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C-Reactive Protein and it's Correlation with Renal Parameters among Patients of Chronic Kidney Disease, not on Dialysis

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Abstract

***Background:** Chronic kidney disease (CKD) is commonly studied through renal, haematological and metabolic complications, but it also represents a chronic systemic inflammatory state. This analysis evaluated whether advancing non-dialysis CKD is accompanied by a measurable inflammatory gradient and whether C-reactive protein (CRP) correlates with renal dysfunction, anaemia, iron dysregulation and mineral metabolism.*

***Methods:** This cross-sectional analysis included 160 adults with non-dialysis CKD stages G3a to G5. CRP was the primary inflammatory marker. Stage-wise differences were tested using the Kruskal-Wallis test. High CRP was defined as >5 mg/L. Correlations between CRP and clinical-biochemical parameters were assessed using Spearman correlation with false-discovery-rate correction; Pearson's correlation was used as sensitivity analysis.*

***Results:** Mean CRP increased from 3.98 ± 2.24 mg/L in stage G3a to 11.00 ± 3.64 mg/L in stage G5 ($p < 0.001$). CRP >5 mg/L rose from 33.3% in stage G3a to 98.2% in stage G5 (chi-square = 51.82, $p < 0.001$). CRP correlated strongly with creatinine (rho = 0.651), urea (rho = 0.635), GFR (rho = -0.633) and TSAT (rho = -0.651), and significantly with haemoglobin, PCV, calcium, ferritin, TIBC and phosphorus. In the high-CRP group, GFR, haemoglobin, TSAT and calcium were lower, while creatinine and urea were higher. The high ferritin-low TSAT-high CRP phenotype was concentrated in advanced CKD, affecting 21.7% of stage G4 and 87.5% of stage G5 patients.*

***Conclusion:** Advancing CKD was associated with a clear systemic inflammatory signature. CRP rose with worsening CKD stage and tracked renal dysfunction, iron restriction, anemia and mineral-metabolic disturbance. These findings support CKD as an inflammatory systemic disorder, with iron-restricted erythropoiesis representing one downstream consequence rather than the sole manifestation.*

***Key words:** chronic kidney disease; inflammation; C-reactive protein; ferritin; transferrin saturation; anaemia; mineral bone disorder; non-dialysis CKD.*

Introduction

Chronic kidney disease (CKD) is a multisystem disorder traditionally defined by persistent reduction in kidney function or evidence of kidney damage. Beyond progressive nephron loss, CKD is increasingly recognised as a chronic inflammatory condition in which uraemic toxin accumulation, oxidative stress, endothelial dysfunction, altered gut-derived metabolites, comorbid diabetes and hypertension, volume overload and mineral-metabolic dysregulation contribute to persistent immune activation. This inflammatory state has clinical relevance because it links renal dysfunction to anaemia, vascular injury, cardiovascular risk, protein-energy wasting and progression of disease[1-4].

CRP is a pragmatic clinical marker of systemic inflammation. Although it does not define the complete inflammatory network of CKD, it is widely available, inexpensive and interpretable in routine practice. Ferritin, Transferrin Saturation (TSAT), haemoglobin, calcium, phosphorus and PTH may also reflect downstream consequences of inflammation and CKD metabolic disturbance. Ferritin is both an iron-storage marker and an acute-phase reactant; therefore, high ferritin with low TSAT in a high-CRP patient may indicate inflammatory iron sequestration rather than adequate bioavailable iron[5-8].

The present original analysis reframes the parent CKD anaemia dataset around the broader question of whether CKD behaves as a systemic inflammatory state. The primary objective was to evaluate stage-wise CRP behaviour across CKD stages G3a to G5. Secondary objectives were to test correlations of CRP with renal function, anaemia, iron indices and mineral metabolism parameters, and to interpret iron-

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restricted erythropoiesis as one downstream manifestation of CKD-associated inflammation.

Abbreviations

Table A: Abbreviations

Abbreviation	Full form
ACD	Anaemia of chronic disease
CKD	Chronic kidney disease
CRP	C-reactive protein
eGFR	Estimated glomerular filtration rate
FDR	False discovery rate
GFR	Glomerular filtration rate
Hb	Haemoglobin
IDA	Iron deficiency anaemia
MBD	Mineral bone disorder
PCV	Packed cell volume
PTH	Parathyroid hormone
SD	Standard deviation
TIBC	Total iron-binding capacity
TSAT	Transferrin saturation

Material and Methods

Study design and population

This was a prospective cross-sectional analysis of 160 adult non-dialysis CKD patients evaluated between April and September 2024 at Apollo Hospitals, Secunderabad. Patients had GFR <60 mL/min/1.73 m^2 for more than 3 months and were classified into CKD stages G3a, G3b, G4 and G5. Patients on dialysis, post-transplant patients, those with recent transfusion, recent parenteral iron, overt bleeding, malignancy, chronic infections, malabsorption, steroid therapy, haemoglobinopathies or erythropoietin therapy were excluded in the parent study.

