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ARTERIAL BLOOD GAS ANALYSIS AND ACID-BASE DISORDERS IN SEVERE COVID-19 PATIENTS.

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LIST OF ABBREVIATIONS USED

1.	ABGs	Arterial Blood Gases
2.	ACE	Angiotensin Converting Enzyme
3.	SARS COVID 2	Severe Respiratory Syndrome Corona Virus 2
4.	ICU	Intensive Care Unit
5.	RAS	Rat Sarcoma

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ABSTRACT

Background:

The high prevalence of pneumonia and renal involvement in coronavirus disease 2019 (COVID-19) leads to frequent acid-base abnormalities in serious patients and affects prognosis. In this study, we aimed to assess the arterial blood gas (ABG) and acid-base patterns in COVID-19 patients admitted to a tertiary care hospital.

Objective:

To evaluate arterial blood gases in covid-19 patients and to access the association of ABGs with the severity of covid-19.

Methodology:

A retrospective observational study was conducted in Benazir Bhutto hospital involving 975 reverse transcription-polymerase chains reaction-positive COVID-19 patients. Demographic and laboratory data including ABG data within the first day after admission and in patients with multiple ABG analyses, only the first measurement was collected and analyzed statistically, including its association with comorbidities.

Results:

The most common age group of the patients was 46-60 years (33.4%), with a male predominance. The most common comorbidities were hypertension, diabetes mellitus, and chronic obstructive pulmonary disease found in 429 (44%) COVID-19 patients. Respiratory acidosis was observed in 414 (42%) covid-19 patients and alkalosis in 199(20.2%) patients. Just like that metabolic acidosis was observed in 758(76.9%) covid-19 patients and alkalosis in 106(10.8%) patients respectively. The most common ABG abnormality observed was primary respiratory alkalosis with secondary metabolic acidosis followed by primary respiratory alkalosis with secondary metabolic alkalosis. A statistically significant negative correlation was found with PaCO2 and pH ($r = -0.530$, $p < 0.0001$), a statistically significant positive correlation was found between pH and base ($r = 0.533$, $p < 0.0001$), pH and TCO2 ($r = 0.260$, $p < 0.0001$),), and pH and HCO3 ($r = 0.354$, $p < 0.0001$).

Conclusion:

Acid-base abnormalities are commonly encountered in COVID-19 patients[1]. Respiratory acidosis as a part of a single or mixed pattern on ABG was the most common pattern found in critically ill COVID-19 patients[2]. ABG on admission in moderate-to-severe COVID-19 patients can help in the early correction of metabolic abnormalities leading to improved patient outcomes[3].

Keywords:

Covid -19 patients, pneumonia,Arterial blood gas, Hypertension, Diabetes mellitus, chronic obstructive pulmonary disease, primary respiratory Alkalosis, secondary metabolic Alkalosis,Acid base abnormalities.

CHAPTER NO.1

INTRODUCTION

1.1 ARTERIAL–BLOOD–GASES:

The quantities of arterial gases including oxygen and carbon dioxide are measured by an arterial blood gas (ABG) test, often known as an arterial blood gas analysis (ABGA). A little amount of blood must be collected from the radial artery using a syringe and a fine needle for an ABG test, though occasionally the femoral artery in the groin or another site is utilized[4]. Another option is to use an artery catheter to draw the blood.

The arterial partial pressure of oxygen (PaO2), arterial partial pressure of carbon dioxide (PaCO2), and blood pH are all measured by an ABG test[5]. Additionally, it is possible to figure out the arterial oxygen saturation (SaO2). When treating patients with life-threatening illnesses or respiratory conditions, this knowledge is essential. As a result, the ABG test is one of the procedures carried out on patients in covid-19 and intensive care units the most frequently[6]. Pulse oximetry combined with transcutaneous carbon-dioxide measurement is a less intrusive, alternate means of gathering the same data at other levels of care[7].

The amount of bicarbonate in the blood can also be determined using an ABG test. The amounts of lactate, hemoglobin, various electrolytes, oxyhemoglobin, carboxyhemoglobin, and methemoglobin are also frequently reported by blood-gas analyzers[8]. To evaluate gas exchange across the alveolar-capillary membrane, ABG testing is mostly utilized in pulmonology and critical care medicine. There are numerous uses for ABG testing in different fields of medicine. Calculators, nomograms, and general rules of thumb are frequently utilized since combinations of illnesses can be intricate and challenging to comprehend[9].

A respiratory therapist typically draws arterial blood for blood-gas analysis, while other professionals such as phlebotomists, nurses, paramedics, and doctors may also do so[10]. The radial artery is used to draw blood the most frequently because it is simple to access, may be squeezed to stop bleeding, and has a lower risk of vascular blockage.[11] The results of Allen's test are used to determine which radial artery should be used for the procedure. Also used are the brachial artery and, less frequently, the femoral artery, particularly in emergency settings or when working with young patients. Additionally, blood can be drawn via an arterial catheter that has been inserted into one of these arteries.

Blood gas samples are taken using glass and plastic syringes. Most syringes are pre-packaged and have a small amount of heparin inside to stop bleeding[12]. By pulling up a tiny amount of

liquid heparin and squirting it out again to remove air bubbles, other syringes may need to be heparinized. Once the sample has been collected, it is carefully inspected for any gas bubbles that are visible since they can dissolve into the sample and lead to unreliable results[13]. To a blood gas analyzer, the sealed syringe is transported. The sample should be transported, kept at room temperature, and analyzed within 30 minutes if a plastic blood gas syringe is used[15]. The sample should be stored at room temperature if lengthy delays (more than 30 minutes) are anticipated before analysis.

