Contents lists available at Egyptian Knowledge Bank

Labyrinth: Fayoum Journal of Science and Interdisciplinary Studies

Journal homepage: https://lfjsis.journals.ekb.eg/

Altered inflammatory cytokines and mcp-1 chemokine in patients with chronic renal failure

Shaimaa A. Mosaad [a], Samah M. Fathy [a], Dina S. Abdel Fatah [b, c], Asmaa A. Ghanem [d], Mohammed S. Mahmoud [a,*]

[a] Zoology Department, Faculty of Science, Fayoum University, El Fayoum 63514, Egypt.
[b] Biochemistry Department, Faculty of Medicine, Cairo University, Giza 12613, Egypt.
[c] Faculty of Medicine, Badr University, Badr City, Cairo 11829. Egypt.
[d] General Medicine Department, Faculty of Medicine, Fayoum University, El Fayoum 63514, Egypt.

ARTICLE INFO

Keywords:
Chronic kidney disease
Proinflammatory cytokines
Inflammation
Innate immune system

ABSTRACT

Chronic kidney disease (CKD) is a worldwide epidemic that impacts about 10% of the population globally. CKD is associated with high levels of blood inflammatory markers. This study aimed to examine the role of inflammation in CKD patients by monitoring changes in inflammatory biomarkers. The samples were taken from 30 CKD individuals and 30 healthy individuals. Kidney function parameters, haemoglobin (Hb) content, electrolytes, and ferritin levels were colourimetrically assessed in serum using a spectrophotometer. Nuclear factor- kappa B (NF-kB), tumour necrosis factor (TNF)-α, interleukin (IL)-6, kidney injury marker (KIM)-1, and monocyte chemoattractant protein (MCP)-1 were measured using enzyme-linked immunosorbent assay. Creatinine, urea, ferritin, KIM-1, NF-kB, TNF-α, IL-6, and MCP-1 increased significantly in the serum of CKD patients compared to healthy individuals. Hb content and estimated glomerular filtration rate declined remarkably in CKD individuals compared to normal subjects. In conclusion, the current study confirmed the role of inflammation in CKD and hence, targeting certain inflammatory pathways may improve the health outcomes.

1. Introduction

Kidney failure is a case where one kidney or the two cannot work efficiently. This case is called renal failure. Kidney diseases are commonly classified as chronic or acute disorders. Treatments for chronic kidney disease (CKD) are dialysis or kidney transplantation. CKD is usually attributed to diabetes, hypertension, cardiovascular disease (CVD), bone disorders, metabolic syndrome, and autoimmune disorders [1]. Continuous kidney damage for about three months is usually followed by CKD [2]. It has been estimated that 10%–15% of individuals are CKD patients' worldwide [3].

The immune system has a crucial role in the stimulation and development of the disease by stimulating systemic inflammation [1]. People with kidney failure have an immune dysfunction that is responsible for about 30% of CKD deaths. Moreover, the remaining 70% of patients with CKD continue their life with haemodialysis [4] which stimulates an increase in the inflammatory and immune responses with elevated secretion of pro-inflammatory cytokines [5]. The first line of defense against pathogens is the innate immune system, which is rapidly stimulated before the adaptive immune system. The innate immune system makes responses against pathogen-associated molecular patterns, like high-mobility group box1 and adenosine triphosphate [6]. In CKD, renal necrotic or apoptotic cells release chemotactic factors and damage associated molecular patterns (DAMPs) in the extracellular space, where PRRs such as toll like receptors (TLRs) and nucleotide-binding and oligomerization domain (NOD)-like receptors (NLRs) on innate immune cells recognize them. Subsequently, inflammatory mediators are released and more immune cells are activated with subsequent kidney pathogenesis [7]. The principal elements of the innate immunity that participate in kidney disease development are TLRs, dendritic cells, polymorphonuclear leukocytes, complement system, macrophages, monocytes, natural killer cells, and leukocytes [1].

It has been reported that the relationship between the immune system and kidney function is a reciprocal relationship, which means that immune system disorder leads to many kidney diseases and in turn renal deterioration can affect the immune system. As a result of CKD, kidney structure is

* Corresponding author.
E-mail address: msm07@fayoum.edu.eg (M. S. Mahmoud); Tel.: +201096863521

DOI: 10.21608/ifjsis.2025.406302.1122
Received 21 July 2025; Received in revised form 27 August 2025; Accepted 06 September 2025
Available online 06 September 2025

damaged leading to protein excretion from the patient's body, which has a pivotal role in immune function. Subsequently, the excretion of proteins limits the active ingredients for making enzymes and antibodies involved in the immune system. In addition to the loss of proteins, the increase of toxins in the body ascribed with kidney damage was proven in many cases [1]. These substances harm body organs and can affect the immune system. For instance, these toxins can interfere with bone marrow proliferation, a vital organ in the immune system [8]. Moreover, anaemia, which is a conjoint problem of CKD, is due to bone marrow deterioration [9].

Active mononuclear phagocyte cells associated with kidney injury secret free radicals and inflammatory mediators such as interferon (IFN)-ɣ and interleukin (IL)-6. The previous mediators were proven to accelerate inflammation by activating other immune cells at the site of injury [10]. Nuclear factor- kappa B (NF-kB) was documented to be found in the cytoplasm of all cell types as a transcription factor. After activation, NF-kB is transported to the nucleus and exerts a vital effect in regulating of the gene expression of cytokines and adhesion molecules. Moreover, it can control adaptive immunity, cell growth, cell apoptosis, and ageing [11, 12]. NF-kB is stimulated by pro-inflammatory cytokines as TNF-α and IL-1 and participates in the formation of genes of adhesion molecules, chemokines, and cytokines along with promoting B lymphocyte maturation. Furthermore, NF-kB was recognized as a marker of the inflammatory response [11, 12].

