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Article

Estimating the Levels of Some Biomarker in Patients with Chronic Kidney Disease

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Abstract

Background: Chronic kidney disease (CKD) constitutes a significant global health of populations concern due to its rising prevalence, elevated morbidity and mortality rates, correlation with diminished quality of life, decreased life expectancy, and substantial financial implications, thereby imposing a considerable burden on healthcare systems. **Objective:** The present study aimed to determine some biochemical parameters (glutathione (GSH), urea, uric acid, and creatinine) in individuals suffering from chronic kidney illness . **Materials:** The current research was conducted on 90 people, 30 control groups, and 60 patients aged 18-80 with CKD. Samples were collected from Tikrit Central Teaching Hospital in Saladin, Iraq, from September 2023 to December 2023. **Results:** The findings demonstrated a significantly lower in GSH levels in CKD patients (4.61 ± 0.2 µmol/L) relative to control group (9.06 ± 0.09 µmol/L, urea levels in CKD patients (87.35 ± 3.61 mg/dL) had significant than control group (22.01 ± 0.81 mg/dL, similary for uric acid levels in CKD patients (12.39 ± 0.48 mg/dL) than control

group (4.88 ± 0.27 mg/dL, The findings demonstrated a significantly elevated in creatinine levels in CKD patients (2.38 ± 0.07 mg/dL) compared to control group (1.03 ± 0.05 mg/dL) at $p<0.05$. The results indicate lower levels of glutathione, and higher levels of urea, uric acid, and Creatinine in patients with CKD compared to the healthy group.

Keywords: Chronic kidney disease, Glutathione, Urea, Uric acid, and Creatinine.

Introduction

Chronic kidney disease (CKD) is a kidney disorder marked by an irreversible deterioration in the functioning of the kidneys that typically starts to manifest itself for several years. The only manifestation of this condition at first is a metabolic anomaly. As time passes, the kidney's inability to perform its excretory, metabolic, and endocrine tasks will eventually result in the clinical manifestations and indicators of renal failure, collectively referred to as uremia[1] . About 40% of hospital admissions and 50% of deaths in those with CKD across all stages are attributable to cardiovascular disease (CVD)[2, 3]. The rate of CVD mortality is approx. 10–20 times greater in those suffering end-stage renal disease (ESRD) than in the general people [4]. At the onset, when renal replacement therapy (RRT) is severe, possibly CVD most likely starts in the early (CKD)stages [5]. Higher blood C-reactive protein (CRP) has been caused by atherosclerosis, which develops in individuals with CKD.[6]. One of the pentraxin protein family members is the acute phase reactant C-reactive protein. In reaction to cytokines secreted from macrophages and adipocytes, including interleukin-1, tumour necrosis factor-alpha, interleukin-6, and the liver synthesizes it. A persistent inflammatory state brought on by dialysis-related and patient variables is known as CKD [7]. The infection, oxidative stress, uremic milieu, obesity, co-morbidities, immunologic or genetic variables, and exposure to dialysate and dialyzer membrane in people with dialysis

are some causes. Six people suffering from coronary heart disease (CHD) with CKD have higher inflammatory markers including fibrinogen, homocysteine, and CRP[8]. Chronic inflammation causes CKD patients to become malnourished, anemic, hyporesponsive to erythropoietin, develop cardiovascular disease (CVD), and experience a higher death rate [9-11]. Glutathione (GSH) is essential for cellular protection against reactive free radicals and other oxidizing agents in the human body. Under typical circumstances, GSH and GSH-Px are prevalent in the kidney. The status of GSH and the activity of its dependent antioxidant enzymes may be diminished to manage heightened oxidative stress due to renal injury, or the decline in kidney function may curtail their production. Prior research has demonstrated that plasma or erythrocyte GSH concentration, GSH-Px, and/or GSH reductase activities diminish with the decline of renal function[12]. Urea, uric acid and creatine are important indicators of kidney function and are closely related to levels of granular filtration Low levels indicate kidney dysfunction[13].

