Ir Med J; April 2022; Vol 115; No. 4; P579

April 29th, 2022

Outcomes of Patients with a pH<7.0 Presenting to the Emergency Department (OPpHED Study)

E. Umana[1], B. McNicholas[2], A. Smyth[3], P. O'Shea[4], D. Griffin[5], J. Bates[2], B. McNicholl[1]

1. Department of Emergency Medicine, University Hospital Galway.
2. Department of Intensive Care, University Hospital Galway.
3. Department of Nephrology, University Hospital Galway.
4. Department of Clinical Biochemistry, University Hospital Galway.
5. Department of Pathology, University Hospital Galway.

Abstract

Objectives

The aim of this study was to assess the mortality and predictive factors in patients presenting with a pH<7.0 to the emergency department (ED).

Methods

A retrospective study of patients presenting to the ED of University Hospital Galway with a pH<7.0 from January 2014 to December 2017 was performed. A pH<7.0 on arrival to the ED from either an arterial or venous sample as measured by the blood gas analyser machine were assessed for inclusion.

Results

A total of 130 patients presented to ED over a 4-year period, with a mean age of 58 ±20 years. Eighty-one (63%) patients of the total cohort were male. In terms of aetiology of presentation, 66 (51%) cases were from cardiac arrest (CA), while the remaining 64 (49%) cases were non-cardiac arrest (NCA) related. Twenty-eight-day mortality was 69.5% overall, with significant mortality in the CA group (89%) compared to the NCA group (48%) (p<0.00). A modified early warning score (MEWS) (odds ratio [OR] 1.37, 95% CI: 1.18-1.59) and PCO2 ([OR] 1.35, 95% CI: 1.08-1.68.) were predictive of mortality.

Conclusion

In patients presenting to the ED with a pH of <7.0 the overall mortality was 69.5%, with survival more likely in NCA aetiologies. Mortality was associated with higher pCO2 and MEWS.

Introduction

The pH in extracellular fluid is tightly regulated to maintain normal cellular function.[1] Patient presenting with extreme acidosis (pH<7.0) are in a critical condition and as such their prognosis is poor depending on its aetiology.[2-4] These poor outcomes stem from the negative effects of extreme acidosis on the cardiovascular, pulmonary and immune function in these patients as well as the severity of the aetiology.[5,6] However, several case reports have demonstrated favorable outcomes in patients presenting with extreme acidosis, particularly in those with a reversible cause.[7-13] The potential causes of extreme acidosis are said to be diverse as described in various case reports.[7-13] The management of extreme acidosis will depend on the cause, otherwise the general principle of symptomatic treatment is followed.[14]

There is currently paucity of data on outcomes of extreme acidosis in the emergency department (ED) patients. However, few studies have attempted to assess the outcomes and prognostic factors for mortality of patients presenting with extreme acidosis, with data mostly from intensive care (ICU) settings, and in patients presenting with out of hospital cardiac arrest or trauma.[14-17] Paz et al and Allyn et al evaluated the outcomes of ICU patients who developed extreme acidosis from varied aetiologies with approximated mortality rate of 67%.[14,15] These studies highlight a significant mortality rate in this cohort of non ED patients. The other interesting aspects is, what prognostic factors predict mortality, and can this be applied particularly to patients presenting to the ED with various causes of extreme acidosis?

The primary aim of this study was to assess the mortality of patients who present to the ED with extreme acidosis. Secondly, we also aimed to assess the management received and predictive factors of mortality.

Methods

This is a retrospective observational cohort study of all patients with a pH<7.0 experienced during initial management in the ED of a tertiary university hospital (University Hospital Galway, Ireland). University Hospital Galway has an annual ED attendance of 65,000 patients. This study was approved by the Clinical Research Ethics Committee prior to data collection. All patients > 14 years of age, presenting with a pH<7.0 to the ED from January 01, 2014, to December 31, 2017, on initial assessment were included. Patients with either arterial blood gas (ABG) or venous blood gas (VBG) with pH<7.0 were assessed.

