Original Article

Serum interleukin 18 level in kidney diseases and age

Ghada Abd Eltawab Radwan[1], Ali El-Said Yousef[2], Mohamed Fathy Bayomy[1,3]

[1]Department of Zoology, Faculty of Science, Menoufia University, Shibin El Kom, [2]Department of Rheumatology and Immunology, Internal Medicine, Teaching Benha Hospital, [3]Department of General Biology, Center of Basic Sciences, Misr University for Science and Technology, 6th of October, Banha, Egypt

Abstract

Background: Interleukin-18 (IL-18), also known as interferon-gamma inducing factor is a protein which in humans is encoded by the IL18 gene, it is a member of the IL 1 family and has a molecular weight of 18 kDa. Innate and adaptive immunity can be regulated by IL-18, and disorders involving its dysregulation might result in inflammatory or autoimmune conditions.

Aim of the Work: To distinguish between acute kidney injury (AKI) and chronic renal failure (CRF), this research investigates the utility of IL-18 as a novel biomarker and examines how age affects its level.

Materials and Methods: Three hundred participants were included and divided into three groups using the following methodology. Group I consisted of 100 control subjects who were split up by age and gender. Group II consisted of 100 AKI patients who were divided into two groups and subgroups based on age and gender. Group III, which consisted of 100 CRF (hemodialyzed patients), was divided into two groups and subgroups, as patients with acute renal injury and previously healthy people. Patients' blood was drawn to conduct a laboratory investigation blood urea, serum creatinine, sodium, potassium, *p*H, GFR and PCO_2.

Results: Patients with CRF had higher serum levels of IL-18 than patients with AKI, regardless of gender, and both groups of patients had levels of IL-18 that rise with age.

Conclusion: IL-18 is a reliable indicator for the differentiation between AKI and CRF patients receiving hemodialysis and its level correlates with age independent with gender.

Keywords: Acute kidney injury, aging, chronic renal failure, interleukin 18, hemodialysis

Address for correspondence: Dr. Ghada Abd Eltawab Radwan, Department of Zoology, Faculty of Science, Menoufia University, Shibin El Kom, Egypt.
E-mail: ghadaabdeltawabradwan@gmail.com

Received: 28.10.2022, **Revised:** 11.03.2023, **Accepted:** 02.09.2023, **Published:** 18.04.2024.

INTRODUCTION

The process by which our body's immune system responds to a pathological situation brought on by a variety of internal and external triggers, such as the presence of bacteria, viruses, foreign substances, necrosis, or other harmful chemicals. Inflammation serves primarily to reduce the harmful component, neutralize it, and then restores the tissue that has been harmed.[1]

Many cells in the body, particularly immune cells, create a class of cytokines called interleukins (ILs), a group of protein molecules.

We have identified roughly 40 ILs, and their number is constantly growing, per the literature.[2]

ILs, like cytokines, have three ways to affect other cells:

- Autocrine (the substance affects the cells which produce it)-

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/ua.ua_140_22

How to cite this article: Radwan GA, Yousef AE, Bayomy MF. Serum interleukin 18 level in kidney diseases and age. Urol Ann 2024;16:133-9.

- Paracrine (the substance affects tissue close to the cell that produce it)
- Endocrine (the material the cell produces travels to distant organs via the bloodstream.[3]

Kidney damage stimulates the synthesis and release of vasoactive and inflammatory mediators, which disrupt microcirculatory flow and cause leukocyte adhesion and interstitial infiltration. The primary producers of inflammatory cytokines are endothelial cells and circulating monocytes. The latter's ubiquitous distribution may be the cause of the widespread effects of inflammation in practically every organ, including the bone. With only 25% of the total blood volume going to the kidney, it lacks the detoxifying, anti-inflammatory, and antioxidant defense systems that other highly vascularized tissues like the liver have developed. Thus, in the face of ongoing hostility, the kidney is a prime target.

It is believed that inflammation is an important aspect of the pathogenesis of AKI, namely in the context of local kidney injury, multi-organ failure linked to AKI, renal recovery, and the possible progression to chronic kidney disease (CKD).[4] The mechanisms of CKD that follow AKI include nephron loss and the hypertrophy of the remaining nephrons, which causes interstitial fibrosis; peritubular capillary loss, which causes renal hypoxia and accelerates inflammation and fibrosis; injured renal tubular cells, which can adopt a profibrotic phentotype after cell cycle arrest, affecting other epithelial cells, pericytes, and the immune system; and maladaptive repair, which encourages the activation and growth of fibroblasts, which leads to the deposition of extracellular matrix and subsequent fibrosis.[5]

Chronic renal failure (CRF) is a condition where the kidneys' capacity to remove waste and fluid from the blood decreases. It is chronic, which means that it takes a long time for the condition to develop and there is no way to reverse it. The illness is also frequently referred to as chronic kidney disease (CKD).

