Original Research Article

Electrolyte and acid-base disturbances in the critically ill patients: A retrospective case control study

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Abstract

Background: Electrolyte and acid-base disturbances are common in critically ill patients. Early appreciation and appropriate interventions to maintain this internal milieu are lifesaving and cost effective for the patients.

Objective of the study: To analyze the effects of electrolyte and acid-base disturbances on hospital mortality in critically ill patients.

Materials and methods: A retrospective case control study was done on 100 patients in the intensive care unit of our hospital for six months.

Results: The incidences of electrolyte and acid-base disturbances were higher in non-survivors than survivors. The serum potassium value had both clinical (4.318 in the survivors vs. 4.815 in the non-survivors) and statistical significance (p=0.0298) between the survivor and non-survivor group. Arterial blood HCO3 (0.0304), CO2 (P=0.0396) and pH (P=0.015) at admission were statistically different between the two groups. The incidence rates of hyperkalemia (65%), respiratory acidosis (62.5%) and mixed metabolic acidosis and respiratory acidosis (65%) were higher in the non-survivor group.

Conclusion: Electrolyte and acid-base disturbances hyperkalemia, respiratory acidosis and mixed respiratory with metabolic acidosis are highly associated with hospital mortality.

Key words

Electrolyte disturbances, Acid-base disorders, Hyponatremia, Hyperkalemia, Metabolic acidosis, Respiratory acidosis, Intensive care unit, Acute kidney injury.

Introduction

Acid-base balance is one of the most important mechanisms implied in the internal homeostasis of the human body. Normal pH and electrolyte values are vital for the normal functioning of the body at the cellular level. Extreme ranges of pH and electrolyte abnormalities are potentially life threatening because of disruption of many vital enzymatic reactions and physiological processes [1].

Disturbances in acid-base and electrolytes are the most common clinical problems in the intensive care unit. They commonly occur in the very ill patients or it may be the first presentation and marker of an underlying disease [1]. The presence of these disorders does not only signal severe underlying pathophysiology but also is a significant marker of adverse outcomes, particularly in the case of hyperkalemia and acidosis [2].

The various etiologies of acid base imbalance commonly encountered in the intensive care set up are acute ventilatory or circulatory failure, severe cardiovascular events, diabetic ketoacidosis, uremia and the acidosis of septicemia [3, 4]. Some life threatening imbalances may be due to the therapeutic options like administration of diuretics, transfusion of citrated blood and removal of gastric secretions [5, 6]. Critically ill patients also have a wide range of abnormalities ranging from metabolic, endocrine, nutritional, respiratory and hemodynamic complications.

So, we conducted a retrospective study to detail the prevalence of acid base imbalance and electrolyte abnormalities at admission in our intensive care unit, to describe the relationship between these abnormalities with mortality.

Objectives

- To study the different type of acid base imbalance and electrolyte abnormalities encountered in our intensive care unit.
- To evaluate the metabolic disturbances commonly found in the non-survivors.
- To analyze the etiological factors perpetuating the acid base and electrolyte imbalance.

Materials and methods

Study design and data collection

This retrospective study included all the patients admitted to the intensive care unit of Dhanalakshmi Srinivasan Medical College Hospital, Perambalur between January and August 2018. Only the initial ICU (intensive care unit) admission ABG and electrolyte values were considered in this study. Patients without both electrolyte and blood gas analysis were excluded. The collected data included demographics, diagnosis of the patient, relevant comorbidities, clinical data which included vitals, complete blood count, random blood sugar, renal function and liver function test. The number of days stayed in the hospital and the outcome of the patient were also noted.

Definitions

The samples were analyzed in the central laboratory of the Institution and were defined according to the reference ranges provided by them.

Normal sodium range (135 – 145 mEq/L), normal potassium range (3.5 to 5 mEq/L), normal chloride range (95 to 105 mEq/L).

The anion gap (AG) was calculated by the standard formula {AG = [Na+]-[Cl-]-[Hco3]} with an elevated anion gap defined as greater than or equal to 16 mmol/L [7]. Simple, dual and triple acid-base disturbances were diagnosed according to the flow diagrams [8].

AKI (acute kidney injury) is defined using Kidney Disease: Improving Global Outcomes criteria [9] as an increase in serum creatinine (SCr) ≥0.3 mg/dl within 48 hours, or an increase in Serum creatinine to ≥1.5 time's baseline known or presumed to have occurred within the prior 7 days.