Variables and definitions

The analysis included age, sex, hypertension, diabetes, urea, creatinine, GFR, haemoglobin, RBC count, PCV, red cell indices, WBC count, platelet count, serum iron, ferritin, TIBC, TSAT, CRP, PTH, calcium, phosphorus and anaemia type. CRP was analysed as the principal marker of systemic inflammation. High CRP was defined as CRP >5 mg/L. An inflammatory iron-restriction phenotype was defined as ferritin ≥100 ng/mL, TSAT <20% and CRP >5 mg/L.

Statistical analysis

Continuous variables are presented as mean ± SD. Categorical variables are presented as number and percentage. Stage-wise comparisons were performed using Kruskal-Wallis testing. Associations between CKD stage and categorical inflammatory phenotypes were tested using the chi-square test. Low-CRP and high-CRP groups were compared using the Mann-Whitney test. Spearman's rank correlation was used as the primary correlation test for CRP versus other continuous variables; Pearson's correlation was performed as sensitivity analysis. Multiple comparisons were controlled using Benjamini-Hochberg false discovery rate correction.

Results

Cohort profile

Table I: Cohort characteristics.

Variable	n or mean ± SD	%
Total sample	160	100.0
Age, years	53.21 ± 10.76	-
Male sex	92	57.5
Female sex	68	42.5
Hypertension	150	93.8
Diabetes mellitus	102	63.7
CKD G3a	9	5.6
CKD G3b	35	21.9
CKD G4	60	37.5
CKD G5	56	35.0

The cohort contained 160 non-dialysis CKD patients. Advanced CKD predominated, with 37.5% in stage G4 and 35.0% in stage G5. Hypertension and diabetes were common comorbidities, present in 93.8% and 63.7% respectively.

CRP gradient across CKD stages

Table II: Stage-wise inflammatory burden by CRP

CKD stage	n	CRP, mean ± SD	CRP >5 mg/L	% CRP >5 mg/L
G3a	9	3.98 ± 2.24	3/9	33.3%
G3b	35	5.48 ± 1.86	21/35	60.0%
G4	60	8.87 ± 2.83	58/60	96.7%
G5	56	11.00 ± 3.64	55/56	98.2%
Overall/statistical test	160	Kruskal-Wallis **p = <0.001**	$\chi^2 = 51.82$	**p = <0.001**

CRP increased stepwise across CKD stages, indicating an inflammatory gradient accompanying progressive renal

