International Journal of Medicine Research
ISSN: 2455-7404; Impact Factor: RJIF 5.42
Received: 25-12-2018; Accepted: 05-02-2019
www.medicinesjournal.com
Volume 4; Issue 1; January 2019; Page No. 47-50

Study of acid-base imbalance in critically ill patients and its outcome in emergency medical ward of Hamidia Hospital: A study from Bhopal

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Abstract
Background: In the intensive care unit acid-base imbalance is a frequently observed event among the critically ill patients (CIP). There is limited evidence describing the acid-base imbalance in different diseases and its relation with the anion gap.
Aims and Objectives: To study the incidence, type of acid-base imbalance, its prognosis, and association with the different conditions in CIP admitted in the emergency ward.
Materials and Methods: Hundred CIP were studied in the Department of Medicine Gandhi Medical College, Hamidia Hospital in Emergency Ward-II from October 2011 to November 2012. Detailed demographic profile including details of complications, comorbid conditions, duration of stay in emergency ward, outcome of patients (recovery after treatment), correlation with death of patients, vital parameters at the time of admission, relation between type of disease and acid-base imbalance and relation between mortality and type of acid-base imbalance was recorded.
Results: Maximum number of patients were in the age group of 15-30 years (n=35). Majority of the CIP who did not survive had liver disease (80%), respiratory disease (54.54%) and cerebral (neurological disease) (50%). Most common acid-base disorder among patients who did not survive was metabolic acidosis, respiratory alkalosis. Percentage fatality was highest among the patients who had mixed acidemia (50%) and mixed alkalosis (50%), respiratory alkalosis (36.8%) and Metabolic Acidosis (34.3%). The pH, PCO2 and PO2 were significantly high among the CIP with anion gap <11 as compared to those with anion gap>11.
Conclusion: Acid-base disorders are very common in CIP mainly metabolic acidosis. Considering the anion gap increase the prevalence of acid-base disorders. Unmeasured anion, lactate etc. play important role in mortality and morbidity of patients.

Keywords: acid-base imbalance, critically ill patients, diabetic ketoacidosis, anion gap

1. Introduction
The anticipation of early identification of conditions that alter the body's ability to compensate for acid-base disorders is vital in the management of critically ill patients (CIP). A clear understanding of metabolic respiratory interactions and a systematic approach aimed at identifying the separate components of acid-base disorders not only serves as a diagnostic tool but also helps in formulating therapeutic interventions [1].
Acid-base homeostasis is defined by the plasma pH and by the conditions of the acid-base pairs that determine it. Normally arterial plasma pH is maintained between 7.35 to 7.45. Any of the following indicators serves to identify acid-base disorders [2, 3].
There are three methods of describing and classifying acid-base abnormality, all three threats PCO_2 as the independent variable. The first method quantifies $HCO3^-$ concentration, second by using Standard Base Excess (SBE), third by using strong ion difference. All three yield identical results [4]. The only significant difference is conceptual ones, related to how each approach helps in understanding the mechanism of the disorder [5, 6].
A healthy individual may achieve an arterial pH lower than 7.15 and a lactate concentration higher than 20 meq/L during maximal exercise with no lasting effects [7]. CIP may not be able to tolerate even a brief episode of academia. In the present study, we tried to study the incidence and type of acid-base imbalance in CIP admitted in emergency ward-II of Hamidia Hospital.

