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Original Research Article

STUDY AMONG PATIENTS ADMITTED IN ICU TO DETERMINE THE PROPORTION OF MIXED ACID-BASE DISORDER AND THE PROPORTION OF LACTIC ACIDOSIS

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Abstract

Background: The mixed acid-base disorder is also known as the existence of more than one primary acid-base disorder. The common mixed disorders are mixed metabolic with respiratory acidosis and mixed metabolic with respiratory alkalosis. The study aimed to determine the proportion of mixed acid-base disorders and the various types among patients admitted to the ICU. **Materials and Methods:** This hospital-based cross-sectional study was conducted at Sri Manakula Vinayagar Medical College in Pondicherry on adult patients between the ages of 20-80 years admitted to the ICU with features suggestive of acidosis were studied for 18 months. Arterial blood gas analysis was done and interpreted along with the anion gap. In patients with a high anion gap, serum lactate levels were measured. **Result:** A study of 150 patients found that the majority were aged 66-80 (35.3%), with 62% males and 38% females. The majority were admitted due to sepsis, pneumonia, or underlying liver disease. The most common co-morbidity was type 2 diabetes mellitus (37%) and systemic hypertension (23%). The most common abnormality was hypoalbuminaemia (43.3%), followed by altered liver enzymes (12%) and hyponatraemia (10.6%). The most common pattern was metabolic acidosis with respiratory alkalosis (28%), followed by metabolic acidosis with respiratory alkalosis and respiratory alkalosis (24.7%). Serum lactate levels were elevated in 73.91% of patients with a high anion gap, with 10 patients having sepsis as the underlying pathology. **Conclusion:** Mixed acid-base disorders are common in ICUs, and analysing arterial blood gas (ABG) with an anion gap and serum lactate levels is valuable for early identification.

INTRODUCTION

The mixed acid-base disorder is also known as the existence of more than one primary acid-base disorder. Usually, the common disorder includes mixed metabolic and respiratory acidosis.[1] The common mixed disorders are mixed metabolic with respiratory acidosis and mixed metabolic with respiratory alkalosis. Lactic acidosis is the main and major cause of metabolic acidosis in patients under critical care.[2] The existence and the symptoms of mixed acid-base disorders are usually understudied. The acid-base state in the body's fluid is determined by independent variables, such as PCO2 and strong ion difference (SID), which constantly change based on other factors.[3,4] Normal acid-base status is determined when these variables have normal values, and normalising these variables is crucial for therapeutic interventions, as dependent variables can't be changed individually.[5] Acute care services face high patient acuity and limited resources, requiring early diagnosis for resource allocation. Traditional measures like vital signs fail to identify occult hypoperfusion, leading to high morbidity and mortality. A biochemical maker, serum lactate level, is needed for early illness prediction.[6]

Serum lactate has been used for many long years to assess perfusion status and measure the level of illness. Lactate, a by-product of anaerobic metabolism, can be easily determined, and it also shows the correlation between central venous, peripheral venous and peripheral arterial samples.[7] Hyperlactatemia has been associated with hypoperfusion and is primarily used for predicting the risk of increased mortality. Also, acidosis due to increased lactate levels denoted a higher mortality risk than acidosis because of the many other root causes.[8] This metabolic derangement occurs along with normal symptoms with no other biochemical abnormalities, including central venous oxygen saturation, base deficit, or anion gaps. The knowledge of increased serum lactate in various diagnoses leads to better assessment and management in the acute care setting.[6]

In-depth findings and analysis into the effectiveness of lactate kinetics as a marker for resuscitative therapies in septic patients have shown a clear connection with clinical outcomes, especially mortality. Most studies have focused on managing the early phase of sepsis, with little focus on later periods. A lot more studies are required, focusing on lactate as a tool for late sepsis management to help in determining the period of the treatment for the physician who deals with the patients during this period and thus help in the improvement of the patients.[8,9]

An article related to severe sepsis found acute hospital mortality was higher in patients with high serum lactate levels than those with lower serum lactate levels.[10] The new septic shock definition will be upgraded and can be differentiated according to BP or serum lactate levels because a high lactate level indicates higher mortality. This new definition should help decide the dosages and types of vasopressors. The new definition of septic shock should indicate that cell-based metabolism and lactate level can be used as a marker instead of relying on vital signs.[10-12]

The study aimed to determine the proportion of mixed acid-base disorders and the various types among patients admitted to ICU. Also, to determine the proportion of lactic acidosis among patients with high anion gap metabolic acidosis and mixed acid-base disorder (metabolic acidosis and alkalosis).

