



Vitamin D as A Risk Factor for Bone Fractures In Pediatric Patients

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ABSTRACT

Background

There are few studies on the aetiology and clinical range of COVID-19 in children. Arterial hypoxaemia is the main respiratory complication of COVID-19. Analyses of arterial blood gases (ABGs) aid in the early detection of changes in acid-base balance. Acid-base imbalance in children with COVID-19 has not been well described.

Methods

Between February 1, 2021, and the end of July 2021, 124 kids with positive nasopharyngeal swabs had their ABG status evaluated at the time of admission in a teaching hospital in India.

Results

Only 3.2% of patients had PaO₂ levels above 100, while 90.3% of patients had hypoxemia (P value 0.001). Amounts of acids and bases were measured,

and it was discovered that 16.1% had high HCO₃ and 48.4% had low HCO₃ (P value = 0.007). As a result and according to the computation of base excess and deficit, 22.6% had normal amounts of bases, 24.2% had excess bases, and 53.2% had base deficits (P value = 0.004). On the other hand, only 32.3% of participants had high levels of lactic acid, while 67.7% substantially had normal levels (P value = 0.005).

Conclusion

Since the majority of children in this study presented with diarrheal GIT manifestations, children have more unusual COVID presentations than adults. Children also have a greater ability to withstand variations in oxygen saturation in order to maintain acid-base balance.

Keywords

Acid Base balance, Acidosis, Alkalosis, Children, COVID-19

INTRODUCTION

The World Health Organisation (WHO) classified the Coronavirus Disease of 2019 (COVID-19) as a pandemic on March 20, 2020 (1). To stop the virus from spreading further, a consistent effort around the globe is required. Numerous research has examined laboratory biomarkers used to diagnose and predict the prognosis of COVID-19 patients during the outbreak, but none have examined arterial blood gas and acid-base alterations in infected children. Rarely have studies done this. Numerous individuals need to be admitted to the intensive care unit (ICU) when COVID-19 grows more severe, necessitating periodic arterial blood gas (ABG) analysis. The staging, monitoring, prognosis, and treatment of COVID-19 patients may be aided by a number of test results that have been identified as risk predictors. (2,3)

Children may experience milder symptoms and need hospitalisation less frequently than adults, according to what is currently known. However, the paediatric multisystem inflammatory syndrome (MIS-C) linked to COVID-19 was reported by the US Centres for Disease Control and Prevention (CDC) on May 14, 2020 (4,5). This claim comes from a subset of paediatric patients who presented with severe inflammation and multiple organ failure and were found to be SARS-CoV-2 positive.

One of the most major complications of COVID 19 is the arterial hypoxemia, thus affecting the lung compliance which could require mechanical ventilation (6,7). Acid base imbalance is a frequent association with patients who suffer from serious viral

illnesses including COVID-19(8). Tropism of the virus for kidneys and lungs might hypothetically result in frequent acid–base changes due to kidney injury and pneumonia (9,10). To monitor acid base balance of COVID-19 patients, ABG should be carried out. Most occurrences of acid–base alterations are minor and rarely symptomatic and may have a low likelihood to influence organ homeostasis. Contrariwise, severe changes of acid– base balance can have severe multi-organ significances. The prevalence and impacts of acid–base disorders in COVID-19 patients have been poorly assessed until now (11).

As angiotensin-converting enzyme 2 (ACE2) is the entry pathway for SARS-CoV-2 (12), the renin-angiotensin system (RAS) is affected by COVID-19. When SARSCoV-2 enters cells, it downregulates ACE2, upregulates RAS signaling, and produces angiotensin II and aldosterone. Both angiotensin II and aldosterone affect renal processing of hydrogen (H+) and bicarbonate (HCO₃) and can cause acid-base disorders. (13) . Reports on the clinical picture of COVID-19 in children are missing and the clinical patterns of children with COVID-19 remain uncertain. The aim of this study was to describe the clinical, ABG finding of children with COVID-19 and the link between them.

METHODS

From February to the end of July 2021, a teaching hospital in India hosted the trial for a total of six months. Children who were hospitalised and whose COVID-19 infection had been verified by PCR (polymerase chain reaction) were enrolled.

