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Comparative Analysis of Protein Fractions and Oxidative Stress Markers in Patients with Chronic Kidney Disease: Clinical and Biochemical Implications

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chronic kidney disease, total protein, albumin, total oxidant status, ceruloplasmin ferroxidase

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ABSTRACT
This study showed the effect of chronic kidney disease (CKD) on serum protein balance and redox homeostasis through a comparative analysis of serum protein fractions and oxidation markers. The results showed a significant reduction in total protein, albumin, and ceruloplasmin ferroxidase activity coupled with marked elevation in globulin levels and total oxidant status(TOS), also a decline in catalase activity compared with the first (healthy) group. This alterations connected with a dual disturbance in nutritional and immune status: tubular damage, malnutrition, and protein loss which cause a decreased in proteins serum. While the increase in globulin levels indicates a chronic inflammatory response. The increase in (TOS) with reduced antioxidant defenses confirms the role of oxidative stress in (CKD) progression. Furthermore, the decrease in ceruloplasmin ferroxidase activity is caused by impaired iron and copper metabolism and the accumulation of labile iron, which promotes Fenton reactions and the generation of reactive oxygen species. Overall these results suggest that assessment of serum proteins and oxidative stress biomarkers provides important diagnostic and prognostic tools for evaluating disease severity and guiding therapeutic interventions, stressing in the importance to but a strategy that include nutritional support and oxidative stress mitigation to advance clinical outcomes in CKD patients.

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1. INTRODUCTION

The kidneys filter the blood and remove waste products produced physiologically by the body, such as urea and creatinine, all of these products are toxic in blood, and the kidneys eliminate these toxins through urine production . This occurs within the nephrons, which number one million per kidney (Maxime, 2021). Kidney failure is a fault in the normal functions of kidneys which filtering the blood from impurities and body by-products, including regulating fluids and electrolytes, which leads to fluid accumulation in the body and the accumulation of waste, resulting in a general imbalance in the human body (Harmon, 2009). Individuals of various ages are impacted by kidney disease, and issues can arise at the social, psychological, and physiological levels. Kidney transplants can also be costly (Coresh et al, 2005). According to recent research, renal failure clearly alters the blood's protein components, particularly albumin, as a decline in this protein is one of the typical vital signs in kidney failure patients, infections, and malnutrition are strongly associated with kidney failure. A study published in 2025

showed that an elevated urea-to-albumin ratio is an important determenent of the disease (He et al., 2025). These changes are not limited to albumin levels, but also include total protein and globulin levels.

Protein loss through urine and impaired hepatic synthesis due to chronic inflammation lead to a decrease in total protein levels. Certain globulin types also rise as a result of inflammation's ongoing immune system stimulation (Zhang et al., 2024). In addition to these alterations in blood proteins, kidney failure also affects oxidative stress and its antioxidants because it causes the oxidation of several large biomolecules, including proteins, lipids, and nucleic acids, which increases oxidative stress (Purwati et al., 2022). Increased stress is associated with decreased antioxidant levels and increased free radical levels. In kidney failure, ROS attack cell membranes thereby reducing the effectiveness of antioxidant enzymes (Ighodaro and Akinloye, 2018). These radicals, such as superoxide radicals, hydroxyl radicals, and hydrogen peroxidase, which are naturally formed from oxygen metabolism, activate macrophages and neurophiles, leading to inflammatory processes (Carrero et al., 2020).

2.MATERIAL AND METHODS

study design

This study was conducted on a number of patients with kidney failure and a number of healthy individuals who were randomly selected in Al-Ishaqi District and Samarra District-Salah al-Din for the period (1/3/2025 to 1/5/2025). The studied samples were divided into two groups: first group included (25) blood samples from healthy individuals, and the second group included (25) blood samples from patients with kidney failure. Blood samples were drawn using 5 ml medical syringes. Blood was then placed in glass tubes containing gelatin (Gel tubes). The samples were then centifuged at 3000 rpm for fifteen min to obtain blood serum, then it was frozen at -20°C until biochemical tests were conducted.

Methods

After taking blood sample collection, kidney function tests were performed, which included estimating urea and creatinine levels, as well as serum proteins, including total protein, albumin, and globulins. Pre-manufactured kits were used for all tests. As for oxidative stress and antioxidant tests, which included total oxidant status (TOS), catalase, and ceruloplasmin ferroxidase, the following methods were used:

Determination of Total Oxidant Status (TOS)

Erel's (2005) colorimetric used the basic idea of this method is that the oxidizing cause the ferrous ion–o-dianisidine complex to oxidize to the ferric ion. The oxidation process was aided by glycerol molecules. In an acidic media, iron (III) and xylenol orange combine to form a colorful complex, and the intensity of the resulting color is evaluated using spectrophotometry. The results are expressed as micromoles of hydrogen peroxide equivalents per liter (μmol H2O2 Equiv./L) were obtained by calibrating the test with hydrogen peroxide. The following reagents were used:

Reagent-1

Prepared by dissolving 114 mg of xylenol orange and 8.18 g of NaCl in 900 ml of 25 mM H2SO4 solution. 100 ml of glycerol was added to the solution to produce a final reagent solution consisting of 150 μM xylenol orange, 140 mM NaCl, and 1.35 M glycerol. The pH value of the reagent is 1.75, and this reagent is stable for at least 6 months at 4°C.

