Sumer Journal for Pure Science (ISSN: 2790-7031)
SJPS 2026 (June), Vol. 5, No. 1, p.p.: 337-353

Diagnostic Performance of Renal Function and Mineral Metabolism Biomarkers in Female Patients with Kidney Failure

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Abstract

The last stage of chronic kidney disease is kidney failure, which is characterized by critical alterations in the renal system's ability to excrete waste, as well as disruptions to body's control mechanisms of the mineral and endocrine system. Urea and creatinine are still valuable markers in assessing renal functions, as changes in calcium and parathyroid hormone (PTH) indicate the beginning of chronic kidney disease and mineral and bone disorder. Thus, these markers can be valuable in diagnosing kidney failure and monitoring disease progression.

Objective: The study aimed to analyze the changes in renal function and mineral metabolism markers in female patients with kidney failure and the potential of these changes to support a diagnosis.

Methodology : A case-control study was conducted at Nasiriyah Teaching Hospital, in Thi-Qar Governorate, Iraq. The study included 200 female participants in the age range of 45 to 55, of which 100 were kidney failure patients, and the other 100 were apparently healthy and served as controls. Standard laboratory tests were performed, and the levels of serum urea, creatinine, calcium, and parathyroid hormone were measured. Data are presented as mean ± standard deviation. Group comparisons were performed using the independent samples t-test. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic potential of the biomarkers. A p-value of less than 0.05 was considered statistically significant.

Results: Kidney failure patients exhibited significantly higher serum urea and creatinine levels compared with healthy controls (110.6 ± 22.8 vs. 27.9 ± 6.3 mg/dL and 6.5 ± 1.9 vs. 0.89 ± 0.19 mg/dL, respectively; $P < 0.001$). Serum calcium levels were significantly reduced in patients (7.4 ± 0.5 mg/dL) compared with controls (9.6 ± 0.7 mg/dL; $P < 0.001$), while serum PTH levels were markedly elevated in the patient group (461.2 ± 133.4 vs. 44.3 ± 16.6 pg/mL; $P < 0.001$). ROC analysis showed high areas under the curve for urea, creatinine, and PTH, demonstrating excellent diagnostic performance. In contrast, calcium showed inverse discriminatory behavior reflecting hypocalcemia in kidney failure.

Conclusions: Kidney failure in female patients is linked with pronounced renal deficiency coupled with considerable imbalances in mineral metabolism, as indicated by increased levels of urea, creatinine, and PTH, and decreased levels of serum calcium. Urea, creatinine, and PTH had considerable diagnostic value in differentiating patients with kidney failure from non-affected subjects, whereas calcium had additional diagnostic value in assessing the status of metabolic imbalances. The findings validate the importance of assessing both renal and mineral metabolism for the diagnosis of kidney failure.

Keywords: Kidney failure, Chronic kidney disease, Renal function biomarkers, Parathyroid hormone.

الأداء التشخيصي للمؤشرات الحيوية لوظائف الكلى وأيض المعادن لدى المريضات المصابات بالفشل الكلوي: دراسة حالة وضبط

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الخلاصة

الخلفية: تُعد المرحلة الأخيرة من مرض الكلى المزمن هي "الفشل الكلوي"، والذي يتميز بتغيرات حرجة في قدرة الجهاز الكلوي على طرح الفضلات، فضلاً عن اختلالات في آليات تحكم الجسم في نظام المعادن والغدد الصماء. ولا يزال اليوريا والكرياتينين مؤشرين قيمين في تقييم وظائف الكلى، كما تشير التغيرات في مستويات الكالسيوم وهرمون الغدة جار الدرقية (PTH) إلى بداية مرض الكلى المزمن والاضطرابات المعدنية والعظمية المرتبطة به. وبالتالي، يمكن أن تكون هذه المؤشرات ذات قيمة في تشخيص الفشل الكلوي ومراقبة تطور المرض.

الهدف : هدفت الدراسة إلى تحليل التغيرات في مؤشرات وظائف الكلى وأيض المعادن لدى المريضات المصابات بالفشل الكلوي، ومدى قدرة هذه التغيرات على دعم التشخيص.

المنهجية : أُجريت دراسة "حالة وضبط" في مستشفى الناصرية التعليمي بمحافظة ذي قار، العراق. شملت الدراسة 200 مشاركة من الإناث ضمن الفئة العمرية من 45 إلى 55 عاماً، من بينهن 100 مريضة بالفشل الكلوي، و100 أخريات أصحاء ظاهرياً كمجموعة ضابطة. أُجريت الاختبارات المختبرية القياسية، وقِيست مستويات اليوريا، والكرياتينين، والكالسيوم، وهرمون الغدة جار الدرقية في المصل. عُرضت البيانات في صورة (المتوسط الحسابي ± الانحراف المعياري). وأُجريت مقارنات المجموعات باستخدام اختبار (t) للعينات المستقلة. كما استُخدم تحليل منحنى خصائص التشغيل المتلقي (ROC) لتقييم القدرة التشخيصية للمؤشرات الحيوية، واعتُبرت القيمة الاحتمالية (P-value) الأقل من 0.05 دالة إحصائياً.

