



Arterial Blood Gas Analysis of Critically Ill Corona Virus Disease 2019 Patients

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Authors' contributions

This work was carried out in collaboration among all authors. Authors JL, HP and AM designed the study, wrote the protocol and the first draft of the manuscript. Author SK performed the statistical analysis and managed the analysis. Authors RG and RC managed literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background/Aims: The aim of present study was to find out profile and sequential pattern of Arterial Blood Gas (ABG) in critically ill Corona Virus Disease 2019 (COVID-19) patients.

Study Design: Observational prospective study.

Methodology: A total of 80 Reverse Transcription Polymerase Chain Reaction (RT PCR) positive cases; that needed ICU admission for their life-threatening conditions were included in this study done at teaching hospital of Gujarat, India. Non consenting patients and patients who could not be followed up as per protocol were excluded. Data of Arterial Blood Gas (ABG), performed on admission, day 5 and day 10 were taken for the analysis. Patients were followed up till they remained in ICU.

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Results: Of 80 patients, 3 patients had normal, 24 patients (30%) had primary disorder on ABG while 53 patients (66.25%) had mixed disorders. The most common ABG abnormality observed was respiratory alkalosis with metabolic acidosis in 16 patients (20%) while respiratory alkalosis with metabolic alkalosis in 15 patients (18.75%). There was difference in ABG pattern observed among survivors and non-survivors ($P=.04$); of which conspicuous was presence of “respiratory acidosis with metabolic acidosis” in 5 non-survivors (15.63%), which was not seen in survivors. Of 80 patients admitted in COVID ICU; 2 improved after day 1; 6 after day 5; 40 after day 10, making total of 48 patients surviving COVID critical condition. Of 32 non-survivors, 14 died within twenty-four hours of admission, 14 within first 5 days and 04 after 10 days of ICU stay.

Conclusion: ABG done on admission and serially in severe COVID-19 patients gives useful information on underlying pathophysiology. Mixed ABG pattern was more common than single disorder which can be sign of multi-organ involvement. Respiratory acidosis with metabolic acidosis was observed significantly higher in non-survivors. Respiratory alkalosis as a part of single or mixed pattern on ABG was the most common pattern found in critically ill COVID patients.

Keywords: SARS CoV-2; COVID-19; ABG analysis; mixed acid-base disorder; respiratory alkalosis.

1. INTRODUCTION

Arterial blood gas analysis is an important routine investigation to monitor the acid-base balance of the patients, effectiveness of gas exchange, and the state of their voluntary respiratory control [1]. Disorders of acid base balance can complicate many disease states and occasionally the abnormality may be so severe that it can be life threatening.

In December 2019, a series of acute atypical respiratory disease which originated from Wuhan, China and rapidly spread to other areas. The novel coronavirus that was discovered was named as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCoV) due to its high homology (~80%) to SARS-CoV, which caused acute respiratory distress syndrome (ARDS). 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 [2,3], producing high levels of inflammatory mediators in COVID-19 infected patients, which was associated with severity and death [4-6]. The COVID-19 patients that are critical may share some similar features with sepsis of respiratory origin, such as thick mucus secretions in airways, diffuse alveolar damage, increased pulmonary inflammation, and high levels of systemic proinflammatory cytokines and micro thrombosis [3], probably as consequence of the increase in angiotensin II caused by SARS-CoV-2 and angiotensin-converting enzyme 2 interaction and high levels of interleukin (IL)-6 and other pro-inflammatory

cytokines that were identified in COVID-19 patients, contributing to coagulopathy [7-9].

The major respiratory feature of COVID-19 is arterial hypoxemia causing great abnormalities in pulmonary mechanics (decreased compliance) [10-12]. Hypoxemia with COVID-19 is usually associated with an increased alveolar-to-arterial oxygen gradient, signifying either ventilation-perfusion mismatch or intrapulmonary shunting [13].

There are many diseases that are evaluated using an ABG which include acute respiratory distress syndrome (ARDS), severe sepsis, septic shock, hypovolemic shock, diabetic ketoacidosis, renal tubular acidosis, acute respiratory failure, heart failure, cardiac arrest, asthma and inborn errors of metabolism. Arterial Blood Gas analysis can help in predicting mortality in COVID-19 patients, to manage the ventilatory settings for the better outcome in these patients and can also help to predict underlying co-morbid conditions in COVID patients.

The present study was carried out to assess acid-base patterns in COVID-19 ICU patients and to find their outcomes in COVID-19 patients admitted to ICU.

