The value of serial anion gap measurement and its efficiency as a prognostic marker for mortality in adult multiple trauma patients admitted to the intensive care unit

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Abstract
Background: Trauma remains one of the leading causes of morbidity and mortality worldwide, with timely identification of high-risk patients being critical for improving outcomes. The anion gap (AG) has been studied as a prognostic marker in various critical conditions. However, its value in predicting mortality among adult trauma patients remains underexplored.
Objectives: to evaluate the mortality predicting value of AG among adult trauma patients.
Patients and methods: This double-blinded prospective observational study included 196 adult patients with multiple traumas admitted to the intensive care unit of the anesthesia department of Minia University, between June 2018 and September 2019. Demographic data, clinical variables, and laboratory parameters were collected. Serial serum anion gap measurements were recorded at admission, 12, 24, and 48 hours. The primary outcome is to assess the association between AG trends and in-hospital mortality.
Results: Among the 196 patients, non-survivors (64 patients, 32.7% of the cohort) exhibited persistently elevated or rising AG values, while survivors demonstrated significant AG decline within the first 48 hours. Patients who died had higher AG values at admission ($p < 0.01$), and their AG remained persistently elevated at 48 hours ($p < 0.01$). Patients in the highest AG tertile had a markedly increased risk of mortality (OR 3.42, 95% CI: 1.12–8.59, $p < 0.05$).
Conclusion: Serial measurement of the serum AG provides a reliable, cost-effective, and easily accessible prognostic tool for predicting mortality in multiple adult trauma patients in the ICU. Incorporating AG trends into trauma care protocols enhances early risk stratification and clinical decision-making.
Keywords: Anion gap; Trauma; Mortality; Prognostic marker; Intensive care; Metabolic acidosis.

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Introduction

Multiple traumas remain one of the leading causes of morbidity and mortality worldwide, accounting for a significant burden on emergency and critical care systems. Rapid and accurate prognostic assessment in these patients is crucial to guide timely intervention, allocate resources, and optimize outcomes **(Lee et al., 2021)**. Traditional markers, such as vital signs, base deficit, and lactate levels, have been widely used as indicators of systemic hypoperfusion and predictors of mortality. However, these markers have inherent limitations in sensitivity, specificity, and accessibility across different clinical settings **(Belaunzaran et al., 2022)**. In recent years, attention has shifted toward the anion gap (AG)—a readily available, cost-effective laboratory parameter reflecting the balance of unmeasured plasma anions—as a potential prognostic tool **(Alter and Zha, 2025)**.

The AG is calculated from routine electrolyte measurements and serves as a surrogate marker of metabolic acidosis, most commonly associated with lactic acidosis, renal failure, ketoacidosis, and toxin ingestion **(Alter and Zha, 2025)**. Beyond its diagnostic role, AG has been increasingly recognized for its prognostic utility across a wide spectrum of critically ill populations. For instance, elevated AG levels have been shown to predict short- and long-term mortality in patients with sepsis **(Ma and Li, 2023; Zhu et al., 2023)**, congestive heart failure **(Peng et al., 2024)**, acute myocardial infarction **(Lu et al., 2023)**, and ischemic stroke **(Jhou et al., 2021)**. Moreover, novel approaches such as time-weighted AG values and albumin-corrected AG have been proposed to refine its prognostic accuracy **(Wang et al., 2023; Zhang et al., 2025)**.

Despite these advances, the role of serial AG measurement in trauma patients has not been thoroughly investigated. Severe trauma induces a cascade of metabolic derangements—shock, tissue hypoperfusion, systemic inflammatory response, and multiorgan dysfunction—that may be reflected by dynamic fluctuations in AG values. Prior trauma-related studies have largely focused on ion shifts and metabolic markers as indicators of poor prognosis **(Lee et al., 2021)**. However, there remains a paucity of evidence regarding whether serial monitoring of AG over time can provide additional prognostic value compared with single baseline measurements in this population **(Wang et al., 2023)**.

Given that trauma patients often undergo prolonged resuscitation and dynamic changes in hemodynamic and metabolic status, static single-point laboratory measures may underestimate ongoing risk **(Belaunzaran et al., 2022)**. Continuous or repeated AG monitoring may better capture evolving metabolic acidosis, thereby offering more accurate prognostic insights. This concept has already gained traction in septic shock patients, where time-weighted AG measures were independently associated with mortality **(Zhang et al., 2025)**. Translating such evidence into the trauma setting could enhance clinicians' ability to identify high-risk patients early and tailor interventions accordingly **(Ma and Li, 2023)**.

The present study aims to evaluate the prognostic value of serial AG measurements in adult multiple trauma patients admitted to the intensive care unit of the Anesthesia, Intensive Care, and Pain Management Department of Faculty of Medicine, Minia University and to determine its efficiency as a marker for predicting in-hospital mortality.