This study aims to identify the particular biomarker parameter and its relationship with the progression of disease in individuals with CKD

Materials and Methods

Sample collection

The present study involved 90 people, 30 control groups, and 60 patients (females and males) aged 18-80 with chronic kidney disease. Samples were collected from Tikrit Central Teaching Hospital in Saladin, Iraq, from September 2023 to December 2023.

Blood Sample Collection

5 ml of venous blood was obtained with a sterile syringe, transferred to a gel tube, and allowed to coagulate for 20 minutes at the ambient temperature (25-30°C). The

tubes were centrifugated at 3000 rpm for 15 minutes to isolate the serum, which was then preserved in Eppendorf tubes at −20°C until utilized for Biochemical assay.

Measurement of biochemical parameters

In this study, analysis of a Japanese company (FUJIFILM, FUJI DRI-CHEM SLIDE) was used to measure urea, uric acid, and creatine levels, GSH measurement by Sandwich-enzyme-linked immunosorbent assay (ELISA) using SunLong kit, China.

Ethical approval

This study was performed according to the ethical principles established in the Declaration of Helsinki. It was conducted following the acquisition of both verbal and written consent from the patients before collecting the samples; this case-control research received approval from the Scientific Committee of the Institute of Genetic Engineering and Biotechnology for post-graduate study at the University of Baghdad, as well as the study was approved by the Ministry of Health and Environment of Iraq (73275 in 30-11-2023).

Statistical Analysis

The study used the Statistical Analysis System (SAS), 2018 to detect the effects of different groups (patients and controls). A T-test was employed to distinguish between means and calculate the correlation coefficient among variables [14].

RESULTS

Levels of GSH in stuided groups

The findings of the current study indicated lower significant GSH levels in CKD patients (4.61 ± 0.2 µmol/L) compared to the control group (9.06 ± 0.09 µmol/L, $p<0.05$), as shown in Figure 1.

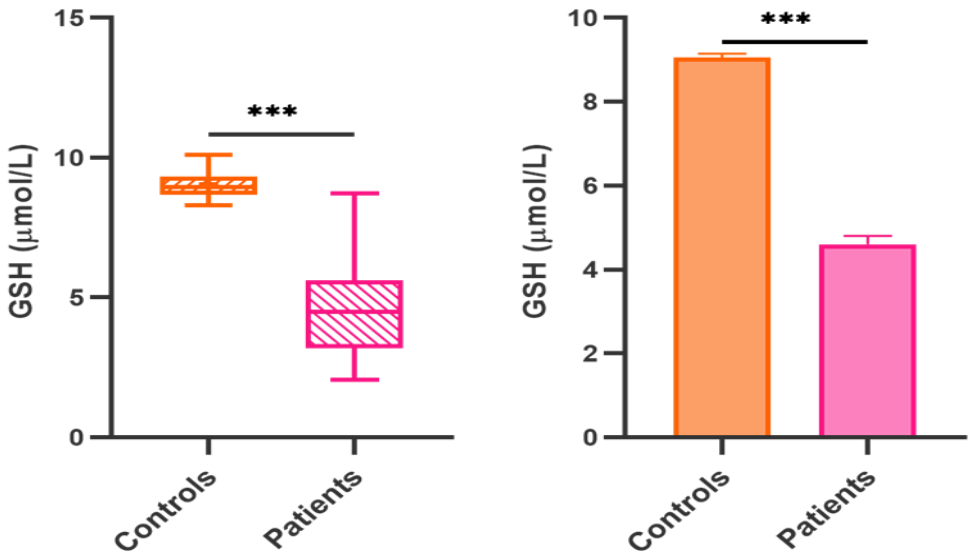

Figure (1): Compare the GSH (µml/L) levels between patients and control groups.