Reagent –2:

Prepared by dissolving 1.96 g of ferrous ammonium sulfate and 3.17 g of o-dianisidine dihydrochloride in 1000 ml of 25 mM H2SO4 solution. The final reagent consiststed of 5 mM ferrous ammonium sulfate and 10 mM o-dianisidine dihydrochloride. This reagent is stable for at least 6 months at 4°C.

Measurement:

11 μL of the second reagent, 35 μL of the sample (blood or other fluids, whether pure or containing complex oxidants), and 225 μL of the first reagent were taken. The wavelengths used for the measurements were 800 nm for the secondary wavelength and 560 nm for the primary wavelength. As a baseline for the sample, the initial absorbance measurement was obtained prior to combining reagents R1 and R2. About three to four minutes after mixing, the reaction achieved a steady state, or when the reaction line became horizontal, at which point the final reading was taken. The concentrations were computed using the standard curve shown in Figure 1.

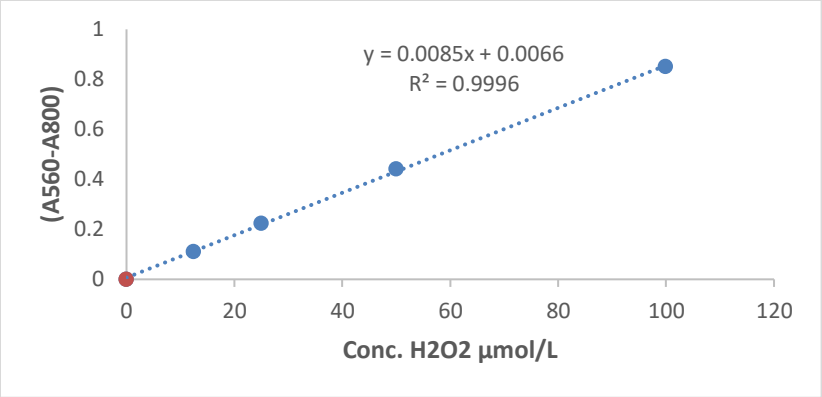

Figure (1) Standard calibration curve for TOS

The Hadwan 2018 colorimetric method was used. The method principle based on the ammonium metavanadate reaction with hydrogen peroxide at acidic pH, reducing vanadium (V) to (III). Hydrogen peroxide causing the formation of an orange-red peroxovanadium complex, which absorbs at 452 nm. As in the following equation:
$H_2O_2 + NH_4VO_3 + H_2SO_4 \rightarrow NH_4[VO(O_2)SO_4] + 2H_2O$
solution.

The following solutions were used for this purpose:
First solution: Vanadium reagent: Prepare a 0.01 M solution of sodium metavanadate in 0.5 M sulfuric acid.
Second solution: Phosphate buffer solution: Prepared at a concentration of 50 mM and pH = 7.
The third solution was: Hydrogen peroxide: Prepared at a concentration of 10 mM using phosphate buffer

Solutions used:, ,	**sample**	**standard**	**cuvette**
serum			
water	.....	25 microliters	2025 microliters
hydrogen peroxide	2000µl	2000µl	……
Mix with a mixer and incubate at 37°C using a water bath.			
Vanadate solution	2000 microliters	2000 microliters	2000 microliters
Once the saturating solution has been zeroed in, let the tubes sit at room temperature for ten min before reading the absorbance at 452 nm.			

Catalase Activity of test kU = 2.303/t * log S°/S

Determination of Ceruloplasmin Ferroxidase

A new spectrophotometric method was used to measure the activity of ceruloplasmin ferroxidase in Hadwan 2024 using a microplate protocol. A mixture of 25 µL of serum diluted fivefold with 0.15 M sodium chloride solution and 100 µL s of 0.45 M acetate buffer (pH 5.8) was prepared and incubated at 37°C for 5 min in a 96-well plate.then 25 µL of 5 mM ferrous ammonium sulfate solution, the second reagent, was then added and mixed well. Then, 100 µL of reagents 3 and 4 were added to each well, and the plate was incubated for an additional 5 minutes at 37°C. The absorbance was then measured at a wavelength of 490 nm using reagent 3 and 450 nm when using reagent 4. Distilled water was used in a blank well.
Calculations: activity was calculated useing to the following equation:
Ferric ion in tube =(ATest/ ASTD)x Conc. of STD
Ferroxidase (U⁄L)=(Conc.of ferric ion in test tube / time(5min))x(Total volume(ml)/ Volume of the sample (ml))
The Concentrations were calculated according to the standard curve shown in Figure 2.

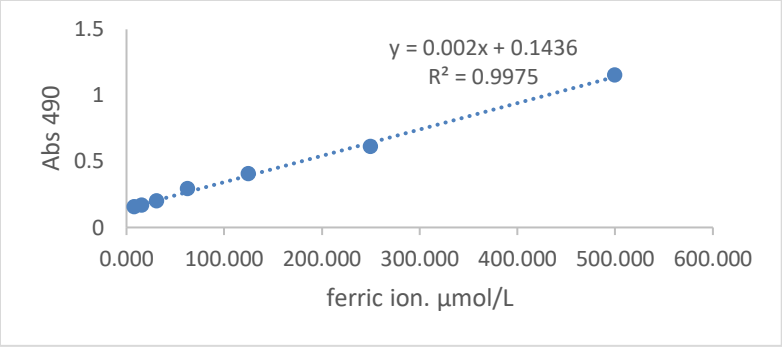

Figure (2) Standard calibration curves for ceruloplasmin ferroxidase.

