Original Research Article

Unusual presentation of acid base abnormalities in critically ill COVID-19 patients: A retrospective observational study in a tertiary care centre, Telangana

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Abstract

Introduction: Since the novel corona virus disease 2019 (COVID-19) was declared a pandemic, the impact globally has been unparalleled. The World Health Organization (WHO) has notified about the novel coronavirus (COVID-19) as pandemic and have been identified as the causative agent for pneumonia and ARDS shortly thereafter. As the severity of COVID-19 progresses, many patients require intensive care unit (ICU) admission requiring frequent arterial blood gas (ABG) analysis which led to discovery of unusual acid base abnormalities in the patients. Arterial blood gas analysis is an important routine investigation to monitor the acid base balance of the patients, effectiveness of gas Exchange. Disorders of acid base balance can complicate many diseases and occasionally the abnormality may be so severe that it can be life threatening. The present study was carried out to assess acid-base patterns in COVID-19 ICU patients and to find their outcomes.

Objective: To find out profile and pattern of Arterial Blood Gas anomalies (ABG) in intensive care (COVID-19) patients.

Materials and methods: A single-center retrospective, observational study in a dedicated COVID-19 intensive care unit from the period of 8 months. A total of 32 Reverse Transcription Polymerase Chain Reaction (RT PCR) positive cases; that needed ICU admission were included in this study done at Malla Reddy Institute of Medical Sciences, Hyderabad, India. Data of Arterial Blood Gas (ABG) performed on day of admission was noted and they were followed up until they remained in ICU.

Results: The age group affected with COVID-19 in this study was 26-75 years. Out of the patients admitted 21 were male (M) and 11 were female (F). Average duration of hospital stay for patients included in study was 22.31 $\pm$ 9.68. Out of 32 patients, there were 81.25% (n=26) survivors and (n=6) (18.75%) were non-survivors. In this study population majority of patients had (n=7) (21.88%) metabolic alkalosis, while 5 patients (15.63%) had Normal ABG. Metabolic acidosis was seen in 4 patients (12.50%), and respiratory acidosis was seen in 4 patients (12.50%) each.

Conclusion: Majority of patients admitted with COVID-19 experienced pH changes with a wide range of acid–base abnormalities, with metabolic alkalosis being the most prevalent. The observed occurrence of metabolic alkalosis on admission in a large number of COVID-19 patients is an undocumented finding that necessitates a multicenter investigation to uncover the disease's pathogenesis, including the importance of other acid-base imbalances that have been discovered in the present study.

Key words

SARS COVID-19, Arterial Blood Gas, Metabolic Acidosis, Metabolic Alkalosis, ARDS.

Introduction

Since the novel corona virus disease 2019 (COVID-19) was declared a pandemic, the impact globally has been unparalleled. The first cases of atypical pneumonia were described in Wuhan, China, late 2019. The World Health Organization (WHO) had notified in January 2020 about the novel corona virus (CoV-2) which was identified as the causative agent shortly thereafter.

As the angiotensin-converting enzyme 2 (ACE2) is the port of entry for SARS-CoV-2, the renin angiotensin system (RAS) is affected in COVID-19. When SARS-CoV-2 enters the cell, there is down regulation of ACE2, with up regulation of the classic RAS pathway leading to angiotensin II and aldosterone production. Both angiotensin II and aldosterone affect the renal handling of hydrogen (H^+) and bicarbonate ($HCO3^-$), which may cause acid–base disturbances. As the severity of COVID-19 progresses, many patients require intensive care unit (ICU) admission leading to frequent arterial blood gas (ABG) analysis [1-3].

The clinical features of the patient infected with SARS-CoV-2 ranges from minimal symptoms to severe respiratory failure with multiple organ failure. Severe Acute Respiratory Syndrome Corona Virus-2 (SARS CoV-2) can induce the cytokine storm in a subgroup of patients producing high levels of inflammatory mediators in COVID-19 infected patients, which was associated with increased severity and death [2, 3].

The COVID-19 patients that are critical may share features similar to Acute respiratory distress syndrome with leakage of protein rich fluid in alveoli impairing gas exchange, other features such as thick mucus secretions in airways, diffuse alveolar damage, increased pulmonary inflammation, and high levels of systemic pro-inflammatory cytokines and micro-thrombosis. Hypoxemia with COVID-19 is usually associated with an increased alveolar-to-arterial oxygen gradient, signifying either ventilation–perfusion mismatch or intrapulmonary shunting [4].