Higher amounts of IL-18 in CKD patients receiving hemodialysis had worse overall survival, greater rates of hospitalization, and increased cardiovascular morbidity and mortality.[6] Reduced renal blood flow, impairment to the renal concentrating capacity, pathological indications of tubular atrophy, vascular sclerosis, worldwide glomerular sclerosis, and decreased cerebral activity are all linked to the age-related decline in GFR.[7] There is growing evidence that one of the main factors causing ageing is inflammation. Very proinflammatory cytokine IL-18 is a strong candidate for aging-related inflammation.

Hence, we aimed in this study to show the utility of IL-18 in the differentiation between AKI and CRF (patients getting hemodialysis) and study the effect of age on its level.

MATERIALS AND METHODS

Study design

There were 300 participants in this study, and they were split into three groups. Group I: For this group, 100 healthy people were placed into equal groups by age and gender and had no diseases as cancer, an active infection, or a chronic metabolic problem, or diabetes, they acted as controls. 100 patients with acute renal injury are part of Group II, which is further split into GPIIa: It is split into 2 subgroups and has 50 male participants. Patients in GPIIa^1 were between the ages of 25 and 35, and those in GPIIa^2 were between the ages of 45 and 60. GPIIb: It is broken into 2 subgroups and has 50 female participants. Patients in GPIIb1 between the ages of 25 and 35 and those in GPIIb2 between the ages of 45 and 60 are included. AKI was identified by Kidney Disease Improving Global Outcomes as rise in serum creatinine of 0.3 mg/dl within 48 hours or by a 50% increase in serum creatinine from baseline within 7 days, or a urine volume of less than 0.5 mL/kg/h for at least 6 hours.[8]

Group III is composed of 100 individuals who have CRF and undergoing hemodialysis is further separated into 50 males make up GPIIIa, which is divided into two subgroups. Patients between the ages of (25–35) and (45–60) are included in GPIIIa1 and GPIIIa2, respectively. 50 females make up GPIIIb, which is separated into two subgroups. Patients in GPIIIb1 between the ages of 25 and 35 and those in GPIIIb2 between the ages of 45 and 60 are included. Exclusion criteria were: presence of malignancy, liver, or infectious diseases. Kidney damage or a glomerular filteration rate 60 ml/min/1.73 m2 for 3 months, with or without kidney damage, are both considered signs of chronic kidney disease (CKD) according to Kidney Foundation Disease Outcomes Quality Initiative Guidelines.[9]

All patients and controls underwent a thorough history-taking process as well as laboratory testing, which included measuring serum urea, creatinine, blood Hb, glomerular filtration rate (GFR), *p*H, and serum IL-18, sodium, potassium, creatinine, and PCO_2.

AKI was identified by a rise in serum creatinine of 0.3 mg/dL or greater in < 48 h.[6] Kidney damage or a GFR 60 mL/min/1.73 m^2 for 3 months, with or without kidney damage, are both considered signs of CKD according

to kidney foundation disease outcomes quality initiative guidelines.[7]

Patients with CRF were sampled at the artificial kidney unit.

Samples collection and storage

Blood samples of AKI patients were collected from Intensive care unit, Department of Internal Medicine and blood samples of CRF patients were collected from Artificial Kidney Unit and were taken at the start of dialysis (pre-hemodialysis). Blood samples were allowed to clot 10-20 minutes at room temperature and centrifuged at 2000-3000 RPM for 20 minutes and sera were collected in Eppendorfs stored at -20˚C or -80˚C. Repeated freeze - thaw cycles were avoided.

Methods of estimation

Estimation of blood urea, serum creatinine, sodium and potassium using Vitros ECIQ chemical auto analyzer made in USA. Measurement of blood Hb by auto hematology analyzer device Celltac Alpha NIHON KOHDEN made in Japan. Estimation of GFR by using Modification of Diet in Renal Disease (MDRD) equation. Estimation of *p*H and PCO_2 values by taking arterial blood samples in heparinized blood- gas syringes and using GEM Premier 3000 blood gas analyzer for measurement made in Italy. Measurement of serum IL-18 by ELISA technique by Tecan sunrise reader made in Austria. IL-18 ELISA kit: Cat. No: E0147Hu manufactured by Shanghai Korain Biotech CO., Ltd. 228 Ningguo Rd.Yangpu Dist. Shanghai. China.

