

# Severe Metabolic Acidosis in Critically Ill Patients and Its Impact on the Outcome; A Prospective Observational Study

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## Abstract

**Background:** Though acid-base abnormalities are common in critically ill patients, the association of metabolic acidosis with their outcome remains uncertain. Though there are many studies on acid-base abnormalities in critically ill patients, the data focusing specifically on severe metabolic acidosis (pH < 7.20) is scanty. This study was carried out in critically ill patients with single severe metabolic acidosis (pH < 7.20) admitted under the Department of General Internal Medicine to JSS Hospital, Mysore, a major tertiary care center.

**Materials and Methods:** It was a prospective observational study. A total of 100 consecutive critically ill patients (APACHE II score of 18 or more) with single severe metabolic acidosis (pH < 7.20) admitted to the intensive care units (ICUs) of JSS Hospital, Mysore under the Department of General Internal Medicine fulfilling inclusion and exclusion criteria were studied. Arterial blood gas analysis along with other relevant investigations was done within first 24 h of ICU admission. The hospitalization details and progress of the patients were collected from the in-hospital records. Patients were followed-up until the end points, i.e. discharge by the treating physician, discharge against medical advice or in-hospital death and discharge for a referral.

**Results:** Out of 100 critically ill patients with single severe metabolic acidosis (pH < 7.20), 70 patients expired compared to 30 patients who were discharged from hospital in stable condition. Out of 86 patients, who had lactic acidosis, 69 (80.2%) patients expired compared to 17 (19.8%) patients who were discharged in stable condition. A high anion gap acidosis was found in 69 patients out of which 47 (68.1%) patients had an adverse outcome. A higher base deficit is associated with high mortality (79.4% compared to 20.6%). Out of 55 patients who were put on mechanical ventilator on the first day, 45 (81.8%) patients expired. 37 patients required vasopressor support on admission out of which 34 (91.8%) patients had lactic acidosis.

**Conclusions:** This study shows a higher mortality in critically ill patients with severe metabolic acidosis. Lactic acidosis and higher base deficit are associated with higher mortality. Patients with lactic acidosis presented with hypotension and required vasopressor support on admission. Monitoring of serum pH, HCO<sub>3</sub><sup>-</sup>, lactate, base excess levels may have prognostic and therapeutic implications.

**Key words:** Acid-base disorders, Critical illness, Metabolic acidosis

## INTRODUCTION

Acid-base abnormalities are common in critically ill patients. Acidosis in critically ill patients may occur due

to a rise in arterial partial carbon dioxide tension (PaCO<sub>2</sub>), i.e. respiratory acidosis or due to fixed acids, i.e. metabolic acidosis.<sup>1</sup> There is a difference between patients with respiratory acidosis and those with metabolic acidosis *vis-a-vis* physiological variables and clinical outcomes prompting some researchers to conclude that it is the cause of acidosis rather than the acidosis per se that determines the clinical outcomes.<sup>2,3</sup> Metabolic acidosis may be due to an increase in endogenous acid production (such as lactate and ketoacids), loss of bicarbonate (as in diarrhea), or accumulation of endogenous acids (as in renal failure). Common causes of metabolic acidosis

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www.ijss-sn.com

Month of Submission : 09-2015

Month of Peer Review : 10-2015

Month of Acceptance : 11-2015

Month of Publishing : 11-2015

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include lactic acidosis, hyperchloremic acidosis, renal failure, and ketoacidosis. Metabolic acidosis can be broadly classified based on Anion Gap as normal anion gap metabolic acidosis and high anion gap metabolic acidosis. This classification has therapeutic implications also. Metabolic acidosis is called “severe” when  $\text{pH} < 7.20$  (metabolic acidosis with  $\text{pH} < 7.20$  is severe metabolic acidosis).<sup>4</sup> Even though metabolic acidosis is common in the intensive care units (ICUs), data on severe metabolic acidosis are scanty.

