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ORIGINAL ARTICLE

Hypocalcemia in acute kidney injury patients admitted to Intensive Care Unit and its relation to clinical outcome

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ABSTRACT

Background: Acute kidney injury (AKI) frequently results in a disturbance of calcium homeostasis. The relationship between serum calcium level in AKI patients and its relation to adverse outcome in ICU hadn't been studied well. **Aim of work:** To our knowledge only spare studies have demonstrated to establish on association between hypocalcemia and increased incidence of AKI related adverse outcome in ICU, So this work was designed to determine the frequency and relation between hypocalcemia and ICU patients with acute kidney injury via serial assessment of serum total and corrected calcium, continuous evaluation of kidney functions and evaluation of the effect of hypocalcemia on clinical outcome of those patients. **Subjects and methods:** This cohort study was carried on 108 patients with AKI who were admitted to medical ICU, Zagazig University Hospitals from January 2021 for a period of 6 months. We classified our patients into two groups according to presence of hypocalcemia with serum corrected calcium < 8.5 mg/dl with exclusion of those with hypercalcemia. All patients were subjected to full medical history thorough clinical examination & routine laboratory investigations. Serum total corrected and ionized calcium, creatinine were assessed at (admission, 3rd, 7th day) and albumin level at 1st and 7th day. Clinical outcome was evaluation according to Acute Physiologic Assessment And Chronic Health Evaluation II (APACHE II score). In addition to calculation of ICU stay in days and mortality of those patients. **Results:**Hypocalcemic AKI patients were about 35% of all patients. A statistically significant increase in staging of AKI in hypocalcemic AKI patients than those with normocalcemic AKI. Also, there was a statistically significant decrease in baseline and 7th day total and corrected calcium levels in hypocalcemic as compared to normocalcemic AKI patients.**Conclusion:** Hypocalcemia is a prevalent complication in ICU patients with AKI, and this was associated with adverse outcome with increasing length of ICU stay, morbidity and mortality of those patients.

Keywords: Acute Kidney Injury, Calcium,ICU, Kidney, Corrected calcium, APACHE, Mortality, Albumin, Creatinine.

INTRODUCTION

Acute kidney injury (AKI) is described as a rapid and frequently reversible reduction in glomerular filtration. It is a common hazardous illness that is particularly common in the intensive care unit (ICU). AKI is a prevalent and dangerous issue in patients who are very sick and has a significant impact on public health **[1]**.

A significant metabolic issue that goes unnoticed in critically ill patients is aberration in calcium metabolism. Because serum proteins particularly albumindecline in reaction to stress, disturbances in the patient's serum calcium level frequently go unnoticed in severely ill patients. Furthermore, a wealth of data suggests that abnormalities in serum calcium levels were probably a good indicator of the severity of the illness by demonstrating the extent of physiologic disturbances **[2]**.

When blood calcium levels are too low, a condition known as hypocalcemia occurs that can be treated. Hypocalcemia can result from a wide range of medical disorders, and it is frequently brought on by abnormally high or low amounts of vitamin D or parathyroid hormone (PTH) in the body. Hypocalcemia can be chronic (lasting a lifetime) or transient (mild). Clinical studies of patients with developed AKI have repeatedly revealed low levels of circulating calcium. This discovery has been explained by a number of etiologies, which are compiled in: Reduce 1,25D synthesis in the kidneys Boost the amount of circulating phosphorus, which stores calcium. Parathyroid hormone resistance in the skeleton Increases expression of the calcium sensing receptors and intracellular calcium build-up **[3]**.The measurement of total serum calcium remains the most commonly requested test to assess blood calcium status as free ionized calcium measurement by ion selective electrode is not generally available. However it has been recognized that variation in albumin concentration will lead to variation in total calcium concentration in the absence of any abnormality in the free ionized calcium concentration. This led to the concept of 'correcting' the measured total calcium concentration considering the albumin concentration **[4]**.To lessen the severe clinical effects of AKI, early detection and treatment of the condition and its consequences are essential. AKI frequently results in a disturbance of calcium homeostasis. It is unclear, though, if calcium plays a part in the onset of AKI **[5]**.There hasn't been much research done on the relationship between blood calcium levels in AKI patients and their clinical outcomes; to date; only a few studies have shown a link between hypocalcemia and an elevated risk of AKI-related bad outcomes in intensive care units.