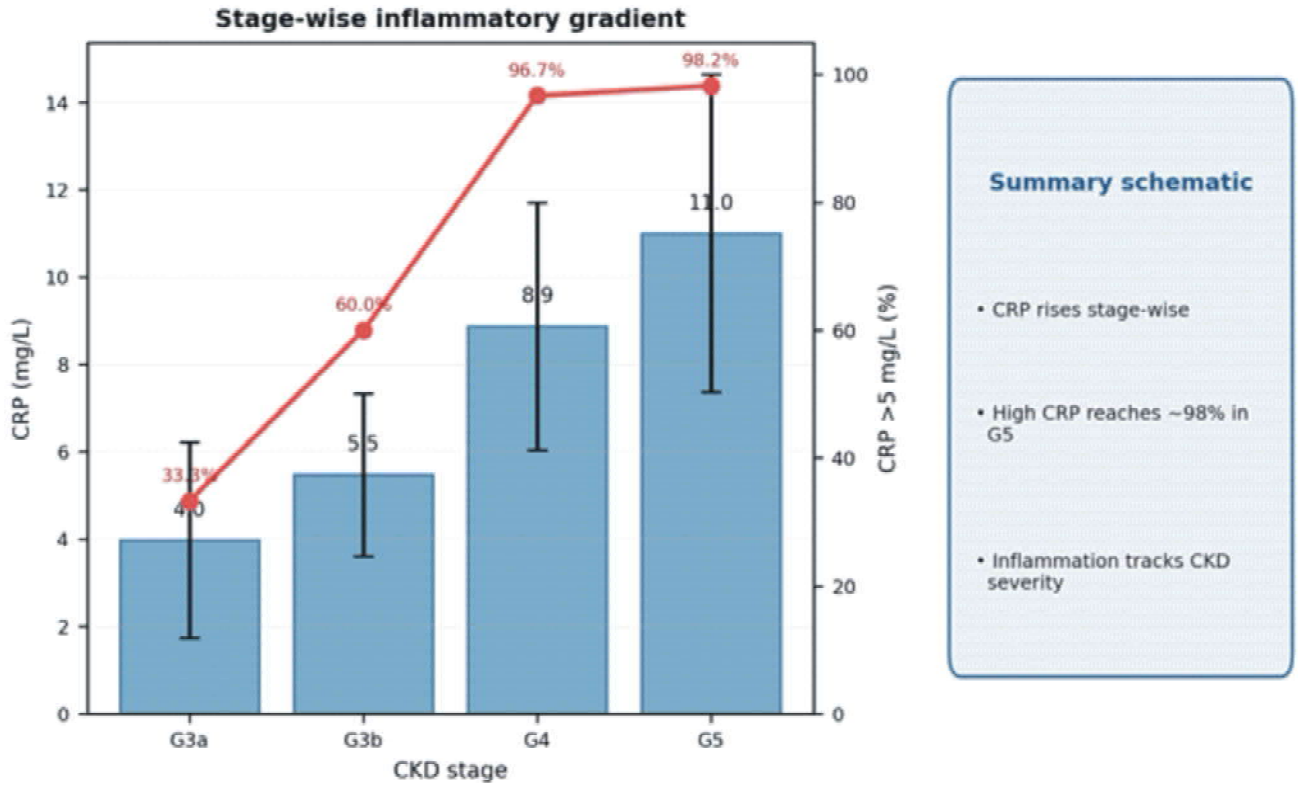

Fig. 1: *Stage-wise CRP gradient and prevalence of high CRP across CKD stages. Bars show mean CRP with SD; the line shows the percentage of patients with CRP >5 mg/L. Take-home: CRP rises progressively with CKD stage, supporting CKD as a systemic inflammatory state.*

dysfunction. The proportion of patients with CRP >5 mg/L increased from 33.3% in stage G3a to 98.2% in stage G5.

Multisystem biochemical pattern accompanying inflammation

Table III: Renal, haematological, iron and mineral parameters across CKD stages.

Parameter	G3a	G3b	G4	G5	p value
GFR	49.33 ± 3.61	36.51 ± 4.18	20.50 ± 4.05	11.14 ± 2.04	**<0.001**
Creatinine	1.69 ± 0.10	2.05 ± 0.29	3.19 ± 0.64	5.00 ± 0.61	**<0.001**
Urea	23.89 ± 4.14	29.34 ± 7.67	46.80 ± 15.05	69.27 ± 16.53	**<0.001**
Haemoglobin	11.67 ± 1.10	10.89 ± 0.99	10.21 ± 1.29	9.79 ± 1.48	**<0.001**
Ferritin	154.11 ± 79.02	177.77 ± 77.45	175.23 ± 84.70	310.61 ± 146.00	**<0.001**
TSAT	28.93 ± 0.93	26.08 ± 2.13	21.37 ± 1.85	15.91 ± 2.61	**<0.001**
Calcium	9.27 ± 0.34	8.91 ± 0.47	8.70 ± 0.40	8.17 ± 0.58	**<0.001**
Phosphorus	4.18 ± 0.65	4.74 ± 0.64	4.73 ± 0.67	5.05 ± 0.70	**0.003**
PTH	47.68 ± 7.62	66.10 ± 30.45	62.70 ± 27.23	74.18 ± 33.02	**0.036**

The CRP gradient was accompanied by worsening renal parameters, lower haemoglobin, increasing ferritin, lower TSAT, lower calcium, higher phosphorus and higher PTH. This pattern supports CKD-associated inflammation as a multisystem phenotype rather than a single haematological mechanism.

High-CRP phenotype versus low-CRP phenotype

Table IV: Biological profile of low-CRP versus high-CRP patients.

Parameter	CRP ≤5 mg/L	CRP >5 mg/L	Mann-Whitney p
GFR	38.83 ± 10.53	19.58 ± 9.77	**<0.001**
Creatinine	2.00 ± 0.67	3.74 ± 1.25	**<0.001**
Urea	26.74 ± 8.53	53.39 ± 20.54	**<0.001**
Haemoglobin	11.23 ± 0.97	10.14 ± 1.39	**<0.001**
Ferritin	178.13 ± 93.85	229.34 ± 129.62	0.141
TSAT	27.03 ± 3.10	19.89 ± 4.24	**<0.001**

Calcium	9.00 ± 0.54	8.52 ± 0.57	**0.002**
Phosphorus	4.59 ± 0.65	4.85 ± 0.70	0.083
PTH	56.02 ± 23.40	68.40 ± 30.68	0.061

Patients with high CRP had significantly lower GFR, higher creatinine and urea, lower haemoglobin, lower TSAT and lower calcium than those with CRP ≤5 mg/L. Ferritin, phosphorus and PTH were numerically higher in the high-CRP group, but the between-group differences were weaker than the renal and TSAT relationships.

