



Metabolic alkalosis in hospitalised COVID-19 patients: A window to the pathogenesis?

To the Editor: South Africa has documented >600 000 confirmed COVID-19 cases within the 6 months since notification of the first case.^[1] During this influx of COVID-19 patients, we have observed an under-reported finding on the arterial blood gas of some hospitalised patients, namely metabolic alkalosis with or without hypoxaemia. No known causes of alkalosis were present in these patients, and as it was clinically associated with SARS-CoV-2 infection, the finding soon became known as the 'COVID gas' among frontline clinicians.

We conducted a prospective cohort study to determine the prevalence and significance of otherwise unexplained metabolic alkalosis in 255 consecutive patients admitted with suspected COVID-19. Standard bicarbonate (sHCO₃) was used as a marker for the metabolic component.^[2]

One hundred and fifty patients tested SARS-CoV-2-positive. The median sHCO₃ was 26.7 (interquartile range (IQR) 23.95 - 29.2) mmol/L, 27.6 (IQR 25.2 - 29.4) mmol/L and 25.2 (IQR 22.1 - 28.1) mmol/L for the whole cohort, the SARS-CoV-2-positive group and the SARS-CoV-2-negative group, respectively. The median pH was 7.46 (IQR 7.4 - 7.49), 7.47 (IQR 7.45 - 7.5) and 7.42 (IQR 7.34 - 7.47) for the respective groups. Metabolic alkalosis (sHCO₃ ≥28 mmol/L and pH ≥7.45) was significantly more common in SARS-CoV-2-positive than SARS-CoV-2-negative patients (60/150 (40%) v. 17/105 (16%); *p*<0.001). The median potassium level was 4.0 (IQR 4.0 - 4.5) mmol/L and 5.0 (IQR 4.0 - 5.0) mmol/L in the SARS-CoV-2-positive and negative groups, respectively. Thirteen patients in the SARS-CoV-2-positive group (9%) had hypokalaemia (<3.5 mmol/L) and 8 had both hypokalaemia and metabolic alkalosis. Urine samples obtained from 4 of these patients all showed an increased potassium-to-creatinine ratio, with a median of 3.1 mmol/mmol. The 'COVID gas' had moderate specificity (84%) but poor sensitivity (40%) for COVID-19 diagnosis. In the 143 COVID-19 patients with available outcomes, neither the presence nor the absence of metabolic alkalosis predicted survival.

We present this unusual observation to assess opinion regarding the consistency of this finding in other centres, and to gather opinion as to the potential causes and clinical significance of the pronounced metabolic alkalosis. We speculate that the metabolic alkalosis may be due to excess mineralocorticoid-like effects or hypokalaemia, either from renal or gastrointestinal losses.^[3] Chen *et al.*^[4] reported a 53% prevalence of hypokalaemia in COVID-19 patients. The renin-angiotensin system (RAS) effects are antagonised by actions of angiotensin-converting enzyme 2 (ACE2). SARS-CoV-2 binds and degrades ACE2, thereby potentially reducing its counter-regulatory effects.^[5] Increased RAS activity with increased angiotensin II and aldosterone effects may therefore promote distal nephron sodium reabsorption and enhanced urinary potassium excretion. Our cohort predominantly had normal concentrations of serum potassium, probably because the acute nature of SARS-CoV-2 infection does not affect total body potassium stores significantly.

The unusual presence of metabolic alkalosis on admission in a significant number of patients admitted with COVID-19 is an unreported finding requiring multicentre investigation to unravel the pathophysiology of the disease, including the significance of the acid-base abnormalities we observed.

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