Kidney injury molecule-1 (KIM-1) is a type 1 transmembrane glycoprotein powerfully stimulated by toxic insults and ischemic to the kidney [13, 14]. Studies on animal models suggest that after kidney injury, the acute upregulation of the KIM-1 reveals to be protective, while its chronic upregulation may cause kidney fibrosis progression [15, 16]. Monocyte chemoattractant protein (MCP)-1, is also considered to be a chemokine ligand 2 (CCL2), which belongs to the extended chemokine family that plays a pivotal role in the mediation of tissue inflammation and innate immune response. It possesses a remarkable role in kidney-induced inflammation. When it binds to its receptor, it can activate the lymphocytes and the NK cells' activation, differentiation, migration, homing, and development, whereas stimulating macrophages' and monocytes' infiltration, herewith facilitating the kidney disease-associated to the inflammation. MCP-1 has made a notable progression in kidney diseases of the primary stage like chronic glomerulonephritis and secondary renal diseases including; lupus nephritis and diabetic nephropathy [17]. IL-6 is a pro-inflammatory cytokine that has varied physiological effects so it is recognized as a hormone-like cytokine [18]. In CKD patients, high levels of plasma IL-6 concentrations were observed [5], which is largely due to chronic inflammation, fluid overload, and oxidative stress. Moreover, the reduced removal of IL-6 due to kidney function defect also contributes to its accumulation.

TNF-α is an essential player in the innate immune system. Its pro-inflammatory influence leads to stimulation and induction of inflammatory cells to the injury niche. Although macrophages and monocytes are considered the basic source of TNF-α, the main production of TNF-α via motivated intrinsic kidney cells seems to be more correlated to renal inflammation [19]. The current study aims to identify the role of immunity in kidney failure through investigating alterations of some immunological parameters in CKD patients by detecting some inflammatory cytokines and chemokines such as; TNF-α, IL-6, KIM - 1, and MCP-1. It also investigated proinflammatory transcription factor NF-kB. Changes in Hb content, kidney function biomarkers, and ions' balance in relation to immunological deterioration in CKD patients were also investigated.

2. Materials and Methods

2.1. Subjects

The present investigation included 30 healthy people (28 males & 2 females), with a mean age of 43.08+16.60 (20-72 years), 30 kidney disease patients (19 males & 11 females), with a mean age of 50.92+11.78 (20-66 years). The subjects were collected at Fayoum University Hospital in Fayoum after obtaining their informed consent. The current research was approved by Fayoum University Supreme Committee for Scientific Research Ethics (FU-SCSRE) with the approval number (EC 2403). All procedures were carried out using commercially available kits following the instructions provided by the manufacturer.

2.2. Laboratory examinations

Venous blood samples were acquired and left to clot for 30 min at room temperature before being centrifuged at a speed of 2000 revolutions per minute at 4°C for 15 minutes. Subsequently, the upper yellowish layer (serum) was stored at -80°C.

2.3. Estimation of kidney function parameters

The concentration of serum creatinine and urea was determined using a quantitative colourimetric method by a Roche modular auto-analyzer (Tokyo, Japan). The estimated glomerular filteration rate (eGFR) is a derived parameter dependent on serum level of creatinine, age, gender and race, and is considered as a measure of kidney function. eGFR was calculated based on the following formula (Hsu and Bansal, 2011):

eGFR = 175 × (SCr)-1.154 × (age)-0.203 × (0.742 if female) × (1.212 if Black), where SCr = serum creatinine in mg/dL

2.4. Measurement of immunological parameters

Human NF-κB, Human KIM-1, Human MCP-1 were assessed using commercial ELISA Kits (Fine Test, Wuhan Fine Biotech Co., Ltd.; Catalogue No.: EH3423, EH0210, EH0222 respectively) following the manufacturer's instructions. (IL-6) (Catalogue No.: SEA079Hu) and TNFα (Catalogue No.: SEA133Hu), were also investigated using ELISA kits (Cloud-Clone Corp.) as per the manufacturer's instructions. The samples' absorbance was detected at 450 nm wavelength by using ELISA reader (Awareness Technology Chromate Microplate Reader).

2.5. Colourimetric assessment of haemoglobin

The colourimetric endpoint cyanmethaemoglobin method [20] was used to assess Hb concentration at 520 - 560 nm wavelength. The whole blood sample was mixed with EDTA as an anticoagulant. 10 µL of the blood sample was added to 2.5 mL of the working solution. Slight shaking of the mix was performed to avoid clumping of the erythrocytes. After incubation for 5 minutes at room temperature, the absorbance was measured against the reagent blank. The following formulae were used to calculate the Hb concentration:

Hb Concentration (g/dl) = Specimen absorbance x 36.7

2.6. Colourimetric assessment of Calcium

A photometric method was used to measure Calcium in serum at 570 nm [21]. Samples were prepared by adding 20 µL of serum sample or standard to 1.0 mL of reagent blank, mixed, and the standard and samples' absorbance was measured as regard to the reagent blank from 5 to 30 minutes. Concentration was calculated according to the following equation: C = (A sample / A standard) × 8 mg/dl.

2.7. Assessment of phosphorus using UV – phosphomolybdate method

To measure phosphorus, UV – phosphomolybdate method was used at 340 nm wavelength [22]. 10 µL from each sample, standard and distilled water was added to 1.0 mL of the reagent, mixed and incubated for 10 minutes at 15 – 25 ° C or 5 minutes at 37° C, then the absorbance of specimen (A specimen) and standard (A standard) was measured against reagent blank within 30 minutes. Serum phosphorus conc. (mg/dl) = (A specimen/A standard) x 5

2.8. Colourimetric assessment of Potassium

Potassium concentration was measured using the spectrophotometry method at 380 nm wavelength [23]. Three labelled cuvettes were used (sample, Calibrator and blank). 1.0 mL of R1 reagent was added to each of them. Then, 25 µL of the sample and Calibrator were added to their respective cuvettes. All cuvettes were mixed and incubated for 5 minutes at 37ºC, then 250 µL of R2 reagent was added in each one, mixed, and incubated for 1 minute at 37ºC and read (A1), mixed again, and incubated for 3 minutes at 37ºC and read (A2). By using the following formulae Potassium concentration was calculated.

mmol/L Potassium = ((A2 – A1) Sample/(A2 – A1) Calibrator) x C Calibrator.