النتائج :أظهرت المريضات المصابات بالفشل الكلوي مستويات أعلى بكثير من اليوريا والكرياتينين في المصل مقارنة بالأصحاء (22.8 ± 110.6) مقابل (6.3 ± 27.9)ملجم/ديسيلتر، و (1.9 ± 6.5) مقابل (0.89 ± 0.19)ملجم/ديسيلتر على التوالي؛ ($P < 0.001$).وانخفضت مستويات الكالسيوم في المصل بشكل ملحوظ لدى المريضات (0.5 ± 7.4) ملجم/ديسيلتر مقارنة بالمجموعة الضابطة (0.7 ± 9.6) ملجم/ديسيلتر؛ ($P < 0.001$)، بينما ارتفعت مستويات هرمون (PTH) في المصل بشكل حاد في مجموعة المريضات (461.2 ±133.4)مقابل (16.6 ± 44.3) بيكوجرام/مل ؛ ($P < 0.001$). أظهر تحليل (ROC) مساحات كبيرة تحت المنحنى (AUC) لكل من اليوريا والكرياتينين وهرمون(PTH) ، مما يثبت أداءً تشخيصياً ممتازاً. وفي المقابل، أظهر الكالسيوم سلوكاً تمييزياً عكسياً يعكس حالة نقص كالسيوم الدم في الفشل الكلوي.

الاستنتاجات : يرتبط الفشل الكلوي لدى المريضات بقصور كلوي واضح مقترن باختلالات كبيرة في أيض المعادن، كما يتضح من زيادة مستويات اليوريا والكرياتينين وهرمون(PTH) ، وانخفاض مستويات الكالسيوم في المصل. تمتلك اليوريا والكرياتينين وهرمون (PTH) قيمة تشخيصية كبيرة في تمييز مريضات الفشل الكلوي عن غير المصابات، بينما يمتلك الكالسيوم قيمة تشخيصية إضافية في تقييم حالة الاختلالات الأيضية. وتؤكد النتائج أهمية تقييم كل من الوظائف الكلوية وأيض المعادن لتشخيص الفشل الكلوي.

1. Introduction

Recent studies have demonstrated how chronic kidney diseases pose a significant threat to global health as a growing concern. It is a major contributor to mortality and morbidity as well as the cost of health care. Recent data from the Global Burden of Disease (GBD) 2023 suggests that hundreds of millions of adults across the globe are suffering from CKD. It ranks as one of the highest casuses of mortality, with it's contribution to the disability adjusted years of life lost (DALY) increasing across all levels of income and region [1, 2]. Increased population and increased incidence of the primary drivers of chronic kidney disease such as diabetes, hypertension, and obesity coupled with increased cardimetabolic risk are the primary determinants that are accelerating the renal injury and progression [1]. Most middle and low income countries are suffering from a lack of resources to offer timely screening and specialist nephrology services, which leads to late presentations. This fuels the progression to end stage kidney disease (ESKD) resulting in an increased need for renal replacement therapy (RRT) and increasing the economic and societal burdens of CKD [1].

CKD is an indicator of abnormalities of kidney structure or function lasting more than three months, with health consequences. It's classified by cause, glomerular filtration rate (GFR) category, and albuminuria category (CGA framework) [3]. The latest update of the KDIGO 2024 guidelines highlight the importance of albuminuria and estimated GFR (eGFR) for risk-based assessments, and how they contribute to prognosis and clinical decision-

making [4]. Although CKD has no clear symptoms in its initial stages, it progressively leads to clinical syndrome of kidney failure (end stage kidney disease) where a patient's life is reliant on a dialysis or transplant. This is a consequence of the loss of kidney function, leading to an inadequate clearance of metabolic waste, disturbed mineral balance, and endocrine dysfunction [4]. CKD is also closely associated with other conditions such as cardiovascular disease, increased infection risk, osteoporosis, and a decline in overall health, which results in harmful consequences for the affected population [1,4].

Serum creatinine is foundational for estimating GFR and CKD monitoring and thus builds the basis for guideline staging. In spite of the fact that it is influenced by factors including, but not limited to, muscle mass, diet, and catabolism, it continues to be employed. This is likely due to the fact that it is inexpensive, widely used, and integrated into eGFR equations [4]. Reflecting urea, which is not excreted when there is diminished renal function, it is understandable that urea and creatinine (often referred to as BUN), which is another urea biomarker used in the same settings, provide a complementary renal function and azotemia severity assessment in advanced renal disease. Especially in underdeveloped settings where advanced biomarkers are not available, their contribution to CKD assessment is invaluable[4-7].

Besides filtration markers, imbalances in mineral metabolism are complications of CKD that demonstrate an exacerbation in relation to the degree of renal insufficiency. Characteristically, CKD–mineral and bone disorder (CKD-MBD) is a systemic disorder with a triad defining it: (i) abnormalities of calcium, phosphate, parathyroid hormone (PTH), and vitamin D metabolism; (ii) alterations in bone turnover, mineralization, volume, linear growth or strength; and (iii) the presence of vascular or extra-skeletal calcification [6–9]. The clinical parameters KDIGO has outlined for CKD-MBD stipulate that, in the advanced stages of CKD and dialysis patients, calcium and PTH need to be monitored more closely due to the frequency of derangements and their clinical significance [6,7,10]. The metabolic derangements extend far beyond lab abnormalities; they are involved in the etiology of bone disease, fractures, vascular calcification, increased (through calcification) arterial stiffness, cardiovascular events, and an increase in mortality [6–11].