*** indicates a highly significant difference between the two groups

This study demonstrated a high significance in urea levels in CKD patients (87.35 ± 3.61 mg/dL) compared to the control group (22.01 ± 0.81 mg/dL, $p<0.05$), as shown in the **Figure 2.**

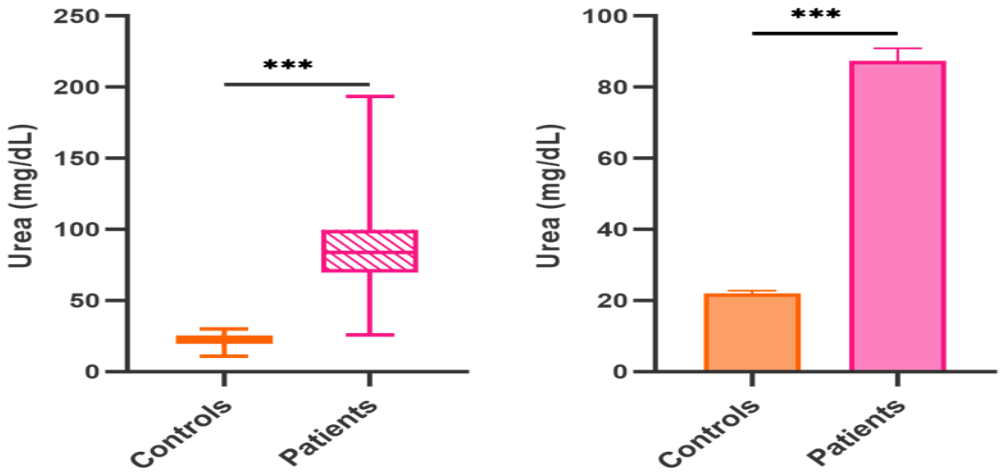

Figure (2): Compare the urea (mg/dL) levels between patients and control groups.

Findings of the current data revealed a high significance in uric acid levels in CKD patients (12.39 ± 0.48 mg/dL) compared to the control group (4.88 ± 0.27 mg/dL, $p<0.05$), as shown in the **Figure 3.**

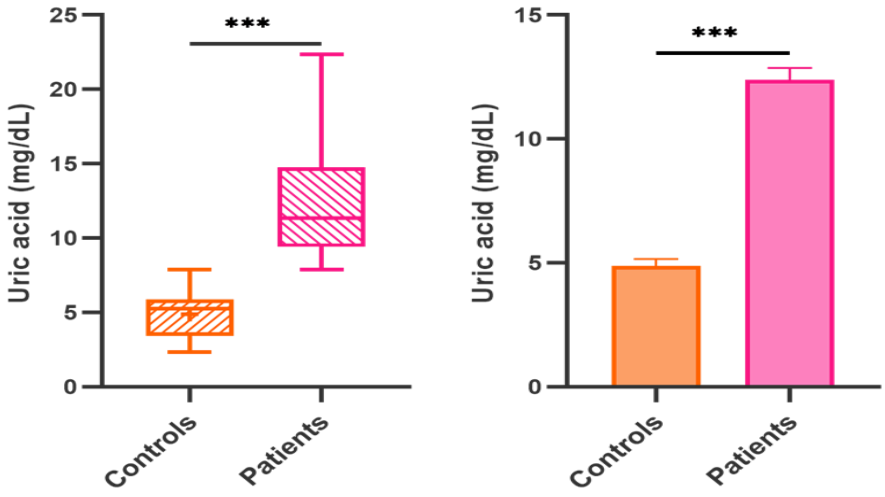

Figure (3): Compare the uric acid (mg/dL) levels between patients and control groups.