2. METHODOLOGY

This was an observational, prospective study carried out at Dhiraj General Hospital COVID ICU attached to Smt. Bhikhiben K. Shah Medical Institute & Research Center of Sumandeep Vidyapeeth Deemed University, Piparia after Institutional Ethics Committee approval. 80 adult

(>18 years of age) consecutive patients of COVID-19 admitted in COVID ICU from period of May to December 2020 with following objectives and fulfilling inclusion/exclusion criteria were selected for this study.

2.1 Objectives of the Study

The primary objective of this observational study was to find out ABG profile at the time of admission (Day 1), Day 5 and Day 10 in severe COVID-19 patients. Secondary objective was to correlate any specific pattern of severe COVID-19 infection to prognosis, pathophysiology, laboratory parameters and resultant outcome observed in this study. Laboratory parameters included Complete Blood Picture, Liver and renal function tests, C-Reactive Protein (CRP), Ferritin, Serum Lactate Dehydrogenase (LDH), and D-Dimer levels as they maybe deranged in these critically ill COVID patients.

2.2 Inclusion Criteria

Reverse Transcription Polymerase Chain Reaction (RT PCR) positive cases; who needed ICU admission, for their life-threatening conditions like acute respiratory distress syndrome (ARDS), multiple organ dysfunction syndrome (MODS), hemodynamic failure and others, were included after obtaining informed consent. In case of a clinical situation like unconsciousness, patient on mechanical ventilator and disability resulting into inability of giving informed consent, it was obtained from a legally acceptable representative (LAR).

2.3 Exclusion Criteria

Patient who refused to participate, those who did not give consent and those patients who took discharge against medical advice (DAMA) were excluded from the study. The patients who took DAMA were excluded from the study in the view that those patients follow up could not carried out properly.

All the patients were monitored by all the important clinical and laboratory parameters. On admission, detailed demographic data (such as name, age, residential address, occupation, ethnicity), presenting history (fever, cough, shortness of breath, sore throat, runny nose, vomiting, diarrhoea, abdominal pain, chest pain, malaise), comorbidity status (Hypertension, Diabetes mellitus, Cerebrovascular accident, Ischemic Heart Disease, Acute Kidney

Injury/Chronic kidney Disease), contact history (whether patient had any contact history with a laboratory confirmed or suspected COVID-19 positive patient) and relevant examination findings (temperature, pulse, blood pressure, respiratory rate, oxygen saturation, use of accessory muscles for respiration) were noted from the patient's record. All the patients were subjected to investigations like Complete Blood Count, Renal and Liver function tests, C-Reactive Protein, Ferritin, Serum Lactate Dehydrogenase enzyme levels, D-dimer levels, X-ray chest and CT Scan, as per the protocol.

Arterial blood gases analysis and serum electrolytes (Sodium, Potassium, Chloride) were done in all patients taken for study before specific management. Arterial blood gas (ABG) sampling was done using a heparinised syringe and processed immediately by GEM Premier 3000 Blood Gas/Electrolyte Analyzer Model 5700 and analysis was done in relation to blood pH, partial pressures of oxygen and carbon-dioxide (pO_2 and pCO_2), Bicarbonate (HCO_3) level, electrolytes, and anion Gap. Arterial Blood Gas was collected in all patients twice in 24 hours, that is, in morning at 6 am and in evening at 6 pm. Second and subsequent ABG analysis was also done as per the need till the patient improved or died. The first analysis criterion which was taken was based on pH. The parameters for oxygen therapy and mechanical ventilation taken into account were respiratory rate, oxygen saturation, use of accessory muscles for respiration on the day of admission and later on, partial pressures of oxygen and carbon-dioxide on ABG along with other clinical parameters were considered.

All patients had ICU admission. All patients' follow-up was possible by clinical assessment and ABG analysis for at least 10 days (in patients who survived for 10 days) or could follow them up to death if occurred before 10 days.

The data collected was entered in Microsoft Excel program and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS, IBM version 20.0). The level of significance was fixed at 5% and P value of less than 0.05 was considered statistically significant.

The definitions considered in the study are:

- Multi-organ failure: Development of potentially irreversible physiologic derangement involving two or more organ systems.