2. Materials and Methods
The present observational cross-sectional study was performed on 100 CIP in Department of Medicine Gandhi Medical College, Hamidia Hospital, Bhopal in Emergency Ward-II from October 2011 to November 2012.
Patients with age between 15-95 years, attending Emergency Ward-II for more than 2 hours and those requiring resuscitation in the form of IV fluid, IV vasopressor, oxygen support, and ventilator support were included. Those who died within 2 hours on arrival in Emergency Ward-II, those who were transferred out of Emergency Ward within 2 hours of arrival and conscious well-oriented patients not requiring any intensive care were excluded from the present study.
The APACHE (acute physiologic and chronic health evaluation) II score was calculated on ICU admission. Organ function was evaluated according to the sequential organ failure assessment (SOFA) score. For each of the six organ systems included in the SOFA score (respiratory, cardiovascular, neurologic, renal, hematologic, and hepatic), organ failure was defined as a score of six. Infection was diagnosed according to usual clinical, laboratory, and microbiological parameters.
Systemic Inflammatory Response Syndrome (SIRS) was confirmed if the patient had two or more of the following

temperature of >38°C or <36°C, heart rate of >90, respiratory rate of >20 and WBC count >12 x 10^9 /L or <4 x 10^9/L or 10% immature forms (bands).

Sepsis was defined as SIRS plus a culture-documented infection. Severe Sepsis is defined as sepsis plus organ dysfunction, hypotension, or hypoperfusion (including but not limited to lactic acidosis, oliguria, or acute mental status changes). Septic Shock is defined as hypotension (despite fluid resuscitation) plus hypoperfusion. Organ dysfunction was defined on basis of SOFA score. SOFA score is a six organ dysfunction/failure score measuring multiple organ failure daily. Each organ is graded from 0 (normal) to 4 (the most abnormal), providing a daily score of 0-24 points. An increase in SOFS score during the first 48 hours in the ICU predicts a mortality rate of at least 50%.

Clinical data of all CIP managed in emergency ward-II collected and an arterial blood sample collected for acid-base gas analysis (ABG machine) which is situated in emergency medical ward-II (Unit).

Clinical data were collected from all CIP who were divided in to patients having cerebrovascular accident, patients having DM with acidosis, patients having chronic kidney disease (CKD), patients having chronic liver disease (CLD), patients having respiratory failure and require oxygen support, poisoning (OP Poisoning, Celphos Poisoning etc.) and Critically ill with Pyrexia (Malaria, MODS, Septicemia). After a detailed demographic profile details of complications, comorbid conditions, duration of stay in emergency ward, outcome of patients (recovery after treatment), correlation with death of patients (type of insult), vital parameters at the time of admission, relation between type of disease and acid-base imbalance and relation between mortality and type of acid-base imbalance was recorded.

All the data analysis was performed using SPSS ver. 20 software. Baseline characteristic of patients was expressed as mean ± standard (quantitative data) deviation and percentage (categorical data). Means of various variables were compared using the student t-test. The p-value of <0.05 is considered as significant.

3. Results

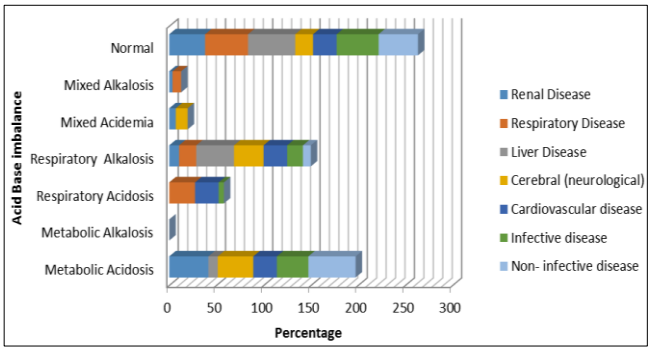
Majority of the patients were in the age group of 15-30 years (n=35) followed by 31-45 years (n=26). There was an equal distribution of gender.

Table 1: Relationship of primary disease and outcome of patients

Primary disease		Total	Survivor	Non Survivor
Renal Disease		28	20 (71.43)	8 (28.57)
Respiratory Disease		11	5 (45.46)	6 (54.54)
Liver Disease		10	5 (20)	5 (80)
Cerebral (neurological)		16	8 (50)	8 (50)
Cardiovascular		4	4 (100)	0 (0)
Other	Infective	21	11(53.39)	10(47.61)
	Non-infective	10	8 (80)	2 (20)

Table 2: Relationship of Acid-base imbalance and outcome

Acid-Base disorder	Survivor	Non Survivor	Percentage Fatality
Metabolic Acidosis	32	11	34.3
Respiratory Acidosis	5	1	20
Respiratory Alkalosis	19	7	36.8
Mixed Acidemia	4	2	50
Mixed Alkalosis	2	1	50



Non infective diseases; poisoning, snake bite etc.