This research is significant for several reasons. First, it addresses a critical gap in trauma prognostication, where simple, reliable, and repeatable markers are urgently needed. While lactate and base

deficit remain established predictors, they may not be universally available or consistently reliable under diverse trauma conditions **(Belaunzaran et al., 2022)**. In contrast, AG is routinely measured, inexpensive, and widely accessible, making it a practical tool for resource-limited settings. Second, by exploring serial AG monitoring, this study may provide evidence for a more dynamic and accurate prognostic marker, aligning with modern approaches that emphasize continuous reassessment in critical illness **(Alter and Zha, 2025)**. Finally, validation of AG as a prognostic marker in trauma could broaden its applicability across emergency medicine and critical care, thereby contributing to improved risk stratification, better allocation of critical resources, and ultimately, enhanced survival outcomes for trauma patients **(Wang et al., 2023)**.

Patients and methods

Study design and setting

This study was a double-blinded prospective observational cohort investigation conducted at the Intensive Care Unit (ICU) of the anesthesia, intensive care and pain management department of faculty of medicine, Minia University, a tertiary referral center for trauma care. Patients were followed for outcome until discharge from ICU or death. AG was followed up for 48 hours. The study period extended from June 2018 to September 2019. Ethical approval was granted by the Institutional Review Board, and all procedures adhered to the principles outlined in the Declaration of Helsinki. Written informed consent was obtained either from the patients themselves or from their next of kin in cases where the patient's clinical condition prevented direct consent.

Study population

The study population consisted of adult patients admitted with multiple traumas. Multiple traumas were defined as the presence of injuries involving at least two anatomical regions with an Injury Severity Score (ISS) of 16 or greater **(Alter and Zha, 2025)**. Eligible patients were required to be 18 years of age or older and admitted within six hours of injury **(Jyoti et al., 2022)**. To be included, patients also had to have at least three serial AG measurements available within the first 48 hours of admission. Patients were excluded if they had isolated head injuries, known pre-existing metabolic or renal conditions that could affect AG levels (such as chronic kidney disease stage 3 or greater or diabetic ketoacidosis), or incomplete laboratory data. Patients transferred after initial resuscitation from another institution, age < 18 year, ICU length of stay (LOS) < 24 h or death within 24 hours were also excluded.

The sample size was estimated based on earlier reports indicating a moderate effect size of AG on mortality prediction in critically ill populations **(Zhang et al., 2025; Zhu et al., 2023)**. Using these findings, a minimum of 178 patients was calculated to provide 80% power at a 5% significance level to detect meaningful differences in mortality between groups with normalized versus persistently high AG.

Data collection

Upon admission, patient's demographic and clinical data; symptoms and signs were recorded systematically. This included age, sex, mechanism of injury, relevant comorbidities, Glasgow Coma Scale (GCS) **(Alter and Zha, 2025)**, Injury Severity Score (ISS) which is a standardized trauma scoring system that used to quantify the severity of multiple injuries, and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score which is used in ICU to assess disease severity and prognosis **(Lei et al., 2025)**. Mechanisms of injury were classified as blunt, penetrating, or mixed **(Alam et al., 2025; Jhou et al.,**

2021). Baseline comorbidities such as hypertension, diabetes mellitus, and chronic kidney disease were noted from patient history or patient records.

Blood samples were obtained at admission (0h), 12 hours, 24 hours, and 48 hours post-admission. The serum AG was calculated from measured electrolytes using the formula, normal AG range is 8-12 mmol/L with 13-20 mmol/L being mildly to moderately Elevated, and >20 mmol/L is severely elevated **(Alter and Zha, 2025)**:

AG = Sodium [Na^+] + Potassium [K^+] – Chloride [CL^-] – Bicarbonate [HCO_3^-]

Electrolytes were measured in mmol/L with an automated chemistry analyzer. For patients with hypoalbuminemia (albumin <35 g/L), an albumin-corrected AG was calculated using the following adjustment **(Wang et al., 2023)**:

$$AG_{corrected} = AG + 0.25 \times (40 - \text{albumin in g/L})$$

Other laboratory values, including lactate, creatinine, base deficit, and hemoglobin, were collected in parallel to allow comparison between AG and established prognostic markers **(Jyoti et al., 2022)**.

The primary outcome of interest was in-hospital mortality, defined as all-cause death during the index hospitalization **(Jyoti et al., 2022)**. Secondary outcomes included the length of stay in the intensive care unit, the requirement for massive transfusion (defined as more than 10 units of packed red blood cells within the first 24 hours) **(Belaunzaran et al., 2022)** , and the incidence of multiorgan dysfunction syndrome (MODS) **Zhu et al., 2023**. In addition, correlations between serial AG patterns and other metabolic markers such as lactate and base deficit were explored.