- Severity of ARDS on basis of PaO₂/FiO₂ ratio was classified as follows according to the Berlin Definition [14]:
- Mild ARDS: 200 millimetres of mercury (mm Hg) less than PaO₂/FiO₂ ratio ≤ 300 mm Hg with PEEP or CPAP ≥ 5 cmH₂O
 - Moderate ARDS: 100 mm Hg less than PaO₂/FiO₂ ratio ≤ 200 mm Hg with PEEP ≥ 5 cmH₂O
 - Severe ARDS: PaO₂/FiO₂ ratio ≤ 100 mm Hg with PEEP ≥ 5 cmH₂O

3. RESULTS

Out of total 80 patients, 55 were male (M) and 25 were female (F). The most common age group to be affected with COVID-19 was 51-60 years (33.75% patients) followed by age group of 61-70 years (26.25%). The mean age between male and female patients was found to be 56.14±12.2 years. Out of 80 patients, there were 48 (60%) survivors and 32 (40%) were non-survivors. After day 1, from 80 patients only 2 patients improved and shifted to ward, while the rest 14 patients died. After Day 5, 6 patients showed an improvement and shifted to the ward or discharged while 14 patients died. After Day 10, there were 40 patients with an improvement while 4 patients died (Table 2). Average length of ICU stay was 9.7±5.7 days.

Out of 48 survivors, the most common co-morbidity found was type 2 diabetes mellitus/hypertension/ thyroid disorders in 24 patients (50%), whereas there was no sepsis or multi-organ failure in survivors. In non-survivors, type 2 diabetes mellitus/hypertension/thyroid disorder was found in 12 patients (37.5%). Multi-organ dysfunction syndrome (MODS) was present in 5 and sepsis in 4 of the non-survivors of COVID-19 infected patients (Table 3). A statistical significance was found in co-morbidities associated between survivors and non-survivors of COVID-19 (*P* value=.001).

3.1 Day Wise Evaluation of Various Arterial Blood Gas Parameters (Table 4)

For pH values, on day of admission (day 1), out of 80 patients, acidemia was present in 13 patients (16.25%), alkalemia in 23 patients (28.75%), whereas 44 patients (55%) had normal pH. On day 5, ABG were repeated in 64 patients, of whom 12 (18.75%) patients had acidemia, 22 (34.37%) patients had alkalemia and 30 (46.88%) patients had normal pH. On day 10, out of 44 patients, only 2 (4.54%) of the patients had acidemia, 15 (34.1%) of the patients had alkalemia and 27 (61.36%) of the patients had normal pH.

Table 1. Demographic data of Corona Virus Disease 2019 patients

1) Age	Frequency (N=80)	Percentage (%)
<30	1	1.25
31-40	8	10
41-50	15	18.75
51-60	27	33.75
61-70	21	26.25
>70	8	10
TOTAL	80	100
2) Sex		
Male	55	68.75
Female	25	31.25
Total	80	100

Table 2. Day wise outcome (Death/Discharge/Shift to ward) of Corona Virus Disease 2019 patients

Parameters	Frequency		
	After Day 1 (out of 80)	After Day 5 (out of 64)	After Day 10 (out of 44)
Shifted to ward/discharge	2	6	40
Death	14	14	4

Table 3. Co-morbidities associated between survivors and non-survivors of Corona Virus Disease 2019

Co-morbidity	Survivors (N=48)	Percentage	Non-survivors (N=32)	Percentage
Chronic Kidney Disease/AKI	1	2	5	15.63
Congestive Cardiac Failure	0	0	0	0
Liver Failure	0	0	0	0
DM-II/HTN/hypothyroidism	24	50	12	37.5
Diabetic Ketoacidosis	1	2	1	3.13
MODS	0	0	5	15.63
Sepsis	0	0	4	12.5
None	22	46	5	15.63
Total	48	100	32	100
Chi square		DF		p-value
24.136		7		0.001

Abbreviation: AKI: Acute Kidney Injury; DM-II: Type 2 Diabetes Mellitus; HTN: Hypertension; MODS: Multi-organ Dysfunction Syndrome

We found that on first day of admission, 42 out of 80 patients had PaCO₂ in the range of <20-35 mm Hg, while subsequently on day 5 and day 10, 28 and 17 patients had low (<20-35 mm Hg) PaCO₂ levels, respectively. Bicarbonate levels were found in the normal range in 34, 27 and 25 of the patients on day 1, day 5 and day 10, respectively. Statistical significance was not found in pH, PaCO₂ and bicarbonate groups. Hyponatremia (sodium level <135 mmol/L) was

found in 21 patients on first day of admission, whereas hypernatremia (sodium level >145 mmol/L) was found in 2 patients. Hypokalaemia (potassium level <3.5 mmol/L) was found in 12 patients on first day of admission while 6 patients had hyperkalaemia (potassium level >5 mmol/L). A statistical significance was found in sodium and potassium levels on day 1, day 5 and day 10 (*P* value=0.03) and (*P* value=0.002), respectively.

