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Original Research Article

Assessment of the acid-base disturbance in COVID-19 patients admitted in an intensive care unit: an observational study

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ABSTRACT

Background: The coronavirus disease 2019, known as COVID-19, became a global pandemic following its initial outbreak in Wuhan, China. COVID-19 illness severity is categorized into three levels: mild, severe, or critical. Arterial blood gas (ABG) testing is considered the definitive method for assessing oxygen levels. It also plays a crucial role in evaluating the sufficiency of ventilation and the balance of acids and bases in the body. To assess the acid base disturbance in COVID 19 patients who were admitted in the intensive care unit (ICU).

Methods: After obtaining ethical committee approval and informed consent from patients this prospective observational study was conducted in a tertiary care hospital, Bengaluru from August 1st to October 31st 2020. The arterial blood gas tests were performed prior to any intervention to manage the patient's condition. The analyses focused on the anion gap, bicarbonate levels, blood pH, $PaCO_2$, and PaO_2.

Results: The mean age of the patients was 58+12.2 years. A high pH level (alkalosis) was observed in 31 (62%) patients. High HCO3 was seen in 14 (28%). A statistical analysis using the Pearson correlation test revealed a significant negative correlation between $PaCO_2$ and pH, with a correlation coefficient (r) of -0.346 and a p value of 0.001.

Conclusion: Consistent monitoring of ABG at regular intervals plays a crucial role in promptly detecting respiratory impairment, silent hypoxia, and cytokine storms. Early identification through such monitoring can lead to timely intervention and ultimately save lives.

Keywords: Acid-base balance, COVID-19, Alkalosis, Hypoxemia

INTRODUCTION

Coronaviruses constitute a group of viruses associated with causing respiratory and gastrointestinal illnesses in a range of animals and humans.[1] The coronavirus disease 2019, known as COVID-19, became a global pandemic following its initial outbreak in Wuhan, China. It primarily targets the respiratory system in humans by binding to angiotensin-converting enzyme 2 (ACE-2) receptors found on the surface of cells in the respiratory tract.[2,3] The World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern on January 30, 2020. Subsequently, on March 11, 2020, the WHO escalated its status, categorizing COVID-19 as a pandemic.[4] COVID-19 illness severity is categorized into three levels: mild, severe, or critical. Mild cases may present with no or mild pneumonia and do not fulfil the conditions for severe or critical classification. Severe cases exhibit symptoms like shortness of breath, rapid breathing (respiratory rate of 30 or more per minute), low blood oxygen levels (below 93% oxygen saturation), a PaO_2/FiO_2 ratio below 300, or a more than 50% increase in lung infiltrates within 24 to 48 hours. Critical cases are marked by respiratory failure, septic shock, or multiple organ dysfunction.[5]

Arterial blood gas (ABG) testing is considered the definitive method for assessing oxygen levels. It also plays a crucial role in evaluating the sufficiency of ventilation and the balance of acids and bases in the body. Arterial hypoxemia is a primary respiratory symptom in patients with COVID-19.[6] Respiratory alkalosis, frequently observed as an acid-base imbalance in patients with COVID-19, has been associated with a heightened risk of severe complications.[7] Utilizing pH, pCO2, and HCO3−levels as reference points can assist in recognizing compensatory mechanisms and mixed acid-base disturbances.[8,9] Indeed, the presence of metabolic acidosis is linked with a higher mortality rate in these patients.[10-13] The anion gap (AG) is defined as the discrepancy between the concentrations of measured anions and cations and is calculated during instances of metabolic acidosis to aid in pinpointing the root cause.[14]

Observed electrolyte imbalances in COVID-19 cases can influence treatment choices, duration of hospitalization, and the risk of death. Since patients with severe COVID-19 typically require extended hospital stays, ongoing analysis of their electrolyte and acid-base balance is of significant interest.

This study was conducted to assess the acid base disturbance in COVID-19 patients who were admitted in the Intensive Care Unit (ICU) during first wave with severe and critical illness.

