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ORIGINAL ARTICLE

Renal Function Parameters, Serum Electrolyte Balance, and Haematological Profile in Beta-thalassaemia Patients with and without Kidney Injury

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ABSTRACT

Beta-thalassaemia is associated with a spectrum of renal impairments, ranging from hyperfiltration to progressive dysfunction, depending on disease severity and treatment. Serum creatinine systematically underestimates renal dysfunction in this population owing to reduced skeletal muscle mass and altered erythropoiesis. This cross-sectional comparative study enrolled 180 participants in four groups: healthy controls (G1, n = 30), beta-thalassaemia with kidney injury (G2, n = 30), non-thalassemic kidney disease (G3, n = 30), and beta-thalassaemia without kidney injury (G4, n = 90). Renal indices (urea, creatinine, estimated glomerular filtration rate [eGFR]), serum electrolytes (Na^+, K^+, Cl^-), and haematological parameters (RBC, WBC, haemoglobin [Hb]) were compared using one-way ANOVA with least significant difference (LSD) post-hoc testing. Pearson correlation coefficients were computed across all variables (n = 180). All parameters differed significantly among groups ($P < 0.01$). G4 showed paradoxically low creatinine (45.78 ± 1.46 µmol/L) and supranormal eGFR (122.85 ± 1.86 mL/min/1.73 m^2), attributable to reduced creatinine generation from muscle depletion and glomerular hyperfiltration. Both thalassaemia groups demonstrated lower serum sodium, elevated WBC counts, and substantially reduced haemoglobin relative to healthy controls. Haemoglobin, meanwhile, was inversely correlated with potassium ($r = -0.50$) and positively correlated with RBC count ($r = 0.77$). Compared with non-thalassaemic chronic kidney disease (CKD), beta-thalassaemia produces a distinctive systemic profile. Creatinine-based assessments alone are insufficient for renal monitoring in this population; a multimodal strategy incorporating eGFR, serum electrolytes, and haematological profiling is recommended. Incorporating these varied metrics improves the accuracy of clinical evaluations significantly, Adopting a multimodal monitoring strategy is crucial for accurate risk stratification and safe clinical management in this population.

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1- INTRODUCTION

Beta-thalassaemia is characterized by reduced or absent synthesis of the beta-globin chains of haemoglobin. β-thalassemia major is a severe anemia involving ineffective red blood cell production and can be life-threatening [1]. Among the most prevalent monogenic haemoglobinopathies worldwide, beta-thalassaemia results from point mutations or deletions in the beta-globin gene that reduce or abolish beta-globin chain synthesis [2, 3]. This imbalance between alpha and beta chains causes excess alpha-globin subunits to precipitate within the bone marrow, generating reactive oxygen species, inducing erythroblast apoptosis, and accelerating peripheral red cell destruction. Together, these processes produce the clinical phenotype of severe microcytic anemia, extramedullary haematopoiesis, and transfusion-dependent iron overload [4, 5].

Renal involvement is a well-recognized complication outside the haematological system. Chronic hemolysis releases free haemoglobin and haem, sustaining oxidative stress and damaging the endothelium. At the same time, compensatory hyperdynamic circulation places hemodynamic strain on the glomerular microvasculature, while iron deposition can cause direct tubular toxicity [6]. Over the course of the disease, measurable renal impairment develops in between 40% and 60% of chronically transfused patients [7]. The researchers found that conventional renal assessments are unreliable because Serum creatinine levels depend heavily on muscle bulk, which is frequently reduced in these patients due to chronic anaemia, nutritional deficiencies, and impaired growth. Serum creatinine levels depend heavily on this skeletal muscle mass, chronic anaemia, nutritional deficiencies, and impaired growth reduce muscle bulk. [8]. Because creatinine production is reduced independently of filtration capacity, serum concentrations may remain within the reference range even when GFR has declined substantially. Electrolyte homeostasis may also be disrupted. Mechanisms include the release of intracellular potassium due to haemolysis, impaired adrenal function and aldosterone-mediated sodium retention resulting from iron overload, and tubular dysfunction that alters acid-base handling [9]. Many local studies demonstrated the physiological and immunological changes among beta-thalassaemia patients [1, 10].

