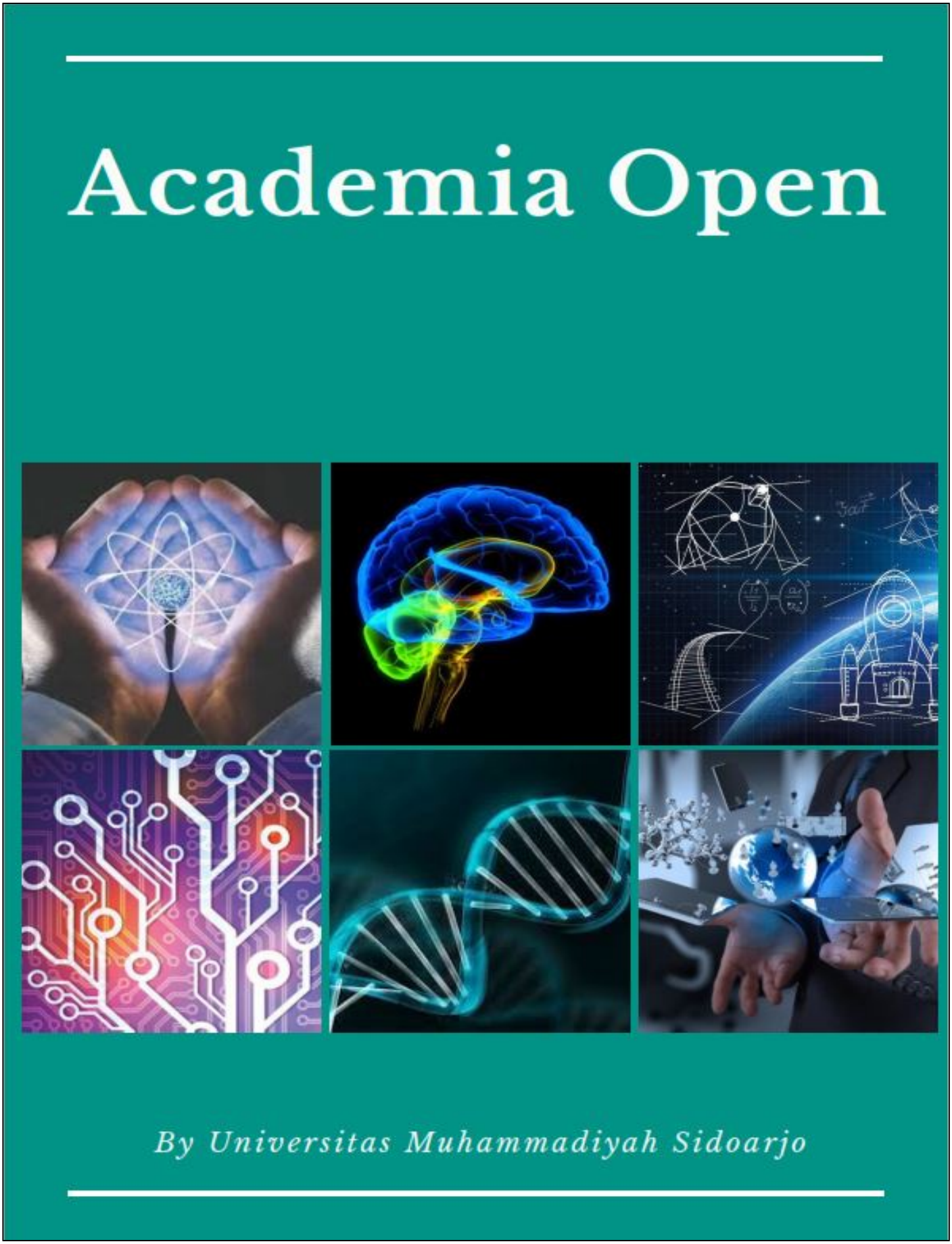
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Evaluation of ?2-microglobulin, IL17, Endostatin levels, and some biochemical variables in patients with Chronic kidney disease in Kirkuk city

Evaluasi kadar ?2-mikroglobulin, IL17, Endostatin, dan beberapa variabel biokimia pada pasien penyakit ginjal kronis di kota Kirkuk