2.9. Colourimetric assessment of sodium

Colourimetric method was used for measuring sodium concentration in serum, at the wavelength of 630 nm [24]. 1.0 mL of R2 reagent was added to 10 µL of the blank, standard, and sample, mixed, and incubated for 5 minutes at room temperature, then the absorbance of the specimen (A specimen) and standard (A standard) was measured against the blank. Serum sodium conc. = (Absorbance of sample/Absorbance of Standard) × Standard value.

2.10. Colourimetric assessment of Ferritin

Ferritin values were determined photometrically at 540 nm (530 – 550 nm) wavelength [25]. The reagent and spectrophotometer were brought to 37°C. The instrument was adjusted to zero using distilled water. 400 µL of diluent (R1), 100 µL of latex (R), and 45 µL of calibrator or sample were added to each cuvette. After mixing, absorbance was measured immediately (A1) and another read was taken 5 minutes later (A2). The absorbance difference (A2-A1) was calculated for each point of the calibration curve, and the concentration of ferritin in the sample was calculated by the interpolation of its (A2-A1) in the calibration curve.

2.11. Statistical analyses

Statistical analyses were done using GraphPad PRISM software (version 6.01, USA) using unpaired t test. The results were expressed as mean ± standard deviation (SD) and statistical significance was set at a p-value of less than 0.05 ($P < 0.05$).

3. Results

Results demonstrating the involvement of immunity in individuals with chronic renal failure are shown by comparing immunological parameters of CKD patients with control subjects. Table 1 shows the age difference between the subjects of the CKD group and the control group. There was no remarkable age variation between different groups as shown in Table 1.

Table 1: Age difference between control and CKD groups

Parameter	Control (n=30)	CKD (n=30)	Statistical significance
Age (Mean±SD); Range	43.08±16.60; (20-72)	50.92+11.78; (20-66)	Not significant ($P > 0.05$)

3.1. Kidney function parameters

Kidney patients showed impaired kidney function, as evidenced by a substantial elevation (P ≤ 0.0001) in serum creatinine (Fig. 1-A) and urea levels (Fig. 1-B) compared to the control group. eGFR (Fig. 1-C) was found to be less than 15 Ml/min/1.73 m2 in CKD groups, while the control group showed a normal eGFR.

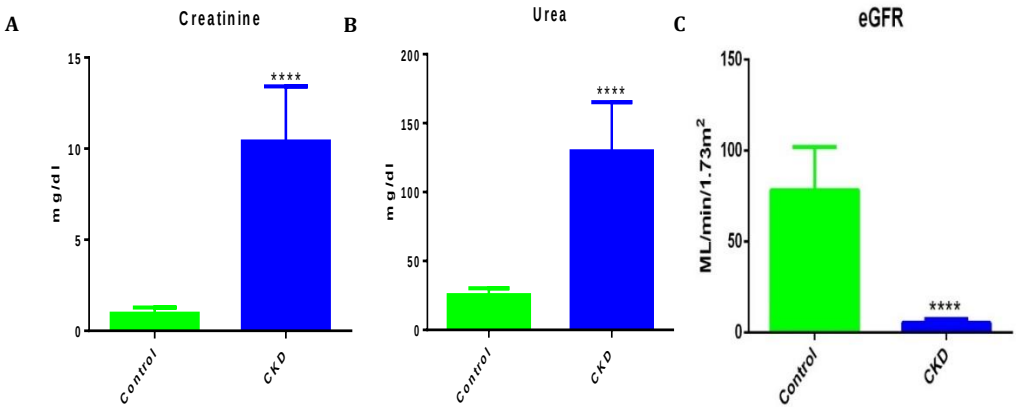

Fig. 1. Serum levels of creatinine (A) and Urea (B), and eGFR (C) in the healthy group (control) and CKD patients expressed as mean ± SD. ****: P ≤ 0.0001 compared to control group.

3.2. *Concentration of Calcium and key ions in serum*

Differences between control and CKD subjects regarding serum concentrations of Calcium and key ions (Na^+, K^+, and PO_4^{3-}) are revealed in Table (2).

Table 2: Serum concentrations of Calcium and key ions (Na^+, K^+, and PO_4^{3-}) in control and CKD subjects

Parameter	Control (n=30)	CKD (n=30)	Statistical significance
Ca	9.057 ± 0.1092	9.303 ± 0.1882	Not significant
Na^+	138.7 ± 0.3113	132.2 ± 0.4213	****
K^+	3.990 ± 0.04324	4.518 ± 0.1279	***
$PO4^{3-}$	3.573 ± 0.09588	5.517 ± 0.3295	****

Serum concentrations of different ions in control and CKD individuals expressed as mean ± SD. ***: *P* ≤ 0.001 ****: *P* ≤ 0.0001 compared to the control group.

3.3. Hb, Ferritin, and KIM-1 levels in CKD patients

Hb content is inversely proportional to renal function impairment. In our study, CKD patients revealed a significant reduction (P ≤ 0.0001) in Hb content relevant to the control group (Fig. 2A). CKD patients showed a significant elevation (*P* ≤ 0.0001) in serum ferritin and KIM-1 levels in comparison with the control group (Fig. 2B, 2C).

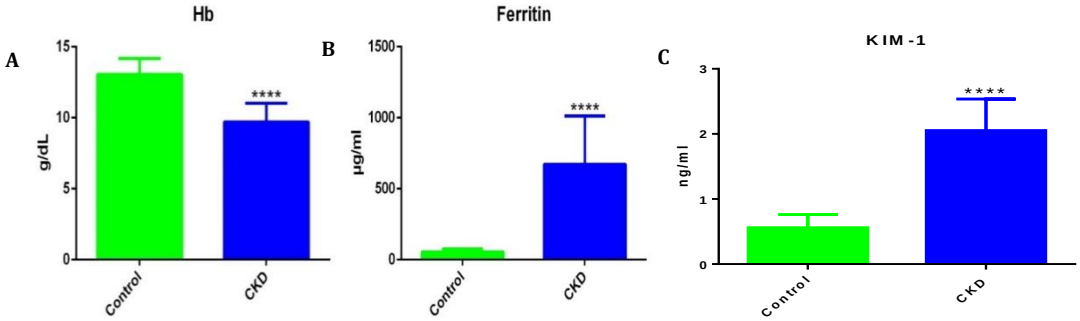

Fig. 2. Hb content (A), Ferritin level (B), and KIM-1 (C) in the healthy group (control) and CKD patients expressed as mean ± SD. ****: *P* ≤ 0.0001 compared to control group.

