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CLINICAL MARKERS PREDICTING MORTALITY IN PATIENTS RECEIVING RENAL REPLACEMENT THERAPY IN THE INTENSIVE CARE UNIT: A ONE-YEAR RETROSPECTIVE STUDY

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Abstract

Objective: Acute kidney injury (AKI) necessitating continuous renal replacement therapy (CRRT) is linked to elevated mortality rates in the intensive care unit (ICU). Finding prognostic markers affects each person's care are still very important. The objective of this study was to determine clinical and biochemical predictors of intensive care unit mortality in patients undergoing CRRT.

Methods: This retrospective single-center study encompassed 130 adult ICU patients who underwent CRRT from January 2024 to January 2025. For the mortality analysis, patients were divided into two groups: surviving and exitus. For the secondary analysis, they were divided into two groups: early CRRT and late CRRT, based on when they started.

Results: The mortality rate in the ICU was 83.8% (n=109). In multivariable logistic regression, a higher SOFA score (OR: 2.18; 95% GA: 1.38–3.45; p=0.001), increased serum creatinine (OR: 0.59; 95% GA: 0.36–0.94; p=0.029), levels were independently linked to mortality. There was no significant difference in mortality between the early (57.7%) and late (42.3%) CRRT initiation groups (p>0.05). The late group, on the other hand, stayed in the ICU and the hospital for a lot longer and got more Prismocal solution (p<0.05).

Conclusion: This study identified several clinical and biochemical parameters as independent predictors of mortality in CRRT-treated ICU patients. Although early CRRT initiation did not significantly impact survival, it was associated with reduced use of dialysis solution and shorter ICU and hospital stays. These findings suggest that integrating prognostic markers into clinical decision-making may improve outcome prediction.

Keywords*: Renal replacement therapy, acute kidney injury, intensive care unit, sepsis-associated AKI, critical care outcomes, mortality.*

Introduction

Acute kidney injury (AKI) is a complication frequently seen in the intensive care unit (ICU) and leads to devastating outcomes. It significantly increases the risk of mortality by affecting between 20% and 50% of intensive care patients.[1] Although there is no definitive treatment for AKI, renal replacement therapy (RRT) is a key intervention for patient survival. However, the mortality rates in patients requiring RRT remain high. Despite advances in the field of intensive care, the 90-day mortality in patients with AKI requiring dialysis can be as high as 50%. [2] Sepsis is the leading cause of AKI in the ICU and is responsible for approximately 50% of all AKI cases. [3] Prognosis is poorer in sepsis-associated AKI than in sepsis or AKI alone and entails longer admission to the ICU and a higher risk of mortality. [4]

The most appropriate management strategies for RRT in the ICU are still debated and researched.[5] The principal questions in this area focus on the time of RRT initiation and module selection (continuous or intermittent).[5] Current evidence shows no significant difference in survival between continuous RRT (CRRT) and intermittent RRT (IRRT).[6] Similarly, no distinct benefit in terms of mortality has been observed for the early initiation of RRT. The *STandard vs. Accelerated Initiation of RRT in AKI* (STARRT-AKI) trial revealed that early RRT did not reduce 90-day mortality more than the late strategy.[7] In clinical practice, the timing and type of RRT generally depend on clinician preference, considering factors such as hemodynamic stability and fluid load. However, these supportive approaches do not significantly reduce the consistently high mortality rates associated with AKI.

Owing to the alarmingly high risk of mortality, interest has grown in the identification of markers capable of predicting clinical outcomes in patients undergoing RRT in the ICU. [8]As emphasized by the latest guidelines, the timely recognition of high-risk patients is critically important. [6] However, reliable prognostic indicators have not yet been adequately identified in this patient group. Earlier research identified several factors linked to unfavorable outcomes in patients receiving RRT. These include advanced age, high disease severity scores (such as Acute Physiology and Chronic Health Evaluation II [APACHE II] and Sequential Organ Failure Assessment [SOFA]), hemodynamic instability, and increased inflammatory biomarkers like C-reactive protein (CRP) or blood lactate. [3,9,10] This retrospective cohort study, conducted over a year, focused on ICU patients who required RRT. This study aimed to identify the main clinical indicators that predict mortality and to explore how these factors are linked to patient outcomes.

