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Estimated Glycation End Products and Oxidative Status in Renal Failure Patients

Salam Khalid Mutlag

Ministry of Education, Directorate of Kirkuk Education, Iraq.

mohaned.bio@gmail.com**Mohanad Hammo Mukhlif1**

Ministry of Education, Directorate of Kirkuk Education, Iraq.

Solidbiology88@gmail.com

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Abstract: The present study conducted to assess the Glycation end products and oxidative status of in patients with renal failure. 100 patients that have had CKD for less than 2 years have been diagnosed by a doctor. A control group of 40 stable individuals was selected. From October 2021 to February 2022, patients were confirmed to be sick with chronic renal disease at Azadi Teaching Hospital and Al-Jumhuri Hospital. the results showed that the largest age group of patients was > 60 years with percent (39%). Body Mass Index (BMI) of patients was 18.5-24.9 kg with percent (52%). Residential Area of patients was urban with percent (83%). Smoking Status of patients was non-smoking with percent (68%). The current outcomes demonstrated a reduction in the concentration of total protein that is significant ($P<0.05$), albumin and globulin in patients compare with healthy volunteers. On the other hand, the results show a significant ($P<0.05$) elevated in levels of carbonyl and amino group, while decreased in thiol levels in patients compare with healthy volunteers. Otherwise, the Glycation level shows significant ($P<0.05$) elevated in in patients compare with healthy volunteers. Its concluded that the CKD lead to elevated Glycation level and changes in oxidative status.

Keywords: Glycation; Chronic kidney disease; amino group; carbonyl group.

Introduction

Chronic kidney disease (CKD) is a form of renal disease in which, over the course of months or years, kidney function steadily declines. Early signs and symptoms include leg swelling, exhaustion, vomiting, loss of appetite, and confusion; later signs and symptoms include leg edema, exhaustion, vomiting, lack of appetite, and confusion. Among the complications include heart disease, hypertension, bone disease, and anemia [1-3]. The incidence of all stages of CKD varies considerably around the globe, falling between 7 and 12%. A frequency of 1.7% for adults with CKD stages G3–G5 has been observed in China [4], 3.1% in the U. S. [5], 5.8% in Australia [6]. Spain [7] has a prevalence of 24.0 percent, and England [8] has a prevalence of 5.2 percent. The causes of CKD According to research from the Chronic Kidney Disease in Queensland registry, the main

causes of CKD before beginning KRT [8]. The cornerstones of CKD care have been the diagnosis and treatment of certain kidney diseases, and also hemodialysis. Evidence suggests that preventative measures could considerably reduce the burden of CKD, but it also suggests that such measures are not currently being used. It is not common practice to use tests for early kidney disease detection when it is most treatable. To effectively address this significant public health concern, CKD management requires a comprehensive public health approach [9-10]. The present study conducted to assess the Glycation level and oxidative status of in patients with renal failure.

Materials & methods

Patients

100 individuals with CKD who had it for less than two years were given the diagnosis by a doctor. We selected a controlled experiment of 40 healthy individuals. Patients at Al-Jumhuri Hospital and Azadi Teaching Hospital were discovered to have chronic renal disease between October 2021 and February 2022.

Estimation of Proteins

Plasma samples are tested for total protein, albumin, and globulin concentration using a colorimetric method in accordance with kit instructions.

Estimation of Thiol and Carbonyl Group Levels

The concentration of thiol is determined using Ellman's method [11]. Principle Thiol groups and 5,5-dithiol-bis-(2-nitrobenzoic acid) were mixed to create a 412 nm yellow color; the color's intensity rises with the number of thiol groups. Glycation, carbonyl, and amino group concentrations are estimated using the [12] technique.

Statistical analysis

The data were analyzed using the Minitab statistical program, which was supported by Microsoft Excel XP and SPSS. Basic interpretations of the data included mean, SD (standard deviation), minimum and maximum values.

Results and Discussion

Socio-demographic variables

Table 1 displayed a few sociodemographic factors. Around 39% of patients were over 60 years old, making up the largest age group. Patients' Body Mass Index (BMI) ranged from 18.5-24.9 kg with a 52% percentile. 83% of the patients' residential areas were urban. Patients had a 68% non-smoking rate for smoking status.

Table (1): socio-demographic variables of studied groups

Characteristics	Classes	Groups	
		Control	Patients

Age	20-30 years	2 (5%)	7 (7%)
	31-40 years	5 (12.5%)	11 (11%)
	41-50 years	7 (17.5%)	19 (19%)
	51-60 years	11 (27.5%)	24 (24%)
	> 60 years	15 (37.5%)	39 (39%)
	Total	40	100
Body Mass Index (BMI)	< 18.5	14 (35%)	37 (37%)
	18.5-24.9	21 (52.5%)	52 (52%)
	25-29.9	5 (12.5%)	11 (11%)
	Total	40	100
Residential Area	Urban	32 (80%)	83 (83%)
	Rural	8 (20%)	17 (17%)
	Total	40	100
Smoking Status	Yes	6 (15%)	18 (18%)
	Non	29 (72.5%)	68 (68%)
	Passive	5 (12.5%)	14 (14%)
	Total	40	100