Levels of creatinine in stuided groups

The present results showed significantly elevated creatinine levels in CKD patients (2.38 ± 0.07 mg/dL) relative to the control group (1.03 ± 0.05 mg/dL, p<0.05), as shown in the **Figure 4.**

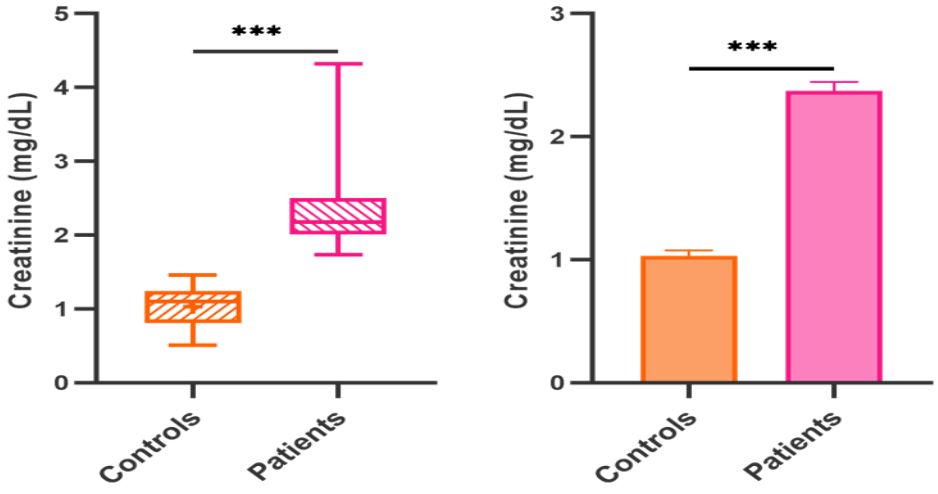

Figure (4): Compare the creatinine (mg/dL) levels between patients and control groups.

Correlation between some biomarker in patient with CKD

Serum urea levels demonstrated a strong negative correlation with GSH (r=-0.66, p<0.05,), In addition, the correlation between serum creatinine a strong negative correlation with GSH (r=-0.64, p<0.05,), which indicates that lower levels of these protective factors are related to higher serum creatinine levels in CKD patients.

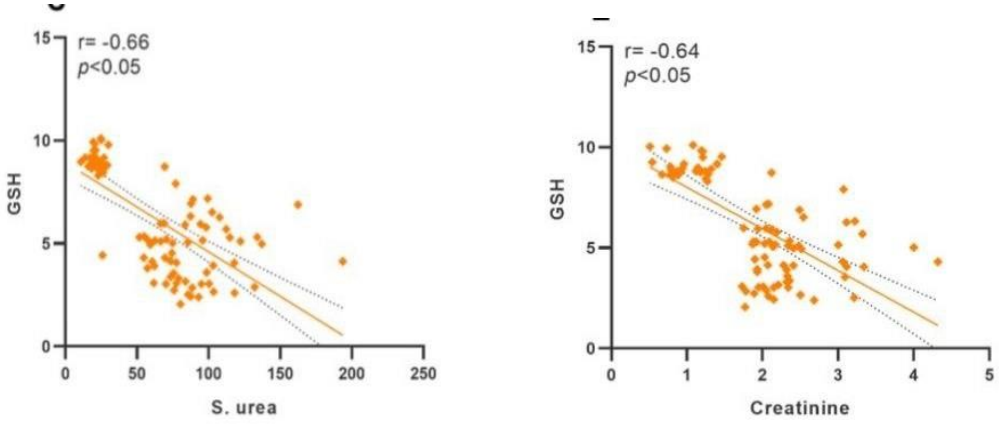

Figure 5: Correlation between GSH with Urea and Creatinine

Discussion

In the present study the results show lower GSH levels in CKD patients contribute to increased oxidative damage, which can exacerbate the progression of kidney disease and related complications. Managing oxidative stress through dietary interventions, supplements, or medications that boost GSH levels might help mitigate some of these effects[15]. The significantly lower GSH levels observed in CKD patients in this study suggest a compromised antioxidant status, which may contribute to oxidative damage and associated complications in CKD. The decreased GSH levels in CKD patients highlight the potential importance of targeting oxidative stress and enhancing antioxidant defenses as a therapeutic strategy in the management of CKD.