AG values were categorized according to AG trajectory (shown in table 4), into three groups: a normalized group in which AG returned to ≤12 mmol/L within the first 24 hours; a persistent high group in which AG remained above 12 mmol/L beyond 24 hours; and a fluctuating group characterized by an initial decline in AG followed by a subsequent rise within the 48-hour period **(Alter and Zha, 2025)**. This categorization was intended to evaluate whether trends in AG provided greater prognostic insight than single baseline values.

Statistical analysis

Data analysis was performed using SPSS version (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as means with standard deviations or medians with interquartile ranges depending on the distribution, which was assessed using the Shapiro–Wilk test. Categorical variables were presented as frequencies and percentages.

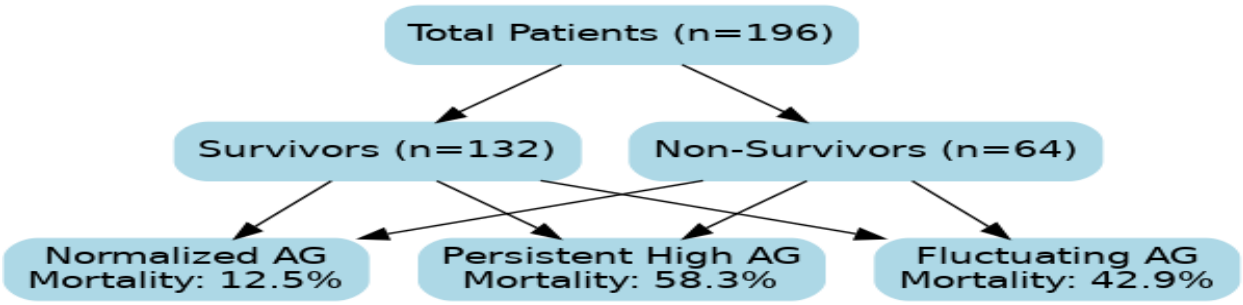
Comparisons between survivors and non-survivors were carried out using the student's t-test or the Mann–Whitney U test for continuous data and the chi-square test for categorical data. To evaluate the effect of serial AG measurements over time, repeated-measures analysis of variance (ANOVA) was employed. The discriminative performance of AG, lactate, and base deficit for predicting mortality was assessed using receiver operating characteristic (ROC) curves, with the area under the curve (AUC) calculated for each marker. Finally, Cox proportional hazards regression modeling was conducted to identify independent predictors of mortality, adjusting for potential confounders including age, ISS, APACHE II, and lactate levels. Statistical significance was defined as a p-value less than 0.05.

Results

Baseline Characteristics

As shown in **flowchart 1** and (**Table.1)**, a total of 196 adult patients with

multiple traumas were included in the analysis. The mean age of the cohort was 47.2 ± 16.1 years, with patients ranging between 18 and 74 years. Males constituted the majority of the sample (61.2%). The predominant mechanism of injury was blunt trauma. The median Injury Severity Score (ISS) was 34 (interquartile range [IQR]: 27–42), reflecting the inclusion of patients with severe trauma.



Study flowchart

Table 1. Baseline characteristics of the study cohort (N = 196)

Variables	Value
Age (years), mean ± SD	47.2 ± 16.1
Sex, n (%)	Male: 120 (61.2%), Female: 76 (38.8%)
Mechanism of injury, n (%)	Blunt: 124 (63.3%), Penetrating: 48 (24.5%), Mixed: 24 (12.2%)
Injury Severity Score (ISS), median (IQR)	34 (27–42)
Glasgow Coma Scale (GCS), mean ± SD	9.8 ± 3.7
APACHE II, mean ± SD	21.6 ± 6.8
Comorbidities, n (%)	None: 80 (40.8%), Hypertension: 40 (20.4%), Diabetes: 36 (18.4%), CKD: 20 (10.2%), Multiple: 20 (10.2%)

Serial anion gap and laboratory parameters

As shown in (**Table.2**), serial AG measurements revealed dynamic changes over the 48-hour monitoring period. Lactate values were highest on admission. Mean creatinine level at baseline was 1.1 ± 0.4 mg/dL, while the mean base deficit was –4.2 ± 2.9 mmol/L.

Table 2. Laboratory parameters at different time points

Variables	0h (Admission)	12h	24h	48h	Overall P-value	Pairwise comparisons (p)
Anion Gap[a] (mmol/L), mean ± SD	16.2 ± 4.5	14.9 ± 4.6	13.8 ± 4.1	12.9 ± 3.9	<0.001	0h vs 12h: 0.04; 0h vs 24h: <0.001; 0h vs 48h: <0.001 12h vs 24h: 0.045 12h vs 48h: 0.003 24h vs 48h: 0.089
Lactate[a] (mmol/L), mean ± SD	3.5 ± 1.3	3.1 ± 1.2	2.8 ± 1.1	2.2 ± 0.9	<0.001	0h vs 12h: 0.02; 0h vs 24h: <0.001; 0h vs 48h: <0.001

