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Original Article

Metabolic alkalosis acquired in intensive care: A retrospective cohort study

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ABSTRACT

Introduction: Alkalosis is a common acid-base disturbance in intensive care unit (ICU) patients. We evaluated the epidemiology of metabolic alkalosis developing during admission to the ICU and its relationship with outcome.
Methods: Multicentre, retrospective cohort study of admissions to 12 ICUs in Queensland, Australia from January 1st, 2015 to December 31st, 2021. We excluded readmissions, patients with metabolic alkalosis within the first 24 h and those with ICU length of stay (LOS) ≤48 h. The primary outcome was the cumulative incidence of metabolic alkalosis during admission, and secondary outcomes were the frequency of potential underlying causes. Multivariable analyses, including adjustment for immortal time bias, were used to explore its relationship with mortality.
Results: Of 24,676 eligible admissions, 8889 (36%) developed metabolic alkalosis during their stay in the ICU. The median time to first development was four days in the ICU (interquartile range 3–6 days). The most common potential causes were diuretics (28%) and steroids (24%), but no cause could be identified in more than 40% of cases. After adjustment for immortal time bias, patients with metabolic alkalosis

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were seen to have increased mortality rates. However, it was not an independent predictor of outcome after adjusting for disease severity and comorbidities using multivariable analysis.
Conclusion: Metabolic alkalosis develops commonly in the ICU, but its association with increased mortality may be attributable to other confounding factors. Further research is required to elucidate its underlying causes and whether treatments to correct alkalosis improve outcomes.

Introduction

Metabolic alkalosis is considered the most common acid-base disorder encountered in intensive care unit (ICU) patients, as demonstrated in a retrospective review of more than 100,000 arterial blood gases [1]. It frequently occurs in the context of a mixed acid-base disturbance following several days of therapy in intensive care. Potential contributory factors include therapies for shock, acidemia, fluid overload, respiratory failure, bowel obstruction, and renal failure [2,3].

Severe alkalosis can lead to major adverse clinical sequelae, including tetany, seizures, cardiac arrhythmias, and delirium. Lesser degrees of alkalosis are still associated with potentially deleterious effects, including inhibition of respiratory drive and leftward shifting of the oxygen-hemoglobin dissociation curve [4,5]. It has been linked with increased patient mortality and prolonged ICU length of stay (LOS), although not all studies have demonstrated this association [6–10].

There is a paucity of data evaluating factors contributing to the development of alkalosis in the ICU, and conflicting evidence regarding its effect on mortality. In this study, we examined the incidence and potential causes of metabolic alkalosis developing in critically unwell patients during their ICU admission. We also aimed to clarify the relationship between metabolic alkalosis and mortality.

Methods

Study design

Multicenter, retrospective cohort study utilizing data extracted from electronic clinical information systems.

Setting

Data was obtained from 12 closed model ICUs in Queensland, Australia, which utilize an electronic medical record, accessed *via* the Queensland Critical Care Research Network (QCCRN) [11]. These sites include 5 tertiary, 3 outer metropolitan, and 4 regional ICUs, which provide intensive care to the majority of Queensland's adult population. The dataset was available for admissions from January 1st, 2015, to December 31st, 2021.

Population

The study population consisted of all patients aged ≥18 years with a calculated standard base excess (SBE) <4 mmol/L in the first 24 h (*i.e.*, no metabolic alkalosis on arrival to ICU). SBE was chosen to define the population of interest as it is most reflective of the metabolic component of acid-base balance, while bicarbonate levels can be influenced by both respiratory and metabolic disturbance. It was calculated using the formula SBE = $[0.0307 \times PaCO_2 \times 10^{(pH - 6.105)}] - 24.8 + [16.2 \times (pH - 7.40)]$ [12]. We defined clinically significant metabolic alkalosis developing during admission as SBE ≥4 mmol/L at any time after the first 24 h [13].

