Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

specifically drug-induced SIAD and pneumonia. Of 34 patients with SIAD related to drugs in our study, 28 (82%) had other identifiable causes. These included malignancies in 20 patients, neuropsychiatric illness in 7 patients, and human immunodeficiency virus–related illness in 1 patient. A cure was not possible for these causes during the study period.

We admit that simply withdrawing medications related to SIAD can result in correction of hyponatremia.[3] However, to do that in patients who have other incurable causes of SIAD may not sufficiently restore serum sodium to a normal level. Also, withdrawal of those medications might not be feasible in some patients; for example, withdrawal of opioid analgesics in patients with cancer. Ten of 34 (29%) patients who received medications that might be associated with SIAD discontinued those medications at the time of enrollment, at the discretion of the primary physician. The proportion of patients who discontinued medications was not different between the treatment assignments.

Pneumonia is another resolvable cause of SIAD. Cuesta et al[4] have demonstrated that SIAD due to pneumonia could be corrected by antimicrobial therapy in 80% of their patients without any specific treatments for SIAD. In our study, 7 patients had nontuberculous pulmonary infection identified as a cause of SIAD. Of those, 4 patients achieved serum sodium level ≥ 135 mmol/L. In 3 patients who did not achieve serum sodium levels ≥ 135 mmol/L, 2 had malignancy as a concomitant disease. The suggestion of a subgroup analysis is useful, but it should be performed in a study with more participants.

Kajohnsak Noppakun, MD, Pathomporn Pin-on, MD, Chidchanok Ruengorn, PhD

Article Information

Authors' Affiliations: Division of Nephrology, Department of Internal Medicine, Faculty of Medicine (KN); and Pharmacoepidemiology and Statistics Research Center, Faculty of Pharmacy, Chiang Mai University, Thailand (KN, PP-o, CR).

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Infections and Collapsing Glomerulopathy

To the Editor:

We read with great interest the review of Ahn and Bomback[1] describing the current diagnosis and management of podocytopathies. As underscored by the authors, the list of underlying processes associated with podocytopathies is growing. Infectious diseases are a major cause of podocytopathies, including collapsing glomerulopathy. We would like to emphasize 2 pathogens, *Plasmodium* species and SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2; the causative agent of coronavirus disease 2019 [COVID-19]), which could be added to the spectrum of infectious agents associated with collapsing glomerulopathy.

We recently reported clinical and pathologic characteristics of 18 patients with collapsing glomerulopathy occurring within 3 months of an acute malaria episode.[2] Interestingly, all 7 tested patients had high-risk variants of *APOL1*. As discussed by Anh and Bomback, infection caused by *Plasmodium* species may act as a second hit leading to collapsing glomerulopathy in genetically predisposed patients. Similarly, compelling evidence suggests that SARS-CoV-2 may act as a trigger for collapsing glomerulopathy occurrence in patients of African ancestry and genetic susceptibility factors.[3] Whether SARS-CoV-2–associated collapsing glomerulopathy is the result of direct podocyte viral infection or may be related to secondary mechanisms remains to be determined.[3] Further studies (including genotyping of *APOL1*) will decipher the role of genetic predisposition in the pathogenesis of this secondary form of collapsing glomerulopathy.

These findings suggest that malaria and COVID-19 may be 2 additional infectious diseases leading to toxic podocytopathies.

Anissa Moktefi, MD, PhD, Vincent Audard, MD, PhD
Khalil El Karoui, MD, PhD

Article Information

Authors' Affiliations: Département de Pathologie, Assistance Publique des Hôpitaux de Paris (AP-HP), Hôpitaux Universitaires

Henri Mondor (AM); Univ Paris Est Créteil, Institut National de la Santé et de la Recherche Médicale (INSERM) U955, Institut Mondor de Recherche Biomédicale, Equipe 21 (AM, VA, KEK); and AP-HP, Hôpitaux Universitaires Henri Mondor, Service de Néphrologie et Transplantation, Centre de Référence Maladie Rare "Syndrome Néphrotique Idiopathique", Fédération Hospitalo-Universitaire "Innovative therapy for immune disorders", Créteil, France (VA, KEK).

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Ahn and Bomback declined to respond.

