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SERUM VITAMIN D STATUS AND RENAL RECOVERY OUTCOMES IN DIABETIC PATIENTS WITH SEPSIS-ASSOCIATED ACUTE KIDNEY INJURY: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT **Background:** Acute kidney injury (AKI) frequently complicates sepsis and is amplified by the vascular and immune dysfunction associated with diabetes mellitus. Vitamin D's immunomodulatory and renoprotective actions raise the possibility that vitamin D status influences renal recovery in this high-risk group, yet evidence remains limited. **Objective:** To evaluate the relationship between serum vitamin D levels at the time of AKI diagnosis and 90-day renal recovery in septic patients with type 2 diabetes mellitus. **Methods:** A prospective observational study was conducted over six months in the nephrology department of a tertiary-care hospital. Two hundred fifty adult patients (143 male, 107 female) meeting Sepsis-3 and KDIGO criteria for AKI, with type 2 diabetes, were enrolled and followed for 90 days. Serum 25-hydroxyvitamin D was categorised as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Renal recovery was defined as serum creatinine <1.5 times baseline without ongoing renal replacement therapy. Data were analysed in SPSS v25 using chi-square/Fisher's exact and independent-sample t-tests; $p<0.05$ was considered significant. **Results:** Vitamin D deficiency was present in 56.8% of patients, and only 28.0% recovered renal function by 90 days. Recovery was significantly associated with vitamin D status ($p=0.005$), KDIGO stage ($p<0.001$), absence of hypertension ($p<0.001$) and chronic kidney disease ($p=0.001$), normal thyroid function ($p=0.037$), lower discharge creatinine, blood urea nitrogen, potassium and phosphorus, and absence of albuminuria ($p=0.007$) and altered mental status ($p=0.048$). Dialysis dependence was strongly linked to non-recovery ($p<0.001$). **Conclusion:** Vitamin D status, alongside several modifiable biochemical and clinical variables, is significantly associated with renal recovery from sepsis-associated AKI in diabetic patients, supporting further investigation of vitamin D as an adjunct therapeutic and prognostic target.

KEYWORDS : Acute Kidney Injury; Vitamin D; Sepsis; Diabetes Mellitus; Renal Recovery; KDIGO

INTRODUCTION

Acute kidney injury (AKI) is an abrupt decline in renal function that disproportionately affects critically ill patients with sepsis, where systemic inflammation, microvascular dysfunction, and tissue hypoperfusion combine to injure the renal tubules[1]. Type 2 diabetes mellitus compound's this risk: chronic hyperglycaemia, endothelial dysfunction, and impaired neutrophil function leave the diabetic kidney more vulnerable to acute insult and slower to recover once injury has occurred [2]. The coexistence of sepsis, diabetes, and AKI therefore represents a particularly high-risk clinical triad associated with prolonged intensive care stay, need for renal replacement therapy (RRT), and elevated mortality [3].

Vitamin D, beyond its classical role in calcium homeostasis, exerts immunomodulatory, anti-inflammatory, and antifibrotic effects through vitamin D receptors expressed on renal tubular and immune cells. Experimental evidence links active vitamin D metabolites to suppression of the renin-angiotensin-aldosterone system (RAAS), down-regulation of pro-inflammatory cytokines, and promotion of tubular epithelial repair, mechanisms directly relevant to recovery from AKI [4, 5]. Also vitamin D modulates immune cell infiltration and macrophage polarization towards a reparative M2 phenotype, supporting tissue remodeling and healing in the post-AKI phase [6].

Vitamin D deficiency is highly prevalent among critically ill patients and has previously been linked to worse outcomes in sepsis and AKI [7,8], yet most available evidence comes from heterogeneous, predominantly non-diabetic intensive-care cohorts, and the specific contribution of vitamin D status to renal recovery in diabetic, septic AKI patients remains inadequately characterised.

The Kidney Disease: Improving Global Outcomes (KDIGO) staging system[9], together with the Sepsis-3 consensus criteria[10], has standardised AKI diagnosis and severity grading, allowing clinical and biochemical predictors of recovery to be studied more reliably [10, 11]. Identifying modifiable predictors, particularly an inexpensive and correctable factor such as vitamin D, could meaningfully inform risk stratification and adjunct management strategies in this vulnerable population.