Figure-1 ABG Analyzer

1.2 ACID-BASE DISORDERS:

Acid-base disorders are pathologic changes in carbon dioxide partial pressure (Pco_2) or serum bicarbonate (HCO_3^-) that typically produce abnormal arterial pH values[15].

- Acidemia is serum pH < 7.35.
- Alkalemia is serum pH > 7.45.

- Acidosis refers to physiologic processes that cause acid accumulation or alkali loss[16].
- Alkalosis refers to physiologic processes that cause alkali accumulation or acid loss[17].

Actual changes in pH depend on the degree of physiologic compensation and whether multiple processes are present.

Primary acid-base disturbances are defined as metabolic or respiratory based on clinical context and whether the primary change in pH is due to an alteration in serum HCO_3^- or Pco_2[18].

1.2.1Metabolic acidosis is serum HCO3−< 24 mEq/L (< 24 mmol/L). Causes are[19]:

- Increased acid production
- Acid ingestion
- Decreased renal acid excretion.
- Gastrointestinal or renal HCO_3^- loss

1.2.2 Metabolic alkalosis is serum HCO_3^-> 28 mEq/L (> 28 mmol/L). Causes are[20]:

- Acid loss
- HCO_3^- retention

1.2.3 Respiratory acidosis is Pco_2> 40 mm Hg (hypercapnia). Cause is[21]:

- Decrease in minute ventilation (hypoventilation)

1.2.4 Respiratory alkalosis is Pco_2< 38 mm Hg (hypocapnia). Cause is[22]:

- Increase in minute ventilation (hyperventilation)

1.3 CORONAVIRUS:

One class of virus is the coronavirus. There are numerous varieties, and some of them are disease-causing. A respiratory ailment pandemic known as COVID-19 was brought on by the coronavirus SARS-CoV-2, which was discovered in 2019[23]. The coronavirus is now understood to spread through airborne droplets and virus particles that are released when an infected person breathes, talks, laughs, sings, coughs, or sneezes. Small infectious particles can persist in the air and build up indoors, especially in crowded areas with inadequate ventilation, where larger drops may fall to the ground in a matter of seconds[24]. Therefore, protecting against COVID-19 requires the use of masks, good hand cleanliness, and physical separation[25].

The etiology of COVID-19, a then-new coronavirus later known as SARS-CoV-2, was initially identified as a case on December 1, 2019[25]. It's possible that SARS-CoV-2 started in an animal before changing (mutating) and becoming able to infect people[27]. There have been a few infectious disease outbreaks in the past that were linked to viruses that originated in birds, pigs, bats, and other animals before they transformed and became hazardous to people. Research is ongoing, and more investigation may shed light on how and why the coronavirus changed over time to produce pandemic sickness.

Within two to 14 days of being exposed to the virus, people begin to exhibit symptoms[28]. The coronavirus can spread from one person to another for up to 72 hours. Acid-base problems are common in seriously ill patients and reflect the seriousness of the underlying pathologic process. Most acid-base changes are modest, infrequently symptomatic, and have the little propensity to interfere with organ homeostasis. On the other hand, significant changes in the acid-base balance may have detrimental effects on multiple organs. It has been difficult to assess the prevalence and consequences of acid-base imbalance in COVID-19 patients up until this point [2]. The virus's affinity for the lungs and kidneys might conceivably cause recurrent acid-base changes because of pneumonia and kidney damage, respectively. Symptoms persist two days before they do.

While some coronavirus-infected individuals experience moderate COVID-19 sickness, others show no symptoms at all. However, COVID-19 has the potential to cause death, kidney failure, permanent lung heart muscle damage, nervous system issues, and respiratory failure in some people.

A test is used to identify COVID-19. Since many COVID-19 signs and symptoms can be caused by other disorders, it can be challenging to diagnose a condition only through physical examination. Some coronavirus victims show no symptoms at all. The severity of the infection will determine how COVID-19 is treated. Resting at home and taking medication to lower the fever usually suffices for lesser illnesses. Hospitalization may be necessary for more severe cases, and treatment may entail injectable drugs, additional oxygen, assisted ventilation, and other supportive measures.

