Children presenting with diabetes and diabetic ketoacidosis to Emergency Departments during the COVID-19 pandemic in the UK and Ireland: an international retrospective observational study

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ABSTRACT

Objectives To describe the incidence of new onset paediatric diabetes mellitus, clinical characteristics and patterns of presentation to emergency departments (ED) during the COVID-19 pandemic, and to assess whether this increase was associated with SARS-CoV-2 infection.

Design Retrospective medical record review.

Setting Forty nine paediatric EDs across the UK and Ireland.

Patients All children aged 6 months to 16 years presenting to EDs with (1) new onset diabetes or (2) pre-existing diabetes with diabetic ketoacidosis (DKA), during the COVID-19 pandemic (1 March 2020–28 February 2021) and the preceding year (1 March 2019–28 February 2020).

Results There were increases in new onset diabetes (1015 to 1183, 17%), compared with background incidence of 3%–5% in the UK over the past 5 years. There were increases in children presenting with new onset diabetes in DKA (395 to 566, 43%), severe DKA (141 to 252, 79%) and admissions to intensive care (38 to 72, 89%). Increased severity was reflected in biochemical and physiological parameters and administration of fluid boluses. Time to presentation from symptom onset for children presenting with new onset diabetes and DKA were similar across both years; healthcare seeking delay did not appear to be the sole contributing factor to DKA during the pandemic. Patterns of presentation changed in the pandemic year and seasonal variation was lost. Children with pre-existing diabetes presented with fewer episodes of decompensation.

Conclusions There were increases in new onset diabetes in children and a higher risk of DKA in the first COVID pandemic year.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Incidence of new onset diabetes and diabetic ketoacidosis (DKA) has been reported to have increased in children during the COVID-19 pandemic.

⇒ Proposed reasons for the increased incidence of new onset diabetes and DKA at diagnosis were delay in presentation and SARS-CoV-2 infection.

WHAT THIS STUDY ADDS

⇒ The Diabetes Mellitus in Children and Young People in the SARS-CoV-2 Pandemic study describes this pattern in a large patient population.

⇒ The study adds detailed data on presentation, severity of illness, diagnostic intervals and documented delay in presentation in both new onset and pre-existing diabetes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We may see further high incidence years with new onset diabetes, especially if SARS-CoV-2 has triggered the process of seroconversion in susceptible children.

⇒ Studies to characterise DKA in new onset diabetes are important to understand the factors for the high incidence of DKA despite public awareness campaigns.

⇒ Resource allocation and planning services will be key combined with a targeted approach of raising awareness for early identification of new onset diabetes in children.

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INTRODUCTION

While paediatric emergency department (ED) attendances declined during the COVID-19 pandemic, the proportion of severely unwell patients presenting to ED increased.[1] Among the high acuity presentations, an unseasonal spike in new onset paediatric diabetes and diabetic ketoacidosis (DKA) presenting to ED was observed during the first pandemic wave.

While this increase has been reported for both new onset diabetes[2–4] and DKA[2–8] at diagnosis, speculation on contributing factors has varied. Some hypothesise that the rise in DKA may be due to a direct effect of SARS-CoV-2 infection,[2 3] while others speculate that delay in presentation was the main reason.[5–7] Studies have also proposed an association between new onset diabetes and SARS-CoV-2.[9–11] While studies reported that hospitalised adults with COVID-19 developed new-onset diabetes,[12 13] evidence of a similar association between new onset diabetes and SARS-CoV-2

in children varied.[2–8] Children generally present with mild or asymptomatic COVID-19, and selection bias in testing for SARS-CoV-2 existed as only symptomatic and hospitalised children were tested. Combined with a paucity of testing for SARS-CoV-2 antibodies in the first pandemic year, it was difficult to establish whether a relationship existed between new onset diabetes and SARS-CoV-2.

In the DIMPLES study, we aimed to describe the characteristics of new onset and decompensation of existing diabetes in children presenting to paediatric EDs during the COVID-19 pandemic and compare this to the prepandemic era.