This study was undertaken to evaluate the association between serum 25-hydroxyvitamin D levels measured at the time of AKI diagnosis and renal recovery at 90 days in septic patients with type 2 diabetes mellitus, and to identify other clinical and biochemical correlates of recovery in this group.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Nephrology of a tertiary-care super-specialty hospital in Kannur, Kerala, over a six-month period, with each enrolled patient followed for 90 days. Adult patients (≥18 years) admitted with a confirmed diagnosis of sepsis (Sepsis-3 criteria), type 2 diabetes mellitus (American Diabetes Association criteria) [12], and AKI (KDIGO criteria) were eligible. Patients who were dialysis dependence prior to admission, those already receiving vitamin D supplementation exceeding 800 IU/day, individuals with hypercalcaemia or known metabolic bone disease, and those who declined consent were excluded. A sample size of 250 was calculated to provide 80% power at a 5% significance level.

Two hundred fifty patients (143 male, 107 female) were enrolled after written informed consent. Demographic data, comorbidities, glycaemic control (HbA1c), and serum 25-hydroxyvitamin D at the time of AKI diagnosis were recorded. Vitamin D status was classified

as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Serum creatinine, blood urea nitrogen, electrolytes, urine albumin, and dialysis requirement were monitored. The primary outcome, renal recovery, was defined as serum creatinine falling to less than 1.5 times the baseline value without ongoing RRT, assessed at 90 days. Secondary outcomes included ICU stay duration, dialysis frequency, and 90-day all-cause mortality.

Data were entered in Microsoft Excel and analysed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation and compared using the independent-sample t-test; categorical variables were expressed as frequencies and percentages and compared using the chi-square or Fisher's exact test as appropriate. A p-value <0.05 was considered statistically significant. The study was approved by the Institutional Human Ethics Committee (Ref. No. 003/2024/CCOPS/IEC) and conducted in accordance with the Declaration of Helsinki.

RESULTS

Two hundred fifty patients with sepsis-associated AKI and type 2 diabetes were studied; the mean age was 63.75 ± 14.12 years, and 57.2% were male (Table 1). Most patients presented with severe AKI, with 88.8% classified as KDIGO Stage 3, 8.8% as Stage 2, and only 2.4% as Stage 1. Vitamin D deficiency was present in 56.8% of the cohort, while 22.4% were insufficient and 20.8% were sufficient, with a mean admission level of 21.98 ± 16.84 ng/mL. Only 70 patients (28.0%) achieved renal recovery by 90 days; the remaining 180 (72.0%) did not, of whom 62.4% of the overall cohort remained dialysis-dependent and 5.2% died within the follow-up period.

Table 1 Baseline Characteristics of the Study Population (N = 250)

Variable	n (%) or mean ± SD
Age, years	63.75 ± 14.12
Male sex	143 (57.2)
Female sex	107 (42.8)
Serum 25-hydroxyvitamin D at admission, ng/mL	21.98 ± 16.84
Deficient (<20 ng/mL)	142 (56.8)
Insufficient (20–29 ng/mL)	56 (22.4)
Sufficient (≥30 ng/mL)	52 (20.8)
KDIGO Stage 1	6 (2.4)
KDIGO Stage 2	22 (8.8)
KDIGO Stage 3	222 (88.8)
Recovered from AKI at 90 days	70 (28.0)
Did not recover from AKI at 90 days	180 (72.0)

A statistically significant association was observed between vitamin D status at admission and 90-day renal recovery (p = 0.005). The relationship was notably non-linear: patients with vitamin D levels 20–29 ng/mL, recovered most frequently (44.6%), compared with 24.6% in the deficient group. Mean admission vitamin D levels did not differ significantly between those who recovered and those who did not (20.32 ± 10.84 vs. 22.63 ± 18.65 ng/mL, p = 0.331), suggesting that categorical status carried a stronger association with outcome than the absolute admission value.

