The North African Journal of Scientific Publishing (NAJSP)
مجلة شمال إفريقيا للنشر العلمي (NAJSP)
E-ISSN: 2959-4820
Volume 4, Issue 2, 2026
Page No: 404-415
Website: https://najsp.com/index.php/home/index
SJIFactor 2024: 5.49 0.69 :2025 (AIF) معامل التأثير العربي ISI 2024: 0.696

Evaluation of Calcium–Phosphate–Parathyroid Hormone Axis in Secondary Hyperparathyroidism Among Renal Failure Patients

Laila H. Faraj Shaglouf[1*], Bhumikha Upadhyay[2]
[1]Department of Medical Laboratory Technology, Medical college, Almergib University, Libya.
[2]Department of Biochemistry, Medical college, Hamdard university, India

تقييم محور الكالسيوم والفوسفات وهرمون الغدة جار الدرقية في فرط نشاط الغدة جار الدرقية الثانوي المصاحب لمرضى الفشل الكلوي

ليلي حامد فرج شقلوف[1*]، بوميكا اوبادهي[2]
[1]قسم المختبرات الطبية، كلية التقنية الطبية، جامعة المرقب، مسلاته، ليبيا.
[2]قسم الكيمياء السريرية، جامعة همدرد للعلوم الطبية والأبحاث، دلهي، الهند.

*Corresponding author: Lailashaglouf@gmail.com

Received: March 28, 2025 | Accepted: May 08, 2026 | Published: May 24, 2026

Abstract:
Background: Chronic kidney disease (CKD) leads to profound disturbances in mineral metabolism, culminating in secondary hyperparathyroidism (SHPT), a central component of CKD–mineral and bone disorder (CKD-MBD). Objective: To evaluate the biochemical interplay between calcium, phosphate, and parathyroid hormone (PTH) in renal failure patients and assess the severity of SHPT. Methods: A cross-sectional analytical study was conducted on 80 patients with advanced renal failure. Biochemical parameters including calcium, phosphate, PTH, vitamin D, and renal function markers were analyzed. Statistical comparisons were made against healthy reference midpoints using one-sample t-tests. Correlation and regression analyses were performed to assess interrelationships. Results: Mean PTH levels were markedly elevated (789.26 pg/mL, $p<0.001$), with concomitant hyperphosphatemia (6.49 mg/dL) and vitamin D deficiency (20.53 ng/mL). Despite near-normal mean calcium (9.50 mg/dL), significant endocrine dysregulation was evident. Strong associations were observed between renal dysfunction and metabolic derangements. Conclusion: Severe disruption of the calcium–phosphate–PTH axis is evident in renal failure patients, characterized by vitamin D deficiency, phosphate retention, and compensatory PTH elevation. Early intervention targeting mineral metabolism is critical to reduce morbidity associated with CKD-MBD.

Key words: Chronic Kidney Disease, Secondary Hyperparathyroidism, Vit D, Calcium and Phosphate.

الملخص:
إلى اضطرابات عميقة في استقلاب (أيض) المعادن، مما يؤدي في النهاية إلى الإصابة بفرط نشاط الغدد جارات الدرقية الثانوي (SHPT)، وهو مكون أساسي للاضطرابات العظمية والمعدنية المصاحبة لمرض الكلى المزمن.(CKD-MBD) الهدف: تقييم التداخل الكيميائي الحيوي بين الكالسيوم والفوسفات وهرمون الغدة جارة الدرقية (PTH) لدى مرضى الفشل الكلوي، وتقييم مدى شدة فرط نشاط الغدد جارات الدرقية الثانوي.(SHPT) المنهجية: أُجريت دراسة تحليلية مستعرضة

(Cross-sectional)على 80 مريضاً يعانون من فشل كلوي متقدم. وتضمنت الدراسة تحليل المؤشرات الكيميائية الحيوية، بما في ذلك الكالسيوم، والفوسفات، وهرمون الغدة جارة الدرقية(PTH) ، وفيتامين (د)، بالإضافة إلى مؤشرات وظائف الكلى. كما أُجريت مقارنات إحصائية مع القيم المرجعية المتوسطة للأصحاء باستخدام اختبار (t) لعينة واحدة (One-sample t-tests)، إلى جانب إجراء تحليلات الارتباط والانحدار لتقييم العلاقات المتبادلة. النتائج: أظهرت النتائج ارتفاعاً ملحوظاً في متوسط مستويات هرمون الغدة جارة الدرقية (789.26 بيكوغرام/مل)، بقيمة احتمالية (p<0.001)، مصحوباً بفرط فوسفات الدم (6.49 ملغ/ديسيلتر) ونقص فيتامين (د ((20.53 نانوغرام/مل). وعلى الرغم من أن متوسط مستوى الكالسيوم كان قريباً من المعدل الطبيعي (9.50 ملغ/ديسيلتر)، إلا أن هناك خللاً واضحاً في التنظيم الهرموني. كما لوحظ وجود ارتباطات قوية بين القصور الكلوي والاضطرابات الاستقلابية.

الكلمات المفتاحية: مرض الكلى المزمن، فرط نشاط الغدد جارات الدرقية الثانوي، فيتامين (د)، الكالسيوم، والفوسفات.

Introduction:

Chronic kidney disease is a progressive condition characterized by irreversible loss of renal function and widespread metabolic disturbances (Yan et al, 2021, Romagnani et al, 2017). Among its systemic complications, disruption of mineral metabolism plays a pivotal role, leading to secondary hyperparathyroidism (SHPT). This condition arises due to impaired phosphate excretion, reduced activation of vitamin D, and altered calcium homeostasis (Shin-Hwa Tsai et al., 2024).

The calcium–phosphate–PTH axis is tightly regulated under physiological conditions. However, in CKD, decreased renal 1α-hydroxylase activity reduces calcitriol synthesis, leading to hypocalcemic stimuli and compensatory PTH hypersecretion (Maranduca et al, 2024, Mazzaferro et al., 2025). Persistent elevation of PTH contributes to bone resorption, vascular calcification, and increased cardiovascular risk (Khundmiri et al., 2016).

The relationship between kidney function and mineral metabolism is highly significant, particularly in the regulation of calcium and vitamin D (Holick,2020). This renal activation step is crucial, as calcitriol is responsible for enhancing calcium absorption in the intestines and maintaining calcium balance in the body (Ross et al.,2021). Calcium is one of the most important minerals in the human body and is involved in numerous physiological processes (Guyton & Hall, 2021). The concentration of calcium in the blood is tightly regulated within a narrow range, as even small deviations can lead to serious physiological disturbances (Peacock et al., 2010).