Table 4. Day wise evaluation of pH, Partial pressure of Carbon Dioxide (PaCO₂), Bicarbonate, Sodium and Potassium levels in Corona Virus Disease 2019 patients

Parameters	Frequency			p value
1) pH	Day 1 n (%)	Day 5 n (%)	Day 10 n (%)	
<7.2 to 7.35	13 (16.25%)	12 (18.75%)	2 (4.54%)	0.23
7.35 to 7.45	44 (55%)	30 (46.88%)	27 (61.36%)	
7.45 to ≥7.55	23 (28.75%)	22 (34.37%)	15 (34.1%)	
2) PaCO ₂				0.08
<20-35 mm Hg	42 (52.5%)	28 (43.75%)	17 (38.64%)	
35-45 mm Hg	33 (41.25%)	21 (32.81%)	24 (54.55%)	
45 to >55 mm Hg	5 (6.25%)	15 (23.44%)	3 (6.81%)	
Bicarbonate (HCO ₃ ⁻)				0.218
< 22 mmol/L	28 (35%)	22 (34.4%)	7 (16%)	
22-26 mmol/L	34 (42.5%)	27 (42.2%)	25 (56.7%)	
>26 mmol/L	18 (22.5%)	15 (23.4%)	12 (27.3%)	
4) Sodium				0.03
<135 mmol/L	21 (26.25%)	9 (14.06%)	3 (6.82%)	
135-145 mmol/L	57 (71.25%)	52 (81.25%)	41 (93.18%)	
>145 mmol/L	2 (2.5%)	3 (4.69%)	0 (0)	
5) Potassium				0.002
<3.5 mmol/L	12 (15%)	7 (10.94%)	0 (0)	
3.5-5 mmol/L	62 (77.5%)	57 (89.06%)	44 (100%)	
>5 mmol/L	6 (7.5%)	0 (0)	0 (0)	

3.2 Type of Arterial Blood Gas Disorder Observed in Corona Virus Disease 2019 Patients (Tables 5 to 7)

In Table 5, normal ABG pattern was observed in 3 (3.75%) patients on day 1, in 1 (1.56%) patient on day 5 and in 3 (6.82%) patients on day 10. Single disorder in ABG was found in 20 (30%) patients on day 1, whereas mixed ABG pattern was found in 53 (66.25%) patients. On day 1 of admission, the most common ABG pattern observed was primary respiratory alkalosis with secondary metabolic acidosis in 16 patients (20%) followed by primary respiratory alkalosis with secondary metabolic alkalosis in 15 patients (18.75%). The most common ABG pattern observed in survivors was respiratory alkalosis with metabolic acidosis in 12 patients (25%) followed by respiratory alkalosis with metabolic alkalosis in 11 patients (23%). The similar ABG pattern was observed in non-survivors too, in which, respiratory alkalosis with metabolic alkalosis and respiratory alkalosis with metabolic acidosis were recorded higher frequency percent (18.75% for both) compared to other ABG pattern (Table 7). Also, statistical significance was found in ABG pattern between survivors and non-survivors on day 1 of admission (P value=0.04). It was observed that the most common co-morbidity found was diabetes mellitus type 2 or hypertension which was associated with primary respiratory alkalosis with secondary metabolic acidosis. Anion gap was

less than 8 in 9 patients, 32 patients had anion gap between 8-12 and 40 patients had anion gap more than 12. Out of 4 patients of sepsis, 1 patient had anion gap of 11, 2 patients had anion gap of 12 while 1 patient had anion gap of 22.

3.3 Severity of Acute Respiratory Distress Syndrome in Corona Virus Disease 2019 Patients

On day 1 of admission, 13 patients had mild ARDS, 39 patients had moderate ARDS and 11 patients had severe ARDS. On day 5, 18 patients had mild ARDS, 30 patients had moderate ARDS and 11 patients had severe ARDS. On day 10, 14 patients had mild ARDS, 15 patients had moderate ARDS and 7 patients had severe ARDS (Fig. 1).