Statistical methods

The data were analyzed using SPSS version 18.0 software. Continuous variables were presented as mean ± SD if they were statistically normally distributed and categorical variables as numbers and percentages. They were compared using the Student t-test for continuous variables and the $\chi 2$ test for categorical variables. A P-value <0.05 was considered indicating statistical significance

Results

A total of 100 patients met the inclusion criteria. The baseline characteristics of the critically ill patients were listed in the **Table - 1**. Age, co-morbidities and the baseline parameters of blood chemistry at ICU admission, the incidence of acute kidney injury were statistically different and matched accordingly between the survivors and non survivors groups.

In this study, though the number of males (70) was more compared to the females (30), there was no significant difference regarding the gender between the survivor and the non-survivor group. The p value (0.275) was not statistically significant ($p < 0.05$).

Regarding the co-morbidities, the p values were significant for the incidence of chronic obstructive pulmonary disease, bronchial asthma ($p = 0.04986$) and acute kidney injury ($p = 0.020921$) in the non-survivor group. Patients presenting with acute exacerbations of chronic obstructive airway disease and bronchial asthma often had severe respiratory acidosis, had to be intubated due to type 2 respiratory failures and subjected to disturbances in the electrolyte and acid base balance. Similarly patients presenting with acute kidney injury had severe metabolic acidosis and hyperkalemia which predisposes for the worsening of the patient's condition in the intensive care unit.

Table - 1: Baseline characteristics of the critically ill patients.

	Survivor	Non survivor	P value
Age, years	54.68	52.66	0.875
Male sex, (n)	38	32	0.275
Female sex, (n)	12	18	
Diabetes, (n)	19	16	0.473289
Hypertension, (n)	24	11	0.001886
CAD, (n)	7	7	1
CKD, (n)	34	22	0.023342
COPD/ BA, (n)	4	9	0.04986
AKI, (n)	1	5	0.020921
ALF, (n)	0	4	*
DCLD, (n)	0	4	*
Stroke, (n)	3	2	0.527089

*Since there were no survivors in the intensive care unit admitted with acute liver failure or decompensated chronic liver disease, the significance of p value could not be calculated with fishers' exact test.

Table - 2: Baseline clinical data of the critically ill patients at admission.

	Survivor	Non survivor	P value
MBP mmHg	96.1	72.64	0.171325
Haemoglobin g/L	9.77	10.07	0.682
WBC, 1000 cells/ mcl	13.33	15.53	0.171
AST U/L	28.4	266.06	0.018*
ALT U/L	27.44	196.32	0.027*
Total bilirubin mg/dl	1.002	2.2118	0.009*
Albumin g/L	3.52	3.328	0.075
Sr Creatinine, mg/dL	4.846	4.743	0.925
Blood Urea	81.34	98.66	0.225
eGFR, ml/min	29.24	33.56	0.650619
Serum Uric acid	6.008	6.22	0.679
Na, mEq/dl	132.06	131.7	0.212
K, mEq/dl	4.318	4.815	0.0298*
Cl, mEq/dl	101.24	100.86	0.788
PaCO2, mmHg	32.956	40.924	0.0396*
pH	7.25	7.17	0.015*
HCO3-, mEq/dL	17.76	14.936	0.0304*
Hospital stay, days	9.38	3.604	0.000*

* Correlation was significant at the 0.05 level.

Chart - 1: Comparison of the eGFR values between the survivor and the non-survivor group.

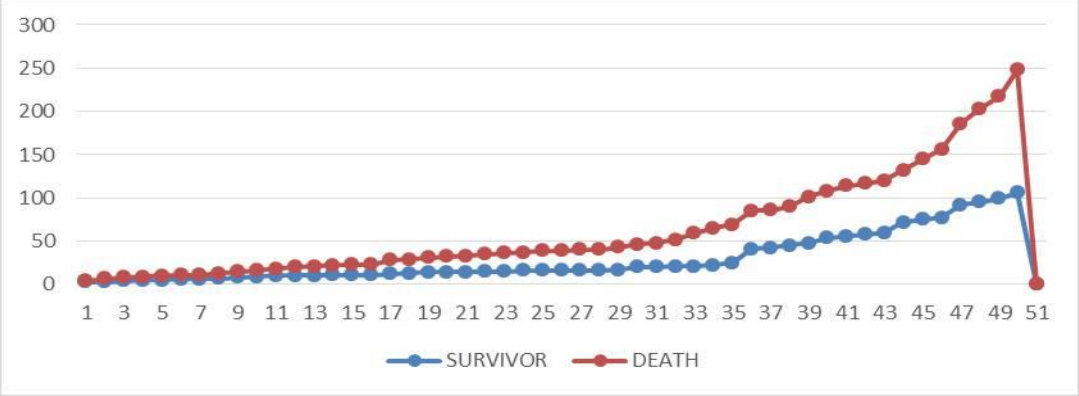

Chart - 2: Incidence of electrolyte imbalance in our intensive care unit.