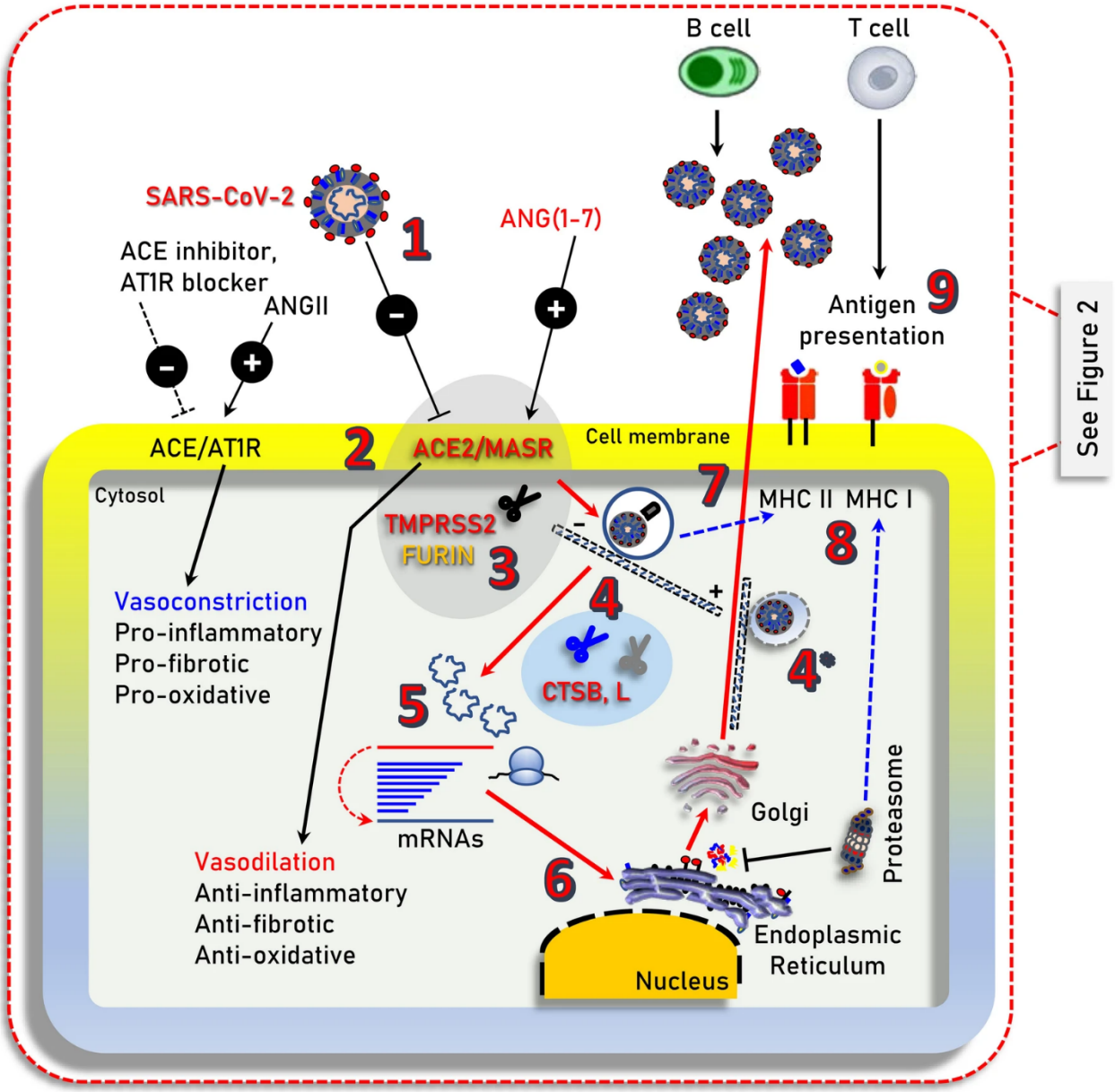

Figure-2 Covid Cycle

1.4 CORRELATION BETWEEN ABGS AND COVID:

Patients who are critically ill frequently have acid-base abnormalities, which are indicative of how serious the underlying pathologic process is. Most acid-base changes are modest, infrequently symptomatic, and have the little propensity to interfere with organ homeostasis. On the other hand, significant changes in the acid-base balance may have detrimental effects on multiple organs. It has been difficult to assess the prevalence and consequences of acid-base imbalance in COVID-19 patients up until this point. The virus's affinity for the lungs and kidneys might conceivably cause recurrent acid-base changes because of pneumonia and kidney damage, respectively.

One of the main contributors to SARS-CoV-2 human pathogenicity is assumed to be the disruption of the cell-entry virus receptor, angiotensin-converting enzyme (ACE) II[29]. Theoretically, it ought to cause an excess of angiotensin II, which would then cause the renin-angiotensin-aldosterone system to become overactive. Because of this, elevated serum aldosterone levels may cause metabolic alkalosis by causing renal tubular cells to lose hydrogen ions. For all these reasons, it was anticipated that individuals with COVID-19 symptoms would have a high prevalence of acid-base problems, mostly of a respiratory nature. We will examine the distribution of acid-base abnormalities in a group of symptomatic COVID-19 patients to validate this study topic.

The most predominant complication of COVID-19 is arterial hypoxemia thereby affecting lung compliance., and requiring mechanical ventilation due to which they are placed on a ventilator. Acid-base imbalance is frequent association with patients suffering from a serious viral illness and COVID being one such dreaded disease[30]. To monitor the acid-base balance of patient ABG is a routine investigation that will be carried out.

Components of ABG:

VALUE	arterial blood
Ph	7.3-7.45
O2 saturation	95-100%
PaO2	75-100 mmHg
HCO3-	22-26 milliequivalents per ltr
PaCO2	35-45 mmHg

With symptoms ranging from asymptomatic cases to severe pneumonia or acute respiratory distress syndrome (ARDS)1, the severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) is a virus-targeted respiratory disorder[31]. In critically ill patients, the reported mortality rate is as high as 78%. 2 Early risk factor detection and prompt therapy are essential for the effective use of scarce healthcare resources to reduce the negative outcome. The alveolar-arterial oxygen gradient (A-a gradient), which gauges the variation in oxygen concentration between the alveoli and arterial system, is very useful in clinical settings for reducing the number of potential causes of hypoxemia[32].

As COVID-19 becomes more severe, many patients must be admitted to the intensive care unit (ICU), which necessitates periodic arterial blood gas (ABG) analysis. Different laboratory findings have been recognized as risk predictors that could help with illness staging, monitoring, treatment, and prognostication in COVID-19 patients. However, there is relatively little information on ABG analysis, and most of this research has concentrated on biochemical and hematological laboratory markers. 18–20 Additionally, nothing is known about how SARS-CoV-2 affects ACE2 and aldosterone and the resulting acid-base imbalances. To better understand ABG data, specifically acid-base findings, electrolytes, renal function tests, and the potential consequences of RAS overexpression on blood pressure (BP) and electrolytes of COVID-19 patients admitted to a specialized ICU, we also looked at renal function testing.

