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Determination of High-Sensitivity C-reactive protein in Chronic Kidney Disease Patients in Al-Hawija General Hospital in Kirkuk City-Iraq

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Abstract

Chronic kidney disease (CKD) is a serious worldwide health problem due to the gradual and irreversible damage it causes. Although hemodialysis (HD) is an essential renal replacement treatment, little is known about its effectiveness and prevalence in Iraq. This study aimed to determine high- sensitivity c-reactive protein(hs-CRP), interleukin-6(IL-6), complement components C3 and C4, and the novel renal biomarker fibroblast growth factor-23 (FGF-23) in Iraqi patients with CKD, alongside selected biochemical parameters including estimated glomerular filtration rate (eGFR), serum creatinine, phosphate, albumin, sodium, potassium. The study was conducted at Al-Hawija General Hospital during September 2024 and May 2025, and included 160 participants: 80 CKD patients (aged 35–65 years) and 80 age- and sex-matched healthy controls. Spectrophotometry was used for biochemical measurements, ELISA for IL-6, C3, C4, and FGF-23, and immunoturbidimetry for CRP. The majority of CKD patients were in the 35–65-year age group (mean 46.08 ± 6.29 years), with females constituting 71.25%. Diabetes mellitus was the most common comorbidity (24%). Inflammatory and complement assays revealed significantly higher levels of hs-CRP and IL-6 in CKD patients. Serum C3 levels were significantly elevated, while C4 showed no significant difference. FGF-23 levels were significantly elevated in CKD patients and demonstrated a strong negative correlation with estimated eGFR. Compared with controls, CKD patients had significantly lower eGFR, serum albumin and serum sodium. In contrast, serum creatinine, serum phosphate and serum potassium were significantly higher. ROC curve analysis indicated that FGF-23 had the highest diagnostic performance (AUC = 0.92, sensitivity = 91.2%, specificity = 90.5%), followed by IL-6 (AUC = 0.85), CRP (AUC = 0.78), and C3 (AUC = 0.74).These findings indicate that integrating inflammatory markers (CRP, IL-6), complement components (C3, C4), and the novel renal biomarker (FGF-23) provides a broader pathophysiological assessment of CKD and could enhance early detection, risk stratification, and potentially guide anti-complement therapeutic approaches in nephropathy within the Iraqi healthcare setting.

Keywords: Chronic Kidney Disease (CKD); High-Sensitivity C-Reactive Protein (Hs-CRP); Interleukin-6 (IL-6); Fibroblast Growth Factor-23 (FGF-23)

1. Introduction

Chronic kidney disease (CKD) is a major worldwide health concern, with a rising prevalence among the population. Precise and prompt forecasting of CKD is essential for efficient therapy [1]. The prevalence of end-stage renal disease (ESRD) has been increasing over time and significantly impacts morbidity and death rates [2]. ESRD necessitates continuous therapy, leading to various physical and emotional pressures for patients. Patients with ESRD face challenges in maintaining employment, social interactions, financial stability, and adhering to dietary limitations regarding liquids and solid meals [3]. CKD is linked to prolonged exposure to toxins and mostly pertains to the

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subsequent pathological alterations induced by the original insult. The secondary alterations serve as compensatory strategies to preserve overall kidney function, ultimately resulting in diminished glomerular performance and subsequent tubular and interstitial modifications [4]. Nephrology widely uses conventional inflammatory indicators, especially CRP, to identify systemic inflammation and predict adverse outcomes [5]. Nonetheless, CRP has insufficient specificity for renal disease, hence constraining its use as an independent diagnostic instrument [6].

Pro-inflammatory cytokine production in injured renal tissue promotes immune cell infiltration, which helps eliminate cellular debris and promotes tissue recovery. However, immune-mediated tissue damage, nephron loss, and the development of renal fibrosis have all been connected to an overabundance or sustained inflammatory response [7]. IL-6, a multifunctional cytokine implicated in immune control, has surfaced as a more robust prognostic marker in (CKD). Increased IL-6 levels facilitate mesangial proliferation, endothelial dysfunction, and renal fibrosis and have been demonstrated to independently forecast all-cause and cardiovascular death in both dialysis and non-dialysis patients [8, 9]. The activation of the complement system, particularly components C3 and C4, is widely acknowledged as a pathophysiological characteristic of renal damage. Complement activation induces glomerular inflammation, exacerbates tubular injury, and enhances chronic inflammatory responses. Research indicates that increased or dysregulated levels of C3 and C4 are associated with worse renal outcomes and, in some situations, may forecast a rapid deterioration in eGFR [10; 11].

FGF-23 (fibroblast growth factor 23) is a hormone synthesised by osteoblasts that regulates mineral and bone metabolism. Factors that regulate FGF-23 production include elevated concentrations of calcium, phosphates, parathyroid hormone, and 1,25-dihydroxycholecalciferol in serum [12]. The significance of FGF-23 as a biomarker for chronic renal disease has recently been emphasised. Phosphate retention is one of the initial metabolic abnormalities observed in the early stages of chronic renal disease. The secretion of FGF-23 and PTH is elevated in response to this procedure [13;14]. The elevated levels of FGF-23 in chronic renal disease coincide with the kidneys' adaptation to reduced urine phosphate excretion [15]. However, the levels of FGF-23 also rise in response to oxidative stress, inflammation, heightened activation of the renin-angiotensin-aldosterone system (RAAS), and iron deficiency [16;17;18]. Due to the intricate nature of CKD pathophysiology, which encompasses inflammatory, immunologic, and metabolic pathways, there is increasing support for multi-biomarker strategies to enhance diagnosis, risk assessment, and monitoring. The amalgamation of CRP, IL-6, C3, C4, and FGF-23 into a unified evaluative framework may provide a more thorough comprehension of the disease state, especially in demographics with restricted access to sophisticated nephrology services.