CRP correlation analysis

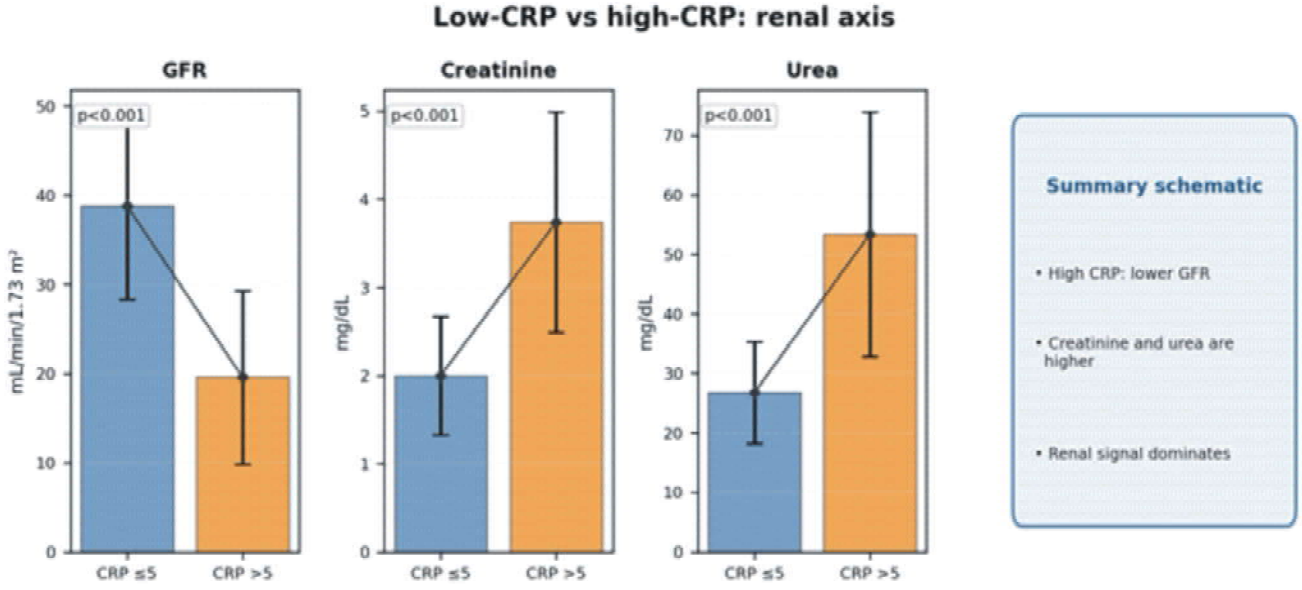

Fig. 2: *Low-CRP versus high-CRP renal phenotype. Mean ± SD plots compare GFR, creatinine and urea. Take-home: high CRP identifies worse renal dysfunction.*

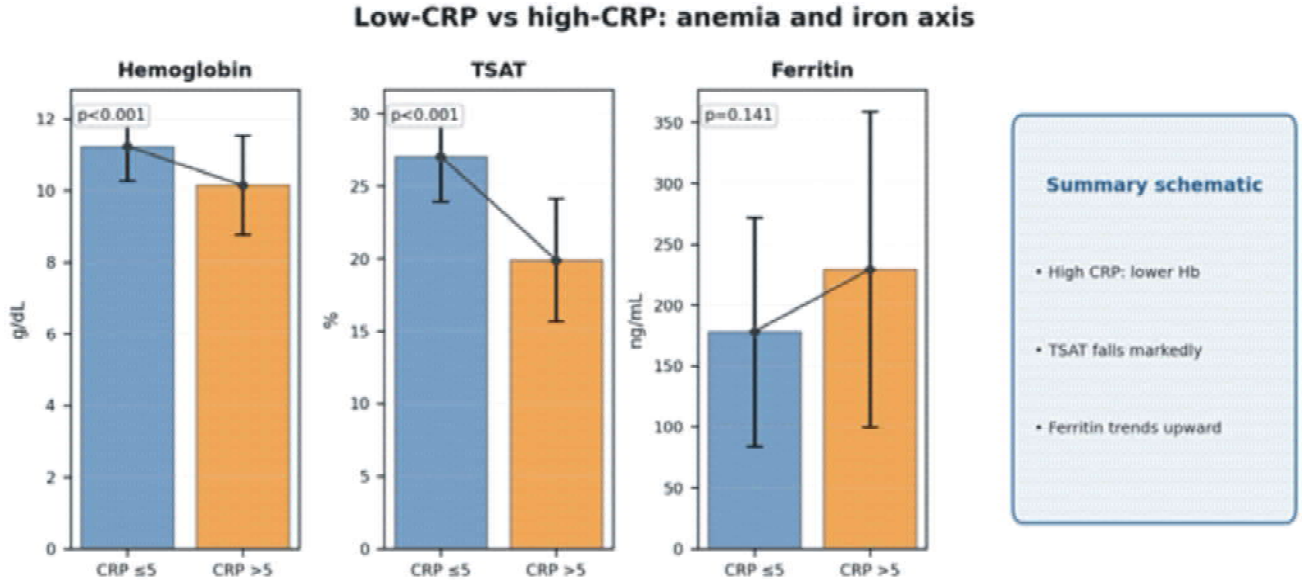

Fig. 3: *Low-CRP versus high-CRP anaemia/iron phenotype. Mean ± SD plots compare haemoglobin, TSAT and ferritin. Take-home: high CRP is accompanied by lower haemoglobin and lower TSAT.*