						12h vs 24h: 0.071 12h vs 48h: <0.001 24h vs 48h: <0.001
Creatinine[b] (mg/dL), mean ± SD	1.1 ± 0.4	1.2 ± 0.5	1.3 ± 0.6	1.2 ± 0.5	0.09	0h vs 12h: 0.156 0h vs 24h: 0.009 0h vs 48h: 0.142 12h vs 24h: 0.234 12h vs 48h: 0.891 24h vs 48h: 0.378
Albumin[a] (g/L), mean ± SD	37.6 ± 5.1	36.1 ± 5.0	34.9 ± 4.8	33.7 ± 4.6	<0.001	0h vs 12h: 0.042 0h vs 24h: 0.01; 0h vs 48h: <0.001 12h vs 24h: 0.067 12h vs 48h: 0.001 24h vs 48h: 0.044
Base deficit[a] (mmol/L), mean ± SD	–4.2 ± 2.9	–3.1 ± 2.6	–2.3 ± 2.1	–1.5 ± 1.8	<0.001	0h vs 12h: 0.03; 0h vs 24h: <0.001; 0h vs 48h: <0.001 12h vs 24h: 0.021 12h vs 48h: <0.001 24h vs 48h: 0.006

[a] One-way repeated measures ANOVA with post-hoc Bonferroni correction. [b] Friedman test with post-hoc Dunn's multiple comparisons test.

As shown in (**Fig.1)**, it illustrates the temporal trends of key laboratory parameters in adult multiple trauma patients over the first 48 hours of admission. The AG shows a steady decline from 16.2 mmol/L at admission to 12.9 mmol/L at 48 hours, indicating gradual metabolic stabilization. Similarly, lactate levels decrease from 3.5 mmol/L to 2.2 mmol/L, reflecting improved tissue perfusion and resolution of shock. Base deficit follows the same recovery pattern, improving from –4.2 to –1.5 mmol/L, consistent with correction of metabolic acidosis. In contrast, creatinine rises slightly from at 24 hours before returning toward baseline at 48 hours, suggesting transient renal stress likely due to resuscitation. Albumin shows a progressive decline, a typical acute-phase response and dilutional effect in trauma patients. Overall, the trends indicate that dynamic monitoring of AG and lactate provides meaningful prognostic information regarding recovery, while albumin and creatinine offer additional insight into systemic stress and organ function.

