Estimation of IL-18 and TNFα in Iraqi Patients with Chronic Renal Failure

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Goals of Study

Chronic Renal Failure (CRF) also called chronic kidney disease (CKD) is defined as the presence of kidney damage, and eventually leads to a gradual loss of kidney function, which means the need for renal replacement therapy (dialysis or transplantation). The goal of our study it is to measures some immunological parameters (IL-18& TNF-a) in chronic kidney disease (CKD) & then compare between them and assess some biochemical parameters include (urea, creatinine, sodium, potassium and calcium).

Material and Methods

This study included 60 cases and classified as 30 patients suffering from chronic renal failure, these patients with age range between (15 years & above), and compared with 30 apparent healthy controls with age range (15years and above). Laboratory diagnosis was depended on using spectrophotometry for detection biochemical tests. IL-18 & TNFα levels were estimation by Enzyme Linked Immuno-sorbent assay (ELISA).

Results

It was observed that majority of patients with chronic renal failure within age group with in aged (40-60) years that account (60%) and most of these patients were females that constituted (73.3%). Furthermore, preponderance diseases associated with chronic renal patients were associated with Diabetes Mellitus (23.33%).

Considering some cytokines (IL-18, TNFα) revealed increase levels of IL-18 &TNFα significantly (26.26 ±1.48), (92.96 ±1.80) respectively in chronic renal patients when compared with control group (13.02 ±0.34), (66.55 ±0.45).

Conclusion

Our conclusion stated that chronic renal diseases indicated these cytokines participate in the pathophysiology of reduced renal function and role of these cytokines as principle mediators of inflammatory reaction in renal damage and these cytokines could be potential therapeutic targets.

Key words: Biochemical tests, Immunomarkers, kidney diseases.

INTRODUCTION:

The term chronic renal failure (CRF) as a same chronic kidney disease (CKD) is defined as the presence of kidney damage (1), and eventually leads to a gradual loss of kidney function, which means the need for renal replacement therapy (dialysis or transplantation) (2).

Worldwide, CKD accounted for three million and over two million of life-years lost in 2012 (3). Various symptoms and disorders including water electrolyte balance disorders, metabolic acidosis, anemia, hypertension, hypophosphatemia with bone disease (4). The role of pathological abnormalities through the study of kidney biopsy, as well as abnormalities in urinary sediment or increased secretion of albumin in the end leads to kidney damage **(**5). Race, gender, age, and family history are strong risk factors for kidney disease, as are factors such as excessive smoking, blood pressure, diabetes mellitus, and obesity(6). Exposure to heavy metals and excessive use of sedative medications are among the risk factors for kidney disease, in addition to cardiovascular disease, hyperlipidemia, metabolic syndrome, hepatitis C, AIDS and malignant tumors(7).Patients with other risk factors including cardiovascular disease, older age, history of low birth weight, obesity, and a family history of CKD, should be considered in the examination(8) .

Inflammation is one of the body's defense mechanisms resulting from infection and tissue injury (9). In the body' first line of defense against the pathogens is innate immunity and is activated by pattern recognition receptors (PRRs), that are common to pathogens. There are several classes pattern of recognition receptors (PRRs), including Toll-like receptors (TLRs), C-typeLectin receptors, Which in turn identifies pathogen- associated molecular patterns (PAMPs) nucleotide-bindingoligomerization domain-like receptors (NLRs), retinoic acid-inducible geneI-like receptors (RLRs), and missing in melanoma2 (AIM2)like receptors. The inflammasome, a multiprotein complex formed intracellularly in response to PAMPs and DAMPs, converts procaspase-1 to active caspase-1 and induces pro-inflammatory cytokines such as interleukin 1beta (IL-1b) and IL-18 (10).The NLR family member leucine rich repeat and pyrin domain containing 3 (NLRP3) forms the NLRP3 inflammasome together with the adapter molecules apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) and procaspase-1 and activates caspase-1 to processes IL-1b and IL-18 to the bioactive mature form (11, 12). The NLRP3 inflammasome hasbeen implicated in the pathogenesis ofmany diseases, includingmicrobial pathogens, inflammatory diseases, cancer, and metabolic and autoimmune disorders (11, 12), and it has also been implicated in various kidney diseases (13). A member of the IL-1 superfamily, IL-18 is a pro-inflammatory cytokine that is structurally similar to IL-1b (14, 15). IL-18 promotes the production of interferon gamma (IFN-g) and strongly induces a Th1 response. Tumor necrosis factor (TNF-α) is one of an important proinflammatory cytokines and essential factors of inflammatory tissue injury. Which are released by dendritic cells (DCs) in the renal interstitium. It has important immune regulatory functions. Most researchers reported a role of TNF in acute and chronic renal disease pathogenesis. Thus, after renal injury the early proinflammatory mediator is TNF-α. (16).