Evaluating renal function, electrolyte balance, and haematological indices simultaneously, groups were stratified by both thalassaemia status and kidney injury in few studies. The combination of all three parameter domains across four clinically defined groups were compared in this study, the researchers computed a complete Pearson inter-parameter correlation matrix. This study aimed to characterise the systemic biochemical profile of beta-thalassaemia and to identify the limitations of conventional renal biomarkers in this population.

2- MATERIALS AND METHODS

2.1 Study Design and Setting

This cross-sectional comparative study was conducted at a tertiary haematology and nephrology referral center in Iraq. This study complied with the Declaration of Helsinki. Institutional Review Board approval was obtained and written informed consent provided by all participants or their legal guardians.

2.2 Study Population

One hundred and eighty participants were allocated to four groups: healthy controls (G1, n = 30), confirmed by normal complete blood count, renal indices, and haemoglobin electrophoresis; beta-thalassaemia with kidney injury (G2, n = 30); non-thalassaemic kidney disease (G3, n = 30), comprising CKD of non-haematological origin without haemoglobin disorders; and beta-thalassaemia without kidney injury (G4, n = 90). Kidney injury was defined as eGFR < 60 mL/min/1.73 m^2 and/or creatinine exceeding the age-adjusted reference interval, per KDIGO (2013) criteria [11].

2.3 Inclusion and Exclusion Criteria

Thalassaemia diagnosis was confirmed by haemoglobin electrophoresis and/or molecular genetic testing; all thalassaemia patients were receiving regular transfusion therapy. Healthy controls were frequency matched for sex. Exclusion criteria included acute infection, diabetes mellitus, primary hypertension unrelated to renal disease, pregnancy, autoimmune disorders, immunosuppressive therapy, and acute hepatic failure.

2.4 Blood Collection and Laboratory Measurements

Venous blood (5–10 mL) was collected after a minimum overnight fast of 8 hours during morning hours by standard antecubital venipuncture. In transfusion-dependent patients, samples were taken immediately before scheduled transfusion to avoid hemodilution. Serum was separated by centrifugation (3,000 rpm, 10 min, 4 °C) and stored at −20 °C; all analyses were completed within 72 hours. Serum urea was measured by the urease-Berthelot method; creatinine by the kinetic Jaffé method on a calibrated automated analyser. eGFR was calculated using the 2009 CKD-EPI creatinine equation

adjusted for age and sex [12]. Serum Na+, K+, and Cl− were measured by indirect ion-selective electrode potentiometry. RBC count, WBC count, and haemoglobin were determined with an automated haematology analyser (Sysmex XN-380).

2.5 Statistical Analysis

Data are presented as mean ± standard error (SE). Group comparisons used one-way ANOVA followed by LSD post-hoc testing; categorical variables were analysed by chi-square test. Pearson product-moment correlation analysis was conducted on pooled data (n = 180). $P < 0.05$ was considered statistically significant; $P < 0.01$ was considered highly significant. All analyses were performed using IBM SPSS Statistics v26.0 (IBM Corp., Armonk, NY, USA).

3- RESULTS AND DISCUSSION

3.1 Participant Characteristics

Age differed significantly among groups ($P < 0.01$; Table 1). G3 participants were substantially older (35.23 ± 1.35 years) than those in G1 (31.07 ± 1.43), G2 (33.70 ± 1.67), and G4 (29.83 ± 0.81), reflecting the older demographic typical of non-haematological CKD. Sex distribution was comparable across all groups ($P > 0.05$), confirming adequate demographic balance.

Table (1): Age distribution across study groups

Group	n	Mean ± SE Age (years)
G1: Healthy controls	30	31.07 ± 1.43^{bc}
G2: Beta-thalassaemia with KI	30	33.70 ± 1.67^{b}
G3: Non-thalassaemic with KI	30	35.23 ± 1.35^{a}
G4: Beta-thalassaemia without KI	90	29.83 ± 0.81^{c}
LSD		3.642**
P-value		0.001

Note: Means with different superscript letters differ significantly ($P \leq 0.01$). ** Highly Significant ($P \leq 0.01$). LSD = Least Significant Difference; KI = Kidney Injury.

The significant age difference between G3 and the other groups, particularly G1 and G4, represents a notable confounder, as age is a primary determinant of renal function.