Method of estimation of interleukin 18

Bring all reagents, standard solutions, and samples to room temperature. Add 50 ul standard to standard well. Do not add antibody to standard well because the standard solution contains biotinylated antibody. Add 40 ul sample to sample well and then add 10 ul anti-IL-18 antibody to sample wells, then add 50 ul streptavidin-HRP to sample wells and standard wells (NOT blank control well). Mix well. Cover the plate with a sealer. Incubate 60 min at 37°C. Remove the sealer and wash 5 times with wash buffer. Add 50 ul substrate solution A to each well and then add 50 ul substrate solution B to each well. Incubate plate covered with a new sealer for 10 min at 37°C in the dark. Add 50 ul stop solution to each well, determine the optical density of each well immediately using a microplate reader set to 450 nm within 10 min after adding stop solution.

Statistics

Statistical study was performed using Minitab statistics version 17. The values were expressed by mean ± standard deviation. One-way analysis of variance and *t*-test were used to compare between different study groups. $P < 0.05$ was considered statistically significant and $P < 0.01$ was considered statistically highly significant.

Table 1: Comparison between AKI and CRF of males patients their age (25-35) years

variable	Control	AKI GPIIa[1]	CRF GPIIIa[1]	*P* AKI vs CRF
Urea (mg/dl)	10.50±1.51	88.50±35.22	145.25±43.94	*P*=0.004
Creatinine (mg/dl)	0.64±0.10	3.70±4.47	7.63±3.28	*P*=0.006
Hb (g/dl)	15.97±0.68	8.6±0.97	9.58±1.29	*P*=0.08
Sodium, mmol/L	1.62±138	134±5.95	130±4.97	*P*=0.154
Potassium, mmol/L	0.55±3.89	4.66±0.89	4.84±0.63	*P*=0.424
pH	7.40±0.015	7.34±0.06	7.25±0.06	*P*=0.001
PCO_2 mmHg	1.58±38.0	33.2±8.23	32.4±6.43	*P*=0.417
GFR, ml/min/1.73 m^2	123.50±16.45	17.37±8.27	7.62±1.30	*P*=0.004
Serum IL-18, ng/L	45.17±3.92	134±16.71	278±70.9	*P*=0.002

The results are expressed as mean±standard deviation. AKI, acute kidney injury; CRF, chronic renal failure; IL-18, interleukin18. Highly significant $P<0.01$, significant $P<0.05$. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, $P<0.01$

Table 2: Comparison between AKI and CRF of males patients their age (45-60) years

variable	Control	AKI GPIIa[2]	CRF GPIIIa[2]	*P* AKI vs CRF
Urea (mg/dl)	12±2.70	80.62±16.46	136.50±35.18	*P*=0.001
Creatinine (mg/dl)	0.75±0.18	3.95±1.86	7.96±2.16	*P*=0.002
Hb (g/dl)	14.88±0.69	8.58±0.62	9.03±0.83	*P*=0.079
Sodium, mmol/L	3.18±140	133±5.78	131±4.8	*P*=0.258
Potassium, mmol/L	0.37±3.95	5.17±0.61	5.27±0.83	*P*=0.352
pH	7.41±0.04	7.31±0.08	7.22±0.06	*P*=0.002
PCO_2 mmHg	2.69±41.43	33±10.41	31.43±5.26	*P*=0.364
GFR, ml/min/1.73 m^2	112±24.21	20.87±8.44	6.02±2.26	*P*=0.001
Serum IL-18, ng/L	44.67±3.98	213±53.3	386±73.5	*P*=0.001

The results are expressed as mean±standard deviation. AKI, acute kidney injury; CRF, chronic renal failure; IL-18, interleukin18. Highly significant $P<0.01$, significant $P<0.05$. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, $P<0.01$

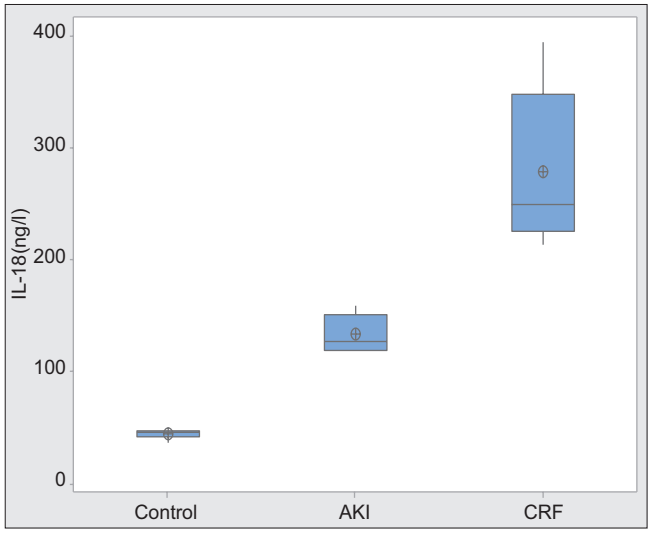

Figure 1: Serum IL-18 level in males patients of age (25-35) years. AKI, acute kidney injury. CRF, chronic renal failure. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, $P<0.01$