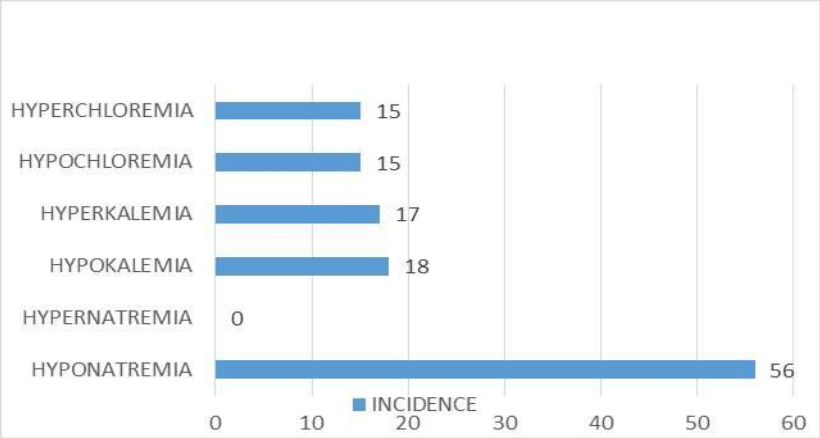

Table - 3: Incidence of electrolyte imbalance in the survivor and non-survivor group.

	SURVIVOR	NON SURVIVOR	N	CHI SQUARE	P VALUE
HYPONATREMIA	26 (46%)	30 (54%)	56	0.6494	.420345
NORMAL SODIUM	24 (54.5%)	20 (45.5%)	44		
HYPERNATREMIA	0	0	0		
HYPOKALEMIA	9 (50%)	9 (50%)	18	0	1
NORMAL POTASSIUM	35 (54%)	30 (46%)	65		
HYPERKALEMIA	6 (35%)	11 (65%)	17	1.7718	.18316
HYPOCHLOREMIA	7 (47%)	8 (53%)	15	0.0784	.779435
NORMAL CHLORIDE	36 (51%)	34 (49%)	70		
HYPERCHLOREMIA	7 (47%)	8 (53%)	15	0.0784	.779435

* Correlation was significant at the 0.05 level (2-tailed).

The incidence of acute liver failure and complications of liver cirrhosis were more in the non-survivor group, but the p value could not be calculated since there were no survivors. But the clinical significance was evident from the study, of all the 8 patients admitted either with acute fulminant liver failure or decompensated chronic liver disease, no one survived. The reason being the poor prognosis of the disease, its reduced life expectancy unless active interventions like liver transplant were initiated.

But on the contrary, the incidence of systemic hypertension ($p = 0.001$) and chronic kidney disease ($p = 0.023$) were comparatively higher in the survivor group than in the non-survivor group in our hospital setup. This may be attributed to

the effective functioning of the hemodialysis centre and renal transplant units of our hospital.

No clinical or statistical significance were found between the disease groups, diabetes mellitus (p=0.4732), coronary heart disease (p=1) and cerebrovascular diseases (p=0.52) as per **Table - 2**.

From comparing the clinical data at admission between the survivor and the non-survivor groups, there was clinical significance in the mean blood pressure (mmHg) between the two groups. The mean blood pressure of the survivor group (96.1 mmHg) was comparatively higher than the non-survivor group (72.6 mmHg), the reason being the incidence of hemodynamic instability in the non-survivor group. The incidence of septic shock, cardiogenic shock, distributive shock were often the initiating factors in the down spiralling of the patient's condition, often resulting in complex electrolyte and acid base disorders. But there was no supporting statistical significance for mean blood pressure (p=0.171) between the two groups to confirm our hypothesis.

The mean hemoglobin was more in the non-survivor group (10.07) than the survivor group (9.77), the probable reason being the majority of the patients who survived had chronic kidney disease (34 of survivors vs. 22 of non-survivors) but the statistical analysis was not significant (p=0.682). The serum creatinine levels which were increased in chronic kidney disease patients was marginally higher in the survivor group (4.846 vs.4.743) and the estimated glomerular filtration rate lower in the survivor group (29.24 vs. 33.56) showed an increased survival rate in chronic kidney disease in spite of statistical insignificance ($p > 0.05$). As discussed above, although chronic kidney disease with end stage renal disease had poor prognosis, early interventions in the nephrology unit significantly increased the survival rate of those with terminal kidney disease. Comparison of the eGFR values between the survivor and the non-survivor group was as per **Chart – 1**.