3.2 Renal Function Parameters

All renal parameters differ significantly among groups ($P < 0.01$; Table 2). Serum urea was highest in G3 (18.23 ± 1.33 mmol/L), approximately 3.4-fold above the upper reference limit, followed by G2 (9.93 ± 0.63 mmol/L), while G1 and G4 remained within normal ranges. Serum creatinine revealed a clinically important reversal in G4 (45.78 ± 1.46 µmol/L), decreasing below the healthy control value (59.30 ± 1.60 µmol/L). This contradictory finding low creatinine in the absence of kidney injury indicates substantially reduced creatinine generation due to muscle depletion, independent of filtration status. Creatinine was markedly elevated in G2 and G3 (141.71 and 181.20 µmol/L, respectively), consistent with advanced glomerular insufficiency.

eGFR showed the clearest difference between groups. G4 had the highest eGFR (122.85 ± 1.86 mL/min/1.73 m²), exceeding that of healthy controls (114.76 ± 1.94 mL/min/1.73 m²). This is consistent with glomerular hyperfiltration caused by chronic anaemia-driven hyperdynamic circulation and/or reduced creatinine generation, which can lead the CKD-EPI equation to overestimate filtration. G2 fell below the kidney injury threshold (57.20 ± 3.16 mL/min/1.73 m²; KDIGO Stage 3), whereas G3 showed the most severe damage (38.17 ± 2.38 mL/min/1.73 m²; approaching Stage 4 CKD).

Table (2): Renal function parameters across study groups

Group	Urea (mmol/L)	Creatinine (µmol/L)	eGFR (mL/min/1.73 m²)
G1	4.56 ± 0.09^{c}	59.30 ± 1.60^{c}	114.76 ± 1.94^{b}
G2	9.93 ± 0.63^{b}	141.71 ± 6.43^{b}	57.20 ± 3.16^{c}
G3	18.23 ± 1.33^{a}	181.20 ± 6.67^{a}	38.17 ± 2.38^{d}
G4	5.32 ± 0.18^{c}	45.78 ± 1.46^{d}	122.85 ± 1.86^{a}
LSD	1.630**	10.765**	7.400**
P-value	0.001	0.001	0.001

Note: Means with different superscript letters within each column differ significantly. ** P ≤ 0.01. KI = Kidney Injury; eGFR = Estimated Glomerular Filtration Rate.

3.3 Serum Electrolytes

Serum Na+, K+, and Cl− differed significantly among the groups (Table 3). Sodium was lowest in G2, at 135.76 ± 1.41 mmol/L, close to the hyponatraemia threshold (< 135 mmol/L). It was also significantly lower in G4 (137.33 ± 0.37 mmol/L) than in the controls. Despite established CKD, G3 had near-normal sodium levels (139.53 ± 0.55 mmol/L). This indicates that, in this cohort, hyponatraemia is more closely associated with thalassaemia-specific mechanisms than with reduced GFR per se. Potassium showed the opposite pattern: G2 had the highest concentration (4.96 ± 0.11 mmol/L), approaching the upper reference limit of 5.0 mmol/L. The finding reflects impaired tubular potassium secretion as kidney function declines, together with haemolysis-driven release of intracellular potassium. G4 potassium was also higher than in the controls (4.66 ± 0.03 mmol/L), although it remained within the reference range. This suggests that haemolysis-driven release can occur independently of overt renal dysfunction. Chloride showed the smallest difference between groups (P = 0.0054). G3 had the highest concentration, at 102.34 ± 0.36 mmol/L, consistent with hyperchloraemic metabolic acidosis in Stage 3–4 CKD.

Table (3): Serum electrolyte concentrations across study groups

Group	Na^{+} (mmol/L)	K^{+} (mmol/L)	Cl^{-} (mmol/L)
G1	140.87 ± 0.43^{a}	4.15 ± 0.04^{c}	100.77 ± 0.33^{b}
G2	135.76 ± 1.41^{b}	4.96 ± 0.11^{a}	100.43 ± 1.15^{b}
G3	139.53 ± 0.55^{a}	4.59 ± 0.04^{b}	102.34 ± 0.36^{a}
G4	137.33 ± 0.37^{b}	4.66 ± 0.03^{b}	99.93 ± 0.23^{b}
LSD	1.998**	0.162**	1.475**
P-value	0.001	0.001	0.0054

Note: Means with different superscript letters within each column differ significantly. ** P ≤ 0.01. * P ≤ 0.05.