It was observed that out of 48 survivors, 22 (45.8%) patients had moderate ARDS, while in non survivors 17 (53.1%) patients had moderate ARDS. Severe ARDS was present in 4 (8.33%) of the survivors and in 7 (21.9%) of the non-survivors (Table 8). Also, we found that all the survivors (100%) were on non-invasive ventilation while within non-survivors group, 19 (59.38%) patients were on non-invasive ventilation whereas 13 (40.625%) patients were on invasive ventilation (Table 9). Statistical differences for non-invasive and invasive ventilation between survivors and non-survivors groups were significant (P value<.000).

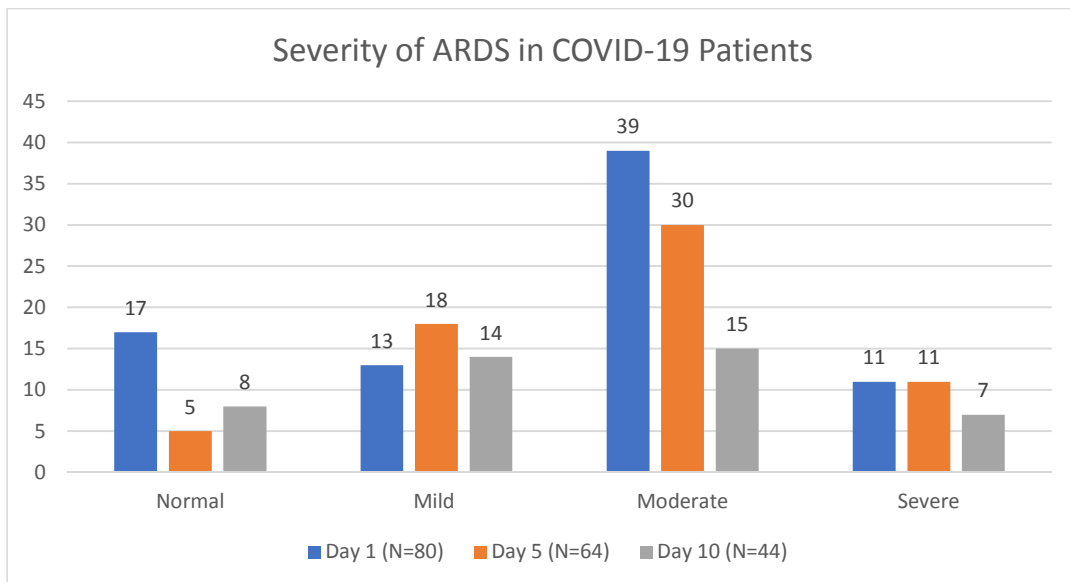


Fig. 1. Day wise evaluation of severity of ARDS in Corona Virus Disease 2019 Patients

Table 5. Normal, Single, Double and Triple disorders in Corona Virus Disease 2019 Patients

Parameter	Frequency		
	Day 1 N (%)	Day 5 N (%)	Day 10 N (%)
Normal ABG	3 (3.75%)	1 (1.56%)	3 (6.82%)
Single Disorder	24 (30%)	20 (31.25%)	13 (29.54%)
Mixed ABG disorder	53 (66.25%)	43 (67.19%)	28 (63.64%)
Total	80	64	44

Table 6. Type of Arterial Blood Gas disorders in Corona Virus Disease 2019 Patients

Type of ABG Disorders	Frequency		
	Day 1 N (%)	Day 5 N (%)	Day 10 N (%)
Normal ABG	3 (3.75%)	1 (1.56%)	3 (6.82%)
Metabolic acidosis	6 (7.5%)	6 (9.38%)	3 (6.82%)
Metabolic alkalosis	7 (8.75%)	5 (7.81%)	4 (9.1%)
Respiratory acidosis	2 (2.5%)	2 (3.12%)	0 (0)
Respiratory alkalosis	9 (11.25%)	7 (10.94%)	6 (13.64%)
Primary respiratory alkalosis with secondary metabolic alkalosis	15 (18.75%)	16 (25%)	11 (25%)
Primary respiratory acidosis with secondary metabolic acidosis	4 (5%)	4 (6.25%)	1 (2.3%)
Primary respiratory acidosis with secondary metabolic alkalosis	1 (1.25%)	3 (4.69%)	2 (4.55%)
Primary respiratory alkalosis with secondary metabolic acidosis	16 (20%)	5 (7.81%)	7 (16%)
Primary metabolic acidosis with secondary respiratory alkalosis	2 (2.50%)	3 (4.69%)	2 (4.55%)
Primary metabolic alkalosis with secondary respiratory acidosis	1 (1.25%)	3 (4.69%)	3 (6.82%)
Primary metabolic alkalosis with secondary respiratory alkalosis	2 (2.50%)	0 (0)	1 (2.3%)
Primary metabolic acidosis with secondary respiratory acidosis	1 (1.25%)	1 (1.56%)	0 (0)
Respiratory Alkalosis + secondary metabolic acidosis + metabolic alkalosis	6 (7.50%)	5 (7.81%)	0 (0)
Respiratory acidosis + secondary metabolic acidosis + metabolic alkalosis	5 (6.25%)	3 (4.69%)	0 (0)
Metabolic acidosis + secondary respiratory alkalosis + Metabolic alkalosis	0 (0)	0 (0)	1 (2.3%)
Total	80	64	44