3.4. *Immunological parameters changes in CKD patients*

Serum level of NF-κB, TNF-α, IL-6, and MCP-1 elevated remarkably (P≤ 0.0001) in CKD compared to the control group (Fig. 3A-D).

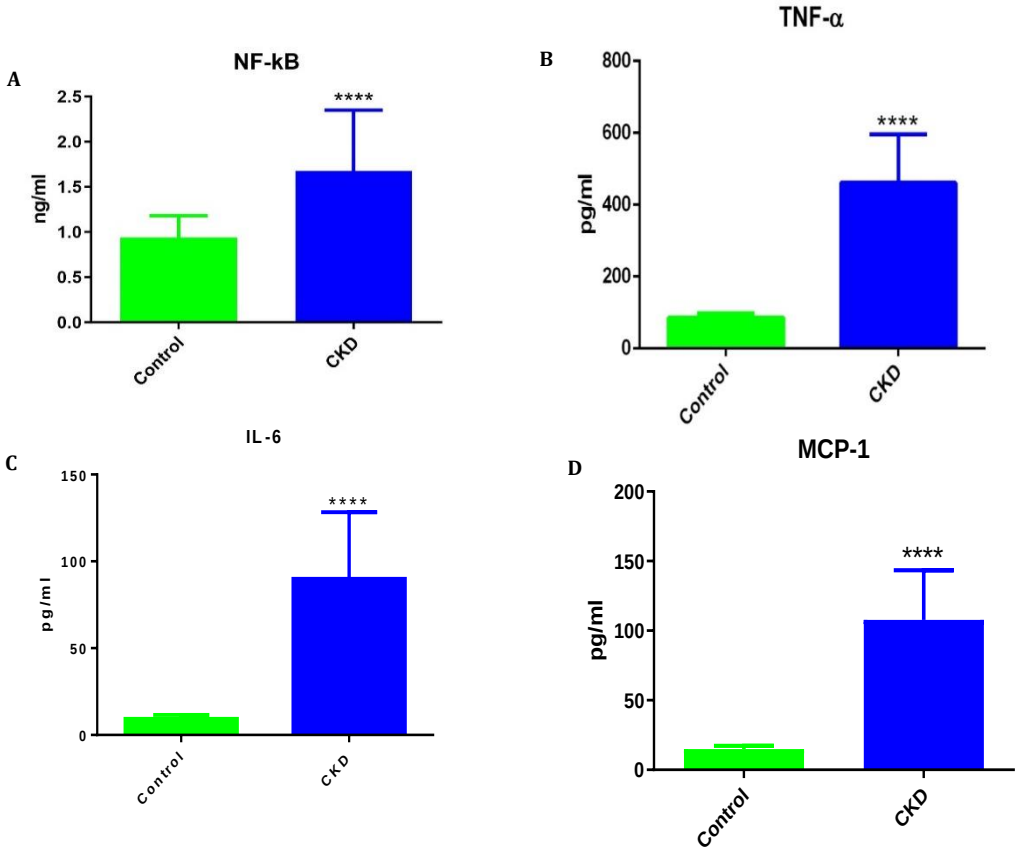

Fig. 3. Serum levels of NF-kB (A), TNF-α, IL-6 (C), and MCP-1 (D) in the healthy group (control) and CKD patients expressed as mean ± SD. **: $P \leq 0.01$, and ****: $P \leq 0.0001$ compared to control group.

4. Discussion

In the current study, it was observed that reduced levels of Hb concentration were attributed to the impairment of renal function. In agreement with our findings, other studies published on CKD patients showed that the average RBCs count is lower than that in non-CKD patients, and low levels of blood cells are indicative of anaemia [26]. Moreover, the obtained results were also in accordance with [27], showing a decreased RBCs count and a low Hb concentration in patients. The previous outcome might be attributed to the removal of blood during dialysis in CKD, which led to a low Hb level and then the development of anaemia [28]. The kidneys are the key organ for the elimination of the waste products of metabolism, such as creatinine (from the muscle creatine), urea (from amino acid metabolism), and other products. Creatinine level is regulated by the kidneys, which make the balance between creatinine generation and excretion [29]. In the present investigation, the levels of serum urea and creatinine elevated significantly in CKD patients compared with healthy controls, concurrent with previous studies [30].

Calcium, potassium, sodium, chloride, phosphorus, and magnesium are included among the major ions, and they contribute to osmotic balance regulating enzymatic reactions, mineralization of the bone, impulse conduction of the nerve, and muscle contraction [31]. The normal concentrations are essential for the smooth function of the body. Furthermore, electrolyte disorders are convenient serum biochemical parameters that can be used to evaluate kidney physiology [32]. These severe biochemical derangements in CRF patients can be corrected by regular dialysis and renal transplantation [33]. Notably, potassium and sodium are necessary mineral salts needed for our bodies. However, it is possible to exceed the daily limit intake, as with water. The excess fluids and salts are removed regularly by the kidneys, but the problem appears when impairment in kidney function is manifested. This leads to build-up of the fluid in the bloodstream and tissues, causing hypertension, fatigue, queasiness, and abnormality of the heart rhythms [34]. Agreeing with previous results [27], serum sodium levels showed a significant decrease in CKD patients in comparison with healthy individuals, which may be due to the impaired kidney ability to excrete solute-free water. However, a different study on 120 patients revealed that 71 patients had normal serum sodium levels, 48 patients had declined levels, whereas only one patient showed an increased level of sodium [35]. Moreover, serum calcium levels in patients with CKD who undergo dialysis were in normal ranges. Similarly, a previous result exhibited that the calcium concentration of 90 out of 120 patients showed normal serum levels, 28 patients had decreased serum calcium, and 2 had increased levels [35]. On the contrary, the levels of potassium were remarkably higher in CKD patients than in normal individuals. In agreement with our results, a previous study recorded that potassium

increased significantly in CKD in pre-haemodialysis compared with controls [30]. Phosphorus in the present study demonstrated upregulated levels in most patients.