Objectives

To assess the acid base disturbance/abnormalities in COVID-19 patients admitted in the Intensive Care Unit (ICU).

METHODS

Study design

This was a prospective observational study.

Study place

The study was conducted in the main Intensive Care Unit (ICU) in the Trauma Care Centre of Victoria Hospital, attached to Bangalore Medical College and Research Institute (BMCRI), Bangalore, India

Study duration

The study was conducted from 1st August 2020 to 31st October 2020.

Sample size

50 patients participating in the study who were selected based on simple random sampling by random number generator.

Inclusion criteria

Patients with a laboratory-confirmed diagnosis of COVID-19, patients who are admitted to the ICU, adult patients aged 18 years and older (or a different age range as per the study design), patients who have undergone ABG testing as part of their clinical assessment upon admission and during their ICU stay, patients who are willing to give written informed consent

Exclusion criteria

Patients with a history of chronic acid-base disorders prior to COVID-19 infection, pregnant women, if pregnancy is determined to be a risk factor or not the focus of the study, patients with COVID-19 who are admitted to the hospital but not in the ICU, patients with incomplete medical records or missing ABG results, patients suffering from other comorbidities or conditions that may independently affect acid-base balance, such as severe kidney, liver, or lung diseases unrelated to COVID-19.

Method of data collection

After obtaining ethical clearance from Institutional Ethical Committee and written informed consent from patients admitted in ICU who fulfilled inclusion criteria. This study was conducted in the department of Pulmonary medicine, Victoria Hospital attached to BMCRI, Bengaluru from 1st August 2020 to 31st October 2020. Based on similar study conducted we considered around 50 samples. Upon admission to the emergency department, demographic information, existing comorbidities, and ongoing treatments were documented. At the attending physician's judgment, respiratory assistance was administered using either helmet continuous positive airway pressure (CPAP) or mask-based non-invasive ventilation (NIV) to keep the peripheral oxygen saturation (SpO_2) above 92% and the respiratory rate below 25 breaths per minute. If any clarification was needed, the patient's records were verified with the attending physician. All patients underwent consistent monitoring of vital clinical and laboratory indicators.

Trained personnel collected ABG samples using heparinized syringes, which were then immediately analyzed using a bedside device (Abbott i-STAT analyzer, Abbott Park, IL, USA). Blood gas assessments were conducted for all patients on the day they were admitted. For those with multiple ABG tests, the initial reading was the one evaluated. The arterial blood gas tests were performed prior to any intervention to manage the patient's condition. The analyses focused on the anion gap, bicarbonate levels, blood pH, $PaCO_2$, and PaO_2. A pH range of 7.35 to 7.45 was deemed normal. Normal PaO2 levels were identified as being between 75 to 100 mmHg, PaCO2 levels from 35 to 45 mmHg, and the corrected standard bicarbonate concentration in ABG was considered normal at 22 to 26 mmol/l.[16]

Statistical analysis

The data collected was analysed using JAMOVI version 1.2.19. Socio-demographic variables were analysed in terms of mean, standard deviation (SD), frequency (n) and percentage (%). Pearson correlation test was performed to assess correlation between ABG parameters. A p value of <0.05 was taken as statistically significant. Data results were represented in the form of Tables and Figures.

RESULTS

An analysis was conducted on data from 50 critically ill COVID-19 patients who were admitted to the Intensive Care Unit (ICU). The baseline characteristics are summarised in Table 1. The mean age of the patients was 58+12.2 years. In this study 37 (74%) were males and 13 (26%) were females. In total majority of patients, 23(46%) of the patients were between the ages of 51 and 60 years. Mean duration of hospital stay was 6.1+4.1 days.