Table 7. Type of Arterial Blood Gas pattern on day of admission (Day 1) between survivors and non-survivors of Corona Virus Disease 2019 infection

ABG Pattern	Survivors (N=48)	Percentage	Non-survivors (N=32)	Percentage
Normal ABG	2	4.2	1	3.13
Metabolic Acidosis	4	8.3	2	6.25
Metabolic Alkalosis	4	8.3	3	9.38
Respiratory Acidosis	0	0	2	6.25
Respiratory Alkalosis	7	14.6	2	6.25
Respiratory acidosis + Metabolic Acidosis	0	0	5	15.63
Respiratory alkalosis + Metabolic Alkalosis	11	23	6	18.75
Respiratory Acidosis + Metabolic Alkalosis	2	4.2	0	0
Respiratory Alkalosis + Metabolic Acidosis	12	25	6	18.75
Respiratory Alkalosis + secondary metabolic acidosis + metabolic alkalosis	5	10.4	1	3.13
Respiratory acidosis + secondary metabolic acidosis + metabolic alkalosis	1	2.1	4	12.5
Total	48	100	32	100
Chi square	DF		p-value	
18.39	10		0.04	

Table 8. Severity of Acute Respiratory Distress Syndrome on day of admission (Day 1) between survivors and non-survivors

Severity of ARDS	Survivors (N= 48) n (%)	Non-survivors (N=32) n (%)
Normal	14 (29.17%)	3 (9.37%)
Mild	8 (16.67%)	5 (15.63%)
Moderate	22 (45.83%)	17 (53.13%)
Severe	4 (8.33%)	7 (21.87%)
Chi square	DF	p-value
6.322	3	0.09

Table 9. Corelation of Oxygen therapy/Mechanical Ventilation between survivors and non-survivors

Mode of therapy	Survivors (N=48)	Non-survivors (N=32)	p-value
On NRBM/ NIV (bipap/cpap)	48 (100%)	19 (59.38%)	0.000014
On Invasive Ventilation	0	13 (40.62%)	

Abbreviation: NRBM: Non-Rebreather Mask; NIV: Non-Invasive Ventilation

4. DISCUSSION

Corona virus disease 2019 (COVID-19) is caused by SARS-CoV-2. Severe acute respiratory syndrome corona virus 2(SARS-CoV-2) infection is characterised by an initial cytokine storm that can result in ARDS and macrophage activation syndrome. This initial phase is then followed by a period of immune dysregulation, which is the major cause of sepsis-related fatalities [15]. During outbreak of COVID-19, many studies have investigated the role of laboratory biomarkers in management and prognostication of COVID-19 patients, however to the best of our knowledge, there are very few studies are done regarding ABG, acid-base patterns and its association with the outcomes in COVID-19 patients admitted to ICUs. Arterial blood gas (ABG) analysis is an essential part of diagnosing and managing a patient's oxygenation status and acid–base balance.

In this study of critically ill COVID-19 patients admitted to ICU, with laboratory confirmed COVID-19 from May to December 2020, the majority were male patients. The most common age group to be affected was 51-60 years (33.75% patients) followed by 21 patients (26.25%) in age group of 61-70 years with mean age of 56.14±12.2 years. The overall mortality rate of COVID-19 is much lower than for severe acute respiratory syndrome (9.6%) and Middle East respiratory syndrome (34.4%) [16]. Here we report a high mortality of up to 40%.

