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RESEARCH ARTICLE

Biochemical Observations in Patients Suffered From Acute and Chronic Kidney Diseases with Reference to Thyroxin

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Abstract

Blood samples of acute kidney injury (AKI) patients (20) ;chronic kidney disease(CKD) patients (20) and normal persons(20), were collected from the central dialysis unit and private clinical diagnostic laboratories in Mosul city/Iraq during the period from (Jan. to March.2018), for investigation of blood urea, serum creatinine, serum thyroxin (T4) and serum total protein, Albumin and Globulin. Results reviled that only urea and creatinine were significantly reduced in AKI patients, but all studied parameters except albumin were significantly reduced in CKD patients in comparison with normal persons. Health significance of all parameter s levels was discussed.

Introduction

Acute kidney injury (AKI) is a syndrome characterized by a rapid (hours to days) deterioration of kidney function , i.e., is an abrupt loss of kidney function that develops within 7 days [1], Acute kidney injury has been increased in the last two decades and now it is considered as a global problem [2]. Prerenal, intrinsic and post renal categorizations of acute Kidney injury are multi-factorial health problems [3]. One of the major effects of AKI is the failure in glomerular filtration which leads to imbalance in body fluids ended either to CKD or in patient's death [4].

Although different definitions and classifications to AKI were used like (RIFLE) and (KDIGO) through 2007 t0 2012 [5], and many indicators were proposed for its diagnosis, but the 5-fold rise in creatinine level within 7 days of disease onset still the main diagnostic criteria in AKI cases [6]. In the other hand, chronic kidney disease (CKD) is also a growing public health burden around the world. End stage renal disease is the suggestive irreversible CKD condition of glomerular filtration reduction rate (10% of the normal), coupled with persistent hypertension and neuropathology [7].

The 5 stages which characterize CKD [8] could involve sever body multisystem deteriorations that enforce the initiation of dialysis or kidney transplantation [9].

The interrelation between endocrine abnormalities like thyroid gland function disorders in synthesis, metabolism and excretion of thyroid hormones and CKD are common [10]. Moreover, CKD is associated with disturbance of acid-base balance and a range of electrolyte disorders (potassium derangements, hyperkalemia, metabolic acidosis, derangements of bone mineral metabolism) and those with ESRD who cannot survive without kidney transplant or regular-usually thrice-weekly-dialysis treatment. [11].

Total serum or plasma protein (total protein) concentration is generally assayed as part of a health check-up to assess nutritional status or to help diagnose certain liver, kidney, and bone marrow disorders and other metabolic disease processes [12]. The total protein level is the amount of the two major protein classes in the blood, albumin and globulin and the decreased total protein (hypoproteinemia) may be observed in conditions where production of albumin or

globulin proteins is impaired, such as malnutrition or severe liver disease; conditions that accelerate the breakdown or loss of protein as in kidney disease (e.g., nephrotic syndrome); malabsorption disorders such as celiac disease, Crohn's disease, and short-bowel syndrome; and conditions that increase plasma volume, thereby diluting the blood, such as congestive heart failure [13].

The most abundant protein in the body is albumin, comprising about 50% of total protein and this protein is an indicator of how well the liver and kidneys are functioning and how well the diet provides protein, and may determine the cause of excess fluid retention. So the aim of this study is to find the effect of renal diseases (AKI and CKD) on some of serum biochemical parameters (Urea, creatinine, serum thyroxin T4, Total serum protein, Albumin and Globulin) in patients admitted to the hospitals and private clinical laboratories in Mosul city.

Materials and Methods

Test samples were collected from 60 persons; 20 patients with AKI (aged 25-75years); 20 patients with CKD (aged16-82 years) and from 20 individuals with no claim from AKI or CKD (normal) (aged 18- 62 years). Samples of patients with acute kidney injury (AKI) were collected from 3 private clinical diagnostic laboratories in Mosul city/Iraq, while samples of patients with CKD were collected from the central dialysis unit in Mosul city/Iraq. Control group samples were collected from 20 healthy individuals. All samples were gathered during the period from (Jan. to March .2018). Informed consent was obtained from all patients. Detailed clinical history and clinical examination were undertaken with preference to thyroid and renal diseases. The general symptoms of tested AKI patients were polyuria, decreased appetite, hypertension, large kidneys with uroliths.

The symptoms of CKD patients were

polyuria, decreased appetite, vomiting, large kidneys, hypertension, anaemia, uroliths, and parathyroid hyperplasia. Risk factors information's such as diabetes mellitus, hypertension, chronic glomerulonephritis, family history of CKD and others were recorded. Blood samples (5 ml) were taken from cubital vein before heparin administration for hemodialysis procedure from patients and normal persons.