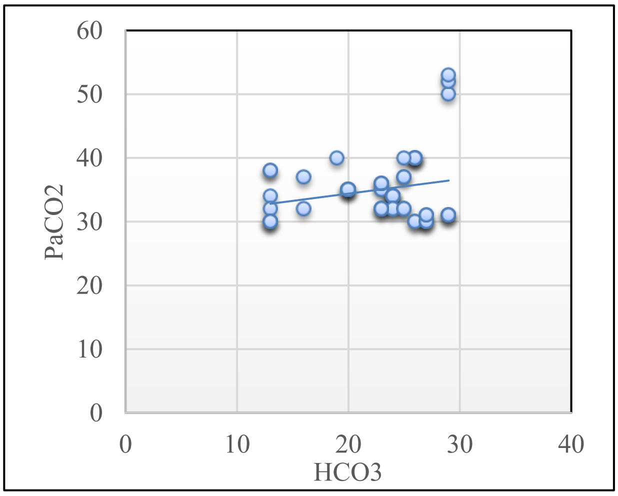

Figure 1: Correlation between paCO2 and bicarbonate.

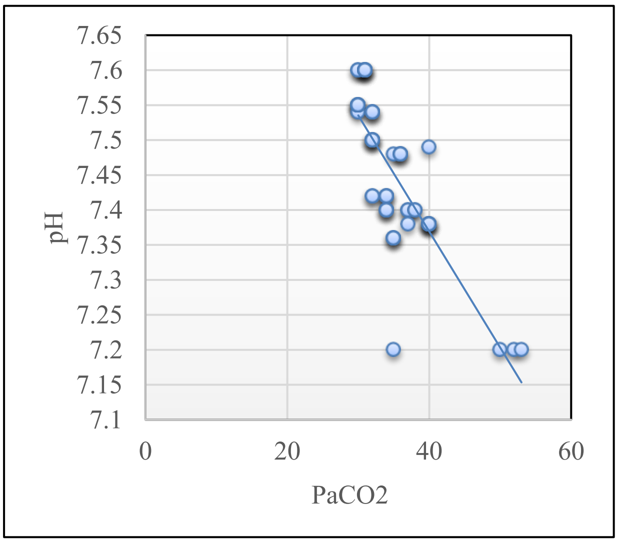

Figure 2: Correlation between paCO2 and pH.

On ABG analysis, A high pH level (alkalosis) was observed in 31 (62%) patients. Acidosis, indicated by a pH level of less than 7.35, was uncommon, occurring in just 1 (2%) patient. Hypoxemia, characterized by low PaO_2, was detected in 37 (74%) patients. High HCO_3 was seen in 14 (28%). All ABG parameters are summarized in Table 2.

A statistical analysis using the Pearson correlation test revealed a significant negative correlation between $PaCO_2$ and pH, with a correlation coefficient (r) of -0.346 and a p value of 0.001, as well as a significant positive correlation between $PaCO_2$ and HCO_3 standard, with a correlation coefficient (r) of 0.48 and a p value of 0.03 (as shown in Figure 1,2). Additionally, a positive correlation was observed between PaO_2 and $PaCO_2$, suggesting a concurrent presence of hypoxia and hypocapnia, although this correlation was not statistically significant (r=0.05, p>0.05). The study shows the sample population to have acute respiratory alkalosis with partially compensated metabolic acidosis.

Table 1: Baseline characteristics of the study population (n=50).

Variables	Values
Mean age (in years)	58±12.2
Age group distribution (in years)	
≤50	12 (24%)
51-60	15 (30%)
>60	23 (46%)
Gender	
Male	37 (74%)
Female	13 (26%)
Hospital-stay	
<7 days	33 (66%)
≥7 days	17 (34%)

Table: ABG analysis of study subjects (n=50).