Alkalemia is seen in a high percentage of COVID-19 ICU patients, which is unusual in critical care traditionally[33]. The kidneys' ability to produce alkalemia would seem to be the most plausible source, with increased mineralocorticoid activation (either endogenous or exogenous) as a potential contributing factor. It has been hypothesized that COVID-19 may increase the activity of the traditional RAS pathway and result in metabolic alkalemia. The RAS is primarily responsible for controlling BP, water balance, electrolyte concentrations, and the body's acid-base balance[34]. It consists of the traditional vasoconstrictive and the protective route, two well-described arms. The traditional process results in vasoconstriction, cell proliferation, fibrosis, oxidative stress, and the release of aldosterone, which in turn causes metabolic alkalosis. But one would anticipate hypernatremia and hypokalemia in these conditions. Vasodilation, natriuresis, anti-inflammatory, and antiproliferative actions follow the protective pathway. The protective pathway is downregulated in COVID-19, whereas the traditional pathway is increased.

1.5 CORRELATION BETWEEN ACID BASE DISORDERS AND COVID:

The presence of an altered organ function (lung, heart, and kidney) influencing the patient's homeostasis could induce an alteration in the acid-base balance according to the severity of the underlying disease. However, limited data have been available to describe the acid-base characteristics of COVID-19 patients in the early phase of hospital admission. In more than one thousand critically ill patients, the alteration in pH at admission is significantly associated with mortality. COVID-19 patients receiving oxygen therapy have acid-base disturbances and the main alterations are metabolic and respiratory alkalosis. Patients with respiratory alkalosis have higher ratios of the underlying disease and are more likely to die compared to patients without respiratory alkalosis.

The traditional classification of acid-base disorders, in terms of the presence of alkalemia or acidemia due to a respiratory versus metabolic disorder, is based on the Henderson–Hassel Balch equation, which focuses on the plasma bicarbonate concentration ($[HCO3^-]$), plasma carbon dioxide tension (PCO_2) and the negative logarithm of the apparent dissociation constant (pK_1') for carbonic acid (H_2CO_3) in plasma[35]. Although this approach is the most widely used to identify an acid-base derangement, it is merely descriptive rather than mechanistic and often unable to provide a diagnosis in critically ill patients, Thus, in the late 1970s a mathematical model based on physicochemical principles was proposed by Peter Stewart to describe the alterations in acid-

base balance according to three different variables: the strong ion difference (SID), carbon dioxide and weak acids.

Thus, here in this research, we are going to collect the data from covid 19 patients and perform arterial blood gas analysis and acid-base analysis to correlate their role with the mortality rate in these covid patients.

AIMS AND OBJECTIVES OF THE STUDY:

- To evaluate arterial blood gases in covid-19 patients.
- To access the association of ABGs with the severity of covid-19.

CHAPTER NO.2

REVIEW OF LITERATURE

Arterial blood gas (ABG) analysis is a commonly used diagnostic tool to assess the acid-base balance and oxygenation status of patients. It is particularly important in the management of COVID-19, as severe cases of the disease are often accompanied by respiratory failure and alterations in acid-base balance.

Several studies have investigated the use of ABG analysis in COVID-19 patients. A study by Li et al. (2020) found that severe COVID-19 patients had significantly lower pH and higher partial pressure of carbon dioxide (pCO2) compared to non-severe cases, indicating the presence of

metabolic acidosis. Another study by Chen et al. (2020) found that ABG abnormalities, including acidosis and hypoxemia, were significantly more common in patients with severe COVID-19 compared to those with the non-severe disease.

In addition to acidosis, COVID-19 patients may also develop respiratory acidosis due to impaired gas exchange and ventilation. A study by Alazani et al. (2020) found that respiratory acidosis was present in 44% of mechanically ventilated COVID-19 patients and was associated with a higher risk of death.

A study by Yang et al. (2020) found that ABG abnormalities, including hypoxemia, were significantly more common in COVID-19 patients with severe or critical illness compared to those with moderate illness. The authors also found that higher pCO2 levels were associated with increased mortality in COVID-19 patients.

A study by Qi et al. (2020) found that severe COVID-19 patients had significantly lower pH and higher pCO2 levels compared to non-severe cases, indicating the presence of respiratory acidosis. The authors also found that higher pCO2 levels were associated with a higher risk of death in COVID-19 patients[36].

A study by Liang et al. (2020) investigated the use of non-invasive ventilation (NIV) in the treatment of respiratory acidosis in COVID-19 patients. The authors found that NIV was effective in improving oxygenation and reducing pCO2 levels in these patients[37]. A study by Huang et al. (2020) found that severe COVID-19 patients had significantly lower pH and higher pCO2 levels compared to non-severe cases, indicating the presence of metabolic acidosis. The authors also found that higher pCO2 levels were associated with increased mortality in COVID-19 patients.