In accordance with the recent reports on characteristics of patients with COVID-19 who

needed management in intensive care units, advanced age (>60), male sex, and co-morbidities (particularly hypertension) are believed to be risk factors for severe disease and death from SARS-Cov-2 infection [6,17,18]. In our study, there were 24 survivors (50%) and 12 non-survivors (37.5%) who had co-morbidities like hypertension and diabetes mellitus. In non-survivors, there were 5 patients (15.63%) who had MODS while 4 patients (12.5%) had sepsis. Also, a significant correlation (p value=0.001) was found in co-morbidities associated with COVID-19 infection between survivors and non-survivors.

Majority of patients in this study had ABG abnormality which suggests that the homeostasis of various organs which maintains acid base balance was affected. On day 1 of ICU admission, out of 80 patients, acidemia was present in 13 patients (16.25%) and alkalemia in 23 patients (28.75%). Normal pH does not mean normal ABG, as it may happen in mixed ABG disorder which was reported in 8 out 36 patients of sepsis reported by Lakhani JD et al in their study on ABG in sepsis patients [19]. In the study by Lakhani JD et al, out of 36 patients, acidemia was present in 19 (52.77%), alkalemia in 9 (25%) and normal pH in 8 (22.22%) patients [19]. In the present study, out of 80 patients, 44 patients (55%) had normal pH of which only 3 had normal ABG while two third had mixed disorders. Again, mixed ABG disorders were more common than single disorder on first day of admission and also on sequential days; on fifth and tenth day. This may be due to multi-organ involvement, sepsis or due to associated co-morbidities present. Sepsis can be one of the important causes of multi-

organ dysfunction [20,21]. Critical outcomes have been described in the previous literature to be secondary to a rapid decline in renal function with development of severe metabolic acidosis due to cytokine storm associated with COVID-19 [22].

Double and triple disorders on ABG can be marker of multi organ dysfunction. Traditional way of detecting multi-organ dysfunction by scores like MODS or Sequential Organ Failure Assessment (SOFA); may detect lesser number of patients than presumption by ABG abnormality; where mixed pattern can be early indicator of simultaneous involvement of more than one organ [19,23]. In COVID, multi-organ involvement is common which may indicate unfavourable outcome. Assessment of organ dysfunction by different criteria is done in COVID patients by different prognostic scores [24]. Most scoring system uses oxygen saturation (SpO₂), PaO₂/ FiO₂ ratio as one of criterion in prognostic scores of ICUs [24,25]. In COVID-SARS patients, it may reflect lung involvement and hypoxemia, however ABG picture can give overall scenario of haemostasis of the body which will reflect not only lungs but kidney, liver, endocrine and overall metabolic milieu of a critically ill patient.

In addition to hypoxemia, ABG often initially show a respiratory alkalosis which was very commonly observed in the current study. Respiratory alkalosis can be due to hyperventilation syndrome which can lead to hypocapnia as breathing is in excess of metabolic requirements [26]. Anxiety, panic attitude towards COVID apart from ARDS occurring in the context with or without sepsis, pulmonary embolism, mechanical ventilator rate and complex interplay of all these factors can be responsible for respiratory alkalosis present in such patients [26]. Additionally, metabolic acidosis with or without respiratory compensation may be present. As the condition progresses and the work of breathing increases, the PCO₂ begins to rise and respiratory alkalosis gives way to respiratory acidosis. Arterial Blood Gas abnormality may point to an underlying pathology. This may be early indicator of multi organ involvement as blood pH homeostasis is maintained by kidney, lung and various other cellular mechanisms which involve membrane transport of protons [27]. When alveolar ventilation is increased or decreased out of proportion to CO₂ production, a respiratory acid-base disorder exists. Respiratory alkalosis may be the most frequently encountered acid-base

disorder. It may occur in a number of pathologic conditions, including salicylate intoxication, early sepsis, hepatic failure and hypoxic respiratory disorders. The most common mixed ABG abnormality detected in present study was primary respiratory alkalosis with secondary metabolic acidosis in 20% patients on day 1 of ICU admission, while on day 5 and day 10, primary respiratory alkalosis with secondary metabolic alkalosis was present in 25% patients.

In early COVID-19 studies, some evidence has been provided that electrolyte disorders may also be present upon patients' presentation, including sodium, potassium, chloride and calcium abnormalities [6,28]. Others have postulated that patients with more severe COVID-19 tend to display a higher proportion of hypokalaemia at baseline compared with those with less severe forms of disease [29]. Hypokalaemia is known to exacerbate acute respiratory distress syndrome (ARDS) and acute cardiac injury, which are common complications in COVID-19, especially in patients with underlying lung or heart disease [29]. In this study, 21 patients had hyponatremia while hypernatremia was found in 2 patients on day 1 whereas, hypokalaemia was present in 12 patients and hyperkalaemia was found in 6 patients.

