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Original Article

Community Section

Blood Gas Analysis among COVID-19 Patients: A Single Centre Retrospective Observational Study

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ABSTRACT

Introduction: The dominant respiratory feature of Coronavirus Disease 2019 (COVID-19) is arterial hypoxaemia, greatly exceeding abnormalities in pulmonary mechanics. Arterial Blood Gas (ABG) analysis helps to find out respiratory, metabolic acidosis and alkalosis.

Aim: To evaluate the blood gas levels among critically ill COVID-19 positive patients admitted in Intensive Care Unit (ICU).

Materials and Methods: A retrospective, observational study was conducted in East Midnapore district of West Bengal, India from July 2020 to February 2021. Data of ABG analysis {pH, PaO_2 (partial pressure of oxygen in arterial blood), $PaCO_2$ (partial pressure of carbon dioxide in arterial blood) and bicarbonate (HCO_3)} in 314 adult COVID-19 positive cases, were obtained from ICU records. All critically ill COVID-19 patients those who were admitted in ICU with more than 15 years of age were included in this study. Data were analysed and Pearson correlation test was applied for statistical significance.

Results: Among the study subjects, 234 (74.5%) were males. Most affected age group was 51-60 years among males and above 60 years among females. Most common ABG finding was high pH indicating alkalosis, found among 183 (58.3%) patients. Acidosis was rare and seen in only 19 (6.0%) patients. A total of 174 (55.4%) patients developed respiratory alkalosis with low $PaCO_2$. Hypoxaemia was found in 144 (45.9%) patients. High HCO_3, indicating metabolic alkalosis, was seen in 144 (45.9%) patients. Statistically significant correlation was found between $PaCO_2$ and pH (pearson correlation coefficient (r)=-0.153, p=0.007) and $PaCO_2$ and HCO_3 standard (r=0.185, p=0.001).

Conclusion: ABG should be done in all COVID-19 patients during admission. A regular interval monitoring of ABG can help in early identification of respiratory damage, silent hypoxia and cytokine storm and with early detection many lives can be saved with early initiation of management.

Keywords: Alkalosis, Bicarbonate, Hypoxaemia, Metabolic acidosis

INTRODUCTION

Coronaviruses are a family of viruses that are known to cause both respiratory and intestinal diseases in various animal species and in humans [1]. These viruses tend to target the upper respiratory tract, which in extreme cases can progress to severe pneumonia. While most COVID-19 cases have been identified as mild, extreme diagnoses have led to respiratory failure, septic shock, and/or multiple organ dysfunction [2]. As this infectious disease continues to spread, further clinical and epidemiological characteristics must be elucidated to improve our understanding of the true extent of the virus, in order to improve diagnostic and treatment capabilities and reduce its overall impact on morbidity and mortality.

Arterial hypoxemia is key respiratory feature among COVID-19 patients. Patients' oxygenation is evaluated initially using a pulse oximeter. Pulse oximetry estimates SaO_2 (oxygen saturation as measured by blood analysis) by measuring changes in light absorption by oxyhaemoglobin in arterial blood [3]. Saturation (SpO_2) thus estimated by pulse oximetry can differ from true SaO_2 (measured with a CO-oximeter) by as much as ±4% [4].

Hypocapnic hypoxia, also termed as silent hypoxia, has multi-factorial causation in case of COVID-19. Fever, prominent with COVID-19, causes the oxygen dissociation curve to shift to the right; thus any given PaO_2 will be associated with a lower SaO_2. It is also seen that Angiotensin-Converting Enzyme 2 (ACE 2), the cell receptor of Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), is expressed in the carotid body, the site at which chemoreceptors sense oxygen [5]. Carotid bodies are responsible for respiratory drive, respond only to PaO_2 and not SaO_2. Due to this rightwards shift, substantial desaturation of oxygen occurs without change in carotid body stimulation which is responsible for occurrence of silent hypoxemia [6]. Silent hypoxemia, with increased thrombogenesis leading to the development of thrombi within the pulmonary vasculature, has been noted in patients with COVID-19 [7]. Thrombi within the pulmonary vasculature can cause severe hypoxemia and dyspnoea is related to pulmonary vascular obstruction and its consequences. Dyspnoea can also arise from the release of histamine or stimulation of juxtacapillary receptors within the pulmonary vasculature leading to serious complications [8].