The kidneys also contribute directly to calcium balance by regulating its excretion and reabsorption. Approximately 98–99% of filtered calcium is reabsorbed along different segments of the nephron, and this process is influenced by PTH and other factors (Koeppen & Stanton, 2021). In the other hands, one of the most used biomarkers to evaluate kidney function is serum creatinine. It is freely filtered by the glomeruli and minimally reabsorbed by the renal tubules, making it a reliable indicator of glomerular filtration rate (GFR) (Ávila et al.,2025). Elevated levels of serum creatinine are strongly associated with impaired kidney function and are widely used in clinical practice to diagnose and monitor kidney diseases, particularly in CKD (Shlipak et al.,2009).

In addition, elevated serum creatinine levels in CKD patients reflect declining glomerular filtration rate and worsening kidney function. This decline further exacerbates disturbances in vitamin D metabolism and calcium balance, creating a complex cycle of metabolic dysregulation (Levey et al., 2020). Meanwhile, the result of reduced calcitriol levels, intestinal calcium absorption decreases, leading to hypocalcaemia (Ross et al.,2021). This hypocalcemia stimulates the parathyroid glands to secrete more PTH in an attempt to restore calcium levels. This condition is known as secondary hyperparathyroidism and is a common complication in patients with CKD (Moe et al.,2020). By the time, persistent elevation of PTH can lead to excessive bone resorption and skeletal abnormalities, collectively referred to as renal osteodystrophy (Cunningham et al., 2021).

The interrelationship between vitamin D, calcium, creatinine, kidney function, and parathyroid hormone becomes particularly evident in pathological conditions, especially chronic kidney disease (CKD). Which characterized by a progressive decline in kidney function over time, resulting in the accumulation of metabolic waste products and disturbances in electrolyte and mineral balance (KDIGO et al., 2024). One of the early consequences of CKD is the reduced ability of the kidneys to convert vitamin D into its active form, leading to decreased levels of calcitriol (Holick et all., 2020, Alazoumi et al. 2024).

These alterations not only affect bone health but are also associated with increased cardiovascular risk and morbidity in patients with chronic kidney disease (Kovesdyet, et al., 2022).

Furthermore, recent studies have emphasized the importance of early detection and management of abnormalities in vitamin D, calcium, and PTH levels in patients with impaired kidney function. Monitoring these parameters alongside serum creatinine can provide valuable insights into disease progression and help guide therapeutic interventions (KDIGO,2024).

This study aims to quantitatively evaluate this axis in renal failure patients and elucidate the biochemical and pathophysiological mechanisms underlying SHPT.

Materials and Methods:

Study Design and Population:

A cross-sectional observational study was conducted on 80 patients diagnosed with advanced renal failure. To evaluate the clinical significance of the cohort’s metabolic derangement, statistical comparisons were performed against the midpoints of established healthy reference intervals. Because clinical parameters are typically reported as a range (e.g., Calcium 8.5–10.2 mg/dL), a single midpoint (e.g., 9.3 mg/dL) was utilized as a benchmark for one-sample t-tests. This methodology allows for a rigorous quantification of how far the renal failure cohort has drifted from healthy physiological norms.

Biochemical Parameters:

The following parameters were analyzed:

- Serum calcium (Ca)
- Serum phosphate (P)
- Parathyroid hormone (PTH)
- 25-hydroxy vitamin D
- Renal function markers (urea, creatinine)
- Electrolytes and inflammatory markers (CRP, ferritin)

Statistical Analysis:

- Mean and standard deviation were calculated.
- One-sample t-tests were performed against reference midpoints.
- Pearson correlation coefficients were used to assess interrelationships.
- Linear regression was applied to evaluate endocrine feedback dynamics.
- Reference intervals were derived from standard clinical guidelines.

Results:

Clinical Reference Intervals and Statistical Midpoints:

The table below summarizes the reference ranges used to evaluate the cohort. The "Test Midpoint" was calculated as the mathematical centre of the healthy range to serve as the baseline for the one-sample t-tests. The sample size equal to 80.

Table (1): Clinical reference intervals and statistical midpoints

Parameter	Reference Range	Units	Test Midpoint
Ca (Calcium)	8.5 – 10.2	mg/dL	9.3
PTH (Parathyroid H.)	10 – 65	pg/mL	37.5
Vit D (25-Hydroxy)	30 – 100	ng/mL	65.0
Cr (Creatinine)	0.7 – 1.3	mg/dL	1.0
Glucose (Fasting)	70 – 99	mg/dL	84.5
Urea (BUN)	7 – 20	mg/dL	13.5
K (Potassium)	3.6 – 5.2	mmol/L	4.4
Cl (Chloride)	96 – 106	mmol/L	101.0
Phe (Phosphate)	2.5 – 4.5	mg/dL	3.5
Mg (Magnesium)	1.7 – 2.2	mg/dL	1.95
Na (Sodium)	135 – 145	mmol/L	140.0
Fe (Serum Iron)	60 – 170	µg/dL	115.0
Fer (Ferritin)	30 – 150	ng/mL	90.0
U.Acid (Uric Acid)	3.5 – 7.2	mg/dL	5.35
T.pr (Total Protein)	6.0 – 8.3	g/dL	7.15
Alb (Albumin)	3.4 – 5.4	g/dL	4.4
CRP (C-Reactive Pr.)	< 1.0	mg/L	0.5

The mean and stander deviation of the samples:

Table (2): (Cohort vs. Healthy Normal) (Sample no= 80 Patients of CKD)

Sample size (80)	Parameter	Mean	Std Dev	p-value	Significance
1	Ca	9.50	0.85	0.0399	Significant
2	PTH	789.26	10.05	0.0001	Significant
3	Vit D	20.53	1.08	0.0001	Significant
4	Cr	17.93	3.18	0.0002	Significant
5	Glucose	131.62	16.31	0.0001	Significant
6	Urea	169.23	7.11	0.0001	Significant
7	K	5.21	2.45	0.0041	Significant
8	Cl	104.05	11.73	0.0870	Non-Sig
9	Phe	6.49	1.87	0.001	Significant
10	Mg	2.59	1.49	0.0003	Significant
11	Na	138.87	5.66	0.0782	Non-Sig
12	Fe	60.05	5.47	0.001	Significant
13	Fer	372.58	12.31	0.0001	Significant
14	U.Acid	6.64	1.23	0.001	Significant
15	T.pr	6.92	0.59	0.0078	Significant
16	Alb	4.10	0.52	0.001	Significant
17	CRP	11.05	2.91	0.001	Significant

The statistical findings in the table (3.2) reveal a cohort in a state of advanced physiological crisis. The renal function biomarkers are critically elevated, with a mean Creatinine of 17.93 mg/dL and Urea of 169.23 mg/dL (p<0.001), confirming severe azotemia and renal failure. This renal impairment has triggered a profound disruption of the endocrine axis, evidenced by Secondary Hyperparathyroidism with an extremely high mean PTH of 789.26 pg/mL and a significant Vitamin D deficiency (20.53 ng/mL). Additionally, the significantly high mean Phosphate (6.49 mg/dL) and elevated CRP (11.05 mg/L) indicate that the patients are suffering from both chronic kidney disease-Mineral and Bone Disorder (CKD-MBD) and systemic chronic inflammation.