It was hypothesised that in patients with CKD, serum ferritin levels are always elevated compared to normal persons and this elevation was attributed to inflammation [36, 37]. In the current study, the CKD patients showed high serum ferritin levels compared to non-CKD patients, which can be due to inflammation. These findings were consistent with research assessing ferritin level changes in patients with CKD [36, 37]. Noteworthy, CKD was characterised by increasing pro-inflammatory cytokine levels, such as TNF-α and IL-6 [38, 39], which are inversely correlated with the eGFR decline [40, 41]. These outcomes were confirmed by our results. KIM-1 was revealed to be expressed on the renal proximal tubule epithelial cells at a very little amount in the normal kidney. Meanwhile, it was elevated in different primary and secondary renal disorders. The extracellular part of KIM-1 can split and enter tubule lumens. It is known to be a delicate and specific marker for nephron proximal tubule deterioration [42]. Moreover, it is upregulated in undifferentiated proximal tubule epithelial cells following ischemic or toxic insult [43, 44]. Despite the KIM-1 expression may impact the regenerating process of tubule epithelial cells in normal people, it was associated with inflammation in CKD and renal fibrosis [42, 45]. In our study, the high expression level of KIM-1 in CKD patients was demonstrated as a progressive consequence of inflammation. Noteworthy, KIM-1 expression in CKD was confirmed to induce inflammation and tubule interstitial fibrosis, which is characterised by elevation of MCP-1 levels and induction of MCP-1-dependent macrophage chemotaxis [15]. Similarly, the MCP-1 level significantly increased in CKD of the present investigated CKD patients.

In our study, an elevated level of MCP-1 in patients with the late stage of CKD was detected. The previous findings were in agreement with [46], where an association between CKD and inflammatory markers, as MCP-1, and TNF-α receptor-1 and -2 (TNFR1 and TNFR2) was also demonstrated. Further studies have confirmed that MCP-1 is an effective chemokine produced by the kidney cells and acts as a mediator in acute ischaemic and toxic renal injury [47]. Besides, many studies have shown that polycystic kidneys have abnormally large numbers of macrophages [48]. Another study identified the tubular cells of aged kidneys as the predominant source of MCP-1 [49].

Other cytokines were also tested to investigate the involvement of inflammatory cytokines in CKD including TNF-α and IL-6. TNF-α is essentialy produced by the macrophages and monocytes and is considered as a multifunctional pro-inflammatory cytokine. It reveals a wide range of pathological and normal physiologic outcomes, besides being a master switch for initiating and perpetuating inflammatory responses [50, 51]. Some observations showed that TNF-α is a cell-signalling cytokine exhibiting an effect in mediating inflammation. When TNF-α binds to TNF-R1, it stimulates the transcription of NF-kB, combined with an increase of adhesion molecules expression, such as VCAM-1 and MCP-1 in endothelial cells [52, 53].

It was shown that high expression levels of TNF-α and IL-6 were independent predictors of the decline of eGFR [40]. In the current study, both pro-inflammatory cytokines; TNF-αand IL-6 expression levels are upregulated remarkably in CKD patients. This prominent outcome was confirmed previously by other researchers who demonstrated that several inflammatory markers such as TNF-α and IL-6 were correlated with increasing renal function impairment and they were sensitive markers of inflammation in CKD patients [54- 56]. This association between biomarkers of inflammation and kidney function was further verified in numerous cases of CKD patients, and it was shown that plasma levels of fibrinogen, IL-6, and TNF-α were elevated in individuals with lower levels of eGFR [57].

In CKD, NF-kB is considered the master regulator of pro-inflammatory cytokines, playing an important role in augmenting pro-inflammatory cytokines including IL-6 and TNF-α, compared with healthy controls [40, 58]. In this study, high concentrations of NF-kB in CKD patients were demonstrated. The signalling pathway of NF-kB plays a pivotal role in promoting inflammation, and accumulated evidence advocates that NF-kB plays a role in the pathogenesis of kidney inflammation caused by autoimmune factors, infection, or injury [59]. NF-κB is considered the key transcription factor in several cells as M1 macrophages and is important in the expression of many inflammatory genes, such as those encoding for IL-6 and TNF-α [60, 61]. Moreover, NF-kB was known to be responsible for cytokines' gene production and B lymphocyte stimulation [62, 63]. Besides, two isoforms of ferritin were documented: the heavy chain (FtH) and the light chain (FtL). Both isoform syntheses were shown to be induced by pro-inflammatory cytokines such as TNF-α and IL-β [64, 65] through the NF-kB pathway [66].

5. Conclusions

This study highlights the strong association of chronic kidney disease (CKD) with systemic inflammation, biochemical imbalances, and impaired haematological profiles. This was revealed by the significantly elevated levels of serum creatinine, urea, phosphorus, potassium, ferritin, and inflammatory cytokines (TNF-α, IL-6, and MCP-1), along with reduced haemoglobin content in CKD. Notably, the activation of NF-κB and its downstream pro-inflammatory cascade appears to exhibits a pivotal effect in CKD progression. Monitoring these biomarkers may contribute to disease management and evaluation of therapeutic interventions in CKD patients.

Author Contributions

SAM, SMF, and MSM suggested the research point of the study and designed the experimental protocol. SAM, SMF, DSA, AAG, and MSM were involved in the implementation of the overall study, performed the statistical analyses of the study, researched the data, and wrote the manuscript. All authors contributed to the critical revision of the manuscript.