METHODS

Study design

This retrospective medical record review was conducted across 49 paediatric EDs who were member sites of Paediatric Emergency Research in the UK & Ireland (PERUKI).[14] Participating sites included tertiary paediatric and general hospitals seeing both adults and children. Two distinct time periods were studied in order to compare the pandemic and prepandemic eras: 1 March 2020–28 February 2021 (year 2) and 1 March 2019–28 February 2020 (year 1). Data were collected between 1 May and 31 December 2021, and the study is reported in line with the Strengthening the Reporting of Observational Studies in Epidemiology statement (online supplemental appendix).

Study population

Participants were eligible for inclusion if they were aged 6 months–16 years at the time of attending ED with (1) any new onset diabetes or (2) decompensation of existing diabetes resulting in DKA. Inclusion was at an individual attendance level; data from more than one attendance were captured provided severity criteria were satisfied at each attendance. Patients were identified by site study leads through searches of electronic clinical coding systems using International Classification of Diseases, 10th Revision codes for diabetes and DKA; this cohort was screened through review of medical notes to confirm eligibility. DKA was defined as a pH less than 7.3 or bicarbonate of <15 mmol and severe DKA as a pH less than 7.1 or serum bicarbonate of <5 mmol and ketones of >3.0 mmol/L in line with national and international guidance.[15]

Procedures

Data were collected according to standard methods for retrospective chart reviews, with all study variables in keeping with international definitions. Data were extracted by site investigators from the clinical records directly into an electronic case report form. All study staff underwent training delivered by the chief investigator prior to study commencement. Data included demographics, presence and duration of symptoms, physical examination findings, physiological parameters at presentation, family history, comorbidities, laboratory results (including COVID testing, HbA1c and pancreatic autoantibodies at diagnosis), duration and type of hospital admission and factors contributing to any delay in presentation. Diagnostic intervals were calculated from the period of reported symptoms of diabetes to the date of presentation to the hospital.

Data management

Study data were collected and managed using Research Electronic Data Capture tools (REDCap), hosted at University Hospitals Bristol and Weston NHS Foundation Trust and University College Dublin. REDCap is a secure, web-based software platform designed to support data capture for research studies.[16] Data entry was monitored for quality and completeness by the data manager. Prior to analysis, data were checked for completeness and accuracy, and queries on missing or potentially erroneous data were resolved by the site study lead using data quality checks.

Sample size

All ED visits that met the criteria for 'new onset diabetes' or DKA ('decompensation') were included for both the pre-COVID-19 pandemic period and the COVID-19 pandemic period.

Outcomes

The primary outcomes were to describe the incidence, clinical and biochemical characteristics of new onset paediatric diabetes presenting to EDs during the pandemic and to evaluate whether a relationship to SARS-CoV-2 existed. Secondary outcomes were to establish whether there was any change in the incidence and severity of DKA during the pandemic in cases of new onset and decompensated disease, compared with pre-COVID historical data.

Statistical analyses

Variables are expressed as absolute numbers and relative frequencies, or median with IQR (or range) where appropriate. χ^2 analyses were used for categorical and dichotomous variables, and Fisher's exact test was used when ≤5 cases were present; nonparametric Wilcoxon rank-sum tests were used for non-normally distributed continuous variables; and Student's t-test was used for normally distributed continuous variables. All analyses were planned a priori; no post hoc analyses were undertaken. Missing data were treated as missing; no imputation was performed. All analyses were performed in R statistical software V.4.0.0.

RESULTS

Incidence and cohort characteristics

In total, 2618 individuals were identified during the study period. There was a 17% increase in new onset diabetes from 1015 in year 1 to 1183 in year 2, 97% of which were type 1 diabetes and 2% were type 2 diabetes (table 1 and online supplemental table A,B). There was a 27.8% reduction in attendances during the pandemic year (year 2) for patients with DKA due to decompensation of existing diabetes (online supplemental table C, D). Participant demographic characteristics did not differ significantly between the 2 years (table 1 and online supplemental table C). The normal seasonal pattern of new onset type 1 diabetes cases (winter peak with summer trough) was disrupted in year 2 (figure 1).