Different pathological mechanism like fever, inflammation involving multiple organs, thrombogenesis, respiratory tract infection (both upper and lower) and carotid body suppression are possible in different stages of COVID-19 disease. Depending on the underlying mechanism, predominant blood acid base balance can shift either towards acidosis or alkalosis. Recently some studies were conducted on acid base balance and ABG of COVID-19 patients in different countries like China, Italy and South Africa [9-12]. These studies concluded that alkalosis is more prevalent among the ICU admitted COVID-19 patients which is unusual as acidosis is more common in patients admitted to ICU (for other diseases). Hence, the present study was conducted among the patients suffering from severe form of COVID-19 disease with the aim of finding out pH, PaO_2, $PaCO_2$ and HCO_3 (bicarbonate) levels as per ABG analysis, which are suggestive of respiratory and metabolic acidosis/alkalosis.

MATERIALS AND METHODS

A retrospective observational was conducted at a designated COVID-19 Hospital in East Midnapore district of West Bengal, India.

Data of 314 critically ill COVID-19 patients admitted in ICU from 1st July 2020 to 1st February 2021 were analysed. Data of seven patients were excluded who succumbed before their ABG analysis could be done. Analysis of data was conducted in March 2021. The study was approved by the Institutional Ethics Committee (MC/KOL/IEC/NON-SPON/1051/02/2021 dated 23.02.2021). Permission from the medical superintendent of the institute was also obtained for accessing records.

Inclusion criteria: All patients of 15 years of age and above who were admitted due to severe form of COVID-19 in ICU within the study period were included.

Exclusion criteria: Those patients who succumbed before ABG analysis could be done were excluded.

Sample size was calculated using complete enumeration method. Data of ABG were collected from ICU records register. For each patient, only the first ABG data was collected. As per the protocol, ABG was conducted among all patients immediately after ICU admission. In case of repeat ABG reports the first one collected immediately after ICU admission was considered for analysis. Apart from ABG, SpO_2 was measured using pulse oximeter at the time of ICU admission.

COVID-19 was diagnosed on the basis of clinical features like flu-like symptoms, fever, tachypnoea, hypoxemia and SARS-COV-2 detection through Real-time PCR [12,13]. Patients admitted in ICU and Fraction of inspired Oxygen (FiO_2) atleast 60% or more and/or those who were under mechanical ventilation were considered as critically ill patients [14].

For operational purpose, pH values of 7.35-7.45 was taken as normal. As for PaO_2, normal value was taken as 75-100 mmHg, for $PaCO_2$-35-45 mmHg and for standard bicarbonate value (after adjusting actual bicarbonate value automatically in ABG) 22-26 mmol/L was taken as normal [15].

STATISTICAL ANALYSIS

Collected data were compiled in MS excel and analysed using Statistical Package for Social Sciences (SPSS) version 20. Frequency of different variables was calculated and presented as percentage. Variables like pH, $PaCO_2$, PaO_2, standard HCO_3 was recoded as low, normal and high. Pearson correlation was applied for statistical significance and $p<0.05$ was considered as significant.

RESULTS

Data of total 314 critically ill COVID-19 patients admitted in ICU were analysed. There were 234 (74.5%) males. Most affected age group was 51-60 years in male followed by 41-50 years. Among females most affected age group was above 60 years, followed by 51-60 years [Table/Fig-1].

Age (years)#	Males (%)	Females (%)
21-30	6 (1.9)	2 (0.6)
31-40	14 (4.4)	12 (3.8)
41-50	74 (23.6)	18 (5.7)
51-60	84 (26.7)	22 (7)
>60	56 (17.8)	26 (8.3)
Total	234 (74.5)	80 (25.5)