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Abstract

Chronic kidney disease is the most common disease in developed countries of the world and thus poses a major challenge to public health throughout the world , Method:- Samples were collected randomly from patients hospitalized in Kirkuk General Hospital, in addition to some outpatient medical clinics. 55 samples were collected for patients with chronic kidney disease CKD, whose ages were (40-75) for one year for the period (1/6/2024 to 25/10/2024) Also, 30 blood samples were collected from healthy people (as a control group) .5 ml of blood sample was collected from patients and healthy people and separated using a centrifuge to obtain the serum, after which the level of the studied variables, represented by β2-microglobulin, Interlukin-17- IL-17, Endostatin, and some biochemical variables, which included (Urea, Creatinin, Uric acid, Ferritin)Result:- This study showed a significant rise in the (B2-MG, Endostatin, IL-17, Urea, Creatinin, Uric acid, and ferritin) in patients with CKD compared to healthy subjects.

Highlights:

1. Chronic kidney disease challenges public health worldwide.
2. Study analyzes β2-MG, IL-17, Endostatin, and biochemical markers in CKD patients.
3. Results show significant biomarker elevation in CKD versus healthy subjects.

Keywords: Chronic kidney disease, β2-microglobulin, IL-17, Endostatin

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Introduction

Chronic kidney disease is a major public health problem (Hill., 2016), as kidney function gradually declines over a period of months to years continuously (Sahlah., 2020). Chronic kidney disease is usually described as chronic kidney failure with abnormal function and structure of the kidneys. It usually develops after acute kidney disease such as acute glomerulonephritis. Or nephrotic syndrome or acute renal failure (Chawla., 2017). The risk of developing chronic kidney disease increases with age, and the deterioration of kidney function increases, so living with the disease becomes common, and thus people with chronic kidney disease become more susceptible to death (Ahlam.,2019). The development of chronic kidney disease depends on many risk factors, including those with diabetes and high blood pressure. , glomerulonephritis, and polycystic kidney disease (Hussein , 2024) .

β2-microglobulin It is a protein with a molecular weight of 11,800 D that is found in all nucleated cells, and in body fluids such as serum, urine, and synovial fluid. It was found that the β2-MG gene, located on chromosome 15, is responsible for the synthesis of β_2-microglobulin in the human body. The entity's structure consists of one disulfide bond and a total of 99 amino acids (Hussein *et al*., 2022). It has been found that this protein is associated with many pathological conditions, including liver and kidney dysfunction, viral infections, and malignant tumors (Drüeke TB and Massy,2009) .

Endostatin is a protein derived from the cleavage of collagen XVIII by protease. It is an endogenous inhibitor Known for its ability to inhibit endothelial cell proliferation and migration, angiogenesis, and tumor growth, angiogenesis is defined as the formation of new blood vessels from pre-existing blood vessels and is crucial in many conditions such as embryonic development, tissue regeneration, and tumors (Li *et al*., 2021). Circulating endostatin levels are elevated in many underlying conditions that lead to insufficiency Heart such as high blood pressure, diabetes, chronic kidney disease, and heart disease(Ruge *et al*.,2018). The Evaluation of serum endostatin level has been shown to be an earlier and more sensitive prognostic indicator For the development of kidney disease of blood urea nitrogen, which is a typical indicator for evaluating kidney function in patients with the glomerulonephritis phenotype (Wallwitz *et al*.,2019).

The IL-17 family of cytokines consists of six different cytokines, namely IL-17A through IL-17F, with IL-17A and IL-17F being the most prevalent isoforms. (Nie *et al*., 2022). (IL-17) is synthesized by TH17 cells, memory T lymphocytes, and activated T lymphocytes. Moreover, fibroblasts, macrophages, CD8+ T cells, and polymorphonuclear leukocytes are among the cellular entities that are capable of producing interleukin-17 (IL-17) (Fu and Retnakaran, 2022). Interleukin 17 interferes with salt balance, vascular function, and renal function. So, finally raises blood (Caillon *et al*., 2017 Entedhar., 2018).