Epidemiological data on CKD in Iraq are limited, and biomarker-based risk assessment has not been integrated into standard clinical practice. This study seeks to address this deficiency by assessing the diagnostic and prognostic efficacy of various biomarkers in Iraqi patients with chronic renal disease, thereby informing the future application of multi-biomarker panels in nephrology clinics.

2. Materials and Methods

2.1. Study Design and Location

This study was done at Al-Hawija General Hospital in Kirkuk, Iraq, from September 2024 and May 2025. The research complied with the Declaration of Helsinki criteria, and informed consent in writing was acquired from all individuals before enrolment.

2.2. Participants

One hundred sixty participants were recruited and allocated into two equal groups: CKD cohort: 80 individuals diagnosed with CKD (duration > 3 months), aged 35–65 years, with a verified estimated eGFR of less than 60 ml/min/1.73 m^2, accompanied by a corroborative clinical history. Control group: 80 healthy participants, matched by age and sex, had an eGFR > 90 ml/min/1.73 m^2 and lacked a history of renal illness.

2.3. Inclusion and Exclusion Criteria

Eligible participants were people aged 35 to 65 years, with chronic kidney failure verified clinically and biochemically according to KDIGO 2024 criteria. The exclusion criteria comprised: acute kidney damage (AKI) or recent hospitalisation (within the last 3 months), active infection, autoimmune illness, malignancy, pregnancy or lactation, and current administration of immunosuppressive treatment.

2.4. Clinical and demographic information

A comprehensive patient history was documented, encompassing age, gender, disease duration, comorbidities (including diabetes and hypertension), medication history, and dialysis status. Body mass index (BMI) and blood pressure were assessed for all individuals.

2.5. Sample Collection, Processing, and Biomarker Assessment

Venous blood samples (10 ml) were obtained from all subjects following an overnight fast (10 hours or more), utilising sterile tubes. To isolate serum, the samples were allowed to coagulate at ambient temperature and subsequently centrifuged at 3,000 rpm for 10 minutes; sera were separated and kept at – 20°C until used. Standard biochemical assays, encompassing serum creatinine, phosphate, albumin, and electrolytes (sodium and potassium), were conducted utilising an automated spectrophotometer (Mindray BS-480, China). High-sensitivity CRP was quantified utilising an immunoturbidimetric test (Cobas c 311, Roche Diagnostics, Germany).

IL-6 was assessed employing enzyme-linked immunosorbent assay (ELISA) kits (RandD Systems, USA) with a sensitivity of 0.92 pg/ml. Complement components C3 and C4 were quantified utilising nephelometric (Siemens BN ProSpec System, Germany). Fibroblast growth factor-23 (FGF-23) was quantified utilising an ELISA technique (Kainos Laboratories, Japan) with a sensitivity of 3.0 pg/ml. The estimated eGFR was calculated using the CKD-EPI 2021 equation, normalized to 1.73 m^2 body surface area.

2.6. Statistical Analysis

The normal distribution was evaluated using the Shapiro-Wilk test and Q-Q plots, while Levene's test checked homogeneity of variance. Welch's t-test was employed for group comparisons when variances were unequal; otherwise, Student's t-test was utilised; the Mann-Whitney coefficient was applied for non-normally distributed data. Effect sizes were presented as Hedges' g, accompanied by a 95% confidence range. Pearson's r was employed for correlations with estimated eGFR, whereas Spearman's ρ was utilised in sensitivity analyses. Multiple testing was regulated via Benjamini-Hochberg's false discovery rate (q = 0.05). ROC analysis indicated the area under the curve (AUC) with a 95% confidence interval, employing DeLong, where raw data were accessible and the Hanley-McNeil approximation for summary-based confidence intervals. Cut-off points were determined using Youden's J statistic. A composite prognostic model utilising multivariate logistic regression, incorporating FGF-23, IL-6, hs-CRP, and C3, was pre-defined. This model employed 10-fold cross-validation and 2000 bootstrap resampling to derive optimism-corrected AUC and calibration metrics (Hosmer-Lemeshow, calibration slope/intercept), in addition to decision curve analysis.

3. Results and Discussion

3.1. Demographic and Clinical Features

The study had 160 volunteers, consisting of 80 individuals with CKD and 80 ostensibly healthy controls. The average age was 46.08 ± 6.29 years in the CKD group and 44.8 ± 8.3 years in the control group ($p = 0.50$), with a higher proportion of females (71.25% vs. 68.75%, $p = 0.62$). Diabetes mellitus was observed in 25% of CKD patients, hypertension in 41.25%, and co-morbidities in 12.5%. The median duration of CKD was 5.8 years (IQR 4.0–8.0), hs-CRP and IL-6 concentrations were markedly increased in CKD patients (14.89 ± 0.98 mg/L vs. 5.69 ± 0.39 mg/L and 27.43 ± 1.89 pg/ml vs. 13.02 ± 0.31 pg/ml, respectively; , $P < 0.0011$ for both). Complement C3 levels were markedly increased (155.45 ± 2.95 vs. 130.38 ± 2.53mg/dL, , $P < 0.0011$), although C4 levels exhibited no significant variation between the two groups. Serum FGF-23 concentrations were nearly doubled in CKD patients (59.81 ± 2.07vs46.56 ± 1.77pg/ml, , $p < 0.0011$).