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted at a tertiary health care setup of Sri Manakula Vinayagar Medical College, Kalitheerthalkuppam, Pondicherry, for 18 months on adult patients with features suggestive of acidosis. Patients were included after getting informed written consent from the patient and clearance from the Research and Ethics Committees.

Inclusion Criteria

All patients admitted to the intensive care unit, aged between 20-80 years, with ABG showing Mixed Acid-Base disorder, were included.

Exclusion Criteria

Patients with Seizure disorder within 3 hrs post admission in ICU and patients who are on Linezolid, Anti-retroviral therapy, and Metformin were excluded.

After identifying patients admitted to the ICU with hypoxic-acidotic and non-hypoxic states, an appropriate questionnaire was used to collect data on patients. About 2 ml of arterial blood sample from the radial or femoral artery was collected in a heparinised syringe. In patients whose ABG shows high anion gap metabolic acidosis and mixed acid-base disorder (metabolic acidosis with metabolic alkalosis), about 2ml of venous blood Samples from the cubital vein were collected in a fluoride liquid-containing vacutainer. (Fluoride inhibits glycolysis, i.e., it is responsible for stabilising blood lactate). Based on routine investigations and clinical history, patients with systemic manifestations/illnesses that can alter blood lactate levels were excluded from the study. Patients with type A lactic acidosis were initiated with early oxygen therapy to help in early correction and early recovery.

Detailed history and physical examination were collected, 2ml of arterial blood sample was collected, the arterial blood gas analysis was done, and 2ml of venous blood sample was collected for serum lactate levels.

Statistical Analysis

Data were entered using the software Epi Info version 7.2.2.6, and analysis was done using the software SPSS version 24.0. Description of categorical variables like gender and disease status was done in frequency and percentage. Continuous variables like age, laboratory parameters, mean and standard deviation were used to summarise. Comparison of laboratory parameters between patients with different types of acid-base disorder was made using the sample t-test for continuous independent variables and the chi-square test for the categorical independent variable. The sensitivity, specificity, positive, and negative predictive values of serum lactate to identify patients with metabolic acidosis and metabolic alkalosis were calculated and presented with a 95% confidence interval.

RESULTS

Among the 150 patients admitted to the ICU, 53(35.3%) members were 66-80 years old. The second major group of 41(27.3%) members were 51-65 years old.

Most of the study patients were male, constituting 62% and females, constituting 38%. Among the male patients, the maximum were between the age group of 66-80. Among the female patients, the maximum were between the age group of 51-65.

56 (37%) of the patients had a history of type 2 diabetes mellitus, 34(23%) of the patients had a history of systemic hypertension, and 23(15.3%) patients had a history of coronary artery disease. 14(9.3%) patients had a history of COPD, 10(6.6%) patients had a history of pulmonary hypertension, and 23(15.3%) patients had a history of chronic kidney disease [Table 1].

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Among the 150 patients admitted to ICU, 51(34%) patients were admitted secondary to sepsis, which constitutes the major cause for ICU admission, followed by Pneumonia 32(21.3%), Acute kidney injury 28(18.7%), and Urosepsis 20(13.3%). Few patients have more than one clinical diagnosis.
Fifty-six patients had a history of diabetes mellitus, which was the commonest co-morbidity, followed by systemic hypertension, chronic kidney disease, coronary artery disease and COPD. Few patients have more than one co-morbidity [Table 2, Figure 1].