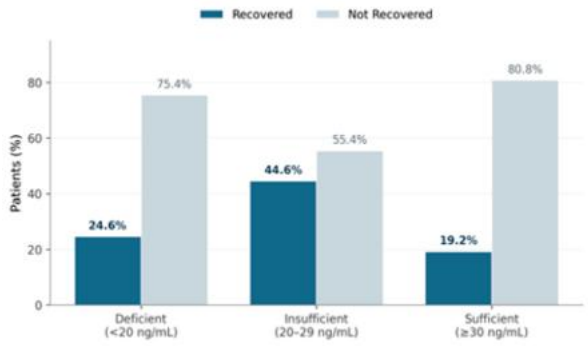

Figure 1. Renal Recovery at 90 Days by Serum Vitamin D Status at Admission

Several clinical and biochemical variables were independently associated with recovery (Table 2). AKI severity strongly predicted outcome: all six KDIGO Stage 1 patients recovered, compared with 45.5% of Stage 2 and only 24.3% of Stage 3 patients (p < 0.001). Recovery was significantly less likely among patients with hypertension (25.0% vs. 78.6% without, p < 0.001), pre-existing chronic kidney disease (22.0% vs. 41.6%, p = 0.001), hypothyroidism (0% vs. 29.3%, p = 0.037), altered mental status at admission (11.5% vs. 29.9%, p = 0.048), and albuminuria (26.4% vs. 75.0% among those without urine albumin, p = 0.007). Dialysis utilisation showed the strongest association with non-recovery: patients who did not recover underwent a mean of 2.83 ± 1.87 dialysis sessions, compared with 0.09 ± 0.44 among those who recovered (p < 0.001).

Discharge biochemical parameters also differed significantly between groups. Patients who recovered had lower mean blood urea nitrogen (86.40 ± 39.98 vs. 106.60 ± 61.67 mg/dL, p = 0.012), serum creatinine (3.33 ± 1.42 vs. 4.10 ± 1.52 mg/dL, p < 0.001), serum potassium (4.43 ± 1.10 vs. 4.91 ± 1.09 mEq/L, p = 0.002), serum phosphorus (5.39 ± 1.47 vs. 6.21 ± 2.53 mg/dL, p = 0.012), and thyroid-stimulating hormone (1.74 ± 1.25 vs. 3.23 ± 5.29 µIU/mL, p = 0.021) than those who did not recover. Age (p = 0.989) and sex (p = 0.086) showed no significant association with recovery, although females recovered numerically more often than males (33.6% vs. 23.8%).

Table 2 Impact of Various Parameters on Renal Recovery

Factor / Parameter	Recovered	Not Recovered	p-value
Panel A: Categorical Clinical Factors, n (%)			
Hypertension – Present	59 (25.0)	177 (75.0)	<0.001*
Hypertension – Absent	11 (78.6)	3 (21.4)	
Chronic kidney disease – Present	38 (22.0)	135 (78.0)	0.001*
Chronic kidney disease – Absent	32 (41.6)	45 (58.4)	
Hypothyroidism – Present	0 (0.0)	11 (100.0)	0.037*
Hypothyroidism – Absent	70 (29.3)	169 (70.7)	
Altered mental status – Present	3 (11.5)	23 (88.5)	0.048*
Altered mental status – Absent	67 (29.9)	157 (70.1)	
Urine albuminuria – Present	64 (26.4)	178 (73.6)	0.007*
Urine albuminuria – Absent	6 (75.0)	2 (25.0)	
KDIGO Stage 1	6 (100.0)	0 (0.0)	<0.001*
KDIGO Stage 2	10 (45.5)	12 (54.5)	
KDIGO Stage 3	54 (24.3)	168 (75.7)	
Vitamin D – Deficient	35 (24.6)	107 (75.4)	0.005*
Vitamin D – Insufficient	25 (44.6)	31 (55.4)	
Vitamin D – Sufficient	10 (19.2)	42 (80.8)	
Panel B: Continuous Biochemical Parameters, Mean ± SD			
Blood urea nitrogen at discharge, mg/dL	86.40 ± 39.98	106.60 ± 61.67	0.012*
Serum creatinine at discharge, mg/dL	3.33 ± 1.42	4.10 ± 1.52	<0.001*
Serum potassium, mEq/L	4.43 ± 1.10	4.91 ± 1.09	0.002*
Serum phosphorus, mg/dL	5.39 ± 1.47	6.21 ± 2.53	0.012*
TSH, µIU/mL	1.74 ± 1.25	3.23 ± 5.29	0.021*
Number of dialysis sessions	0.09 ± 0.44	2.83 ± 1.87	<0.001*

Note. *p < 0.05, statistically significant (chi-square/Fisher's exact test for categorical variables; independent-sample t-test for continuous variables).