Children whose COVID-19 positivity had been confirmed and whose guardians or parents had given

their permission to take part in the study were included. Children who had not undergone PCR testing for COVID-19 and whose parents or legal guardians had not given their agreement to participate in the study were excluded. At the time of admission, 124 kids in all were evaluated for ABG estimation. Their romantic behaviour was tracked.

In accordance with the reference ranges of PH for age and sex, acidemia and alkalemia were specified. In order to define acidosis, alkalosis, hypoxemia, and the base excess and deficit, references for PaCO₂, PaO₂, and HCO₃ were also examined (15,16). We only selected the first ABG analysis in kids who had several analyses. All children suspected of having COVID-19 infection had their nasal/oropharyngeal swabs taken in accordance with WHO recommendations. To monitor the respiratory gas exchange and acid-base status, ABG analysis was required.

Nasopharyngeal swabs have been gathered in accordance with the safety precautions and contamination manipulation suggestions and advice. Following the loading of samples into the tubes used for viral delivery, viral RNA was extracted. PCR primers are subsequently mixed with the extracted nucleic acid. Following that, samples from the used biosystems were put into the Rotor gene heat cycler. Preliminary denaturation was carried out after transcription was completed at 55°C for 10 minutes. This was followed by 45 cycles, each of which consisted of a preliminary denaturation step at 95°C for 10 seconds and an annealing and extension step at 60°C for 60 seconds. When a positive SARS-CoV-2 RT-PCR test result was found, children were deemed to have COVID 19 positive infections (17,18).

The protocol of the current study was approved by Institutional Ethical Committee. Informed consent was obtained from each patient's parents or guardians prior to inclusion in the study. No penalties were imposed if parents refused to participate in the study. This study was conducted in accordance with the Declaration of Helsinki, considering the ethical principles of medical research involving humans.

The SPSS (Statistical Package for Social Sciences) version 20 for Windows® (IBM SPSS Inc, Chicago, IL, USA) was used to code, process, and analyse the obtained data. Frequencies and relative percentages were used to depict qualitative data. To determine the difference between two or more groups of qualitative variables, use the chi square test (2) and Fisher's exact test. Standard deviation (SD) and mean were used to express quantitative data. To compare two or more independent groups of quantitative variables, independent samples t-test and ANOVA were utilised. P value less than 0.05 was regarded as significant.

RESULTS

Children who had COVID-19 infection and confirmation and were admitted to a teaching hospital were assessed for their demographic and clinical status during the trial. There were 124 kids enrolled in all. Regarding the demographic criteria, about 51% of the children under the age of two, 24% of the children between the ages of two and six, and 25% of the children between the ages of six and thirteen were included in the study (Figure 1A). 33 patients, or 53% of the study sample, were male. Patients who were female made up 47% (N=29) of the study group. The ratio of men to women was 1.1:1.

In terms of clinical manifestations, 53% were GIT symptoms (fever, nausea, vomiting, and diarrhoea),

37% were respiratory symptoms (fever, cough, and dyspnea), and 10% were other symptoms (such as myocarditis and Gilian Barre syndrome).The majority of patients (50%) had relatively normal PH values according to ABG studies, while 37.1% of them had acidosis and 12.9% had alkalosis (P value = 0.001). PaCo2 levels among infected toddlers showed no discernible difference (P value = 0.374).

On the other hand, only 3.2% of patients had PaO2 levels above 100, while 90.3% of patients had

hypoxemia (P value 0.001). Amounts of acids and bases were measured, and it was discovered that 16.1% had high HCO3 and 48.4% had low HCO3 (P value = 0.007). As a result and according to the computation of base excess and deficit, 22.6% had normal amounts of bases, 24.2% had excess bases, and 53.2% had base deficits (P value = 0.004). On the other hand, only 32.3% of participants had high levels of lactic acid, while 67.7% substantially had normal levels (P value = 0.005). table 1