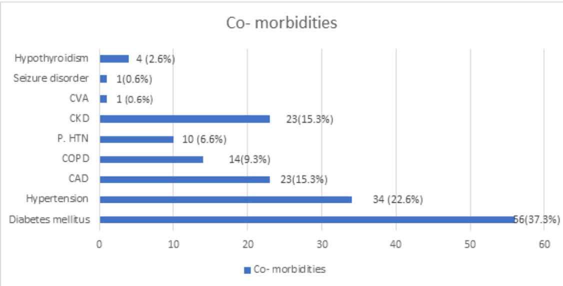

Figure 1. Distribution of the patients based on their co-morbidities.

23 (15%) of the 150 patients admitted to the ICU had a GCS <15 and were admitted to ICU as a result of it. Among the 150 patients, 106(70.7%) had a pulse rate in the range of 60-100bpm, and 41(27.3%) had a pulse rate >100bpm. 59(39.3%) had systolic blood pressure <90mmhg. 129(86%) patients had a high anion gap of >12mEq/L, and 19(12.6%) patients had a normal anion gap. 2 patients had a low anion gap [Table 3].

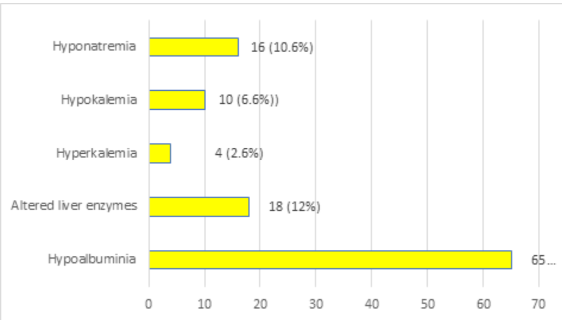

Figure 2: Distribution of patients-based electrolyte levels, altered liver enzymes and albumin levels

Out of which, hypoalbuminaemia was the most common finding in 65(43.3%) patients, followed by altered liver enzymes in 18(12%) patients and hyponatremia in 16(10.6%) patients [Figure 2].

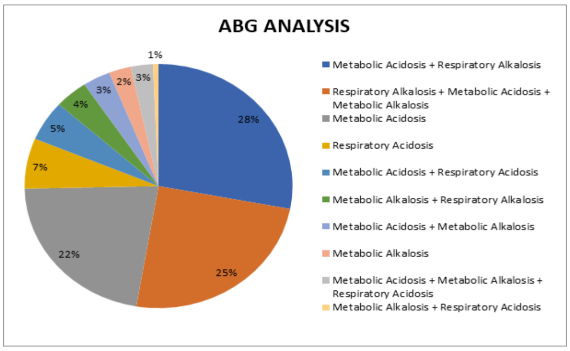

Figure 3: Distribution of patients based on Arterial Blood Gas (ABG) analysis

42(28%) had a combination of metabolic acidosis, and 37(24.7%) had a triple disorder of respiratory alkalosis with metabolic acidosis and metabolic alkalosis. 33(22%) had only metabolic acidosis, and 10(6.7%) had only respiratory acidosis.
Serum lactate levels were checked for 23 patients with high anion gaps. Among them, 17(11.3%) had higher lactate levels than 9mg/dl.
A total of 103 patients among the 150 had mixed acid-base disorder. Out of these, 62(41.3%) patients had double acid-base disorder and 41(27.3%) patients had triple acid-base disorder. 47(31.3%) patients had simple acid-base disorder.
119(79.3%) patients had only high anion gap metabolic acidosis, and 10(6.6%) patients had high and normal anion gap metabolic acidosis.
10(40%) patients with high anion gap had sepsis, 3(12%) patients had diabetic ketoacidosis and another 3(12%) patients had acute kidney injury. 2(8%) had cellulitis/ skin infections and 2(8%) had ARDS. Other causes for raised serum lactate are pneumonia, urosepsis, poisoning, post-cardiac arrest, liver disease, ARDS, and Acute Kidney Injury.