Methods

This retrospective, single-center study was performed with 1375 patients followed-up between January 2024 and January 2025 at the Kocaeli University Medical Faculty General ICU, Türkiye. Patients who developed AKI and underwent RRT according to the KDIGO criteria either at hospital admission or during subsequent ICU stay were included in the study. [11]

The study was approved by the Kocaeli University Non-Interventional Clinical Research Ethical Committee (Decision No. GOKAEK-2025/11/30). The study was performed retrospectively and all patient data were anonymized.

Data were retrieved from the hospital information management system via retrospective examination of patient files. Data recorded within the scope of routine clinical procedures were used.

The variables examined included demographic data (patient name, number, age, and sex), comorbidities, (hypertension, diabetes mellitus, cerebrovascular event, coronary artery disease, chronic obstructive pulmonary disease, lymphoma/leukemia, and malignancy), clinical scores (SOFA and APACHE II), parameters related to intensive care and RRT (duration of stay in the ICU, day of commencement of CRRT, RRT modality, cause of AKI and CRRT indications, and early/late commencement), treatments applied and device characteristics (M150 dialysis set, cytokine filter, dialysate, PrismOcal, citrate fluid, vasopressor use, mechanical ventilation [MV], presence of shock, and hydrazone use), prognosis (survival/exitus), laboratory parameters (hemoglobin, hematocrit, platelet, blood urea nitrogen [BUN], creatinine, albumin, potassium, phosphorus, CRP, osmolality, glomerular filtration rate, international normalized ratio (INR), aPTT, aspartate transferase (AST), alanine transaminase (ALT), total bilirubin, pH, bicarbonate, base excess, lactate, ionized calcium, procalcitonin, and pro-brain natriuretic peptide).

Definitions of early and late RRT: RRT commencement times were classified according to KDIGO guideline. [11]

Early RRT: Patients meeting KDIGO stage 2 AKI criteria (diuresis < 0.5 mL/kg/hour ≥ 12 hours v or a ≥ 2-fold increase in serum creatinine basal values, urea > 100 mg/dL) and started on treatment within 8 hours. [12]

Late RRT: Patients meeting KDIGO stage 3 AKI criteria (diuresis < 0.3 mL/kg/hour ≥ 24 hours refractory hyperkalemia, pulmonary edema, urea > 150 mg/dL, severe acidosis [pH < 7.15]) and started on treatment within 12 hours.[12]

RRT Modalities

According to the records in the patient files, the patients underwent CRRT (continuous venovenous hemofiltration, hemodiafiltration) or intermittent hemodialysis. Data on the devices used for CRRT, filter types, and treatment parameters were retrieved from patient records. Based on these records, Prismaflex® (Baxter International Inc., Deerfield, IL, USA) was used in all RRT procedures. In citrate-based set-ups, PrismOcal® (Baxter) was used, while in non-citrate set-ups, Dialisan® (Baxter) was used as the replacement fluid and PrismOcal® or Dialisan® (Baxter) as the dialysate. According to the data obtained, the prescribed effluent dose was planned at an average of 25 mL/kg/hour, which varied among patients depending on their clinical condition. In patients receiving intermittent hemodialysis, the records showed that the effluent dose was determined based on different parameters.

AKI Classification

The causes of AKI were classified into three groups based on the clinical, laboratory, and imaging findings in the patient records: prerenal, renal (intrinsic), and postrenal. Renal-cause cases were further divided into sub-groups: sepsis-related, nephrotoxic, ischemic, or multifactorial.

The primary study outcome was survival status. Patients were categorized into two groups, survivors and exitus, based on discharge from the ICU or mortality. The two groups were analyzed by comparing their demographic, clinical, and laboratory data.

Inclusion Criteria

1. Age 18 or over
2. Hospitalization >24 hours in the Kocaeli University Medical Faculty ICU
3. Follow-up between 1 January, 2024, and 1 January, 2025
4. Indication for RRT having been established, and RRT being initiated

Statistical Analysis

IBM SPSS 29.0 version (IBM Corp., Armonk, NY, USA) was employed to conduct statistical analyses. The Kolmogorov-Smirnov and Shapiro-Wilk tests were implemented to evaluate normality. The mean ± standard deviation was used to express normally distributed continuous variables, while the median and interquartile range (IQR) were used to express non-normally distributed continuous variables. Counts and percentages were used to represent categorical variables. The independent samples t-test or Mann-Whitney U test were employed to compare continuous variables between survivors and fatalities. The chi-square test was employed to compare categorical variables between the two groups. A binary logistic regression analysis was implemented to conduct multivariable analysis. Statistical significance was defined as a *p*-value of less than 0.05.