Table 1 Inflammatory and Complement Biomarkers and FGF-23 (CKD vs Controls)

Measure	CKD Mean ± SD	Control Mean ± SD	Mean Diff (CKD−Ctrl)	95% CI (Diff)	p (Welch)	Hedges g	95% CI (g)
hs-CRP (mg/L)	14.89 ± 0.98	5.69 ± 0.39	9.20	[8.97, 9.43]	1.03e-93	12.28	[10.89, 13.67]
IL-6 (pg/mL)	27.43 ± 1.89	13.02 ± 0.31	14.41	[13.98, 14.84]	2.36e-74	10.59	[9.38, 11.80]
C3 (mg/dL)	155.45 ± 2.95	130.38 ± 2.53	25.07	[24.21, 25.93]	2.14e-106	9.08	[8.03, 10.13]
C4 (mg/dL)	33.43 ± 2.04	32.66 ± 1.78	0.77	[0.17, 1.37]	1.19e-02	0.40	[0.09, 0.71]
FGF-23 (pg/mL)	59.81 ± 2.07	46.56 ± 1.77	13.25	[12.65, 13.85]	1.58e-88	6.85	[6.03, 7.66]

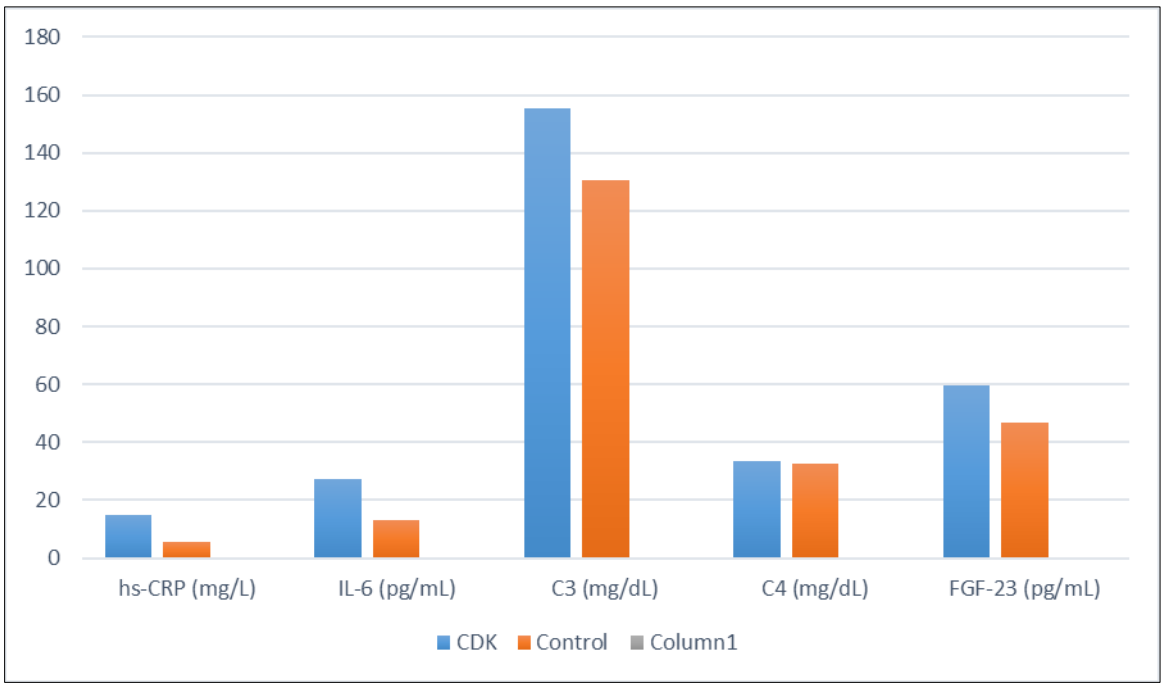

Figure 1 Group Differences (Inflammation/Complement/FGF-23): Mean ± SD for CKD vs Controls

Table 2 ROC performance with 95% CI

Marker	AUC	95% CI
FGF-23	0.92	[0.876, 0.964]
IL-6	0.85	[0.790, 0.910]
hs-CRP	0.78	[0.708, 0.852]
C3	0.74	[0.663, 0.817]
Composite	0.95	[0.915, 0.985]

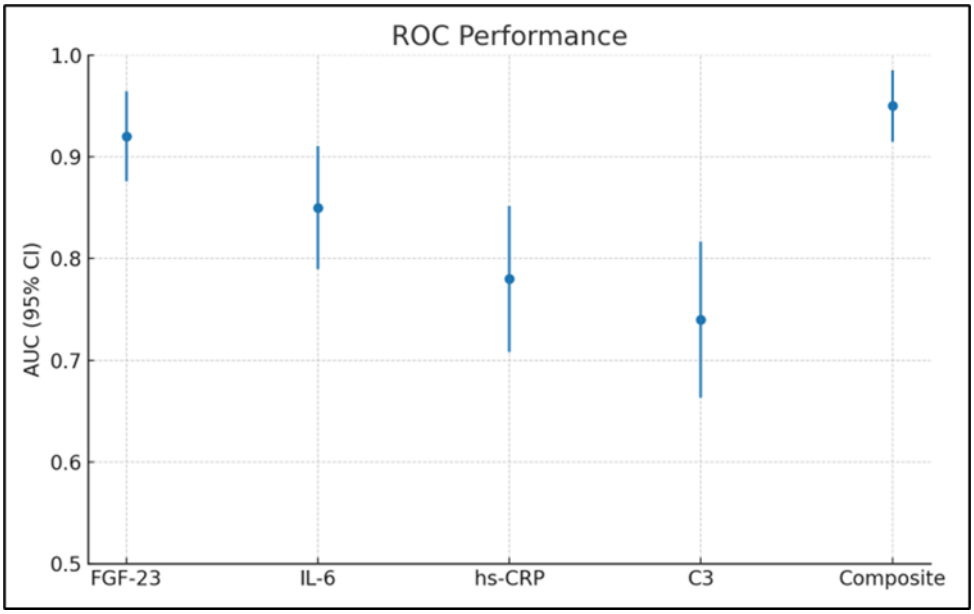

Figure 2 Reported AUCs with 95% Confidence Intervals (Hanley and McNeil)