Fig 1

Table 3: Relationship with Anion Gap

Variables	Anion gap <11 (n=15)	Anion gap >11(n=85)	P value
Apache	10.93±0.73	9.07±0.34	NS
Sofa	4.4±0.86	5.65±0.33	NS
pH	7.35±0.35	7.35±0.01	<0.001
PCo2	38.44±6.96	23.84±1.09	0.002
PO2	63.52±8.19	73.63±3.3	0.001
HCO3	21.17±2.85	14.31±0.73	NS
Outcome	1.33±0.12	1.4±0.05	NS
ICU stay	5.33±0.38	5.15±0.18	NS
Anion Gap	10.37±0.09	12.63±0.11	NS

4. Discussion

The incidence of Acid-Base disorder in CIP was found to be 63% in the present study. After taking anion gap into consideration the incidence of acid-base abnormality was found to be very high (85%) for anion gap more than 11, which suggest the presence of an increased level of the unmeasured anion in CIP. Brenner *et al.* [8] found that those patients who had high anion gap had higher admission rates as compared with normal anion gap cases. Palange *et al.* described the frequent incidence of acid-base abnormality in CIP. It reinforces that a high prevalence of hidden case of mixed acid-base disturbance can be recognized by concomitant analysis of acid-base and electrolyte parameters including anion gap into consideration [9] Goodkin *et al.* [10] emphasized the importance of equality of increment in anion gap (delta anion gap) and decrement in serum bicarbonate (delta HC03) in diagnosing a simple high anion gap metabolic acidosis in experimental studies.

Among the CIP the most common type of acid-base disorder was metabolic acidosis which was 32% of total CIP and case fatality in the patient of metabolic acidosis group was 34.3%. The total incidence of metabolic acidosis in the acid-base imbalance group was 51.61%. Glasmacher *et al.* found that metabolic acidosis due to the presence of unmeasured anion is a clinically relevant phenomenon, which is proportionally related to mortality.[11] Progressive metabolic acidosis may be ongoing in the early phase of critical illness despite the absence of academia. Jung *et al.* found the patient with severe metabolic or mixed acidemia was associated with a mortality rate of 57% in ICU [12]. Gunnerson *et at.* found that CIP with metabolic acidosis was nearly twice as likely to die as a patient without metabolic acidosis which correlates with present study findings [13].

In the present study respiratory alkalosis was found in 30.64% of patient in acid-base imbalance group. Respiratory alkalosis was associated with a case fatality rate of 36.8%. Bang *et al.* reported that post hypercapnic alkalosis is overlooked as a complication of mechanical ventilation in the

patient with exacerbation of chronic obstructive pulmonary disease (COPD). Development of post hypercapnic alkalosis was associated with an increased incidence of ventilator dependence and duration of ICU stay but no increase in mortality [14].

In the present study, mixed acidemia was found in 6.4% of the patient which was associated with the highest case fatality rate (50% of total). A similar study of Jung *et al.* found 8% CIP present with mixed acidemia and all patient needed mechanical ventilator support and vasopressor drugs during a hospital stay. Mixed acidemia was associated with a mortality rate of 57% in the intensive care unit [12]. Delay of acidemia recovery, as opposed to initial pH, was associated with increased mortality in the ICU. The type of academia did not influence the decision to administer bicarbonate therapy. Prompt correction of acid-base disorder and treatment of underlying cause as soon as possible is key to reduce mortality and morbidity. It suggests that we should pay more attention to the diagnosis and management of acid-base disorder in CIP.