## MATERIALS AND METHODS

It was a prospective observational study (descriptive non-interventional study). Institutional ethics committee approval was obtained. This study was undertaken at JSS Hospital, a tertiary care referral teaching hospital attached to JSS Medical College, a constituent college of JSS University, Mysore, Karnataka State, South India. Written informed consent was obtained in all cases. APACHE score was calculated for each patient on the day of admission to ICU using APACHE II scoring system. Critically ill adult patients above the age of 18 years admitted in ICUs with APACHE II score of 18 or more were considered. Critically ill adult patients above the age of 18 years admitted in ICUs with APACHE II score of 18 or more and who were found to have single severe metabolic acidosis with  $\text{pH} < 7.20$  on first 24 h of admission were included for the study. Critically ill patients with single respiratory acidosis and mixed acidosis were excluded. Arterial blood gas (ABG) analysis done within first 24 h of admission into the ICU were taken and patients in critical care areas with single severe metabolic acidosis with  $\text{pH} < 7.20$  on first 24 h of admission were enrolled and the following data were noted: Age, gender, presenting symptoms and signs, diagnosis, relevant investigation reports, treatment and intravenous fluids used, duration of stay in ICU and any complications thereof, any new developments in ICU, use of mechanical ventilation and its duration and mortality in the ICU, initial pH levels, initial  $\text{HCO}_3^-$  levels, serum lactate levels, anion gap, APACHE II score and mortality, etc. This study included 100 such patients during a period of 2 years. Inclusion in the study would not affect the routine patient care in the ICU. Patients were followed up until discharge (from ICU) or death. Quantitative data are represented as mean  $\pm$  standard deviation. To assess the association among qualitative variables the Chi-square test, *t*-test, and ANOVA were used. Differences were considered statistically significant if  $P < 0.05$ . Statistical analysis was performed using SPSS version 16.0 for Microsoft windows.

## RESULTS

Out of the total 100 patients, a total of 66 patients were males and 34 were females. Mean age of presentation was  $59.39 \pm 17.05$  years for males and  $56.41 \pm 17.81$  years for females. Out of 100 critically ill patients with single severe metabolic acidosis ( $\text{pH} < 7.20$ ), the average pH value was 7.08 with lowest being 6.62 and highest being 7.19. Mean duration of ICU stay was  $3 \pm 1$  day.

Out of total 100 cases who had single severe metabolic acidosis ( $\text{pH} < 7.2$ ) on admission, 70 cases expired, and 30 cases were discharged in stable condition (Figure 1). Severe metabolic acidosis on admission is associated with significant mortality in critically ill patients ( $P = 0.001$ ).

Out of 100 patients, 88 patients had APACHE II score of  $>20$  and 12 patients had APACHE II score between 18 and 20. Of the 88 patients who had APACHE II score more than 20, 64 patients expired (72.7%) compared to 20 patients (27.8%) who were discharged with stable condition (Figure 2) which is statistically significant ( $P = 0.001$ ).

Out of 86 patients who had high lactate levels, 69 (80.2%) patients expired compared to 1 patient out of 13 with