Table 3: Comparison between AKI and CRF of females patients their age (25-35) years

variable	Control	AKI GPIIb[1]	CRF GPIIIb[1]	*P* AKI vs CRF
Urea (mg/dl)	10.30±6.70	93.66±64.38	134.80±23.55	*P*=0.038
Creatinine (mg/dl)	0.45±0.13	4.38±3.45	9.50±1.32	*P*=0.002
Hb (g/dl)	12.70±0.90	8.91±1.47	10.41±1.28	*P*=0.028
Sodium, mmol/L	2.58±140	134±6.05	131±5.06	*P*=0.166
Potassium, mmol/L	0.67±3.98	5.05±0.89	5.01±0.64	*P*=0.506
pH	7.38±0.02	7.30±0.07	7.23±0.06	*P*=0.035
PCO_2 mmHg	2.18±38.71	30.14±6.72	33.29±5.53	*P*=0.241
GFR, ml/min/1.73 m^2	176.80±42.40	16.58±7.79	9.01±2.91	*P*=0.009
Serum IL-18, ng/L	40.33±4.63	123±17.58	9.03±238	*P*=0.001

The results are expressed as mean±standard deviation. AKI, acute kidney injury; CRF, chronic renal failure; IL-18, interleukin18. Highly significant *P*<0.01, significant *P*<0.05. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, *P*<0.01

Table 4: Comparison between AKI and CRF of females patients their age (45-60) years

variable	Control	AKI GPIIb[2]	CRF GPIIIb[2]	*P* AKI vs CRF
Urea (mg/dl)	10.67±3.56	89.41±23.91	121.60±21.78	*P*=0.078
Creatinine (mg/dl)	0.60±0.08	4.19±2.77	7.88±1.62	*P*=0.002
Hb (g/dl)	12.39±0.68	8.25±0.98	9.54±1.35	*P*=0.015
Sodium, mmol/L	3.35±138	132±4.07	132±3.58	*P*=0.414
Potassium, mmol/L	0.21±4.1	5.12±0.67	5.05±0.41	*P*=0.475
pH	7.37±0.02	7.29±0.07	7.21±0.07	P=0.004
PCO_2 mmHg	2.16±38	32.43±7.89	32.23±5.97	P=0.507
GFR, ml/min/1.73 m^2	120±22.68	18.24±9.99	9.80±1.30	P=0.002
Serum IL-18, ng/L	37±9.74	168±50.3	292±56.2	P=0.001

The results are expressed as mean±standard deviation. AKI, acute kidney injury; CRF, chronic renal failure; IL-18, interleukin18. Highly significant *P*<0.01, significant *P*<0.05. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, *P*<0.01

RESULTS

Our results in all tables show high significant elevation in the level of serum IL-18 in CRF groups (GPIII) in compared to AKI groups (GPII), *P*<0.01 regardless of gender.

In Table 1, the values of IL-18 of males patients of GPIIIa[1] are significantly higher than those of GPIIa[1], *P*<0.01. The results are (278±70.9) ng/L and (134±16.71) ng/L respectively. The values represented by Figure1.

Males patients in the CRF group GPIIIa[2] had IL-18 level significantly greater than those in the AKI group GPIIa[2], *P*<0.01. The results are (386±73.5) ng /L and (213±53.3) ng /L. The results explained by Table 2 and Figure 2.

Our findings represent high significant increase in IL-18 level of females patients of GPIIIb[1] than GPIIb[1], *P*<0.01. The results are (238 ±9.03) ng/L and (123± 17.58) ng/L. The results illustrated by Table 3 and Figure 3.

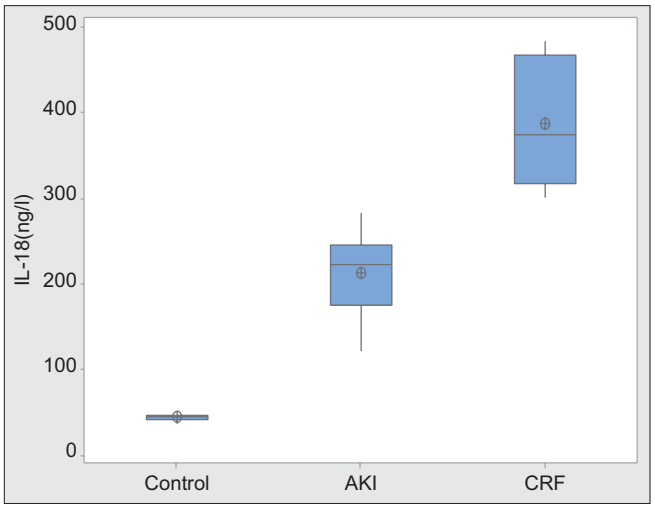

Figure 2: Serum IL-18 level in males patients of age (45-60) years. AKI, acute kidney injury. CRF, chronic renal failure. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, *P*<0.01