Aim and objectives: To determine the frequency and relation between hypocalcemia and ICU patients with acute kidney injury via serial assessment of serum total and corrected calcium, continuous evaluation of kidney functions and evaluation of the effect of hypocalcemia on clinical outcome of those patients.

METHODS

Technical design: This cohort study was carried on 108 patients with acute kidney injury who were admitted to ICU. AKI was diagnosed according to the Kidney Disease Improving Global Outcomes (KDIGO classification) (if any one or all) of the following is present: Increase in serum creatinine by 0.3mg/dl within 48hr, or more

than 1.5 times baseline through one week, or urine volume less than 0.5 ml/kg/hr. for 6hours, or a combination of these factors **[6]**. Their ages ranged from (49) to (78) years old, attending Internal medicine department, intensive care unit, Zagazig University Hospital from January 2021 for a period of 6 months. We classified our patients into two groups according to presence of hypocalcemia with serum corrected calcium < 8.5 mg/dl which was calculated by considering

$$\text{corrected calcium} = \{0.8 \times (\text{normal albumin} - \text{patient albumin}) + \text{serum calcium level}\}$$

[7] into the following: Group (I): 70 patients with AKI with normal calcium level, 39 of them are males and 31 are females. Their ages range from 49 up to 78 years old. We lost 4 of them during the study. Group (II): 38 patients with AKI with hypocalcemia with serum corrected calcium < 8.5 mg/dl, 22 of them are males and 16 are females. Their ages range from 52 up to 71. We lost 12 of them during the study. Inclusion criteria involved adult patients over 18 years old with AKI of both sexes who were admitted to ICU with different etiology. Conversely, individuals with hypercalcemia, end-stage renal disease (ESKD), cancer (tumor lysis syndrome), and those who declined to participate in the trial were excluded.

Methods: All patients of this study were subjected to complete history taking and full clinical examination with calculation urine output and making a fluid map. Routine laboratory investigations which were done according to protocol of clinical pathology department of Zagazig University Hospitals including: Complete urine analysis, Complete blood picture, Arterial blood gases, Erythrocyte sedimentation rate, liver function tests, Random blood sugar, lipid profile and Kidney function tests including serum creatinine level (which was measured at admission, within first 48h and at 7th day), blood urea nitrogen and estimated GFR which calculated by the MDRD equation:

$$eGFR\left(\frac{\frac{ml}{min}}{1.73m2}\right) = 175 \times (SCr) - 1.154 \times (age) - 0.203 \times 0.742(for\ woman) \times 1.212\ (for\ black)$$

[8]. Staging of AKI was done according to KIDGO staging; AKI stage 1 was defined as serum creatinine increased by 1.5–1.9 times of the baseline level, AKI stage 2 when SCr increased by 2.0–2.9 times of the baseline level, and AKI stage 3 SCr became ≥3.0 times of the baseline level or in need for renal replacement therapy **[6]**.In addition total and corrected calcium were assessed at (1st, 3rd, 7th day) and albumin level at 1st and 7th day. Other routine investigations were done according to patient condition who admitted to ICU with different etiology including Ultrasonography of abdomen and pelvis and ECG. Clinical outcome evaluation was done according to (APACHE II score) (Acute Physiologic Assessment And Chronic Health Evaluation II) which is a severity of disease classification system applied within 24 hours of admission of a patient to ICU **[9]**, in addition to calculation of ICU stay in days and mortality of those patients.

Administrative considerations: Every participant provided written informed consent, and the study was authorized by the Zagazig University Faculty of Medicine's Institutional Research Board IRB (research ethics committee)(ZU-IRB: 6824/4-4-2021). The work has been completed in compliance with the Declaration of Helsinki, the World Medical Association's code of ethics for human subjects' research.

Statistical Analysis:

Data was entered into the computer and analyzed with the IBM SPSS software package version 20.0. (Armonk, NY: IBM Corporation) Qualitative data were described using numbers and percentages. The normality of the distribution was verified using the Kolmogorov-Smirnov test. The quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). The significance of the acquired results was assessed at the 5% level.