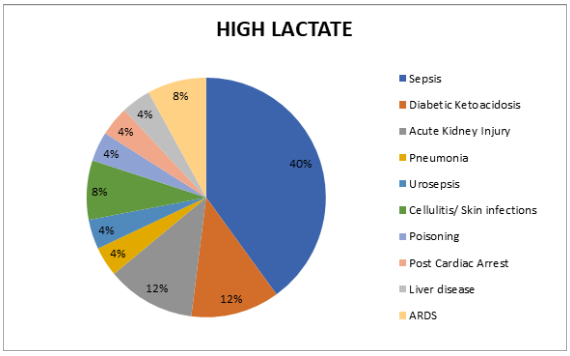

Figure 4: Distribution of the patients with high lactate based on their diagnosis.

8(47%) patients with high lactate levels had metabolic acidosis with respiratory alkalosis, and 4(23.5%) patients with high anion gap had metabolic acidosis only. 3(17.6%) patients had respiratory alkalosis with metabolic acidosis and metabolic alkalosis. 1(5.8%) participant had metabolic acidosis and respiratory alkalosis, and another 1(5.8%) participant had metabolic acidosis with metabolic alkalosis.

Seventeen patients with high anion gap had high lactate levels, and six patients with high anion gap had normal lactate levels.

The commonest simple acid-base disorder is metabolic acidosis, among which the commonest cause is sepsis (16) and acute kidney injury (9), followed by septic shock (6), pneumonia (6), liver disease (6). 5 patients with respiratory acidosis had an acute exacerbation of COPD as the cause. No case of isolated respiratory alkalosis was seen.

The commonest double acid-base disorder is metabolic acidosis with respiratory alkalosis, among which 16 patients had sepsis as the commonest cause and 13 patients had pneumonia, followed by cellulitis/skin infection (7), acute kidney injury (7) and liver disease (7).

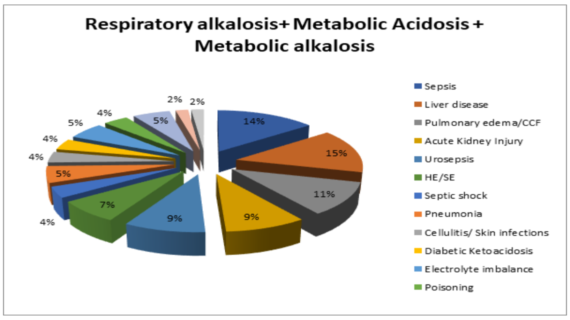

Figure 5: Distribution of triple acid-base disorders based on the clinical diagnosis.

Respiratory alkalosis with metabolic acidosis and metabolic alkalosis was the commonest pattern observed. Among these, the commonest cause is sepsis (8) and liver disease (8), followed by pulmonary oedema/CCF (6), urosepsis (5) and acute kidney injury (5).

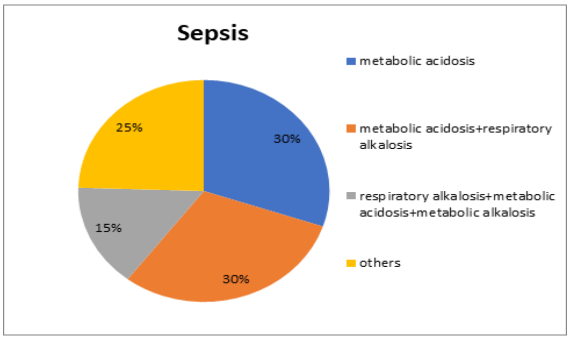

Figure 6: Distribution of ABG pattern among the septic patients.

The most common pathology among the patients admitted to the ICU was found to be sepsis (51). Among the septic patients, the most common ABG pattern was metabolic acidosis in 30%, followed by metabolic acidosis with respiratory alkalosis in another 30% of patients and metabolic acidosis with respiratory alkalosis and metabolic alkalosis in 15%, and all other patterns constituted the remaining 25%.