DISCUSSION

This prospective study found that only 28% of diabetic, septic patients with AKI recovered renal function by 90 days, underscoring the poor prognosis of this high-risk triad. Vitamin D status at diagnosis was significantly associated with recovery, broadly consistent with previous reports linking vitamin D status to renal and survival outcomes in critically ill patients with AKI[13, 14, 15]. Vitamin D's putative renoprotective mechanisms – suppression of RAAS activity, attenuation of pro-inflammatory cytokine release, and support of tubular epithelial regeneration – offer plausible biological explanations for an association between vitamin D adequacy and renal recovery[4,5].

An unexpected finding was the non-linear relationship between vitamin D category and recovery, with the insufficient group (20–29 ng/mL) recovering more often than either the deficient or the

conventionally "sufficient" (≥30 ng/mL) group. While most prior studies describe a more straightforward dose-response relationship, a few have similarly reported attenuated or reversed associations at higher vitamin D concentrations in critically ill cohorts, reflecting reverse causation, such as pre-admission supplementation in less acutely unwell patients, or unmeasured confounding by nutritional status and sun exposure. This pattern, although statistically significant in the present sample, should be interpreted cautiously and warrants confirmation in larger cohorts with serial vitamin D measurement.

The strong association between AKI severity (KDIGO stage) and recovery aligns with the understanding that more extensive tubular injury reduces regenerative capacity[16], consistent with established KDIGO-based prognostic literature[11,17]. Similarly, pre-existing hypertension and chronic kidney disease were associated with markedly poorer recovery, likely reflecting underlying microvascular and structural renal changes that limit the kidney's regenerative reserve [18]. The association between hypothyroidism and non-recovery is consistent with established effects of thyroid hormone on renal blood flow and glomerular filtration rate[19]. Elevated discharge potassium and phosphorus in the non-recovery group likely reflect persistent tubular dysfunction and reduced glomerular filtration, while higher discharge creatinine and blood urea nitrogen directly indicate incomplete resolution of the acute insult. The marked association between dialysis dependence and non-recovery reinforces dialysis requirement as a marker of AKI severity rather than merely a consequence of it.

Albuminuria and altered mental status at admission, both markers of more severe systemic and renal insult, were also associated with poorer recovery, consistent with their recognised roles as indicators of glomerular damage[20] and sepsis-related encephalopathy or multi-organ dysfunction, respectively[21]. Age and sex did not significantly influence recovery in this cohort, although the numerically higher recovery rate among females is consistent with reports by Curtis (2024)[22], even though other studies have shown contrary sex-based outcomes in sepsis-associated AKI.

These findings should be interpreted within the limitations of a single-centre, observational design with a comparatively short follow-up period, which precludes causal inference and limits generalisability beyond similar diabetic, septic AKI populations.

CONCLUSION

In this cohort of diabetic patients with sepsis-associated AKI, serum vitamin D status at diagnosis was significantly associated with 90-day renal recovery, alongside AKI severity, hypertension, pre-existing chronic kidney disease, hypothyroidism, albuminuria, altered mental status, and dialysis dependence. Patients with insufficient, rather than frankly deficient or conventionally sufficient, vitamin D levels recovered most often, a pattern that merits further mechanistic and epidemiological investigation. Lower discharge creatinine, blood urea nitrogen, potassium, and phosphorus levels emerged as useful prognostic markers of recovery[23]. While these results support vitamin D as a potential modifiable factor in AKI recovery among diabetic septic patients, the observational design and single-centre setting warrant cautious interpretation. Larger, multicentre, longitudinal studies, ideally incorporating vitamin D supplementation arms, are needed to clarify causality and to determine whether correcting vitamin D status can improve renal outcomes in this high-risk population.

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