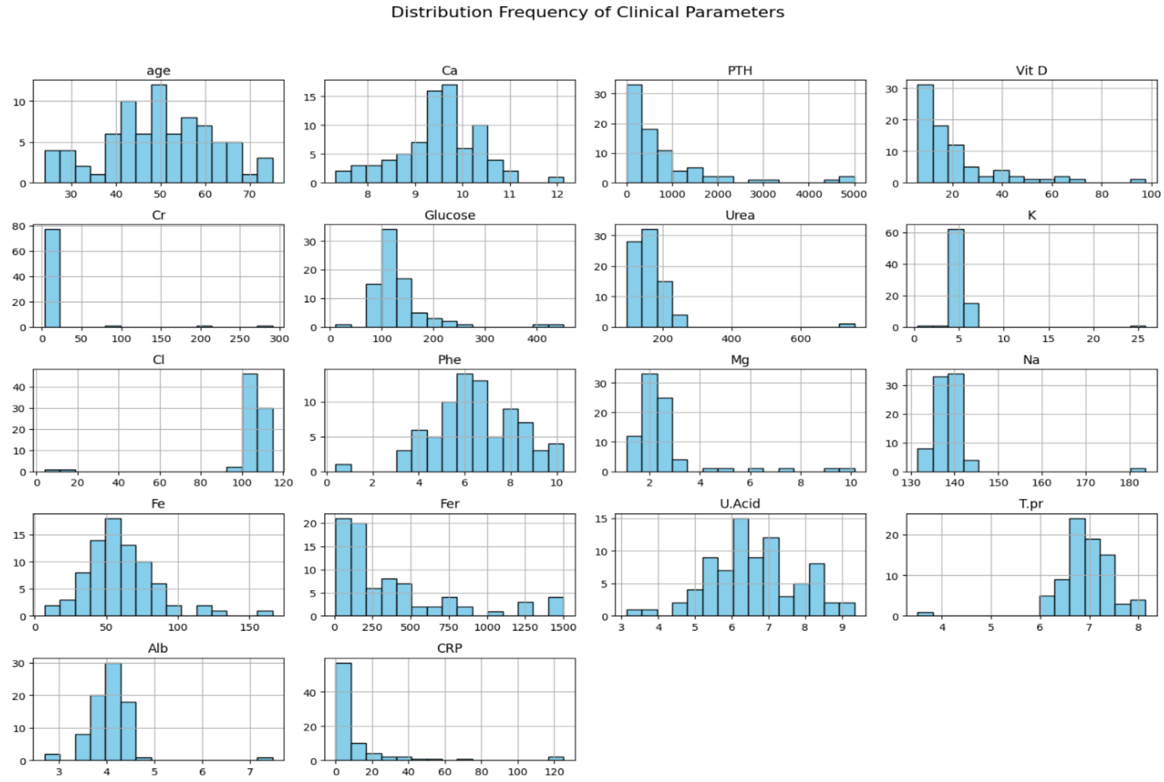
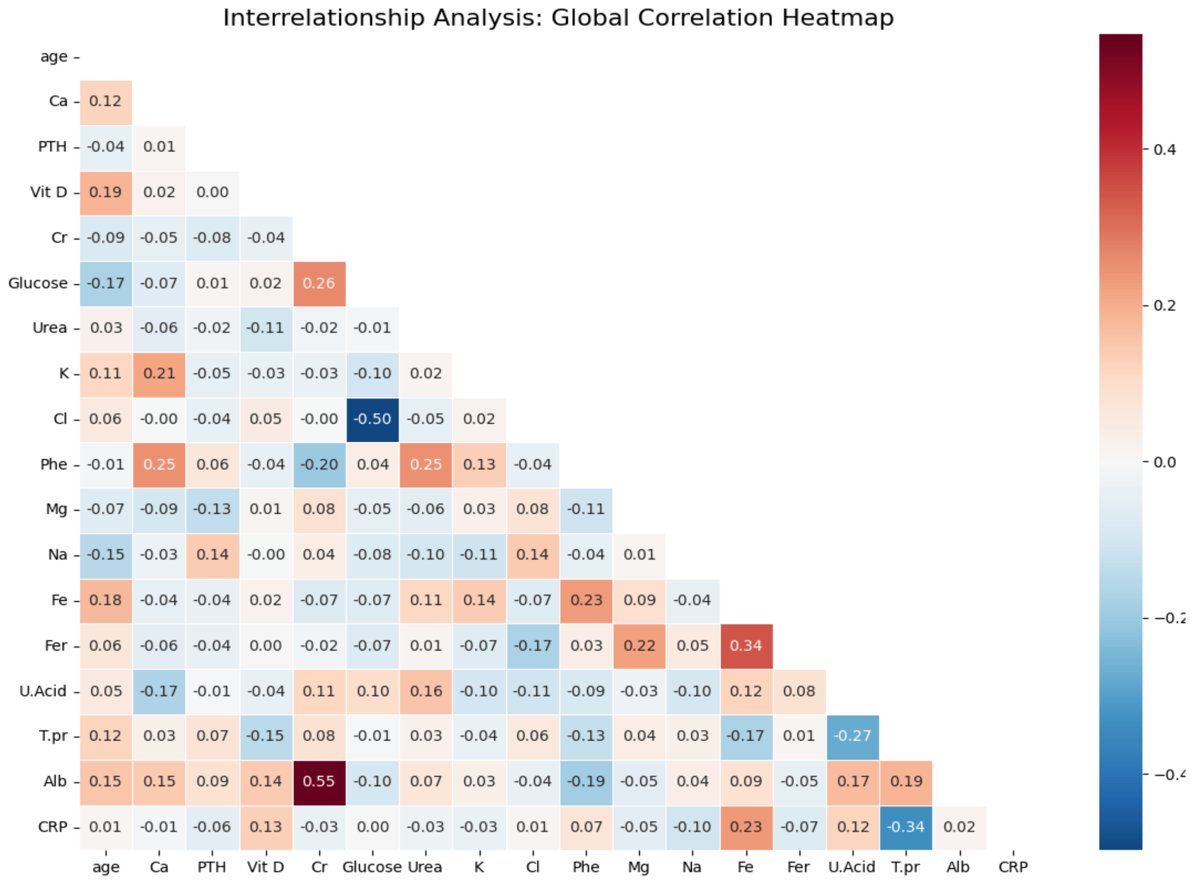


Figure (1): (A, B&C) Distribution frequency.