Table 1: Demographic data of the study

		Frequency	Percentage (%)
Gender	Male	93	62
	Female	57	38
Age group	<18	2	1.3
	19-35	13	8.7
	36-50	31	20.7
	51-65	41	27.3
	66-80	53	35.3
	>80	10	6.7
Diabetes mellitus	Present	56	37
	Absent	94	63
Systemic hypertension	Present	34	23
	Absent	116	77
Coronary artery disease	Present	23	15.3
	Absent	127	84.6
COPD	Present	14	9.3
	Absent	136	90.6
Pulmonary hypertension	Present	10	6.6
	Absent	140	93.3
Chronic kidney disease	Present	23	15.3
	Absent	127	84.6

Table 2: Clinical diagnosis distribution

Clinical diagnosis distribution	Frequency	Percentage (%)
Sepsis	51	34
Septic shock	13	8.7
Pneumonia	32	21.3
Urosepsis	20	13.3
Cellulitis/ Skin infections	10	6.7
Exacerbation of COPD	9	6
Renal Failure	4	2.7
Tuberculosis	4	2.7
Pulmonary oedema/CCF	10	6.7
Pleural effusion	4	2.7
Diabetic Ketoacidosis	8	5.3

Electrolyte imbalance	17	11.3
Poisoning	5	3.3
Post Cardiac Arrest	8	5.3
Liver disease	24	16
HE/SE	14	9.3
Coagulopathy/DIC/MODS	5	3.3
ARDS	6	4
Acute Kidney Injury	28	18.7

Table 3: Distribution of Glasgow Coma Scale, Pulse rate, Systolic Blood Pressure, and Anion gap

		Frequency	Percentage (%)
Glasgow Coma Scale	<15	23	15
	≥15	127	85
Pulse rate	<60bpm	3	2
	60-100bpm	106	70.7
	>100bpm	41	27.3
Systolic Blood Pressure	<90mmhg	59	39.3
	>90mmhg	91	60.7
Anion gap	Low	2	1.3
	Normal	19	12.6
	High	129	86

Table 4: Distribution of patients based on Arterial Blood Gas (ABG) analysis. N=150

ABG Analysis	Frequency	Percentage (%)
Metabolic Acidosis	33	22
Metabolic Alkalosis	4	2.7
Respiratory Acidosis	10	6.7
Respiratory Alkalosis	0	0
Metabolic Acidosis + Metabolic Alkalosis	5	3.3
Respiratory Acidosis + Respiratory Alkalosis	0	0
Metabolic Alkalosis + Respiratory Alkalosis	6	4
Metabolic Acidosis + Respiratory Acidosis	8	5.3
Metabolic Acidosis + Respiratory Alkalosis	42	28
Metabolic Alkalosis + Respiratory Acidosis	1	0.7
Metabolic Acidosis + Metabolic Alkalosis + Respiratory Alkalosis	4	2.7
Respiratory alkalosis + Metabolic Acidosis + Metabolic Alkalosis	37	24.7

Table 5: Distribution of clinical diagnosis of the patients with high lactate levels (>9). N=150

Clinical diagnosis distribution	Normal lactate level (n=6)	High lactate level (n=17)
Sepsis	5	10
Septic shock	0	0
Pneumonia	1	1
Urosepsis	1	1
Cellulitis/ Skin infections	0	2
Exacerbation of COPD	0	0
Renal Failure	0	0
Tuberculosis	0	0
Pulmonary oedema/CCF	0	0
Pleural effusion	0	0
Diabetic Ketoacidosis	0	3
Electrolyte imbalance	1	0
Poisoning	0	1
Post Cardiac Arrest	1	1
Liver disease	0	1
HE/SE	0	0
Coagulopathy/DIC/MODS	0	0
ARDS	0	2
Acute Kidney Injury	4	3

Table 6: Distribution of ABG analysis results of the patients with high lactate levels (>9). N=150

ABG Analysis	Normal lactate level		High lactate level	
	(n=6)	Percentage (%)	(n=17)	Percentage (%)
Metabolic Acidosis	1	16.6	4	23.5
Metabolic Alkalosis	0	0	0	0
Respiratory Acidosis	1	16.6	0	0
Respiratory Alkalosis	0	0	0	0
Metabolic Acidosis + Metabolic Alkalosis	0	0	1	5.8
Respiratory Acidosis + Respiratory Alkalosis	0	0	0	0
Metabolic Alkalosis + Respiratory Alkalosis	0	0	0	0
Metabolic Acidosis + Respiratory Acidosis	0	0	0	0
Metabolic Acidosis + Respiratory Alkalosis	3	50	8	47