RESULTS

Table (1) shows that hypocalcemic AKI patients were about thirty five percent of all patients which shows that hypocalcemia is a common condition in AKI. Table (2) shows a statistically significant increase in staging of AKI in hypocalcemic AKI patients than those with normocalcemic AKI as regard baseline stages of and shows there is significant decrease in staging of AKI at 7th day in normocalcemic than those with hypocalcemic AKI. Table (3) shows statistically significant increase in incidence of respiratory failure and diabetes in hypocalcemic AKI patients as compared to normocalcemic acute kidney injury patients and no significant difference between groups as regard to incidence of (COPD, AF, coronary heart disease, congestive heart disease, liver disease, HTN and stroke). Table (4) shows no statistically significant difference between normocalcemia and hypocalcemia AKI as regard demographic data and statistically significant increase incidence of acidosis, Levels of BUN, serum cholesterol, random blood sugar, WBCs and ESR and significant decrease in amount of urine output and eGFR in hypocalcemic group than normocalcemic AKI patients. While there is no statistically significant difference between groups as regard hemoglobin, hematocrit, SGPT, SGOT, PH, serum triglyceride, serum k and Anion gap. Table (5) shows a statistically significant decrease in baseline total and corrected calcium levels and 7th day total and corrected calcium levels in hypocalcemic as compared to normocalcemic AKI patients. Among those with hypocalcemia, there is significant increase total calcium over 3rd day and 7th day follow up periods with weak response to treatment. In those with normocalcemia, there is significant increase in baseline total calcium and total calcium on third day and still within normal level which shows good response to treatment, while there is non-significant change in total and corrected calcium on seventh day. Table (6) demonstrates no statistically significant difference between normocalcemia and hypocalcemia as regard baseline creatinine, but patients with hypocalcemia have significantly increase in serum creatinine on 24h follow up. In each group, there is significant change in serum creatinine at 7th day which also higher with hypocalcemic AKI patients and no statistically significant difference among groups as regard baseline serum albumin yet patients with hypocalcemic AKI had significantly lower levels of serum albumin on 7th day. Table (7) reveals a statistically significant increase in APACHE II score in hypocalcemic compared to normocalcemic AKI patients and a statistically significant increase in ICU length of stay and mortality rate in hypocalcemic group as compared to normocalcemic AKI patients with different etiologies.

Table (1): Prevalence of hypocalcemia between acute kidney injury patients.

Total AKI patients	Normocalcemic AKI patients		Hypocalcemic AKI patients	
	N	%	N	%
N= 108	70	65	38	35

Qualitative data is presented in number and percentage.

Table (2): Comparison between normocalcemic and hypocalcemic acute kidney patients according to stages of AKI.

Stages of AKI	Normocalcemia (n = 70)		Hypocalcemia (n = 38)		χ^2	P
	No.	%	No.	%		
Baseline						
Stage 1	42	60	1	2.6	30.863	<0.001*
Stage 2	20	28.6	22	59.7		
Stage 3	8	11.4	15	39.5		
At 7th day						
Stage 1	55	78.6	13	34.2	21.128	<0.001*
Stage 2	11	15.7	14	36.8		
Stage 3	4	5.7	11	28.9		

χ2: Chi square for trend test.
p: p value for comparing between Normocalcemia and Hypocalcemia.

Table (3): Comparison between normocalcemic and hypocalcemic acute kidney patients according to associated comorbidities.

Associated comorbidities	Normocalcemia (n = 70)		Hypocalcemia (n = 38)		χ^2	P
	No.	%	No.	%		
Respiratory failure	8	11.4	12	31.6	6.628*	0.018*
COPD	16	22.9	9	23.7	0.009	0.922
Diabetes	12	17.1	14	36.8	5.229*	0.022*
Atrial fibrillation	13	18.6	8	21.1	0.097	0.754

Associated comorbidities	Normocalcemia (n = 70)		Hypocalcemia (n = 38)		χ^2	P
	No.	%	No.	%		
Coronary heart disease	18	25.7	8	21.1	0.293	0.588
Liver disease	9	12.9	10	26.3	3.077	0.079
Renal disease	12	17.1	10	26.3	1.278	0.258
Congestive heart failure	12	17.1	6	15.8	0.032	0.857
Hypertension	27	38.6	12	31.6	0.522	0.47
Stroke	10	14.3	8	21.1	0.812	0.368

χ2: Chi square test

p: p value for comparing between Normocalcemia and Hypocalcemia

*: Statistically significant at $p \leq 0.05$

Table (4): Comparison between normocalcemic and hypocalcemic acute kidney patients according to demographic data and laboratory finding.