Global Interrelationship and Correlation Matrix:

To evaluate the systemic associations and co-dependencies between metabolic markers, we calculated a global correlation matrix using Pearson's (r) coefficients; this comprehensive interrelationship analysis is clinically vital to identify how renal deterioration influences electrolyte balance, protein status, and the endocrine axis simultaneously.

The correlation heatmap reveals several critical physiological links within the cohort. The strongest positive correlation is observed between Albumin and Creatinine (r=0.55), suggesting a complex relationship between nutritional status and the severity of renal waste accumulation in this specific patient group. Conversely, a significant inverse relationship exists between Glucose and Chloride (r=−0.50), which likely reflects the osmotic shifts and electrolyte imbalances common in diabetic patients with renal impairment. We also observe expected pathological clusters, such as the positive correlation between Iron and Ferritin (r=0.34), and a notable negative correlation between Total Protein and CRP (r=−0.34), indicating that as systemic inflammation (CRP) increases, the biosynthetic capacity for proteins tends to decline, a hallmark of Malnutrition-Inflammation Complex Syndrome (MICS) in renal failure.



	age	Ca	PTH	Vit D	Cr	Glucose	Urea	K	Cl	Phe	Mg	Na	Fe	Fer	U.Acid	T.pr	Alb	CRP
age																		
Ca	0.12																	
PTH	-0.04	0.01																
Vit D	0.19	0.02	0.00															
Cr	-0.09	-0.05	-0.08	-0.04														
Glucose	-0.17	-0.07	0.01	0.02	0.26													
Urea	0.03	-0.06	-0.02	-0.11	-0.02	-0.01												
K	0.11	0.21	-0.05	-0.03	-0.03	-0.10	0.02											
Cl	0.06	-0.00	-0.04	0.05	-0.00	-0.50	-0.05	0.02										
Phe	-0.01	0.25	0.06	-0.04	-0.20	0.04	0.25	0.13	-0.04									
Mg	-0.07	-0.09	-0.13	0.01	0.08	-0.05	-0.06	0.03	0.08	-0.11								
Na	-0.15	-0.03	0.14	-0.00	0.04	-0.08	-0.10	-0.11	0.14	-0.04	0.01							
Fe	0.18	-0.04	-0.04	0.02	-0.07	-0.07	0.11	0.14	-0.07	0.23	0.09	-0.04						
Fer	0.06	-0.06	-0.04	0.00	-0.02	-0.07	0.01	-0.07	-0.17	0.03	0.22	0.05	0.34					
U.Acid	0.05	-0.17	-0.01	-0.04	0.11	0.10	0.16	-0.10	-0.11	-0.09	-0.03	-0.10	0.12	0.08				
T.pr	0.12	0.03	0.07	-0.15	0.08	-0.01	0.03	-0.04	0.06	-0.13	0.04	0.03	-0.17	0.01	-0.27			
Alb	0.15	0.15	0.09	0.14	0.55	-0.10	0.07	0.03	-0.04	-0.19	-0.05	0.04	0.09	-0.05	0.17	0.19		
CRP	0.01	-0.01	-0.06	0.13	-0.03	0.00	-0.03	-0.03	0.01	0.07	-0.05	-0.10	0.23	-0.07	0.12	-0.34	0.02	

Figure (2): Global correlation matrix using Pearson's (r) coefficients.

- **PTH levels** showed extreme elevation, often exceeding 1000 pg/mL.
- **Phosphate retention** was significant due to reduced renal clearance.
- **Calcium levels remained near-normal**, suggesting compensatory bone resorption.

Correlation Analysis:

Key findings:

A- Positive correlation between albumin and creatinine (r = 0.55)
B- Negative correlation between total protein and CRP (r = −0.34)
C- Association between iron and ferritin (r = 0.34)

These findings indicate interplay between:

Renal dysfunction, Nutritional status, and Systemic inflammation:

This reflects a dysregulated endocrine feedback loop, where PTH remains elevated despite apparently adequate calcium levels.

Assessment of the Endocrine-Renal Feedback Axis:

To evaluate the integrity of the endocrine-renal axis, we performed bivariate linear regression analysis on the relationships between serum Parathyroid Hormone (PTH) and its primary regulators, Vitamin D and Calcium; this analysis was conducted to assess the presence and severity of secondary hyperparathyroidism, a hallmark complication where renal failure impairs Vitamin D activation and calcium homeostasis.

The regression analysis illustrates a profound state of metabolic derangement characterized by Secondary Hyperparathyroidism. The scatter plots show that a vast majority of the cohort exhibits profound Vitamin D deficiency (clustering significantly below 30 ng/mL) coinciding with pathologically elevated PTH levels, which frequently exceed 1,000 pg/mL and reach extreme values near 5,000 pg/mL. While the linear regression lines appear relatively flat in this visualization-primarily due to the extreme variance and outliers in the PTH data.

The clinical distribution confirms a severe failure of the endocrine feedback loop. The parathyroid glands are demonstrating massive overactivity despite Calcium levels appearing within a standard range for many patients, suggesting that the kidneys' inability to activate Vitamin D has led to uninhibited PTH secretion and potential bone mineral resorption to maintain serum Calcium.