Metabolic Alkalosis + Respiratory Acidosis	0	0	0	0
Metabolic Acidosis + Metabolic Alkalosis + Respiratory Alkalosis	0	0	1	5.8
Respiratory alkalosis + Metabolic Acidosis + Metabolic Alkalosis	1	16.6	3	17.6

Table 7: Distribution of simple acid-base disorders based on the clinical diagnosis. N=150

Clinical diagnosis distribution	Metabolic Acidosis	Metabolic Alkalosis	Respiratory Acidosis	Respiratory Alkalosis
Sepsis	16	1	2	0
Septic shock	6	0	1	0
Pneumonia	6	2	2	0
Urosepsis	5	1	0	0
Cellulitis/ Skin infections	1	0	0	0
Exacerbation of COPD	0	0	5	0
Renal Failure	0	0	0	0
Tuberculosis	1	0	2	0
Pulmonary oedema/CCF	1	1	2	0
Pleural effusion	2	0	0	0
Diabetic Ketoacidosis	4	0	0	0
Electrolyte imbalance	5	0	2	0
Poisoning	2	0	0	0
Post Cardiac Arrest	2	0	0	0
Liver disease	6	0	0	0
HE/SE	3	1	0	0
Coagulopathy/DIC/MODS	3	0	0	0
ARDS	3	0	0	0
Acute Kidney Injury	9	0	1	0

DISCUSSION

In this study, a total of 150 patients admitted to ICU were studied. The sample size was chosen based on a similar study by Maciel AT et al., which studied acid-base disorders among ICU patients by comparing survivors and non-survivors.[13] In our study, among the 150 patients admitted to the ICU, 53(35.3%) members were 66-80 years. The second major group of 41(27.3%) members were 51-65 years old. Most of the study patients were male, constituting 62% and females, constituting 38% among the 150 patients. These findings were similar to a study by Modi et al. to assess acid-base disorders in critically ill patients. As per the study, 42% were female, and 58% were male. The mean of direct admission to the ICU was 59.80±7.9 years.[14]

In this study, 51(34%) patients were admitted secondary to sepsis, which constitutes the major cause for ICU admission, followed by Pneumonia 32(21.3%), Acute kidney injury 28(18.7%), and Urosepsis 20(13.3%). Few patients have more than one clinical diagnosis. Similarly, in the study by Modi et al., 80% were admitted to ICU due to non-infectious causes and 8% were admitted due to sepsis. Another 12 % were admitted due to other infectious causes.[14]

56(37%) patients had a history of diabetes mellitus, which was the commonest co-morbidity, followed by systemic hypertension, chronic kidney disease, coronary artery disease and COPD. 23% of the patients had a history of systemic hypertension. Other patients with various medical conditions, including coronary artery disease, COPD, systemic hypertension, diabetes, chronic kidney disease, cerebrovascular accident, seizure disorder, and hypothyroidism. Few patients have more than one co-morbidity. Esper AM et al., in a study on the impact of co-morbidities on ICU admission, found that 54% to 65% of the patient has chronic comorbid conditions.[15]

In our study, 15% of the patients had a GCS <15, 106(70.7%) had a pulse rate in the range of 60-100bpm, and 41(27.3%) had a pulse rate >100bpm. 59(39.3%) had systolic blood pressure <90mmhg. Most of the patients in the ICU setup had abnormal vital parameters. Systolic blood pressure <90mmhg is a criterion for diagnosing septic shock and a heart rate of >100 bpm. Low blood pressure is associated with high lactate levels, according to a study by Van den Nouland et al. The study also shows that type A hyperlactatemia is associated with low MAP (77±23) and increased heart rate (106±27) than type B hyperlactatemia.[16]

Laboratory parameters and ICU admission: In our study, hypoalbuminaemia was the most common finding in 65(43.3%) patients, followed by altered liver enzymes in 18(12%) patients and hyponatremia in 16(10.6%) patients. 129(86%) patients had a high anion gap of >12, and 19(12.6%) patients had a normal anion gap. 2 patients had a low anion gap. These findings were similar to those in a study by Fencl et al., in which hypoalbuminaemia was the most common finding among ICU patients. It is a major confounding factor in the interpretation of acid-base disorder. When serum albumin is low, it underestimates the calculated anion gap.[5]