Arterial blood gas analysis is an important routine investigation to monitor the acid-base balance of the patients, effectiveness of gas Exchange. Disorders of acid base balance can complicate many diseases and occasionally the abnormality may be so severe that it can be life threatening [5]. The present study was carried out to assess acid-base patterns in COVID-19 ICU patients and to find their outcomes.

Aim and objectives

The aim of the present study was to find out pattern of acid base disorders using Arterial Blood Gas (ABG) in critically ill (COVID-19) patients.

Materials and methods

A single-center retrospective, observational study in a dedicated COVID-19 intensive care unit in Malla Reddy institute of medical sciences from May 2020 to December 2020 was done.

Total of 32 Adult patients (>18 years) with Reverse Transcription Polymerase Chain Reaction (RT PCR) positive cases that needed ICU admission for their life-threatening conditions were included in this study. Non-consenting patients were excluded.

Arterial Blood Gas (ABG), performed on day of admission was performed on a Gem Premier 3500 TM ABG analyzer in the ICU. A potentiometric method is used to calculate partial pressure of carbon dioxide (pCO2) and pH, while partial pressure of oxygen (pO2), HCO3 and base excess (BE) are calculated parameters. The instrument is subject to regular internal quality control with the onboard Intelligent Quality Management system, and the patients were followed up until they remained in Intensive care unit.

Inclusion criteria

- Age > 18 years old admitted to our hospital, irrespective of severity and possible co-morbidities.
- Patients with confirmed diagnosis of COVID-19 with Reverse Transcription Polymerase Chain Reaction (RT PCR) positive; that needed ICU admission for their life threatening conditions were included in this study.

Exclusion criteria

- Age < 18 years old,
- Patients not consenting to study.
- Those patients who took discharge against medical advice (DAMA) were excluded from the study in the view that follow up could not carried out properly.

Results

The age group affected with COVID-19 in this study was 26-75 years. Out of the patients admitted, 21 were male (M) and 11 were female (F). Average duration of hospital stay for patients included in study was 22.31$\pm$9.68. Out of 32 patients, there were 81.25% (n = 26) survivors and 18.75% (n = 6) were non-survivors. In this tudy population, majority of patinets had (n = 7) (21.88%) metabolic alkalosis, while 5 patients (15.63%) had normal ABG. Metabolic acidosis was seen in 4 patients (12.50%) and respiratory acidosis was seen in 4 patients (12.50%) (**Table – 2**) each. Results were depicted as per **Table – 1 to 5**. **Table – 1** depicts maximum (7.6) and minimum (6.9) PH and HCO3 maximum (36) and miniumum (18) values which were obsevred during the study.

Discussion

Acute respiratory distress syndrome (ARDS) is a severe form of SARS-CoV2 infection seen in critically ill-covid 19 patients because of cytokine. Following this initial phase, there comes a period of immunological dysregulation which is the leading cause of sepsis-related deaths [6].

Many studies have investigated the importance of laboratory biomarkers in the care and prognosis of COVID-19 patients during the

outbreak but to our knowledge very few studies have looked into ABG, acid-base patterns, and their relationship with outcomes in COVID-19 patients admitted to ICUs. The study of a patient's arterial blood gas (ABG) is crucial for identifying and maintaining their oxygenation status and acid–base balance.

In the present study of critically ill COVID-19 patients admitted to ICU the majority were male patients i.e. 21 and 11 were female.

The out come, death occured in totlal of 6 outof 32 patients, 4 patients had respiratory acidosis, 2had meatabolic acidosis (**Table –3 & 5**), even though most observed was metabolic alkalosis no deaths were associated with it. P-value was significant with ABG analysis and Outcome, in both alive and dead (**Table - 5**).

The most common age group to be affected was 31-40 years with10 patients (31.25%) followed by 7 patients (21.87%) in age group of 51-60 years with mean age of 49.40 +14.93 years. The overall mortality rate of COVID-19 is much lower than for severe acute respiratory syndrome and Middle East respiratory syndrome [7]. Average duration of hospital stay for patients included in study was 22.31 + 9.68 days. Average duration of stay for survivors is 19.63+8.23 days for non survivors is 32.5 +7.93 days. In accordance with the recent reports on characteristics of patients with COVID-19 who needed management in intensive care units, advanced age (>50), male sex, and co-morbidities (particularly hypertension and diabetes) are believed to be risk factors for severe disease and death from SARS-Cov-2 infection [8, 9].

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There were 26 survivors (81.25 percent) and 6 non-survivors (18.75 percent) with co-morbidities such as hypertension and diabetes mellitus in our study. The majority of the patients in this study had an abnormal ABG, implying that the homeostasis of numerous organs that regulate acid-base balance was disrupted.