3.RESULTS AND DISCUSSION

Kidney Function Test

Kidney function tests, including urea and creatinine levels, were performed for the study groups to compare samples from the patient group with those from the healthy group. The results are shown in Table (1).

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Groups	Urea mg\d	Creatinine mg\dl
Control	36.14 ±6.33 b	0.87± 0.176 b
Patients	207.62±65.491 a	10.15±2.42 a

The mean ± standard deviation (mean ± SD) of urea level in patients was 207.62 ± 65.49 mg/cm3 and in healthy controls was 36.142 ± 6.33 mg/cm3, as shown in Table (1) and Figure (3).

The urea levels in the kidney failure in patients were significantly higher than those in the healthy group, according to the above data, at the probability level of P≤0.05. The reduced excretion of urea, which comprises nitrogen from the metabolism and synthesis of proteins produced in the liver and eliminated by the kidneys, is the cause of the elevated urea level in patients with renal failure (Hayakawa et al., 2018). Because they are sensitive to all changes, urea levels are regarded as a crucial signal in assessing the effectiveness and function of the kidneys (Cauthen et al., 2008). Its rise indicates that the blood of renal contains more urea, and elevated levels of it cause more damage. Increased oxidative stress, cell death, insulin resistance, and inflammatory variables are all part of this rise, (Martinon et al., 2006).

The mean±standard deviation (mean±S.D) of creatinine level in patients was 10.15±2.42 mg/cm3 and in healthy controls was 0.87±0.17 mg/cm3, as shown in Table (1) and Figure (4). Total protein levels in the patient group were significantly lower than those in the healthy group (p≤0.05), according to the results. The glomerular filtration rate is weakened as a result of renal tubule injury, which causes this decline. Because of their huge molecular size, protein molecules cannot pass through the kidneys; yet, in circumstances of glomerular injury and kidney failure, they can (Cravedi and Remuzzi, 2013). The mean ± standard deviation (mean ± SD) of total protein level in patients was 5.703 ± 1.14 mg/cm3 and in healthy controls was 7.081 ± 0.378 mg/cm3, as shown in Table 2 and Figure (5).

There are also other indirect factors, such as malnutrition, which is the most common adverse effects of kidney failure. The body's need for proteins to repair damaged tissue and defend the immune system increases the need for proteins, thus lowering their levels in patients. Therefore, it is an indicator of kidney disease (Madhuvanthi and Lathadevi, 2016). The mean±standard deviation (mean±S.D) of albumin level in patients was 3.68±0.62 mg/cm3 and in healthy controls was 5.017±0.33 mg/cm3, as shown in Table (2) and Figure (6). The results showed a significant decrease in albumin levels at p≤0.05 in the patient group compared to the healthy group. This is because renal failure patients have elevated oxidative stress as a result of the illness. Because albumin is an endogenous antioxidant that inhibits the oxidation-reduction chain and cooperates with uric acid, glutathione, and vitamin C, the body needs to consume antioxidants, including albumin (Watanabe et al., 2025). Albuminuria is the loss of albumin from the blood through the urine as a result of renal disease-induced damage to the glomeruli (Comper, 2022). Reduced albumin levels and increased protein loss in the urine are caused by

high levels of inflammation linked to increasing renal failure. Substances released by inflammatory cells alter protein metabolism and accelerate albumin degradation. In addition, a decrease in albumin levels in the blood due to reduced kidney function causes a build-up of toxins (Sheinenzon et al, 2021).The mean±standard deviation (mean±S.D) of globulin level in patients was 2.63±0.63/cm3 and in healthy controls was 1.96±0.41 mg/cm3, as shown in Table (2) and Figure (7).