An ABL90 FLEX PLUS blood gas analyser (Radiometer accurate testing, UK) located in the resuscitation area of the ED was used for analysis of all samples of patients during initial presentation to the ED. The blood gas analyser is linked directly to the biochemistry laboratory database. A standardized data report form was used in retrieving data from the online ED hospital records (Therefore Navigator), Mediweb laboratory system and the ICU clinical information system (Metavision) by trained data abstractors. Data collated included demographic data, aetiology of presentation, Glasgow coma scale (GCS), laboratory variables including pH, PCO2, HCO3, base excess and lactate, modified early warning score (MEWS) based on vital signs plus GCS and management outcomes. The MEWS is made up of 5 physiological variables which include: systolic blood pressure, heart rate, respiratory rate, temperature, and neurological status. The grading of MEWS is as follows, low risk (score: 0 – 1), intermediate risk (score: 2 – 3), high risk (score: 4 – 6) and very high risk (score: > 6) to enable identification of deteriorating patients requiring review and intervention.

The primary outcome was 28-day mortality. Other outcomes assessed were: 1.) Management received (such as: a.) Intubation- Patients requiring intubation on admission to ED or ICU on initial presentation, b.) Bicarbonate administration and dialysis- Patient receiving bicarbonate administration and dialysis secondary to presentation with extreme acidosis.), 2.) ICU admission, 3.) Factors predicting mortality in patients presenting with extreme acidosis.

Data analysis was performed using Microsoft Excel (Microsoft, Redmond, WA) and SPSS version 17 (SPSS, Chicago, IL). Continuous variables were presented as mean (standard deviation) or median (interquartile range), while categorical variables were summarized as counts and percentages. Student's t-test and the Mann–Whitney U test were respectively used for comparisons of normally and non-normally distributed continuous data. A chi-square and Fisher's exact test were used for categorical data. A multivariate binary logistical regression analysis was performed. Mortality was the dependent variable, with independent variables including age, gender, MEWS, PCO2, base excess and lactate were assessed according to their clinical significance. A p value <0.05 was considered statistically significant.

Results

One hundred and thirty patients presented to the ED with a pH<7.0 over a 4 year period. Eighty-one (63%) patients of the total cohort were male. The mean age of patients was 58 $\pm$20 years. Table 1 displays the demographics and clinical data of these patients. Of the 130 blood gas samples, 74 were arterial, while 56 were venous. Cardiac arrest (CA) patients accounted for 80% of venous samples obtained.

	Survivor N=40 (%)	Non-survivors N=90 (%)	p value
Age (years +/- SD)	49 ± 22	62.7 ± 19	<0.00
Gender			0.50
Male	23 (57)	58 (64)	
Female	17 (43)	32 (36)	
Etiology of Presentation			<0.00
Cardiac arrest	7 (18)	59 (67)	
DKA	13 (33)	1 (1)	
Seizure	10 (25)	2 (2)	
Sepsis	2 (5)	6 (7)	
Respiratory arrest	2 (5)	6 (7)	
Multiorgan failure	2 (5)	4 (4)	
Trauma	2 (5)	3 (3)	
Gastrointestinal	1 (2)	3 (3)	
Haemorrhagic shock	1 (2)	2 (2)	
No documentation	0	4 (4)	
GCS (mean +/- SD)	10 ± 5	5 ± 4	<0.00
MEW-Score (mean +/- SD)	7 ± 4	12 ± 4	<0.00
pH (mean +/- SD)	6.90 ± 0.06	6.86 ± 0.09	<0.00
PCO2 (mean +/- SD) mmHg	7.5 ± 4	11.5 ± 4	<0.00
Bicarbonate (mean +/SD) mmol/L	11.4 ± 6.4	15.8 ± 5.7	<0.00
Comorbidities			
Hypertension	12 (30)	28 (31)	0.91
Ischeamic heart disease	6 (15)	17 (19)	0.58
Congestive heart failure	1 (3)	7 (8)	0.28
Stroke	3 (8)	5 (6)	0.67
Diabetes	16 (40)	14 (14)	<0.00
Hepatic cirrhosis	0 (0)	2 (2)	0.37
Chronic renal failure	0 (0)	8 (9)	0.05
Malignancy	4 (10)	13 (14)	0.53
COPD	1 (3)	14 (16)	0.03
Others	33 (83)	55 (61)	0.01
Others- Atrial fibrillation, Epilepsy, Depression, Alcoholism and Hypercholesterolemia.			

