

## Could the QTc prolongation seen in diabetic ketoacidosis be due to more than just a raised anion gap?



### To the Editor:

Perez et al<sup>1</sup> demonstrated that nearly one-third of patients presenting with diabetic ketoacidosis (DKA) had QTc prolongation. The authors demonstrated a significant correlation between the QTc and anion gap and, therefore, hypothesized that the QTc prolongation seen was secondary to an elevated anion gap and metabolic acidosis.

The authors evaluated whether the change in QTc was related to electrolyte abnormalities, but they did not assess other features of the clinical presentation that may have caused the QTc prolongation observed.

The patients' temperatures are not documented in the study. As cold sepsis could be a precipitant for ketosis, the associated hypothermia should, therefore, be considered as a cause for QTc prolongation.<sup>2</sup>

Hypothyroidism is another autoimmune endocrine condition that is closely associated with type 1 diabetes mellitus and often related to poorer diabetic control.<sup>3</sup> Raised thyroid-stimulating hormone levels is a well-established cause of QTc prolongation,<sup>4</sup> however, thyroid function was not assessed in the acute setting or during follow-up of the Perez et al study.<sup>1</sup>

Lastly, a well-established complication of DKA treatment in the pediatric population is cerebral edema.<sup>5</sup> Raised intracranial pressures are another cause of QTc prolongation, but the authors have not assessed whether this may have occurred during their study.

Although we acknowledge that there is a strong correlation between QTc prolongation and anion gap in patients with DKA, the above confounding factors that could also cause QTc prolongation should be assessed.

**Rebecca Clarke, MBBS, BSc**  
Pediatric Emergency Medicine  
North Middlesex Hospital  
London, United Kingdom

**Adam Ioannou, MBBS, BSc, MRCP**  
Department of Cardiology  
Hammersmith Hospital  
London, United Kingdom

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*The authors declare no conflicts of interest.*

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## Reply



### To the Editor:

We read with interest the letter from Clarke and Ioannou regarding our study. Although we acknowledge the risk of confounding, given the retrospective nature of our manuscript, we feel it is highly unlikely that these factors had an impact on our results.

Although hypothermia has been associated with QTc prolongation,<sup>1</sup> infection is a rare cause of diabetic ketoacidosis (DKA) in developed countries and accounts for only 15% of cases of DKA.<sup>2</sup> Hypothermia could not be attributed as a cause of QTc prolongation in our cohort, as none of the 96 patients had a temperature <35°C during their course of illness on further review of the data.

The authors acknowledge the association between type 1 diabetes mellitus and thyroid disorders; however, DKA has been shown to be associated with sick euthyroid syndrome and a normal thyroid-stimulating hormone.<sup>3</sup> It is difficult to imagine a consistent relationship between DKA severity and thyroid-stimulating hormone elevation that could drive the association with QTc prolongation.

Cerebral edema occurs in <1% of cases of DKA,<sup>4</sup> so this rare potential confounder was not specifically assessed. Our data (Table I) did demonstrate a statistically significant heart rate elevation by severity of DKA, which would challenge the assertion that increased intracranial pressure had a clinical impact, especially in the severe DKA group. Furthermore, the association between elevated intracranial pressure and QTc prolongation has mostly been observed in cases of subarachnoid hemorrhage.<sup>5</sup>

We would again like to thank our colleagues for their interest in our article.

**Michelle M. Perez, MD**  
**Bradley C. Clark, MD**  
Children's Hospital at Montefiore, Bronx  
New York

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## Changes in hospitalization in children during COVID-19 pandemic quarantine in a single center in Turkey



### To the Editor:

Li et al<sup>1</sup> reported the variations in healthcare visits of children to hospitals during the coronavirus disease 2019 (COVID-19) pandemic in China. In Turkey, the first case of severe acute respiratory syndrome coronavirus 2 infection was authoritatively reported by the Ministry of Health on March 11, 2020.<sup>2</sup> The schools and universities were closed on March 16, 2020. The government took further steps to mitigate disease spread, including travel restrictions, social distancing, and home quarantine from March to June 2020.

We report the effects on healthcare utilization data derived from a tertiary pediatric hospital in the middle of Turkey and accepting complicated patients from all over the country. The electronic database system of the hospital was evaluated for the containment period of the country; the same period in 2019 was chosen for comparison. The diagnoses of the hospitalized patients were classified by

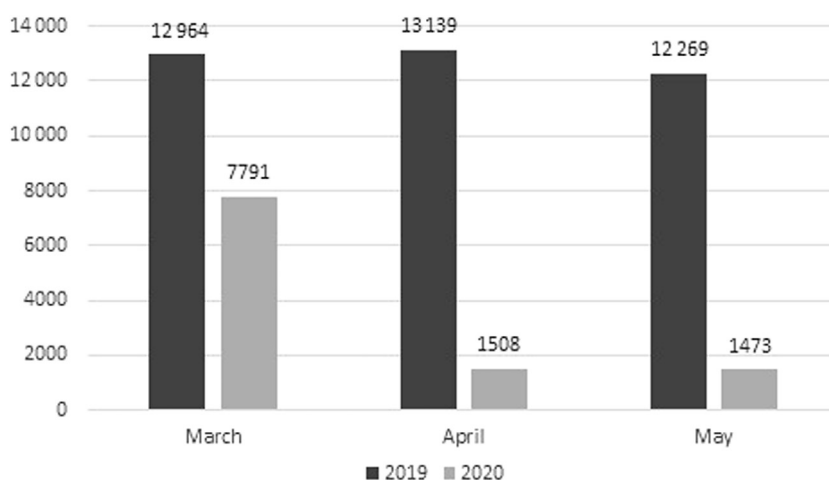
types of infectious diseases, organ system diseases, oncologic diseases, and intoxications. We calculated the change rate of the diseases according to percentage rates. The diseases having a change rate  $>1$  was accepted to be increased,  $<1$  was accepted to be decreased during the pandemic period. With the start of quarantine restrictions and school holidays, a prominent decline in the number of patients occurred not only in outpatient clinics (**Figure 1**) but also in hospitalized patients (**Figure 2**). Patients suspected or diagnosed with COVID-19 infection were excluded. Data indicating the rates of diagnosis and the change rates are shown in **Figure 3**.

As expected, the major decline occurred in infections, including acute lower respiratory infections because of social distancing and restricted close contacts during the pandemic. Other infections spread by close interactions, such as diarrhea, were also diminished.

There was an increase in the number of patients hospitalized for allergic diseases, especially severe urticaria and anaphylaxis. Li et al<sup>1</sup> also noted an increase in atopic dermatitis and related skin problems in China and speculated on the role of lack of sunlight exposure and reduction of vitamin D levels during the long period of home quarantine.

In 2020, there was an increase in rheumatologic diseases including IgA vasculitis (Henoch-Schonlein purpura), juvenile idiopathic arthritis, and juvenile idiopathic arthritis-related macrophage activation syndrome compared with the same period in 2019. The relationship between viral infections and the trigger of both T cell-associated damage and post-translational modification of peptides activating T cells have been reported.<sup>3</sup> Although the highly suspected and confirmed cases of COVID-19 were excluded from the study, multisystem inflammatory syndrome in children without the active symptoms of COVID-19 infections might contribute to this finding.<sup>3</sup>

Intoxication by drugs was 3.5 times higher during COVID-19 quarantine. Intoxication as suicide attempt



**Figure 1.** Number of patients admitted to outpatient clinics in the department of pediatrics in 2020 compared with 2019.