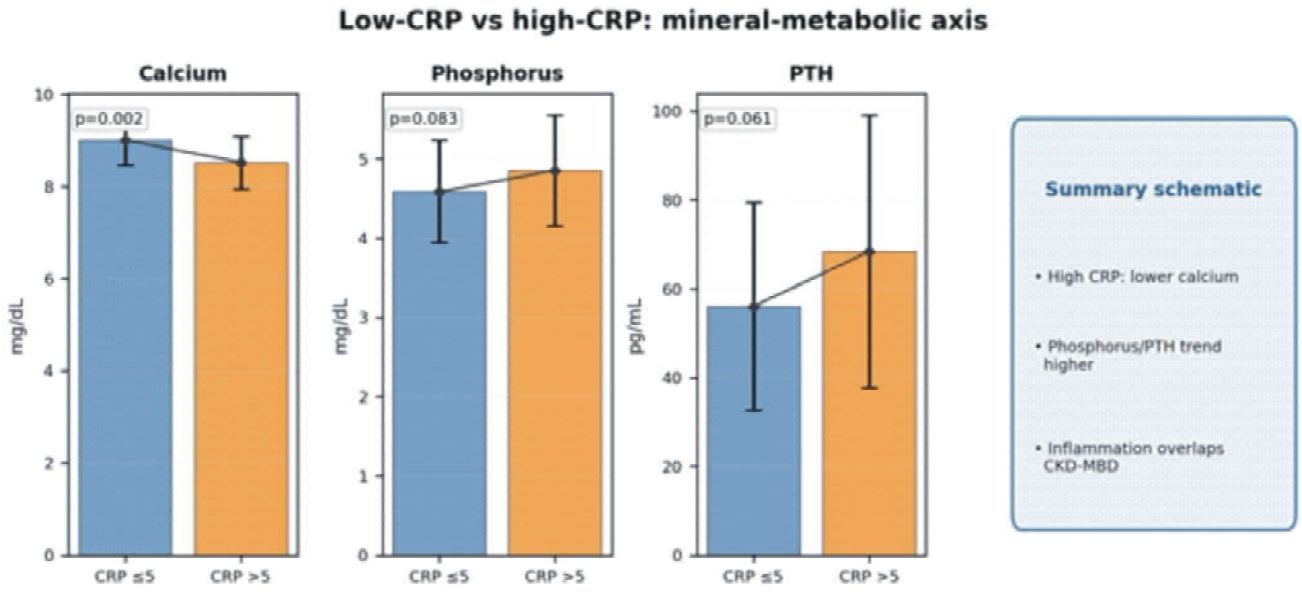

Fig. 4: *Low-CRP versus high-CRP mineral-metabolic phenotype. Mean ± SD plots show calcium, phosphorus and PTH by CRP category. Take-home: high CRP is associated with lower calcium and a trend toward greater CKD-MBD burden.*

Table V: Correlation of CRP with all continuous parameters.

Parameter	Domain	Spearman ρ	p	FDR q	Pearson r	Strength	FDR sig.
Creatinine	Renal	0.651	**<0.001**	**<0.001**	**0.623**	**Strong**	Yes
Urea	Renal	0.635	**<0.001**	**<0.001**	**0.571**	**Strong**	Yes
Ferritin	Iron profile	0.215	**0.006**	**0.012**	0.283	Weak	Yes
TIBC	Iron profile	0.202	**0.011**	**0.018**	0.178	Weak	Yes
Phosphorus	Mineral metabolism	0.180	**0.023**	**0.034**	0.207	Very weak	Yes
PTH	Mineral metabolism	0.058	0.465	0.551	0.069	Very weak	No
Platelet count	Haematological	0.055	0.493	0.551	0.010	Very weak	No
Age	Demographic	0.020	0.801	0.832	0.066	Very weak	No
MCH	Haematological	0.017	0.832	0.832	0.021	Very weak	No
Serum iron	Iron profile	-0.080	0.316	0.401	-0.093	Very weak	No
WBC count	Haematological	-0.099	0.214	0.291	-0.116	Very weak	No
MCHC	Haematological	-0.188	**0.017**	**0.027**	-0.201	Very weak	Yes
MCV	Haematological	-0.214	**0.007**	**0.012**	-0.262	Weak	Yes
RBC count	Haematological	-0.236	**0.003**	**0.006**	-0.263	Weak	Yes
Calcium	Mineral metabolism	-0.301	**<0.001**	**<0.001**	-0.307	Weak	Yes
PCV	Haematological	-0.323	**<0.001**	**<0.001**	-0.382	Weak	Yes
Haemoglobin	Haematological	-0.327	**<0.001**	**<0.001**	-0.390	Weak	Yes
GFR	Renal	-0.633	**<0.001**	**<0.001**	**-0.646**	**Strong**	Yes
TSAT	Iron profile	-0.651	**<0.001**	**<0.001**	**-0.624**	**Strong**	Yes

CRP correlated most strongly with TSAT, creatinine, urea and GFR. Significant correlations after FDR correction were also observed with haemoglobin, PCV, calcium, ferritin, TIBC, phosphorus, RBC count, MCV and MCHC. These results show that CRP tracked multiple biological domains of CKD severity.