Secondary hyperparathyroidism (SHPT) stands out as one of the most important illnesses brought on by CKD's most important clinical complications, and features an increase in the blood concentration of the parathyroid hormone (PTH). The explainable origin of paradoxical episodes of SHPT is complex, and is characterized by the elements of phosphate retention, a decrease in renal secretion of the active form of vitamin D (calcitriol), an elevation of the parathyroid hormone (PTH) due to hypocalcemia, the respective modulation of the calcium-sensing receptor, and an incremental hyperplasia of the parathyroid [6,9,12]. The reduction in nephron mass triggers a decrease in phosphate excretion while simultaneously increasing the retention of phosphate, leading to a reduction in p calcium and an increase of p calcitriol, thus stimulating secretion of parathyroid hormone as a compensatory mechanism [6,10-12]. Over the course of these processes, the relentless stimulation raises the hyperplasia of the parathyroid gland which, in turn, raises p PTH to a significant level, and this has become the norm to observe in instances of renal failure [6,9]. The hypocalcemia associated with CKD is classically attributed to a reduction in PTH production concurrent with calcitriol in addition to diminished intestinal absorption of calcium, and the combined elements of phosphate retention along with disordered bone remodeling and the respective modulation reinforces the disorder of the elements of the mineral balance [6,9]. Recent literature highlight the less recognized HPT syndrome the bone, and the HPT syndrome the calcification outside of the skeleton, and the increased risk

on the cardiovascular system, thus, these become the phenomena qualifying this situated within monitoring and intervention treatment [9,11].

Considering the systemic complications associated with CKD, along with the clinical relevance of both the filtration markers and the elements pertaining to the metabolism of minerals, it seems plausible that assessing urea, creatinine, calcium, and PTH together may yield more valuable insights into the biochemical constituents of kidney failure. Within a hospital context, these tests are typically easy to conduct, inexpensive, and straightforward to assess within standard clinical workflows. Moreover, the changes in their direction and magnitude mirror the essence of the pathophysiological changes in the context of renal failure: the accumulation of nitrogenous waste (urea), filtration deficiency (creatinine), imbalance of minerals (calcium), and end organ over / under PTH activity. [4–6,13] From the translational research perspective, it has certain merits to evaluate these parameters in terms of differentiating kidney failure from non-failure, and thereby offer a preliminary understanding of the differentiation, to guide the refinement of clinical practice in the most.
Receiver Operating Characteristics (ROC) analysis provides information summarizing the sensitivity and specificity of biomarker performance assessments. The Area Under the Curve (AUC) provides a summary of discriminatory performance for the test, while the calculation of the optimal Youden index cut-off can help identify clinically actionable thresholds. In research pertaining to Chronic Kidney Disease (CKD) and Kidney Failure, ROC analysis is often utilized to evaluate the efficacy of various biochemical markers in differentiating diseased states, assisting in the stratification of risk, and suggesting thresholds to be a compromise between sensitivity and specificity for given target populations. However, cut-off points suggested by ROC analysis can be dependent on the given population and the context in which the analysis is done, thus highlighting the importance of in-country, local data, and the need for careful consideration of the cut-off in relation to the specific clinical goal and the prevalence of the disease [10-14].

Studies based in hospitals are important in Iraq and Iraq-like countries for documenting the patterns of biochemicals of failure of the kidneys and related complications of the condition and for providing evidence for local clinical practice. This is why the current study examines adult women and caregives the details of biochemicals and compares patients of kidney failure and healthy controls. The study is focusing on urea, creatinine, calcium, and PTH, which are all common biochemicals. This study is attempting to integrate the routine filtration markers and the parameters related to CKD-MBD. The hope here is to demonstrate excretory impairment and the accompanying endocrine–mineral disorders of kidney failure. This study is recommending biochemical profiling, supporting diagnostic discrimination, and justification for more sophisticated studies to assess the clinical and biochemical consequences of the disease to recommend CKD-MBD markers, as outlined in the more recent gold-standard documents. [6,8,11-17].

2. Materials and Methods

2.1. Study Design and Setting

This **case–control study** was conducted at **Nasiriyah Teaching Hospital**, Thi-Qar Governorate, Iraq, between **October 1, 2025 and April 1, 2025**.

2.2. Study Population

A total of **200 female participants** were enrolled in the present study and categorized into two groups:

- **Patient group (n = 100):** women with a confirmed diagnosis of **kidney failure**.
- **Control group (n = 100):** apparently healthy women with no history of renal disease.

All participants were aged between **45 and 55 years**.

2.3. Inclusion and Exclusion Criteria

Inclusion criteria comprised female subjects aged 45–55 years. Patients had a confirmed diagnosis of kidney failure, while controls were clinically healthy.

Exclusion criteria included women with:

- Hypertension
- Malignant tumors
- Acute or chronic infectious diseases

2.4. Blood Sample Collection and Processing

Approximately **6 mL of venous blood** was collected from each participant under aseptic conditions into plain tubes. Samples were allowed to clot at room temperature and then centrifuged at **3000 rpm for 10 minutes**. The resulting serum was separated and stored at **−20°C** until biochemical analysis.

2.5. Biochemical Analysis

Serum samples were analyzed for:

- **Renal function markers:** urea and creatinine
- **Serum calcium (Ca^{2+})**
- **Parathyroid hormone (PTH)**

All analyses were performed according to the manufacturers' instructions.

2.6. Data Collection

Demographic and clinical data, including age, diagnosis, and laboratory findings, were recorded using a standardized data collection sheet.

2.7. Statistical Analysis

Statistical analyses were performed using appropriate statistical software. Data were expressed as **mean ± standard deviation (SD)**. Comparisons between groups were

conducted using the **independent samples t-test**. A **p-value < 0.05** was considered statistically significant.

Ethical Considerations

The study protocol was approved by the local ethical committee, and **written informed consent** was obtained from all participants prior to sample collection.

3. Results

The biochemical parameters measured in the present study are summarized in Table 1. Statistically significant differences were observed between kidney failure patients and healthy controls for all investigated parameters ($P < 0.001$).