Admissions with an ICU LOS ≤48 h were excluded, as well as readmissions for the same patient and cases with critical missing data. The ICU length of stay >48 h criterion was selected to define a truly critically ill population and exclude low-risk patients who would be relatively unlikely to develop metabolic alkalosis (for example, those requiring brief post-operative monitoring or support).

Patients with chronic respiratory acidosis may have a baseline compensatory metabolic alkalosis, which is not apparent on admission due to acidosis associated with their acute disease process. The elevated SBE in these individuals arguably represents a return to baseline rather than a true "ICU-acquired alkalosis". As it is not possible to identify and exclude these individuals using admission blood gases alone, we performed two sensitivity analyses:

Excluding all patients with a history of chronic lung disease according to ICD coding and APACHE-II respiratory comorbidities

Excluding all patients with respiratory failure identified as a cause of alkalosis (see definition under outcomes below).

Data sources

Data from patient electronic medical records was collected from all sites using the eCritical MetaVision clinical information system. Further data was obtained from the Australia and New Zealand Intensive Care Society (ANZICS) Centre for Outcome and Resource Evaluation (CORE) Adult Patient Database (APD), Queensland Hospital Admitted Patient Data Collection, and linkage to the Queensland Registry of Births, Deaths and Marriages. Admission diagnoses were categorized by APACHE diagnostic group, and comorbidities were classified according to the Charlson Comorbidity Index (CCI). Laboratory testing and reference ranges were standardized across all sites by the statewide diagnostic pathology service.

Outcomes

The primary outcome was the cumulative incidence and timing of metabolic alkalosis developing during ICU admission. As a secondary outcome, we assessed the incidence of potential underlying causes, defined by meeting the following criteria prior to the development of alkalosis [2,5,7,14,15]:

- Diuretic use: minimum 2 doses of total >80 mg intravenous furosemide equivalent
- Steroid use: total minimum equivalent to 100 mg prednisone or any fludrocortisone administration
- High gastrointestinal losses (upper or lower gastrointestinal tract): >750 mL per 24 h period
- Respiratory failure: two blood gases at least 24 h apart with $pCO_2 > 50$ mmHg
- Bicarbonate administration of ≥100mmol

Additional secondary outcomes were the relationship between alkalosis and 90-day all-cause mortality, and ICU and hospital lengths of stay.

Statistical analysis

Continuous data is presented as median (IQR) or mean (SD) according to its distribution. We conducted survival analyses considering the potential for immortal time bias as alkalosis develops at variable time points during admission. Unadjusted analyses were performed using Kaplan-Meier curves with log-rank testing.

For adjusted analyses, a flexible parametric survival model was created as described by Royston and Parmar [16]. APACHE III score, diagnostic category, and Charlson Comorbidity Index (CCI) were chosen as confounders a priori. The baseline hazard was modelled on the log hazard scale with 6 knots, and surviving patients were censored at 90 days. To relax the proportional hazard assumption, the diagnostic groups and CCI were interacted with the spline function of the log time to allow the coefficients to vary with time. The APACHE III score was modelled using restricted cubic splines with 4 knots, and CCI was categorized into 4 groups.

To explore the relationship between the severity of alkalosis and mortality, a second model was created where the maximal calculated base excess was entered as a continuous variable using a restricted cubic spline with 4 knots. The model incorporates time to maximal base excess, and maximal base excess interacts with time. Otherwise, it is identical to the first model. To facilitate interpretation, marginal survival curves were estimated using regression-based standardization. Model performance was assessed using Harrell's C-index and visual inspection of calibration plots at 30, 60, and 90 days. There were only two patients with missing data for the regression modelling, and these two patients were hence excluded from the modelling.

Data was analysed using Stata/IC 16.1 (Stata Statistical Software: Release 16. College Station, TX: StataCorp LP 2020). User-written packages stpm3, standsurv, and sommersd were utilised in the analyses [17–19].