Inflammatory iron restriction as a downstream manifestation

Table VI: Downstream inflammatory iron-restriction phenotype by CKD stage (ferritin ≥100 ng/mL, TSAT <20%, CRP >5 mg/L).

CKD stage	n	Phenotype present (n)	%
G3a	9	0	0.0%
G3b	35	0	0.0%
G4	60	13	21.7%
G5	56	49	87.5%
Statistical test	160	$\chi^2 = 91.29$	**p = <0.001**

The high ferritin-low TSAT-high CRP phenotype was absent in stage G3a and G3b and became common in advanced CKD, particularly stage G5. This supports iron-restricted erythropoiesis as one consequence of systemic inflammation in CKD, but the broader CRP correlation pattern demonstrates that inflammation extends beyond anaemia.

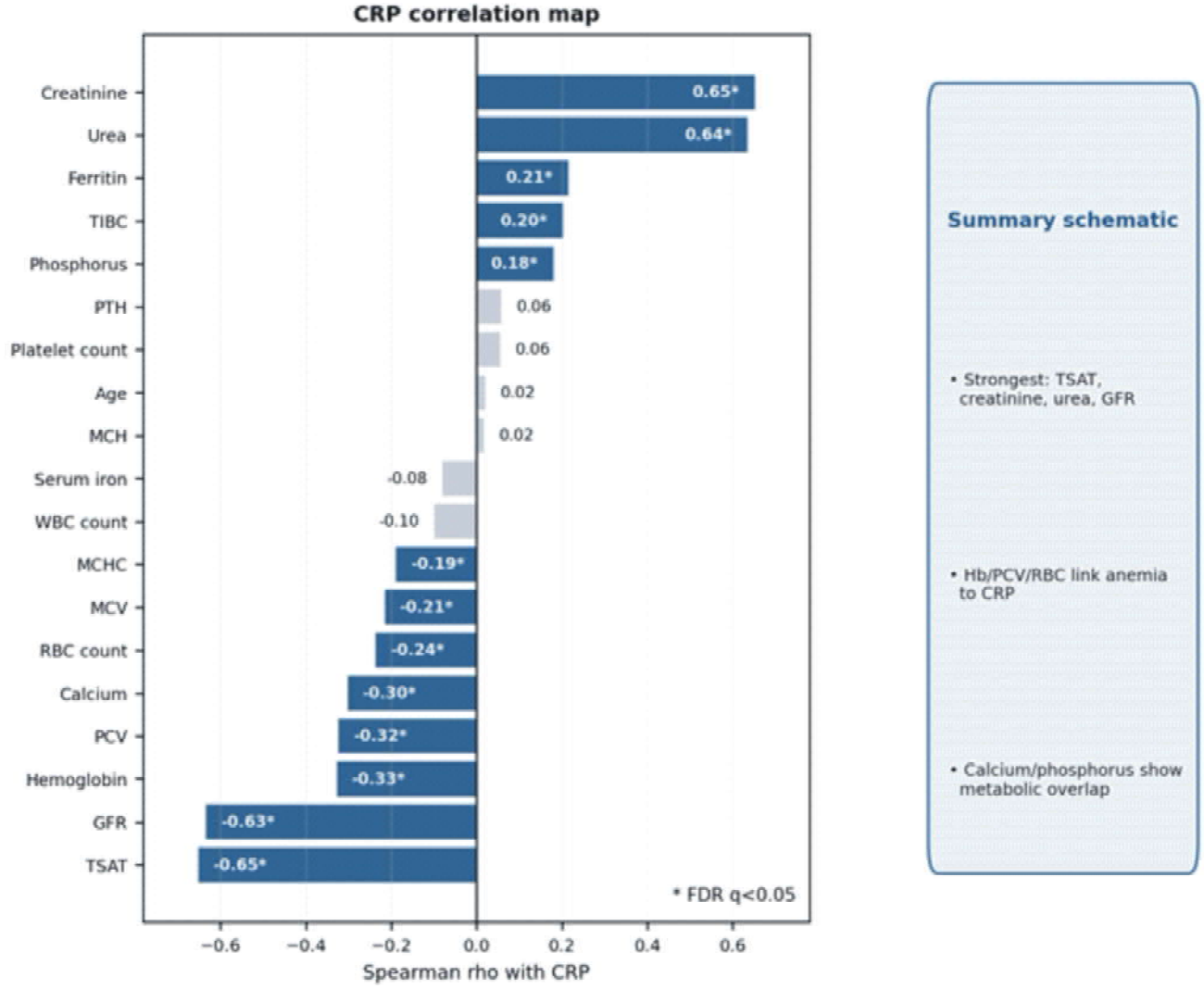

Fig. 5: *CRP correlation map. Bars represent Spearman rho; asterisks indicate FDR q <0.05. Take-home: the strongest links are renal dysfunction and iron restriction.*