This study indicates a significant decrease in the concentration of GSH in CKD compared to healthy subjects, so the present study agreed with a previous study by Azouaou *et al*. [15], and Giustarini *et al*. [16]. The GSH is a crucial intracellular antioxidant that protects cells from oxidative stress by neutralizing reactive oxygen species (ROS). The liver produces GSH. Oxidative stress has been implicated in the pathogenesis and progression of CKD, as impaired kidney function leads to an imbalance between ROS production and antioxidant defense mechanisms[17].

According to the findings, there is a discernible increase in the levels of urea, uric acid and Creatinine in the serum of patients with CKD in comparison to the control group. This result validated the findings of the other studies. There were a few research that explained the key solute that was removed by the renal system, which included blood urea and serum creatinine. Some studies have explained the key

solutes removed by the renal system, including blood urea and serum creatinine [18]. A rise in urea and creatinine levels is observed in patients with CKD due to the kidney's diminished capacity to remove nitrogenous wastes from the bloodstream, leading to these compounds' buildup in the bloodstream. Other factors, such as excessive protein consumption, shock, gastrointestinal bleeding, and so on, could also contribute to this increase in urea and creatinine levels in the blood.

Uric acid is an important biomarker in the context of CKD. Uric acid is an end product of purine metabolism, which found in certain foods and drinks and also produced by the body. Normally, uric acid is dissolved in the blood, processed by the kidneys, and excreted in the urine [19]. The normal ranges for uric acid levels in the blood (for adult men: 3.5 - 7.2 mg/dL) and (for adult women: 2.6 - 6.0 mg/dL), levels above these ranges can indicate hyperuricemia, which is common in CKD patients [20]. In CKD, the impaired kidney function leads to decreased uric acid excretion and consequent hyperuricemia. Elevated uric acid levels have been associated with increased risk of CKD progression, cardiovascular events, and mortality in CKD patients.

Elevated uric acid levels can have several implications for CKD patients such as: Gout: High uric acid levels can lead to the formation of urate crystals in the joints, causing gout, a type of inflammatory arthritis. Kidney stones: uric acid can crystallize in the kidneys, forming stones that can further impair kidney function. Cardiovascular risk: Hyperuricemia is associated with an increased risk of CVD, which is particularly concerning for CKD patients who are already at elevated cardiovascular risk[8].

The significantly higher uric acid levels in CKD patients in this study underscore the potential role of uric acid as a marker of kidney dysfunction and a contributor to

the complex pathophysiology of CKD. The present study's findings confirm those of Miftari *et al*. [21]. Creatinine levels are an important indicator in the diagnosis and management of CKD. Creatinine is a byproduct of muscle metabolism that is typically filtered out of the blood by the kidneys and excreted in the urine[20].

In CKD, the kidneys ability to filter waste products diminishes, leading to an accumulation of creatinine in the blood. Measuring blood creatinine levels helps assess kidney function. Higher levels indicate poorer kidney function. CKD is classified into five stages based on GFR which can be estimated using serum creatinine levels [9]. The normal serum creatinine level is 0.5 to 1.0 mg/dL. In CKD creatinine levels can be significantly higher than this range, depending on the severity of kidney impairment. Serum creatinine level was higher than normal range in CKD patients undergoing dialysis before dialysis. Dialysis has positive impact on serum creatinine level and reduced its level towards normal. The higher serum creatinine levels observed in CKD patients in this study are consistent with the expected pathophysiological changes associated with chronic kidney disease.

CONCLUSION

The results of this study indicated a decrease in glutathione levels and a significant increase in urea, uric acid, and creatine levels in patients with chronic kidney disease, suggesting that these levels are important indicators for predicting kidney disease.

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