Results

There were a total of 89,116 admissions during the study period, of which 24,676 were eligible for inclusion in the final analysis. A flowchart of the reasons for patient exclusion is shown in Fig. 1, and a description of the population characteristics is in Table 1. Of the study population, 8889 (36%) developed metabolic alkalosis during their stay in the ICU. Patients who developed metabolic alkalosis had similar APACHE-III scores to those who did not develop alkalosis, but a higher frequency of mechanical ventilation (90% *vs.* 71%). Fig. 2 depicts mean SBE and pH for the whole population over time, and the median time to development of alkalosis was four days (interquartile range 3–6 days). The incidence of alkalosis plateaued from day 10 of admission.

Patient outcomes are listed in Table 2. Alkalotic patients were seen to have a slightly increased duration of mechanical ventilation, as well as ICU and hospital LOS. Although unadjusted mortality was similar, after accounting for immortal time bias, the alkalosis group is seen to have significantly reduced survival (log-rank test P-value < 0.001) as shown in the Kaplan-Meier curves in Fig. 3 as well as Supplementary Fig. S1, which depicts survival curves stratified by maximal base excess.

Potential causes of metabolic alkalosis are described in Table 3. Diuretics were seen to be the most frequent contributory factor, present in 28% of cases. We identified a single factor in 3255 cases (37%), two potential causes in 1683 cases (19%), and three or more in 692 cases (8%). In a high number of cases (43%), no causal factors were identified. Fig. 4 depicts Kaplan-Meier survival curves stratified by the cause of alkalosis, and patients with respiratory acidosis are seen to have the highest mortality.

Multivariable analyses

After adjustment for baseline severity of illness, there was no significant association between the development of metabolic alkalosis and mortality (Fig. 5). Estimated standardized survival according to maximum SBE level is shown in Fig. 6 and the supplementary material (Fig. S2). The graphs suggest that a maximal SBE of around 3 mmol/L was associated with the best survival (82.2%, 95% confidence interval 81.6–83.0 %), but the

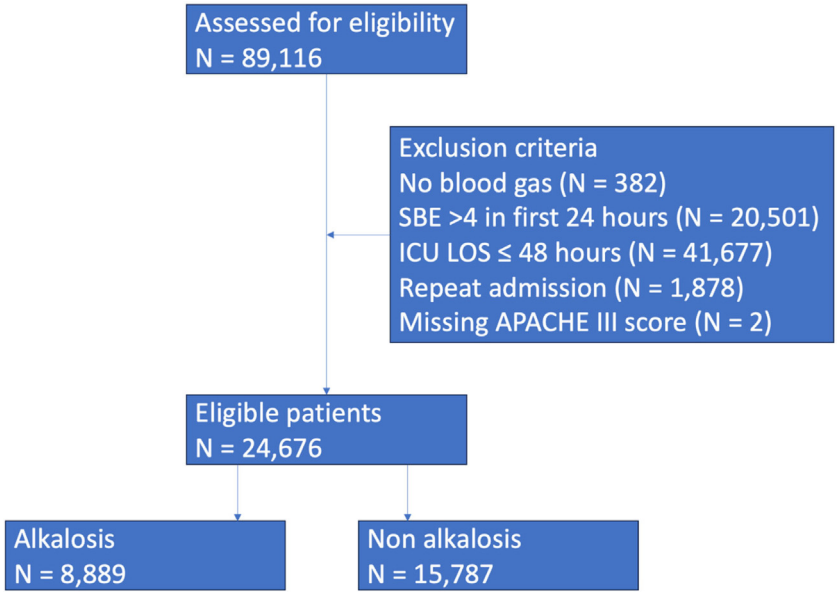

Fig. 1. Flowchart of patient selection.

Table 1
Population characteristics.