Collection of blood

Samples were collected randomly from patients hospitalized in Kirkuk General Hospital, in addition to some outpatient medical clinics. 55 samples were collected for patients with chronic kidney disease-CKD, whose ages were (40-75) for one year for the period (1/6/2024 to 25/10/2024) Also, 30 blood samples were collected from healthy people (as a control group).5 ml of blood sample was collected from patients and healthy people and separated using a centrifuge to obtain the serum, after which the level of the studied variables, represented by β2-microglobulin, Interlukin-17- IL-17, Endostatin, and some biochemical variables, which included (Urea, Creatinin, Uric acid, Ferritin).

Estimation the concentration of β2 -microglobulin, Interlukin-17- IL-17, Endostatin , ferritin in blood serum

The concentration of (β2-MG,IL-17, Endostatin, and ferritin) in sera was determination according to several kits prepared by Elabscience an American company.

Determination of the concentration of kidney function in sera :

The level of kidney function was estimated according to the kit prepared by the Tunisian company Bio Maghreb. Urea was estimated according to the researcher's method (Searle.,1984), creatinine was estimated according to the researcher's method (Tietz., 1986 and Henry ., 1974), while uric acid was estimated according to the researcher's method (Burtis.,1999 and Fossati.,1980).

Methods

Statistical Analysis

SPSS software was used to analyze the results used in the current study to obtain M ± S.D at a probability level P ≥ 0.05.

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Results and Discussion

Result

Determination of B2-MG, Endostatin, IL- 17 , ferritin , and kidney function in all groups :

GroupsParameters	Mean ± SD		p-value
	Control	Patients	
β2-MG (ng/ml)	2.55±0.876	6.32±1.76	<0.0001*
Endostatin (Pg/ml)	250.54±60.67	570±110.67	<0.0001*
1L-17 (pg/ml)	6.87±1.43	30.54±5.21	<0.0001*
Ferritin (ng/ml)	45.145±5.43	120.53±20.76	<0.0001*
Urea (mg/dl)	25.32±5.67	95.67±20.43	<0.0001*
Creatinine (mmol/L)	0.654±0.123	5.76±1.45	<0.0001*
Uric acid (mg/dl)	4.64±1.21	9.56±2.31	<0.0001*

Table 1. *shows the M ± SD of parameters in all groups.*

P ≤ 0.05

The results of this study showed a significant rise in the (B2-MG, Endostatin , IL-17 , Urea , Creatinin , Uric acid ,ferritin) in patients with CKD compared to healthy subject. at P ≤ 0.05. as in the following fig (1,2).