ROC curve study determined FGF-23 as the optimal biomarker (AUC = 0.92, sensitivity = 91.2%, specificity = 90.5%). IL-6 (AUC = 0.85) and hs-CRP (AUC = 0.78) demonstrated robust discriminatory capacity, but C3 exhibited moderate efficacy (AUC = 0.74). The integrated biomarker model (FGF-23 + IL-6 + hs-CRP + C3) enhanced the AUC value to 0.95, signifying synergistic diagnostic efficacy.

Patients with CKD exhibited markedly elevated serum creatinine (6.42 ± 0.38 vs. 0.92 ± 0.06 mg/dL, , P < 0.0011), serum phosphate (6.10 ± 0.35vs. 4.02 ± 0.21mg/dL, , P < 0.0011), serum albumin(3.10 ± 0.27 vs. 4.02 ± 0.16 g/dL),serum sodium(132.80 ± 1.90vs. 139.40 ± 1.30) and potassium (5.6 ± 0.22vs. 4.1 ± 0.15 mmol/L, , P < 0.0011), alongside diminished serum albumin (3.10 ± 0.27 vs. 4.02 ± 0.16 g/dL, , P < 0.0011) and sodium (132.8 ± 1.9 vs. 139.4 ± 1.3 mmol/L, , P < 0.0011). The average estimated eGFR in CKD patients was 24.97 ± 4.08 ml/min/1.73 m^2, in contrast to 124.35 ± 4.09 ml/min/1.73 m^2 in the control group. (interquartile range: 4.0–8.0 years).

Table 3 Biochemical Parameters and eGFR (CKD vs Controls)

Measure	CKD Mean ± SD	Control Mean ± SD	Mean Diff (CKD−Ctrl)	95% CI (Diff)	p (Welch)	Hedges g	95% CI (g)
Serum Creatinine (mg/dL)	6.42 ± 0.38	0.92 ± 0.06	5.50	[5.41, 5.59]	4.89e-97	20.12	[17.88, 22.36]
Serum Phosphate (mg/dL)	6.10 ± 0.35	4.02 ± 0.21	2.08	[1.99, 2.17]	1.50e-81	7.17	[6.32, 8.02]
Serum Albumin (g/dL)	3.10 ± 0.27	4.02 ± 0.16	-0.92	[-0.99, -0.85]	2.14e-53	-4.13	[-4.68, -3.58]
Serum Sodium (mmol/L)	132.80 ± 1.90	139.40 ± 1.30	-6.60	[-7.11, -6.09]	1.10e-54	-4.04	[-4.58, -3.49]
Serum Potassium (mmol/L)	5.60 ± 0.22	4.10 ± 0.15	1.50	[1.44, 1.56]	2.38e-91	7.93	[7.00, 8.86]
eGFR (mL/min/1.73 m^2)	24.97 ± 4.08	124.35 ± 4.09	-99.38	[-100.66, -98.10]	5.04e-174	-24.21	[-26.90, -21.53]

C4 exhibited a modest, although statistically significant, disparity across groups (CKD: 33.43 ± 2.04 vs. Controls: 32.66 ± 1.78 mg/dL; p≈0.012, Welch t-test).

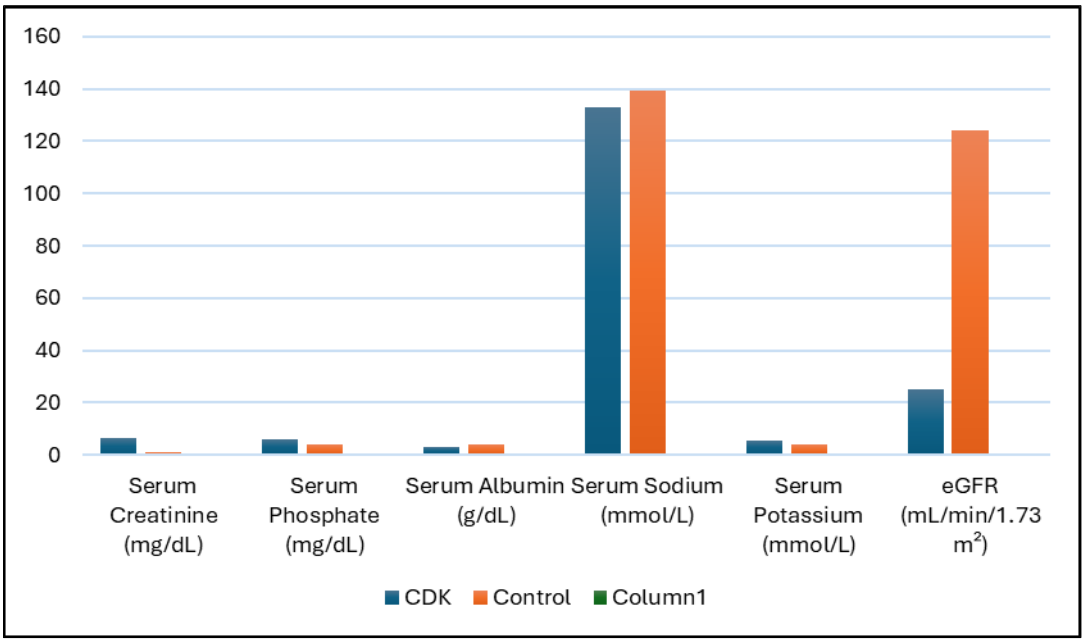

Figure 3 Group Differences (Renal and Electrolytes): Mean ± SD for CKD vs Controls