Proteins

1. Male

According to table (2), the total protein concentration in the blood of patients with renal failure is lower than control group (7.298 ± 0.357 mg/dl) and the reduction is significant ($P < 0.05$). As indicated in table, the blood albumin level of patients with renal failure is significantly lower ($P < 0.05$) than that of the control group (4.205 ± 0.443 mg/dl) (2). As indicated in the table (2), there are no non-significant ($P < 0.05$) differences between the control group's serum hemoglobin level (3.041 ± 0.868 mg/dl) and that of renal failure patients (2.91 ± 0.461 mg/dl).

Table (2): protein profile in male groups

Parameter \ Groups	Control (40)	Patients (100)	P-Value
TP mg/dl	7.298 ± 0.357	$5.794 \pm 0.657^*$	0.000
Albumin mg/dl	4.205 ± 0.443	$2.703 \pm 0.517^*$	0.000
Globulin mg/dl	2.91 ± 0.461	3.041 ± 0.868	0.635

2. Female

The total protein level in renal failure patients' serum (5.751 ± 0.535 mg/dl) is lower than in the control group (7.198 ± 0.51 mg/dl) that is significant ($P < 0.05$)., as shown in table (3). Albumin levels in renal failure patients' serum (2.855 ± 0.437 mg/dl) are significantly lower ($P < 0.05$) than in the control group (4.225 ± 0.398 mg/dl), as shown in table (3). Globulin levels in renal failure patients' serum (2.749 ± 0.305 mg/dl) are lower ($P < 0.05$) than in the control group (3.406 ± 0.51 mg/dl) that is significant ($P < 0.05$), as shown in table (3).

Table (3): protein profile in female groups

Parameter \ Groups	Control (40)	Patients (100)	P-Value
TP mg/dl	7.198±0.51	5.751±0.535*	0.000
Albumin mg/dl	4.225±0.398	2.855±0.437*	0.001
Globulin mg/dl	3.406±0.51	2.749±0.305*	0.003

According to Abdulkader's (2010) findings, the total protein protein level in the serum of patients with CKD reduced and reached (4.9) g/dl with a significant ($P<0.001$) difference because the renal is unable to retain formed substances like RBC, WBC, and proteins at the glomerulus level. The results of the current study revealed that the level of total protein demonstrate a substantial ($P<0.05$) reduced compare healthy individuals. Protein consequently exits the circulation through the kidney and into the urine [13].

The mean total protein level in diabetic nephropathy was 5.95 g/dl ($P\leq 0.001$), which was substantially lower than the total protein level in chronic kidney disease (CKD). Due to the infiltration of specific low molecular weight protein that contained albumin and was excreted outside the body through urine, the albumin concentrations in CKD (male and female) significantly decreased, which was consistent with other findings [14].

The most prevalent plasma protein, albumin, is made in the liver and released into the vascular system, where it is then transported throughout the body. Inside the arteries, it is essential to maintain homeostasis and a compromise between hydrostatic pressure and colloid osmotic pressure [15]. In addition, serum albumin serves a number of physiological functions, including binding to several molecules, including hormones, electrolytes, and medications [16], as well as having anti-inflammatory and antioxidant activities [17].

Regardless of the conditions involved, hypoalbuminemia is a substantial risk factor and predictor of elevated morbidity and death [18]. According to mounting evidence, it is brought on by inadequate calorie or protein intake, compromised hepatic release, decreased intestine absorption, elevated the catabolism process in cells and tissue, or elevated loss.

In the current investigation, it was discovered that when compared with control, albumin levels reduced significantly in both males and females ($P 0.05$). An earlier Japanese study found an independent relationship between blood albumin levels and proteinuria in Japanese DN individuals, and a subsequent study examined the effects of albumin reducing on the progression of renal disease in 343 Caucasian (77%) and black DN patients. They found that a quicker rate of GFR decline was also associated with hypoalbuminemia [19].

However, rather than pathology, clinical signs were mostly used in their research to diagnosis DN. The results of their study might not be as compelling given the significant prevalence of non-diabetic renal disease (NDRD) among diabetes patients undergoing renal biopsy (27-82.9%). The results of this study, which involved people who had DN identified by biopsy, may therefore be more justified [20–22].

Carbonyl, thiol and amino group

1. Male

Carbonyl levels in serum of CKD patients (0.779 ± 0.032 mg/dl) are significantly higher ($P < 0.05$) than in the control group (0.415 ± 0.039 mg/dl), as shown in table (4). Thiol levels in serum of CKD patients (14.11 ± 4.01) are lower ($P < 0.05$) than in healthy individuals group (26.078 ± 2.89) that is significant ($P < 0.05$), as shown in table (4). As shown in table (4), the amino group level in serum of CKD patients (65.61 ± 17.08) shows non-significant ($P < 0.05$) changes compared to the control group (7.933 ± 2.19).