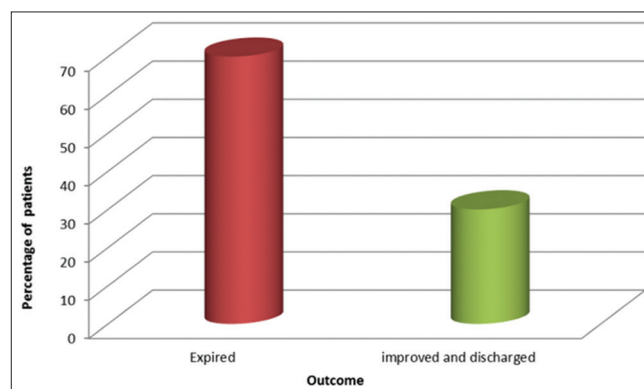


Figure 1: Outcome in severe metabolic acidosis

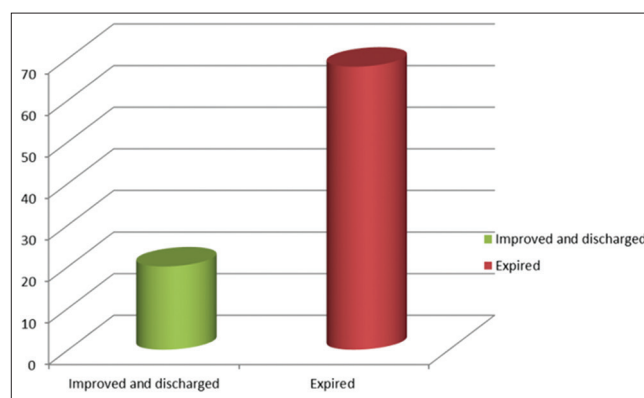
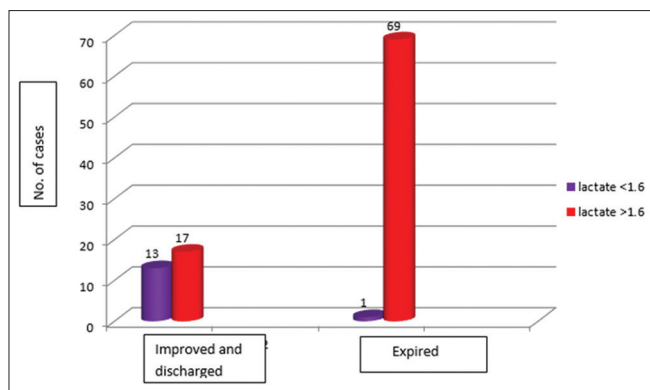


Figure 2: APACHE II score  $> 20$  and outcome



**Figure 3: Lactate levels and mortality**

normal lactate levels which are statistically significant ( $P = 0.04$ ). Out of 86 patients, who had lactic acidosis, 69 (80.2%) patients expired compared to 17 (19.8%) patients who were discharged in stable condition (Figure 3).

31 patients had normal anion gap severe metabolic acidosis while 69 patients had high anion gap severe metabolic acidosis; There was no statistically significant difference in the outcome of two groups ( $P = 0.540$ ). Out of 100 patients, 68 patients had base excess value  $< -2$ . Out of these 68 patients, 54 (79.4%) patients expired compared to 14 (20.6%) patients with normal base excess. The higher mortality was seen in base excess group  $< -2$  compared to normal base excess group, and this was statistically significant ( $P = 0.003$ ). Out of 55 patients who were put on mechanical ventilator on the first day, 45 (81.8%) patients expired compared to 10 (18.2%) patients who did not need mechanical ventilation. Patients who needed mechanical ventilation on admission had significantly higher mortality compared to patients who did not need mechanical ventilator support ( $P = 0.04$ ). Out of 37 patients who required vasopressor support, 34 (91.8%) cases had lactic acidosis and 3 (8.2%) cases were non-lactic acidosis cases. Most common diagnosis in patients with severe metabolic acidosis in the present study was lactic acidosis. Most common diagnosis in patients with lactic acidosis in the present study was sepsis with septic shock. Most common diagnosis in patients with high anion gap non-lactic acidosis was diabetic ketoacidosis, whereas bicarbonate loss from gastrointestinal (GI) tract (acute gastroenteritis [GE]) was common cause of normal anion gap acidosis

## DISCUSSION

The term “severe” metabolic acidosis is used when pH is lower than 7.20.<sup>4</sup> Severe metabolic acidosis is not uncommon in critically ill patients. Jung *et al.*<sup>5</sup> reported higher mortality in critically ill patients with severe metabolic acidosis. In the present study, severe metabolic