Table 1: *Demographics and clinical characteristics.*

Primary outcome

The overall mortality rate in this cohort was 69.5% (90 of 130 patients). There was a male predominance among non-survivors (64%). Based on aetiology, mortality was higher in the CA (89%) than non-cardiac arrest (NCA) (48%) group. Non-survivors demonstrated higher MEW-Score and PCO2, with lower GCS and pH compared to survivors as shown in Table 1. The Lactate and base excess were measurable in 125 and 109 patients, respectively.

There was no difference in median lactate level in survivors (10.2 mmol/L ±SD-7) and non-survivor group (11.4 mmol/L ±SD-5) (p-0.27). A difference was noted in the mean base excess level between the survivor group (-21.5 mmol/L ±SD-5) and the non-survivor group (-18 mmol/L ±SD-5) (p-0.02).

Secondary outcomes

Management received, and ICU admission are displayed in tables 2 and 3. The tables compared survivors versus non-survivors and CA versus NCA aetiologies respectively. Non-survivors had a lower proportion admitted to ICU compared to survivors. In terms of aetiology of presentation with extreme acidosis, 66 patients presented with CA compared to 64 with NCA based aetiology. Of the 66 CA patients, 36 (55%) had return of spontaneous circulation (ROSC) with only 29 (44%) surviving to ICU admission. In the CA group a higher proportion were intubated compared to the NCA group.

Variables	Survivor N=40 (%)	Non-survivors N=90 (%)	p value
ICU admission	31 (78)	38 (42)	0.01
Intubation	12 (30)	53 (59)	<0.00
Bicarbonate administration	6 (15)	22 (24)	0.28
Dialysis	3 (8)	4 (4)	0.68
ICU- intensive care unit.			

Table 2: *Mortality and management outcomes for survivors and non-survivors.*

Variables	Cardiac arrest N=66 (%)	Non-Cardiac arrest N=64 (%)	p value
Mortality (28 days)	59 (89)	31 (48)	<0.00
ICU admission	29 (44)	40 (63)	0.03
Intubation	45 (68)	20 (31)	<0.00
Bicarbonate administration	13 (20)	15 (23)	0.60
Dialysis	1 (2)	6 (9)	0.04
ICU- intensive care unit.			

Table 3: *Mortality and management outcomes by etiology of presentation.*

The results showed that MEWS and PCO2 were predictive of mortality after correction of other factors (Table 4). The other factors in the regression model were not predictive of mortality even after adjusting for other variables.

Variables	OR	CI (95%)	p value
Age	1.03	1.0 – 1.1	0.54
Gender	0.66	0.2 – 1.9	0.45
MEWS	1.37	1.2 – 1.6	0.00
PCO2	1.35	1.1 – 1.7	0.01
Base excess	0.98	0.9 – 1.1	0.73
Lactate	0.98	0.9 – 1.1	0.72

Table 4: *Multivariate analysis and predictive factors of mortality in patients with pH <7.0.*

Discussion

This study adds to the current evidence on mortality outcomes in patient presenting with varied aetiologies of extreme acidosis, with emphasis on the ED. The mortality reported in this study was 69.5%, which was similar to studies looking at the same outcome in ICU, trauma and CA patients presenting with extreme acidosis.[4,15,17,18] Based on etiopathology, the CA group had a higher mortality (89%) compared to the NCA group (48%). Allyn et al reported a 90% mortality in adult patients presenting with CA with extreme acidosis prior to ICU admission, which resonates with our findings.[14] Several studies have demonstrated positive correlation between acidosis and mortality in CA patients.[16,18,19] As the pH falls, the normal physiological and biochemical mechanisms are hampered resulting in lower likelihood of ROSC and intact neurological survival. Even though mortality was high in patients presenting with extreme acidosis post CA in our cohort, a few did survive to ICU admission which is in keeping with other studies.[16,19]

Of the patients with extreme acidosis presenting with NCA aetiology, those with diabetic ketoacidosis (DKA) and seizures had good chances of survival. Our data resonates with the findings of Paz et al and several case reports, which identified increased survival in patients presenting with reversible causes of extreme acidosis.[7,8,15] These findings address the need for aggressive resuscitation measures in such patients with extreme acidosis to increase chances of survival.

In terms of management received, most non-survivors were likely to be intubated and less likely to be admitted to ICU. This could be explained by the CA patients making up the majority of non-survivors.