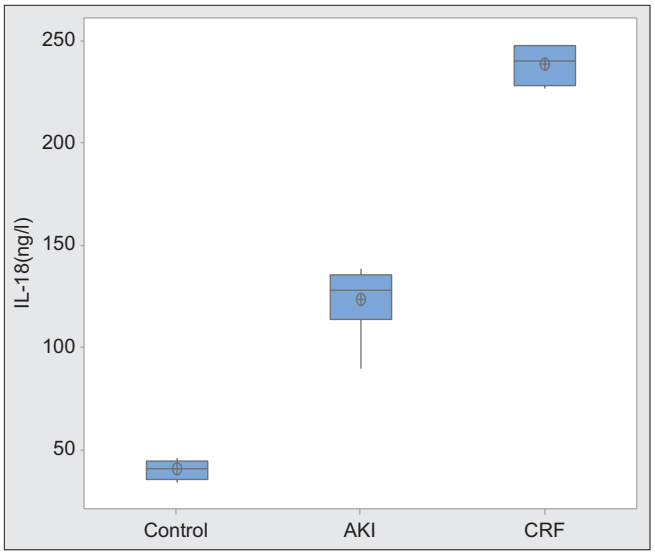

Figure 3: Serum IL-18 level in females patients of age (25-35) years. AKI, acute kidney injury. CRF, chronic renal failure. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, *P*<0.01

The recorded data show high significant increase in IL-18 level in females patients of GPIIIb[2] than GPIIb[2], *P*<0.01. The data are (292 ± 56.2) ng/L and (168 ± 50.3) ng/L, represented by Table 4 and Figure 4.

Regardless of gender, there is a significant increase in the level of IL-18 with age *P*<0.01 in males patients, and *P*< 0.05 in females patients. The values represented by Figure 5.

All examined groups' levels of IL-18 in AKI and CRF had considerably risen as compared to their controls, *P*<0.01.

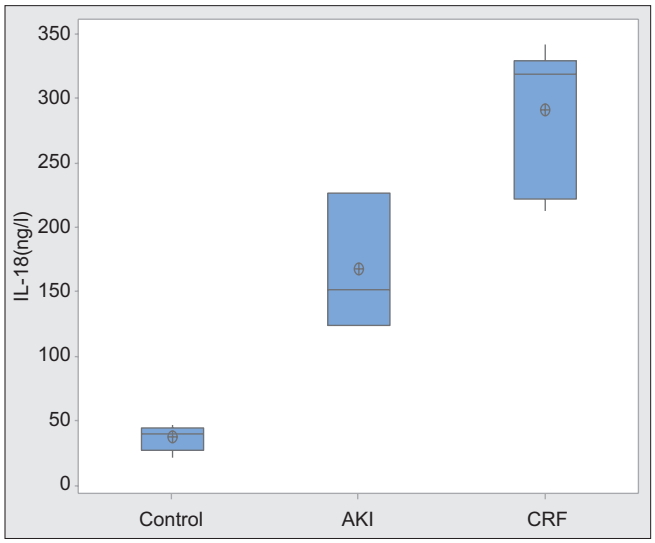

Figure 4: Serum IL-18 level in females patients of age (45-60) years. AKI, acute kidney injury. CRF, chronic renal failure. The level of IL-18 is higher in CRF (hemodialized patients) than in AKI, *P*<0.01