But the blood urea levels which were more of a predictor of acute kidney injury were increased in the non-survivor group (98.66) than the survivor group (81.34) confirming the decreased survival rates in patients with AKI despite statistical insignificance (p=0.225).

On comparing the total WBC (white blood cell) count, there was a clinically significant increase in the non-survivors, on account of more severe sepsis and other acute inflammatory states in this group. But the statistical analysis was not significant (p=0.171) between the two groups.

In the liver function test, the enzymes aspartate transaminase (AST) and alanine transaminase (ALT) were significantly increased in the non-survivor group than the survivor group (AST levels p=0.018) (ALT levels p=0.027). The mean total bilirubin was also increased in the death group (2.2118) than the survivor group (1.002) and the p value significant (p=0.009) implying the poor prognosis of patients with terminal liver disease. The mean serum albumin was significantly decreased in the death group (3.328 vs. 3.52), though it was clinically significant, it could not be correlated with statistical significance (p=0.075).

Regarding the electrolyte values between the survivor and non-survivor group, there was no clinical or statistical significance for sodium and chloride values. This could be attributed be to the small sample size and lack of hypernatremia in our study group. Incidence of electrolyte imbalance in our intensive care unit was as per **Chart – 2** and **Table - 3**.

On comparing the potassium values, there was a both clinical (4.318 in the survivors vs. 4.815 in the non-survivors) and statistical significance (p=0.0298) confirming the decreased survival rates as the serum potassium level spikes in the study group.

On analyzing the acid-base values, there was a clinically significant difference in the PaCO2 (partial pressure of carbon dioxide) levels, serum

HCO3 (bicarbonate) and pH between the survivor and the non-survivor groups which was also confirmed by statistical significance (PaCO2 p=0.0396) (pH p=0.015) (HCO3 p=0.0304). There was an increased mortality in patients presenting with respiratory acidosis and mixed metabolic acidosis with respiratory acidosis compared to other acid-base disturbances. Incidence of the acid base imbalance in the survivor and the non-survivor group was as per **Table – 4**.

The number of days stayed in the intensive care unit was clinically (9.38 in survivors vs. 3.64 in non-survivors) and statistically (p=0.000) significant as patients who presented with hemodynamic instability, severe acid-base and electrolyte disturbances at admission succumbed to death earlier compared to the other group. This also implied that patients whose electrolyte and acid-base imbalance were rapidly corrected, who survived the initial 3 days of admission often improved and got discharged.

Table - 4: Incidence of the acid base imbalance in the survivor and the non-survivor group.

	Survivor group	**Non survivor group**	**N**	**Chi square**	**P value**
Metabolic acidosis	19 (56%)	15 (44%)	34	0.713	0.39844
Metabolic alkalosis	3 (100%)	NIL	3		0.1
Respiratory acidosis	6 (37.5%)	10 (62.5%)	16	1.1905	0.27523
Respiratory alkalosis	2 (100%)	NIL	2		0.3333
Mixed metabolic acidosis with respiratory acidosis	7 (35%)	13 (65%)	20	2.25	0.13361
Mixed metabolic acidosis with respiratory alkalosis	13 (52%)	12 (48%)	25	0.0533	0.81736

* Correlation was significant at the 0.05 level (2-tailed).

Discussion

We investigated the influence of electrolyte and acid-base disturbances on outcomes among critically ill patients in a single-center retrospective case control study. The incidences of electrolyte and acid-base disturbances are higher in non-survivors than survivors because both increase and decrease in levels of electrolyte and acid-base parameters are associated with poor prognosis. It is worth noting that several disorders in the non-survivors are higher than that in the survivors at ICU admission, such as hyponatremia, hyperkalemia, respiratory acidosis and dual acid-base disorders.

The various distribution characteristics of electrolyte and acid-base disturbances among the study group may be due to various diseases. Hyponatremia in cardiac failure patients is a marker of neurohormonal activation, but it may also result from the heart failure therapy [10]. Diuretics are one of the most common causes of drugs induced hyponatremia. Several clinical studies have shown that hyponatremia is associated with adverse prognosis and reduced survival in HF [11]. But in our study population, though the incidence of hyponatremia is more common in the non-survivor, it could not be proven with statistical significance.