	No alkalosis (n = 15,787)	Alkalosis (n = 8889)	Overall (N = 24,676)
Age	58 (±17)	57 (±17)	58 (±17)
Female	6290 (38%)	3361 (38%)	9651 (38%)
Charlson comorbidity index			
<4	8926 (57%)	5279 (59%)	14,205 (58%)
4–5	3651 (23%)	2002 (23%)	5653 (23%)
6–7	1751 (11%)	888 (10%)	2639 (11%)
>7	1459 (9%)	720 (8%)	2179 (9%)
Diagnostic groups			
Cardiovascular	4959 (31%)	2536 (29%)	7495 (31%)
Gastrointestinal	1959 (12%)	947 (11%)	2906(12%)
Metabolic	1170 (7%)	627 (7%)	1797 (7%)
Neurological	2101 (13%)	1240 (14%)	3341 (14%)
Respiratory	1532 (10%)	978 (11%)	2510 (10%)
Sepsis	1614 (10%)	830 (9%)	2444 (10%)
Trauma	1541 (10 %)	1295 (15%)	2836 (11%)
Other	911 (6%)	436 (3%)	1347 (5%)
APACHE-III			
Score	56 (41–76)	57 (42–76)	56 (42–76)
Mean predicted mortality	19% (±24)	20% (±23)	19% (±23)
Blood gas with highest SBE			
SBE	0.5 (±2.7)	7.1 (±3.1)	2.9 (±4.3)
pH	7.42 (±0.06)	7.46 (±0.05)	7.44 (±0.06)
HCO_3	25 (±2.6)	31 (±3.0)	27 (±4.0)
PCO_2	39 (±6.6)	45 (±7.9)	41 (±7.6)
Anion gap	5.7 (±3.1)	4.9 (±3.4)	5.5 (±3.2)
Ventilation			
Invasive	11,277 (71%)	7957 (90%)	19,234 (78%)
Non-invasive	663 (4%)	557 (6%)	1220 (5%)
Renal replacement therapy	2108 (13%)	1249 (14%)	3357 (14%)
Acetazolamide use	64 (0.4%)	766 (9%)	830 (3%)

Results are presented as n (%), mean (± standard deviation), or median (interquartile range).
SBE = Standard base excess.

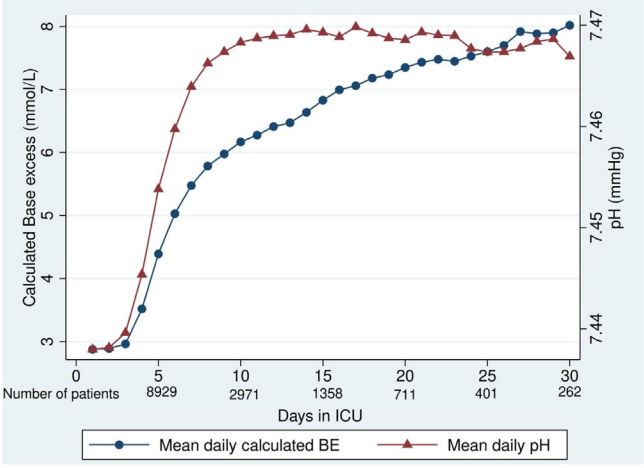

Fig. 2. Development of metabolic alkalosis over time.

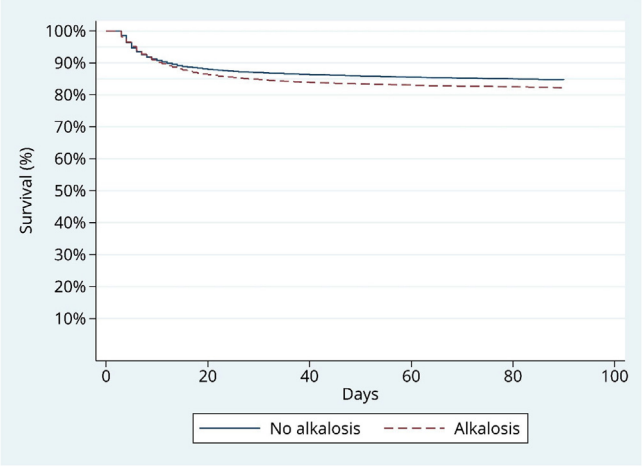

Fig. 3. Kaplan Meier survival curves with adjustment for immortal time bias.

graph plateaued rapidly, and a minimal decrement in survival was noted with increasing SBE levels. By comparison, at a maximal SBE of 10 mmol, the estimated 90-day survival is 81.3% (95% confidence interval 79.7–82.9 %).