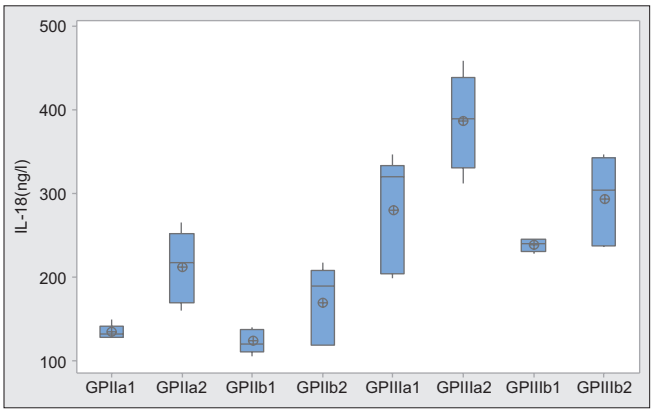

Figure 5: Serum IL-18 level and its relation to age. GPIIa1, males patients of AKI of (25-35) years. GPIIa2, males patients of AKI of (45-60) years. GPIIb1, females patients of AKI of (25-35) years. GPIIb2, females patients of AKI of (45-60) years. GPIIIa1, males patients of CRF of (25-35) years.GPIIIa2, males patients of CRF of (45-60) years. GPIIIb1, females patients of CRF of (25-35) years. GPIIIb2, females patients of CRF of (45-60) years. AKI, acute kidney injury. CRF, chronic renal failure. There is a significant increase in the level of IL-18 with age *P*<0.01 in males patients, and *P*<0.05 in females patients

The average of blood Hb levels in each of the groups under investigation demonstrate a substantial decrease, *P*<0.01 contrasted with controls.

The mean values of blood urea and serum creatinine show high significant increase in all study groups in comparison to their control groups, *P*<0.01.

In compared to controls the mean values of *p*H and GFR in all tested groups exhibit high significant decrease, *P*<0.01.

There is a significant decrease in the levels of PCO*2* and sodium, *P*<0.05 while the potassium levels increased significantly, *P*<0.05, in comparison with controls

DISCUSSION

In human, increased disease severity can be associated with an imbalance of IL-18 to IL-18BP such that the levels of free IL-18 are elevated in the circulation. Tubular epithelial cells are the main producer of IL-18 in the kidney.[10] Another important mechanism in the evolution of kidney disease appears to be chronic systemic inflammation. In community-based populations,[11] elevated inflammatory markers are predictive of incident CKD and loss in renal function as well as eGFR decline and ESRD progression in individuals with prevalent CKD.[12] Pro-inflammatory cytokines may contribute to mesangial cell proliferation, fibrosis, monocyte and macrophage infiltration, and glomerular damage mechanistically.[13] Renal damage also triggers the Nlrp3 inflammasome, and cytokines that are dependent on the inflammasome aid in the advancement of kidney disease.[14] IL-1 β and IL-18 are two examples of the many pro-inflammatory cytokines that are produced under the direction of the inflammasome, which is activated and then assembled.

Our results in this study demonstrate that regardless of the gender, serum IL-18 levels were higher in CRF groups (hemodialyzed patients) than in AKI groups, *P*<0.01. This may be consistent with the findings of Vanholder *et al*.[15] who demonstrated that the kidneys are likely the primary sites of cytokine elimination. It should be noted that IL-18 is a middle-molecule and protein-bound uremic toxin that is challenging to remove by any of the dialysis techniques that are currently in use, which accounts for the observed increase of IL-18 in dialyzed patients. Several inflammatory cytokines are produced during dialysis session by the monocyte/macrophage network, which may also account for the rise in IL-18 levels in the serum. Moreover, it might follow Chiang *et al*.[6] who claimed that increased IL-18 levels in CKD patients may be caused by uremia-specific variables such the buildup of active monocytes, the cytokine's main cellular source. Another class of middle molecule that exhibits elevated levels in the bloodstream in conjunction with the deterioration of renal function is cytokines. In fact, pro- and anti-inflammatory cytokine imbalances have been linked to poor outcomes in patients with CKD.[16] In addition to a number of factors linked to elevated production of these molecules, the issue worsens due to inadequate metabolic and renal clearance of these molecules, which is not offset by insufficient removal by most dialysis methods in use today. This raises the allostatic load and presents a challenge in the care of this

already fragile population. Another unique inflammatory component in patients receiving hemodialysis is the dialysis membrane's ability to directly or indirectly excite monocytes and increase cytokine production through complement activation. Hemodialysis membranes exhibit a wide range of behaviors, with some obviously being more biocompatible than others.

Our data demonstrate a highly significant increase in serum IL-18 levels of CRF groups (hemodialyzed patients) compared to control groups ($P<0.01$), which may be consistent with Fornoni *et al*.[17] who established the link between lower renal function and higher blood serum or urine levels of IL-18 in CKD patients. The elevated serum levels of IL-18 in CKD patients are probably due to a higher proportion of active circulating monocytes, which are the primary biological source of this cytokine.[18] Inflammation in dialysis is caused by the bioincompatibility of dialysis membranes, an inflammatory process within the vascular access, and inadequate sterility of dialysis fluid.[19] Dialysis patients exihhibt increasing circulating levels of pro-inflammatory cytokines such IL-18 and non-specific indicators of inflammation that clearly demonstrate an active inflammatory response.[20]

The data from our investigation demonstrate a highly significant elevation in serum IL-18 levels of AKI groups in comparison with their controls, $P<0.01$ and this may be consistent with Jayaraman *et al*.[21] who reported that IL-18 is a protein that is particular to renal tubules; its levels are low before surgery and rise in those who develop AKI.

