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Estimation of NLRP3 Inflammasome Role and some Biochemical Parameters in Patients with Chronic Kidney Diseases (CKD)

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***Abstract*— Chronic kidney disease (CKD) is a widespread condition that poses a major threat to human health. With substantial public health costs, severe morbidity, and mortality, CKD prevalence is increasing. The study aimed to look at NLRP3 inflammasome , hsCRP , Urea , Creatinine, Uric acid and GFR levels. Serum NLRP3 inflammasome , hsCRP , Urea , Creatinine, Uric acid and GFR levels were determined in 90 patients with Chronic Kidney Diseases (CKD) , and 85 healthy subjects, an age range (30-75). The results of current study show a significant increase in the concentration of serum NLRP3 inflammasome, hs-CRP, urea , creatinine and uric acid in (CKD) patients group in comparison with controls group ($p<0.05$). While shows a significant decrease in GRF in (CKD) patients group in comparison with controls group ($p<0.05$). The aim of this study is estimated the NLRP3 inflammasome , Inflammation marker , kidney function tests and Glomerular filtration rate (GFR) in patients with Chronic Kidney Disease.**

***Keywords*— Chronic Kidney Disease , NLRP3 inflammasome , Inflammation marker , kidney function tests.**

I. INTRODUCTION

Chronic kidney disease (CKD) is a widespread condition that poses a major threat to human health. With substantial public health costs, severe morbidity, and mortality, CKD prevalence is increasing [1, 2, 3]. The United States Renal Data System 2019 yearly Report estimates that by 2030, the yearly prevalence rate of CKD in the country will rise to 14.5% and it is expected to increase 16.7%. [4]. The diagnosis, management, and staging of chronic kidney disease (CKD) and the risk of CKD-related events and fatalities are all based on glomerular filtration rate (GFR) [5]. The rate of glomerular filtration is Values less than 60, 30, and 15 mL/min/1.73 m2, when expressed in milliliters per minute to body surface area normalized, respectively, indicate mild to moderate and severe declines in function and renal failure [6].

Classification of chronic kidney disease [2].

Stage	Description	Glomerular filtration rate (GFR)(ml/min per 1.73 m)
1	Kidney damage with normal GFR	>90
2	Kidney damage with mild decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–20
5	Kidney failure	<15(or dialysis)

The factors that may increase a person's risk of developing CKD include older age, race/ethnicity, other systemic diseases that affect the kidneys (such as systemic lupus erythematosus, HIV infection), family history of kidney disease, genetic risk factors, limited access to health care or low socioeconomic status, high-risk occupations and environmental exposures, and prior acute kidney injury also impact on CKD patients [7]. Finally, a lcohol consumption, high blood pressure, coronary artery disease, cerebrovascular disease, retinopathy, albuminuria, long-standing diabetes (>10 years), high levels of uric acid and uric acid in the blood, poor glycemic control, and taking multiple antihypertensive medications (beta-blockers, loop diuretics, other antihypertensive drugs, antiplatelet drugs, allopurin) are additional risk factors for chronic

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kidney disease [8]. NLRP3 (NOD-like receptor family, pyrin domain containing protein 3), There is a cytosolic protein that is important for recognizing incoming infections; When this protein is activated, it forms the inflammasome a large protein aggregate that also contains caspase-1 and the Apoptosis-Associated Speck-Like Protein. Each cell includes one oligomer, which is composed of seven NLRP3 molecules When all the inflammasomes combined together measuring around 2 m in diameter [9,10]. The NLRP3 inflammasome stimulates the immune system to respond to insults, but when it is triggered repeatedly, it has the potential to be pathologically harmful. Recently, several nephrologists have become interested in the NLRP3 inflammasome because of how it affects sterile renal inflammation in CKD. As a result, inhibiting the NLRP3 inflammasome may reduce renal inflammation in CKD [11]. ESRD patients with CKD have high levels of high sensitivity C-reactive protein (hs-CRP), a condition that affects immune homeostasis and results in a protracted inflammatory state [12]**.** A common substitute for the severity of CKD and the effectiveness of dialysis in clinical settings is urea, a by product of protein metabolism. Urea is a direct and indirect uraemic poison [13]. Creatinine a by product of skeletal muscle's creatine phosphate and dietary meat. Its body production is reliant on muscular mass [14]. Serum uric acid (SUA) has been shown to be able to predict the onset of chronic kidney disease (CKD) [15].

The Purpose of this study is to look at the levels of the NLRP3 inflammasome, an inflammation marker, kidney function tests, and glomerular filtration rate (GFR) in individuals with chronic kidney disease.

II. MATERIALS AND METHODS

A. Design of study

This study was conducted at AL- Nasiriyah Teaching Hospital, and specialist clinics under the supervision of specialist doctors in Thi-Qar province. It included (175) subjects, control (85) (40 female and 45 male) and patients (90) (40 female and 50 male) diagnosed with Chronic Kidney Diseases (CKD) , an age range (30 to75) years old.

B. Methods

About (5mL) of blood samples of the patients with Chronic Kidney Diseases (CKD) and controls were taken and allowed to clot at room temperature in empty disposable tubes centrifuge to separate it in the centrifuge at 3000 (xg) for 10min, the serum samples were separated and stored at (-20ºC) until analyzed for serum NLRP3 inflammasome and hs –CRP were determined using ELISA technology, by spectrophotometer, serum Urea, Creatinine and Uric acid were purchased from Biolabo (France).GFR was calculated according to a method of (Moss, *et al*.) [16] . Patients with Obesity and Dialysis were excluded from the study.