RESEARCH LETTER

Pseudohypobicarbonatemia in Severe Hypertriglyceridemia

To the Editor:

Erroneously low serum CO_2 level (sCO_2) determination or pseudohypobicarbonatemia (PHB) has been reported in severe hypertriglyceridemia.[1–4] Artifactual sCO_2 values may occur due to lipid interference in some analyzers (primarily Abbott Architect).[4] Analyzers measure sCO_2 through a phosphoenolpyruvate (PEP) carboxylase reaction. CO_2 and PEP are converted to phosphate and oxaloacetate, which is reduced to malate, resulting in the oxidation of nicotinamide adenine dinucleotide. The decrease in absorbance is proportional to the sample's CO_2 content,[5] and triglycerides (TG) can disrupt spectrophotometry by absorbing light. Volume displacement by lipids may contribute to the artifact.[6] Abbott Architect is used in 10.8% of US laboratories.[7] We sought to determine the incidence and clinical implications of PHB and develop a protocol to overcome the artifact.

The study was approved by the Institutional Review Board with waiver of informed consent. We searched for cases from 2015 to 2018 of serum TG > 1,000 mg/dL with a Abbott Architect–measured sCO_2 the same day. Prioritizing clinical relevance, we selected those with $sCO_2 \leq 12$ mEq/L. Each sCO_2 was compared to a calculated HCO_3^- from an arterial blood gas (ABG) obtained within 6 hours of the venous blood draw. Calculated HCO_3^- is derived from the Henderson-Hasselbach equation, which uses pH and P_{CO_2} values measured using direct and indirect potentiometry, respectively.[8] We conservatively opted to consider a difference between calculated HCO_3^- and measured sCO_2 of ≤4 mEq/L as medically plausible.[9] Thus, PHB was defined as erroneous sCO_2 ($errCO_2$) gap = (calculated HCO_3^- − measured sCO_2) ≥ 5 mEq/L.

Subsequently, we identified consecutive samples of TG > 1,000 mg/dL over 2 months to measure sCO_2 with/without centrifugation (2 minutes, 12,000*g*) for lipemic layer removal. A separate sCO_2 was determined using an Abbott i-STAT Chem8+ analyzer, which measures pH, P_{CO_2}, and ionic strength; reports total CO_2 [tCO_2, or HCO_3^- + dissolved CO_2 ($0.03 \times P_{CO_2}$)]; and has direct metrologic traceability that categorizes it as a measured analyte.[8] Simultaneously, we calculated HCO_3^-.

We found 2,630 events (1,251 patients) of TG > 1,000 mg/dL with a same-day sCO_2. TG level inversely correlated with sCO_2 ($r = -0.38$; $P < 0.001$). We found 273 events (91 patients) of $sCO_2 \leq 12$ mEq/L. In 144 events, an ABG was either not available or done more than 6 hours apart from the venous sample. The remaining 129 events included 51 instances (11 patients) of true hypobicarbonatemia and 78 instances (39 patients) of PHB (60% instances, 78% of patients). In 78% of events (100/129), the ABG was obtained within 0 to 3 hours of the venous sample. For those with ABGs within 0 to 1 or 0 to 3 hours, the incidence of PHB was 69% (18/26 and 38/55, respectively). Among the PHB cases, the median $errCO_2$ gap was 13 (range, 5-25) mEq/L (Table 1). Median pH was 7.37 (range, 7.05-7.56) and true metabolic acidosis was either absent (47%) or spuriously magnified (53%). Alkalosis was observed among the most extreme PHB cases (Table 2). There was no acid-base disturbance in 21% and either metabolic or respiratory alkalosis was seen in 46% (Table S1). TG level correlated with the magnitude of the $errCO_2$ gap ($r = 0.59$; $P < 0.001$; Fig S1). Bicarbonate was administered to 29% of PHB cases

Table 1. Laboratory Values for Cases of PHB (n = 78)

	Median (Range)	Reference Range
Na, mEq/L	132 (121-156)	13-145
K, mEq/L	4 (3.2-6.9)	3.5-5.1
Cl, mEq/L	101 (89-117)	95-110
sCO_2, mEq/L	8 (<5-12)	23-29
AG, mEq/L	22 (14-31)	8-16
HCO_3^- (ABG), mEq/L	21 (10-34)	22-26
pH (ABG)	7.37 (7.05-7.56)	7.36-7.44
$errCO_2$, mEq/L	13 (5-25)	
TG, mg/dL	3,140 (1,082->3,600)	30-150
Glucose, mg/dL	272 (98-636)	70-110
Lactate,[a] mmol/L	1.8 (0.7-15.6)	0.5-2.2

Abbreviations: (ABG), on arterial blood gas; AG, anion gap; $errCO_2$, erroneous CO_2 gap; sCO_2, serum carbon dioxide; TG, triglycerides.
[a]Only obtained in 56 (72%) cases.