Table 1- The biochemical parameters measured in the present study

Parameter	Healthy controls (Mean ± SD)	Kidney failure patients (Mean ± SD)	Statistical significance
Urea (mg/dL)	27.9 ± 6.3	110.6 ± 22.8	P < 0.001
Creatinine (mg/dL)	0.89 ± 0.19	6.5 ± 1.9	P < 0.001
Calcium (Ca^{2+}) (mg/dL)	9.6 ± 0.7	7.4 ± 0.5	P < 0.001
Parathyroid hormone (PTH) (pg/mL)	44.3 ± 16.6	461.2 ± 133.4	P < 0.001

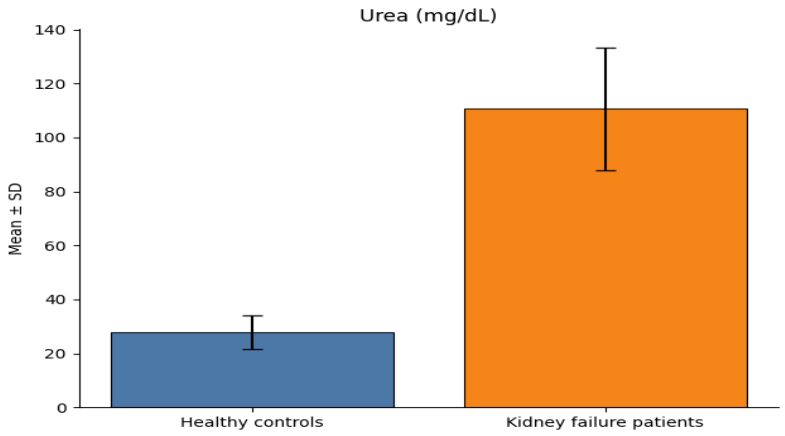

Figure -1 Comparison of serum urea levels between healthy controls and kidney failure patients.

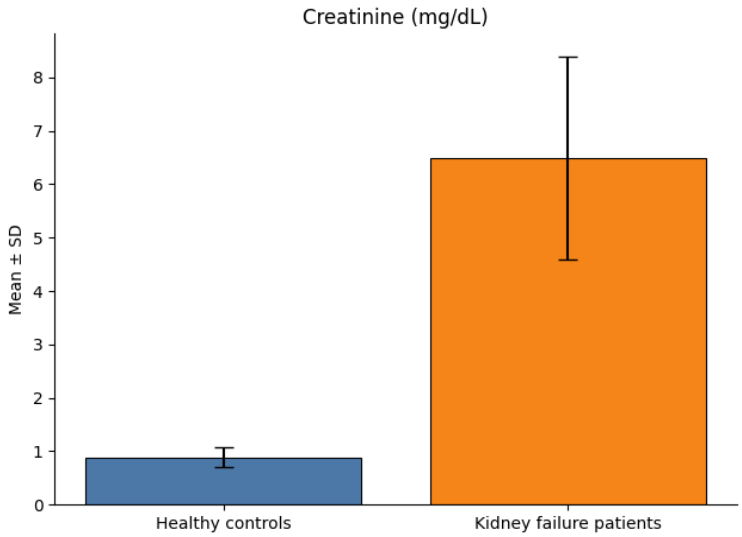

Figure -2 Serum creatinine levels in healthy controls and kidney failure patients.

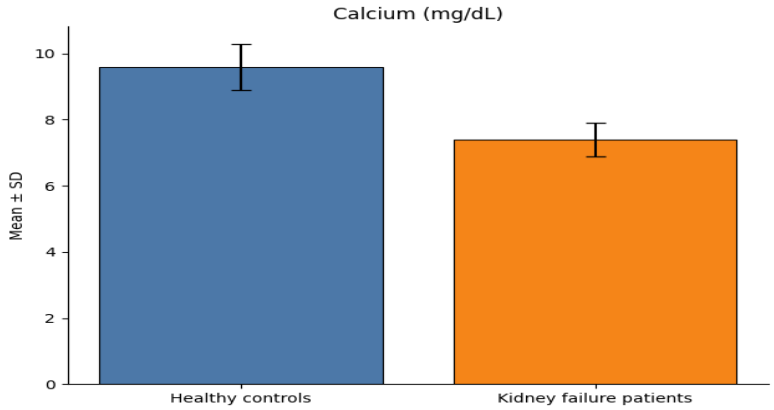

Figure -3 Comparison of serum calcium levels between study groups.

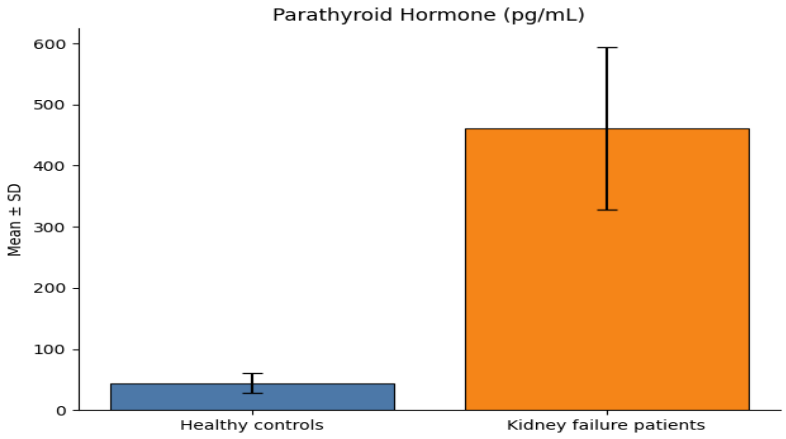

Figure -4 Serum parathyroid hormone (PTH) levels in healthy controls and kidney failure patients.