When ABG abnormality pattern was compared between survivors and in non-survivors, respiratory alkalosis + metabolic acidosis was observed in 12 patients (25%) followed by respiratory alkalosis with metabolic alkalosis in 11 patients (23%) was present in survivors. The similar ABG pattern was observed in non-survivors too, that is, respiratory alkalosis with metabolic alkalosis and respiratory alkalosis with metabolic acidosis. Hence, the most common ABG pattern in non-survivors and survivors were same, inferring that ABG patterns cannot be used as prognostic indicator for need of mechanical ventilation in these patients. However, respiratory acidosis + metabolic acidosis was observed in 5 non-survivors (15.63%) which was not seen in survivors, which can be a bad prognostic indicator for need of mechanical ventilation in these patients and probably the reason for it can be decreased alveolar ventilation leading to carbon-dioxide retention, whereas metabolic acidosis which causes hyperventilation and can be due to sepsis, but in these patients with respiratory acidosis + metabolic acidosis, the ventilation was impaired. In the study by Lakhani JD et al on arterial blood gas analysis in patients of sepsis,

there were 9 patients with respiratory acidosis + metabolic acidosis pattern, which can suggest that metabolic acidosis can be one of the major abnormality in patients with sepsis [19]. Also, Respiratory Alkalosis + secondary metabolic acidosis + metabolic alkalosis was seen in 10.4% of the survivors and 3.13% of the non-survivors. Whereas, Respiratory acidosis + secondary metabolic acidosis + metabolic alkalosis was found in 2.1% of the survivors and 12.5% of the non-survivors. Hypocapnia appears to be a particularly bad prognostic indicator in patients with critical illness [30]. The compensatory ventilatory response to hypoxaemia, increased minute ventilation can lead to extreme hypocapnia. Carbon dioxide (CO₂) diffuses through tissues about 20 times more rapidly than does oxygen (O₂), and these properties are likely to point to the disproportional pulmonary exchange of CO₂ and O₂ in these patients [31].

The majority of the patients in the current study were admitted to the ICU because of acute hypoxemic respiratory failure that required respiratory support. Endotracheal intubation and invasive mechanical ventilation were needed in 40.62% of the non-survivors, whereas 59.38% of non-survivors were on non-invasive ventilation. Acute Respiratory Distress Syndrome causes a marked increase in intrapulmonary shunting which can lead to severe hypoxemia. Although a high FiO₂ is required to maintain adequate tissue oxygenation, additional measures, like lung recruitment with Positive End Expiratory Pressure (PEEP), are often required. Theoretically, high FiO₂ levels may cause diffuse alveolar damage (DAD) via oxygen free radical and related oxidative stresses, collectively called oxygen toxicity. Generally, oxygen concentrations higher than 65% for prolonged periods (days) can result in DAD, hyaline membrane formation, and, eventually, fibrosis. It was observed that out of 48 survivors, 22 patients had moderate ARDS while in non survivors 17 patients had moderate ARDS. Severe ARDS was present in 4 survivors and 7 non-survivors in our study.

Other common laboratory abnormalities in COVID-19 patients included coagulation disorder, impaired liver and kidney functions, elevated inflammatory markers and cytokine storm. In this study, we tried to evaluate the various parameters between survivors and non-survivors, and most of the findings were found similar. In the later stages of the disease, patients who die may develop pulmonary and

extra-pulmonary organ damage, including ARDS, type I respiratory failure, sepsis, acute cardiac injury, heart failure, acute kidney injury, hypoxic encephalopathy, shock, acidosis or alkalosis, disseminated intravascular coagulation, and acute liver injury. Development of respiratory, cardiac, and neurological complications is strongly associated with poor outcome in patients with COVID-19.

5. CONCLUSION

Acid base abnormality is common in COVID patients. Arterial Blood Gas and electrolytes on day of admission and done sequentially may signal the development of metabolic and gas exchange derangement with or without multi-organ involvement. Mixed ABG pattern is commonly found on admission as well as on follow-up which may predict multi organ involvement due to COVID infection, sepsis or because of associated co-morbidities. Respiratory alkalosis as a part of single or mixed pattern was common finding in critically ill COVID patients. Respiratory acidosis with metabolic acidosis was observed significantly higher in non-survivors.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline, participant consent and ethical approval has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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