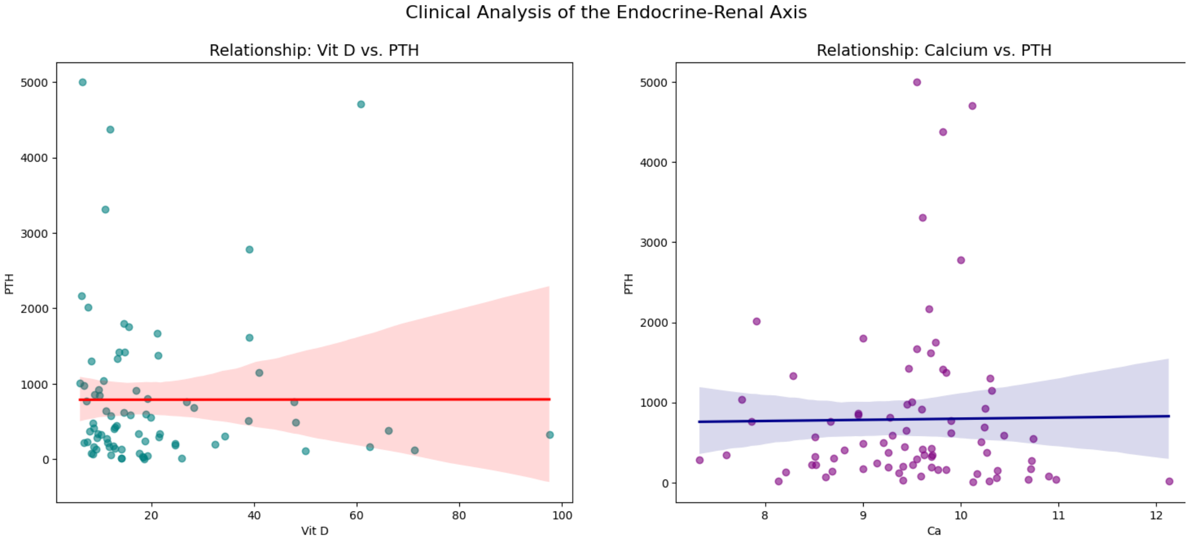


Figure (3): Clinical Analysis of the renal endocrine axis.

Regression analysis demonstrated:

1. Weak linear relationship between PTH and calcium.
2. Persistent PTH elevation despite calcium normalization.
3. Strong association between vitamin D deficiency and PTH elevation.

This confirms loss of physiological feedback control.

Renal Excretory Function and Azotemia Severity:

To quantify the severity and consistency of renal dysfunction within the cohort, we performed a joint-distribution analysis of serum Urea and Creatinine using a bivariate regression model and marginal frequency histograms; this approach was used to determine the degree of synchronized accumulation of nitrogenous waste products, which serves as a definitive indicator of the loss of glomerular filtration rate (GFR).

The joint plot demonstrates that the entire cohort is in a state of sustained azotemia, with the majority of Urea levels clustered between 100 and 250 mg/dL. The marginal histograms reveal a right-skewed distribution, indicating that while most patients are experiencing severe chronic renal failure, a subset of the population has progressed to a state of catastrophic renal collapse, with Urea values exceeding 700 mg/dL. The notably wide confidence interval and the presence of extreme outliers suggest an asynchronous accumulation of these waste products. Clinically, this indicates that in these patients, Urea levels may be further aggravated by factors such as dehydration or high protein catabolism, whereas Creatinine remains the more direct marker of the near-total loss of kidney filtration capacity.

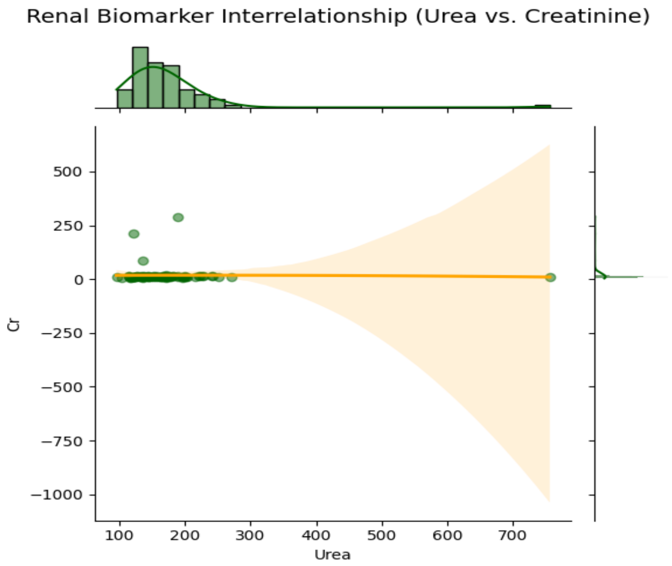


Figure (4): Renal Biomarker interrelationship

The Renal Dysfunction and Azotemia results shows:

a- Urea levels clustered between 100–250 mg/dL.
b- Extreme values (>700 mg/dL) observed in advanced cases.
c- Creatinine consistently elevated.

These findings confirm severe and sustained azotemia.

Nutritional Status and Systemic Inflammatory Burden:

To evaluate the nutritional and inflammatory status of the cohort, we performed a distribution analysis of serum Albumin and Total Protein alongside a multi-dimensional correlation between renal failure severity (Cr), systemic inflammation (CRP), iron stores (Fer), and parathyroid activity (PTH); this integrative approach was employed to identify the "Malnutrition-Inflammation Complex Syndrome" (MICS), which is a major predictor of morbidity in chronic kidney disease.

The results indicate a significant burden of systemic stress and biochemical instability.

While most patients maintain serum Albumin levels within a low-normal range (Mean: 4.10 g/dL), the Presence of outliers on the lower end suggests a risk of protein-energy wasting. The multi-dimensional scatterplot reveals a critical finding: several patients exhibit massive inflammatory spikes (CRP > 80 mg/L and up to 125 mg/L) that do not necessarily correlate with the highest levels of Creatinine, indicating that acute-on-chronic inflammation can occur at any stage of renal failure in this cohort. Furthermore, the largest data points (High Ferritin) coincide with these inflammatory spikes, confirming that Ferritin is acting as an acute-phase reactant rather than just a measure of iron stores. The color gradient highlights that extreme Secondary Hyperparathyroidism (yellow dots, PTH > 4000 pg/mL) is prevalent among those with established renal failure, illustrating the synchronized collapse of the renal-iron-endocrine axes.