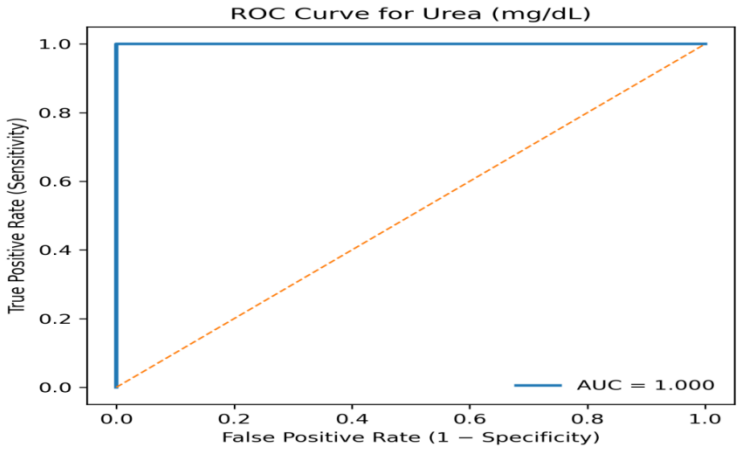

Figure -5 Receiver operating characteristic (ROC) curve of serum urea for distinguishing kidney failure patients from healthy controls.

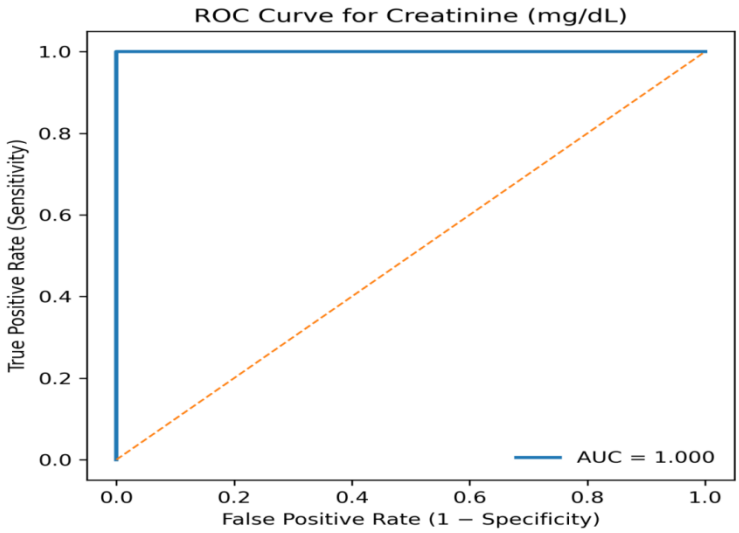

Figure -6 Receiver operating characteristic (ROC) curve of serum creatinine for differentiating kidney failure patients from healthy controls.

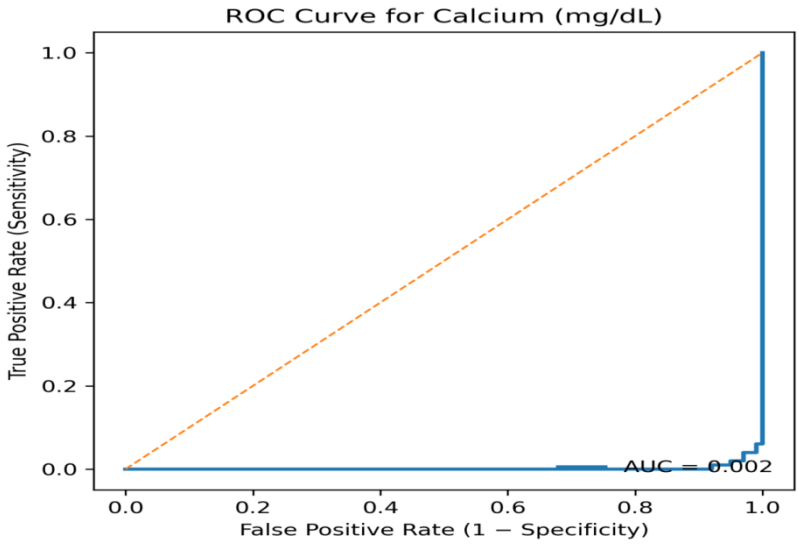

Figure -7 Receiver operating characteristic (ROC) curve of serum calcium for discriminating kidney failure patients from healthy controls.

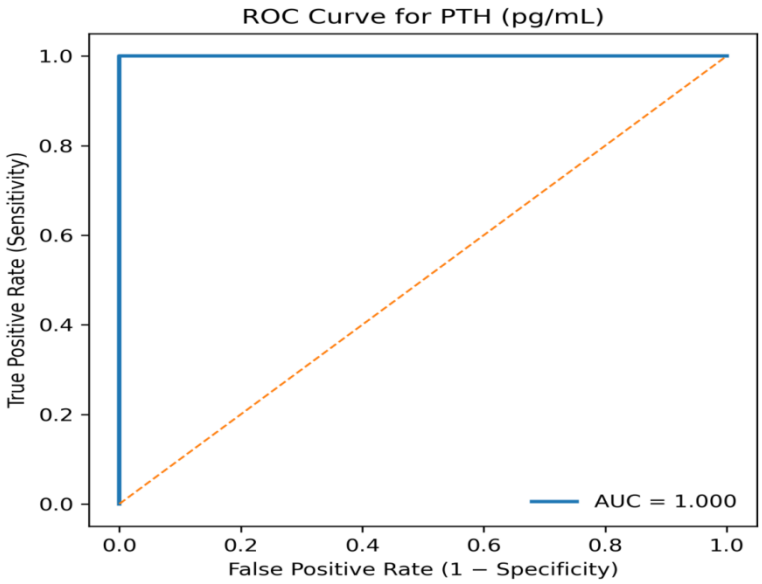

Figure -8 Receiver operating characteristic (ROC) curve of serum parathyroid hormone (PTH) for differentiating kidney failure patients from healthy controls.