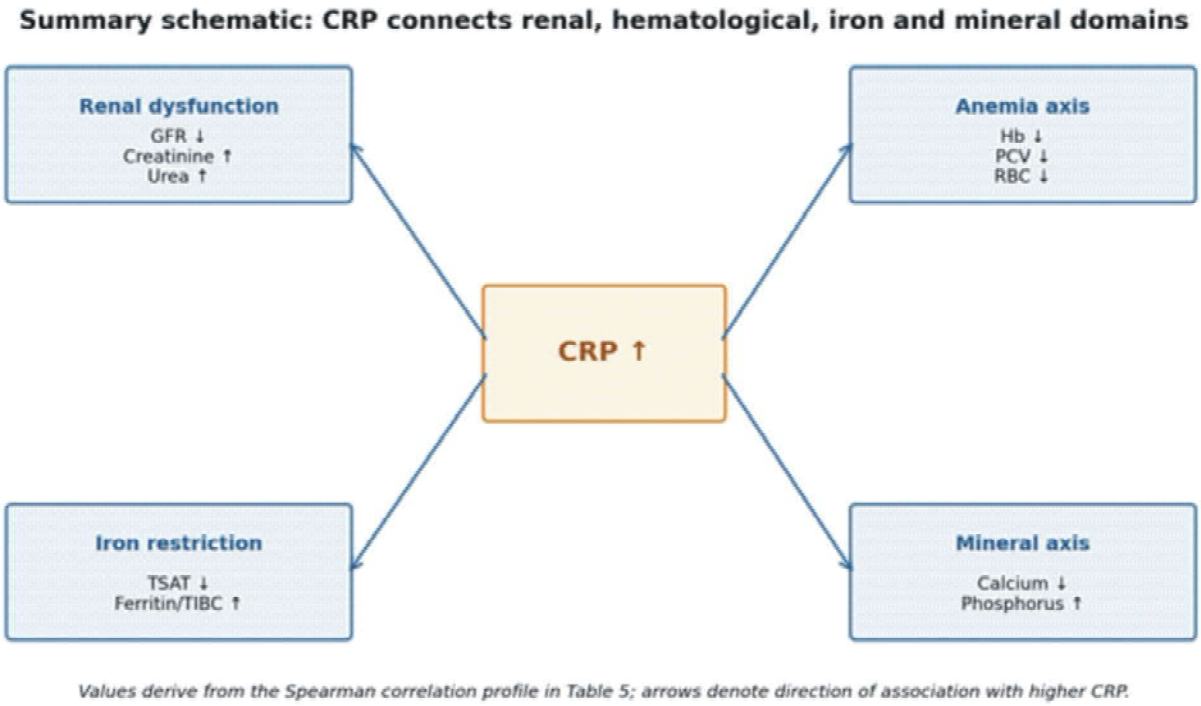

Fig. 6: *Multidomain summary schematic of CRP correlations. The schematic summarizes the main statistically supported directions of association from Table V. Take-home: CRP connects renal dysfunction, iron restriction, anaemia and mineral-metabolic change.*