Hypernatremia is relatively more common in neurologic critically ill patients and often an indicator of the severity of the underlying disease process [12]. Causes of hypernatremia in critically ill patients include central and nephrogenic diabetes insipidus, dehydration, fever and osmotic diuresis. It should be noted that hypernatremia, and the associated hyperosmolar state have major untoward effects on a broad range of physiological functions and consecutively on organ systems. Studies showed that hypernatremia in the critically ill are an independent risk factor for mortality [13]. But in our study group of 100 ICU patients, there is no documented case of hypernatremia. Moreover no statistically significant baseline values of sodium and chloride are found between the survivors and

non-survivors groups at admission, which could be attributed to the limited sample size taken for this study.

Hypokalemia in the intensive care unit is usually iatrogenic and rarely due to conditions like hypokalemia periodic paralysis, mineralocorticoid excess or Cushing's syndrome. Use of potassium free I.V. fluids (normal saline, 5% and 10% dextrose) and continuous nasogastric aspiration are the common inciting factors for the potassium deficiency. Diuretics, commonly used in the intensive care increase urinary potassium excretion whereas insulin therapy, salbutamol nebulisation redistribute the K^+ ions into the cell causing hypokalemia. In our study, hypokalemia is equally distributed between the survivor and the non-survivor groups showing neither clinical nor statistical significance (p=1).

Hyperkalemia is very common in the critically ill patients with acute or chronic renal failure, diabetic ketoacidosis, and uncontrolled diabetes due to insulin deficiency, hemolysis and rhabdomyolysis. Malignancies particularly hematological cause marked thrombocytosis, leukocytosis, and tumor lysis syndrome predisposing to hyperkalemia. There is a statistically significant difference in the potassium value between the survivor and the non-survivor (P=0.0298). Incidence of hyperkalemia is more common in the non-survivor group (65%) than the survivor group. The reason for hyperkalemia could be the more number of chronic kidney disease patients (n=56) admitted in our hospital.

Critically ill patients with metabolic acidosis are twice as likely to die as patients who do not. A study [14] showed that the mortality rate among patients with metabolic acidosis is highest for patients with lactic acidosis (high AG). But in our study, we found metabolic acidosis more common in the survivors (56%) than non-survivors at admission. The reason for this paradox could be due to the more prevalence of CKD cases and more effective hemodialysis center of our Institution.

Respiratory acidosis is not the only acid-base disturbance observed in patients with acute and chronic respiratory failure. Metabolic acidosis can also coexist with respiratory acidosis. Heart failure, acute pulmonary edema, renal failure, and the onset of sepsis or severe hypoxia are the most common causes of metabolic acidosis associated with hypercapnia [15]. Metabolic alkalosis in respiratory failure patients may be the consequence of a too rapid removal of CO2 in patients undergoing mechanical ventilation. In our case study, respiratory acidosis and dual ABD (mixed metabolic and respiratory acidosis) are more common in the non-survivors than survivors. Arterial blood HCO3 (0.0304), CO2 (P=0.0396) and pH (P=0.015) at admission are statistically different between the survivors and non-survivors group. The incidence rates of respiratory acidosis (62.5%) and mixed metabolic acidosis and respiratory acidosis (65%) at ICU admission are clinically significant as evident by the increased mortality rate in these two groups.

Limitations

- Although we attempted to control for confounders by matching, this retrospective case control study did not establish causal relationships of electrolyte and acid-base disturbances with hospital mortality.
- Only the initial ICU admission values were considered in this study, which may have led to potential bias and limited sample size. Many kinds of electrolyte and acid disorders occurred during hospitalization and were not included in the study.
- We failed to analyze the risk factors for the development of acute kidney injury, for the critically ill patients admitted to intensive care with AKI.

Conclusion

The relationship of electrolyte and acid-base disturbances and hospital mortality is complex. They may often be a para-phenomenon, as an indicator of the severity of the underlying diseases. Electrolyte and acid-base disturbances, especially hyperkalemia, respiratory acidosis and mixed metabolic and respiratory acidosis were highly associated with hospital mortality. These disturbances should be monitored closely, diagnosed early and managed correctly during hospitalization and iatrogenic factors should be avoided. Metabolic abnormalities constitute a major chunk of problems in critical care units. Setting the parameters right can influence in a positive way, the outcomes in a critically ill patient. The success lies in recognition of the problem, and employing prompt measures in correcting the problems in a scientific manner, thereby preventing morbidity and mortality.

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