Serum urea levels were markedly elevated in kidney failure patients compared with healthy controls (110.6 ± 22.8 mg/dL vs. 27.9 ± 6.3 mg/dL, $P < 0.001$), as illustrated in Figure 1. This pronounced increase reflects impaired renal excretory function and accumulation of nitrogenous waste products in patients with renal failure. Concentrations of serum creatinine were also significantly higher in the patient group (6.5 ± 1.9 mg/dL) than in the control group (0.89 ± 0.19 mg/dL) ($P < 0.001$), shown in Figure 2. Elevated creatinine levels confirm the reduction in glomerular filtration rate and the severity of renal dysfunction in this patient cohort. Conversely, there was a remarkably large decrease of serum calcium levels among the kidney patients compared to the healthy controls (7.4 ± 0.5 mg/dL vs 9.6 ± 0.7 mg/dL, $P < 0.001$), as shown in Figure 3. In renal failure, hypocalcemia is usually due to insufficient renal conversion of vitamin D, diminished calcium absorption, and the unnecessary retention of phosphates. Moreover, Figure 4 shows a significant increase in the levels of serum parathyroid hormone (PTH) in patients with kidney failure (461.2 ± 133.4 pg/mL) compared to the healthy controls (44.3 ± 16.6 pg/mL) ($P < 0.001$). This increase is due to the abnormality of having secondary hyperparathyroidism which is a common complication of chronic kidney disease and is a result of hypocalcemia with altered metabolism of the minerals.

To analyze the potential discrimination ability of the serum biomarkers in differentiating the patients with kidney failure from the healthy controls, we conducted receiver operating characteristic (ROC) curve analysis. As illustrated in Figures 5 and 6, serum urea and serum creatinine possessed exceptional discrimination capability with the areas under the curve (AUCs) approaching 1, implying both high sensitivity and specificity. Calcium serum showed diagnostic behavior in the reverse direction (Figure 7) where concentrations are in fact lower in the patients with kidney failure than in the controls, which, despite the inverse direction of the change, is clinically important. Moreover, serum PTH showed again, a remarkable high diagnostic capability (Figure 8), leading to a high AUC and again, in strong support of distinguishing patients with kidney failure from the healthy population. Overall, urea, creatinine, and PTH a part from calcium, can reliably serve as

biomarkers for kidney failure while calcium also indicates the associated impairment of mineral metabolism.

4. Discussion

The last phase of chronic kidney disease (CKD) is kidney failure. This stage indicates the loss of the kidneys' ability to perform any of its functions, including the excretory functions. In the current case-control study, kidney failure patients exhibited a stark difference against healthy controls (Table 1) concerning biochemical patterns: (i) blood urea and creatinine levels were elevated as shown in (Figures 1-2), (ii) blood calcium levels were significantly low (hypocalcemia), shown in Figure 3, and (iii) there was a significant rise in parathyroid hormone (PTH) levels, demonstrated in Figure 4. As a whole, the above pieces of evidence corroborate the current state of the art on the systems of CKD, and the systems in the surrounding the framework, due particularly to the disorder of bone and mineral as CKD-MBD (CHronic Kidney Disease-Mineral and Bone Disorder) and secondary type 2 hyperparathyroidism (SHPT) [18-22].Dysfunction of renal excretory system: Urea and Creatinine

Patients of kidney failure have abnormally high values of both urea and creatinine (as shown in Table 1 and Figures 1 and 2). This reflect significant reduction in clearance of nitrogenous waste due to more serious failure in glomerular filtration. Serum creatinine is the most common utilized parameter in the assessment of renal function and is the primary determinant in estimating the GFR in various international guidelines and regulations [23, 24]. Even though there are non-renal factors, in addition to, muscle mass and nutritive factors that impact the value of creatinine, the increase of creatinine observed in the case (as shown in Table 1) is commonly expected in more advanced stages of renal failure and aligns with the expectancy in kidney failure states [23-25]. Inversely, renal urea excretion deficient states culminate in higher retention of urea, however, more protein intake or a catabolic condition can inverse the retention. Regardless of these drawbacks, Urea and creatinine collectively characterize marginally in laboratory diagnostics, their differentiation is more often employed to monitor the severity of a disease especially in the developing countries where other advanced and costly markers are unobtainable [23, 26, 27]. Clinically, significant increase in the distance between the groups is evidence that these parameters can be relied upon to differentiate patients with renal failure from the control healthy population in this particular analysis (Figures 1–2).

The present results hold merit concerning the implications for the stratification and monitoring of patients. The KDIGO 2024 CKD guideline seeks to standardize and encourages practitioners to evaluate kidney functions basin and contextualize the lab results and the clinical picture [28] When brought into the context of real-life practice, the urea and creatinine levels may provide a basis for referral to other clinical processes, interventional/ replacement therapies by the kidneys, and adjust medications concerning the complications of uramia, and evaluate how far along the uremia complications the patient is. Therefore, the current findings restate the importance of the clinical scenario where urea and creatinine levels provide important lab values for evaluating how far along a patient is in terms of renal failure.