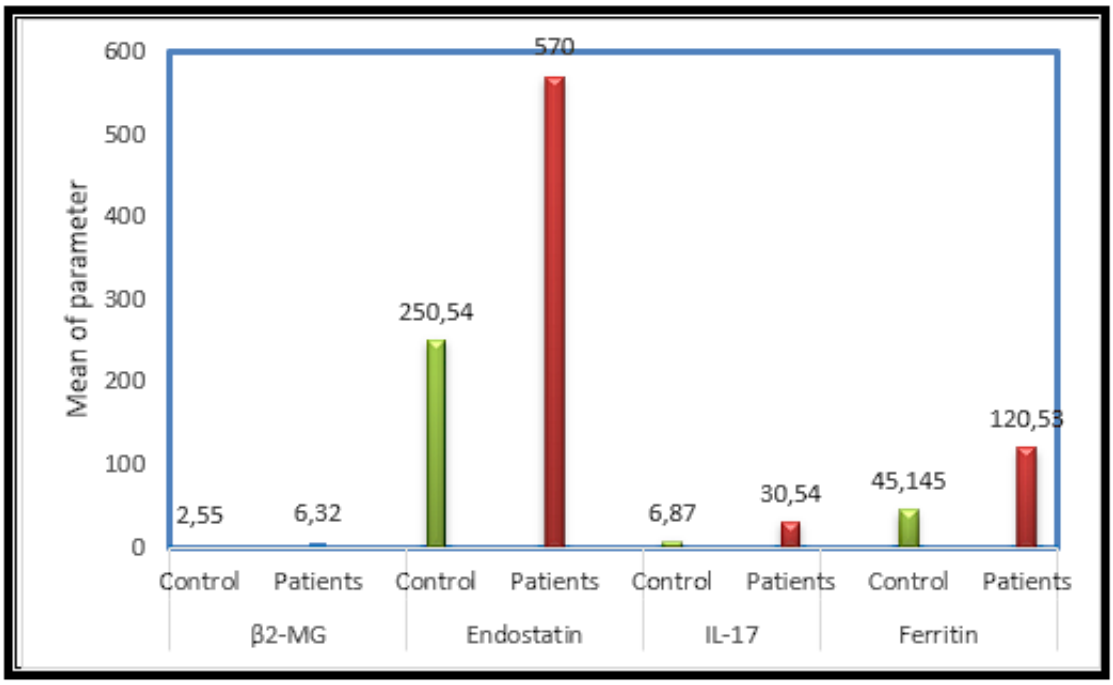


Figure 1. *levels of β2-MG, Endostatin, IL-17, Ferritin in all groups*

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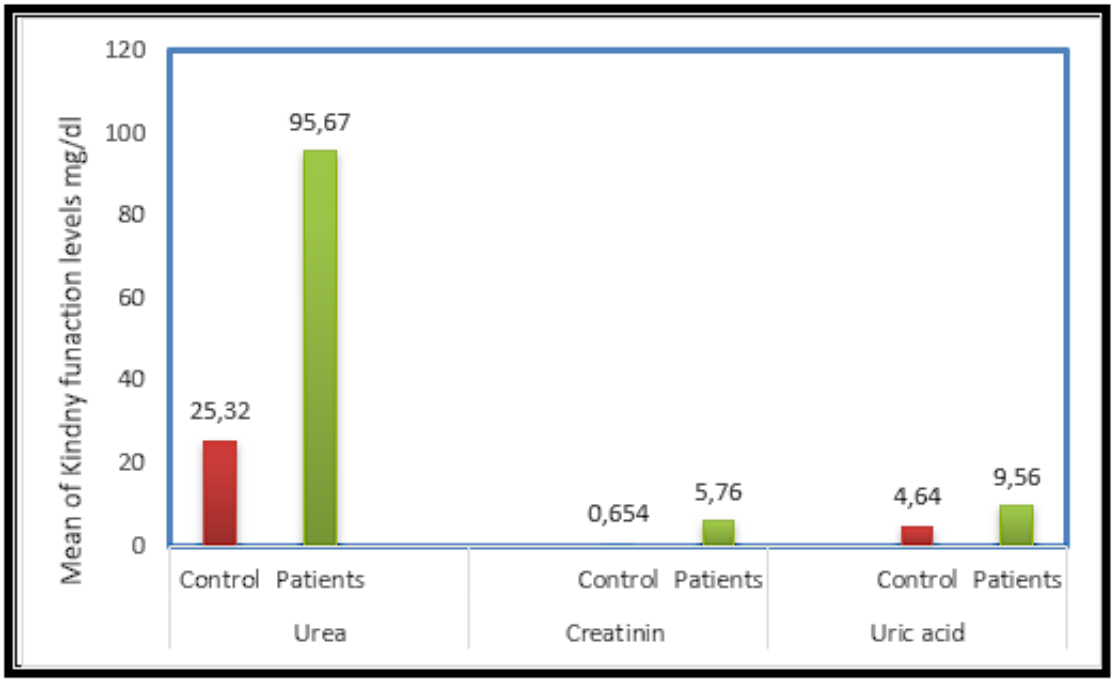


Figure 2. *levels of renal function in all groups*

Discussion

The dysfunction of kidney dysfunction is one of the most common diseases among people on a global scale (Eman., 2023). The result of this study showed a significant increase in urea in patients suffering from chronic kidney disease, as the results agreed with the findings of (Hasan., 2018), as the reason for the increase in urea is that urea is the basic nitrogenous substance resulting from metabolic wastes that are formed and excreted externally through urine. In the event of a defect and deficiency in kidney function, it leads to a decrease in the secretion of urea, which leads to its accumulation in the blood and an increase in its concentration (Pillitteri ., 1999). High levels of urea lead to the emergence of serious complications, including diabetic nephropathy, which causes a high rate of death, and decreased kidney efficiency results from a defect in the efficiency of hormones such as angiotensinogen or structural deformities with a decrease in the number of nephrons or filtration areas that are related to glomerular filtration (Mackenzie.,1995).