The collected blood were allowed to clot and centrifuged to separate serum. Serum was taken to perform the following investigations: blood urea, serum creatinine, serum total thyroxin (T4), serum protein, Albumin and Globulin by qualified laboratory personnel using Standard Operating Procedures (SOPs). Urea and creatinine levels were measured using the Urea reflotron tape (Roche HITACHI of Japan); with reference range (RR) 7-20 mg/dl and 0.8-1.4 mg/dl respectively. Serum T4 was measured using Minividas (Frence); with reference range (RR) 70.0-140.0 nmol/l. Total serum proteins and albumin were measured by enzymatic method (Biolabo, France), Globulin fraction was calculated by using the formula:

Total Protein (g/dl) - Albumin (g/dl) = Globulin (g/dl), with reference range (RR) 6.0-8.0 g/dl, 3.9-5.0 g/dl and 2.0-3.5 g/dl respectively. Patients with recent surgery, trauma or burns, and diabetes mellitus, with liver diseases, patients taking drugs altering thyroid profile were excluded. Statistical analysis of was done by SPSS (Statistical Package for the Social Sciences, version 21.0, SPSS Inc., Chicago, USA). The level of significance (P value) was set at 0.05.

Results

The comparison between AKI and CKD patients in their serum concentrations of urea and criatnine is illustrated in Table 1.

Table 1: Mean concentration of Urea and creatinine in sera of AKI, CKD patient and normal persons

Group studied	No.	Urea (Mean ± SD) (mg/dl)	Creatinine (Mean ± SD) (mg/dl)
Normal persons	20	30.890±8.438	1.001±0.244
AKI patients	20	*106.980±44.611^{B}	*3.502±1.784 ^{B}
CKD patients	20	*246.600±26.76^{A}	*7.821±1.015 ^{A}

*= Significance (P<0.05) between normal persons and (AKI and CKD) patients in the same column

A, B= Different letters indicate significance (P<0.05) between AKI and CKD patients in the same column

The comparison between AKI and CKD patients in their serum concentrations of Thyroxin T4 is illustrated in (Table 2).

Table 2: Mean concentration of Thyroxin T4 in sera of AKI, CKD patient and normal persons.

Group studied	No.	Thyroxin T4 (Mean ± SD) (mmol/l)
Normal persons	20	95.028±15.721
AKI patients	20	*81.778±23.900
CKD patients	20	*81.778±23.900

*= Significance (P<0.05) between normal persons and (AKI and CKD) patients in the same column

The comparison between AKI and CKD patients in their serum concentrations of total protein, albumin and globulin are illustrated in (Table 3).

Table 3: Mean concentration of total protein, albumin and globulin in sera of AKI , CKD patient and normal persons.

Group studied	No.	total protein (Mean ± SD) (g/dl)	Albumin (Mean ± SD) (g/dl)	Globulin (Mean ± SD) (g/dl)
Normal persons	20	5.937±1.037	4.405±0.636	1.458±1.595
AKI patients	20	5.770±0.927^{B}	4.083±0.398	1.687±0.964
CKD patients	20	*5.217±0.534^{A}	*3.940±0.471	1.278±0.840

*= Significance (P<0.05) between normal persons and (AKI and CKD) patients in the same column
A, B= Different letters indicate significance (P<0.05) between AKI and CKD patients in the same column

Discussion

AKI is diagnosed on the basis of characteristic laboratory findings, such as elevated blood urea nitrogen and creatinine, or inability of the kidneys to produce sufficient amounts of urine [14]. In the current study the mean average level of the urea in AKI and CKD patients were106.980 ± 44.611 mg/dl and 246.600±26.764 mg/dl respectively, which were highly significantly differ (p≤0.000) from that of control persons of 30.890 ± 8.438 mg/dl and reference value of 7-20 mg/dl(Table 1).The possible or the expected sequel of AKI is either disease progression to CKD, renal replacement therapy, end stage failure of kidney (so need to perform lifelong dialysis) or prematurely death [15].

CKD results here were also highly significantly differ (p≤0.000) from that of AKI patients value (Table 1), but nearly similar to result gained by [16], who found 209.76 mg/dl, and more than that found by [31] in male and female patients of 135.47± 72.74mg/dl and 134.97 ± 80.91respectively. A similar picture was found with creatinine values in both AKI and CKD patients' 3.502±1.784 mg/dl and 7.821±1.015 mg/dl respectively.

Both values were highly significantly differ (p≤0.000) from that of control persons value of 1.00±0.244 mg/dl and reference range of 0.8-1.4 mg/dl (Table 1), and from each other. Our findings were less than that found by [16] of 10.95 mg/dl, and more than that value of 1.3±0.4 (mg/dl) found by [18] and1.6 ± 0.7 mg/dl by [19], but similar to 6.27 ±4.22 mg/dl in male and 6.13± 4.4mg/dl in female found by [16]. Most of the highest urea and creatinine values especially in CKD patients were seen with older ages [20]. These observations are confirmed by the study of [21], who found that serum creatinine level >1.3 mg/dl in women and >1.5 mg/dl in men, rise rapidly in those aged 60 years and over who mostly suffer from the main causes of CKD, diabetes and hypertension [22].