Results of the sensitivity analysis, excluding patients with chronic respiratory disease and a respiratory cause of alkalosis, are presented in Supplementary Figs. S3-S4 and S5-S6, respectively. The overall trends were consistent across all the populations

Table 2
Unadjusted outcomes in patients with and without alkalosis.

	Non-alkalosis (n = 15,787)	Alkalosis (n = 8889)	Overall (n = 24,676)
90-day mortality	2405 (15%)	1249 (14%)	3654 (15%)
ICU length of stay (days)	4 (2–6)	5 (3–10)	4 (2–7)
Hospital length of stay (days)	11 (7–19)	14 (8–24)	12 (7–20)
Days free of ventilation until day 30	28 (24–29)	24 (19–27)	27 (22–29)

Table 3
Potential contributory factors for the development of metabolic alkalosis.

Potential causes of alkalosis	*N* (%)
Respiratory failure	1686 (19%)
Diuretic use	2489 (28%)
Steroid use	2151 (24%)
Gastrointestinal losses	828 (9%)
Bicarbonate administration	501 (6%)
Multiple causes identified	1932 (22%)
No cause identified	3794 (43%)

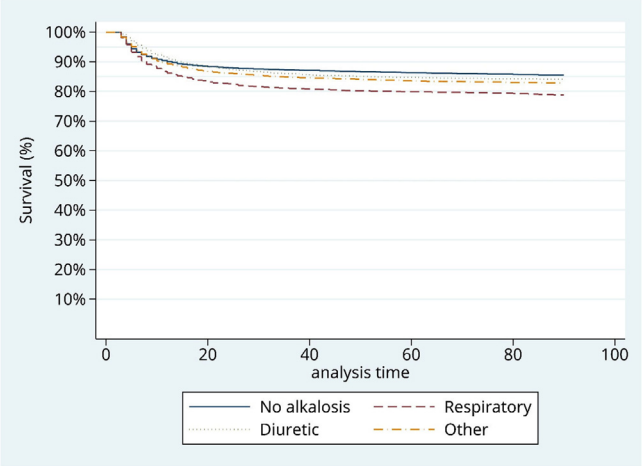

Fig. 4. Kaplan-Meier survival curves stratified by cause of alkalosis.

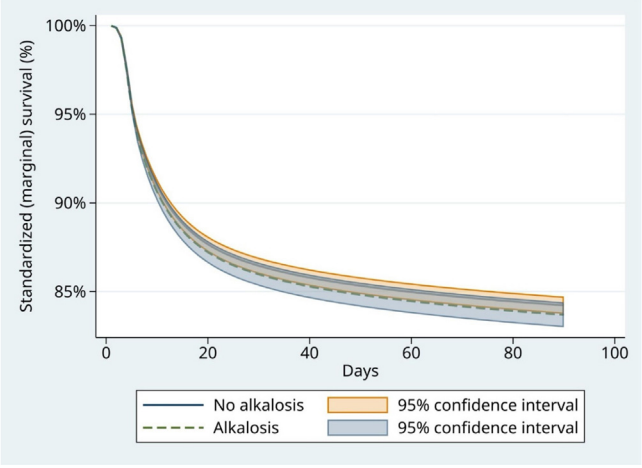

Fig. 5. Standardized (marginal) survival curves based on multivariable analysis. *Adjusted for Apache III score, diagnostic category, and Charlson Comorbidity Index.

evaluated. Calibration plots of all multivariable models can be found in Supplementary Figures S7-S12.