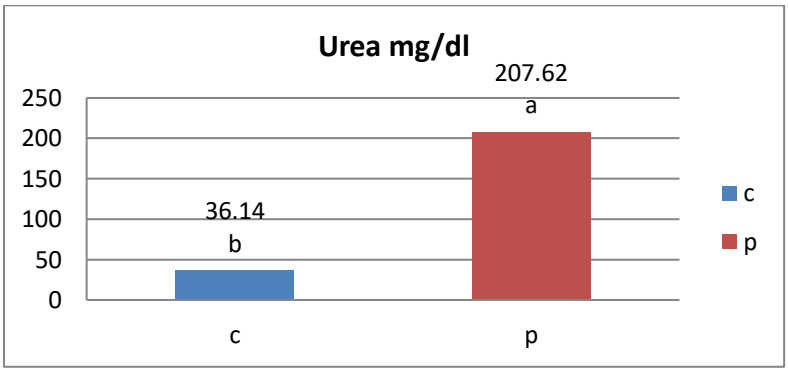

Figure (3) urea levels in serum

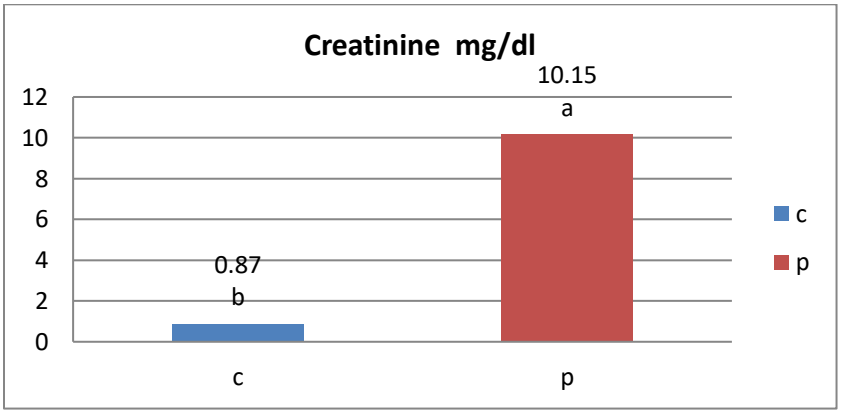

Figure (4) Creatinine level in serum

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Groups	Total protein mg\d	Albumin mg\dl	Globulin g/dl
Control	7.08±0.37a	5.01±0.33a	1.96±0.41 b
Patients	5.70±1.14 b	3.68±0.62 b	2.63±0.63 a

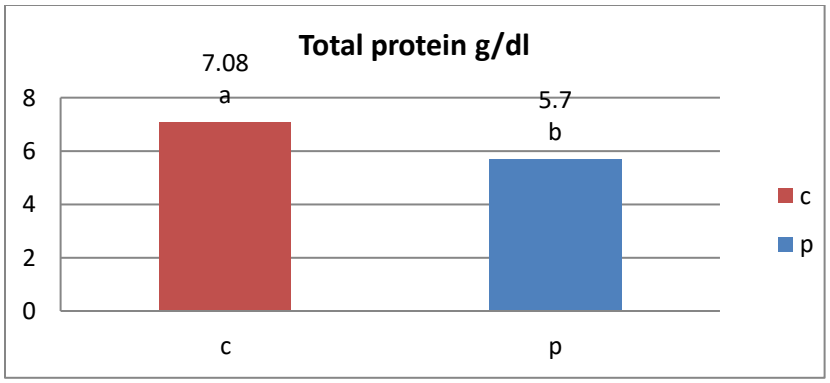

Table (5) Total protein level in serum

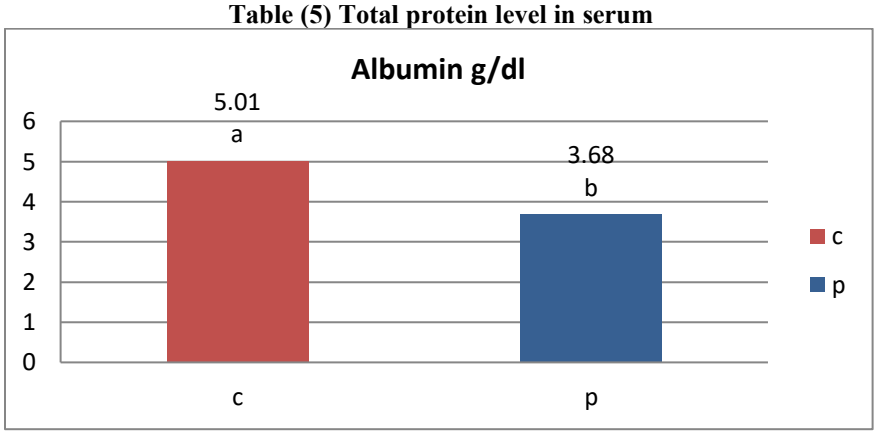

Figure (6) albumin level in serum

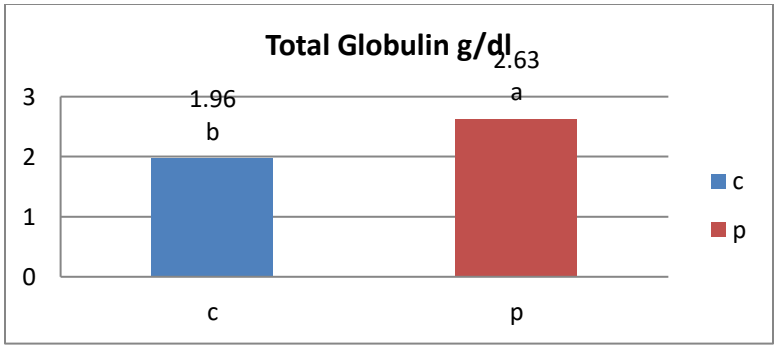

Figure (7). globulin level in serum

At a significance threshold of P≤0.05, the study found that patients' serum globulin levels were higher than those of healthy pepole. These findings are in line with a study performed in 2023 by Clingan et al., which showed that patients with renal failure had higher amounts of globulin, a significant component of total protein. An inflammatory condition or immunological response is indicated by an increase in globulin, the main component of non-albuminuric total protein, which is made up of several inflammatory proteins (Du et al., 2016). Serum globulin levels are related with conditions such as infection, inflammation, and liver disease, or they may decrease when there are problems that cause decreased globulin synthesis or increased globulin loss (Dispenzieri et al., 2001). The inflammation is common in patients with kidney failure, caused by urinary toxins, oxidative stress, and dialysis-related factors (Frąk et al,224). Patients with kidney failure are at increased risk of death if they have high globulin levels and coexist with several conditions such as coronary artery disease or chronic obstructive pulmonary disease (COPD). Furthermore, those with elevated ferritin and globulin levels above 3.2 g/cm3 are at higher risk of death (Boixeda et al., 2017).