Results

In total, 130 patients participated in this study. Among them, 60.8% had hypertension, 34.6% had diabetes mellitus, 37.7% had coronary artery disease, and 36.9% had a history of malignancy. Vasopressor use was present in 83.1% of patients, mechanical ventilation support in 75.4%, and shock in 71.5%.

The most common indications for RRT were oliguria/anuria (65.4%), fluid load (131), and resistant metabolic acidosis (10.8%). The causes of AKI, in descending order of frequency, were kidney disease (32.3%), sepsis (23.8%), postoperative trauma (16.9%), and nephrotoxic agent exposure (13.1%).

Comparison of the surviving (n=21) and exitus (n=109) groups revealed a lower mean age of the survivors (61(47.5-74.5) vs 69(61-78) years, respectively, p=0.031). The SOFA (p<0.001) and APACHE II (p<0.001) scores were significantly higher in the exitus group. The exitus group had a longer duration of stay in the ICU (p=0.001) and longer time to the start of CRRT in the ICU (p=0.001). Platelet (p=0.006), albumin (p=0.001), and creatinine (p=0.007) levels were also lower in the exitus group, while CRP (p=0.049), INR (p=0.001), AST (p<0.001), ALT (p=0.004), and total bilirubin (p=0.014) levels were higher (Table 1).

Table 1. Prognostic indicators of mortality between the surviving and exitus patients

	Total (n=130)	Surviving (n=21)	Exitus (n=109)	*p*
Age (years), median (IQR)	68 (59-75)	61 (47.5-74.5)	69 (61-78)	0.031[a]
SOFA, median (IQR)	9 (7-12)	4 (2.5-6)	10 (8-12.5)	<0.001[a]
APACHE II, median (IQR)	25 (22-31)	20 (12.5-24)	27 (23-32)	<0.001[a]
Days in the ICU, median (IQR)	12.5 (4.7-24.2)	5 (3.5-8)	16 (7-25.5)	0.001[a]
Day of CRRT initiation in the ICU, median (IQR)	3 (2-7)	2 (1-3)	4 (2-7)	0.001[a]
PLT (x10^3/µl), median (IQR)	127.5 (52-212.2)	194 (107-373)	113 (48.5-205)	0.006[a]
Creatinine (mg/dL), median (IQR)	2.8 (1.8-4.5)	4.2 (2.6-6.8)	2.6 (1.7-4.1)	0.007[a]
Albumin (g/L), median (IQR)	23.8 (20.6-28)	29.3 (23-35.7)	23.2 (20.2-26)	0.001[a]
CRP (mg/L), median (IQR)	134.2 (61.3-218)	75 (11.6-198.5)	142 (75.9-242)	0.049[a]
Osmolarity (mOsmol/kg), median (IQR)	313 (298-333.2)	303 (292-318)	316 (300-335)	0.049[a]
GFR (mL/min/1.73 m^2), median (IQR)	20 (11.2-37.8)	15 (7-25.5)	21 (13-38.2)	0.027[a]
INR, median (IQR)	1.2 (1.1-1.5)	1.1 (1-1.3)	1.3 (1.1-1.6)	0.001[a]
AST (U/L), median (IQR)	42.5 (22-97.5)	14.5 (11.8-26)	54 (28-142)	<0.001[a]
ALT (U/L), median (IQR)	21 (8.1-55.8)	8.2 (5.6-17)	23 (10.5-74.6)	0.004[a]
T. Bilirubin (mg/dL), median (IQR)	0.7 (0.3-1.8)	0.4 (0.2-0.7)	0.8 (0.3-2.3)	0.014[a]
Procalcitonin (µg/L), median (IQR)	3.2 (1-8.9)	0.9 (0.2-5.5)	3.6 (1.3-10.1)	0.002[a]
Hemoglobin (g/dL), mean ± SD	8.9±1.8	9.3±1.9	8.8±1.8	0.279[b]
Hematocrit (%), mean ± SD	26.9±5.6	27.6±6.1	26.7±5.5	0.543[b]
Phosphorus (mg/dL), mean ± SD	4.9±2.3	4.5±1.7	4.9±2.4	0.446[b]
Bicarbonate (mmol/L), mean ± SD	20.1±5.6	20.1±6.4	20.1±5.4	0.997[b]
Base deficit (mmol/L), mean ± SD	-4.8±6.5	-4.9±7.6	-4.8±6.4	0.974[b]
Vasopressor use, n (%)	108 (83.1)	5 (23.8)	103 (94.5)	<0.001[c]
Mechanical ventilator requirement, n (%)	98 (75.4)	2 (9.5)	96 (88.1)	<0.001[c]
Malignancy, n (%)	48 (36.9)	4 (19)	44 (40.4)	0.108[c]