On the first day of ICU admission, 5 patients (15.6%) of 32 patients had normal acid base analysis, while 27 patients (84.4%) had abnormal ABG analysis. Normal pH does not always imply normal ABG, as evidenced by Lakhani JD, et al. study on ABG in sepsis patients [5], which found mixed ABG abnormality in 8 out of 36 patients with sepsis.

In research by Lakhani JD, et al., acidemia was found in 19 (52.77%) of the 36 patients, alkalemia in 9 (25%) of the patients, and normal pH in 8 (22.22%) of the patients [10]. In study by Lakhani JD, et al., 44 individuals (55%) had normal pH, with only three having normal ABG and two-thirds having mixed diseases. Sepsis is one of the most common causes of multi-organ failure [11, 12].

Critical consequences have previously been documented as secondary to a rapid loss in renal function and the development of severe metabolic acidosis as a result of cytokine storm associated with COVID-19 [13]. Traditional methods of detecting multi-organ dysfunction(MODS) by Sequential Organ Failure Assessment (SOFA) may miss a smaller number of patients but ABG analysis can be an early indicator of simultaneous involvement of several organs [9].It may reflect lung involvement and hypoxemia in COVID-SARS patients and can provide a comprehensive picture of body homeostasis, reflecting not just the lungs but also the kidneys, liver, endocrine, and overall metabolic milieu of a critically ill patient [14].

In addition to hypoxia, ABG exhibits respiratory alkalosis, which was seen frequently in the current investigation. Hyperventilation syndrome can cause respiratory alkalosis, which can lead to hypocapnia because breathing exceeds metabolic needs. There may also be metabolic acidosis, which can be corrected or not. The PCO2 level rises as the situation worsens and the amount of work required to breathe increases, and respiratory alkalosis is replaced by respiratory acidosis. An abnormal Arterial Blood Gas may

indicate an underlying pathology. Because blood pH homeostasis is maintained by kidney, lung, and other cellular systems that entail protons being transported across membranes, this could be an early indicator of multi-organ involvement [15]. A respiratory acid–base imbalance occurs when alveolar ventilation is increased or decreased in relation to CO_2 generation. Respiratory alkalosis is possibly the most common acid–base condition. In the current study, however, the majority of the patients (21.88 percent) exhibited metabolic alkalosis. In a study conducted by Jacques, et al. the unusual presence of metabolic alkalosis on admission in a significant number of patients admitted with COVID-19 [16].

When the ABG abnormality pattern was compared between survivors and non-survivors, one patient (3.13 percent) had respiratory alkalosis with metabolic acidosis, while two patients (6.25 percent) had respiratory acidosis with metabolic alkalosis. Non-survivors showed a similar ABG pattern, with respiratory acidosis evident in four patients (66.6%) and metabolic acidosis seen in 33.33 percent. Respiratory acidosis was the most prevalent ABG pattern in non-survivors while metabolic alkalosis was the most common ABG pattern in survivors (21.88%), implying that ABG patterns can be used as a predictive signal for the requirement for mechanical ventilation in these individuals.

However, respiratory and metabolic acidosis were found in 6 non-survivors (18.75%), which could be a bad prognostic indicator for the need for mechanical ventilation in these patients. The cause of respiratory acidosis is likely to be decreased alveolar ventilation, which leads to carbon-dioxide retention, whereas metabolic acidosis causes hyperventilation and could be due to sepsis. There were 9 patients with respiratory acidosis with metabolic acidosis pattern in the study by Lakhani JD, et al. on arterial blood gas analysis in patients with sepsis, suggesting that metabolic acidosis could be one of the significant abnormalities in patients with sepsis [10].

Increased minute ventilation, a compensatory ventilatory response to hypoxemia, can result in significant hypocapnia. The disproportional pulmonary exchange of CO_2 and O_2 in these patients is likely due to the fact that carbon dioxide (CO_2) diffuses through tissues 20 times faster than oxygen (O_2) [17]. The majority of the patients in this study were brought to the ICU due to acute hypoxemic respiratory failure that necessitated mechanical ventilation.

The metabolic alkalosis could be caused by excess mineralocorticoid-like effects or hypokalemia, which could be caused by renal or gastrointestinal losses [17]. Hypokalemia was found to be common in COVID-19 patients, according to Chen, et al. [18]. Actions of angiotensin-converting enzyme 2 counteract the effects of the renin-angiotensin system (RAS) .SARS-CoV-2 binds to ACE2 and degrades it, potentially lowering its anti-regulatory effects [19].

