New-Onset Type 1 Diabetes in Children During COVID-19: Multicenter Regional Findings in the U.K.

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Rebecca Unsworth,[1] Susan Wallace,[2] Nick S. Oliver,[1] Shunmay Yeung,[3,4] Archana Kshirsagar,[2] Harshini Naidu,[5] Ruth Min Wai Kwong,[6] Priya Kumar,[6] and Karen M. Logan[4]

Data on new-onset type 1 diabetes during the coronavirus disease 2019 (COVID-19) pandemic, particularly in children, is limited. A recent U.S. multicenter study reported outcomes in sixty-four adults and children with type 1 diabetes, and confirmed or suspected COVID-19. However, only six patients presented with new-onset type 1 diabetes (1).

We report multicenter regional data from North West London (NWL) of new-onset type 1 diabetes and diabetic ketoacidosis (DKA) in children up to the age of 16 years during the peak of the COVID-19 pandemic. We collected data from five inpatient units (four National Health Service [NHS] Trusts) comprising the NWL Pediatric Diabetes Network between 23 March (coinciding with the commencement of the U.K. Government lockdown) and 4 June.

Thirty children aged 23 months to 16.8 years presented with new-onset type 1 diabetes (Table 1). We observed an apparent increase in two units, with 10 cases each (versus typically 2 and 4 cases, respectively, for April/May combined in the previous 5 years). Rates in the other three units were similar to previous years. A high proportion of children (21/30, 70%) presented with DKA, with severe DKA (pH range 6.82–7.05) in over half (11/21, 52%). Twelve children presented with clinical shock and four were managed in pediatric intensive care. Two children presented with reduced conscious level, one received hyperosmolar therapy, and both recovered without complications. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) PCR was performed from nasopharyngeal swabs in 21 children meeting local testing criteria; two tested positive. SARS-CoV-2 serum IgG antibody was tested in a subgroup of children attending one of two units; 3 of 16 children (19%) tested positive. Of the five children with positive results, three presented with severe DKA and refractory hypokalemia, and one child with positive SARS-CoV-2 PCR suffered a hypokalemia-related cardiac arrest but recovered fully following 1 day of ventilation. Only three children with known type 1 diabetes presented with DKA during the same time period.

In comparison with a typical year, we estimate this represents an additional 12–15 new type 1 diabetes cases (80% increase) during the COVID-19 pandemic, with apparent clusters of cases observed in two units. The angiotensin converting enzyme 2 (ACE2) receptor is the binding site for SARS-CoV-1 and -2 (2) and is strongly expressed in pancreatic endocrine cells (3). Previous evidence suggests that SARS-CoV-1 virus may have entered pancreatic islet cells via the ACE2 receptor leading to β-cell damage and new-onset, mainly transient diabetes (3). While our data does not prove a link, we postulate that SARS-CoV-2 exposure contributed to the observed increase in cases by precipitating or accelerating type 1 diabetes onset.

Reports from China and Italy describe a number of children presenting with new-onset type 1 diabetes or severe DKA during the COVID-19 pandemic, apparently unrelated to infection (4). This prompted concerns of delayed presentation, but we suggest that a number of these cases may be attributed to prior SARS-CoV-2 exposure. In accordance with previous reports, we observed a high rate of severe DKA, but delayed presentation did not appear to be a significant factor, with

[1]Imperial College London, London, U.K.
[2]Chelsea and Westminster NHS Foundation Trust, London, U.K.
[3]London School of Hygiene & Tropical Medicine, London, U.K.
[4]St Mary's Hospital, Imperial College Healthcare NHS Trust, London, U.K.
[5]The Hillingdon Hospitals NHS Foundation Trust, Uxbridge, U.K.
[6]London North West University Healthcare NHS Trust, London, U.K.