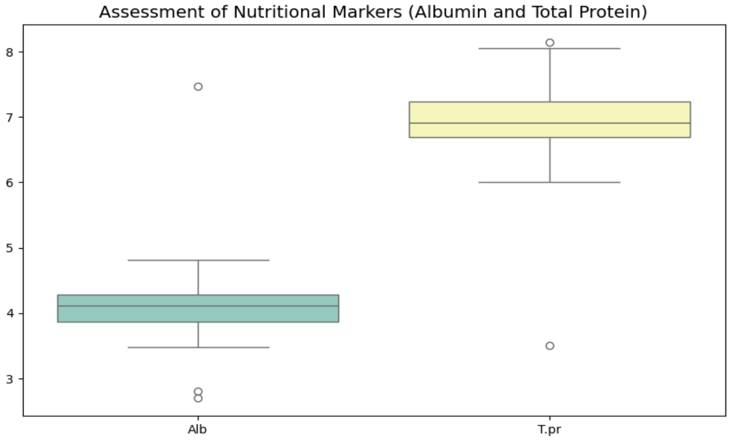


Figure (5): Assessment of Nutritional Markers Total Protein and albumin.

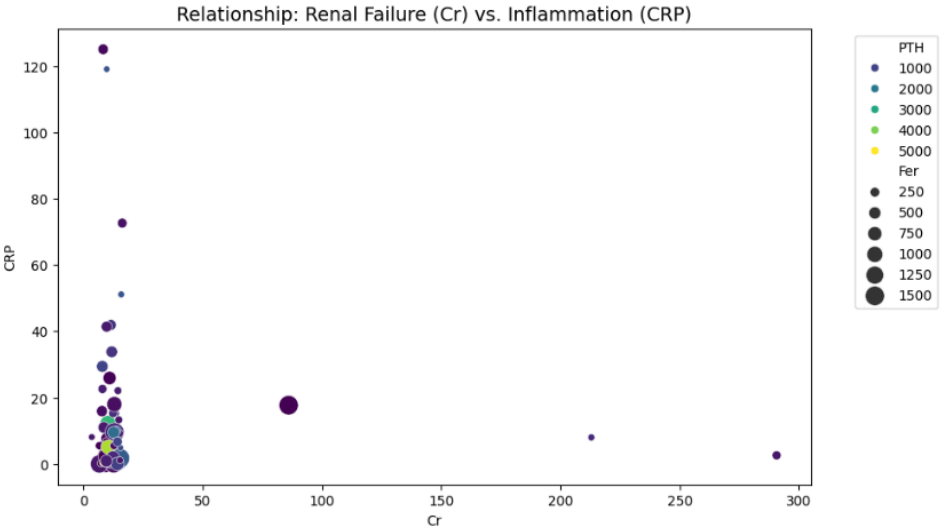


Figure (6): Relationship of renal failure and inflammation.

Inflammation and Nutritional Status shows:

a- Elevated CRP (mean 11.05 mg/L).
b- High ferritin levels (acute phase reactant).
c- Evidence of Malnutrition-Inflammation Complex Syndrome (MICS).

Table (3): Integrated Comparison of Calcium–Phosphate–PTH Axis and Associated Parameters in Renal Failure

Domain	Parameter(s)	Observed Finding	Statistical Significance	Pathophysiological Interpretation	Graph Reference
Calcium Homeostasis	Serum Calcium	9.50 mg/dL (near-normal)	p = 0.0399	Maintained via compensatory bone resorption despite CKD	Figure 4.3 (PTH vs Calcium)
Phosphate Balance	Serum Phosphate	6.49 mg/dL (elevated)	p < 0.001	Reduced renal excretion → hyperphosphatemia → PTH stimulation	Figure 4.1 (distribution frequency)
Parathyroid Function	PTH	789.26 pg/mL (markedly elevated)	p < 0.001	Secondary hyperparathyroidism due to CKD-MBD	Figure 4.2 & 4.3
Vitamin D Status	25(OH) Vitamin D	20.53 ng/mL (deficient)	p < 0.001	Reduced renal activation → decreased calcium absorption → ↑ PTH	Figure 4. 3 (PTH vs Vit D)
Renal Function	Creatinine, Urea	Cr: 17.93 mg/dL; Urea: 169.23 mg/dL	p < 0.001	Severe azotemia indicating advanced renal failure	Figure 4.4 (Urea vs Creatinine)
Electrolyte Balance	Potassium, Sodium, Chloride	K ↑, Na & Cl ~ normal	Mixed significance	Reflects impaired renal regulation and fluid shifts	Figure 4.1 (distribution frequency)
Inflammation	CRP	11.05 mg/L (elevated)	p < 0.001	Chronic systemic inflammation in CKD	Figure 4.6 (Inflammation Plot)
Iron Metabolism	Ferritin, Iron	Ferritin ↑ (372.58 ng/mL)	p < 0.001	Ferritin acting as acute-phase reactant	Figure 4.5
Nutritional Status	Albumin, Total Protein	Mildly reduced/low-normal	Significant	Protein-energy wasting, MICS	Figure 4.2 & 4.5
Endocrine Feedback	PTH vs Ca, Vit D	Weak/flattened relationships	—	Loss of feedback control in CKD	Figure 4.3

Table (4): Graph-wise Interpretation Summary.

Figure No.	Graph Type	Parameters Compared	Key Observation	Clinical Interpretation
Figure 1	Correlation Heatmap	All biochemical markers	Clustered associations (Cr–Alb, CRP–Protein)	Demonstrates systemic interaction (renal–inflammatory–nutritional axis)
Figure 4.3	Scatter + Regression	PTH vs Vitamin D	High PTH with low Vitamin D	Vitamin D deficiency drives SHPT
Figure 4.3	Scatter + Regression	PTH vs Calcium	Flat slope, wide dispersion	Loss of calcium-mediated feedback
Figure 4.4	Joint Plot	Urea vs Creatinine	High clustering with outliers	Confirms severe azotemia
Figure 4.6	Multi-dimensional Scatter	CRP, Ferritin, Cr, PTH	High CRP & ferritin clusters	Confirms MICS and inflammation-driven pathology

Baseline Biochemical Profile:

The cohort demonstrated significant deviations from normal physiology:

Table (5): These findings confirm advanced CKD with severe SHPT.

Parameter	Mean	p-value	Interpretation
Calcium	9.50 mg/dL	0.0399	Mildly elevated
Phosphate	6.49 mg/dL	<0.001	Elevated
PTH	789.26 pg/mL	<0.001	Markedly elevated
Vitamin D	20.53 ng/mL	<0.001	Deficient
Creatinine	17.93 mg/dL	<0.001	Severe renal failure

Calcium–Phosphate–PTH Axis Evaluation:

- PTH levels showed extreme elevation, often exceeding 1000 pg/mL.
- Phosphate retention was significant due to reduced renal clearance.
- Calcium levels remained near normal, suggesting compensatory bone resorption.