acidosis in critically ill patients was associated with statistically significant mortality, i.e. 70% patients expired compared to 30% patients who were discharged in stable condition ( $P = 0.001$ ) which is consistent with the study by Jung *et al.*<sup>5</sup> Serum lactate levels is an important prognostic marker in metabolic acidosis and when elevated is associated with higher mortality levels as reported by Jung *et al.*<sup>5</sup> Gunnerson<sup>1</sup> compared outcomes in patients with high lactate levels and normal lactate levels and demonstrated significant mortality in patients with high lactate level. Smith *et al.*<sup>6</sup> reported similar findings. In the present study, lactic acidosis is associated with higher mortality compared to non-lactic acidosis cases and higher serum lactate levels are associated with statistically significant mortality ( $P = 0.04$ ) which is consistent with previous studies. High anion gap metabolic acidosis may be associated with higher mortality compared to normal anion gap acidosis as reported by Jung *et al.*<sup>5</sup> whereas Cusack *et al.*<sup>7</sup> and Rocktaeschel *et al.*<sup>8</sup> reported no statistical significance in outcomes between these two groups. In our study, 31 patients had normal anion gap severe metabolic acidosis while 69 patients had high anion gap. There was no significance in the outcome between these two groups ( $P = 0.540$ ). Jung *et al.*<sup>5</sup> and Kaplan and Kellum<sup>9</sup> reported that lower base excess is associated with high mortality. In our study, lower levels of base excess on admission are associated with statistically significant mortality compared to normal base excess levels ( $P = 0.003$ ) which are consistent with previous studies.

This study focused on only single severe metabolic acidosis excluding mixed acidosis. Whether metabolic acidosis is an etiologic contributor to organ dysfunction or just a marker of severity of underlying illness has been a matter of debate. Of late, there are reports about severe metabolic acidosis playing a contributory role in organ dysfunction, decreased cardiac output, arterial dilatation and hypotension, arrhythmia, impaired oxygen delivery, increase in respiratory muscle workload, decrease in adenosine triphosphate generation, and altered immune response.<sup>5</sup>

The uncertainty over the timing and indications of bicarbonate buffer therapy and the controversy regarding the pros and cons of bicarbonate therapy was highlighted in an online survey by Kraut and Kurtz.<sup>10</sup> Gehlbach and Schmidt<sup>11</sup> reported high mortality after bicarbonate therapy and Stacpoole<sup>12</sup> reported higher mortality in lactic acidosis with bicarbonate therapy. Jung *et al.*<sup>5</sup> reported no significant outcome between patients who received bicarbonate therapy and patients who did not receive it. Bicarbonate therapy in acute high anion gap metabolic acidosis is controversial.<sup>13,14</sup> From the time of its conception, this study was never meant to assess the effect of sodium

bicarbonate on the outcome or to explore the reasons for sodium bicarbonate administration. However, the present study may be helpful as a primer to design a future interventional, randomized study to examine the effects of buffers in severely acidotic critically ill patients.

### Limitations of this Study

- It was a prospective observational study. No intervention was done in this study.
- ABG analysis on the first day of admission was used for the study. No follow-up ABG analysis was taken into consideration.
- Lack of clear-cut guidelines for administration of bicarbonate buffer therapy.

### CONCLUSION

This study highlights the magnitude of single severe metabolic acidosis on admission in critically ill patients admitted to ICUs under the Department of General Internal Medicine of JSS Hospital, Mysore, Karnataka, India. Severe metabolic acidosis in critically ill patients is associated with significant mortality. Higher serum lactate levels and base deficit, on admission, are excellent predictors of mortality. Patients with higher APACHE II score on admission had high mortality. Most common diagnosis in patients with severe metabolic acidosis in the present study is lactic acidosis. Most common diagnosis in patients with lactic acidosis in the present study is sepsis with septic shock. Most common diagnosis in patients with high anion non-lactic acidosis is diabetic ketoacidosis, whereas bicarbonate loss from GI tract (acute GE) is a common cause of normal anion gap acidosis. Early recognition of mortality predictors may improve the final outcome of the patient. Whether severe metabolic acidosis in critically ill is a significant abnormality in itself contributing to the causality of complications and mortality,

which needs to be corrected, or is it just an association with underlying severe illnesses is difficult to ascertain.

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**How to cite this article:** Kiran HS, Anil GD, Murthy KAS, Gowdappa HB. Severe Metabolic Acidosis in Critically Ill Patients and Its Impact on the Outcome: A Prospective Observational Study. *Int J Sci Stud* 2015;3(8):168-171.

**Source of Support:** Nil, **Conflict of Interest:** None declared.