Parameter	Values
pH	
Acidosis (<7.35)	1 (2%)
Normal (7.35–7.45)	18 (36%)
Alkalosis (>7.45)	31 (62%)
Mean pH=7.5±0.1	
PaCO2	
80-100	45 (90%)
>100	5 (10%)
Mean paCO2 = 27.8±5.1	
PaO_2	
Low (<35)	37 (74%)
Normal (35-45)	12 (24%)
High (>45)	1 (2%)
Mean paO_2 = 64.9±16.6	
HCO_3	
<22	36 (72%)
22-28	14 (28%)

DISCUSSION

The COVID-19 pandemic persists in its global spread. A key clinical manifestation of the disease is pneumonia, typically characterized by bilateral ground-glass opacities, which may or may not be accompanied by consolidations on high-resolution computed tomography scans. This primary symptom is detected in nearly all patients hospitalized with COVID-19.[17] Pneumonia that extensively affects large portions of both lungs can lead to a serious infectious condition, as it disrupts the exchange of respiratory gases and results in alterations to minute ventilation. Consequently, an acid-base imbalance of respiratory nature was an anticipated outcome among our patients with COVID-19.[18]

The study showed the pH to range from 7.3 to 7.9 with a mean of 7.5 indicating alkalosis. The partial pressure of oxygen in the sample population ranged from 38 mmHg to 108 mmHg, with a mean of 64.9 mmHg indicating hypoxemia. The partial pressure of CO2 is shown to range from 17.9 mmHg to 37.6 mmHg, with a mean of 27.8 mm Hg indicates that compensatory mechanism is at play. Bicarbonate concentration in the study population is seen to be ranging from 12.1 mEq/l to 26.5 mEq/l, with a mean of 19.6 mEq/l.

The study shows the sample population to have acute respiratory alkalosis with partially compensated metabolic acidosis. Our research indicated that about 62% of the participants experienced alkalosis. The presence of low PaCO2 in 90% of the patients suggests that respiratory alkalosis is predominantly seen in cases of severe COVID-19. When contrasting our metabolic data with findings from other research, our study found a higher incidence of metabolic alkalosis at 28%, compared to the lower rate observed in the study by Alfano et al.[18]

As confirmed by a negative Pearson correlation between pH and PaCO2. Theories for the unexpected respiratory alkalosis include one where COVID-19 suppresses the carotid body's response to oxygen deprivation, thus preventing hyperventilation and CO2 buildup, potentially through the interaction with ACE2 receptors, which the virus targets.[19] This study predominantly identified respiratory alkalosis accompanied by hypoxemia, a finding that aligns with the results from a similar study carried out by Balzenelli et al.[20] While less frequent, a subset of COVID-19 patients in our study exhibited respiratory acidosis, a condition typically associated with a sense of air hunger.

Notably, a study conducted by Zubieta-Calleja et al, observed that respiratory acidosis coupled with hypoxemia can result in pneumolysis and fatalities.[21] The high incidence of alkalosis among COVID-19 ICU patients, an unusual finding in critical care, remains unexplained.[22] Ventilator support, particularly with high positive end-expiratory pressure, could be a contributing factor to respiratory alkalosis. The prior use of corticosteroids in clinical settings, while possibly causing metabolic alkalosis through mineralocorticoid activation, cannot be directly linked to respiratory alkalosis.[23]

The study primarily focused on severely ill ICU-admitted COVID-19 patients, suggesting the inclusion of ABG analysis for patients with milder and moderate illness would be beneficial. It did not explore the relationship between ABG results and patient outcomes or how ABG patterns change over time, both needing further research. Operational factors like pre-ICU home oxygen support or BiPAP therapy may have influenced respiratory alkalosis presence. The study revealed acid-base abnormalities linked to comorbidities but didn't identify the exact causes, necessitating further investigation.

Limitations include being single-location, retrospective, lacking a control group, and not considering chronic drug use or alternative medications, warranting larger, unbiased investigations.

CONCLUSION

COVID-19 patients frequently experience acid-base disorders, primarily respiratory alkalosis but also respiratory acidosis with mixed metabolic imbalances. The study revealed significant correlations between pH and $PaCO_2$, as well as between $PaCO_2$ and HCO_3, underscoring the importance of regular ABG monitoring for early detection of respiratory issues, silent hypoxia, and cytokine storms, allowing for prompt life-saving interventions.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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