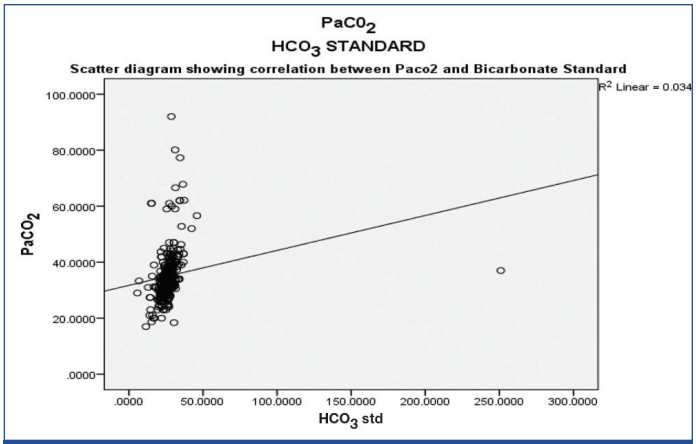
[Table/Fig-1]: Distribution of study subjects according to age and sex (n=314).
#No study subjects were found between 15-20 years age.

High pH (alkalosis) was found in 183 (58.3%) patients. Only 19 (6.1%) patients' pH was <7.35, indicating that acidosis was rare. Total 174 (55.4%) patients developed respiratory alkalosis (low $PaCO_2$) in ABG. Low PaO_2 (hypoxaemia) was found in 144 (45.9%) patients. As per pulse oximeter, 146 (46%) patients had hypoxaemia as indicated by SpO_2 less than 95 percent. Surprisingly, 103 (32.8%) patients had high PaO_2. High HCO_3 was seen in 144 (45.9%) patients [Table/Fig-2].

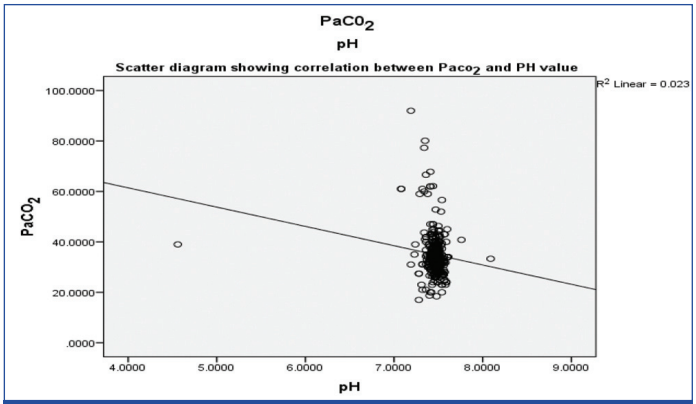
Parameters	Frequency	Percentage
pH		
Acidosis (<7.35)	19	6.0
Normal (7.35-7.45)	112	35.7
Alkalosis (>7.45)	183	58.3
$PaCO_2$ (mmHg)		
Acidosis (>45)	21	6.7
Normal (35-45)	119	37.9
Alkalosis(<35)	174	55.4
PaO_2 (mmHg)		
Low (<75)	144	45.9
Normal (75-100)	67	21.3
High (>100)	103	32.8
HCO_3 (standard) (mmol/L)		
Low (<22)	50	15.9
Normal (22-26)	120	38.2
High (>26)	144	45.9

[Table/Fig-2]: ABG parameters of study subjects (n=314).

Pearson correlation test was done and statistically significant correlation was found with $PaCO_2$ and pH (pearson correlation coefficient (r)=-0.153, p=0.007) and $PaCO_2$ and HCO_3 standard (r=0.185, p=0.001) [Table/Fig-3,4]. A positive correlation was found between PaO_2 and $PaCO_2$ indicating coexistence of hypocapnia and hypoxia (r=0.008, p>0.05).



[Table/Fig-3]: Correlation between $PaCO_2$ and Bicarbonate Standard (n=314).



[Table/Fig-4]: Correlation between $PaCO_2$ and pH.

DISCUSSION

The study was aimed at finding the blood picture, suggestive of respiratory and/or metabolic acidosis or alkalosis, among severely ill ICU admitted COVID-19 patients. A clear and significant pattern, helps in understanding the underlying pathophysiology

in the study population. Results indicate alkalosis in about 58% of the subjects. Low $PaCO_2$ among 56% study subjects indicated that mostly respiratory alkalosis occurs in severe COVID-19. Pearson correlation between pH and $PaCO_2$ showed negative correlation which is expected in case of respiratory alkalosis. Many hypotheses were postulated for possible reasons of respiratory alkalosis in COVID-19 patients instead of acidosis. One hypothesis says that by suppressing response of carotid body towards lack of oxygen COVID-19 prevents hyperventilation and subsequently CO_2 accumulation in blood. ACE2 receptors present in carotid body are probably involved in this process, as the COVID-19 causing virus has shown affinity towards ACE2 receptors [6].