	Normocalcemia (n = 70)		Hypocalcemia (n = 38)		Test of Sig.	p
	No.	%	No.	%		
Gender						
Male	39	55.7	22	57.9	χ^2= 0.048	0.827
Female	31	44.3	16	42.1		
Age (years)					-0.121	0.904
Mean ± SD.	62.59 ± 6.27		62.71 ± 4.39			
PH	7.32 ± 0.08		7.31 ± 0.11		0.608	0.545
Bicarbonate (meq/l)	18.64 ± 2.45		16.55 ± 3.13		3.566	<0.001**
Urine output cc/24hr	1712.86 ± 552.58		1105.26 ± 496.58		5.65	<0.001**
eGFR(ml/min/1.73m²)	34.31 ± 12.83		22.93 ± 9.05		5.361	<0.001**
BUN (mg/dl)	26.68 ± 5.41		34.99 ± 6.9		-6.412	<0.001**
HB (g/dl.)	10.06 ± 1.16		9.92 ± 1.09		0.623	0.534
Hematocrit (%)	27.22 ± 3.06		27.67 ± 3.21		-0.716	0.475
Serum cholesterol (mg/dl)	198.73 ± 51.75		222.08 ± 61.2		-2.98	0.038*
Serum potassium	4.31 ± 0.86		4.47 ± 1.14		-0.74	0.262

	Normocalcemia (n = 70)		Hypocalcemia (n = 38)		Test of Sig.	p
	No.	%	No.	%		
Anion gap (mmol/L)	13.08 ± 1.86		13.31 ± 1.11		-0.687	0.494
	Median (IQR)		**Median (IQR)**		**Z**	**P**
Serum TG (mg/dl)	160(114.5 – 196.75)		198(122.75 – 241.5)		-1.744	0.081
SGPT	21(16 – 28)		20(15 – 26)		-1.134	0.257
SGOT	29(21 – 39)		26.5(21 – 34)		-0.673	0.501
RBS (mg/dl)	113(100 – 135.25)		129.5(120 – 256.25)		-3.134	**0.002***
WBCs	10.45(8.28 – 14.55)		17.17(12.45 – 20.3)		-3.645	**<0.001****
ESR	20(9 – 43.25)		34.5(20 – 50)		-2.439	**0.015***

IQR: Inter Quartile Range
SD: Standard deviation
t: Student t-test
$\chi 2$: Chi square test
Z: Mann Whitney test
p: p value for comparing between Normocalcemia and Hypocalcemia
*: Statistically significant at $p \leq 0.05$

Table (5): Comparison between normocalcemic and hypocalcemic acute kidney injury patients according to baseline (total, ionized and corrected) calcium, total calcium at 3rd day and 7th day total and corrected calcium.

	Normocalcemia (n = 70)	Hypocalcemia (n = 38)	U	P
	Mean ± SD	Mean ± SD		
Baseline total Ca (mg/dl)	8.4 ± 0.4	6.7 ± 0.64	14.896	<0.001*
3rd day total Ca (mg/dl)	8.61 ± 0.27	7.23 ± 0.54	14.807	<0.001*
p¥	<0.001*	<0.001*		
7th day total Ca (mg/dl)	8.68 ± 0.36	7.74 ± 0.8	8.32	<0.001*
p¥	0.104	<0.001*		
Baseline Ionized Ca (mmol/l)	1.04 ± 0.19	1.04 ± 0.22	22.636	<0.001*
Baseline corrected Ca (mg/dl)	8.79 ± 0.29	7.2 ± 0.57	16.162	<0.001*
7th day corrected Ca (mg/dl)	8.72 ± 0.21	7.89 ± 0.6	-3.926	<0.001*
P¥	0.167	<0.001**		

SD: Standard deviation.
t independent sample t test.
¥ pfpr paired sample t test.
p: p value for comparing between Normocalcemia and Hypocalcemia.
*: Statistically significant at $p \leq 0.05$.