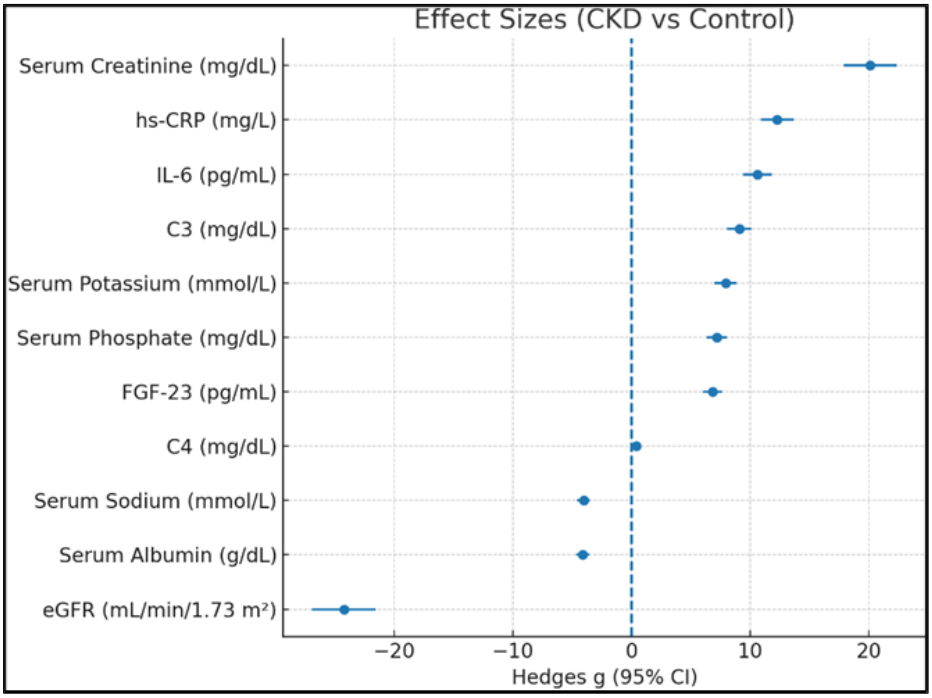

Figure 4 Effect sizes (Hedges g) with 95% CI for all markers

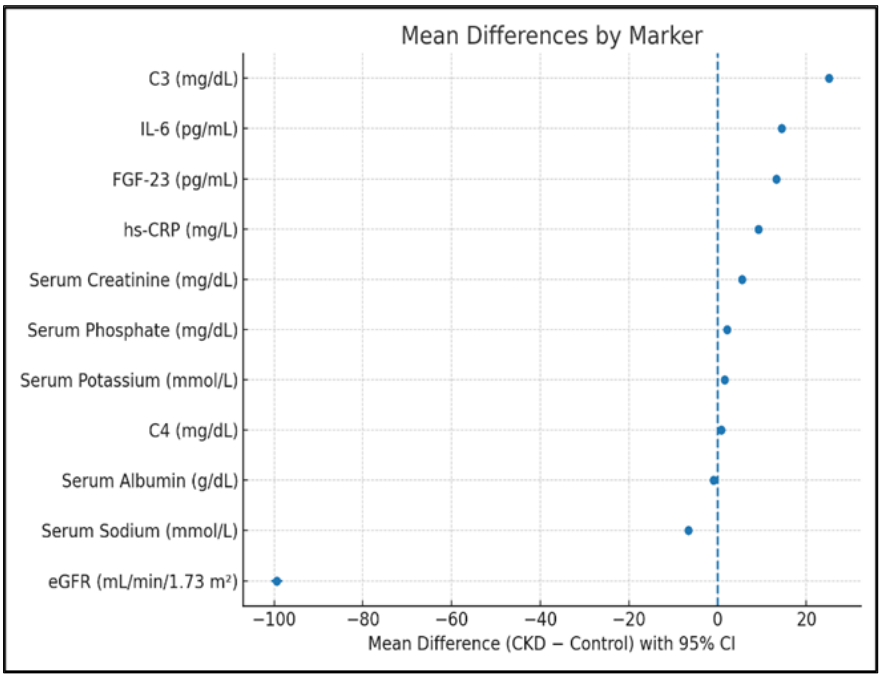

Figure 5 Mean differences (CKD − Control) with 95% CI for all markers

The Pearson correlation revealed a robust negative connection between estimated eGFR and FGF-23 ($r = -0.82$, , $p < 0.0011$), IL-6 ($r = -0.74$, , $p < 0.0011$), hs-CRP ($r = -0.69$, , $p < 0.0011$), and C3 ($r = -0.58$, , $p < 0.0011$). No substantial association exists between eGFR and C4 ($p = 0.31$).