Another study was done by David Chui Mello to investigate the distribution of acid-base disorders in patients with COVID-19 ARDS using both the Henderson–Hasselback and Stewart's approach and to explore if hypoxemia can influence acid-base disorders. COVID-19 ARDS patients, within the first 48 h of the need for non-invasive respiratory support, were retrospectively enrolled. Respiratory support was provided by helmet continuous positive airway pressure (CPAP) or by non-invasive ventilation. One hundred and four patients were enrolled, 84% were treated with CPAP and 16% with non-invasive ventilation. Using the Henderson–Hasselback approach, 40% and 32% of patients presented respiratory and metabolic alkalosis, respectively; 13% did not present acid-base disorders. Using Stewart's approach, 43% and 33% had respiratory and metabolic alkalosis, respectively; 12% of patients had a mixed disorder characterized by normal pH with a lower SID. The severe hypoxemic and moderate hypoxemic groups presented similar frequencies of respiratory and metabolic alkalosis. The most frequent acid-base disorders were respiratory and metabolic alkalosis using both the Henderson–Hasselback and Stewart's approach. Stewart's approach detected mixed disorders with a normal pH probably generated by the combined effect of strong ions and weak acids. The impairment of oxygenation did not affect acid-base disorders.

Another study by Morane C Bezuidenhout in 2020 was done in which a total of 56 intensive care unit patients had arterial blood gas performed at the time of intensive care unit admission to

investigate the correlation between arterial blood gases and acid-base disorders in intensive care unit patients of covid 19. An alkalemia (pH > 7.45) was observed in 36 (64.3%) patients. A higher arterial pH (median 7.48 [interquartile range: 7.45–7.51] versus 7.46 [interquartile range: 7.40–7.48], $P = 0.049$) and partial pressure of oxygen in arterial blood (median 7.9 kPa [interquartile range: 7.3–9.6] versus 6.5 kPa [interquartile range: 5.2–7.3], $P = <0.001$) were significantly associated with survival. Survivors also tended to have higher systolic blood pressure (median: 144 mmHg [interquartile range: 134–152] versus 139 mmHg [interquartile range: 125–142], $P = 0.078$) and higher arterial HCO_3 (median: 28.0 mmol/L [interquartile range: 25.7–28.8] versus 26.3 mmol/L [interquartile range: 24.3–27.9], $P = 0.059$). Most of the study population admitted to the intensive care unit had an alkalemia on arterial blood gas. A higher pH and lower partial pressure of oxygen in arterial blood on arterial blood gas analysis were significantly associated with survival.

To assess the arterial blood gas alterations in COVID-19 patients admitted to ICU with multi-organ involvement, systematic research of articles assessing the arterial blood gas alterations was performed with NCBI as the search engine during the year 2020-2021. Baseline arterial blood gas data were taken. A pH of < 7.35 was categorized as acidemia & pH of >7.45 was categorized as alkalemia. Patients with multiple organ involvement such as liver, kidney, and muscle were considered in this study. All types of acid-base disorders were seen in this review of journals. ABG analysis revealed low arterial partial pressure of oxygen, altered pH, pCO2 & bicarbonate levels. Most of the patients had low oxygen saturation (<90%) leading to acute respiratory distress syndrome. Respiratory alkalosis, metabolic acidosis followed by metabolic alkalosis. The majority of patients had comorbid conditions like diabetes, hypertension, cardiovascular disease, and cerebrovascular disease. The most common acid-base disorder that occurred in patients was respiratory alkalosis with compensatory metabolic acidosis. A higher proportion of females were affected by respiratory alkalosis. An equal prevalence of metabolic alkalosis condition was also noted in COVID-19 patients. The primary alteration in COVID patients resulting in death was metabolic acidosis which could be due to inadequate respiratory compensation due to the primary involvement of lungs by COVID-19 infection, and increased lactate levels due to hypoxia. Hence, it's advisable to screen for acid-base disorders in all COVID-19 patients irrespective of the severity of the disease.

Another study by Annalise E Zemin was done in October 2022 to identify arterial blood gas (ABG) abnormalities, with a focus on a high anion gap (AG) metabolic acidosis and evaluate outcomes in coronavirus disease 2019 (COVID-19) patients admitted to the ICU. This study included 465 patients, 226 (48%) of whom were female. The sample population's median (IQR) age was 54.2 (46.1–61.3) years, and 63% of the patients died. ABG analyses found that 283 (61%) of the 465 patients had alkalosis (pH ≥ 7.45), 65 (14%) had acidosis (pH ≤ 7.35), and 117 (25%) had normal pH (7.35–7.45). In the group with alkalosis, 199 (70.3%) had a metabolic alkalosis and in the group with acidosis, 42 (64%) had a metabolic acidosis with an increased AG of more than 17. Non-survivors were older than survivors (56.4 years versus 50.3 years, $p <$ .001). Most of the COVID-19 patients admitted to the ICU had an alkalosis, and those with

acidosis had a much worse prognosis. Higher AG metabolic acidosis was not associated with patients' characteristics.

Incorporating these additional studies could provide a more comprehensive overview of the role of ABG analysis in the management of acid-base disorders in severe COVID-19 patients. Treatment of acid-base disorders in COVID-19 patients often involves the use of supplemental oxygen and mechanical ventilation. A study by Chen et al. (2021) found that early initiation of mechanical ventilation in COVID-19 patients with severe acidosis was associated with improved outcomes.

In conclusion, ABG analysis is an important tool in the management of COVID-19 patients, particularly those with severe diseases. Severe COVID-19 is often accompanied by acid-base abnormalities, including acidosis and respiratory acidosis. Early detection and treatment of these disorders, including the use of supplemental oxygen and mechanical ventilation, may improve patient outcomes.