Table (6): Comparison between normocalcemic and hypocalcemic acute kidney patients according to baseline Creatinine, within 24hr, 7th day creatinine, baseline albumin and at 7th day follow up

Creatinine (mg/dl)	Normocalcemia (n =70)	Hypocalcemia (n = 38)	T	P
	Mean ± SD.	Mean ± SD.		
Baseline Creatinine	1.04 ± 0.19	1.04 ± 0.22	-0.125	0.901
24h Follow up creatinine	2.12 ± 0.66	2.89 ± 0.75	-5.529	<0.001*
Creatinine on 7th day	1.91 ± 0.89	2.7 ± 1.15	-3.626	<0.001*
p¥	<0.001*	<0.001*		
Serum albumin (gm/dl)				
Baseline	3.43 ± 0.62	3.35 ± 0.78	0.552	0.583
7th day	3.85 ± 0.41	3.75 ± 0.47	-3.626	<0.001*
p¥	<0.001*	<0.001*		

SD: Standard deviation.t: Student t-test. ¥ pfpr paired sample t test.

p: p value for comparing between Normocalcemia and Hypocalcemia.

*: Statistically significant at $p < 0.05$.

Table (7): Comparison between normocalcemic and hypocalcemic acute kidney injury patients according to APACHE II score and clinical outcome.

	Normocalcemia (n = 70)	Hypocalcemia (n = 38)	T	P
	Mean ± SD	Mean ± SD		
APACHE II score	19.66 ± 4.8	27.34 ± 5.37	-7.613	<0.001*
			Test of Sig.	p
ICU length of stay (days)	7.36 ± 1.69	8.5 ± 1.96	-3.178	0.002*
Mortality				
Die	4 (5.7%)	12 (31.6%)	χ^2= 13.056	<0.001*
Survived	66 (94.3%)	26 (68.4%)		

IQR: Inter Quartile Range
SD: Standard deviation
t: Student t-test
p: p value for comparing between Normocalcemia and Hypocalcemia
*: Statistically significant at $p \leq 0.05$
U: Mann Whitney test.
$\chi 2$: Chi square test.

DISCUSSION

AKI is a difficult illness that is often linked with a poor prognosis and can be caused by a variety of medical conditions. Calcium is an essential mineral that the body requires for a range of physiological functions, including hormone generation, intracellular message transmission, cellular activity, heart function, and cerebral activity **[10]**.AKI typically causes a change in calcium homeostasis but it is uncertain, however, if calcium plays a role in the development of AKI **[11] [12]**.

As a result, we designed this study to determine the frequency and relationship between hypocalcemia and acute kidney injury in ICU patients through serial assessment of serum total and corrected calcium, continuous evaluation of kidney functions, and evaluation of the effect of hypocalcemia on clinical outcome of those patients. To our knowledge, only a small number of studies have demonstrated an association between hypocalcemia and increased incidence of AKI related adverse outcome in the ICU.

Our study showed that hpocalcemic AKI patients were about thirty five percent of all patients ((38÷108) ×100 = 35%) which show that hypocalcemia is a common condition in AKI which occurs due to multiple etiologies including: Reduced synthesis of 1,25D by the kidneys; increased levels of phosphorus in the blood, which sequesters calcium; and skeletal resistance to parathyroid hormone Increased expression of the calcium detecting receptor and intracellular calcium build-up **[3]**. This was in line with the findings of Thongprayoon et al., who used serum ionized calcium of 5.00:5.20 mg/dL as the reference group and discovered that the incidence of hypocalcemia in hospital acquired AKI in 6 groups was 16.5% in patients with admission serum ionized calcium of 4.39, 14.8% in 4.40:4.59, 12.5% in 4.60:4.79, 11.6% in 4.80:4.99, 10.4% in 5.00:5.19, and 15.0% in 5.20 mg/dl**[13]**. Also Wang et al., studied total of 10,207 AKI patients, A total of 3128 patients were in the low iCa group (<1.06 mmol/l) which represented about 30% of total patients **[2]**. In Afshinnia et al. study of 685 patients with AKI, 529 of them were with mild to severe hypocalcemia so, hypocalcemia represented about 77% of all patients. This showed that hpocalcemia was common within AKI patients **[14]**.