Globulin is biggest component of total serum protein and is calculated as the difference

between total protein and albumin. (Dispenzieri et al., 2001). Low total protein and albumin combined with high globulin levels lead to a condition called protein-energy wasting (PEW), which define as the decrease in the body's protein and energy stores due to malnutrition and inflammation and is associated with negative health outcomes for kidney failure patients (Wu et al., 2019). From these results, it is clear that low total protein levels are a common feature of CKD patients, which contributes significantly and directly to the body's ability to confront oxidative stress, especially with low albumin, which is an important antioxidant and reduces free radicals. Therefore, low total protein is an indicator of deterioration in the patient's nutritional and defensive status and increases the aggravation of oxidative stress damage associated with kidney failure (Uddinet al, 2021).

Total oxidant status, catalase, and ceruloplasmin ferroxidase were examined for the study groups to confirm the similarity of the patient and healthy group samples. The results were as shown in Table (3). The mean±standard deviation (mean±S.D) of TOS levels in patients was 60.87±13.14 µmol/L and in healthy controls was 31.56±9.42 µmol/L, as shown in Table (3) and Figure (8).

The findings demonstrated that, at a probability level of ($P \leq 0.005$), the patient groups catalase activity level was lower than of the healthy group. By breaking down hydrogen peroxide (H_2O_2) and turning it into oxygen and water, the vital antioxidant enzyme catalase lessens the effects of oxidative stress. Numerous illnesses, including diabetes, anemia, and high blood pressure, are linked to any decline in catalase function. As a result, some research facilities seek to develop it as a remedy for certain illnesses (Nandi et al., 2019). The reason for the decrease in catalase levels in CKD patients is due to ischemia, which is one of the stimulants of oxidative stress. And the main source of reactive oxygen species is the Mitochondria (Su et al, 2019). During ischemic injury, reactive oxygen species (ROS) such as peroxynitrite and hydroxyl radicals are generated. At the same time, antioxidant enzymes such as catalase and glutathione peroxidase, which are produced in kidney tissue after increased nephrotoxicity, are depleted (Dennis and Witting, 2017). According to a study's findings (Sulaiman et al., 2021), patients with CKD had considerably lower catalase activity. High concentrations of catalase, which lowers ROS and prevents lipid peroxidation, are found in the aerobic cells of the kidneys, additionally, a lack of catalase results in the buildup of ROS within mitochondria, breaking down their structure and function and causing mitochondrial malfunction (Ratliff et al., 2016). CKD pathology leads to increased in oxidative stress, and that causes varying levels of catalase in patients with the disease, indicating a connection between worsening kidney damage and reduced antioxidant capacity (Duni et al., 2019). The mean ± standard deviation (mean ± SD) of ceruloplasmin ferroxidase activity level in patients was 167.01 ± 43.63 µmol/L and in healthy controls was 285.7 ± 41.59 µmol/L, as shown in Table (3) and Figure (10).

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Groups	TOS	Catalase	CP- FeOx
Control	31.56±9.42 b	44.68±10.29 a	285.7±41.59a
Patients	60.87±13.14 a	26.16±4.81 b	167.01±43.63b

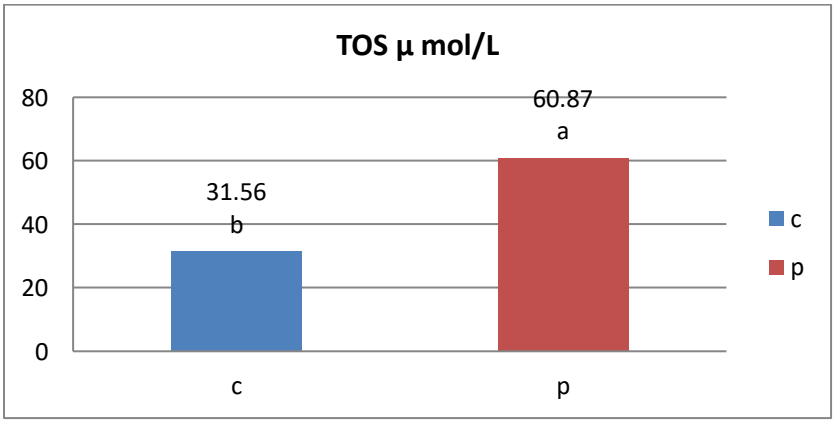

Figure (8) TOS level in serum

The results showed an increase in the overall stress level in the infected group compared to the control group (healthy individuals), at a probability level of p≤0.005. The study results are in agreement with the findings of Abod et al. (2021), which confirmed elevated TOS levels in patients with renal failure and the resulting impaired kidney function. Stress was observed to develop and antioxidant capacity decreased due to several factors, including lipid peroxidation and the resulting elevated levels of malondialdehyde (MDA) (Fahad and Mohammed, 2020). Additionally, NADPH-ox is overexpressed in the kidney and immune cells of CKD patients, which results in higher superoxide generation and less free radical scavenging (Ling and Kuo, 2018). In CKD, there is a decrease in antioxidant enzymes such glutathione peroxidase, catalase, and vitamins C and E. ROS builds up as a result of this shortage, which raises TOS (Yonova et al., 2018). Chronic kidney disease (CKD) is characterized by a high immunological response and elevated CRP, TNF-α, and IL-6. These factors, in turn, cause elevated TOS (Duni et al., 2019). The mean ± standard deviation (mean ± SD) of catalase activity level in patients was 44.68 ± 10.29 U/L and in healthy controls was 26.16 ± 4.81 U/L, as shown in Table (3) and Figure (9).