Declaration of Competing Interest

The authors declare that no competing interests exist.

References

[1] J.D. Imig, M.J. Ryan, Immune and inflammatory role in renal disease, Compr. Physiol. 3 (2013) 957–976.
[2] A. Razmaria, Chronic kidney disease, JAMA. 315 (2016) 2248.
[3] S. White, K. Polkinghorne, R. Atkins, S. Chadban, Comparison of the prevalence and mortality risk of CKD in Australia using the CKD-EPI and MDRD equations: the AusDiab Study, Am. J. Kidney Dis. 55 (2010) 660–670.
[4] United States Renal Data System, USRDS 2013 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States, NIH, NIDDK (2014).
[5] R. Pecoits-Filho, O. Heimbürger, P. Bárány, M. Suliman, I. Fehrman-Ekholm, B. Lindholm, P. Stenvinkel, Associations between circulating inflammatory markers and residual renal function in CRF patients, Am. J. Kidney Dis. 41 (2003) 1212–1218.
[6] R. Medzhitov, C. Janeway Jr., Innate immunity, N. Engl. J. Med. 343 (2000) 338–344.
[7] C. Kurts, U. Panzer, H.J. Anders, A.J. Rees, The immune system and kidney disease: basic concepts and clinical implications, Nat. Rev. Immunol. 13 (2013) 738–753.
[8] I.C. Macdougall, Role of uremic toxins in exacerbating anemia in renal failure, Kidney Int. 59 (2001) S67–S72.
[9] M.R. Tamadon, A. Khatibinezhad, R. Ghorbani, A. Soleimani, F. Malek, M. Jalalzadeh, M. Malek, Impact of human recombinant erythropoietin on renal function in CKD patients, Nephro Urol. Mon. 3 (2011) 114–116.
[10] J. Tecklenborg, D. Clayton, S. Siebert, S. Coley, Role of the immune system in kidney disease, Clin. Exp. Immunol. 192 (2018) 142–150.
[11] M. Serasanambati, S.R. Chilakapati, Function of nuclear factor kappa B (NF-κB) in human diseases – a review, South Indian J. Biol. Sci. 2 (2016) 368–387.
[12] C. Guldenpfennig, E. Teixeiro, M. Daniels, NF-κB's contribution to B cell fate decisions, Front. Immunol. 14 (2023).
[13] S.S. Waikar, V. Sabbisetti, J. Ärnlöv, A.C. Carlsson, J. Coresh, H.I. Feldman, M.C. Foster, G.D. Fufaa, J. Helmersson-Karlqvist, C.Y. Hsu, Relationship of proximal tubular injury to CKD as assessed by urinary KIM-1 in five cohort studies, Nephrol. Dial. Transplant. 31 (2016) 1460–1470.
[14] J. Song, J. Yu, G.W. Prayogo, W. Cao, Y. Wu, Z. Jia, A. Zhang, Understanding kidney injury molecule-1: a novel immune factor in kidney pathophysiology, Am. J. Transl. Res. 11 (2019) 1219–1229.
[15] B.D. Humphreys, F. Xu, V. Sabbisetti, I. Grgic, S.M. Naini, N. Wang, G. Chen, S. Xiao, D. Patel, J.M. Henderson, T. Ichimura, S. Mou, S. Soeung, A.P. McMahon, V.K. Kuchroo, J.V. Bonventre, Chronic epithelial KIM-1 expression causes murine kidney fibrosis, J. Clin. Invest. 123 (2013) 4023–4035.
[16] E. Kuehn, K. Park, S. Somlo, J. Bonventre, Kidney injury molecule-1 expression in murine polycystic kidney disease, Am. J. Physiol. Renal Physiol. 283 (2002) F1326–F1336.
[17] L. Yanlong, X. Ke, X. Yuhua, M. Boyan, L. Hailong, L. Yuan, S. Yue, L. Shuju, B. Yan, Role of MCP-1 as an inflammatory biomarker in nephropathy, Front. Immunol. 14 (2023) 1303076.
[18] S. Rose-John, Interleukin-6 signalling in health and disease, F1000Res. 9 (2020) 1013.
[19] J.R. Timoshanko, J.D. Sedgwick, S.R. Holdsworth, P.G. Tipping, Intrinsic renal cells are the major source of TNF contributing to renal injury in murine crescentic glomerulonephritis, J. Am. Soc. Nephrol. 14 (2003) 1785–1793.
[20] International Council for Standardization in Haematology (ICSH), ICSH recommendations for hemoglobinometry in human blood, Int. J. Lab. Hematol. 43 (2021) S1–S13.
[21] K.A. Sikaris, Calcium, magnesium, and phosphate, in: N. Rifai, A.R. Horvath, C. Wittwer (Eds.), Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics, 9th ed., Elsevier, 2023, pp. 502–511.