AKI: Acute kidney injury; ALT: Alanine aminotransferase; APACHE II: Acute Physiology and Chronic Health Evaluation II; AST: Aspartate aminotransferase; BE: Base excess; BUN: Blood urea nitrogen; CRP: C-reactive protein; CRRT: Continuous renal replacement therapy; GFR: Glomerular filtration rate; INR: International normalized ratio; MV: Mechanical ventilation; SOFA: Sequential Organ Failure Assessment; ICU: Intensive care unit

Values are presented as median (interquartile range, IQR) or mean ± standard deviation (SD), as appropriate.

n: Count

[a]Mann-Whitney U test

[b]Independent samples t-test

[c]Chi-square test

In univariable logistic regression analysis, age (p=0.019), SOFA score (p<0.001), RRT modality (p=0.011), duration of ICU stay (p=0.003), day of commencement of CRRT (p=0.02), and platelet (p=0.04) and creatinine (p=0.001) levels were associated with mortality. In the multivariable analysis, only the SOFA score (OR: 2.18; 95% CI: 1.38-3.45; p=0.001) and creatinine level (OR: 0.59; 95% CI: 0.36-0.94; p=0.029) were identified as independent predictors (Table 2).

Table 2. Uni- and multivariable logistic regression analysis of factors affecting survival

	Univariate Analysis OR (95% CI)	***p***	**Multivariate Analysis aOR (95% CI)**	***p***
Age (years)	1.03 (1-1.05)	0.019	1.04 (0.97-1.1)	0.194
SOFA	2.5 (1.7-3.67)	<0.001	2.18 (1.38-3.45)	0.001
RRT modality	5.36 (1.46-19.6)	0.011	9.92 (0.67-146.5)	0.095
Number of days in the ICU	1.11 (1.03-1.19)	0.003	1.1 (0.95-1.28)	0.179
Day of initiation of CRRT in the ICU	1.33 (1.04-1.7)	0.020	0.98 (0.71-1.35)	0.904
PLT (x10^3/µl)	0.99 (0.99-1)	0.040	0.99 (0.99-1)	0.337
Creatinine (mg/dL)	0.67 (0.53-0.84)	0.001	0.59 (0.36-0.94)	0.029

CRRT: Continuous renal replacement therapy; PLT: Platelet count; RRT: Renal replacement therapy; SOFA: Sequential Organ Failure Assessment; ICU: Intensive care unit; OR: Odds ratio; aOR: Adjusted odds ratio; CI: Confidence interval

In addition to the analysis in the surviving and exitus groups, comparisons of patients who started early and late RRT showed that 57.7% started early and 42.3% started late. The late RRT group had later CRRT initiation in the ICU (2(1-3) vs 7(5-12) days; p<0.001), longer ICU stays (6(3-20) vs 19(13-27) days; p<0.001), and longer hospital stays (13 (4-31) vs 25 (17-40) days; p<0.001). BUN (p=0.009) and osmolarity (p=0.001) were also higher in the late RRT group. The number of PrismOcal dialysis solutions was also higher in the late RRT group (6(3-16) vs 9 (8-13); p=0.006) (Table 3).