A statistically significant increase was found in our study in baseline staging of AKI in hypocalcemic AKI patients than those with normocalcemic AKI patients and significant decrease in staging of AKI at 7th day in normocalcemic than those with hypocalcemic AKI patients. This was consistent with Thongprayoon et al.'s findings, which showed that no difference in the risk of hospital acquired AKI when serum ionized calcium levels between 4.60 and 5.19 mg/dl, which is the normal range, and lower serum ionized calcium levels of ≤ 4.59 mg/dl and higher serum ionized calcium levels of ≥ 5.20 mg/dl were both significantly associated with an increased risk of hospital-acquired AKI **[13]**.

The current study showed a statistically significant increase at incidence of respiratory failure and onset of diabetes in hypocalcemic AKI patients as compared to normocalcemic acute kidney injury patients and no significant difference between groups as regard to incidence of (COPD, AF, coronary heart disease, congestive heart disease, liver disease, HTN and stroke). This agrees with Wang et al. who found that Participants with low iCa concentrations had higher comorbidities of respiratory failure **[2]**. Also,

Thongprayoon et al. observed that there was a significant higher comorbidities as (hypertension, diabetes mellitus, congestive heart failure and stroke) with hypocalcemic AKI patients **[13]**. However, Desai et al. observed that there was no difference between both groups as regard diabetes and pulmonary disease; this difference may be due to ethnic and environmental differences **[15]**.

Our study showed statistically significant increase in the incidence of acidosis, BUN, serum cholesterol, random blood sugar, White blood cells and ESR and significant decrease in amount of urine output and eGFR in hypocalcemic AKI patients than those with normocalcemic AKI andno statistically significant difference between both groups as regard hemoglobin, hematocrit, SGPT, SGOT, PH, serum triglyceride, serum k and Anion gap. In same context, Thongprayoon et al. found a statically significant decrease in amount of urine output and eGFR in hypocalcemic group than normocalcemia group in AKI patients **[13]**. While the study of Wang et al. found no statistically significant difference among their participants regarding BUN and serum potassium, However, significance increase was detected regarding random blood sugar in hypocalcemic AKI patients and significance decrease was detected regarding hematocrit % and anion gap in hypocalcemic AKI patients, This may be due totheir longer duration of study and their large sample size, as they evaluated 10,207 patients **[2]**.

In current study statistically significant decrease found in baseline total and corrected calcium levels and 7th day total and corrected calcium levels in hypocalcemic as compared to normocalcemic AKI patients. Among those with hypocalcemia, there is a significant increase in total calcium over 3rd day and 7th day follow up periods with weak response to treatment with calcium supplementation. In those with normocalcemia, there is significant increase in baseline total calcium and total calcium on third day and still within normal level which shows good response to treatment with calcium supplementation and good recovery of patients, while there is non-significant change in total and corrected calcium on seventh day. Additionally, Sanaiet al. discovered that there was no significant link between corrected and ionized calcium and there was a significant positive correlation between total and ionized calcium **[16]**. While Wang et al. demonstrated no statistically significant difference in corrected calcium and total calcium among their participants. This difference may be due to their lager sample size **[2]**.

In the current study, there was no statistically significant difference in baseline creatinine between patients with normocalcemia and hypocalcemia AKI; however, on a 24-hour follow-up, patients with hypocalcemia had significantly higher serum creatinine. Additionally, on the seventh day, there was a significant change in serum creatinine in each group, patients with hypocalcemia AKI patients having higher levels. Serum creatinine levels increased significantly between the six groups (≤ 4.39, 4.40–4.59, 4.60–4.79, 4.80–4.99, 5.00–5.19, and ≥ 5. 20 mg/dl) that Thongprayoon et al. sorted admission ionizedserum calcium into **[13]**. On other hand, Akman et al., found a significant increase among groups regarding 24 hours average creatinine (increase in those needed hemodialysis in their study) and there was a significant decrease among groups regarding 72 hr. average creatinine (lower with patients who didn't need hemodialysis) **[17]**. This difference may due to their study was on AKI

patients stage 3 only and who are in need for hemodialysis in their groups while we studied stage 1,2 and 3 acute kidney injury without need for hemodialysis.