Disturbance in mineral metabolism: the hypocalcemia and CKD-MBD phenotype

An important aspect of the current study is the lower serum calcium level in kidney failure patients (Table 1; Figure 3). Hypocalcemia constitutes a part of CKD-MBD, and as kidney function declines, it becomes more common and more clinically important [22-25]. KDIGO CKD-MBD recommends that calcium, phosphate, PTH, and vitamin D should be abnormal, as it captures core biochemical signals in CKD-MBD that are important in lieu of altered bone turnover and vascular calcification, in the downstream consequences [23,24]. The change in question, i.e., lower calcium in patients is undoubtedly plausible and congruent with the mechanisms at play.

Nephron mass is lost progressively, which lessens renal 1α-hydroxylase activity and in turn lowers levels of 1,25-dihydroxyvitamin D (calcitriol), which then leads to an intestinal calcium absorption deficiency. Additionally, phosphate retention can largely contribute to the declines serum calcium and can further escalate the compensatory response on the endocrine [23,26]. More recently, the calcium disturbance report at the Kidney International Conference underscored the complexity and interdependence of CKD-MBD and the various elements within the phosphate-vitamin D-bone turnover-therapeutic (binders, vitamin D analogs, calcimimetic) continuum, thereby underscoring the need to consider calcium disturbances in relation to the full CKD-MBD phenotype and the individual [25].

Hypocalcemia in kidney failure may cause neuromuscular dysfunction and reflects the overall mineral imbalance associated with CKD-MBD, which is a complication of chronic kidney disease. Total serum calcium can be confounded by the concentration of serum albumin; therefore, future studies can improve by adjusting for albumin in serum calcium, using calcium measurements, particularly in patients who are hospitalized or malnourished. Despite the above, the observed cohort's significant calcium decrease remains adequate evidence for the presence of a clinically significant mineral imbalance consistent with the syndrome of CKD-MBD.

An important endocrine observation processes document is PTH level. In table 1 and figure 4 we show the drastic PTH levels of the kidney failure patients. De la Cruz et al. argue that the Under-active parathyroid hormone production and consequent parathyroid gland hyperplasia [31,32] during SHPT may occur due to the phosphate retention, hypocalcemia, subnormal calcitriol, bone resistance to PTH, and progressive parathyroid hyperplasia. The PTH levels from the SHPT and the range from the present research is congruous with current research regarding SHPT and its correlating bone morbidity and vascular calcification to the population of patients with CKD [31-33]. SHPT and its correlate have adverse effects, including but not limited to bone pain and fractures, cardiovascular events and a higher incidence of mortality, especially in the population of patients enduring dialysis. Most recent authoritative works in the area of CKD-MBD indicate that PTH levels must be evaluated in conjunction with calcium and phosphate levels and that repeated aggressive suppression of PTH may have deleterious effects, especially for patients with CKD and dialysis [23,24,33].

In the present cohort, the combination of low calcium and high PTH (Table 1) supports a mechanistic link consistent with SHPT physiology. However, because phosphate and vitamin D metabolites were not assessed, the full CKD-MBD biochemical phenotype

could not be completely characterized. Future studies incorporating phosphate, 25-hydroxyvitamin D, and (if feasible) fibroblast growth factor 23 (FGF-23) could provide deeper mechanistic insight and allow better alignment with contemporary CKD-MBD frameworks [24,33].

The substantial separation between controls and kidney failure patients for urea, creatinine, and PTH (Figures 1–2 and Figure 4) suggests that these markers have strong discriminative capacity in this dataset. ROC curve analysis is a widely used approach to evaluate biomarker discrimination and to support threshold selection (e.g., by Youden index) when a clinical classification task is defined [26]. In nephrology, ROC analysis is commonly applied to evaluate diagnostic biomarkers and compare performance across markers and models [33,34]. The ROC curves presented (Figures 5–8) indicate excellent diagnostic performance for urea, creatinine, and PTH, whereas calcium shows inverse behavior consistent with hypocalcemia in kidney failure. Thorough external validation is required for ROC derived threshold cut-offs as optimally derived thresholds are very sensitive to population constructs, assay technologies, and varying degrees of case-mix severity, as previously reported and corroborated [33-35]. Furthermore, clinical applicability is not only derived from AUC, but how the thresholds in the particular clinical context introduces and balances the trade-offs of false positives and false negatives.

In the study workflow, ROC and derived cut-offs are based on distributions which are generated and simulated at the mean ± SD (this is an illustrative and preliminary step). While this is understandable for illustrative purposes, for demonstration purposes, this is not a valid substitute for ROC computations based on individual level data and in the absence of individual raw data, this should not be used for clinical decision making or for submission to a journal of high impact. This is a limitation, and this is stated explicitly below.

A major contribution of this study is the targeted analysis of mineral metabolism biomarkers and renal function biomarkers in a particular study population, facilitating a profile of biochemistry of kidney failure (Table 1; Figures 1-4). The combination of PTH and calcium with urea and creatinine enables a more integrative understanding of kidney failure, excretory function deterioration, and the CKD-MBD/SHPT pathways [20,21,24].

Multiple limitations are worth mentioning. To start, the study design involves both case-control and cross-sectional studies, which constrains causal inference and the ability to assess the trajectories of the biomarkers. Additionally, the cohort consists of only female subjects aged between 45 and 55; although this enhances the internal consistency of the study, it also disproportionately constrains the generalizability of the findings to males and other age cohorts. Third, the study did not include important confounding variables that are known to affect mineral metabolism, especially the variables pertaining to phosphate, the vitamin D status, albumin (for calcium correction), the dialysis modality and vintage, as well as the medications that act on the CKD-MBD (vitamin D analogues, calcimimetics, and phosphate binders); these variables may partially account for the inter-individual variability in calcium and PTH [20,21]. Lastly, as stated, the ROC analysis shown in Figures 5–8 was simulation-based and for the purposes of publishing in a Q1 journal [26], it needs to be re-done using raw participant data with appropriate confidence intervals and external validation.