Discussion

Metabolic alkalosis was a common acid-base disturbance in this population, occurring in over one-third of patients, generally after four or more days of admission. Our observed rate of alkalosis was lower than some studies conducted in hospitalized patients, where it has been reported in up to 51% of cases [20,21]. The variation may be partially explained by the differing thresholds used to define

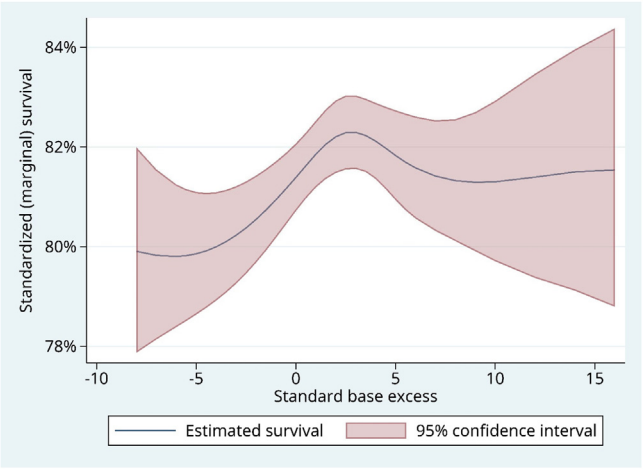

Fig. 6. Association between maximal base excess and standardized mortality at 90 days.

metabolic alkalosis, with some studies considering pH and others focusing on bicarbonate levels [1,2,9,20]. Our study also specifically excludes patients who were already alkalotic on admission to the ICU. It may also be related to patients' illness trajectory, as the time delay before the development of metabolic alkalosis in the ICU may indicate that it occurs during the recovery phase after critical illness. It is possible that if we had access to blood gas results following discharge to the ward, we may have seen more patients develop alkalosis than were detected with the available data.

Diuretics and steroids were the most frequently identified factors that may have contributed to the development of metabolic alkalosis. Only one prior study has investigated possible causes of alkalosis in ICU patients, which was a retrospective analysis using the Multiparameter Intelligent Monitoring in Intensive Care II (MIMIC-II) database [2]. The most common causes in their population were diuretic usage, alkali administration, COPD, and gastrointestinal losses. Other associations included hypokalemia, hypernatremia, and hypoalbuminemia, with the majority of patients (58%) having 3 or more potential risk factors. Of note, for 40% of the cases in our study, no identifiable cause was found despite similar risk factors to Liborio's analysis. In this study, we have deliberately omitted electrolyte disorders as primary "causes", as they have a complex interplay with acid-base status and can be both contributory to and the result of alkalosis. Derangements in sodium and potassium levels are also an intermediate in the causal pathway between diuretic use and acid-base disorders. Hypokalemia was around twice as frequent as hypernatremia in the study by Liborio, but we note that this is unlikely to be a primary cause of alkalosis unless severely depleted, which occurs infrequently following ICU admission, as potassium levels should be routinely monitored and corrected [22].

Multiple authors have reported associations between alkalosis and higher patient morbidity and mortality [2,6–8]. By contrast, one Swedish study looking at patients with severe sepsis and septic shock found no association between metabolic alkalosis and mortality [9]. We observed that the relationship between alkalosis and outcome was subtle and nuanced, as it is more frequent in patients with greater illness severity, but patients must also survive long enough to develop it. Without careful adjustment, mortality can appear similar or even slightly lower in the alkalosis group due primarily to immortal time bias [23]. We found that alkalosis was strongly associated with mortality after adjustment for immortal time bias, but this was predominantly accounted for by patients' underlying disease severity. Alkalosis was not an independent predictor of risk after multivariable analysis, adjust-

ing for the current illness and patient comorbidities. When considering the severity of alkalosis, a maximal SBE of around 3 mmol/L was associated with slightly greater survival. However, the difference in absolute mortality is very small compared to the most severely alkalotic patients, and these differences may still be due to residual confounding. Baseline mortality rates were higher in patients with respiratory diseases, but the sensitivity analyses, excluding individuals whose alkalosis may have occurred purely as compensation for respiratory acidosis, produced similar trends to the primary models.