4. Discussion

CKD is a chronic ailment marked by deteriorating kidney function, varying from modest impairment to end-stage renal failure. The global prevalence is expected to range from 8% to 16%, with elevated rates observed in low- and middle-income nations. Factors contributing to the condition include diabetes, hypertension, and genetic predisposition [19,20]. The multifactorial etiology of CKD is influenced by genetic predispositions, renal function evaluation, anaemia, electrolyte imbalances, and other risk factors.

Furthermore, several studies [21,22] demonstrate that the epidemiology of CKD varies by sex, with a higher prevalence in women than in males. The findings of these investigations align with the current study. 2020 Iraqi research [23] reported a greater prevalence of CKD in males (60.8%) than in females (39.2%). This leads to a discrepancy with our data. This fluctuation is attributable to the disparity in sample size.

Complement activation has been associated with the etiology of several kidney disorders, indicating the kidney's structural and functional vulnerability to complement-mediated damage [24]. The excessive and unregulated activation of this system leads to chronic inflammation, fibrosis, and the advancement of CKD. Consequently, complement inhibition has been suggested as a viable treatment approach to maintain renal function and mitigate tissue damage [25;26;27].

In the present study C3 levels exhibited a notable change in comparison to the control, however C4 levels showed no variation relative to the control and remained within the normal range. This outcome may pertain to the activation of the alternate pathways. These findings concur with others results [28;29]. Another study conducted in 2017 differed from the current study, showing elevated serum C4 levels and decreased serum C3. Their study was conducted in patients with immune A nephropathy. Elevated C3 levels reflect increased kidney disease activity [30]. The observation of elevated C3 levels further supports the role of the alternative pathway in CKD, which may result from endothelial cell injury and immune complex deposition [31,32,33]. Experimental investigations confirm that C3 accumulation accelerates glomerulosclerosis, while its deficiency reduces interstitial fibrosis [34]. The absence of any significant change in C4 reinforces the limited role of the classical pathway in non-autoimmune CKD variants [35]. These findings have therapeutic implications, as targeted C3 inhibitors are undergoing clinical studies for proteinuric kidney disease [36;37].

Our findings indicate markedly elevated concentrations of high-sulfonyl-CRP, IL-6, and FGF-23 in CKD patients relative to matched healthy controls, exhibiting robust negative relationships with estimated eGFR [38;39,40]. This indicates that kidney injury is not only a localised occurrence, but a systemic process involving several interrelated disease pathways. The elevated levels of IL-6 and hs-CRP in our CKD group align with prior research that has recognised inflammation as both a marker and mediator of CKD development [1;3;22;]. IL-6 is crucial in kidney illness, promoting mesenchymal proliferation, glomerular cell damage, and tubulointerstitial fibrosis via the activation of the JAK/STAT3 and NF-κB pathways [41,42]. Consequently, inflammatory signals stimulate CRP production in the liver, worsening vascular inflammation and endothelial dysfunction [43]. Our results corroborate previous interventional evidence indicating that IL-6 inhibition might decelerate CKD development and diminish the risk of cardiovascular disease in individuals with highly inflammatory phenotypes [44]. Moreover, hs-CRP, while less specific to renal pathology, maintains predictive significance for mortality and the commencement of dialysis [45].

Inflammation induces the synthesis of fibroblast growth factor 23 (FGF23), elevated concentrations of which are independently correlated with mortality in CKD (CKD) [46].Among all assessed biomarkers, FGF-23 exhibited the most excellent diagnostic precision, corroborating findings from extensive observational studies [47;48]. FGF-23, historically regarded as a regulator of phosphate balance, functions as a pro-inflammatory mediator that may induce IL-6 production through FGFR4-dependent signalling in cardiac and renal tissues [49;50]. This connection establishes a detrimental loop in which mineral imbalance exacerbates inflammation, and inflammation, in turn, elevates FGF-23 production [46;51]. Increased levels of FGF-23 have been independently linked to left ventricular hypertrophy, cardiovascular mortality, and the advancement of CKD [50;51]. Our data indicate that FGF-23 is a superior predictive marker compared to CRP and IL-6, underscoring its potential for early diagnosis of subclinical disease activity.

Our analysis reveals that the composite biomarker model (FGF-23 + IL-6 + hs-CRP + C3) attained an area under the curve (AUC) of 0.95, surpassing the efficacy of any individual biomarker. This aligns with previous studies advocating for multi-indicator approaches to assess the complex pathophysiology of CKD [52;53]. This method may detect individuals at elevated risk for fast disease advancement, even when standard indicators, such as serum creatinine, are within the near-normal limits [53]. This might provide targeted interventions—such as anti-inflammatories, dietary phosphate reduction, or early referral to nephrology—prior to the onset of irreparable kidney impairment.

Incorporating inflammatory and complement biomarkers into CKD monitoring regimens in Iraq might address existing diagnostic deficiencies. Contemporary management predominantly depends on estimated (eGFR) and serum creatinine, which do not promptly reflect genuine structural damage. Incorporating hs-CRP, IL-6, C3, and FGF-23 into clinical cohorts may enhance diagnostic precision and inform individualised treatment approaches. Patients exhibiting excessive levels of IL-6 and C3 may be candidates for anti-inflammatory or anti-complement therapeutic trials, whilst those with markedly increased FGF-23 levels may be prioritised for rigorous phosphate management.