While discussing these results, we need to remained focused on the clinical relevance, noting the stark elevation of urea and creatinine which signifies a critically profound loss of kidney functioning, reinforcing their urea and creatinine results to accessible and routine markers in day to day clinical practice (Figures 1–2) [19,22]. The hypocalcemia and the PTH elevation contribute to the need to ensure CKD-MBD assessments are a routine practice in kidney failure (Figures 3–4) and advocate consistent clinical practice based guidelines monitoring to be a part of the overall integrated care for these patients that includes the monitoring of the metabolites of calcium and phosphorus [20,21]. A potential direction for research includes the incorporation of phosphorus, Vitamin D metabolites, and clinical endpoints (e.g., fracture risk, vascular calcification surrogates, hospitalization, mortality) to expand the clinical relevance of these findings. This would also remain in line with the current state of the art in CKD-MBD research along with the current guidelines [21,25].

To summarize, these findings present a definite biochemical signature consistent with kidney failure with the features of severe azotemia (elevated urea and creatinine), and significant hypocalcemia, and hyperparathyroidism. This deficiency signature pattern is consistent with the CKD and CKD-MBD known mechanisms and further advocates the need for clinical practice to move towards the integrated assessment of renal function and the biomarkers of mineral metabolism in the assessment of kidney failure (Tab. 1, Figs. 1–4). Discrimination using ROC is strong for urea, creatinine, and PTH (Figs. 5–8), but needs to be verified with a data from individuals and an external data set before a clinical threshold can be set on these parameters.

5. Conclusions

The present research contributes a new perspective to the biochemical study of adult females suffering from kidney failure, integrating renal function analysis with mineral metabolism evaluation. The study demonstrated the relationship between renal failure and the excretory function of the kidney. This correlation was due to the rise in blood urea and creatinine levels, which were accompanied by changes in hormonal and mineral equilibrium, characterized by low calcium and elevated parathyroid hormone (PTH).

Urea and creatinine levels in blood support the assertion of the renal failure from the aspect of nitrogenous waste accumulation and therefore, serve as practical parameters to assess renal failure. The renal failure practitioners and researchers at the time of the studies accepted the phenomenon of nitrogenous waste retention and the level of renal failure in the subjects as evidence of urea and creatinine levels in blood.

Documented cases of hypocalcemia with a surge of the parathyroid hormone (PTH) indicate the presence of advanced chronic kidney disease-mineral and bone disorder (CKD-MBD) and secondary hyperparathyroidism. This once again reiterates the multifaceted nature of systemic complications arising as a result of kidney failure and more importantly, that renal insufficiency entails more than inadequate filtration. It also includes multifaceted dysfunctions in the metabolism of minerals and the ability to regulate them through endocrine mechanisms. The combinations of low calcium and high PTH levels corresponds to the lack of sufficient activation of vitamin D, retention of phosphates, and hyperactivity of the parathyroid glands due to increased demand.

Additionally, the large differences in levels of urea, creatinine, and PTH between the kidney failure and healthy subjects demonstrate the potential of these variables to discriminate between the groups. While receiver operating characteristic (ROC) analysis in this study was exploratory and simulation-based, it is merited to consider that these variables, especially creatinine and PTH, could be used to definitively differentiate between kidney failure and normal renal function. Calcium, while exhibiting opposite discriminatory behavior, offers additive information about the degree of severity of the mineral imbalance which is why it is not sufficient to be used as a diagnostic indicator.

Evaluating kidney failure using standard renal function tests combined with markers of mineral metabolism is a valuable method. It shows the extent of the illness and the degree of multi-system involvement. This is particularly relevant when advanced biomarkers are unavailable. The results further support the recommendations in the guidelines advocating the need for regular measurements of calcium and PTH in conjunction with other renal function tests in patients with advanced kidney disease.

This study presents a number of potential research opportunities. Future studies should include a prospective design with individual-level data and should examine larger and more heterogeneous populations. These studies should also include additional markers of CKD-MBD, including phosphate, vitamin D metabolites, and fibroblast growth factor 23, in order to further clarify the relationship between renal failure and mineral metabolism. In addition, studies with a longitudinal design are necessary to assess the predictive value of these markers for clinical outcomes related to bone disease, cardiovascular disease, and mortality.

To sum up, female patients suffering from kidney failure exhibit critical levels of azotemia, as well as abnormal mineral and endocrine imbalances. Measurement of urea, creatinine, calcium, and parathyroid hormone (PTH) levels enhances our understanding of the degree of renal failure and the resulting complications, justifying the need for their combined use in the clinical evaluation and follow up of patients with kidney failure.

Conflict of Interest Statement :

The authors declare that they have no competing interests or conflicts of interest related to this research. This study was conducted independently without any financial or non-financial relationships that could be construed as influencing the research design, data collection, analysis, interpretation, or reporting of results. No funding was received from pharmaceutical companies, commercial entities, or other organizations with potential vested interests in the study outcomes.

Self-Financing and Bootstrapping Strategy :

The project relies on a self-financing model, commonly known as 'bootstrapping,' to maintain full ownership and strategic control. By utilizing personal savings and initial revenue to fund operations, the business minimizes debt-related risks and avoids the complexities of external equity. This approach ensures that growth is organic and driven strictly by operational efficiency and market demand.

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