It is found that the air sacs in the lungs of COVID-19 patients are not filled with fluid or pus but instead here virus causes the water sacs to collapse, thereby causing hypoxia in the patients. On the other hand the normal lungs' ability to expel carbon dioxide is not hampered in this process. As there is no accumulation of CO_2, patients do not feel Shortness of Breath (SOB) [16].

Respiratory alkalosis with hypoxaemia was most common finding in this study which was similar to the findings of a study conducted in Italy [17]. A positive correlation between PaO_2 and $PaCO_2$ suggests presence of hypocapnic hypoxia which is responsible for the so called 'silent' or 'happy' hypoxia. Hypocapnic hypoxia is not associated with air hunger; rather, a feeling of calm and well-being may arise which makes the determination of severity of disease difficult resulting in delay in hospitalisation. As per an aviation medicine [18] study, decompression to high altitude causes severe hypoxaemia, which triggers the carotid chemoreceptors and sparks a brisk respiratory response with ensuing hypocapnia. Triggering carotid chemoreceptors may be the reason of hypocapnia in COVID-19 disease also. It is interesting to note that all patients were suffering from severe form of disease and many of them presented with SOB leading to air hunger and hypercapnia. In spite of that, overall weak positive correlation between PaO_2 and $PaCO_2$ suggests that there is possibility of having positive correlation between these two if the ABG is conducted before initiation of SOB.

Though less in number, some COVID-19 patients also presented with respiratory acidosis which is expected in case of air hunger. Another study, conducted in Bolivia, found that respiratory acidosis with hypoxaemia leads to pneumolysis and death [19].

As compensatory mechanism to respiratory alkalosis it is expected that metabolic acidosis would develop. But in this study, metabolic alkalosis was found among 46% patients. Hyperpyrexia due to cytokine storm could be a cause of metabolic alkalosis. Similar findings were also seen among intubated COVID-19 patient with obstructive lung disease and hyperpyrexia [15]. Many COVID-19 patients also presented with vomiting, diarrhoea and dehydration which may lead to metabolic alkalosis due to deficiency of potassium. Operationally, prior use of corticosteroid at home or any other hospital setting can also lead to metabolic alkalosis by triggering mineralocorticoid system. In this study approximately 16% patient developed metabolic acidosis. Multiorgan failure, especially acute kidney injury triggered by cytokine storm and microvascular thrombosis indicated by elevated D-dimer and low platelet count, was the main cause of metabolic acidosis in COVID-19 patient [20]. Though metabolic alkalosis was predominant finding but significant positive correlation (r=0.185) between $PaCO_2$ and standard bicarbonate indicates that patients with hypocapnia are also having low bicarbonate level leading to metabolic acidosis which may be compensatory in nature.

Limitation(s)

The study was conducted among seriously ill ICU admitted COVID-19 patients. It would have been better if ABG analysis of mild and moderately ill patients were also included. The relationship of ABG with outcome of the patients in terms of survival and the change of pattern of ABG report over time with disease progression were not included in the present study which needs further research. One important limitation was the presence of operational causes of respiratory alkalosis found in the study. Though all the ABG reports were taken at the time of admission in the ICU but many of the patients were in home oxygen support before admission or even on BiPAP (Bilevel Positive Airway Pressure) support in some other nursing homes from where they were referred out. These may have caused over correction of natural respiratory acidosis leading to the picture found out in the present study.

CONCLUSION(S)

Acid base disorder is very common in COVID-19 patients. Though respiratory alkalosis was predominant but respiratory acidosis with mixed metabolic acidosis and alkalosis was also seen in the study. A significant correlation between pH and $PaCO_2$; and $PaCO_2$ and HCO_3 were found in the study. A regular interval monitoring of ABG can help in early identification of respiratory damage, silent hypoxia and cytokine storm. With early detection many lives can be saved with early initiation of management.

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