Severity of presentations

Presenting symptoms, severity, treatment and outcomes of patients with new onset diabetes are demonstrated in table 2. On comparing severity of new onset disease during year 2 to that of year 1, we found there was a 43% increase in DKA (from 395 to 566, figures 1 and 2). This was most marked in severe DKA, which increased by 79% (from 141 to 252, $p<0.001$ (table 2) and intensive care admissions, which increased by 89% (from 38 to 72, $p<0.05$). The number of children with DKA who received a fluid bolus in ED of 20 mL/kg or more increased from 64 to 161 ($p<0.001$) (table 2). Increased severity of new-onset disease was also reflected in other biochemical and physiological parameters, including pH, tachycardia and tachypnoea (all $p<0.001$) (table 2 and online supplemental table D).

Table 1 Characteristics of patients with new-onset diabetes in the Diabetes Mellitus in Children and Young People in the SARS-CoV-2 Pandemic cohort

Characteristic	Overall, N = 2198*	Year 1 (2019–20), N = 1015*	Year 2 (2020–21), N = 1183*	P value†
Presenting symptoms				
Polyuria				0.2
Yes	1,974 (90%)	898 (88%)	1,076 (91%)	
No	159 (7.2%)	82 (8.1%)	77 (6.5%)	
Unknown	65 (3.0%)	35 (3.4%)	30 (2.5%)	
Polydipsia				0.6
Yes	1,994 (91%)	914 (90%)	1,080 (91%)	
No	140 (6.4%)	69 (6.8%)	71 (6.0%)	
Unknown	64 (2.9%)	32 (3.2%)	32 (2.7%)	
Weight loss				0.8
Yes	1,263 (57%)	576 (57%)	687 (58%)	
No	548 (25%)	259 (26%)	289 (24%)	
Unknown	387 (18%)	180 (18%)	207 (17%)	
Lethargy				<0.001
Yes	1,219 (55%)	505 (50%)	714 (60%)	
No	578 (26%)	312 (31%)	266 (22%)	
Unknown	401 (18%)	198 (20%)	203 (17%)	
Confusion				0.018
Yes	110 (5.0%)	38 (3.7%)	72 (6.1%)	
No	1,365 (62%)	653 (64%)	712 (60%)	
Unknown	723 (33%)	324 (32%)	399 (34%)	
Vomiting				0.043
Yes	517 (24%)	214 (21%)	303 (26%)	
No	1,331 (61%)	636 (63%)	695 (59%)	
Unknown	350 (16%)	165 (16%)	185 (16%)	
Fever				0.3
Yes	68 (3.1%)	29 (2.9%)	39 (3.3%)	
No	1,753 (80%)	799 (79%)	954 (81%)	
Unknown	377 (17%)	187 (18%)	190 (16%)	
Tachycardia	706 (33%)	260 (26%)	446 (38%)	<0.001
missing	55	33	22	
Tachypnea	783 (37%)	312 (32%)	471 (41%)	<0.001
Missing	86	48	38	
Level of consciousness				0.6
Alert	2,026 (92%)	938 (92%)	1,088 (92%)	
Verbal	67 (3.0%)	30 (3.0%)	37 (3.1%)	
Pain	16 (0.7%)	7 (0.7%)	9 (0.8%)	
Unresponsive	10 (0.5%)	2 (0.2%)	8 (0.7%)	
Not documented	79 (3.6%)	38 (3.7%)	41 (3.5%)	
Oxygen saturations				0.6
Normal %O2 saturations	2,183 (99%)	1,009 (99%)	1,174 (99%)	
%O2 saturations <94%	15 (0.7%)	6 (0.6%)	9 (0.8%)	
Duration of symptoms (days)	14 (7,28)	14 (7,30)	14 (7,28)	0.13
Missing	55	26	29	
Laboratory values				
HbA1c	106 (89,125)	105 (88,125)	107 (91,125)	0.092
missing	232	122	110	
HbA1c percentage	12 (11,14)	12 (10,14)	12 (11,14)	0.003
Missing	1,208	585	623	
Measures of severity				
Triage urgency classification				
Immediate	212 (9.6%)	89 (8.8%)	123 (10%)	
Very urgent	897 (41%)	421 (41%)	476 (40%)	
Urgent	532 (24%)	247 (24%)	285 (24%)	
Non-urgent	142 (6.5%)	68 (6.7%)	74 (6.3%)	