This reflects a dysregulated endocrine feedback loop, where PTH remains elevated despite apparently adequate calcium levels.

Discussion:

Pathophysiological Insights:

The findings align with established CKD-MBD mechanisms:

Phosphate retention due to reduced GFR stimulates PTH secretion, Vitamin D deficiency impairs calcium absorption, Parathyroid hyperplasia results in persistent PTH elevation and Bone resorption maintains serum calcium at the cost of skeletal integrity.

Interestingly, calcium levels remained within near-normal range despite severe SHPT. This reflects a compensatory equilibrium, often masking underlying bone disease.

This study highlights the profound disruption of the calcium–phosphate–PTH axis in renal failure patients, confirming the central role of chronic kidney disease–mineral and bone disorder (CKD-MBD) in the development of secondary hyperparathyroidism (SHPT). The biochemical profile of the studied cohort revealed markedly elevated levels of PTH, phosphate, creatinine, urea, ferritin, and C-reactive protein (CRP), together with significant vitamin D deficiency, indicating severe metabolic and endocrine dysregulation. These findings are consistent with established mechanisms of CKD-MBD (KDIGO, 2017; Moe et al., 2006).The significant elevation of PTH level (mean=789.26 pg/mL), reflecting severe secondary hyperparathyroidism. This agrees with previous studies showing progressive elevation of PTH as renal function declines (Arora et al., 2018; Chowdary et al., 2015). In CKD, reduced glomerular filtration rate leads to phosphate retention and decreased calcitriol synthesis, resulting in reduced intestinal calcium absorption and increased PTH secretion (Holick, 2007; Shah et al., 2024).

Comparison with Literature, its well know that the advanced CKD is associated with calcium, phosphorus, and magnesium distribution. As result increased parathyroid hormone secretion maintains serum calcium normal level by increasing calcium efflux from bone, renal calcium reabsorption, and phosphate excretion (Felsenfeld et al., 2015). Studies by Block et al. (2004) and KDIGO guidelines (2017) report similar elevations in PTH and phosphate in advanced CKD.

Vitamin D deficiency (20.53 ng/mL) was also evident, consistent with reduced renal activation of vitamin D and its role in PTH elevation (Dusso et al., 2005; Chen et al., 2022). In addition, vitamin D deficiency is consistently reported as a key driver of SHPT (Holick, 2007, Wang, H et al., 2025). Elevated CRP and ferritin support the presence of chronic inflammation, a known contributor to CKD progression, these findings are in the sync with the study reported by Tsai et al., 2012, and other study reported by Sultana et al; 2025.

Serum phosphate was significantly elevated (6.49 mg/dL), supporting its role as a major contributor to SHPT. Hyperphosphatemia stimulates PTH secretion and suppresses vitamin D activation, worsening mineral imbalance (Block et al., 2004). In the other hands, despite severe endocrine disturbances, serum calcium remained near normal (9.50 mg/dL), likely due to compensatory bone resorption under persistent PTH stimulation (Moe et al., 2006; Drüeke, 2021).

Renal function markers confirmed advanced renal failure, with markedly elevated creatinine (17.93 mg/dL) and urea (169.23 mg/dL), indicating severe loss of filtration capacity (Levey et al., 2009). Inflammatory markers (CRP and ferritin) were also elevated, suggesting chronic inflammation and possible Malnutrition-Inflammation Complex Syndrome (Kovesdy et al., 2022).

Correlation and regression analyses demonstrated disrupted physiological relationships between variables, particularly a weak feedback response between calcium and PTH, reflecting impaired parathyroid regulation in CKD (Brown, 2013).

Clinically, these findings emphasize that serum calcium alone is insufficient for assessing mineral metabolism in CKD patients. Comprehensive evaluation of phosphate, PTH, vitamin D, and inflammatory markers is essential. Therapeutic strategies include vitamin D supplementation, phosphate restriction, phosphate binders, and calcimimetics (KDIGO, 2017; Thadhani et al., 2021).

In the conclusion*,* the comprehensive analysis of this 80-patient cohort characterizes a state of profound physiological derangement, primarily driven by the catastrophic collapse of renal filtration capacity and the subsequent disintegration of the endocrine-mineral axis. The data provides definitive evidence of Secondary Hyperparathyroidism, where severe Vitamin D deficiency and impaired phosphate excretion have triggered a massive, compensatory surge in Parathyroid Hormone (PTH) levels to maintain calcium homeostasis. This endocrine failure is mirrored by advanced azotemia, with critically elevated Creatinine and Urea levels signaling near-total renal exhaustion. Furthermore, the multi-dimensional correlation analysis confirms that the cohort is burdened by Malnutrition-Inflammation Complex Syndrome (MICS), as evidenced by high-magnitude inflammatory spikes (CRP) and the conversion of Ferritin into an acute-phase reactant. Ultimately, these results illustrate that renal failure in this population is not an isolated organ pathology but a result of systemic metabolic derangement where the synchronized failure of the renal, iron, and endocrine axes creates a high-risk environment for bone mineral disease and cardiovascular stress, necessitating aggressive, multi-targeted clinical intervention.

In the other hands, the study demonstrates that secondary hyperparathyroidism in renal failure is characterized by a severe disruption of the calcium–phosphate–PTH axis, driven by:

Persistent hyperphosphatemia, profound vitamin D deficiency, and compensatory but maladaptive PTH elevation, despite near-normal calcium levels, the underlying endocrine imbalance is profound and clinically significant. Additionally, the coexistence of azotemia, inflammation, and nutritional disturbances highlights the systemic nature of CKD.

Clinical Implications:

- Reliance on serum calcium alone may underestimate disease severity.
- PTH and phosphate should be routinely monitored.

Early intervention with:

- Vitamin D analogues, Phosphate binders and Calcimimetics `is essential to prevent complications.

Clinical*:* Recommendation*:*

A multi-targeted approach addressing mineral metabolism, inflammation, and nutrition is crucial to improving patient outcomes and reducing CKD-related morbidity.

References:

1. Alazoumi, Khadega, et al. "Assessment of Calcium, Phosphorous Parathyroid Hormone in End Stage Renal Disease in Ibn Sina Teaching Hospital, Sirt." Libyan Medical Journal (2024): 172-177.
2. Ávila, M., Mora Sánchez, M. G., Bernal Amador, A. S., & Paniagua, R. (2025). The metabolism of creatinine and its usefulness to evaluate kidney function and body composition in clinical practice. Biomolecules, 15(1), 41.
3. Arora, K., et al. (2018). Correlation of parathyroid hormone levels with mineral metabolites in chronic kidney disease. Journal of Clinical and Diagnostic Research, 12(12), BC01–BC05.