MATERIALS AND METHODS

The current study included 30 patients with chronic renal failure, these patients with age group (17 years and more) who were admitted to the Baghdad Teaching Hospital during the period from December 2020 - March 2021. These patients were diagnosed as having acute renal failure based on previous medical examinations. The results of those patients were compared with (30) healthy subjects with age group 17 years and above as a control group. The control group was chosen from people who had no history of kidney disease; they do not have kidney stones and do not suffer from diabetes or hypertension depending on previous

medical reports and laboratory investigation. 5 ml of venous blood was collected from each patient and healthy individuals. We collected serum according to the technique low speed centrifugation at 3000 × g at 4 °C, for 15 min. The serum was removed, aliquoted and stored at -20 °C until the time of assay. Laboratory diagnosis was depended on using ELISA test, Human reader, Germany. Methods were conducted according to the instructions of manufacturing companies leaflet to identified IL-18 , TNFα cytokines

Data analysis:

In this study, Chi-square test was used to detect the significances between variables. All the statistical analysis was done by SPSS program (version-20). Data was presented as Mean ± Stander error. P-value was considered significant when < 0.05.

RESULT

The current study involved 60 samples divided into two groups (30 chronic renal failure and 30 healthy apparent controls). The age of the study population ranged from 17-80 years shows CKD patients aged (40-60) had the highest prevalence of 18 (60%) when compared with other groups while only 6 (20%) of patients within age group (more than 60) and 6 (20%) within (under 40). There are highly significant differences between the incidences of the different age groups among chronic renal patients (P<0.001) table (1).

In same table the study groups were categorized according to gender in chronic group 22 (73.3%) female whereas 8 (26.7%) were male.

According to gender there was significance difference at (p=0.107). In addition, this table demonstrated other diseases associated with study groups which included that highest frequency of chronic 7 (23.33%) was among diabetic mellitus (DM) followed by 3 (10%) hypertension (HT).

Table (1):- Distribution of study groups according to clinical characteristics (Age, gender and other diseases).

Characteristics		**Chronic group**	
		NO	**%**
Age	**Under 40**	**6**	**20**
	40-60	**18**	**60**
	More than 60	**6**	**20**
	Total	**30**	**100**
	P-value	**0.0007****	
Gender	**Male**	**8**	**26.7**
	Female	**22**	**73.3**
	Total	**30**	**100**
Other Diseases	**P-value**	**0.0001****	
	diabetic mellitus (DM)	**7**	**23.33**
	Hypertension (HT)	**3**	**10**

	Heart Diseases	**0**	**0.0**
	Total	**10**	**33.33**
	P-value	**DM=0.0983 NS , HT=0.0983 NS , Heart diseases=0.0001****	

As shown in Table (2) the result of IL-18 between chronic renal patients and control group that mean for CKD was (26.26± 1.80) and mean of control (13.02± 0.34) the results revealed highly significance difference at (p=0.0001).

Regarding to the TNF-α level mean in chronic group was (92.96± 1.80) while mean for control (66.55± 0.45) Statistically, Highly significane at (p=0.0001). Figures (1 &2) confirmed this data .

Table (2): levels of cytokines between chronic renal patients and control group.