Creatinine values in AKI and CKD put the patients in the third or the end-stage stage according to Kidney Disease Improving Global Outcomes (KDIGO) or Risk, Injury, Failure, Loss, and End-stage renal disease (RIFLE) classification, since the patients in our study had mean creatinine (Cr) level ≥ 200% creatinine (Cr) rise from baseline of (2.00–2.99_baseline) [23], and AKI cases is diagnosed if there is a rise in creatinine of 50% from its baseline value [24].

The third or the end stage of AKI and CKD manifested with high increase in Cr level [25], and that a rise in creatinine of ≥0.3 mg/dl, (≥26 mmol/l), was independently associated with an approximately fourfold increase in hospital mortality [26]. Endocrine abnormalities like disruption in thyroid function, degradation and excretion, or

insufficient binding to carrier proteins, altered iodine storage in the thyroid gland of thyroid hormones are common in CKD. Although serum T4 values in AKI and CKD patients in our observations occurred within reference range of 70.0-140.0, mmol/l, but a non-significant reduction in serum T4 level was seen in AKI patients of 93.555±16.039 mmol/l when compared with control serum person's 95.028±15.721 mmol/l (Table 2). A significant reduction in serum T4 levels (hypothyroidism) was noticed in CKD patient's 81.778±23.900 mmol/l when compared with control serum person's 95.028±15.721 mmol/l and AKI patients 93.555±16.039 mmol/l (Tables 2).

Such results agreed with what Lo *et al*., [27], that hypothyroidism seems to be more common in CKD patients, and is associated with increased mortality [28]. In this study, patients with low T4 does not correlate with AKI (Table 2), resembling those normal individuals in control group, a conclusion supported by [29]. Uremic acidosis as one of the sequels of CKD, has been associated with hypothyroidisim (euthyroid sick syndrome) which end in abnormalities in thyroid hormone secretion (THs) (T3 and T4) [30], and patients with CKD usually had low T4 level [31].

The increased level of creatinine in AKI was not enough to induce hypothyroidisim because creatinine level was less than 6 mg/dl as the case in CKD patients who exhibit creatinine level of 7 mg/dl (> 6 mg/dl) [32]. In CKD patients, low T3 level is always recovered, due to low turnover of T4 to T3 and its binding protein [33].

Moreover, inflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-1 in AKI and CKD patients inhibit the expression of type 1 5'-deiodinase, which is responsible for peripheral conversion of T4 to T3 [34]. The reductions in total serum T4 in CKD patients rather than AKI patients could be roughly proportional to the severity of hypoalbuminemia in CKD than AKI with values of 3.940±0.471g/dl and 4.083±0.398 g/dl respectively [35].

Total serum protein concentration reflects all of the different proteins in plasma, and used to detect kidney protein-wasting state. In the current experiment, total serum protein in AKI patients show no significant difference value of 5.770±0.927 g/dl in comparison to control persons 5.937±1.037 g/dl and in the same time within the reference range of serum total protein values of 6.0-8.0 g/dl (Table 3). The significant (P≤0.000) reduction in total serum protein was noticed in CKD patients 5.217±0.534 g/dl compared with control level of 5.937±1.037 g/dl and AKI patients 5.770±0.927 g/dl (Tables 3).The state of uremia in CKD patients obscure the reality of nutrition assessment reflected by serum total protein level [36], but Kidney and liver disease are usually associated with decreased total protein [37].

All values of total serum protein in AKI and CKD patients were lower than the optimal range of 7.2-8.0 g/dl, especially in CKD patients, and this could be attributed to hungry or inadequate food intake or food indigestion, proteinuria or low protein fraction (albumin and globulin [38], which is the situation here regarding albumin and globulin low values (discussed later). Albumin accounts for about 50% of total serum protein concentration, and so its reduction here (as one of a vital indicator of health) is associated with Hypothyroidism (as the case here in CKD patients), Malnutrition-Protein deficiency, Kidney losses (Nephrotic Syndrome) [39].

In the current study, serum hypoalbumenia was detected only in CKD patients 3.940±0.471g/dl but not with AKI patients 4.083±0.398 g/dl when compared to control persons with mean value of 4.405±0.636 g/dl (Tables 3). Our results of serum albumin in CKD patients were more than those reported by [17], who stated mean value of 2.52±0.53 g/dl, and [34] of 4.1 ± 0.5 g/dl, and [40] of 4.04±0.31 g/dl. Hypoalbominemia is so risky when serum albumin level reduced to 4-4.5 g/dl, and may be fatally if reduced to 2.5 g/dl [41].

As kidney is one of the main contributors in albumin catabolism with 40-60% of catabolism occur in kidney, liver and muscle [42] so, Kidney and liver disease are usually associated with decreased albumin and total protein [43]. The optimal range of globulin is between 2.3-2.8 g/dl. Here in this study, all serum globulin values in AKI and CKD patients or control persons were lower than the optimal range, but they did not differ significantly from each other, and were 1.687±0.964 g/dl, 1.278±0.840 g/dl and1.458±1.595 g/dl respectively (Tables 3).

Our serum globulin values were not in normal sense, since they were 5.770±0.927 g/dl and 5.217±0.534 g/dl in AKI and CKD patients which is assign of bad health condition due to many disease conditions [44].

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