Continued

Table 1 Continued

Characteristic	Overall, N = 2198*	Year 1 (2019–20), N = 1015*	Year 2 (2020–21), N = 1183*	P value†
Standard	5 (0.2%)	2 (0.2%)	3 (0.3%)	
Not documented	391 (18%)	184 (18%)	207 (17%)	
Unknown	19 (0.9%)	4 (0.4%)	15 (1.3%)	
pH	7.32 (7.15,7.39)	7.34 (7.19,7.39)	7.30 (7.11,7.39)	<0.001
Missing	111	53	58	
Fluid bolus >=20 mls/kg	225 (10%)	64 (6.3%)	161 (14%)	<0.001
Inotropes / vasopressors	11 (0.5%)	4 (0.4%)	7 (0.6%)	0.5
Mechanical ventilation	20 (0.9%)	5 (0.5%)	15 (1.3%)	0.056
Route of initial insulin administration				<0.001
Subcutaneous	1,247 (57%)	621 (61%)	626 (53%)	
Intravenous	936 (43%)	390 (39%)	546 (47%)	
Missing	15	4	11	
Presentation in diabetic keto-acidosis				<0.001
Not in DKA	1,235 (56%)	620 (61%)	615 (52%)	
Mild	301 (14%)	140 (14%)	161 (14%)	
Moderate	268 (12%)	114 (11%)	154 (13%)	
Severe	394 (18%)	141 (14%)	253 (21%)	
Disposition‡				
Admission to inpatient ward	1,766 (80%)	828 (82%)	938 (79%)	0.2
High dependency unit	345 (16%)	138 (14%)	207 (17%)	0.012
Paediatric intensive care unit	110 (5.0%)	38 (3.7%)	72 (6.1%)	0.012
Critical care retrieval	21 (1.0%)	10 (1.0%)	11 (0.9%)	0.9
Transfer to other hospital	68 (3.1%)	26 (2.6%)	42 (3.6%)	0.2
Discharged home from ED	25 (1.1%)	12 (1.2%)	13 (1.1%)	0.9
Admitted to short stay unit	40 (1.8%)	28 (2.8%)	12 (1.0%)	0.002
Patient died	1 (<0.1%)	0 (0%)	1 (<0.1%)	>0.9
Length of stay in hospital (days)	4 (2,5)	4 (2,5)	4 (2,5)	0.2
Missing	12	3	9	
Length of stay in hospital >72 hrs	1,587 (73%)	709 (70%)	878 (75%)	0.013
Missing	12	3	9	

*Median (25%–75%); n (%).
†Wilcoxon rank-sum test; Pearson's χ^2 test; Fisher's exact test.
‡Tick all that apply.

SARS-CoV-2 testing

In children with new onset and pre-existing diabetes, 1028 were negative for SARS-CoV-2 on nasopharyngeal swabs (reverse transcription polymerase chain reaction), while 316 children were not tested. Of 12 children with new onset diabetes who tested positive for SARS-CoV-2 on nasopharyngeal swab, 10 presented in DKA (online supplemental table E). Four of 155 children with pre-existing diabetes tested positive for SARS-CoV-2 on nasopharyngeal swab; all four presented in DKA. In total, 37 children were tested for SARS-CoV-2