Table 3. A comparison of patients started on RRT late and early

	Total (n=130)	**Early (n=75)**	**Late (n=55)**	***p****
PrismOcal® use, median (IQR)	6 (3-22)	6 (3-16)	9 (8-13)	0.006
Days in the ICU, median (IQR)	12.5 (4.7-24.2)	6 (3-20)	19 (13-27)	<0.001
Day of initiation of CRRT in the ICU, median	3 (2-7)	2 (1-3)	7 (5-12)	<0.001
Days of hospitalization, median (IQR)	19 (8.7-33)	13 (4-31)	25 (17-40)	<0.001
BUN (mg/dL), median (IQR)	65 (46-97.5)	59 (41-81)	79.5 (52-104)	0.009
Osmolarity (mOsm/kg), median (IQR)	313 (298-333.2)	308 (295-322)	325 (305-348)	0.001

BUN: Blood urea nitrogen; CRRT: Continuous renal replacement therapy; SD: Standard deviation; ICU: Intensive care unit, IQR: Interquartile range
*Mann-Whitney U test

Discussion

This study examined the clinical and biochemical parameters associated with mortality in intensive care patients who received CRRT for AKI, a 50% risk factor for mortality in intensive care, and revealed various markers that may affect survival. The findings showed that parameters such as age, SOFA and APACHE II scores, the day on which CRRT was initiated in the ICU, platelet levels, creatinine, albumin, CRP, INR, hepatic enzymes, and total bilirubin were significantly associated with mortality.

Various machine-learning models developed for predicting mortality in AKI patients receiving CRRT also emphasize similar prognostic variables. For example, Järvisalo et al. described age, SOFA score, and creatinine levels as exhibiting the greatest significance in predicting mortality.[8] Similarly, Ahn et al. created a machine-learning algorithm aimed at forecasting mortality among AKI patients receiving CRRT. [13] The variables with the highest significance in the model were age, SOFA score, and creatinine levels. Similarly, in the present study, these parameters exhibited significant effects on survival in both univariate and multivariate analyses. The fact that both traditional statistical methods and AI models yield similar results suggests that these indicators may represent the basis of clinical decision-support systems.

Debates over the effectiveness of RRT initiated early or late have led to the development of multi-center and large-scale clinical studies. The first of these was the ELAIN study (2016) – *Early vs. Late Initiation of Dialysis in AKI*. In this single-center, randomized, controlled study from Germany, 231 patients who developed KDIGO stage 2 AKI and met the high-risk criteria were placed into either the "early RRT" group, which involved treatment within 8 hours of meeting stage 2 criteria, or the "delayed RRT" group, where treatment occurred within 12 h of reaching stage 3 or when urgent dialysis was necessary. [12] The results revealed a significantly lower 90-day mortality with early RRT (early arm, 9.3%; late arm, 54.7%; p=0.03). The early treatment group experienced a 15% absolute reduction in survival risk (HR=0.66, 95% CI 0.45–0.97). Secondary benefits were also reported in patients undergoing early RRT, such as shorter mechanical ventilation time and shorter ICU/hospital stays. However, it should be noted that the ELAIN population largely consisted of patients after cardiovascular surgery, and that almost all the late-arm patients eventually required dialysis, with 91% progressing to stage 3 AKI, among whom RRT was administered. The significant improvement in mortality observed with early RRT

in this selected high-risk patient group has emerged as an important finding in favor of early RRT in the literature.

The second was the *Artificial Kidney Initiation in Kidney Injury* (AKIKI) study (2016).[14] This multicenter randomized controlled study conducted in 31 centers in France compared early and postponed RRT in a larger patient population than ELAIN. Six hundred twenty critically ill patients meeting stage 3 AKI criteria underwent either 'early RRT' (initiation of dialysis within ≤6 hours following stage 3 diagnosis) or a 'delayed/surveillance strategy.' In the delayed strategy, patients were followed up without initiation of RRT, unless indications requiring emergency dialysis emerged (dialysis was initiated in case of criteria such as BUN >40 mmol/L, potassium >6 mmol/L, pH <7.15, or >72 h oliguria). In contrast to ELAIN, AKIKI results showed that early RRT conferred no benefit in terms of survival. Sixty-day mortality was almost identical between the early and late initiation groups (48.5% vs. 49.7%, respectively; HR=1.03, p=0.79). Twenty-eight mortality also exhibited no significant difference (41.6% vs. 43.5%). Notably, only approximately half of the patients in the delayed intervention group were able to leave intensive care without requiring dialysis (49% of patients in the delayed arm discontinued follow-up without requiring RRT owing to spontaneous recovery of kidney function or death). That study suggests that early dialysis is not routinely superior in the general population, and that delaying dialysis can be safe in many patients. The dialysis-related side effects and dialysis dependence rates on day 60 in the early group were not different from those in the delayed group. The AKIKI findings were inconsistent with those of ELAIN, and this led to a questioning of the 'early RRT for all' approach.