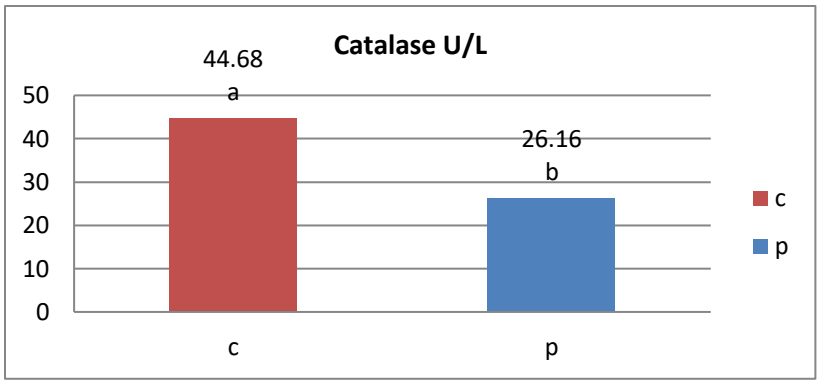

Figure (9) Catalase activity level in serum

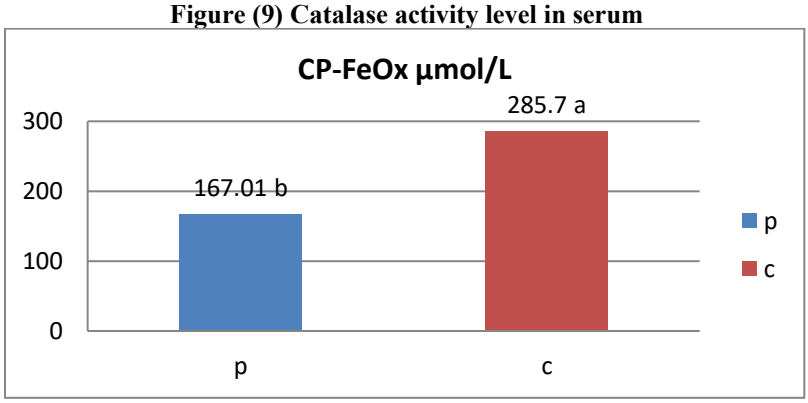

Figure (10) Ceruloplasmin ferroxidase activity level in serum

The results showed a significant decrease in the CP-FeOx activity level in the patients group compared to the healthy group at a probability level of (P≤0.005). Ceruloplasmin is a human protein found in blood serum that carries 95% of the total copper and is the largest enzymatic antioxidant which play a protection role by inhibiting iron-dependent lipid peroxidation and preventing the formation of hydroxyl radicals [OH] from hydrogen peroxide through its participation in the ferroxidase reaction. It also inhibits copper-catalyzed lipid peroxidation, in addition to consuming nitric oxide in plasma through its activity as NO oxidase, and enhances the oxidation of LDL lipoprotein (Arenas et al, 2020; Hughan et al, 2017).

As a ferroxidase-active protein, ceruloplasmin contributes to iron metabolism by oxidizing iron ions (Fe^{2+}) to Fe^{3+}, which then binds to transferrin and stops the production of harmful iron products (Linder, 2016; Gaware et al., 2010). Ceruloplasmin is one of the ferrooxidase enzymes that are crucial for maintaining iron balance. Thus, iron buildup brought on by ferroxidase deficiency impacts immunological response and brain function (Helman et al., 2023). Iron buildup in tissues, including iron deposited in the body and liver, is

one of the most significant signs of kidney failure. This increases oxidative stress, which in turn increases vascular disease and kidney damage overall (Nakanishi et al., 2019).

When iron accumulates due to disease, free iron increases, which is very reactive and generates hydroxyl radicals through Fenton reactions, causing damage to plasma proteins and depleting antioxidants, including ceruloplasmin, which reduces its effectiveness (Hellman and Gitlin, 2002), In addition, CKD causes changes in copper and iron metabolism, which leads to a decrease in the effectiveness of ceruloplasmin ferroxidase (Siotto et al, 2014). With the increase of iron, it collapses, which exceeds the ability of ceruloplasmin to regulate, leading to disruption of its function and a decrease in its activity (Hasan and Rozoqi, 2023).

5.CONCLUSIONS

The Damage to renal tubules and protein loss, which results in lower levels of total protein and albumin, impact the nutritional and immunological condition of individuals with renal failure. Elevated globulin and acute-phase proteins are also caused by the inflammatory response linked to renal failure. Because of the buildup of free radicals, this chronic inflammatory disease and reduced renal function undoubtedly cause an imbalance of oxidants and antioxidants. This comes on top of the body's diminished capacity to expel hydrogen peroxide as a result of ischemia-induced reductions in antioxidants, such as catalase, and mitochondrial dysfunction in kidney cells. Furthermore, decreased ceruloplasmin ferroxidase is due to impaired antioxidant capacity, impaired iron and copper metabolism, and the accumulation of free iron, which exacerbates oxidative Fenton reactions. Therefore, all of these factors are important in monitoring the deterioration of the clinical condition of these patients.

6.References

Abod, K. S., Mohammed, M. T., & Taay, Y. M. (2021, March). Evaluation of total oxidant status and antioxidant capacity in sera of acute-and chronic-renal failure patients. In *Journal of Physics: Conference Series* (Vol. 1853, No. 1, p. 012038). IOP Publishing.