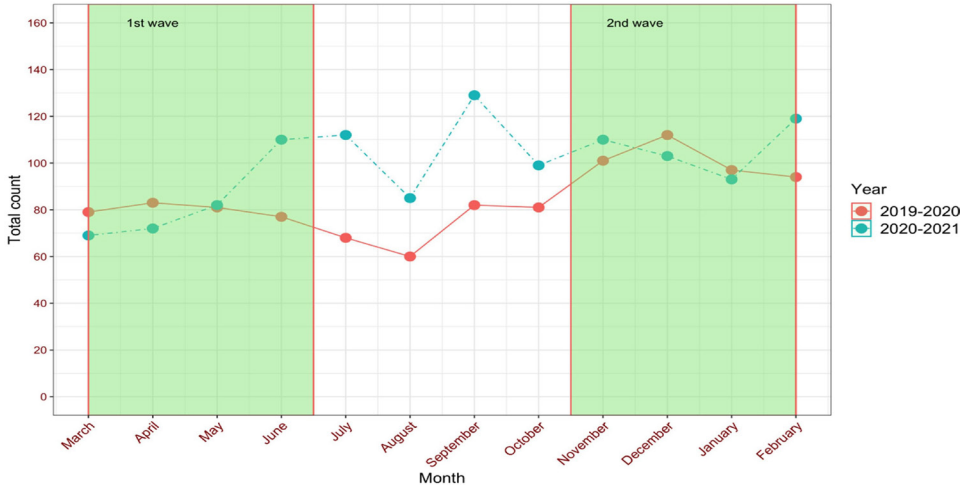

Figure 1 Number of cases of new onset diabetes in the Diabetes Mellitus in Children and Young People in the SARS-CoV-2 Pandemic study.

Table 2 Severity and outcomes of patients with new-onset diabetes in cohort

Characteristics	Overall, N=2198*	Year 1 (2019–2020), N=1015*	Year 2 (2020–2021), N=1183*	P value†
Measures of severity				
Triage urgency classification				
Immediate	212 (9.6)	89 (8.8)	123 (10)	
Very urgent	897 (41)	421 (41)	476 (40)	
Urgent	532 (24)	247 (24)	285 (24)	
Non-urgent	142 (6.5)	68 (6.7)	74 (6.3)	
Standard	5 (0.2)	2 (0.2)	3 (0.3)	
Not documented	391 (18)	184 (18)	207 (17)	
Unknown	19 (0.9)	4 (0.4)	15 (1.3)	
pH	7.32 (7.15–7.39)	7.34 (7.19–7.39)	7.30 (7.11–7.39)	<0.001
Missing	111	53	58	
Fluid bolus ≥20 mL/kg	225 (10)	64 (6.3)	161 (14)	<0.001
Inotropes/vasopressors	11 (0.5)	4 (0.4)	7 (0.6)	0.5
Mechanical ventilation	20 (0.9)	5 (0.5)	15 (1.3)	0.056
Route of initial insulin administration				<0.001
Subcutaneous	1247 (57)	621 (61)	626 (53)	
Intravenous	936 (43)	390 (39)	546 (47)	
Missing	15	4	11	
Presentation in DKA				<0.001
Not in DKA	1235 (56)	620 (61)	615 (52)	
Mild	301 (14)	140 (14)	161 (14)	
Moderate	268 (12)	114 (11)	154 (13)	
Severe	394 (18)	141 (14)	253 (21)	
Disposition‡				
Admission to inpatient ward	1766 (80)	828 (82)	938 (79)	0.2
High-dependency unit	345 (16)	138 (14)	207 (17)	0.012
Paediatric intensive care unit	110 (5.0)	38 (3.7)	72 (6.1)	0.012
Critical care retrieval	21 (1.0)	10 (1.0)	11 (0.9)	0.9
Transfer to other hospital	68 (3.1)	26 (2.6)	42 (3.6)	0.2
Discharged home from ED	25 (1.1)	12 (1.2)	13 (1.1)	0.9
Admitted to short stay unit	40 (1.8)	28 (2.8)	12 (1.0)	0.002
Patient died	1 (<0.1)	0 (0)	1 (<0.1)	>0.9
Hospital length of stay (days)	4 (2–5)	4 (2–5)	4 (2–5)	0.2
Missing	12	3	9	
Hospital length of stay >72 hours	1587 (73)	709 (70)	878 (75)	0.013
Missing	12	3	9	