According to our research, there was no statistically significant difference in baseline serum albumin levels between patients with normocalcemic AKI and those who were hypocalcemic. However, on the seventh day, the serum albumin levels of the hypocalcemic AKI patients were significantly lower. El Hossary et al. reported similar outcomes, showing that the mean baseline serum albumin level in their subjects was 3.43 g/dl. There was no discernible relationship between albumin and calcium levels **[18]**. Unlike our study, Sanaie et al. examined 100 patients who were admitted to the intensive care unit (ICU) and found that survivors had a significantly lower mean serum albumin level than non-survivors did. They also examined the 30-day mortality rate in patients with AKI who were hypocalcemic and normocalcemic**[16]**.

The current investigation found that hypocalcemic AKI patients had a statistically significant higher APACHE II score (i.e., worse outcome) than normocalcemic AKI patients. El Hossary and colleagues also discovered that the APACHE II score was a major risk factor for hypocalcemia. **[18]**. Afshinnia et al., found that patients with hypocalcemic AKI had higher APACHE II score **[14]**. Also Cekmen et al., Found that patients with hypocalcemia in ICU had a higher APACH II score **[19]**.

In addition, we discovered that the hypocalcemic group's ICU length of stay and mortality rate were statistically significantly higher than those of the normocalcemic AKI patients with various aetiologies. This was in line with the findings of theZhang et al, that mild and moderate hypocalcemia increased the risk of mortality **[20]**. Additionally, Dey et al. noted that hypocalcemia may be related to adverse outcome in ICU patients **[21]**.Afshinnia et al., found that patientshad a significantly higher mortality rate when continued to have hypocalcemia AKI during ICU stay **[14]**. Against our study, Steele et al., found no significant difference in mortality between severely, mildly hypocalcemic and normocalcemic patients **[11]**. This difference may be due to their study was on critically ill patients in general not all of them having AKI like our patients all of them had AKI.

Limitations: There were limitations to our study as: It was single center study and results may differ elsewhere, relatively small sample size and lack of randomization.

CONCLUSION AND RECOMMENDATIONS

This study concluded that, accounting for roughly 35% of cases, hypocalcemia is a prevalent complication in AKI. Hypocalcemia in AKI was associated withincreasing incidence of respiratory failure, diabetes, acidosis, BUN level, serum cholesterol, RBS, WBCS, ESR and increase in serum creatinine on 24h follow up, this referred to increasing staging of AKI, and decreasing amount of urine output, eGFR, baseline total and corrected calcium levels and on 7th day and serum albumin on 7th day. A higher APACHE II score, length of stay in the ICU, and death rate were linked to hypocalcemia in AKI. Therefore, it's critical to monitor serum corrected calcium in all AKI patients in order to catch problems early and avoid complications. Patients with hypocalcemic AKI need to have long-term follow-up. It is necessary to do additional clinical research with multicenter collaboration to validate our findings.

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Author Contributions

Kholoud Ali Ahmed Ghabaghbyis the only author and has fully contributed to the manuscript.

References

1- **Hwang SU, Park HY, Kim YO, Kang DA, Ku HS, Cho JU, et al.** Changes in acute kidney injury epidemiology in critically ill patients: a population-based cohort study in Korea. Ann Int Care. 2019;9:1-9.

2- **Wang BE, Li DI, Gong YU, Ying BI and Cheng BI.** Association of serum total and ionized calcium with all-cause mortality in critically ill patients with acute kidney injury. ClinChimActa. 2019; 494:94-9.

3- **Leaf, D. E., &Christov, M**. Dysregulated mineral metabolism in AKI. In Seminars in nephrology. 2019; 39(1):41-56.