3.4 Haematological Parameters

The set of haematological variables differ significantly among groups (P < 0.01; Table 4), RBC counts were markedly reduced in both thalassaemia groups. Counterintuitively, the lowest RBC count were in G4 ($3.07 \pm 0.06 \times 10^{12}$/L), this group bear the full haematological burden of transfusion-dependent thalassaemia ineffective erythropoiesis, chronic haemolysis, and microcytic erythroid output without any additional erythropoietin-deficiency component from kidney injury. Haemoglobin followed the same pattern, with the lowest mean in G4 (8.30 ± 0.12 g/dL), followed by G2 (8.61 ± 0.23 g/dL) and G3 (9.04 ± 0.14 g/dL). Anaemia in the thalassaemia groups results from failed erythropoiesis and haemolysis; in G3, it primarily reflects impaired erythropoietin-driven production. WBC count showed the most striking inter-group contrast. Both thalassaemia groups substantially exceeded the conventional upper limit of approximately 11.0×10^{9}/L: G2 recorded $15.86 \pm 1.52 \times 10^{9}$/L and G4 recorded $13.37 \pm 0.94 \times 10^{9}$/L. G3 showed mild leucocytosis ($9.29 \pm 0.30 \times 10^{9}$/L), considerably less pronounced than either thalassaemia group. The higher WBC in G2 relative to G4 likely reflects the additional inflammatory stimulus of concurrent kidney injury superimposed on chronic haemolysis.

Table (4): Haematological parameters across study groups

Group	RBC (×10¹²/L)	WBC (×10⁹/L)	Hb (g/dL)
G1	4.27 ± 0.06^{a}	5.20 ± 0.19^{c}	12.72 ± 0.22^{a}
G2	3.37 ± 0.16^{b}	15.86 ± 1.52^{a}	8.61 ± 0.23^{bc}
G3	3.41 ± 0.06^{b}	9.29 ± 0.30^{b}	9.04 ± 0.14^{b}
G4	3.07 ± 0.06^{c}	13.37 ± 0.94^{a}	8.30 ± 0.12^{c}
LSD	0.269**	3.358**	0.521**
P-value	0.001	0.001	0.001

Note: Means with different superscript letters within each column differ significantly. ** P ≤ 0.01. RBC = Red Blood Cell; WBC = White Blood Cell; Hb = Haemoglobin.

3.5 Correlation Analysis

3.5.1 Renal function correlations

Creatinine correlated strongly with urea ($r = 0.82$, $P < 0.01$) and the strongest association in the matrix. Urea correlated inversely with eGFR ($r = -0.74$, $P < 0.01$). Weaker associations included urea with potassium ($r = 0.23$, $P < 0.05$) and eGFR with chloride ($r = -0.24$, $P < 0.05$). No significant correlations emerged between renal indices and any haematological parameter.

3.5.2 Electrolyte correlations

Sodium correlated inversely with potassium ($r = -0.69$, $P < 0.01$) and positively with chloride ($r = 0.43$), RBC count ($r = 0.42$), and haemoglobin ($r = 0.40$; all $P < 0.01$), with a weak inverse correlation with WBC count ($r = -0.27$, $P < 0.05$). Potassium correlated inversely with haemoglobin ($r = -0.50$), RBC count ($r = -0.48$), and chloride ($r = -0.36$), and positively with WBC count ($r = 0.37$; all $P < 0.01$).

3.5.3 Haematological correlations

RBC count and haemoglobin showed a strong positive association ($r = 0.77$, $P < 0.01$). WBC count correlated weakly and inversely with both RBC count ($r = -0.25$) and haemoglobin ($r = -0.26$; both $P < 0.05$).

Table (5): Summary of significant Pearson correlation coefficients (n = 180)

Domain	Parameter Pair	r	P-value
Renal	Creatinine vs. eGFR	−0.93	< 0.01
	Creatinine vs. Urea	0.82	< 0.01
	Urea vs. eGFR	−0.74	< 0.01
	Urea vs. K^+	0.23	< 0.05
	eGFR vs. Cl^-	−0.24	< 0.05
Electrolyte	Na^+ vs. K^+	−0.69	< 0.01
	Na^+ vs. Cl^-	0.43	< 0.01
	Na^+ vs. RBC	0.42	< 0.01
	Na^+ vs. Hb	0.40	< 0.01
	Na^+ vs. WBC	−0.27	< 0.05
	K^+ vs. Hb	−0.50	< 0.01
	K^+ vs. RBC	−0.48	< 0.01
	K^+ vs. WBC	0.37	< 0.01
	K^+ vs. Cl^-	−0.36	< 0.01
Haematological	RBC vs. Hb	0.77	< 0.01
	WBC vs. Hb	−0.26	< 0.05
	WBC vs. RBC	−0.25	< 0.05

Note: Only statistically significant correlations are shown. Positive r = direct relationship; negative r = inverse relationship.