Table 1: ABG finding in the studied children

Variable	N (%)	P value
pH value		
Normal (7.35 - 7.45)	62 (50)	0.001
Acidosis (< 7.35)	46 (37.1)	
Alkalosis (> 7.45)	16 (12.9)	
PaCO2 (mmHg)		
Normal (35-45)	42 (33.9)	0.374
Low (< 35)	50 (40.3)	
High (> 45)	32 (25.8)	
PaO2 (mmHg)		
Normal (80-100)	8 (6.5)	<0.001
Low (< 80)	112 (90.3)	
High (> 100)	4 (3.2)	
HCO3 (mEq/L)		
Normal (22-28)	44 (35.5)	0.007
Low (< 22)	60 (44.4)	
High (> 28)	20 (16.1)	
Lactic acid (mmol/L)		
Normal (0.5-2.2)	84 (67.7)	0.005
High (> 2.2)	40 (32.3)	

DISCUSSION

Our data analysis revealed the range of acid-base abnormalities in kids with COVID-19. The primary symptom of this illness in our study was diarrhoea, which was followed by respiratory symptoms like pneumonia and certain children's unusual presentations including myocarditis and Guillain-Barre syndrome. These unusual presentations can show how the COVID-19 presentation in children may vary from that in adults.

As was already noted, children with COVID-19 may present with diarrhoea. This result is consistent with a prior study that found diarrhoea to be the primary symptom in a significant number of individuals (19). In our study, the proportion of kids who have it as a primary symptom is higher. The prevalence of diarrhoea in our developing nation (20) helps to explain this.

Atypical acute distress syndrome, frequently linked to conserved lung gas levels, develops in the majority of patients with severe COVID-19 infection necessitating hospitalisation in the intensive care unit (21). This is consistent with our observations that nearly all patients (90.3%) had hypoxia despite small variability in PaCO₂ levels across infected children; this is known as "silent hypoxia" or "silent hypoxemia" (22-24). The increased pulmonary compliance and focal lung damage may be related to the mechanisms mentioned (25).

One of the most important indicators of the severity and pathophysiology of many diseases, including COVID-19 infections, is acid-base abnormalities (26). Acidosis may result from kidney failure (metabolic acidosis), a significant increase in various compounds like lactic acid and arterial ketones, or a significant

rise in arterial carbon dioxide pressure (respiratory acidosis). All of these conditions can act simultaneously to increase hydrogen protons and, as a result, lower blood and pH levels (27,28). Previous research has suggested that anaerobic glycolysis, which is favoured by hypoxia, may be the cause of lactate-induced metabolic acidosis in COVID-19. Pyruvate, a byproduct of the glycolytic cycle, is not delivered to the mitochondria to proceed with oxidation. Instead, the enzyme lactate dehydrogenase converts it to lactate in the cytosol. Because tissue oxygenation and oxidative phosphorylation are compromised by hypoxia, cells must produce ATP (adenosine triphosphate) by anaerobic glycolysis. As a result, metabolic acidosis worsens and lactate levels start to rise dramatically (29,30).

This shows that children may have different compensatory mechanisms than adults that enable them to endure the hypoxic effects of COVID-19, even though lactic acid levels were only raised in 32.2% of the study participants and 67.7% had normal levels. When this subject was previously investigated, it was discovered that kids had different adaptability principles than adults do. The anaerobic metabolism of carbohydrates in children is less active than that in adults because there is less of the rate-limiting enzyme phosphofructokinase. Less lactic acid is consequently produced. Children also have a larger arteriovenous oxygen difference, which enhances the pattern of cardiorespiratory system adaptation. Compared to adults, children have a 30% higher local flow in the peripheral circulation of the active muscle (31). This may assist to explain why, despite the fact that the study subjects' ABG levels were abnormal, only

37.1% of them experienced acidosis and 50% had normal PH levels.

In the present study, we discovered that the majority of COVID-19 children (53%) displayed gastrointestinal tract (GIT) manifestations in the form of diarrhoea that resulted in HCO₃ loss, resulting in about 48.4% having low HCO₃ levels and approximately 53.2% having base deficit. This was in line with other research that suggested the SARS-CoV-2 virus can infect the intestines, causing diarrhoea that causes considerable loss and, as a result, increases the likelihood that acidosis will develop (32,33). Although a sizable percentage of youngsters had base deficits, not all of them had acidosis. Base deficiency is a weak and unreliable indication of tissue acidity, in fact. This conclusion closely resembles one from an earlier study (34).

CONCLUSION

Since the majority of children in this study presented with diarrheal GIT manifestations, children have more unusual COVID presentations than adults. Children also have a greater ability to withstand variations in oxygen saturation in order to maintain acid-base balance.

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