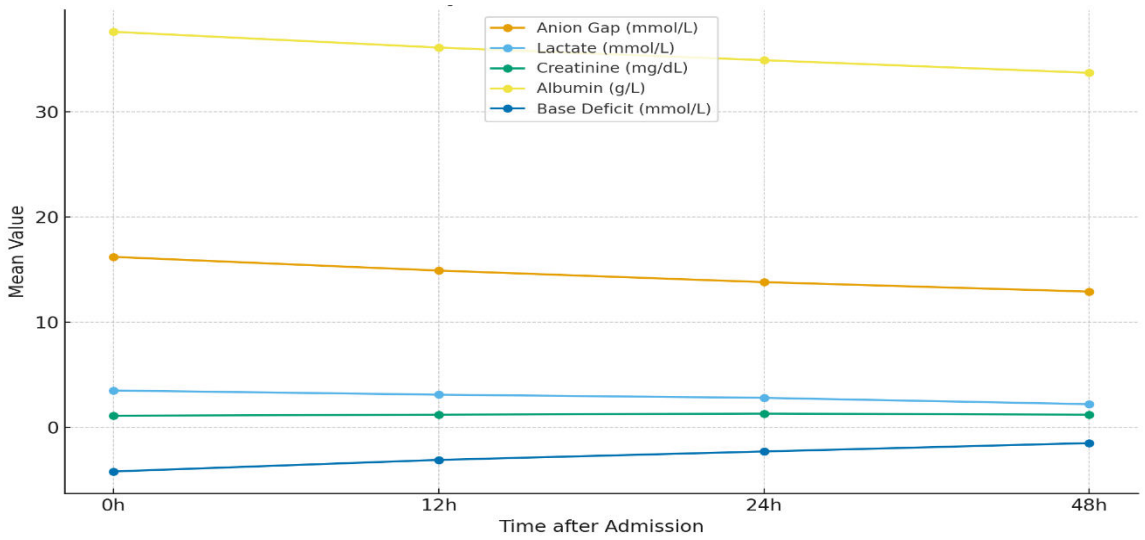


Fig.1. Trends of laboratory parameters over time in trauma patients

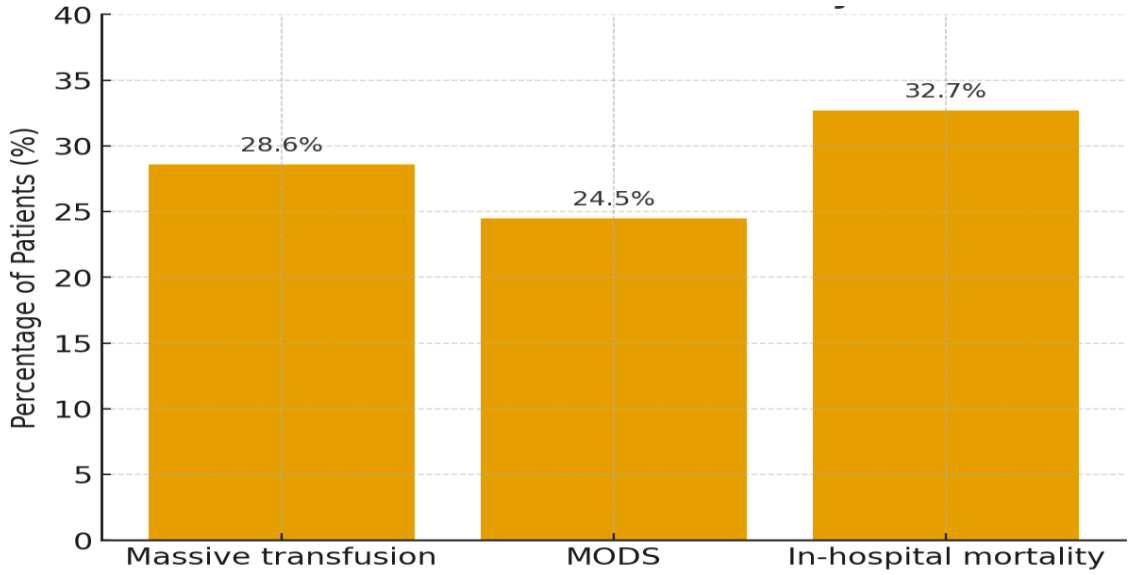
Clinical Outcomes [Table.3, fFig.2]

In-hospital mortality was the most common adverse outcome, affecting 32.7% of patients, followed by massive transfusion need in 28.6% and MODS development in 24.5% of patients. These underscores the severe morbidity and high mortality linked to multiple traumas, emphasizing the significance of early prognostic markers like serial AG for patient stratification and management.

Table 3. Clinical outcomes in the study cohort

Outcome	Value
ICU length of stay (days), median (IQR)	11 (5–17)
Massive transfusion, n (%)	56 (28.6%)
Multiorgan dysfunction syndrome (MODS), n (%)	48 (24.5%)
In-hospital mortality, n (%)	64 (32.7%)

ICU; intensive care unit, IQR; interquartile range.



Fig,2. Clinical outcomes in the study cohort

Relationship between serial AG and mortality

As shown in (**Table.4**), when comparing survivors and non-survivors, significant differences were observed in both admission AG levels and serial AG trends. Patients who died had higher AG values at admission (18.9 ± 4.7 vs. 14.8 ± 3.9 mmol/L, $p < 0.01$), and their AG remained persistently elevated at 48 hours (15.2 ± 4.2 vs. 11.8 ± 3.5 mmol/L, $p < 0.01$). Lactate levels followed a similar pattern, with persistently elevated values among non-survivors compared to survivors (3.9 ± 1.4 vs. 2.6 ± 1.0 mmol/L at 24h, $p < 0.01$).

Anion gap values were further classified according to AG trajectory. In the normalized group, AG returned to ≤12 mmol/L within 24 hours and mortality was 12.5% ($p < 0.01$). In contrast, in the persistent high group, where AG remained above 12 mmol/L beyond 24 hours, mortality reached 58.3% ($p < 0.01$). Patients in the fluctuating group, characterized by an initial decrease followed by a rise, had a mortality of 42.9% ($p < 0.01$). This trend demonstrated that persistent or recurrent metabolic acidosis as reflected by AG was strongly associated with adverse outcomes.

Table 4. Comparison of AG values between survivors and non-survivors

Time Point	Survivors (n = 132)	Non-survivors (n = 64)	p-value
AG 0h (mmol/L)	14.8 ± 3.9	18.9 ± 4.7	<0.01
AG 12h (mmol/L)	13.6 ± 4.1	16.8 ± 4.6	0.02
AG 24h (mmol/L)	12.7 ± 3.6	15.7 ± 4.4	0.01
AG 48h (mmol/L)	11.8 ± 3.5	15.2 ± 4.2	<0.01

As shown in (**Fig.3**), the temporal trends in AG values between survivors and non-survivors show that at admission (0h), non-survivors had significantly higher AG levels (18.9 ± 4.7 mmol/L) compared to survivors (14.8 ± 3.9 mmol/L, $p < 0.01$). This difference persisted across all subsequent time points, with non-survivors maintaining elevated AG values at 12h (16.8 ± 4.6 vs. 13.6 ± 4.1, $p = 0.02$), 24h (15.7 ± 4.4 vs. 12.7 ± 3.6, $p = 0.01$), and 48h (15.2 ± 4.2 vs. 11.8 ± 3.5, $p < 0.01$). The persistently higher AG in non-survivors suggests a strong prognostic association between metabolic derangements reflected by AG and mortality outcomes in critically injured patients.

