

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Diabetic ketoacidosis during COVID-19 pandemic in a developing country



We read with interest the study published by Goldman et al. [1], who identified four patients with diabetic ketoacidosis (DKA) resistant to standard therapy that was triggered by COVID-19 and was associated with high morbidity and mortality. This is also happening in developing countries such as Peru, which has the highest number of COVID-19 cases per million inhabitants and the second-lowest public healthcare spending according to WHO [2].

In our Endocrinology inpatient department at a social security hospital in Peru, from the beginning of the pandemic to date, we have treated 14 patients with DKA who were transferred from the emergency service after they had met the resolution criteria. Of these patients, nine presented with new-onset diabetes. Four tested positive for SARS-CoV-2, three by RT-PCR and one by ELISA, and two patients died. In total, six, six, and two patients had severe, moderate, and mild DKA, respectively. Nine developed acute kidney injury, and six developed acute pancreatitis (Table 1).

The mechanism by which SARS-CoV-2 triggers DKA has not been fully elucidated; however, it has been shown that it uses the receptor for angiotensin-converting enzyme 2 as a gateway, which is expressed in the intestine, kidney, and pancreas [3], organs that are part of the "egregious eleven," the pathophysiological basis of type 2 diabetes mellitus [4]. Accordingly, the virus can cause cellular destruction of the islets of Langerhans, which may explain the higher incidence of DKA [3] in patients with and without known diabetes. This damage can be expressed by an elevation of pancreatic enzyme levels in patients with COVID-19 [5]; however, DKA itself can present with elevated pancreatic enzyme levels in 16–25% of cases [6]. Likewise, a state of insulin resistance triggered by COVID-19 has been described, which, together with pancreatic injury, contributes to an increased risk of hyperglycemic crisis in patients with diabetes [3].

In our experience, an insulin infusion pump was continuously used to manage patients with mild and moderate DKA. Hence, healthcare workers were highly exposed to patients with COVID-19. However, the American Diabetes Association and the Joint British Diabetes Societies have recommended the administration of rapid subcutaneous insulin every 4 h [7]. This regimen is safe and effective. Furthermore, it minimizes the time spent for bedside care and conserves the use of personal protective equipment [8], which should be prioritized in our country considering the shortage of equipment, supplies, and medicines needed for COVID-19.

Funding

The authors received no funding from an external source.

Declaration of competing interest

The authors declare no conflict of interest in this publication.

REFERENCES

- [1] Goldman N, Fink D, Cai J, Lee Y-N, Davies Z. High prevalence of COVID-19-associated diabetic ketoacidosis in UK secondary care. Diabetes Res Clin Pract 2020;166. <u>https://doi.org/10.1016/ i.diabres.2020.108291</u> 108291.
- [2] PAHO COVID-19 RESPONSE [Internet]. Paho-covid19-responsewho.hub.arcgis.com. 2020 [cited 17 August 2020]. Available from: https://paho-covid19-response-who.hub. arcgis.com/pages/paho-south-america-covid-19-response.
- [3] Yang J-K, Lin S-S, Ji X-J, Guo L-M. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol 2010;47:193–9. <u>https://doi.org/10.1007/s00592-009-0109-4</u>.
- [4] Schwartz SS, Epstein S, Corkey BE, Grant SFA, Gavin JR, Aguilar RB. The time is right for a new classification system for diabetes: rationale and implications of the β-cell-centric classification schema. Diabetes Care 2016;39:179–86. <u>https:// doi.org/10.2337/dc15-1585</u>.
- [5] Chee YJ, Tan SK, Yeoh E. Dissecting the interaction between COVID-19 and diabetes mellitus. J Diabetes Investig 2020. <u>https://doi.org/10.1111/jdi.13326</u>. jdi.13326.
- [6] Rizvi AA. Serum amylase and lipase in diabetic ketoacidosis. Diabetes Care 2003;26:3193–4. <u>https://doi.org/10.2337/diacare.26.11.3193</u>.
- [7] Rayman G, Lumb A, Kennon B, Cottrell C, Nagi D, Page E, et al. Guidance on the management of Diabetic Ketoacidosis in the exceptional circumstances of the COVID-19 pandemic. Diabet Med 2020;37:1214–6. <u>https://doi.org/10.1111/dme.14328</u>.
- [8] Palermo NE, Sadhu AR, McDonnell ME. Diabetic ketoacidosis in COVID-19: unique concerns and considerations. J Clin Endocrinol Metab 2020;105. <u>https://doi.org/10.1210/clinem/ dgaa360</u>.