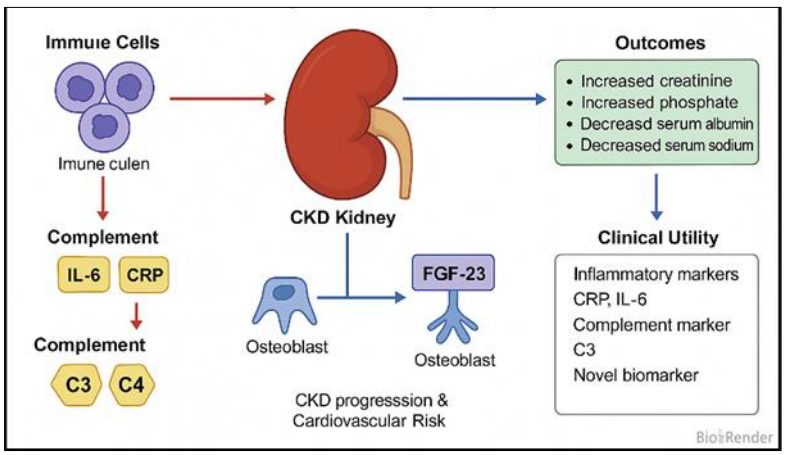

Figure 6 Pathophysiological biomarkers in chronic kidney disease (CKD). The graphic encapsulates the interaction among inflammatory indicators (IL-6, CRP), complement components (C3, C4), and the mineral metabolism regulator FGF-23 in individuals with chronic kidney disease (CKD). Increased levels of IL-6, CRP, C3, and FGF-23 contribute to chronic inflammation, immunological activation, and mineral dysregulation, resulting in diminished eGFR, elevated blood creatinine and phosphate, reduced albumin and salt levels, and heightened cardiovascular risk. This result underscores the prospective therapeutic value of these biomarkers in the early identification and surveillance of CKD development

Elevated serum creatinine concentrations are indicative of kidney dysfunction [54,55]. Significant increases were found in the serum of patients with renal failure. These results are consistent with many previous studies [56; 57;58]. The high serum creatinine concentrations of patients with renal failure are attributed to the fact that they are metabolic wastes that are naturally excreted through urination. In cases of renal failure, kidney dysfunction and impairment occur, which in turn leads to decreased excretion of these wastes. They accumulate and lead to increased serum concentrations [59]. Serum creatinine levels serve as the primary clinical metric for evaluating renal function through the eGFR, owing to their simplicity, rapidity, and cost-efficiency. However, creatinine has limitations since factors such as age, physical activity, high-protein diets, male gender, pharmaceutical drugs, and ethnicity can all have an impact on its levels. Given its little effect on serum creatinine, serum cystatin C combined with it may be used as a substitute. Since the muscles are where creatinine is synthesised chiefly, it is a crucial metric for assessing lean body mass in body composition studies. For the purpose of determining and monitoring nutritional status in patients with chronic renal illness, this assessment is crucial. [59].

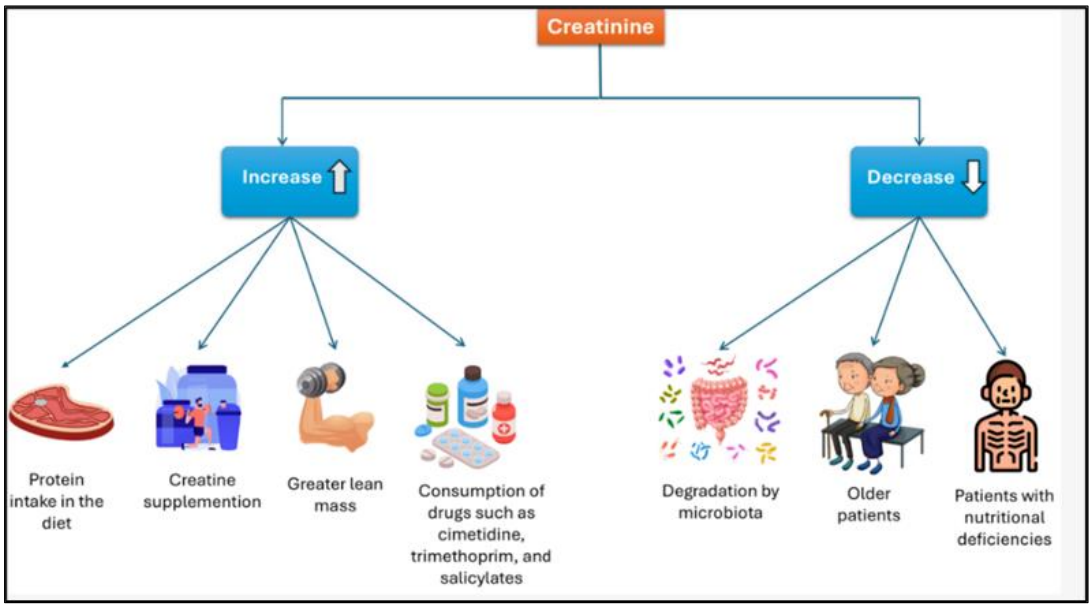

Figure 7 Factors that influence serum creatinine concentration [59]

The marked elevation of serum phosphate in CKD patients (6.10 ± 0.35 mg/dL vs 4.02 ± 0.21 mg/dL; $p < 0.0001$) underscores a hallmark of progressive renal dysfunction. Hyperphosphatemia in CKD arises from reduced glomerular filtration and compromised tubular excretion. Clinically, increased phosphate induces vascular calcification and secondary hyperparathyroidism, both of which substantially boost cardiovascular morbidity and death in renal populations. CKD involves multiple pathophysiological mechanisms that lead to vascular calcifications, such as the osteochondrogenic differentiation of vascular cells, hyperphosphatemia, hypercalcemia, and the depletion of specific vascular calcification inhibitors, including pyrophosphate, fetuin-A, osteoprotegerin, and matrix GLA protein.