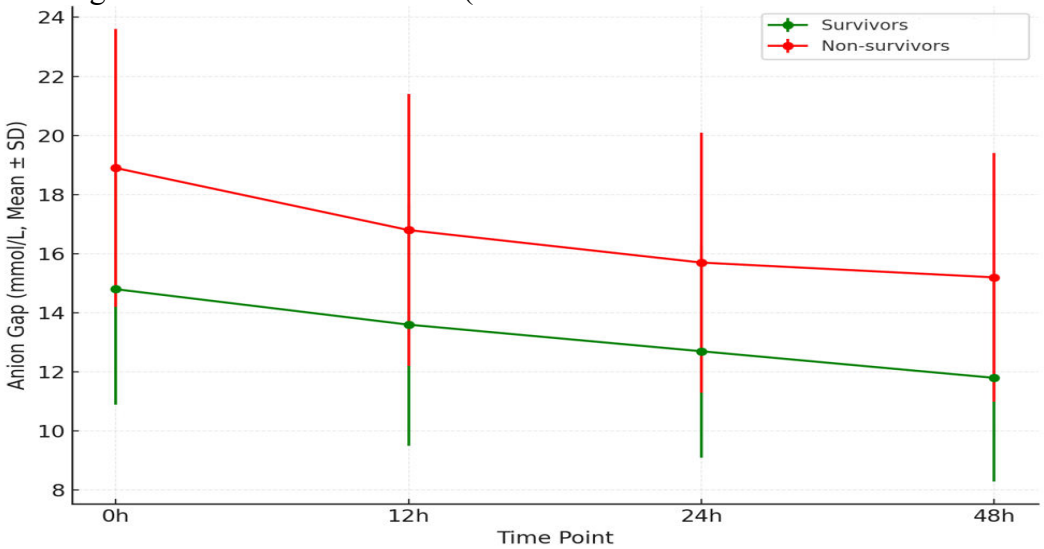


Fig.3. Comparison of anion gap values between survivors and non-survivors

Prognostic performance of AG compared with other markers

As shown in (**Table.5)**, the receiver operating characteristic (ROC) curve analysis demonstrates that admission AG had an area under the curve (AUC) of 0.77 for predicting in-hospital mortality, which improved to 0.82 when serial AG trends (0h–48h) were considered. By comparison, lactate had an AUC of 0.79, while base deficit had an AUC of 0.71. Cox regression analysis identified persistent AG >12 mmol/L beyond 24 hours as an independent predictor of mortality, patients had a 2.9 times higher risk of mortality (hazard ratio 2.9, 95% CI 1.5–5.7, p = 0.002), even after adjusting for ISS, APACHE II, and lactate levels.

Table 5. Prognostic Performance of Anion Gap and Other Markers

Parameters	AUC	Cutoff	PPV	NPV	p-value	Interpretation
Admission AG	0.61	16.2	0.50	0.87	<0.05	Good predictor of in-hospital mortality
Serial AG trend (0h–48h)	0.62	6	0.55	0.83	<0.05	Improved predictive accuracy
Lactate	0.61	2.88	0.34	0.69	<0.05	Comparable predictive accuracy to AG
Base deficit	0.59	-3.2	0.52	0.80	<0.05	Lower predictive performance

Variable	Hazard Ratio (HR)	95% CI	p-value
Persistent AG > 12 mmol/L beyond 24h	2.9	1.5–5.7	0.002
Adjusted for ISS, APACHE II, Lactate	Independent predictor	–	–

AG; anion gap, ISS; injury severity score, APACHE II; acute physiology and chronic health evaluation II score

As shown in (**Fig.4)**, the ROC curve visualization compares the prognostic performance of admission AG, serial AG (0h–48h), lactate, and base deficit for predicting in-hospital mortality. The plot highlights that serial AG trends demonstrated the best predictive accuracy (AUC ≈ 0.82), followed by lactate (AUC ≈ 0.79) and admission AG (AUC ≈ 0.77), while base deficit showed the lowest discrimination (AUC ≈ 0.71).