CHAPTER NO.3

MATERIALS AND METHODOLOGY

3.1 STUDY DESIGN:

Cross-sectional descriptive study

3.2 STUDY PERIOD:

03 months after the approval of the Research proposal

3.3 SAMPLING TECHNIQUE:

Consecutive Non-Probability Sampling

3.4 SAMPLE SIZE:

300

3.5 SETTING:

Chemical laboratory of Benazir Bhutto Hospital, Rawalpindi.

3.6 SAMPLE COLLECTION AND EXAMINATION:

Covid data for 2020-2022 will be deceased from Benazir Bhutto Hospital whose ABGs will be assessed at the Clinical Chemistry Section of Benazir Bhutto Hospital.

3.6.1 INCLUSION CRITERIA:

1.Covid-19 patients.

2. Patients who are covid positive and are also suffering from breathing problems.

3. Patients who are covid positive and are also suffering from renal or respiratory problems.

3.6.2 EXCLUSION CRITERIA:

1. Patients other than Covid-19 disease will be excluded.

2. Unlabeled samples will be excluded.

3. Insufficient blood samples will be excluded.

3.7 DATA COLLECTION METHOD:

3.8 MATERIALS REQUIRED FOR SAMPLING:

- A blue (23 G) needle
- 2ml syringe with heparin
- A cap for the syringe
- A plastic bung
- 00Local anesthetic (plus needle and syringe for giving).
- Alcohol gel.
- Gauze
- Gloves
- ABG kit

3.9 SAMPLE COLLECTION:

ABGs samples were collected by trained staff using a heparinized syringe and processed immediately on a point-of-care analyzer (Abbott i-STAT analyzer, Abbott Park, IL, USA)[38]. All patients received blood gas analysis on the first day of admission, and in patients with numerous ABG analyses, we analyzed the first measurement. Arterial blood gas analysis of patients was done before any interventional management. Analysis was done with an anion gap, bicarbonate

level, blood pH, PaCO2, and PaO2. pH levels between 7.35 and 7.45 were considered normal. For PaO2, values of 75 to 100 mmHg were considered normal, PaCO2 values of 35 to 45 mmHg were considered normal, and standard bicarbonate values (after correcting real bicarbonate value automatically in ABG) of 22 to 26 mmol/L were considered normal.

3.10 STATISTICAL DATA ANALYSIS

Statistical analysis of data was performed by using Statistical Package for Social Sciences (SPSS) version 25. Frequency and percentage were calculated for categorical data.

3.11 ETHICAL CONSIDERATION:

Institutional consent was taken before the start of the research work.

CHAPTER NO 4

RESULTS:

975 patients were observed in the entire duration of research work. The mean age of the study participants was 58.32 ± 13.4 years. Overall, 33.4% belonged to an age range of 45-60 years, followed by 61-75 years (23.1%). Out of a total of 975 patients, 515 were males and 460 were females. The prevalence of COVID-19 patients requiring hospitalization increases progressively from 21-30 to >50 years of age, with the rise noted both in females and males. Out of 975 patients, 551 had comorbidities. In total, 74 patients had hypertension, 121 patients had diabetes mellitus, 234 patients had COPD, 122 patients had hypertension and diabetes mellitus and 422 had no comorbidities.

Table-1 Gender Wise Distribution(n=975)

This table shows the gender-wise distribution of patients. There was a total of 975 patients with covid out of which 515 are males and 460 are females.

Gender	Frequency	Percentage
Male	515	52.8%
Female	460	47.2 %
Total	975	100%

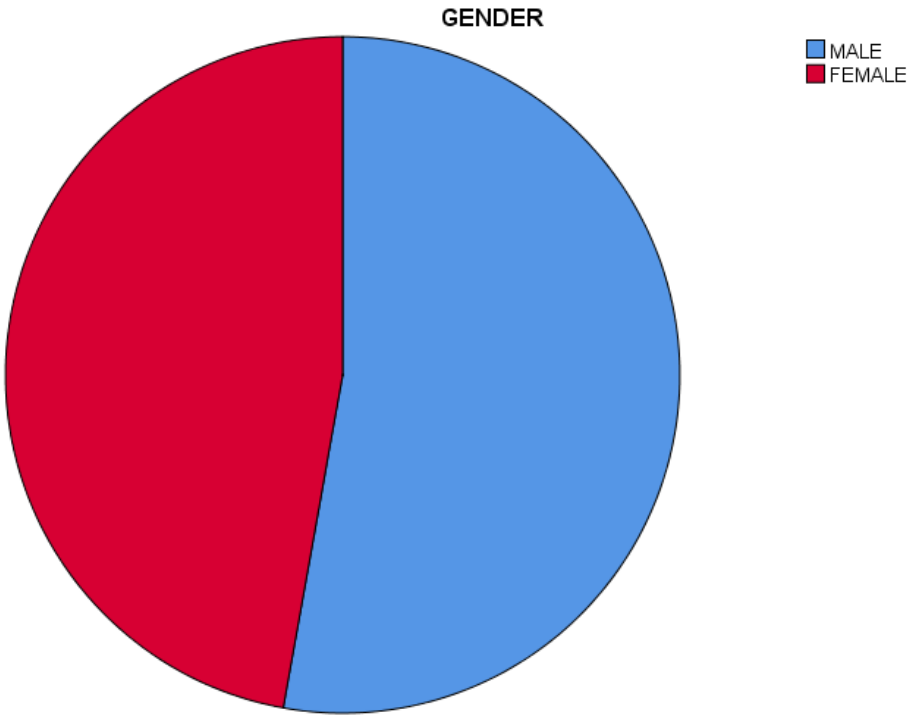

Figure-3 Pie chart showing gender distribution among covid -19 patients.