The high intubation rates among CA patient may represents intubations performed as part of post ROSC care. There was no significant difference between survivors and non-survivors for bicarbonate administration or dialysis. Treating reversible causes and symptomatic management are the mainstay managements for these patients. For those presenting with respiratory acidosis, ventilation with either non-invasive ventilation or intubation would be a corrective measure. Patients presenting with mixed or metabolic acidosis are more difficult to manage as they have varied causes such as DKA, medication ingestion (aspirin and metformin), lactic acidosis, chronic renal failure and poising with carbon monoxide or cyanide. Several studies analysed the benefits of bicarbonate in patients with extreme acidosis from trauma and out of hospital CA without improvement in outcomes.[20-22] Therefore, it advised to use bicarbonate with caution as it only corrects the pH values and does not reverse the negative impact of acidosis.[17]

A number of studies have assessed the prognostic factors for survival and mortality in patients presenting with extreme acidosis.[14,15,17] Interestingly, injury or illness severity scores (injury severity score (ISS), acute physiology and chronic health evaluation II (APACHE II) and simplified acute physiology score II (SAPS II)) have been associated with mortality in these studies. [14,15,17] In our study, the MEWS was predictive of mortality even after adjusting for other variables. The MEW score has been extensively investigated and validated in ED patients.[23] A MEWS of 4 or greater can predict inpatient hospital mortality with an OR of 14.3 (95% [CI]: 12.185 to 16.730) and area under the curve (AUC) of 0.78 (95% [CI]: 0.715 to 0.841).[24] The advantage of the MEWS is its clinical applicability in the ED due to its dependence on physiological variables and GCS. Majority of patients in our study had a low GCS and therefore were obtunded which could lead to hypoventilation and elevated PCO2. Also, PCO2 was higher in non-survivors and could explain its predictive ability for mortality in our cohort. Paz et al and Allyn et all reported other variables associated with mortality which differed from our analysis, such as: GCS, creatinine, potassium, and A-type lactic acidosis.[14,15]

This study had several limitations. It was a retrospective study and using the electronic records and biochemical laboratory data to extract information. Patients where only selected if their initial pH was <7.0. As such, patients who had low pH but had treatment prior first initial blood gas analysis might have been missed. We included patients in our study that had a low pH from either ABG or VBG. Current literature suggests that pH correlates well between an ABG and VBG.[25] The majority of the VBG samples were from the CA group indicating the difficulty in gaining arterial access during CA. Our cohort was heterogenous for both age and presentation. Finally, this was a single center study; hence, findings may not be generalizable to other institutions or EDs.

In patients presenting to the ED with a pH of <7.0, the reported overall mortality was 69.5%, which is higher in CA patients. Mortality was associated with the level of PCO2 and MEWS. Our study reported the various aetiologies of extreme acidosis. Understanding the causes and prognostic factors, would help guide resuscitative efforts and help focus on therapies that would ensure better outcomes for patients. Particularly for those with NCA causes, where aggressive resuscitative efforts are necessary to increase chances of survival.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

Corresponding Author:
Dr Etimbuk Umana
Department of Emergency Medicine,
University Hospital Galway,
Galway,
Ireland.
E-Mail: etimbukumana@rcsi.com

References:

1. Ganong W. *Review of medical physiology*. 19th ed. Stamford: Appleton & Lange, 1999.
2. Rhoades RA, Bell DR. *Medical physiology: principles for clinical medicine*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2009.
3. Sherwood L. *Human physiology: from cells to systems*. 7th ed. United States: Brooks/Cole, Cengage Learning, 2010.
4. Fumeaux T, Borgeat A, Cuénoud PF, Erard A, de Werra P. Survival after cardiac arrest and severe acidosis (pH = 6.54). *Intensive Care Med* 1997; 23:594.
5. Mitchell JH, Wildenthal K, Johnson RL. The effects of acid-base disturbances on cardiovascular and pulmonary function. *Kidney Int* 1972; 1:375–89.
6. Kellum JA, Song M, Venkataraman R. Effects of hyperchloremic acidosis on arterial pressure and circulating inflammatory molecules in experimental sepsis. *Chest* 2004; 125:243–8.
7. Kamarzaman Z, Turner C, Clark F. How low can you go: a case presentation on a patient with diabetic ketoacidosis. *Resuscitation* 2009; 80:967–8.
8. Opdahl H. Survival put to the acid test: extreme arterial blood acidosis (pH 6.33) after near drowning. *Crit Care Med* 1997; 25:1431–6.
9. Giuliani E, Albertini G, Vaccari C, Barbieri A. pH 6.68—surviving severe metformin intoxication. *QJM* 2010; 103:887–90.
10. Willcox N, Oakley P. Survival with an arterial pH of 6.57 following major trauma with exsanguinating haemorrhage associated with traumatic amputation. *Resuscitation* 2002; 53:217–21.
11. Bey TA, Walter FG, Gibly RL, James ST, Gharahbaghian L. Survival after ethylene glycol poisoning in a patient with an arterial pH of 6.58. *Vet Hum Toxicol* 2002; 44:167–8.
12. Di Rollo N, Caesar D, Ferenbach DA, Dunn MJ. Survival from profound metabolic acidosis due to hypovolaemic shock. A world record? *BMJ Case Rep* 2013; 2013:bcr2012008315.
13. Ulvin O, Nielsen E. Unexplained severe lactic acidosis in emergency medicine. *J Case Rep & Studies* 2013; 1(2).

14. Allyn J, Vandroux D, Jabot J, Brulliard C, Galliot R, Tabatchnik X, et al. Prognosis of patients presenting extreme acidosis (pH <7) on admission to intensive care unit. *J Crit Care* 2016; 31:243–8.
15. Paz Y, Zegerman A, Sorkine P, Matot I. Severe acidosis does not predict fatal outcomes in intensive care unit patients: a retrospective analysis. *J Crit Care* 2014; 29:210–3.
16. Chien D-K, Lin M-R, Tsai S-H, Sun F-J, Liu T-C, Chang W-H. Survival prediction of initial blood pH for nontraumatic out-of-hospital cardiac arrest patients in the emergency department. *Int J Gerontol* 2010; 4:171–5.
17. Ross SW, Thomas BW, Christmas AB, Cunningham KW, Sing RF. Returning from the acidotic abyss: Mortality in trauma patients with a pH < 7.0. *Am J Surg* 2017; 214:1067-1072.
18. Shin J, Lim YS, Kim K, Lee HJ, Lee SJ, Jung E. Initial blood pH during cardiopulmonary resuscitation in out-of-hospital cardiac arrest patients: a multicenter observational registry-based study. *Crit Care* 2017; 21:322
19. Jamme M, Ben Hadj Salem O, Guillemet L, Dupland P, Bougouin W, Charpentier J et al. Severe metabolic acidosis after out-of-hospital cardiac arrest: risk factors and association with outcome. *Ann Intensive Care* 2018; 8:62
20. Sandra Sabatini, Neil A. Kurtzman. Bicarbonate Therapy in Severe Metabolic Acidosis*. J Am Soc Nephrol* 2009; 20:692-5.
21. Jaber S, Paugam C, Futier E, Lefrant JY, Lasocki S, Lescot T, et al. Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the Intensive Care Unit (BICAR-ICU): A multicentre, open-label, randomised controlled, phase 3 trial. *Lancet* 2018; 392:31–40.
22. Liu X, Nozari A, Rubertsson S, Wiklund L. Buffer administration during CPR promotes cerebral reperfusion after return of spontaneous circulation and mitigates post-resuscitation cerebral acidosis. *Resuscitation* 2002; 55:45-55.
23. Van Oppen J, Challen K. BestBets: Does the Early Warning Score measured in the Emergency Department predict the need for life-saving intervention? [Internet]. *Bestbets.org* 2016 [cited 21 November 2018]. Available from: https://bestbets.org/bets/bet.php?id=2834
24. Suwanpasu S, Sattayasomboon Y. Accuracy of Modified Early Warning Scores for Predicting Mortality in Hospital: A Systematic Review and Meta-analysis. *J Intensive & Crit Care* 2016; 02:02.
25. Byrne AL, Bennett M, Chatterji R, Symons R, Pace NL, Thomas PS. Peripheral venous and arterial blood gas analysis in adults: are they comparable? A systematic review and meta-analysis. *Respirology* 2014; 19:168–175.