. The intensity of the color formed is proportional to the amount of enzyme present and is inversely related to the amount of unlabeled fT3 in the sample.

### *G. FT4 Assay*

The fT4 test is a solid phase competitive enzyme immunoassay. Serum samples, standards, and Thyroxine-Enzyme Conjugate Working Reagent are added to wells coated with monoclonal T4 antibody. fT4 in the specimen and the T4 labeled conjugate compete for available binding sites on the antibody. After a 60 minutes incubation at room temperature, the wells are washed with water to remove unbound T4 conjugate. A solution of $H_2O_2$/TMB is then added and incubated for 20 minutes, resulting in the development of blue color. The color development is stopped with the addition of 3N HCl, and the absorbance is measured spectrophotometrically at 450 nm. The intensity of the color formed is proportional to the amount of enzyme present and is inversely related to the amount of unlabeled fT4 in the sample.

### *H. TSH Assay*

TSH ELISA Test is based on the principle of a solid phase enzyme-linked immunosorbent assay. The assay system utilizes a unique monoclonal antibody directed against a distinct antigenic determinant on the intact TSH molecule. Mouse monoclonal anti-TSH antibody is used for solid phase (microtiter wells) immobilization, and goat anti-TSH antibody is used in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample is allowed to react simultaneously with the antibodies, resulting in the TSH molecule being sandwiched between the solid phase and enzyme-linked antibodies. After a 2 hour incubation at room temperature with shaking, the solid phase is washed with distilled water to remove unbound labeled antibodies. A solution of tetramethylbenzidine (TMB) is added and incubated for 20 minutes, resulting in the development of a blue color. The color development is stopped with the addition of 1N HCl, and the resulting yellow color is measured spectrophotometrically at 450 nm. The concentration of TSH is directly proportional to the color intensity of the test sample.

## III. Results and Discussion

The levels of urea, creatinine, triglyceride (TG), total cholesterol (TC), high density lipoprotein – cholesterol (HDL-C), low density lipoprotein- cholesterol (LDL-C) and very low density lipoprotein –cholesterol (VLDL-L) were estimated using enzymatic methods.

The level of FT3, FT4 and TSH were estimated by using ELISA method.

The results in Table I demonstrated the level of biochemical parameters (urea, creatinine, cholesterol, TG, HDL, LDL, FT3, FT4 and TSH) in both male and female in case of chronic kidney failure patients and control groups.

TABLE I. Biochemical Parameters Changes in Chronic Kidney Patients and Control Groups

| **Biochemical parameters** | **Patients mean N= 50** | **Control mean N= 30** | **P.V.** | **C.S.** |
|---|---|---|---|---|
| Urea | 165.24 ± 34.66 | 32.16 ± 5.74 | P< 0.001 | Hs |
| Creatinine | 7.95 ± 2.44 | 0.64 ± 0.14 | P< 0.001 | Hs |
| Cholesterol | 143.00 ± 32.34 | 164.73 ± 27.19 | P> 0.05 | Ns |
| TG | 113.8 ± 5. 99 | 110.166 ± 38.72 | P> 0.05 | Ns |
| HDL | 33.68 ± 14.09 | 42.06 ± 4.56 | P> 0.05 | Ns |
| LDL | 87.44 ± 24.30 | 102.86 ± 21.63 | P> 0.05 | Ns |
| FT3 | 2.36 ± 0.72 | 2.47 ± 1.13 | P> 0.05 | Ns |
| FT4 | 0.96 ± 0.22 | 1.02 ± 0.21 | P> 0.05 | Ns |
| TSH | 2.49 ± 1.82 | 2.64 ± 2.73 | P> 0.05 | Ns |

The results show significant (P< 0.001) increase in urea and creatinine concentration in chronic renal failure patients when compared with those of the control group.

The doctors rely on plasma concentrations of waste materials from urea and creatinine to determine renal function. These tests are sufficient to determine whether a patient is suffering from kidney disease.

These tests help to measure the efficiency of the kidneys in filtering the blood. It also gets kidney function and the amount of nitrogen and creatinine in the blood increases.

It uses the level of creatinine in the blood to determine the glomerular filtration rate (GFR). GFR is used to show how the renal function of the patient still has. GFR also be used to determine the stage of renal disease and guide decisions about treatment.

The result demonstrated non-significant (P>0.05) reduction in serum Cholesterol, HDL, and LDL-cholesterol, concentration in chronic renal failure patients when compared with those of the control group, while TG concentration is non significantly higher (P>0.05) in

chronic renal failure patients when compared with those of the control group.

On using correlation analysis we found that there is no significant (P>0.05) relationship between the concentrations of lipid profiles and the concentrations of thyroid hormones.

Among the various parameters tested triglyceride was not significantly higher in CRF patients as compared to controls (p>0.05). HDL levels were no significantly lower in CRF patients as compared to control (p>0.05). There was no significant change (p>0.05) observed in total cholesterol and LDL levels in between healthy controls and CRF patients. This study demonstrated that CRF patients with and without hemodialysis are at greater risk of development of dyslipidemias, characterized by hypertriglyceridemia, elevated levels and decreased HDL levels. Total cholesterol and LDL cholesterol levels remain normal or decreased in these patients. Both male and female patients of CRF with and without hemodialysis have dyslipidemias without any discrimination of sex and it is not attenuated by the hemodialysis process.

Serum TSH concentrations are usually normal or elevated in chronic kidney disease (CKD), but its response to its releasing hormone (TRH) is generally low. These findings suggest the presence of intrathyroidal and pituitary disturbances associated with uremia [23]. Also, both TSH circadian rhythms as TSH glycosylation are altered in CKD. The latter may compromise TSH bioactivity.

Free and total T3 and T4 concentrations are usually normal or low in patients with CKD [24]. The reduction in T3 levels (low T3 syndrome) is the most frequently thyroid alteration observed in these patients [25]. This reduction in T3 concentrations has been linked to a decrease in the peripheral synthesis of T3 from T4. Chronic metabolic acidosis associated with the CKD may contribute in this effect. Although free and total T4 concentrations may be normal or slightly reduced, sometimes free T4 may be high due to the effect of heparin used in anticoagulation during hemodialysis (HD), which inhibits T4 binding to its binding proteins [26].

A relationship between T3 levels and mortality has been proven in uraemic patients; however, the relationship between TSH and survival, well established in other population groups, has not been reported in patients with different degrees of kidney insufficiency. Further investigation in this field will provide new insights in our understanding of the biological significance of thyroid hormone changes in patients with kidney disease.

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