Studied Groups	**Mean ± SE**	
	IL-18	**TNF-α**
Chronic group	**26.26 ±1.48**	**92.96 ±1.80**
Control group	**13.02 ±0.34**	**66.55 ±0.45**
P-value	**0.0001****	**0.0001****
**** (P≤0.01) Highly Significant.**		

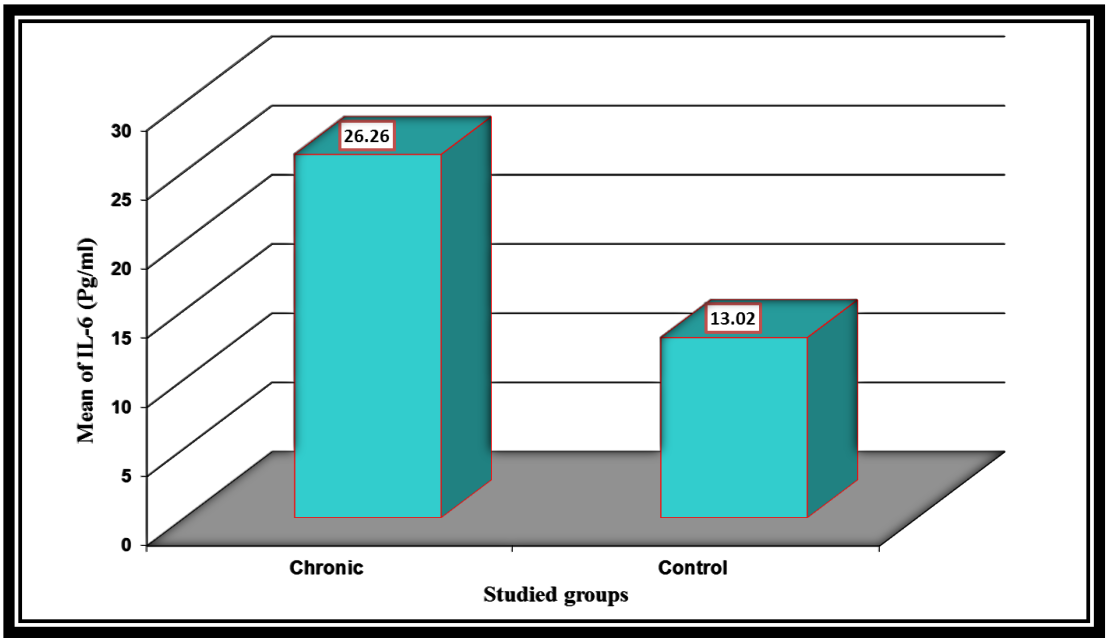

Figure (1): Level of IL-18 between chronic and control groups.