[22] B. Yadav, A. et al., Evaluation of serum phosphorus by UV phosphomolybdate method in comparison with enzymatic method in a clinical laboratory, Int. J. Clin. Biochem. Res. 9 (2022) 165–170.
[23] N. Kumar, D.M. Vasudevan, Electrolytes and their measurement in clinical chemistry, J. Clin. Diagn. Res. 15 (2021) BM01–BM06.
[24] S. Gowda, A. et al., Clinical biochemistry of sodium and potassium: methods of estimation and interpretation in disease, Biomed. Res. 32 (2021) 139–146.
[25] G.G. Klee, Tietz textbook contributors, Ferritin measurement and clinical significance, in: C.A. Burtis, D.E. Bruns (Eds.), Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 7th ed., Elsevier, 2023, pp. 1563–1566.
[26] M.G. Latheef, R. Logeswaran, N.H. Mohtar, Detecting chronic kidney disease from blood samples using neural networks, J. Phys. Conf. Ser. 1712 (2020) 012008.
[27] E.I. El-Zawhry, M.M. Salem, G.H. Abdel-Rached, M. Wafeek, M.S. Galal, E.E.T. Mohamed, Effect of renal dialysis on hematological, electrolyte and biochemical parameters in hepatitis patients, Egypt. Acad. J. Biol. Sci. 5 (2013) 29–34.
[28] R.T. Mahmood, M.J. Asad, M. Noorulamin, Evaluating urea and creatinine levels in chronic renal failure pre- and post-dialysis, J. Cardiovasc. Dis. 2 (2014) 2330–4596.
[29] F. Murphy, Acute kidney injury, in: Principles of Nursing in Kidney Care: Under the Auspices of EDTNA/ERCA and EKPF, Springer, Cham, 2024, pp. 81–113.
[30] A.M.K. Aljebory, T.J.M. Al-Salman, H.W.R. Alasedi, A.Y.A. Beyi, Effect of kidney dialysis on some biochemical variance, J. Phys. Conf. Ser. 1294 (2019) 052019.
[31] A.K. Balcı, O. Koksal, A. Kose, E. Armagan, F. Ozdemir, T. Inal, N. Oner, General characteristics of patients with electrolyte imbalance admitted to emergency department, World J. Emerg. Med. 4 (2013) 113–116. https://doi.org/10.5847/wjem.j.issn.1920-8642.2013.02.005.
[32] T. Dhondup, Q. Qian, Electrolyte and acid-base disorders in chronic kidney disease and end-stage kidney failure, Blood Purif. 43 (2017) 179–188. https://doi.org/10.1159/000452725
[33] C.P. Kovesdy, J.D. Kopple, K. Kalantar-Zadeh, Management of protein-energy wasting in non-dialysis-dependent chronic kidney disease: reconciling low protein intake with nutritional therapy, Am. J. Clin. Nutr. 97 (2013) 1163–1177. https://doi.org/10.3945/ajcn.112.036418.
[34] Bel Marra Health, Sodium-potassium balance in diet critical in chronic kidney disease prevention, (2015). https://www.belmarrahealth.com/sodium-potassium-balance-in-diet-critical-in-chronic-kidney-disease-prevention/
(accessed 10 February 2020).
[35] P.P. Kalyani, V. Balasubramaniyan, A. Saravanan, K. Thamaraiselvi, K. Prabhavathi, S. Kanimozhi, R.L. Bhavya, N.R. B. Nikhil, Serum electrolyte disturbance and significance in late stages of chronic kidney disease, Natl. J. Physiol. Pharm. Pharmacol. 14 (2023) 5.
[36] K. Kalantar-Zadeh, B.R. Don, R.A. Rodriguez, M.H. Humphreys, Serum ferritin is a marker of morbidity and mortality in hemodialysis patients, Am. J. Kidney Dis. 37 (2001) 564–572.
[37] G.M. Nassar, S. Fishbane, J.C. Ayus, Occult infection of old nonfunctioning arteriovenous grafts: a novel cause of erythropoietin resistance and chronic inflammation in hemodialysis patients, Kidney Int. Suppl. 80 (2002) 49–54.
[38] C.C. Grabulosa, S.R. Manfredi, M.E. Canziani, B.M.R. Quinto, R.B. Barbosa, J.F. Rebello, M.C. Batista, M. Cendoroglo, M.A. Dalboni, Chronic kidney disease induces inflammation by increasing Toll-like receptor-4, cytokine and cathelicidin expression in neutrophils and monocytes, Exp. Cell Res. 365 (2018) 157–162.