Tab	Table 1 – Clinical and biochemical characteristics of patients with diagnosis of diabetic ketoacidosis upon admission.													
	Gender	Age	Known diagnosis of DM	Severity of DKA	COVID-19diagnosis	AKI	pН	HCO3⁻	Glucose	Amilase	Lipase	HbA1c	Abdominal CT	
		U	Ũ	2	Ç		-	mmol/L	mg/dL	U/L	U/L	% (mmol/mol)		
1	Male	31	No	Severe	No	Yes	6.9	5.6	888	361	396	17 (162)	Edematous pancreas	
2	Male	66	No	Mild	No	Yes	7.26	20.5	506	413	2421	10.9 (96)	Edematous pancreas	
3	Male	66	No	Severe	ELISA	No	7.05	8.6	781	54	284	12 (108)	No abnormalities	
4	Male	36	No	Severe	No	Yes	6.99	6.1	683	87	1472	11.4 (101)	No abnormalities	
5	Male	73	Yes	Mild	RT-PCR	Yes	7.3	18.6	699	51	315	14.3 (133)	Hipotrofic pancreas	
6	Male	62	Yes	Severe	No	Yes	7.27	13.7	260	600	4837	13.5 (124)	Edematous pancreas	
7	Male	62	Yes	Moderate	RT-PCR	*	7.3	14.6	1218	37	106	*	No abnormalities	
8	Male	48	No	Moderate	No	No	7.23	11	305	159	1004	12.9 (117)	Diffuse edema of the	
													pancreas	
9	Female	36	Yes	Severe	RT-PCR	Yes	6.8	2.5	420	622	15	15.2 (143)	No abnormalities	
10	Male	40	No	Moderate	No	No	7.24	10.6	341	89	143	14.6 (136)	No abnormalities	
11	Male	63	No	Moderate	No	Yes	7.25	11.6	1046	143	353	12.5 (113)	No abnormalities	
12	Male	45	No	Severe	No	Yes	6.9	10.5	1072	86	558	18.4 (178)	No abnormalities	
13	Male	15	Yes	Moderate	No	Yes	7.1	8	637	64	25	9.5 (80)	No abnormalities	
14	Female	53	No	Moderate	No	No	7	12	600	264	16,647	10.4 (90)	Edematous pancreas	

Source: Data obtained from the Endocrinology inpatient department. Guillermo Almenara National Hospital. March-July 2020.

* Not applied: Patient with end stage renal disease.

DM: Diabetes mellitus; DKA: Diabetic ketoacidosis; CT: Computed tomography; RT-PCR: Reverse transcription- polymerase chain reaction; AKI: Acute kidney injury; IPT: Insulin pump therapy; HbA1c:

Division of Obstetrics and Ginecology, Edgardo Rebagliati Martins National Hospital, Lima, Peru Julia Cristina Coronado Arroyo National Hospital, Lima, Peru

Division of Endocrinology, Guillermo Almenara Irigoyen Esteban Alberto Plasencia Dueñas

Covid-19 Unit, Regional Teaching Hospital of Trujillo, Peru * Corresponding author at: School of Medicine, National University of Trujillo, Av. Roma 338, 13011 Trujillo, Peru. E-mail address: davidarmasflorez@gmail.com Cristian David Armas Flórez

Marcio José Concepción Zavaleta Division of Endocrinology, Guillermo Almenara Irigoyen National Hospital, Lima, Peru