*n (%), median (25%–75%).
†Pearson's χ^2 test, Fisher's exact test, Wilcoxon rank-sum test.
‡Tick all that apply.
DKA, diabetic ketoacidosis; ED, emergency department.

antibodies, of which eight were positive (online supplemental table F).

Delays in presentations

Median symptom duration before attendance for new-onset diabetes in year 2 (14 days, IQR 7–28) was similar to year 1 (14 days, IQR 7–30) (online supplemental table D). There was no documented delay in 92% of children presenting with new onset diabetes in the pandemic year, similar to the prepandemic year (tables 3 and 4). Across both years, most instances of documented delay related to referral from primary care to EDs in children with new onset diabetes.

DISCUSSION

We have demonstrated an increase in new onset diabetes and severity of DKA during the first year of the COVID pandemic, in the context of unchanged patient demographics and symptom duration. Increased severity was reflected in biochemical and physiological parameters, administration of fluid boluses, and increases in severe DKA and intensive care admissions. This was contrasted by a reduction in decompensation of established disease during the pandemic year. Rates of delayed presentation to EDs were not different between study years in either new onset or decompensated diabetes. The seasonal variation of a peak in winter and a trough in summer reported in the prepandemic years[17] was lost in the COVID-19 pandemic year.

Comparison to existing literature

The 17% increase in new onset diabetes in the first year of the COVID pandemic appears to represent a true rise, unique to this year. The population incidence of new onset diabetes in children over the past 5 years is 3%–5%, as reported from the National Paediatric Diabetes audit (NPDA).[18] This is also supported by similar findings of a 20.7% rise in the first pandemic year

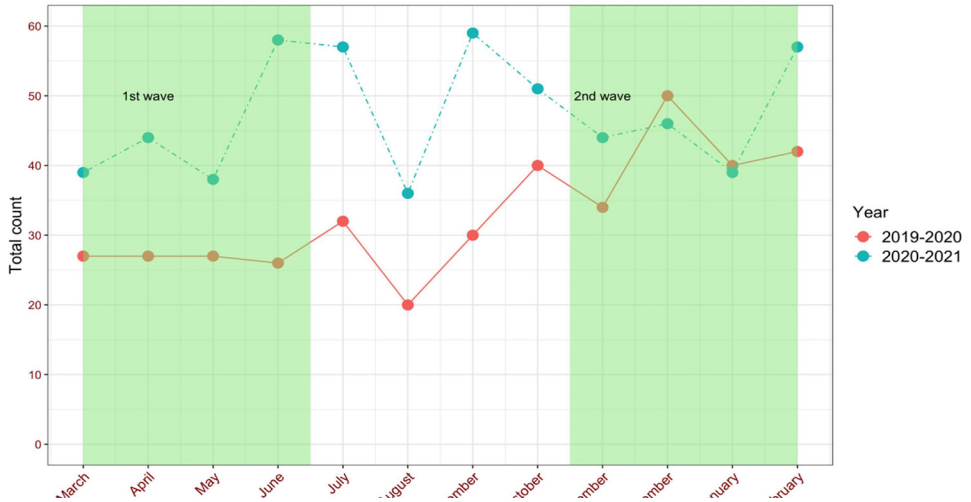

Figure 2 Number of cases of diabetic ketoacidosis in children with new onset diabetes in the Diabetes Mellitus in Children and Young People in the SARS-CoV-2 Pandemic study

reported from NPDA[18] A further study showed an increase of 57% in children diagnosed with type 1 diabetes mellitus (T1DM) during the first pandemic year versus the previous 5 years.[4]

The DIMPLES study is a unique study from the ED that has demonstrated that DKA at presentation in new onset diabetes was greater during the pandemic era compared with the previous year. Children were at higher risk of DKA both during lockdown and during the period of partial restrictions in the pandemic year (figure 2). There were increases in the number of children with DKA who received a fluid bolus of 20 mL/kg. Eighty seven per cent of children who received a fluid bolus of 20 mL/kg or more in the pandemic year had severe DKA. During the study period, national guidance (British Society of Paediatric Endocrinology and Diabetes) changed in regard to fluid management, which could have also contributed.