In our study, 42(28%) had a combination of metabolic acidosis with respiratory alkalosis, and 37(24.7%) had a triple disorder of respiratory alkalosis with metabolic acidosis and metabolic alkalosis. 33(22%) had only metabolic acidosis, and 10(6.7%) had only respiratory acidosis. Serum lactate levels were checked for 23 patients with high anion gaps. Among them, 17(11.3%) had higher lactate levels than 9mg/dl. Similar findings were observed in the study by Modi et al., in which the ABG of 50 patients admitted to ICU were analysed where it was observed the commonest disorder was metabolic acidosis with respiratory alkalosis (10) followed by metabolic acidosis (8).[14]

Our study found that 41.3% of patients had mixed acid-base disorders, with 62 having double, 27.3% having triple, and 31.3% having simple acid-base disorders. Most patients had respiratory alkalosis, but further compensation and anion gap calculation helped identify the underlying metabolic acidosis leading to respiratory alkalosis. The isolated high anion gap was more common than the combination of high and normal anion gap disorders.

ABG patterns in association with underlying pathology: Ten patients with high anion gap had sepsis, three patients had diabetic ketoacidosis, and another three patients had acute kidney injury. 2 had cellulitis/ skin infections, and 2 had ARDS. Other causes for high anion gap are pneumonia, urosepsis, poisoning, post-cardiac arrest, and liver disease. Similar findings were noted in a Gunnerson KJ study to understand the acid-base abnormalities in the ICU setup.[17] Ketoacidosis is a major cause of the high anion gap in ICU setup. Estimating the anion gap and treating the underlying metabolic acidosis early help improve the prognosis of the patients.

Our study found that patients with high lactate levels had metabolic acidosis with respiratory alkalosis, while those with high anion gap had metabolic acidosis only. Lactate is a significant contributor to metabolic acidosis. Various studies suggest the use of lactate as an early prognostic marker in the treatment of patients with sepsis and septic shock.[18-20]

In our study, the most common acid-base disorder is metabolic acidosis, causing sepsis, acute kidney injury, septic shock, pneumonia, and liver disease. It is also common in patients with respiratory acidosis, which often worsens COPD. The most common double acid-base disorder is metabolic acidosis with respiratory alkalosis, causing sepsis, pneumonia, cellulitis/skin infection, acute kidney injury, and liver disease. The most common pattern is respiratory alkalosis with metabolic acidosis and metabolic alkalosis. Similar findings were seen in the study by Van de Nouland; patients in the high lactate group had shock (51.8%) and sepsis (16.2%) as the underlying cause, while the patients with mild elevation in lactate had other infections (22.5%), and no lactate group had gastrointestinal problems. The study also found high lactate levels associated with hospital stays and increased mortality rates. Type A hyperlactaemia was found to have a poorer prognosis and complications with increased ICU admissions than type B hyperlactaemia.[16]

CONCLUSION

Mixed acid-base disorders are a common finding in ICU. Arterial blood gas is a traditional investigation that still has value because of the rapidity of the results and early identification of the ongoing pathologic process. It requires a skilled assistant to take the sample to attain reliable reports. When used with ABG, the anion gap is more reliable and accurate. Hyperlactemia is more common in the ICU than abnormalities in other unmeasured anions. Lactate is elevated predominantly in sepsis and septic shock. Studies have shown the prognostic value of lactate in the initial 6 hours of resuscitation. Type A was associated with a higher mortality than type B hyperlactaemia, and usually, both have been found to co-exist. Hence, treating type A hyperlactaemia initially and then for type B hyperlactaemia is advised. ABG analysis with an anion gap and serum lactate levels helps in the effective management of the patients by adopting the necessary resuscitative measures.

Limitations

It is a hospital-based cross-sectional study. Further studies regarding the mortality benefit and follow-up studies on changes in patterns associated with effective resuscitation are required.

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