[39] S. Mihai, E. Codrici, I.D. Popescu, A.M. Enciu, L. Albulescu, L.G. Necula, C. Mambet, G. Anton, C. Tanase, Inflammation-related mechanisms in chronic kidney disease prediction, progression, and outcome, J. Immunol. Res. 2018 (2018) 2180373.
[40] R.L. Amdur, H.I. Feldman, G. Jayanta, Y. Wei, K. Peter, S. Michael, R. Mahboob, J.P. Lash, R.R. Townsend, O. Akinlolu, C.R. Akshay, A.S. Go, J. Marshall, H. Jiang, V.S. Balakrishnan, P.L. Kimmel, J.W. Kusek, D.S. Raj, Inflammation and progression of CKD: the CRIC study, Clin. J. Am. Soc. Nephrol. 11 (2016) 1546–1556.
[41] E. Castillo-Rodríguez, S. Pizarro-Sánchez, A.B. Sanz, A.M. Ramos, M.D. Sanchez-Niño, C. Martin-Cleary, B. Fernandez-Fernandez, A. Ortiz, Inflammatory cytokines as uremic toxins: "Ni son todos los que están, ni están todos los que son", Toxins. 9 (2017) 114.
[42] C. Yin, N. Wang, Kidney injury molecule-1 in kidney disease, Ren. Fail. 38 (2016) 1567–1573.
[43] P.M.C.S. De Silva, K.S.M. Abdul, E.M.D.V. Eakanayake, S.S. Jayasinghe, C. Jayasumana, H.B. Asanthi, H.S.D. Perera, G.G.T. Chaminda, E.P.S. Chandana, S.H. Siribaddana, Urinary biomarkers KIM-1 and NGAL for detection of chronic kidney disease of uncertain etiology (CKDu) among agricultural communities in Sri Lanka, PLoS Negl. Trop. Dis. 10 (2016) e0004979.
[44] C.R. Parikh, H. Thiessen-Philbrook, A.X. Garg, D. Kadiyala, M.G. Shlipak, J.L. Koyner, C.L. Edelstein, P. Devarajan, U.D. Patel, M. Zappitelli, C.D. Krawczeski, C.S. Passik, S.G. Coca, Performance of kidney injury molecule-1 and liver fatty acid-binding protein and combined biomarkers of AKI after cardiac surgery, Clin. J. Am. Soc. Nephrol. 8 (2013) 1079–1088.
[45] M.M. van Timmeren, M.C. van den Heuvel, V. Bailly, S.J. Bakker, H. van Goor, C.A. Stegeman, Tubular kidney injury molecule-1 (KIM-1) in human renal disease, J. Pathol. 212 (2007) 209–217.
[46] M.A. Niewczas, T. Gohda, J. Skupien, A.M. Smiles, W.H. Walker, F. Rosetti, X. Cullere, J.H. Eckfeldt, A. Doria, T.N. Mayadas, J.H. Warram, A.S. Krolewski, Circulating TNF receptors 1 and 2 predict ESRD in type 2 diabetes, J. Am. Soc. Nephrol. 23 (2012) 507–515.
[47] R. Munshi, A. Johnson, E.D. Siew, T.A. Ikizler, L.B. Ware, M.M. Wurfel, J.M. Himmelfarb, R.A. Zager, MCP-1 gene activation marks acute kidney injury, J. Am. Soc. Nephrol. 22 (2011) 165–175.
[48] A. Karihaloo, F. Koraishy, S.C. Huen, Y. Lee, D. Merrick, M.J. Caplan, S. Somlo, L.G. Cantley, Macrophages promote cyst growth in polycystic kidney disease, J. Am. Soc. Nephrol. 22 (2011) 1809–1814.
[49] M.J. Jo, J.K. Lee, J.E. Kim, G.J. Ko, Molecular mechanisms associated with aging kidneys and future perspectives, Int. J. Mol. Sci. 24 (2023) 16912.
[50] J.M. Fragoso, G. Vargas-Alarcón, S. Jiménez-Morales, O.D. Reyes-Hernández, J. Ramírez-Bello, Tumor necrosis factor alpha (TNF-α) in autoimmune diseases (AIDs): molecular biology and genetics, Gac. Med. Mex. 150 (2014) 334–344.
[51] G.D. Kalliolias, L.B. Ivashkiv, TNF biology, pathogenic mechanisms and emerging therapeutic strategies, Nat. Rev. Rheumatol. 12 (2016) 49–62.
[52] R.J. Mentz, J.P. Kelly, T.G. von Lueder, A.A. Voors, C.S.P. Lam, M.R. Cowie, K. Kjeldsen, E.A. Jankowska, D. Atar, J. Butler, M. Fiuzat, F. Zannad, B. Pitt, C.M. O'Connor, Noncardiac comorbidities in heart failure with reduced versus preserved ejection fraction, J. Am. Coll. Cardiol. 64 (2014) 2281–2293.
[53] A.C. Pouleur, Which biomarkers do clinicians need for diagnosis and management of heart failure with reduced ejection fraction?, Clin. Chim. Acta. 443 (2015) 9–16.
[54] A. Dag, E.T. Fırat, A.K. Kadiroglu, E. Kale, M.E. Yılmaz, Significance of elevated gingival crevicular fluid tumor necrosis factor-alpha and interleukin-8 levels in chronic hemodialysis patients with periodontal disease, J. Periodontal Res. 45 (2010) 445–450.
[55] J. Kamińska, M. Stopiński, K. Mucha, A. Jędrzejczak, M. Gołębiowski, M.A. Niewczas, B. Foroncewicz, IL-6 but not TNF is linked to coronary artery calcification in patients with chronic kidney disease, Cytokine. 120 (2019) 9–14.
[56] P. Stenvinkel, Inflammatory and atherosclerotic interactions in the depleted uremic patient, Blood Purif. 19 (2001) 53–61.
[57] G. Jayanta, M. Nandita, P.A. Kanetsky, D. Joe, M.R. Wing, R. Muredach, V.O. Shah, V.S. Balakrishnan, N.J. Guzman, G. Matthias, B.G. Periera, H.I. Feldman, J.W. Kusek, Association between albuminuria, kidney function, and inflammatory biomarker profile in CKD in CRIC, Clin. J. Am. Soc. Nephrol. 7 (2012) 1938–1946.
[58] V. Losappio, B. Infante, S. Leo, D. Troise, M. Calvaruso, P. Vitale, S. Renzi, G. Stallone, G. Castellano, Nutrition-based management of inflammaging in CKD and renal replacement therapies, Nutrients. 13 (2021) 267.
[59] H. Zhang, S.C. Sun, NF-κB in inflammation and renal diseases, Cell Biosci. 5 (2015) 63.
[60] C. Biswas, N. Shah, M. Muthu, P. La, A.P. Fernando, S. Sengupta, G. Yang, P.A. Dennery, Nuclear heme oxygenase-1 (HO-1) modulates subcellular distribution and activation of Nrf2 impacting metabolic and antioxidant defenses, J. Biol. Chem. 289 (2014) 26882–26894.
[61] A.G. Janiques, V.O. Leal, M.B. Stockler-Pinto, N.X. Moreira, D. Mafra, Effects of grape powder supplementation on inflammatory and antioxidant markers in hemodialysis patients: a randomized double-blind study, J. Bras. Nefrol. 36 (2014) 496–501.
[62] T. Kawaguchi, L. Tong, B.M. Robinson, A. Sen, S. Fukuhara, K. Kurokawa, B. Canaud, N. Lameire, F.K. Port, R.L. Pisoni, C-reactive protein and mortality in hemodialysis patients: the Dialysis Outcomes and Practice Patterns Study (DOPPS), Nephron Clin. Pract. 117 (2011) c167–c178.
[63] N. Ueda, K. Takasawa, Role of hepcidin-25 in chronic kidney disease: anemia and beyond, Curr. Med. Chem. 24 (2017) 1417–1452.
[64] N. Naz, F. Moriconi, S. Ahmad, A. Amanzada, S. Khan, S. Mihm, G. Ramadori, I.A. Malik, Ferritin L is the sole serum ferritin constituent and a positive hepatic acute-phase protein, Shock. 39 (2013) 520–526.
[65] F.M. Torti, S.V. Torti, Regulation of ferritin genes and protein, Blood. 99 (2002) 3505–3516.
[66] C.G. Pham, C. Bubici, F. Zazzeroni, S. Papa, J. Jones, K. Alvarez, S. Jayawardena, E. De Smaele, R. Cong, C. Beaumont, F.M. Torti, S.V. Torti, G. Franzoso, Ferritin heavy chain upregulation by NF-κB inhibits TNFα-induced apoptosis by suppressing reactive oxygen species, Cell. 119 (2004) 529–542.