Strengths and limitations

Strengths of our study include the relatively large sample size, which we believe to be the largest cohort to date evaluating metabolic alkalosis in intensive care patients. The population was sourced from mixed medical and surgical ICUs in regional and metropolitan locations, making the results generalizable to a relatively wide population.

The study is subject to the inherent limitations of retrospective cohort studies, such as errors in data collection and coding, and the inability to adjust for confounding variables that are either unrecorded or unknown. The results may not be applicable to patients managed in health care systems that differ substantially from Australian ICUs. We were also limited in that information was only available from intensive care records, and we did not have access to pathology results or blood gases obtained before or after admission to the ICU.

Conclusion

Metabolic alkalosis is a common acid-base disturbance among critically ill patients in Queensland ICUs, occurring most frequently after the fourth day of admission. Alkalosis was associated with increased mortality rates, but after controlling for underlying illness severity, it was not an independent predictor of outcome. The most common contributory factors identified were steroids and diuretics, but in a large proportion of patients, an underlying cause was not identified. Further study may be required to clarify the determinants of metabolic alkalosis in the ICU and whether specific treatment improves outcome.

CRediT authorship contribution statement

Study conception and design (all authors); data curation (all authors); formal analysis (SPB); writing original draft (GG); manuscript review and editing (all authors).

Ethical considerations

Use of the dataset was approved by the Human Research Ethics Committee at Metro South Hospital and Health Service who granted a waiver of individual consent (HREC/2022/QMS/82024).

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Data availability statement

Data cannot be shared publicly due to institutional ethics, privacy, and confidentiality regulations. Data released for research under Sect. 280 of the Public Health Act 2005 requires an application to the Director-General of Queensland Health (PHA@health.qld.gov.au).

Declaration of competing interest

All authors have no conflict of interest to declare

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.accpm.2025.101591.