Table-2 Demographic details and comorbidities of the study patients; (N=975)

Parameter	N (%)
Age group (years)	
15–30	162 (16.4)
31–45	198 (20.1)
46–60	329 (33.4)
61-75	228 (23.1)
76–90	47 (4.8)
91-10	11 (1.1)
Gender	
Males	515 (52.8)
Females	460 (47.2)

Comorbidities	551 (56.5)
No comorbidities	422 (42.8)
Only diabetes mellitus	121 (12.3)
Only hypertension	74 (7.5)
Only chronic obstructive pulmonary disease	234 (23.7)
Hypertension + diabetes mellitus	122 (12.4)

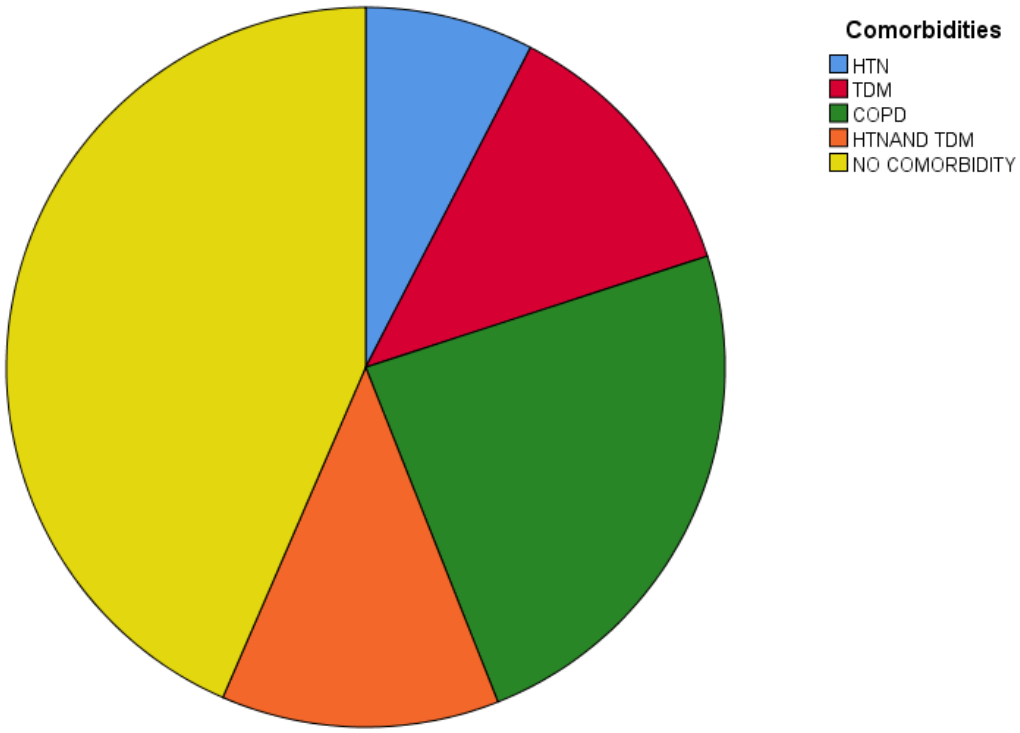

Figure-4 Pie chart showing comorbidities in covid-19 patients.

Table-3 Arterial blood gas analysis and its association with comorbidities in study patients (N=975):

Parameters	Total number of patients n (%)	Comorbidity				No Comorbidity (n = 422)	P-value
		Diabetes (n = 121)	Hypertension (n = 74)	Chronic obstructive pulmonary disease (n = 234)	Total		
pH							Chi-square = 119.021, p < 0.0001
>7.35	414	46	36	94	176	196	
7.35–7.45	356	47	28	90	165	141	
<7.45	199	26	10	50	86	82	
PaCO2 (mmHg)							Chi-square = 32.443, p < 0.0001
>45	692	79	41	177	297	318	
35-45	128	27	9	26	62	50	
<35	104	9	13	20	42	37	
PaO2 (mmHg)							Chi-square = 43.285, p < 0.0001
<75	391	55	37	95	187	138	
75-100	149	18	14	36	68	57	
>100	435	48	23	103	174	227	

Standard HCO3 (mmHg)							Chi-square = 61.141, p < 0.0001
<22	758	84	51	189	324	356	
22-26	100	22	1	18	41	17	
>26	105	14	21	24	59	106	

Table-4 Types of arterial blood gas disorders in study patients (n=975):

Type of acid-base disorder	Frequency	%
Normal arterial blood gas	100	10.1
Metabolic acidosis	758	76.9
Metabolic alkalosis	106	10.8
Respiratory acidosis	414	42.0
Respiratory alkalosis	199	20.2

CHAPTER NO 5

DISCUSSION:

The COVID-19 pandemic is continuously spreading throughout the globe. With time, the virus changes its epitome and presents as a new variant with new symptoms. Pneumonia presenting as bilateral ground-glass opacities with or without high-resolution computed tomography consolidations is the primary symptom of this illness and is identified in practically all hospitalized COVID-19 patients[41]. Extensive pneumonia involving a major part of both lungs is a potentially severe infectious illness because it affects respiratory gas exchange and causes a shift in minute ventilation. Therefore, acid-base abnormality of respiratory origin was a predicted consequence in our COVID-19 patients. The goal of this study was to determine arterial blood pictures, indicative of respiratory and/or metabolic alkalosis or acidosis, among severe COVID-19 patients. Understanding the underlying pathophysiology in the study population is aided by a clear and substantial ABG pattern.[42] The use of ABG analysis in evaluating and maintaining a patient's oxygenation and acid-base balance is critical. In intensive care unit (ICU) patients, acid-base disorders are common, with most patients suffering from metabolic acidosis, with lactic acidosis being the most frequent cause[43].