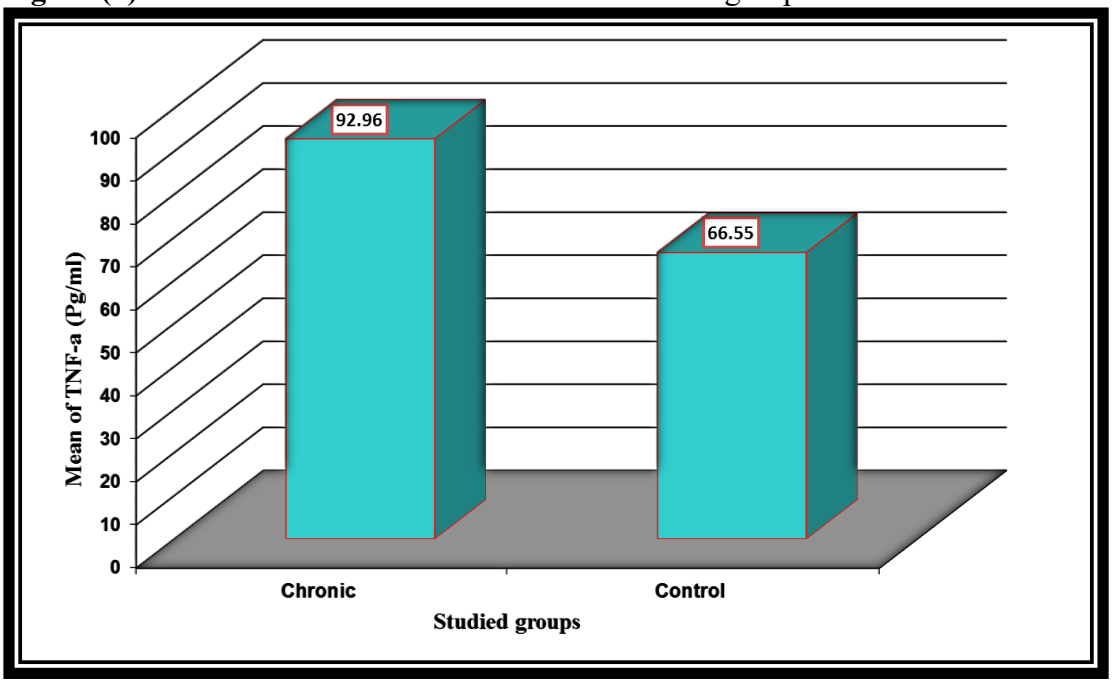

Figure (2): Level of TNFα between chronic and control groups.

DISCASION:

To be considered that Chronic kidney disease is one of the major health and social problems.

The current study demonstrated that highest prevalence (60%) of chronic renal failure within age group (40-60) years as shown in Table (1) similar results were found by (Mary Mall appallil *et* al., 2014) who observed that a high prevalence of CKD in the elderly less than (65 years).The current study showed the prevalence of kidney disease in the elderly 20% within

age group more than 60 years in the same table. These results have shown some compatibility to other studies.(18, 19) which reported that age group more than 60 years constituted (25.8%) from all cases of CKD patients . Regarding data of the (13) **,** CKD is more common in people aged 65 years or older (38%) than in people aged 45–64 years (12%) or 18–44 years. Age has been considered a factor that leads to the increasing prevalence of decreased kidney function and chronic kidney disease (6%) and those results were unlike with the current study. This variation due to the sample size , geographic distribution , life style different from country to country . It was proposed that growing prevalence of decreased renal function in older persons can be due to an increase in age-related risk factors for progression to CKD such as diabetes, hypertension and cardiovascular disease (14) however , Aging undergoes several changes in body that impact kidney function, so GFR declines with age (20).

In concordance to other studies (12 ,14,16) our study showed a higher prevalence of CKD in women (73.3%) compared with men(26.7%) .

The current study found that the female sex is the strongest risk factors for developing kidney disease it may be due to the difference in glomerular structure, muscle mass and hormone metabolism reduced physical activity and cardiac independence may be a reason for the increased prevalence of CKD between women and men (21). Epidemiological study (22) indicates that the rate of infection depends on sex, as its prevalence among women is greater than among men.

The result of this study in line with present study. In Iraq (23) who observed that high percentage of CKD in male (60.8%) more than female (39.20 %) .This results disagreement with our data. The reason for this variation may be to the difference in sample size**.** Many studies have shown that people with chronic kidney disease suffer from various diseases such as kidney disease , AIDS, and this does not occur due to infection with bacteria or viruses, But as a result of the high level of interleukin secreted by T cells, as well as the increase in the level of C reactive protein in chronic kidney patients (24, 25). The present study revealed highly significant increase of **IL-18**level in CKD patients when comparing with control group these results in keeping with other study.(26).

This investigation appeared highly significant increase of TNFα levels among chronic renal failure patients in comparing with control group. These outcomes are consistent with previous studies (27,28).

Conclusion

From our results, it can be concluded that: Highly significant difference was observed in different age groups among acute and chronic renal patients. In addition Age specific frequency in Iraqi patients with acute renal was high in age group above 60 years while age group (40-60) years were high among chronic renal cases. Highly significant difference was detected in the level of IL-18, TNFα in chronic renal cases in comparing with control group. This finding may be reflect the role of pro-inflammatoy cytokines (IL-6, TNFα) in the renal damage.

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