Table (4): carbonyl, thiol and amino group in male groups

Groups Parameter	Control (40)	Patients (100)	P-Value
Carbonyl nmol/mg	0.415 ± 0.039	$0.779 \pm 0.032^*$	0.000
Thiol	26.078 ± 2.89	$14.11 \pm 4.01^*$	0.001
Amino group	7.933 ± 2.19	65.61 ± 17.08	0.000

2. Female

Carbonyl levels in renal failure patients' serum (0.71 ± 0.092 nmol/mg) lower than in healthy individuals group (0.408 ± 0.019 nmol /mg) that is significant ($P < 0.05$), as shown in table (5). Thiol levels in serum of CKD patients (9.432 ± 2.44) are lower than in healthy individuals group (22.801 ± 3.475) that is significant ($P < 0.05$), as shown in table (5). As shown in the table (5), the amino group level in the serum of CKD patients (70.32 ± 13.23) is significantly higher ($P < 0.05$) than in the control group (6.974 ± 1.79).

Table (5): carbonyl and thiol in female groups

Groups Parameter	Control (40)	Patients (100)	P-Value
Carbonyl nmol/mg	0.408 ± 0.019	$0.71 \pm 0.092^*$	0.005
Thiol	22.801 ± 3.475	$9.432 \pm 2.44^*$	0.001
Amino group	6.974 ± 1.79	$70.32 \pm 13.23^*$	0.003

The study discovered an elevated oxidative state and a deteriorating antioxidative defense system, showing a significant oxidative stress levels in the initial stages of chronic uraemia. The results are consistent with those of other investigators and indicate the existence of elevated carbonyl stress in uraemic individuals experiencing or not accepting dialysis [23].

In the current study, protein carbonyl levels in the blood were assessed as a biomarker of protein oxidation. An early sign of oxidative stress-related illnesses in proteins is protein carbonylation, an irreversible oxidative protein change. Protein carbonyls can be created by lysine, proline, arginine, threonine, and tryptophan being directly oxidized by metals, additionally, histidine and cysteine are reactive lipid peroxidation products. Proteins that have been changed must be destroyed by the cell's

proteasome process because carbonylated proteins cannot be restored by cellular enzymes [24].

The protein carbonyl level is the gold standard for determining the level of protein oxidation. It rises in severe cases of CKD but falls following kidney transplant and l-carnitine supplementation [25].

Thiols can be distinguished from other organic substances by the presence of sulfhydryl residues. Cysteine in biological systems contains low and high molecular weight substances called thiols. Less than 3% of the amino acid makeup of most proteins is made up of the amino acid cysteine. Contrarily, the chemical variety of thiols allows them to take part in a wide range of functions, such as catalysis, signaling, metal complexing, structural stability, and antioxidant defense [26].

According to the findings of the current study, renal failure and critically sick patients had blood protein thiol levels that were much lower than those of healthy participants. thiol levels and serum albumin levels were positively correlated in patients with renal failure. Study the causes of low thiol concentrations in critically ill patients and those with kidney failure in further detail. Lower blood albumin levels could be one of the main explanations of this observation [27].

In a different study, children with AKI had lower concentrations of unadjusted thiols than control subjects [28]. Both unadjusted and adjusted thiol levels were related with adjusted thiol levels in this study; however, we used adjusted thiol levels to account for albumin levels.

According to the current study's findings, renal failure patients and critically sick patients had blood amino group levels that were much greater than those of healthy participants. The quantity and severity of abnormalities were to be larger in individuals who had more severe kidney failure, and many plasma amino acid levels were abnormal in people with the mildest forms of renal insufficiency [29].

Estimation of the Glycation end products of (Crude & Purified) HPA

Table (6) compares the glycation levels of the patients' (crude & purified) HSA protein to those of control participants

Table (6): Levels of (Crude & Purified) HPA Glycation in All Study Groups

Parameters \ Groups	Control group	Patients group
Purified HPA mmole/l protein	13.89	158.4
Crude HPA mmole/l protein	12.47	141.5

Non-enzymatic glycation may impair HPA's ability to bind proteins, leading to atypical biological outcomes [30]. The non-enzymatic addition of reducing sugar to protein is known as glycation [31]. Food deterioration was first identified as a result of the maillard reaction cascade, which includes the glycation of proteins. Glycated proteins are most likely directly associated with tissue damage resulting from aging, diabetes, and other chronic illnesses, even though the same processes have been observed in vivo [32]. There are still many unanswered questions about the real mechanisms at action. Since 12–18% of circulating albumin and up to 6% of hemoglobin are glycated, people with diabetes who seem healthy often have the most severe cases of heart disease [33], led to the hypothesis that antioxidants in food could reduce tissue glycation.

Conclusion

Based on the results of the current study, it was found that chronic kidney failure leads to a change in the oxidative status of patients, as the formation of free radicals increases with a decrease in antioxidant enzymes in the body.

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