According to the observed data, serum IL-18 levels rise with age regardless of gender $P<0.01$ for males patients and $P<0.05$ for females patients, which may be consistent with Ferrucci *et al*.[22] who said that age-related increases in IL-18 serum concentrations. AKI and CKD are interrelated syndromes that have been shown to be significantly influenced by renal aging.[5] Also inflammation is a major factor in aging,[23] and IL-18 is a promising candidate for the early onset in elderly individual.

Our results demonstrate a highly significant elevation in blood urea, serum creatinine and highly significant decrease in GFR of study groups in comparison with their controls, $P<0.01$ this finding may be consistent with Baum *et al*.[24] who stated that before plasma urea or creatinine concentrations climb above the upper limits of their respective reference ranges, GFR must be lowered by about 50%.

In the current study there is a highly significant decrease in blood Hb levels of the examined groups compared to their controls P<0.01, which may be related to Cheyron *et al*.[25] who noted that numerous research had shown a connection between AKI and anaemia, which is common in hospitalized patients and linked to worse outcomes. Moreover, this outcome is consistent with Babitt et al. findings's[26] that CKD patients had a severe iron deficit. An increased rate of blood loss during dialysis may be the cause of this. The high rate of iron loss (1-3 g/year) is also brought on by gastrointestinal bleeding brought on by platelet dysfunction and gastritis,[27] this happens often in both CKD patients on dialysis and those who are not.[28]

In addition, there is a highly significant decrease in pH values of the tested groups, $P<0.01$ when compared to controls, which may be connected to the research of Viswanathan *et al*.[29], metabolic acidosis commonly happens when GFR is < 20 to 30 ml/min.

The values of PCO2 decreased significantly, $P<0.05$ in all study groups in comparison with controls, low pH with a low PCO2 suggests a metabolic acidosis.[30]

Our data represent significant decrease in the level of serum sodium in compared to controls, $P<0.05$, a frequent water balance problem known as hyponatremia is characterized as a serum sodium content of less than 135 mEq/l. Acute hyponatremia is defined by a clinical onset that occurs within 48 hours, while chronic hyponatremia develops gradually over a period of days to weeks. In both prevalent and incident hemodialyzed patients, chronic hyponatremia is more common (6%–29%), related to malnutrition and loss of residual renal function, and independently associated with mortality.[31]

According to our results, there was a significant increase in potassium levels when compared to the controls $P<0.05$, a common water balance disorder defined as impaired distribution between the intracellular and extracellular space and impaired potassium excretion (due to an acute or permanent loss of functioning nephrons, impaired distal tubular flow, hyporeninemic hypoaldosteronism, or medication interfering with potassium excretion in the setting of maintained dietary potassium intake) are the causes of hyperkalemia in acute and chronic renal failure.

Serum potassium levels greater than 6 or 5.5 mEq/l, together with clinical symptoms including arrhythmia or other abnormalities on an electrocardiogram (ECG), muscle weakness, and/or ascending paralysis, are considered severe hyperkalemia.[32]