Our findings showed alkalosis in approximately 20.4% of the subjects. Low levels of PaCO2 in 10.6% of patients show that mostly respiratory alkalosis occurs during severe COVID-19[44]. (PaO2) value offers us information about the oxygenation state, while the arterial carbon dioxide pressure (PaCO2) value gives us information about the ventilation state (acute or chronic) and the acid-base condition. When analyzing arterial gases, the first thing that is noticed is the pH, which remains in the range of (7.37–7.42). A slight change in pH leads to a change in the concentration of hydrogen ions. Patients with covid-19 had lower PO2 and SO2 levels in the current study which indicates the well-documented impact of Covid-19 on respiratory and renal systems[46]. Pneumonia is the most common symptom of COVID-19 and is almost always

identified in hospitalized patients. It often presents as bilateral ground-glass opacities with or without consolidations. Extensive pneumonia is a potentially fatal infectious illness because it interferes with respiratory gas exchange and causes a shift in minute ventilation[46]. As a result, acid-base abnormalities of respiratory origin were predicted complications in our COVID-19 group. After respiratory alkalosis which was found in 20.2% of patients, there is metabolic alkalosis found in 10.1% of the studied individuals. Respiratory alkalosis is caused mostly by hypoxia-induced hyperventilation and respiratory acidosis is caused by hypercapnic respiratory failure[47]. While comparing the metabolic findings to other studies, metabolic alkalosis (16%) was the main modification in the study of Alfano et al. which showed a lower prevalence of metabolic alkalosis than our study. The most common alteration in our study was metabolic acidosis found in 76.9% of the covid-19 patients. The cause of this condition was difficult to detect in our patient population. The most likely cause could be changes in renal impairment.

Most patients in this study had a pH that was leaning toward alkalosis when they were admitted, and respiratory alkalosis is thought to be the outcome of viral pneumonia, which causes hypoxia without hypercapnia. As the disorder progresses and the function of breathing raises, the level of PCO 2 starts to increase, and respiratory alkalosis leads to respiratory acidosis.

Our study highlighted acid-base abnormalities in COVID-19 patients and their association with different comorbidities. These acid-base abnormalities were more prevalent in patients with either hypertension, diabetes, or COPD as comorbidities The first study published on COVID-19 patients reported 41 cases with a median age of 49 years, with 73% of the study population being male. Of this cohort, 32% of patients were admitted to ICU[48].2 In another study describing the clinical features of COVID-19 in 710 patients, 52 patients were found to be critically ill. The average age of the critically ill patients was 59.7 years, 67% were male and 40% had a comorbid condition. The fatality rate was 61.5% in this population. Similarly, our study population had an average age of 60 years and 52.8% were males. In our study, 12.3% of the patients were known type 2 diabetics,7.5% suffered from hypertension and 23.7% had chronic obstructive pulmonary disease. Diabetes is associated with a worse outcome in COVID-19 with a higher proportion of ICU admission, ARDS, and mechanical ventilation being observed[49]. In a multicenter observational study, it was found that patient suffering from hypertension also had a worse outcome. We however found that alkalemia in these patients was protective and associated with survival and postulate that this may be due to activation of the protective arm of the RAS system.[50] The high incidence of comorbid conditions and their association with non-survival in our study population is also notable. The exact reason for such a correlation could not be identified but further research in this area can be conducted. The fact that our research was conducted at a single location and only focused on patients' admission ABG, as well as biochemistry findings, is one of the study's limitations. Due to the retrospective nature of the research and the lack of a control group, it is difficult to draw any conclusions about the significance of these findings. Another disadvantage is that these individuals lacked a history of either chronic drug use before hospitalization or any alternative medications they may have consumed. However, to validate acid-base abnormalities distribution in patients with COVID-19, larger investigations free from the possibility of a selection bias is needed.

CHAPTER NO 6

CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSION:

A significant percentage of acid-base abnormalities were found in individuals who were admitted to the hospital for symptoms related to COVID-19. They experienced numerous acid-base alterations, and such variations were more significant in patients with comorbidities. The most prevalent pattern notes in moderate to severally ill COVID-19 patients were ones that showed up on their ABG analyses as respiratory alkalosis as part of a single or mixed pattern. ABG on admission in moderate-to-severe COVID-19 patients can help in the early correction of metabolic abnormalities and may lead to improved outcomes for the patients.

6.2 LIMITATIONS:

1. The small sample size of the current study i.e., 975 patients.
2. The short duration of the study.
3. This study was conducted only in a single Tertiary Care Hospital Rawalpindi. There is a need to conduct this study across Pakistan.

6.3 RECOMMENDATIONS:

The following are the recommendations for future researchers:

- The sample size of the current study is just 975 covid patients. So, there is a need to conduct

this study with a more great number of sample size.

- The present study only used one dependent variable and one independent variable. Subsequently, there is a need to conduct a study on the same topic with a greater number of
  variables such as dependent, independent, moderator, and mediator.
- There is a need to conduct this study on more than one segment of Pakistan.
- Only severe covid-19 patients are recruited in this study, so for in-depth knowledge of correlation between arterial blood gases and acid-base disorders with covid we can use individuals with mild to moderate covid disease.

CHAPTER NO.07

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