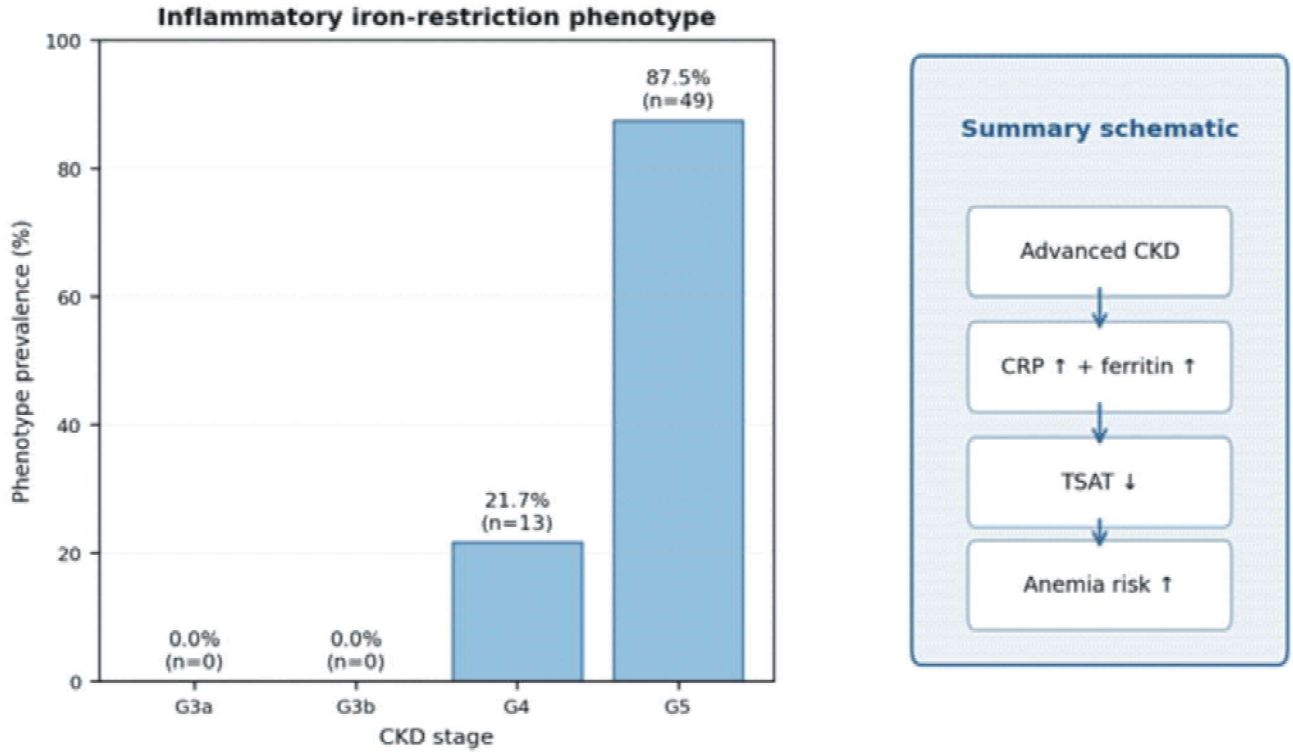

Fig. 7: *Stage-wise prevalence of the inflammatory iron-restriction phenotype. Bars show the percentage of patients meeting ferritin ≥100 ng/mL, TSAT <20% and CRP >5 mg/L. Take-home: this downstream phenotype emerges predominantly in advanced CKD.*

Discussion

This original analysis reframes a non-dialysis CKD anaemia dataset through the broader lens of systemic inflammation. The main finding is that CRP rose in a graded manner across CKD stages, from G3a to G5, and high CRP became nearly universal in advanced disease. This stage-wise inflammatory gradient was accompanied by worsening renal function, anemia, iron dysregulation and mineral-metabolic disturbance.

The strength of the CRP correlations is important. CRP showed strong positive correlations with creatinine and urea and a strong inverse correlation with GFR, indicating that inflammation closely tracked renal dysfunction. These findings are consistent with the concept that progressive CKD promotes inflammation through uraemic toxin accumulation, oxidative stress, endothelial injury, gut dysbiosis and comorbidity-driven immune activation[1-4].

The iron and anaemia findings should therefore be interpreted as part of a wider inflammatory phenotype. CRP correlated strongly and inversely with TSAT, weakly but significantly with ferritin and TIBC, and significantly with haemoglobin and PCV. This supports a model in which inflammation contributes to iron-restricted erythropoiesis through impaired iron mobilisation, while ferritin may partially behave as an acute-phase marker rather than a pure reflection of available iron stores[5-8].

The relationship between CRP and mineral metabolism adds a further systemic dimension. CRP correlated negatively with calcium and positively with phosphorus, while PTH showed only a weak non-significant relationship. This suggests that the inflammatory signature of CKD may coexist with CKD-mineral bone disorder, although the present dataset cannot prove causality. The combination of inflammation, mineral dysregulation, anaemia and iron restriction may help explain the high cardiovascular and metabolic burden of advanced CKD[3,4,9].

The clinical implication is that inflammation should be considered an integral part of CKD assessment rather than an incidental laboratory finding. In advanced CKD, elevated CRP may identify patients with a broader inflammatory-metabolic phenotype, including low TSAT, high ferritin, anemia, lower calcium and higher phosphorus. Such patients may require more careful interpretation of iron markers, evaluation for occult inflammatory triggers, optimisation of CKD-MBD care and individualised anaemia management.

Strengths and limitations

The strengths of this study include a well-defined non-dialysis CKD cohort, availability of CRP across CKD stages, simultaneous assessment of renal, haematological, iron and mineral variables, and use of FDR correction for multiple correlation testing. The main limitations are the cross-sectional design, lack of hepcidin, interleukin-6, albumin, oxidative stress markers, albuminuria and longitudinal outcomes. CRP was measured once, and subclinical infection or comorbidity-related inflammation cannot be completely excluded despite parent-study exclusions. The cohort was hospital-based and enriched for advanced CKD, which may limit generalizability.

Conclusion

CKD in this non-dialysis cohort showed a clear systemic inflammatory signature. CRP increased progressively with CKD stage and correlated with renal dysfunction, iron restriction, anaemia and mineral-metabolic disturbance. These findings support CKD as a systemic inflammatory state, with inflammation-associated iron-restricted erythropoiesis representing one downstream manifestation rather than the sole explanation. Routine interpretation of CRP alongside GFR, ferritin, TSAT, haemoglobin, calcium, phosphorus and PTH may better characterize the inflammatory phenotype of advanced CKD.

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