Corresponding author: Karen M. Logan, k.logan@imperial.ac.uk

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Table 1—Children presenting with new-onset type 1 diabetes or with DKA and known type 1 diabetes

		New onset type 1 diabetes (n = 30)				
		SARS-CoV-2 not tested/ negative* (n = 25)		SARS-CoV-2 PCR or IgG positive (n = 5)		
	All patients (n = 33)	Not in DKA (n = 8, 32%)	DKA (n = 17, 68%)	Not in DKA (n = 1, 20%)†	DKA (n = 4, 80%)‡	Known type 1 diabetes with DKA (n = 3)§
Median age (IQR), year	10.9 (6.8)	12.0 (6.0)	10.3 (6.2)	5.8	11.6 (1.7)	13.2 (2.3)
Male	22 (68)	6 (75)	11 (65)	0 (0)	3 (75)	2 (67)
Median weight for age z score (IQR)	0.12 (1.44)	0.90 (2.09)	0.04 (1.62)	−0.23	0.96 (1.61)	0.12 (0.44)
Ethnicity						
White European	12 (36)	3 (38)	7 (41)	0 (0)	2 (50)	0 (0)
Black African	8 (24)	2 (25)	4 (24)	0 (0)	1 (25)	1 (33)
Arab	6 (18)	1 (13)	3 (18)	1 (100)	1 (25)	0 (0)
Asian	3 (9)	1 (13)	2 (12)	0 (0)	0 (0)	0 (0)
Other	4 (12)	1 (13)	1 (6)	0 (0)	0 (0)	2 (67)
Family history of type 1 diabetes	11 (33)	6 (75)	4 (24)	1 (100)	0 (0)	0 (0)
Comorbidities	2 (6)	1 (13)	1 (6)	0 (0)	0 (0)	0 (0)
Median duration of symptoms (IQR), days	7 (10)	14 (17)	7 (7)	10	10 (10)	1 (2)
Median plasma glucose on presentation (IQR), mg/dL	432 (200)	354 (155)	465 (177)	475	484 (135)	427 (87)
HbA_{1c}, median, % (mmol/mol)	11.6 (103)	11.2 (99)	11.6 (103)	11.3 (100)	12.5 (113)	10.0 (86)
Median pH on presentation (IQR)	7.19 (0.28)	7.37 (0.06)	7.14 (0.29)	7.42	6.90 (0.08)	7.24 (0.11)
Severe DKA (pH <7.1)	12 (36)	—	8 (47)	—	3 (75)	1 (33)
Median plasma lactate on presentation (IQR), mmol/L	1.9 (2.5)	1.0 (0.04)	2.1 (2.3)	1.5	4.6 (0.8)	1.3

Data are n (%) unless otherwise indicated. IQR, interquartile range. *Eight children had no testing, six had SARS-CoV-2 PCR testing only, two had SARS-CoV-2 IgG testing only, nine had both SARS-CoV-2 PCR and IgG. †Positive for SARS-CoV-2 IgG. ‡Two positive for SARS-CoV-2 PCR and two positive for SARS-CoV-2 IgG. §One child had no testing, two children had negative SARS-CoV-2 PCR testing only.

relatively short symptom duration in the majority of children.

SARS-CoV-2 also affects the renin-angiotensin-aldosterone system through reduced ACE2 expression, leading to decreased degradation of angiotensin II and increased secretion of aldosterone and renal potassium loss (5). Although hypokalemia is not uncommon during treatment of DKA, particularly in cases of renal impairment, it is possible that reduction in ACE2 expression may have contributed in the reported cases.

Five children tested positive for SARS-CoV-2 PCR or IgG, but testing was not universal across NWL, and 14 children did not have SARS-CoV-2 IgG testing. This limited our ability to identify possible cases, particularly in children with recent suspected symptoms or known COVID-19 contacts. In addition, SARS-CoV-2 serology was tested soon after diagnosis and did not report IgM, and as antibody responses may not develop until 14–21 days postinfection, further cases may have been missed.

To the best of our knowledge, this is the first report to describe an apparent increase in new-onset type 1 diabetes in children during the COVID-19 pandemic, with evidence of SARS-CoV-2 infection or exposure in a proportion of those tested. Our intention is to raise awareness of a possible link between SARS-CoV-2 and new-onset type 1 diabetes, especially as there are reports of incident type 1 diabetes occurring as apparently small localized outbreaks. Further studies are required to establish a definitive link and any possible impact on the severity of type 1 diabetes presentation, including severe hypokalemia.

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