References

[1] Mæhle K, Haug B, Flaatten H, Nielsen EW. Metabolic alkalosis is the most common acid–base disorder in ICU patients. Critical Care 2014;18(2):420. http://dx.doi.org/10.1186/cc13802.
[2] Libório AB, Noritomi DT, Leite TT, de Melo Bezerra CT, de Faria ER, et al. Increased serum bicarbonate in critically ill patients: a retrospective analysis. Intensive Care Med 2015;41(3):479–86. http://dx.doi.org/10.1007/s00134-015-3649-9.
[3] Achanti A, Szerlip HM. Acid-base disorders in the critically ill patient. Clin J Am Soc Nephrol 2023;18(1):102–12. http://dx.doi.org/10.2215/CJN.04500422.
[4] Pochet JM, Laterre PF, Jadoul M, Devuyst O. Metabolic alkalosis in the intensive care unit. Acta Clinica Belgica 2001;56(1):2–9. http://dx.doi.org/10.1179/acb.2001.002.
[5] Tinawi M. Pathophysiology, evaluation, and management of metabolic alkalosis. Cureus 2021;13(1):e12841. http://dx.doi.org/10.7759/cureus.12841.
[6] Anderson LE, Henrich WL. Alkalemia-associated morbidity and mortality in medical and surgical patients. South Med J 1987;80(6):729–33. http://dx.doi.org/10.1097/00007611-198706000-00016.
[7] Webster NR, Kulkarni V. Metabolic alkalosis in the critically ill. Crit Rev Clin Lab Sci 1999;36(5):497–510. http://dx.doi.org/10.1080/10408369991239286.
[8] Wilson RF, Gibson D, Percinel AK, Ali MA, Baker G, LeBlanc LP, et al. Severe Alkalosis in critically ill surgical patients. Arch Surg 1972;105(2):197–203. http://dx.doi.org/10.1001/archsurg.1972.04180080051009.
[9] Kreü S, Jazrawi A, Miller J, Baigi A, Chew M. Alkalosis in critically ill patients with severe sepsis and septic shock. PLoS One 2017;12(1):e0168563. http://dx.doi.org/10.1371/journal.pone.0168563.
[10] Sithole N, Lalla U, Davids MR, Chothia MY. The frequency of acid-base disorders on admission to the intensive care and its association with in-hospital outcome, Cape Town, South Africa: a retrospective cohort study. Pan Afr Med J 2022;42:130. http://dx.doi.org/10.11604/pamj.2022.42.130.32570.
[11] White KC, Quick L, Ramanan M, Tabah A, Shekar K, Senthuran S, et al. Hypothermia and Influence of Rewarming Rates on Survival Among Patients Admitted to Intensive Care with Bloodstream Infection: A Multicenter Cohort Study. Ther Hypothermia Temp Manag 2024 Oct 23. http://dx.doi.org/10.1089/ther.2024.0047. Epub ahead of print. PMID: 39441721.
[12] Berend K. Diagnostic use of base excess in acid–base disorders. N Engl J Med 2018;378(15):1419–28. http://dx.doi.org/10.1056/NEJMra1711860.
[13] Langer T, Brusatori S, Gattinoni L. Understanding base excess (BE): merits and pitfalls. Intensive Care Med 2022;48(8):1080–3. http://dx.doi.org/10.1007/s00134-022-06748-4.
[14] Do C, Vasquez PC, Soleimani M. Metabolic alkalosis pathogenesis, diagnosis, and treatment: core curriculum 2022. Am J Kidney Dis 2022;80(4):536–51. http://dx.doi.org/10.1053/j.ajkd.2021.12.016.
[15] Emmett M. Metabolic alkalosis. Clin J Am Soc Nephrol 2020;15(12):1848–56. http://dx.doi.org/10.2215/CJN.16041219.
[16] Royston P, Parmar MKB. Flexible parametric proportional-hazards and proportional-odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects. Stat Med 2002;21(15):2175–97. http://dx.doi.org/10.1002/sim.1203.
[17] Lambert P. STANDSURV: Stata module to compute standardized (marginal) survival and related functions. Statistical Software Components. Published online September 5, 2024. Accessed January 6, 2025. https://ideas.repec.org//c/boc/bocode/s458991.html.
[18] Lambert P. STPM3: Stata module to fit flexible parametric survival models. Statistical Software Components. Published online 95 2024. Accessed January 6, 2025. https://ideas.repec.org//c/boc/bocode/s459207.html.
[19] Newson R. SOMERSD: Stata module to calculate Kendall's tau-a, Somers' D and median differences. Statistical Software Components. Published online April 16, 2020. Accessed January 6, 2025. https://ideas.repec.org//c/boc/bocode/s336401.html.
[20] Hodgkin JE, Soeprono FF, Chan DM. Incidence of metabolic alkalemia in hospitalized patients. Crit Care Med 1980;8(12):725–8. http://dx.doi.org/10.1097/00003246-198012000-00005.
[21] Okusawa S, Aikawa N, Abe O. Postoperative metabolic alkalosis following general surgery: its incidence and possible etiology. Jpn J Surg 1989;19(3):312–8. http://dx.doi.org/10.1007/BF02471407.
[22] Gennari FJ. Pathophysiology of metabolic alkalosis: a new classification based on the centrality of stimulated collecting duct ion transport. Am J Kidney Dis 2011;58(4):626–36. http://dx.doi.org/10.1053/j.ajkd.2011.06.004.
[23] Yadav K, Lewis RJ. Immortal time bias in observational studies. JAMA 2021;325(7):686–7. http://dx.doi.org/10.1001/jama.2020.9151.