Proposed reasons for increased frequency and severity of DKA diagnosis in children with new onset diabetes during the COVID pandemic have included delay in presentation.[5–7] We therefore included the duration of symptoms before diagnosis to evaluate this relationship, and the comparable median duration across both years suggests that delay was unlikely to be the sole factor contributing to the increased severity seen in our cohort.

There is growing evidence that increased incidence of new onset diabetes is related to previous SARS-CoV-2 infection.[2–4] A study of two large US databases of more than 2.5 million children reported that those with active/prior COVID-19 exhibited higher risk of new-onset diabetes than those without COVID-19.[2] Several observational and registry studies also showed evidence of a link between COVID-19 and severity of DKA.[3 4 8–11]

Table 3 Reasons for delay and coexisting diagnoses in patients with new onset diabetes

Characteristics	Overall, N=2198*	Year 1 (2019–2020), N=1015*	Year 2 (2020–2021), N=1183*
Delays in presentation†			
No delay documented	2051 (93)	958 (94)	1093 (92)
Delay in getting GP appointment	33 (1.5)	8 (0.8)	25 (2.1)
Delay in GP referral to hospital	50 (2.3)	24 (2.4)	26 (2.2)
General COVID-related advice to stay at home, no consultation with primary care (GP, 111 or equivalent)	5 (0.2)	0 (0)	5 (0.4)
Advised to stay at home as outcome of primary care consultation (GP, 111 or equivalent), either COVID or non-COVID-related	22 (1.0)	6 (0.6)	16 (1.4)
Parent/child concerns over visiting hospital, non-COVID related	4 (0.2)	2 (0.2)	2 (0.2)
Parent/child concerns over visiting hospital, related to COVID exposure	5 (0.2)	1 (<0.1)	4 (0.3)
Other	47 (2.1)	20 (2.0)	27 (2.3)
Coexisting diagnoses†			
Asthma/wheeze	16 (0.7)	8 (0.8)	8 (0.7)
Infection	98 (4.5)	54 (5.3)	44 (3.7)
Mental health crisis	3 (0.1)	2 (0.2)	1 (<0.1)
Trauma	3 (0.1)	1 (<0.1)	2 (0.2)
Other	39 (1.8)	19 (1.9)	20 (1.7)
None of the above	2047 (93)	935 (92)	1112 (94)

*n (%).
†Tick all that apply.
GP, general practitioner.

Table 4 Reasons for delay and coexisting diagnoses in patients with decompensation of pre-existing diabetes