CONCLUSION

IL-18 is a useful marker for distinguishing between patients

of AKI and patients of CRF receiving hemodialysis and its level correlates with age independent with gender.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, *et al.* Inflammatory responses and inflammation-associated diseases in organs. Oncotarget 2018;9:7204-18.
2. Lissoni P, Messina G, Pelizzoni F, Rovelli F, Brivio F, Mozon A, *et al.* The fascination of cytokine immunological science. J Infect 2020;3:18-28.
3. Corwin EJ. Understanding cytokines. Part I: Physiology and mechanism of action. Biol Res Nurs 2000;2:30-40.
4. Lee DW, Faubel S, Edelstein CL. Cytokines in acute kidney injury (AKI). Clin Nephrol 2011;76:165-173.
5. Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute kidney injury and chronic kidney disease as interconnected syndromes. N Engl J Med 2014;371:58-66.
6. Chiang CK, Hsu SP, Pai MF, Peng YS, Ho TI, Liu SH, *et al.* Interleukin-18 is a strong predictor of hospitalization in haemodialysis patients. Nephrol Dial Transplant 2004;19:2810-5.
7. Silva FG. The aging kidney: A review-part1. Int Urol Nephrol 2005;37:185-205.
8. Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl 2012;2:1-138.
9. Levey AS, Coresh J, Bolton K, Culleton B, Harvey KS, Ikizler TA, *et al.* K/DOQ1/ clinical practice guidelines for chronic kidney disease: Evaluation, classification and stratification. Am J Kidney Dis 2002;39: S1-S266.
10. Melnikov VY, Ecder T, Fantuzzi G, Siegmund B, Lucia MS, Dinarello CA, *et al.* Impaired IL-18 processing protects capase-1 deficient mice from ischemic acute renal failure. J Clin Invest 2001;107:1145-52.
11. Hiramoto JS, Katz R, Peralta CA, Ix JH, Linda F, Mary C, *et al.* Inflammation and coagulation markers and kidney function decline: the Multi-Ethnic Study of Atherosclerosis (MESA) Am J Kidney Dis 2012;60:225-32.
12. Amdur RL, Feldman HI, Gupta J, Yang W, Kanetsky P, Shlipak M. *et al.* Inflammation and Progression of CKD: The CRIC Study. Clin J Am Soc Nephrol 2016;11:1546-56.
13. Lee SB, Kalluri R. Mechanistic connection between inflammation and fibrosis. Kidney Int Suppl 2010;119:S22-26.
14. Vilaysane A, Chun J, Seamone ME, Wang W, Chin R, Hirota S, Li Y, *et al.* The NLRP3 inflammasome promotes renal inflammation and contributes to CKD. J Am Soc Nephrol 2010;21:1732-44.
15. Vanholder R, Van laecke S, Glorieux G. What is new in uremic toxicity? Pediatr Nephrol 2008;23:1211-21.
16. Cohen SD, Phillips TM, Khetpal P, Kimmel PL. Cytokine patterns and survival in haemodialysis patients. Nephrol Dial Transplant 2010;25:1239-43.
17. Fornoni A, Ijaz A, Tejada T and Lenz O. Role of inflammation in diabetic nephropathy. " Cur Dia Rev 2008;4:10-17.
18. Descamps- latscha B. The immune system in endstage renal disease. Curr Opin Nephrol Hypertens 1993;2:883-891.
19. Raj DSC, Carrero JJ, Shah VO, Qureshi AR, Bárány P, Heimbürger O, *et al.* Soluble CD14 levels, interleukin 6, and mortality among prevalent hemodialysis patients. Am J Kidney Dis 2009;54:1072-80.
20. Gangemi S, Mallamace A, Minciullo PL, Santoro D, Merendino BA, Savica V, *et al.* Involvement of interleukin-18 in patients on maintenance hemodialysis. Am J Nephrol 2002;22:417-21.
21. Jayaraman R, Sunder S, Sathi S, Gupta VK, Sharma N, Kanchi P, *et al.* Post cardiac surgery acute kidney injury: a woebegone status rejuvenated by the novel biomarkers. Nephrourol Mon 2014;6:e19598.
22. Ferrucci L, Corsi A, Lauretani F, Bandinelli S, Bartali B, Taub DD, *et al.* The origins of age- related proinflammatory state. Blood 2005;105:2294-9.
23. Caruso C, Lio D, Cavallone L, Franceschi C. Aging, Iongevity, inflammation, and cancer. Ann N Y Acad Sci 2004;1028:1-13.
24. Baum N, Dichoso CC, Carlton CE. Blood urea nitrogen and serum creatinine. Physiology and interpretations. Urology 1975;5:583-8.
25. Cheyron D du, Parienti JJ, Fekih-Hassen M, Daubin C, Charbonneau P. Impact of anemia on outcome in critically ill patients with severe acute renal failure. Intensive Care Med 2005;31:1529-36.
26. Babitt JL, Lin HY. Mechanisms of anemia in CKD. J Am Soc Nephrol 2012;23:1631-4.
27. Yang JY, Lee TC, Montez-Rath ME, Paik J, Chertow GM, Desai M, *et al.* Trends in acute nonvariceal upper gastrointestinal bleeding in dialysis patients. J Am Soc Nephrol. 2012;23:495-506.
28. Liang CC, Wang SM, Kuo HL, Chang CT, Liu JH, Lin HH, *et al.* Upper gastrointestinal bleeding in patients with CKD. Clin J Am Soc Nephrol. 2014;9:1354-9.
29. Viswanathan G, Sarnak MJ, Tighiouart H, Muntner P, Inker LA. The association of chronic kidney disease complications by albuminuria and glomerular filteration rate: a cross- sectional analysis: Clin Nephrol 2013;80:29-39.
30. Vema AK, Roach P. The interpretation of arterial blood gases. Aust Prescr 2010;33:124-9.
31. Rhee CM, Ayus JC, Kalantar-Zadeh K. Hyponatremia in the dialysis population. Kidney Int Rep 2019;4:769-80.
32. Abuelo JG. Treatment of severe hyperkalemia: Confronting 4 fallacies. Kidney Int Rep 2018;3:47-55.