Table (1): Data of the studied groups

Groups	No.	Sex (Male / Female)
patients	90	50/40
controls	85	45/ 40
Total	175	

C. Statistical Analysis

Statistical analysis was done using the software **SPSS** version 20.0.The results were expressed as mean ± standard deviations (mean ± SD). To compare parameters in various study groups, the one-way ANOVA test was performed. P-values ($p < 0.05$) were used to determine statistical significance.

III. RESULTS AND DISCUSSION

A. NLRP3 inflammasome

The table (2) shows a significant increase in the concentration of serum NLRP3 inflammasome in (CKD) patients group in comparison with controls group ($p<0.05$).

Table (2): Serum NLRP3 inflammasome concentration of control and CKD groups

Groups	NO.	NLRP3 ng/ml Mean ±SD
Patients	90	50.23±9.80
Controls	85	5.38±1.07
p-value		0.000

* Each value represents Mean ±SD values were considered significantly differences ($P < 0.05$).
No: Number of subjects
Patients group:Chronic Kidney Diseases CKD: Controls Group.

By tracking its levels at various stages, the NLRP3 inflammasome is linked to the seriousness of chronic kidney disease and significantly contributes to its etiology [17] . CKD has a high clinical incidence, and the prognosis for patients is frequently dismal. Independent risk factors for CKD include immunological dysfunction and inflammation that are caused by infections or immune cells. The NLRP3 inflammasome pathway has drawn a lot of interest in nephrology since it is active in CKD. As a result, one of the well-known therapy for renal disorders is reducing or blocking the NLRP3 inflammasome activation cascade [17,18]. In the sections that follow, we will quickly go over the activation of the NLRP3 inflammasome links to the emergence of kidney-related disorders [19].

B. High Sensitivity C Reactive Protein

The table (3) shows a significant increase in the concentration of serum hs-CRP in (CKD) patients group in comparison with controls group ($p<0.05$).

Table (3): Serum hs-CRP concentration of control and CKD groups

Groups	NO.	hs-CRP mg/dL Mean ±SD
Patients	90	30.93± 4.97
Controls	85	1.62 ± 0.35
p-value		0.000

- Legend as in table (2)

Numerous studies have revealed that the blood concentrations of inflammatory markers increased in individuals with CKD, with high levels of inflammation [20]. High sensitivity C-reactive protein (hsCRP) assay is useful for sensitive detection of inflammatory states [21]. CKD is defined as kidney damage or glomerular filtration rate (GFR) < 60 ml/min/1.73 m2 for 3 months or more, irrespective of cause [22]. An established biomarker of inflammation in renal disease is CRP short pentraxin. An acute phase protein is CRP. Since CKD is a persistent inflammatory condition, glomerulosclerosis is encouraged. This process is aided by the presence of inflammatory cytokines such IL-6, TGF-, and PDGF. There is an increase in macrophages and monocytes, which produces type 1 and type 2 collagen and causes glomerulosclerosis. As a result, CKD patients have higher CRP levels [23].

C. Urea, Creatinine, Uric acid and GFR

The table (4) shows a significant increase in the concentration of serum urea , creatinine and uric acid in (CKD) patients group in comparison with controls group ($p<0.05$). While shows a significant decrease in GRF in (CKD) patients group in comparison with controls group ($p<0.05$).

Table (4): Serum Urea, Creatinine, Uric acid and GFR concentration of control and CKD groups

Groups	**NO.**	**Urea mg/dl Mean ±SD**	**Creatinine mg/dl Mean ±SD**	**Uric acid mg/dl Mean ±SD**	**GFR ml /min/ 1.73m^2 Mean ±SD**
Patients	90	112.27±21 .62	3.38 ± 0.83	7.40 ± 1.40	25.75± 8.24
Controls	85	30.38± 5.23	0.98 ± 0.28	3.86 ± 0.95	95.52±23.8 3
p-value		0.000	0.000	0.001	0.004

- Legend as in table (2)

Serum creatinine and urea are well established markers for measurement of Glomerular Filtration Rate (GFR) [24]. Creatinine is a perfect filtration marker and more sensitive index of kidney function compared to blood urea level [25] . Because the glomerulus filters creatinine, the serum creatinine level regarded as an indirect indicator of glomerular filtration. Raising plasma levels of serum creatinine and urea is a consequence of declining glomerular filtration rate. Since this increase implies kidney disease development, serum creatinine has a better predictive capacity than urea for predicting unfavorable outcomes [26 , 27]. According to several studies, the onset of CKD is linked to greater uric acid levels [28 - 30]. It is not known the correlation between uric acid levels and CKD outcomes [31], including whether uric acid is merely a marker for reduced estimated GFR (eGFR) or incidentally linked to unfavorable CKD outcomes [32]**.**

IV. Conclusion

We can infer from the information in this study that serum NLRP3 inflammasome may have a critical diagnostic function in chronic kidney disease (CKD). The diagnostic value of (hs-CRP, Urea, Creatinine, Uric acid, and GFR) in the examined disorders was confirmed.
Finally the serum levels of NLRP3 inflammasome may be used for risk stratification patients with Chronic Kidney Diseases (CKD) and its possible complication.

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CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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