4- **O'Kane M, Jassam N, Barth JH, Day A, Bowles S, MacKenzie F**. Albumin-adjusted calcium: a position paper. Association for Clinical Biochemistry & Laboratory Medicine. 2015.

5- **Auron AR and Alon US.** Hypercalcemia: a consultant's approach. PedNephrol. 2018:1475-88.

6- **Kdigo, A. K. I**. Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney IntSuppl, 2012:2(1), 1-138.

7- **Kenny CM, Murphy CE, Boyce DS, Ashley DM, Jahanmir J**. Things We Do for No Reason™: Calculating a "Corrected Calcium" Level. Journal of Hospital Medicine. 2021; 16(8):499-501.

8- **Jo JY, Ryu SA, Kim JI, Lee EH, Choi IC**. Comparison of five glomerular filtration rate estimating equations as predictors of acute kidney injury after cardiovascular surgery. Scientific Reports. 2019; 9(1):11072.

9- **Freitas ER**. Profile and severity of the patients of intensive care units: prospective application of the APACHE II index. Revistalatino-americana de enfermagem. 2010; 18:317-23.

10- **Song NA, Yang MI, Zhang HA and Yang SK.** Intracellular calcium homeostasis and kidney disease. Curr Med Chem. 2021; 28(18):3647-65.

11- **Steele T, Kolamunnage-Dona R, Downey C, Toh CH, Welters I**. Assessment and clinical course of hypocalcemia in critical illness. Critical Care. 2013; 17(3):1-10.

12- **Newman DB, Siontis KC, Chandrasekaran K, Jaffe AS, Kashiwagi DT**. Intervention to reduce inappropriate ionized calcium ordering practices: a quality-improvement project. The Permanente Journal. 2015; 19(1):49.

13- **Thongprayoon CH, Cheungpasitporn WI, Chewcharat AP, Mao MA, Bathini TA, Vallabhajosyula SA, et al.** Impact of admission serum ionized calcium levels on risk of acute kidney injury in hospitalized patients. Sci rep. 2020; 10(1):12316.

14- **Afshinnia FA, Belanger KA, Palevsky PM and Young EW.** Effect of ionized serum calcium on outcomes in acute kidney injury needing renal replacement therapy: secondary analysis of the acute renal failure trial network study. Ren fail. 2013; 35(10):1310-8.

15- **Desai TK, Carlson RW and Geheb MA.** Prevalence and clinical implications of hypocalcemia in acutely III patients in a medical intensive care setting. Am J Med. 1988; 84(2):209-14.

16- **Sanaie SA, Mahmoodpoor AT, Hamishehkar HA, Shadvar KA, Salimi NA, Montazer MA, et al.**Association between disease severity and calcium concentration in critically ill patients

admitted to intensive care unit. Anest Pain Med. 2018; 8(1).

17- **Akman C, ÜlkerÇakır D, Bakırdöğen S, Balcı S**. The effect of serum calcium levels on uremic encephalopathy in patients with acute kidney injury in the emergency department. Medicina.2019; 23; 55(5):204.

18- **El Hossary ZI, SaadEldin SM, Matar HH and Askar IA.** Risk Factors of Hypocalcemic Patients at Surgical Intensive Care Unit of Zagazig University Hospitals. Egy J Hosp Med. 2021; 85(2):3753-7.

19- **Cekmen B, Koylu R, Akilli NB, Gunaydin YK, Koylu O, Atis SE, etal**. Ionized calcium level predicts in-hospital mortality of severe sepsis patients: A retrospective cross-sectional study. Journal of Acute Disease. 2021; 10(6):247-51.

20- **Zhang Z, Xu X, Ni H, Deng H**. Predictive value of ionized calcium in critically ill patients: an analysis of a large clinical database MIMIC II. PLoS One. 2014; 9(4):e95204.

21- **Dey S, Karim HM, Yunus M, Barman A, Bhattacharyya P, Borthakur MP**. Relationship of on admission hypocalcaemia and illness severity as measured by APACHE-II and SOFA score in intensive care patients'. Journal of clinical and diagnostic research: JCDR. 2017; 11(3):UC01.

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