Finally, the *STandard vs. Accelerated Initiation of RRT in AKI* (STARRT-AKI) trial was conducted (2020). Performed under Canadian leadership with more than 3000 patients from different regions of the world, this is the most extensive randomized controlled study. [7] It compared an 'accelerated' RRT strategy (early, initiation in ≤12 hours) compared to a 'standard' strategy (a waiting time of at least ~48-72 hours in the absence of traditional criteria) in critically ill patients developing AKI. After 90 days, the mortality rates were nearly identical between the two groups, with 43.9% in the early strategy group and 43.7% in the standard strategy group (RR=1.00, p=0.92). In other words, early RRT yielded no improvement in survival. Moreover, the early RRT group experienced several notable negative outcomes; the rate of dialysis dependence among survivors was markedly higher in this group (10.4% compared to 6.0%; RR=1.74, p= 0.007). These findings suggest that early dialysis may hinder renal recovery. Moreover, the early group experienced a significantly higher incidence of severe adverse events related to RRT, such as hypertension, bleeding, and infection, with rates of 23.0% compared to 16.5% (p<0.001). A significant proportion of the patients in the standard (delayed) strategy arm (up to 38%) recovered without requiring dialysis, while almost all patients in the early group were exposed to dialysis (61.8% of patients in the standard arm underwent RRT, compared to 96.8% in the early arm). The STARRT-AKI results showed that early RRT did not reduce mortality in the general ICU population, but in fact revealed, in a powerful manner, that it can increase unnecessary dialysis and complications risks.

While this study found no variation in mortality rates between the early and late groups, the early group's use of a smaller amount of dialysate solution was notably advantageous in terms of cost-effectiveness. Similarly, shorter hospital and ICU stays in the early group were important in terms of hospital resource use.

This study had several limitations. In particular, the study was conducted retrospectively and at a single center; therefore, the generalizability of the findings may be limited. In addition, protocol standardization could not be established since parameters such as the initiation of CRRT, fluid type selection, and length of treatment depend on patient-based clinical decisions. The exclusion from the analysis of important clinical parameters such as the effluent dose, cumulative fluid balance, and long-term outcomes must also be regarded as another limitation.

Nonetheless, this study is important in terms of systematically analyzing a patient population specific to the ICU. Despite its retrospective nature, it has the potential to review the efficacy of the treatment modalities applied and contribute to the improvement of in-service quality. From this perspective, it will prepare the groundwork for further extensive prospective studies to be performed in the clinical setting.

This retrospective study evaluated the clinical and biochemical markers associated with mortality in patients undergoing CRRT due to AKI in the ICU and the results of different RRT initiation timings. A high mortality rate was detected in 109 of the 130 patients. According to the multivariable analysis results, SOFA scores reflecting the degree of organ failure and serum creatinine levels emerged as principal markers predicting survival. We believe that these parameters can contribute to the future development of clinical tools for predicting mortality using both logistic regression and models based on machine learning.

The analysis of CRRT initiation times, the second point of focus in this study, revealed no notable difference in mortality rates between those who received early treatment and those who received it later. However, hospital and ICU stays were longer, and the spread of dialysis solutions employed differed in the late CRRT group. These results suggest that the clinical outcomes of RRT timing may vary depending on the specific patient group, and that individualized treatment strategies are needed.

Conflict of Interest

The authors declare that there is no conflict of interest.

Compliance of Ethical Statement

The study was approved by the Kocaeli University Non-Interventional Clinical Research Ethical Committee (Decision No. GOKAEK-2025/11/30). The study was performed retrospectively and all patient data were anonymized.

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Author Contributions

V.A., A.K.: Study idea/Conceptualization; V.A., M.E.: Methodology; S.K., İ.İ.A.: Data Collection; V.A., Ö.G.: Analysis and Investigation; V.A., Ö.G.: Writing – original draft; N.B., A.K.: Writing – review and editing; All authors: Critical review.

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