The findings point to a distinctive systemic profile in beta-thalassaemia, one that differs substantially from non-thalassaemic CKD. Both kidney injury groups had elevated urea and creatinine, together with reduced eGFR, consistent with established glomerular insufficiency. Impairment was more severe in G3 than in G2, most plausibly because the cohort was older and had a longer natural history. In non-haematological CKD, metabolic comorbidities can produce cumulative nephron loss over decades; renal injury attributable to thalassaemia, by contrast, arises through distinct mechanisms and may progress more variably [13]. Iraqi clinical data independently support the unreliability of serum creatinine as a standalone renal marker in β-TM. Shaalan *et al*. (2022) [14] evaluated 69 pediatric patients with β-TM and 23 with β-TI who were registered at the Basrah Centre for Hereditary Blood Diseases. Compared with healthy controls, the thalassaemic patients had significantly elevated blood urea nitrogen. Their urinary albumin/creatinine and uric acid/creatinine ratios were also substantially higher, while serum creatinine values remained within conventional reference limits. The most clinically consequential finding is the paradoxically supranormal eGFR and low creatinine in G4. Two mechanisms, likely operating together, explain this. First, chronic anaemia drives hyperdynamic renal haemodynamics with increased glomerular plasma flow an analogue of the hyperfiltration described in sickle cell disease [5]. Second, and probably more important, reduced skeletal muscle mass lowers creatinine generation, causing the CKD-EPI equation to assign an artefactually high eGFR when creatinine falls below the age-sex expected range [15]. A cross-sectional Iranian study [16] compared serum cystatin-C directly with creatinine-based eGFR, the β-TM patients receive deferasirox at the Iran University of Medical Sciences in Tehran. Although no independent variable showed a significant effect on serum creatinine levels in that cohort, cystatin-C tracked subclinical impairment more sensitively. Tsiotsios *et al.* (2026) [17] reported that many thalassaemia patients maintain eGFR within the normal range without apparent hyperfiltration, suggesting that the extent of supranormal values may depend on the population and the method used.

Hyponatraemia was more pronounced in the thalassaemia groups than in G3, which had established CKD but near-normal sodium levels. This pattern implicates mechanisms specific to thalassaemia beyond reduced GFR.Iron overload-related adrenal insufficiency impairing aldosterone-mediated sodium retention, plasma volume expansion from chronic anaemia diluting serum sodium, and disrupted hypothalamic osmoregulation from iron deposition are the most plausible contributors [18]. Serum potassium levels in Iraqi β-TM paediatric patients was reported as significantly lower than in healthy controls by Shaalan *et al*. (2022) [14]. This finding shows a direction opposite to the present study, the elevated potassium in G2 (4.96 ± 0.11 mmol/L) and G4 (4.66 ± 0.03 mmol/L) contradict those previous results. This discrepancy is most plausibly attributable to age-related differences in tubular handling and disease stage, these physiological factors change over the course of the illness. The convergent potassium elevation in G2 reflects impaired tubular secretory capacity from kidney injury combined with haemolysis-driven intracellular potassium release [19]. The mildly elevated potassium in G4, despite the absence of kidney injury, also implicates haemolysis as an independent contributor rather than an effect of declining GFR. In G3, the raised chloride fits the hyperchloraemic metabolic acidosis seen in Stage 3–4 CKD: impaired renal acid excretion and bicarbonate regeneration lead to chloride retention.