4. Block, G. A., Klassen, P. S., Lazarus, J. M., Ofsthun, N., Lowrie, E. G., & Chertow, G. M. (2004). Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. Journal of the American Society of Nephrology, 15(8), 2208–2218.
5. Brown, E. M. (2013). Role of the calcium-sensing receptor in extracellular calcium homeostasis. Best Practice & Research Clinical Endocrinology & Metabolism, 27(3), 333–343.
6. Chen, X., et al. (2022). Vitamin D status and its association with parathyroid hormone in patients with chronic kidney disease. Journal of Steroid Biochemistry and Molecular Biology, 222, 106151. https://doi.org/10.1016/j.jsbmb.2022.106151
7. Chowdary, R. D., Nellutla, R., & Reddy, P. K. (2015). Relationship between parathyroid hormone and serum creatinine levels in chronic kidney disease patients. J Med Sci Res, 3(1), 17-21.
8. Cunningham, J., Locatelli, F., & Rodriguez, M. (2021). Secondary hyperparathyroidism: Pathogenesis, disease progression, and therapeutic options. Clinical Journal of the American Society of Nephrology, 6(4), 913–921.
9. Dusso, A. S., Brown, A. J., & Slatopolsky, E. (2005). Vitamin D. American Journal of Physiology–Renal Physiology, 289(1), F8–F28.
10. Drüeke, T. B. (2021). Hyperparathyroidism in chronic kidney disease. In Endotext. MDText.com.
11. Felsenfeld, A.J., Levine, B.S. and Rodriguez, M. (2015), Pathophysiology of Calcium, Phosphorus, and Magnesium Dysregulation in Chronic Kidney Disease. Semin Dial, 28: 564-577.
12. Guyton, A. C., & Hall, J. E. (2021). Textbook of Medical Physiology (14th ed.). Elsevier.
13. Holick, M. F. (2007). Vitamin D deficiency. New England Journal of Medicine, 357(3), 266–281.
14. Holick, M. F. (2020). Vitamin D deficiency. The New England Journal of Medicine, 357(3), 266–281. https://pmc.ncbi.nlm.nih.gov/articles/PMC3944129/
15. KDIGO. (2017). Clinical practice guideline update for chronic kidney disease–mineral and bone disorder (CKD-MBD). Kidney International Supplements, 7(1).
16. KDIGO CKD–MBD Work Group. (2024). KDIGO clinical practice guideline for chronic kidney disease–mineral and bone disorder (CKD–MBD). Kidney International Supplements.
17. Koeppen, B. M., & Stanton, B. A. (2021). Renal Physiology (5th ed.). McGraw-Hill Education.
18. Kovesdy, C. P. (2022). Mineral metabolism and secondary hyperparathyroidism in chronic kidney disease. Kidney International, 79(9), 953–967.
19. Khundmiri, Syed Jalal, Rebecca D. Murray, and Eleanor Lederer. "PTH and vitamin D." Comprehensive Physiology 6.2 (2016): 561-601.
20. Levey, A. S., Stevens, L. A., Schmid, C. H., et al. (2009). A new equation to estimate glomerular filtration rate. Annals of Internal Medicine, 150(9), 604–612.
21. Levey, A. S., Coresh, J., Greene, T., Stevens, L. A., Zhang, Y. L., Hendriksen, S., … & CKD-EPI. (2020). GFR estimation updates. Annals of Internal Medicine.
22. Moe, S., Drüeke, T., Cunningham, J., Goodman, W., Martin, K., Olgaard, K., … & Eknoyan, G. (2020). CKD–MBD classification update. Kidney International.
23. Moe, S., et al. (2006). Definition, evaluation, and classification of renal osteodystrophy. Kidney International, 69(11), 1945–1953.
24. Maranduca, Minela Aida, et al. "The molecular mechanisms underlying the systemic effects mediated by parathormone in the context of chronic kidney disease." Current Issues in Molecular Biology 46.5 (2024): 3877-3905.
25. Mazzaferro, Sandro, et al. "Pathophysiology and therapies of CKD-associated secondary hyperparathyroidism." Clinical Kidney Journal 18. Supplement_1 (2025): i15-i26.
26. Romagnani, Paola, et al. "chronic kidney disease." Nature reviews Disease primers 11.1 (2025): 8.
27. Ross, A. C., Taylor, C. L., Yaktine, A. L., & Del Valle, H. B. (2021). Dietary Reference Intakes for Calcium and Vitamin D. National Academies Press.
28. Shlipak, M. G., Katz, R., Kestenbaum, B., Fried, L. F., Newman, A. B., Siscovick, D. S., ... & Sarnak, M. J. (2009). Rate of kidney function decline in older adults: a comparison using creatinine and cystatin C. American journal of nephrology, 30(3), 171-178.
29. Shah, A., Hashmi, M. F., & Aeddula, N. R. (2024). Chronic kidney disease–mineral bone disorder. In StatPearls. StatPearls Publishing.
30. Sultana, S., Islam, M. J., Lifa, T. H., & Khaled, M. (2025). Association of Anemia and Inflammatory Markers with Chronic Kidney Disease among Elderly Patients. Asia Pacific Journal of Surgical Advances, 2(4), 181-186.
31. Thadhani, R., et al. (2021). CKD–MBD and vitamin D metabolism updates. Journal of Nephrology.
32. Tsai, Shin-Hwa, et al. "Secondary hyperparathyroidism in chronic kidney disease: A narrative review focus on therapeutic strategy." Clinical Medicine 24.5 (2024): 100238.

33. Tsai, Y. C., Hung, C. C., Kuo, M. C., Tsai, J. C., Yeh, S. M., Hwang, S. J., ... & Chen, H. C. (2012). Association of hsCRP, white blood cell count and ferritin with renal outcome in chronic kidney disease patients. PloS one, 7(12), e52775.
34. Wang, H., Yuan, T., Wu, W., & Ou, S. (2025). Vitamin D and chronic kidney disease: Mechanisms, clinical implications, and future perspectives. Frontiers in Medicine, 12, 1643415.
35. Yan, Ming-Tso, Chia-Ter Chao, and Shih-Hua Lin. "Chronic kidney disease: strategies to retard progression." International journal of molecular sciences 22.18 (2021): 10084.