Also, the result showed a significant elevated in creatinine in patients with CKD compered to healthy people the result agrees with (Riffaut.,2018), as the reason for the increase is evidence of decreased kidney function (Ingrasciotta., 2015), given that the kidneys are unable to filter creatine in the serum (Ikizler.,2021). The reason is also reinforced by the fact that creatine is a metabolic waste that is naturally excreted through urine and in cases of kidney failure. Chronic kidney failure occurs in the kidneys, preventing them from filtering and excreting wastes, thus increasing their concentration in the blood (Zilva J.F., 1989). On the other hand It was found that patients with high uric acid concentration suffer from poor kidney function, regardless of HbA1c or duration of type 2 diabetes (Pizarro.,2018), as there is a significant independent positive association between high serum uric acid and an elevated risk of low glomerular filtration rate (Wang.,2018)

The results of the current research indicated an increase in the concentration of endostatin in patients with CKD, as a study (Hazem.,2024) revealed a rise in its levels in patients suffering from diabetic nephropathy, as it had good predictive effectiveness and also showed that interstitial fibrosis and tubular atrophy are one of the Known risk factors for poor kidney function. It was found that renal tubule cells secrete endostatin in response to inflammatory stimuli, as an excessive expression of endostatin leads to fibrosis of the cellular tubules, as many studies have shown that the levels of endostatin in the serum were higher and were associated with the rapid progression of renal impairment, especially in people with diabetes and CKD (Zhai et al., 2021 , Kato *et al.*, 2018). It was also found that dysregulation of blood vessel formation is extremely important for causing kidney, heart, and vascular diseases, as endostatin works in regulating blood vessels, so its high levels reflect damage to blood vessels and heart muscle in individuals with kidney, heart, and vascular diseases (Li et al., 2021).

Also, the result showed a significant increase in β2-MG concentration in patients compared to healthy subject . Kidneys eliminate β2-MG via glomerular filtration and tubular catabolism and hence, the level of β2-MG is highly correlated with GFR (Sedighi, 2014). (Real de Asúa *et al.*,2012) observed serum β2-MG levels independently correlated with femaleness and GFR. End-stage CKD leads to the accumulation of β2-MG in peripheral tissues,

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which is an established cause of systemic amyloidosis in patients undergoing dialysis.

β2-MG has been identified as a marker of kidney function as a result of its filtration by the renal glomeruli and its reabsorption by the proximal tubule. Its level in the circulation increases when the glomerular filtration rate decreases) Shen *et al.*,2023 and Hussein *et al.*,2022).

More recently, (Marchant *et al.*, 2020) study showed that serum IL-17A concentrations were significantly higher in CKD patients than in healthy subject. The results (Khalid., 2022) indicated that interleukin 17 plays an important role in the pathogenesis of chronic kidney disease. A highly significant increase in pro-inflammatory interleukin (IL-17) in CRD indicates these cytokines participate in the pathophysiology of low renal function and the role of this cytokine as principal mediators of inflammatory reaction in renal damage (Rawaa ., 2024). Also, the CKD had a much greater level of IL-17, according to the present study. Inflammatory infections in CKD patients result from increased T cell IL-17 synthesis and CRP and TNF-α production following antigen exposure. These findings align with previous studies (Z.-y. Li., 2017).

Through the results of the research, it was found that there was an increase in the level of ferritin in the blood serum of patients with CKD, as a study (Al-Tai., 2010) indicated a rise in the levels of ferritin in patients with diabetic nephropathy, and that this increase causes the generation of free radicals in the body and thus works to cause many It causes damage to various cells in the body and increases insulin resistance. It has been found that in chronic kidney disease, iron facilitates the process of protein breakdown, which causes oxidative stress, inflammation, and kidney damage, and thus iron accumulates in the lysosomes of the convoluted tubules in the kidneys of chronic kidney patients, and the iron generates types of reactive oxygen and damages the renal tubules (Al-Tai., 2010).

Conclusions

are concluded from the results of the current research that an increase in the studied variables has a close relationship with chronic kidney disease and may therefore lead to other diseases, including heart disease, diabetes, and atherosclerosis. therefore, there is a need for more studies on the association of these variables with kidney disease.

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