In the present study, the patient admitted in ICU in the critically ill condition of chronic liver disease with decompensation either due to hemorrhage or sepsis were 10. All patients have metabolic acidosis and out of 10 patients, the case fatality rate was 50% i.e. only 50% survived. The nonsurvivor patient had renal dysfunction, sepsis and they required vasopressor support during the hospital stay. Similar to present study Funk *et al.* found that stable equilibrium acid-base disorder is lost when the patient of cirrhosis become critically ill. Lactic acidosis and academia were associated with increased mortality. They concluded that stable cirrhotic patient becomes critically ill during hepatic decompensation due to hemorrhage or sepsis and lost equilibrium setting of the metabolic acid-base disorder. The main result of their study was that the patient had net metabolic acidosis owing to unmeasured anion and owing to hyperchloremic dilutional and lactic acidosis. Lactic acidosis, academia and acute renal failure on ICU admission were associated with increased mortality, lactate and pH discriminate between survivor and nonsurvivor [4].

In the present study, the total number of a patient having a disorder associated with respiratory failure was 11. All patients needed mechanical ventilator support due to respiratory failure. Out of 11 patient, 6 (54%) were CIP having COPD. In the present study, 50% of a patient of COPD was found to be in respiratory acidosis and mixed disorder was observed in 30% of patient. The case fatality rate of respiratory acidosis was 20%.

In the present study, 7 patients were found to have sepsis and septic shock. Out of that, 3 patients had metabolic acidosis which is 23% of the total and 4 patients found to be in metabolic acidosis during their hospital stay of 3-4 days. The case fatality rate in patients of sepsis with septic shock was 85.7% which was highest in comparison to any other group of patients. Noritomi *et al.* described the composition of metabolic acidosis with severe sepsis and septic shock at ICU admission and throughout the first 5 days of intensive care unit stay. They studied the contribution ofin organic ion difference, lactate, albumin, phosphate, and strong ion gap metabolic acidosis. Lowest case fatality was found in patients of diabetic ketoacidosis group in which all patients survived [1].

In the present study total number of a patient having diabetes and diabetic ketoacidosis were 11 in number and most common acid-base disorder was metabolic acidosis which was present in 4 patient having diabetes and diabetic ketoacidosis who survived and there was no mortality in this group. Similar to present study Frire *et al.* [15] compared CIP with diabetic ketoacidosis in ICU and general ICU population and found that diabetic ketoacidosis patient is less ill and have lower disease severity score, mortality and shorter length of ICU and hospital stay than in DKA patient. In general population (all P-value <0.001) hospital mortality in the non-DKA patient was 18% and there was no death in a patient with DKA.

In the present study, there is significant correlation exist between anion gap and pH value ($p<0.0001$) between anion gap and bicarbonate concentration ($P<0.0001$) and anion gap and PC02 ($P= 0.0002$). Similar to present study Fujimoto M describe the dependence of cell pH and Buffer capacity on the extracellular acid-base change in skeletal muscle of bullfrog and they found that stability of pH or size of buffer capacity were proportional to external HC03 concentration. A negative correlation was observed between pH and change in pH and PC02 concentration at constant HC03 concentration. The stability of pH or size of Buffer capacity were proportional to external HC03 cone ($P= 0.002$) [16].

Cross-sectional nature was the main limitation of the present study; a large randomized clinical trial is required to strengthen the present study findings.

5. Conclusion

Acid-base disorders are very common in critical illness. Prompt correction of acid-base disorder and treatment of underlying cause as soon as possible is the key to reduce morbidity and mortality. After taking the anion gap into consideration actual figure of acid-base disorder become much higher. Metabolic acidosis was the most common acid-base disorder among CIP. Severe acidosis or mixed acidemia had the highest mortality rate. Metabolic acidosis was present in all patients of sepsis and septic shock and they had the highest case fatality rate. Overall least mortality was observed in diabetic ketoacidosis patients in comparison to non-DKA population. Hence unmeasured anion, lactate etc. play important role in mortality and morbidity of patients.

6. References

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