The kidneys play a role in regulating the levels of sodium, potassium, calcium, and phosphorus ions, so any disturbance in their levels in the blood is related to kidney function. Phosphate is a macronutrient integral to all cellular energy activities. Approximately 90% of the phosphate filtered by the glomerulus is eliminated by the kidneys; hence, renal dysfunction and the resultant overproduction of parathyroid hormone and fibroblast growth factor 23 lead to elevated blood phosphate levels [60]. Our results show that serum phosphate levels gradually increase as renal function deteriorates, which is in line with previous research. A study of Japanese patients with non-dialysis-dependent (CKD) revealed that elevated blood phosphorus levels (≥3.7 mg/dL) correlated with a heightened risk of CKD progression [61]. A longitudinal examination of CKD patients advancing to end-stage kidney disease (ESKD) revealed a moderate rise in blood phosphate levels with time, with alterations becoming apparent around five years prior to the start of ESKD [62]. Another study indicated that mean serum phosphorus levels significantly escalated over CKD stages, with maximum values recorded in advanced stages (CKD stages 4 and 5) [63;64]. The therapeutic implications of our study findings are significant, underscoring the necessity for early phosphate monitoring and dietary modifications in CKD patients, particularly those advancing to advanced stages.

Serum albumin levels were significantly lower among CKD patients (3.10 ± 0.27 g/dL) than controls (4.02 ± 0.16 g/dL; $p < 0.0001$). These findings concur with other results [22;65;66], Hypoalbuminemia occurs when compensatory

mechanisms fail to match the disruptions in catabolism/loss and/or reduced synthesis of albumin. In several illness conditions, such as CKD, hypoalbuminemia is a recognised, independent risk factor for negative outcomes, including death. In the context of CKD, diminished serum albumin levels frequently indicate protein-energy wasting, a condition characterised by metabolic and dietary changes that lead to decreased protein and energy reserves. The advancement of CKD to renal failure and the commencement of continuous HD further increases the susceptibility of an already vulnerable population to hypoalbuminemia, resulting in roughly 60% of HD patients exhibiting albumin levels below 4.0 g/dl [67].

Hypoalbuminemia in CKD frequently indicates a confluence of starvation, systemic inflammation, and proteinuria. Reduced albumin levels are a significant predictor of negative outcomes, including death and complications. Moreover, inflammation inhibits hepatic albumin production, hence increasing risk [68].

Our results indicate a considerable drop in serum salt levels in the CKD patient group compared to their healthy counterparts. These findings concur with other results [22;65;66], demonstrating that hyponatremia essentially increases in dialysis patients due to hypotonic fluid intake or excessive water consumption. Moreover, additional studies [69] have shown that the incidence of hypernatremia, but not hyponatremia, increased in persons with more advanced renal impairment. These results contrast with our data. Potential causes for heterogeneity included illness severity, sample size, research methodology, and the threshold value used for blood sodium assessment. Moreover, assessing blood sodium levels at a singular time point may have resulted in the misdiagnosis of dysmetria due to variations in sodium values between dialysis sessions [22]. An imbalance of sodium in CKD may arise from compromised tubular reabsorption, metabolic acidosis, diuretic use, or diminished aldosterone activity, leading to increased urine salt excretion. The kidney's failure to manage water and cation excretion renders CKD patients susceptible to hyponatremia and hypernatremia, which occur more often than in the general population. Dysmetria in CKD patients correlates with adverse outcomes and heightened death rates. Current therapeutic guidelines for the general population should be adhered to in the management of these disorders, while recognising the necessity for more focused treatments and more research [70].

Elevated serum potassium (5.60 ± 0.22 mmol/L vs 4.10 ± 0.15 mmol/L; $p < 0.0001$) signals early disturbance in electrolyte homeostasis. These findings agree with other results [22;71,72]. This rise is attributable to many factors, notably the kidney's function in excreting around 90-95% of the potassium that enters the body. In cases of chronic renal failure, the efficacy of this mechanism declines. Hyperkaliemia is a prevalent and life-threatening electrolyte condition in CKD [73,74]. The severe drop in eGFR (24.97 ± 4.08 mL/min/1.73 m^2 vs 124.35 ± 4.09; $p < 0.0001$) aligns with the cumulative disruptions observed in electrolytes and proteins. Reduced eGFR reflects substantial nephron loss and correlates strongly with the clinical and biochemical derangements characteristic of CKD. The reduction in GFR observed in the current study aligns with the results of prior research [75], which suggested that the S.Cr. The level rose, but the eGFR declined due to impaired kidney function, resulting in less creatinine filtration and its subsequent buildup in the circulation.

5. Conclusion

The study demonstrates that CKD progression in Iraqi patients closely linked to inflammation, complement activation and mineral imbalance. Elevated levels of FGF-23, IL-6, hs-CRP and C3 were strongly associated with reduced eGFR, highlight their value as diagnostic and prognostic biomarkers. Among all evaluated markers, FGF-23 showed the greatest diagnostic accuracy, while the combined panel (FGF-23, IL-6, hs-CRP, C3) achieved superior predictive performance. These results suggest that a multi -marker approach offers a more comprehensive assessment than reliance on serum creatinine or eGFR alone. Incorporating these biomarkers into routine practice may facilitate earlier diagnosis, patient stratification, and targeted interventions, ultimately improving outcomes for CDK patients. Larger multi-center studies are recommended to confirm theses results and guide the integration of biomarker-based monitoring into clinical nephrology in Iraq.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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