Arenas de Larriva A P, Limia-Pérez L , Alcalá-Díaz J F , Alonso A , López-Miranda J and Delgado-Lista J 2020 *Nutrients,* **12** 3219.

Boixeda R, Capdevila JA, Vicente V *et al.*(2017*)* Gamma globulin fraction of the proteinogram and chronic obstructive pulmonary disease exacerbations.*Med Clin (Barc)*; 149: 107–113

Carrero, J. J., González-Ortiz, A., Avesani, C. M., Bakker, S. J., Bellizzi, V., Chauveau, P., ... & Fouque, D. (2020). Plant-based diets to manage the risks and complications of chronic kidney disease. *Nature Reviews Nephrology*, *16*(9), 525-542.

Cauthen CA, et al.(2008). Relation of blood urea nitrogen to long-term mortality in patients with heart failure. The American journal of cardiology.; 101(11): 1643-7

Clingan MJ, et al(2023). Imaging Patients with Kidney Failure. RadioGraphics.; 43(5): e220116.

Comper, W. D., Vuchkova, J., & McCarthy, K. J. (2022). New insights into proteinuria/albuminuria. *Frontiers in Physiology*, *13*, 991756.

Coresh , J. Byrd – Holt , D. ; Astor , B. C. ; Briggs, J. P.; Eggers, P.W. ; Lacher, D. A. and Hostetter, T. H.(2005). Chronic kidney disease awareness prevalence and trends among U. S. adults 1999 to 2000. J. Am. Soc. Nephrol ; 16: PP: 180 -188 .

Cravedi, P., & Remuzzi, G. (2013). Pathophysiology of proteinuriaand its value as an outcome measure in chronic kidney disease. British journal of clinical pharmacology, 76(4), 516-523.

Dennis, J. M., & Witting, P. K. (2017). Protective role for antioxidants in acute kidney disease. *Nutrients*, *9*(7), 718.

Dispenzieri A, Gertz MA, Therneau TM et al. 2001Retrospective cohort study of 148 patients with polyclonal gammopathy. Mayo Clin Proc; 76:476–487.

Dispenzieri A, Gertz MA, Therneau TM et al. 2001Retrospective cohort study of 148 patients with polyclonal gammopathy. Mayo Clin Proc; 76:476–487.

Du, X. J., Tang, L. L., Mao, Y. P., Guo, R., Sun, Y., Lin, A. H., & Ma, J. (2016). Circulating EBV DNA, globulin and nodal size predict distant metastasis after intensity-modulated radiotherapy in stage II nasopharyngeal carcinoma. *Journal of Cancer*, *7*(6), 664.

Dundar ZD, Kucukceran K, Ayranci MK.(2021) .Blood urea nitrogen to albumin ratio is a predictor of in-hospital mortality in older emergency department patients. The American Journal of Emergency Medicine; 46: 349-54.

Duni, A., Liakopoulos, V., Roumeliotis, S., Peschos, D., & Dounousi, E. (2019). Oxidative stress in the pathogenesis and

evolution of chronic kidney disease: untangling Ariadne's thread. *International journal of molecular sciences*, *20*(15), 3711.

Erel, O. (2005). A new automated colorimetric method for measuring total oxidant status. *Clinical biochemistry*, *38*(12), 1103-1111.

Fahad, D. and M.T. Mohammed, OXIDATIVE STRESS: IMPLICATIONS ON SKIN DISEASES. Plant Archives, 2020. 20(2): p. 4150-4157.

Farhan, Layla O.(2017). Determanation of Several Biochemical Markers in Sera of Patients with Kidney Diseases. Journal of AlNahrain University-Science 16.3: 40-45.

Frąk, W., Dąbek, B., Balcerczyk-Lis, M., Motor, J., Radzioch, E., Młynarska, E., ... & Franczyk, B. (2024). Role of uremic toxins, oxidative stress, and renal fibrosis in chronic kidney disease. *Antioxidants*, *13*(6), 687.

Gaware, V., Kotade, K., Dhamak, K., & Somawanshi, S. (2010). Ceruloplasmin its role and significance: a review. *Pathology*, *5*(6), 10-7439.

Guyton A, Hall J(2004). Text book of medical physiology. 11th Ed.: Eleventh Edition.

Hadwan, M. H., & kadhum Ali, S. (2018). New spectrophotometric assay for assessments of catalase activity in biological samples. *Analytical biochemistry*, *542*, 29-33.

Hadwan, M. H., Rahi, A. K., Abass, E. R., Hadwan, A. M., Mohammed, R. M., Alta'ee, A. H., ... & Al-Talebi, Z. A. (2024). A new spectrophotometric method for measuring ceruloplasmin ferroxidase activity: an innovative approach. *BioMetals*, *37*(6), 1699-1712.

Harmon, W., (2009). Glomerular filtration rate in children with chronic Kidney disease. Clinical chemistry.,55: pp:400-441.

Hasan, H. R., & Rozoqi, S. S. (2023). Determination of Ceruloplasmin Ferroxidase Activity, Iron & Transferrin in Patients with Brain Tumor. *American J Neurol Res*, *2*(1), 1-4.

Hayakawa, K., Kato, T. A., Watabe, M., Teo, A. R., Horikawa, H., Kuwano, N., ... & Kanba, S. (2018). Blood biomarkers of Hikikomori, a severe social withdrawal syndrome. *Scientific Reports*, *8*(1), 2884.