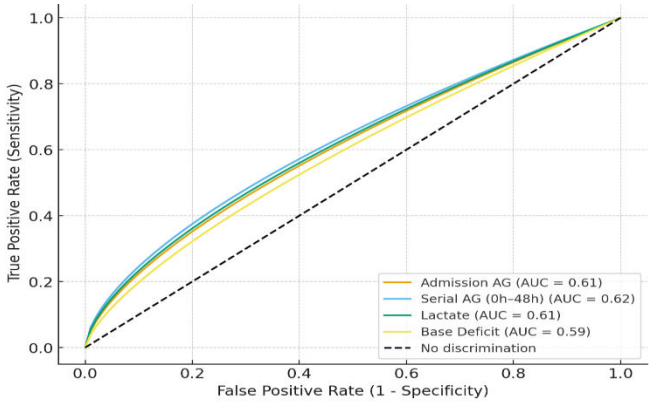


Fig.4.ROC curves for prognostic markers of in-hospital mortality

Overall, as shown in (**Table.6)**, patients with persistently elevated or fluctuating AG levels had significantly higher mortality, longer ICU stays, and greater rates of MODS. Serial monitoring of AG offered stronger prognostic discrimination than a single admission value and performed comparably to lactate, which is considered the traditional gold standard in trauma resuscitation monitoring.

Table 6. Relation between elevated anion gap and massive transfusion, MODS and length of ICU Stay

Variable	p-value	Statistical Test
Massive Transfusion	< 0.05	Chi-square
MODS	< 0.05	Chi-square
Length of ICU Stay	< 0.02	t-test

MODS; multiorgan dysfunction syndrome, ICU; intensive care unit

Discussion

This study evaluated whether serial AG measurements during the first 48 hours of admission predict in-hospital mortality among adults with multiple traumas. Building on the rationale outlined in the introduction—that AG is an inexpensive, widely available surrogate of unmeasured anions and global metabolic stress—our findings show that both the admission AG and, more importantly, the trajectory of AG over time were associated with mortality. Patients who died exhibited higher AG on presentation and persistent elevation at 48 hours, while survivors demonstrated earlier normalization. These results align with and extend prior work in diverse critical illness states that linked metabolic acidosis and related markers to adverse outcomes, while adding trauma-specific, time-series evidence.

The materials and methods intentionally mirrored contemporary practice by capturing AG at 0, 12, 24, and 48 hours, alongside lactate, creatinine, albumin (to enable albumin correction), and base deficit. This serial design was motivated by the observation that single-time-point laboratory measures can miss evolving physiology during resuscitation. Our analysis strategy—grouping patients by AG trajectories (normalized, persistent, and fluctuating) and comparing outcomes—showed that persistent elevation beyond 24 hours carried the highest risk. This dynamic perspective resonates with literature emphasizing that trends in acid–base markers outperform static values for risk stratification in critical care (confer the growing interest in time-weighted or longitudinal indices). Although specific to sepsis rather than trauma, investigations of time-weighted or serial measurements support the value of repeated assessment to capture ongoing shock physiology (e.g., longitudinal electrolytes and acid–base disturbances) and anticipate prognosis **(Lei et al., 2025)**.

Our results complement the well-established prognostic role of lactate and base deficit in polytrauma. In an observational cohort of polytrauma patients, higher lactate and more negative base deficit were associated with mortality, lending support to their routine use in early risk assessment **(Jyoti et al., 2022)**. A systematic review across emergency department populations similarly affirmed serum lactate as a broad prognostic marker of mortality **(Alshiakh, 2023).** In the current cohort, lactate behaved as expected—non-survivors maintained higher values at 24 hours—but serial AG provided comparable discrimination and, in some models, incremental information beyond lactate. This observation suggests that AG trends may serve as a practical adjunct in settings where

lactate is delayed, unavailable, or limited by preanalytical variability, a theme highlighted in the emergency and intensive care medicine literature **(Alshiakh, 2023)**. Moreover, AG integrates contributions from lactate and other unmeasured anions generated by shock, renal hypoperfusion, and tissue injury, which may explain its independent association with outcome even after adjustment for lactate and injury severity **(Si et al., 2025; Xu et al., 2025)**.

Our use of albumin measurements allowed, when indicated, albumin-corrected AG, addressing the known influence of hypoalbuminemia on the AG. Evidence from non-trauma cohorts indicates that albumin-corrected AG may better reflect the true burden of unmeasured anions and may relate to organ function. In hypertensive individuals from NHANES, higher albumin-corrected AG associated with impaired kidney function **(Jiang et al., 2024)**. Pediatric critical care data also connect metabolic acidosis measures to outcome, underscoring the cross-population relevance of acid–base derangements **(Datta et al., 2024)**. Even in neonatal intensive care settings, corrected AG has shown prognostic promise for mortality and ventilatory needs **(Alam et al., 2025)**. Taken together, these studies suggest that corrected or serial AG captures systemic metabolic stress across ages and diagnoses; our trauma findings add that the trajectory of AG within the first 48 hours is clinically meaningful in adult polytrauma.