The haematological phenotype observed in both thalassaemia groups is consistent with findings reported by several Iraqi centers. RBC counts and haemoglobin were markedly reduced in both groups, while leukocytosis was pronounced, matching data from other regions. Al-Allawi *et al*. (2020) [20] evaluated 150 consecutive β-TM patients at a thalassaemia center. Pre-transfusion haemoglobin was ≤ 9.0 g/dL in 38.7% of the cohort, a figure close to the mean haemoglobin of 8.30 ± 0.12 g/dL recorded in G4. The research team attributed this pattern to difficulties with timely transfusion access and chelation optimization. Despite the absence of kidney injury, G4 had lower haemoglobin and RBC than G2. This most likely reflects a greater contribution from ineffective erythropoiesis and haemolysis in the thalassaemia groups, whereas G2 patients with concurrent CKD may have received erythropoiesis-stimulating agent therapy. Taher et al. (2018) [5] estimated that optimally managed patients maintain pre-transfusion haemoglobin at 9.5–10.5 g/dL; the 8.30 g/dL recorded in G4 suggests sub-optimal transfusion or pre-transfusion sampling. Both thalassaemia groups showed marked leukocytosis: G2 at 15.86 ± 1.52 × 10^9/L and G4 at 13.37 ± 0.94 × 10^9/L, both well above the upper reference limit of 11.0 × 10^9/L. Four mechanisms are likely responsible. First, chronic haemolysis releases free haemoglobin, haem, and erythroid membrane fragments that activate Toll-like receptor signalling and complement, sustaining a granulopoietic drive and prolonging neutrophil survival [4, 5]. The added cytokine burden of concurrent kidney injury most plausibly explains why G2 ran approximately 18.6% higher than G4 despite comparable thalassaemia disease burden. Second, splenectomy eliminates the principal neutrophil margination site, releasing a sequestered pool back into the circulation and producing a structural leukocytosis unrelated to any active inflammatory signal [19]; because splenectomy status was not individually recorded, its contribution cannot be quantified from the present data. Third, extramedullary haematopoiesis expands myeloid progenitors at ectopic sites when the bone marrow cannot keep pace with chronic erythroid destruction, releasing granulocytic precursors outside the normal regulatory environment of the marrow [4]. Fourth, repeated allogeneic transfusions provide a recurrent antigenic stimulus: even with optimised crossmatching, subclinical alloimmune reactions transiently enlarge the leukocyte pool, and cumulative sensitisation may sustain a raised baseline over years of transfusion

dependence [21]. G3 showed comparatively mild leukocytosis (9.29 ± 0.30 × 10^9/L), consistent with uraemia-driven impairment of neutrophil apoptosis rather than any of the thalassaemia-specific mechanisms above. WBC elevation in this population should not be read as a straightforward marker of acute infection without accounting for splenectomy history, transfusion frequency, and disease severity.

The correlation between creatinine and eGFR ($r=-0.93$) is mathematically expected because the CKD-EPI formula depends on serum creatinine across the broad filtration range represented by the four groups. It is also consistent with the validation data of Zhu (2022) [22]. More informative are the links between electrolytes and haematological measures. As the haematological burden of thalassaemia increases, haemolysis-related potassium release and sodium dilution associated with plasma volume expansion led to parallel electrolyte changes: haemoglobin falls as potassium rises ($r=-0.50$) and sodium falls ($r = 0.40$). In the pooled analysis, renal function indices showed no significant correlations with haematological parameters. That finding differs from the inverse GFR–haemoglobin relationship well documented in non-thalassaemic CKD [23, 24]. These findings have three practical implications, although the limitations of creatinine deserve particular attention. In beta-thalassaemia, it should not be treated as a stand-alone renal marker. Reporting eGFR alongside creatinine should be the minimum standard, while cystatin C-based GFR estimation is preferable for patients with markedly reduced muscle mass [25].

4- CONCLUSION

Beta-thalassaemia produces a distinctive systemic profile, characterized by paradoxically low serum creatinine, preserved or supranormal eGFR, hyponatraemia, elevated potassium, and profound anaemia with leukocytosis. This pattern differs substantially from that seen in non-thalassaemic CKD. Creatinine-based assessments alone fail to detect or exclude renal impairment reliably in this population, so routine clinical care should combine eGFR calculation with electrolyte surveillance and haematological profiling. Prospective longitudinal studies incorporating cystatin C, urinary tubular injury biomarkers, and direct GFR measurement are needed to clarify causality, validate the prognostic significance of early electrolyte and filtration abnormalities, and establish evidence-based monitoring thresholds for this patient population.

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