He, K., Zhu, Y., Wang, W., Wang, Z., Guo, S., & Wu, J. (2025). Association between the blood urea nitrogen to serum albumin ratio and the risk of mortality in patients with chronic kidney disease: a cohort study. *BMC nephrology*, *26*(1), 275.

Hellman, N. E., & Gitlin, J. D. (2002). Ceruloplasmin metabolism and function. *Annual review of nutrition*, *22*(1), 439-458.

Helman, S. L., Zhou, J., Fuqua, B. K., Lu, Y., Collins, J. F., Chen, H., ... & Frazer, D. M. (2023). The biology of mammalian multi-copper ferroxidases. *Biometals*, *36*(2), 263-281.

Hughan K S , Wendell S G, Delmastro-Greenwood M , Helbling N , Corey C , Bellavia L, Shiva S 2017 *Hypertension,* **70** 634.

Ighodaro, O. M., & Akinloye, O. A. (2018). First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid. *Alexandria journal of medicine*, *54*(4), 287-293.

Linder, M. C. (2016). Ceruloplasmin and other copper binding components of blood plasma and their functions: an update. *Metallomics*, *8*(9), 887-905.

Ling, X. C., & Kuo, K. L. (2018). Oxidative stress in chronic kidney disease. *Renal Replacement Therapy*, *4*(1), 1-9.

Madhuvanthi, M., & Lathadevi, G. V. (2016). Serum proteins alteration in association with body mass index in human volunteers. Journal of clinical and diagnostic research: JCDR, 10(6),CC05.

Martinon F, et al.(2006)**.**Gout-associated uric acid crystals activate the NALP3 inflammasome. Nature.; 440(7081): 237-41

Maxime Raffray (2021), etude des parcours de soins des insuffisants renaux chroniques terminaux ayant demarre la dialyse en urgence par une approche methodologique mixte (these de doctorat, sante publique), ecole doctorale, biologie sante, universite de Rennes, France,p21.22.

Nakanishi, T., Kuragano, T., Nanami, M., Nagasawa, Y., & Hasuike, Y. (2019). Misdistribution of iron and oxidative stress in chronic kidney disease. *Free Radical Biology and Medicine*, *133*, 248-253.

Nandi, A., Yan, L. J., Jana, C. K., & Das, N. (2019). Role of catalase in oxidative stress-and age-associated degenerative diseases. *Oxidative medicine and cellular longevity*, *2019*(1), 9613090.

Purwati, D. D., Mustika, A., Hakim, L., & Thaha, M. (2022). Correlation of serum nitric oxide and urine malondialdehyde levels in non-hemodialysis chronic kidney disease patients. *Molecular and Cellular Biomedical Sciences*, *6*(1), 43-9.

Ratliff, B. B., Abdulmahdi, W., Pawar, R., & Wolin, M. S. (2016). Oxidant mechanisms in renal injury and disease. *Antioxidants & redox signaling*, *25*(3), 119-146.

Sheinenzon, A., Shehadeh, M., Michelis, R., Shaoul, E., & Ronen, O. (2021). Serum albumin levels and inflammation. *International journal of biological macromolecules*, *184*, 857-862.

Siotto, M., Pasqualetti, P., Marano, M., & Squitti, R. (2014). Automation of o-dianisidine assay for ceruloplasmin activity analyses: usefulness of investigation in Wilson's disease and in hepatic encephalopathy. *Journal of Neural Transmission*, *121*(10), 1281-1286.

Su, H., Wan, C., Song, A., Qiu, Y., Xiong, W., & Zhang, C. (2019). Oxidative stress and renal fibrosis: mechanisms and therapies. *Renal fibrosis: mechanisms and therapies*, 585-604.

Sulaiman, S. H., Demir, H., Soyoral, Y. U., & Demir, C. (2021). Determination of oxidative stress levels and some antioxidant activities in acute and chronic renal failure patients. *International Journal of Clinical Chemistry and Laboratory Medicine (IJCCLM)*, *7*(1), 12-19.

Uddin, M. J., Kim, E. H., Hannan, M. A., & Ha, H. (2021). Pharmacotherapy against oxidative stress in chronic kidney disease: Promising small molecule natural products targeting nrf2-ho-1 signaling. *Antioxidants*, *10*(2), 258.

Watanabe, K., Kinoshita, H., Okamoto, T., Sugiura, K., Kawashima, S., & Kimura, T. (2025). Antioxidant Properties of Albumin and Diseases Related to Obstetrics and Gynecology. *Antioxidants*, *14*(1), 55.

Wu, P. P., Hsieh, Y. P., Kor, C. T., & Chiu, P. F. (2019). Association between albumin–globulin ratio and mortality in patients with chronic kidney disease. *Journal of clinical medicine*, *8*(11), 1991.

Yonova, D., Trendafilov, I., Georgieva, I., Dimitrova, V., Arabadjieva, D., & Velkova, N. (2018). Oxidative stress (OS) in chronic kidney disease (CKD): a mini review. *Nephrol. Renal Dis*, *3*, 1-3.

Zhang, L., Deng, T., Zeng, G., Chen, X., & Wu, D. (2024). The association of serum albumin with 28 day mortality in critically ill patients undergoing dialysis: a secondary analysis based on the eICU collaborative research database. *European Journal of Medical Research*, *29*(1), 530.