At the same time, acid–base markers sit within a broader ecosystem of predictive analytics. Machine-learning approaches applied to large ICU datasets in sepsis and hypertensive kidney disease demonstrate that combining physiologic time series, laboratory values, and comorbidities can enhance early mortality prediction **(Si et al., 2025; Xu et al., 2025)**. While our study used traditional regression and ROC analysis, the strong signal carried by serial AG suggests that data-driven models incorporating AG trajectories, chloride dynamics, and albumin-corrected calculations might further improve trauma risk stratification. Notably, longitudinal chloride behavior—another key determinant of strong ion difference—has been linked with mortality in septic critical illness, reinforcing that electrolytes beyond sodium and bicarbonate contain prognostic information **(Lei et al., 2025)**. In metabolic states dominated by ketoacids, as in diabetic ketoacidosis, composite scores that integrate acid–base indices discriminate risk effectively **(Munsakul et al., 2024)**, again underscoring the value of multi-marker panels where AG is a central component.

Methodologically, several design choices strengthen internal validity. First, by restricting inclusion to adults with multiple traumas and ensuring early sampling within six hours of injury, we reduced heterogeneity in timing of presentation and initial resuscitation. Second, measuring AG at predefined, clinically relevant intervals paralleled decision windows in trauma ICU care. Third, adjustment for ISS, APACHE II, and lactate addressed confounding by injury severity and global shock burden. And fourth, exclusion of patients having any chronic disease states that may alter the metabolic panel and AG.

Clinically, our findings have several implications. First, serial AG is a low-cost, immediately available adjunct to lactate and base deficit that can be measured in virtually all laboratories without specialized equipment. In environments where frequent lactate testing is constrained—or where albumin is low and lactate alone incompletely reflects total acid burden—AG offers complementary insight. Second, trajectory-based thresholds may be more actionable than a single admission cut point. For example, failure of AG to normalize to

≤12 mmol/L by 24 hours identified a subgroup with substantially higher mortality, paralleling the way persistent lactatemia flags ongoing shock **(Alshiakh, 2023; Jyoti et al., 2022)**. Third, integration of AG with chloride and albumin trends could inform fluid and transfusion strategies, in line with data linking chloride trajectories and outcomes in sepsis **(Lei et al., 2025)** and the associations between albumin-corrected AG and organ function **(Jiang et al., 2024)**. Finally, because corrected AG has shown utility in neonatal and pediatric cohorts **(Alam et al., 2025; Datta et al., 2024)**, protocolized serial AG monitoring may have broad applicability across age groups and pathophysiologic contexts, with trauma being a logical domain for wider adoption.

In relation to prior literature, our trauma-focused results dovetail with the broader theme that metabolic acidosis—quantified by lactate, base deficit, corrected AG, or combinations thereof—tracks with severity and mortality in acute critical illness **(Alam et al., 2025; Alshiakh, 2023; Datta et al., 2024)**. Where this study adds value is in demonstrating that serial AG measures during the early inpatient window carry independent prognostic information comparable to lactate and that persistent elevation is particularly ominous. The convergence of evidence across conditions—sepsis, DKA, neonatal and pediatric ICUs, and hypertensive kidney disease—suggests that acid–base perturbations share common mechanistic underpinnings of tissue hypoxia, impaired clearance, and inflammatory dysregulation, all of which are present in major trauma. Future work should test whether AG-guided resuscitation targets, perhaps embedded in interpretable ML tools, can improve outcomes beyond standard care **(Si et al., 2025; Xu et al., 2025)**.

Serial AG monitoring in adult multiple trauma patients provides clinically meaningful prognostic information. In this cohort, higher admission AG and, critically, failure of AG to normalize within 24–48 hours were associated with increased in-hospital mortality, independent of injury severity and lactate. These findings support incorporating AG trajectories alongside lactate and base deficit into routine early risk assessment. Given corroborating evidence that corrected AG and related acid–base markers predict adverse outcomes across neonatal, pediatric, and adult critical care—including links to kidney function, chloride dynamics, and disease-specific mortality **(Alam et al., 2025; Jiang et al., 2024; Lei et al., 2025).** Prospective, multi-center studies should validate AG-based thresholds, explore integration with interpretable machine-learning models, and determine whether AG-targeted resuscitation strategies can improve survival in major trauma **(Jyoti et al., 2022; Munsakul et al., 2024)**.

Limitations : Nonetheless, limitations should be acknowledged. The single-center design and modest sample size particularly for subgroup analyses limit generalizability and precision. Residual confounding (e.g., variability in fluid type, chloride load, renal replacement therapy, and transfusion practices) could influence AG and outcomes despite statistical adjustment. Other advanced acid–base frameworks (e.g., the Stewart approach), was not evaluated. Finally, we did not implement machine-learning classifiers in this research.

Recommendations: Nevertheless, larger multicenter prospective studies are warranted to validate the results of our research and to explore the integration of corrected AG with other metabolic and clinical parameters for enhanced prognostic accuracy.

Conclusion

This study demonstrated that serial measurement of the AG is a valuable

prognostic marker for mortality in adult multiple trauma patients and underscored the clinical utility of the AG as a simple, cost-effective, and widely available marker that can complement established scoring systems in predicting outcomes in trauma patients.

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