Higher RAS activity, in combination with increased angiotensin II and aldosterone effects, may promote salt reabsorption in the distal nephron and increased urine potassium excretion coupled with hypokalemic effects due to use of nebulized or inhaled Beta 2 adreno-receptor agonists [20, 21]. The occurrence of metabolic alkalosis on admission in a large number of COVID-19 patients is an undocumented finding that necessitates a multicenter investigation to uncover the disease's pathogenesis, including the importance of the acid-base imbalances we discovered.

We publish this unexpected discovery in order to get feedback on whether this finding has been replicated in other centers and to learn more about the probable reasons and clinical implications of the significant metabolic alkalosis.

Table - 1: ABG Analysis.

	Minimum	**Maximum**	**Mean ± SD**
PH	6.9	7.6	7.38 ± 0.13
PCO2	8.6	105	41.64 ±16.28
PO2	30.4	226	84.09 ±30.25
HCO3	18	36	25.50 ±4.74

Table - 2: ABG analysis with Acid-Base disorders.

Acid-base disorder	**Patient**	**Percentage**
Metabolic acidosis with compensation	2	6.25%
Metabolic alkalosis	7	21.88%
Metabolic acidosis	4	12.50%
Metabolic acidosis with respiratory alkalosis	1	3.13%
Mixed respiratory acidosis with metabolic alkalosis	2	6.25%
Normal ABG	5	15.63%
Respiratory acidosis	4	12.50%
Respiratory acidosis compensated	1	3.13%
Respiratory acidosis uncompensated	1	3.13%
Respiratory acidosis with metabolic acidosis	1	3.13%
Respiratory alkalosis	3	9.38%
Respiratory alkalosis uncompensated	1	3.13%
Total	32	100.00%

Table - 3: Interpretation.

Interpretation	**Outcome**		**Total**
	Alive	**Dead**	
Metabolic acidosis with compensation	1	1	2 (6.2%)
Metabolic alkalosis	3	0	3 (9.4%)
Metabolic acidosis	2	1	3 (9.4%)
Metabolic acidosis with respiratory alkalosis	1	0	1 (3.1%)
Mixed respiratory acidosis with metabolic alkalosis	2	0	2 (6.2%)
Metabolic acidosis	1	0	1 (3.1%)
Metabolic alkalosis	4	0	4 (12.5%)
Normal ABG	5	0	5 (15.6%)
Respiratory acidosis	2	2	4 (12.5%)
Respiratory acidosis compensated	0	1	1 (3.1%)
Respiratory acidosis uncompensated	0	1	1 (3.1%)
Respiratory acidosis with metabolic acidosis	1	0	1 (3.1%)
Respiratory alkalosis	3	0	3 (9.4%)
Respiratory alkalosis UNCOMPENSATED	1	0	1 (3.1%)
	26 (81.2%)	6 (18.8%)	32
Chi-squared	17.778		
Df	13		
Significance level	P = 0.1661		

Table - 4: ABG analysis and Outcome.

	Alive (n=26)	Dead (n=6)	P value
PH	7.42 ± 0.10	7.23 ±0.17	0.001*
PCO2	42.10 ±17.33	39.66 ±11.63	0.74
PO2	85.48 ±33.34	78.10 ±7.90	0.59
HCO3	25.26 ±4.66	26.56 ±5.37	0.55

Table – 5: Acid base abnormality observed in non – survivors.

Age group (Years)	Non survivor male	Non survivor Female	Acid base disorder
18-30	0	0	
31-40	0	0	
41-50	0	1 (Respiratory acidosis)	Respiratory acidosis
51-60	1 (metabolic acidosis)	1 (Respiratory acidosis)	Respiratory acidosis and metabolic acidosis
61-70	1 (Respiratory acidosis)	1 (Respiratory acidosis)	Respiratory acidosis
71-80	0	1 (Metabolic acidosis)	Metabolic acidosis
Total	2	4	

Limitations

There are certain limitations to our research. To begin with, this was a modest, single-center study with small sample size. Furthermore, the study only looked at the patient's initial ABG and biochemistry findings.

Though P value is not significant, similar trends have been reported in other studies. No other data or urine electrolytes were examined during their ICU stay to track trends. Another drawback in these people is a lack of medication history.

Conclusion

Majority of patients admitted with COVID-19 experienced pH changes with a wide range of acid–base abnormalities, with metabolic alkalosis being the most prevalent. The observed occurrence of metabolic alkalosis on admission in a large number of COVID-19 patients is an undocumented finding that necessitates a multicenter investigation to uncover the disease's pathogenesis, including the importance of other acid-base imbalances that have been discovered in the present study.

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