Characteristics	Overall, N=420*	Year 1 (2019–2020), N=244*	Year 2 (2020–2021), N=176*
Delays in presentation†			
No delay documented	409 (97)	238 (98)	171 (97)
Delay in getting GP appointment	0 (0)	0 (0)	0 (0)
Delay in GP referral to hospital	1 (0.2)	1 (0.4)	0 (0)
General COVID-related advice to stay at home, no consultation with primary care (GP, 111 or equivalent)	1 (0.2)	0 (0)	1 (0.6)
Advised to stay at home as outcome of primary care consultation (GP, 111 or equivalent), either COVID or non-COVID-related	0 (0)	0 (0)	0 (0)
Parent/child concerns over visiting hospital, non-COVID related	0 (0)	0 (0)	0 (0)
Parent/child concerns over visiting hospital, related to COVID exposure	0 (0)	0 (0)	0 (0)
Other	9 (2.1)	5 (2.0)	4 (2.3)
Coexisting diagnoses†			
Asthma/wheeze	1 (0.2)	1 (0.)	0 (0)
Infection	66 (16)	47 (19)	19 (11)
Mental health crisis	10 (2.4)	5 (2.0)	5 (2.8)
Trauma	0 (0)	0 (0)	0 (0)
Other	7 (1.7)	3 (1.2)	4 (2.3)
None of the above	337 (80)	188 (77)	149 (85)
Contributing factors†			
Patient compliance with treatment	144 (34)	80 (33)	64 (36)
Availability/supply of therapeutic treatment	11 (2.6)	6 (2.5)	5 (2.8)
Travel (eg, left drug at home)	5 (1.2)	2 (0.8)	3 (1.7)
Family-related issues	38 (9.0)	17 (7.0)	21 (12)
Equipment failure	39 (9.3)	17 (7.0)	22 (12)
Other	22 (5.2)	12 (4.9)	10 (5.7)
None	215 (51)	130 (53)	85 (48)

*n (%).
†Tick all that apply.
GP, general practitioner.

From our data, the corelation with previous SARS-CoV-2 infection and new onset diabetes could not be tested as there was a paucity of testing for SARS-CoV-2 antibodies. It was also not possible to determine whether incidence of new onset diabetes or risk of decompensation was increased during acute SARS-CoV-2 infection due to the low volume of positive RT-PCR tests. The peaks of new-onset diabetes we have demonstrated followed surges of COVID-19 by approximately 3 months (figure 1). We hypothesise that there may be an association between COVID-19 and new-onset diabetes that cannot be captured by acute SARS-CoV-2 testing, akin to the late temporal association with PIMS-TS (Paediatric multisystem inflammatory syndrome temporally associated with COVID-19)

The DIMPLES data demonstrates a reduction in ED presentations for children with decompensated pre-existing diabetes during the pandemic, a phenomenon which has not previously been reported. Additionally, the DIMPLES study showed that there was no increase in severity of DKA or duration of hospital stay in children with pre-existing diabetes. Children with DKA usually present through ED; hence, the reduction in numbers is likely to be a true reduction. However, some participating institutions created alternative pathways for children with diabetes and implemented new ways of managing these patients effectively and safely. DKA in children with pre-existing type 1 diabetes is usually precipitated by insulin omission, concurrent illness or both. The pandemic offered opportunities for virtual diabetes clinics which may have contributed to increased engagement.[19] The NPDA audit also reported better glycaemic control in the pandemic compared with previous years.[18] Young people and families were managing their pre-existing diabetes and emergencies well with better implementation of sick day rules, resulting in reduced DKA. Learning from this and finding a system that allows flexibility between virtual and hospital clinics and is responsive to clinical needs may be of benefit and cost effective in the management of chronic diseases.

Implications for clinical practice and future research

Awareness of the increased incidence of new onset paediatric diabetes and the severity of DKA in the pandemic among both healthcare professionals and parents is vital. A targeted approach of educating people who will be in most contact with children (families, teachers and primary care clinicians) may help in increasing vigilance, recognising subtle symptoms, early identification of new onset diabetes and reducing the incidence of DKA.

The estimated incidence of new-onset T1DM in children was 3%–5% annually in the prepandemic period; an increase of 17% placed unexpected pressure on services. It is possible that we may see further high incidence years with new onset diabetes. Resource allocation and planning services are vital. Capture of pancreatic autoantibodies in all children with new onset diabetes is important.

It has historically been difficult to prove a causal relationship between viruses and T1DM due to the natural history and complexity of the disease. However, evidence exists in the form of animal studies and observational studies of new onset diabetes after viral infections to suggest that a link between these entities is likely.[20] Autoimmunity and beta cell destruction start long

before the clinical symptoms of T1DM, infectious triggers may accelerate the diagnosis or initiate the disease.[21] Additionally, the sensitivity, the specificity and the paucity in testing for SARS-CoV-2 in children makes it difficult to associate previous SARS-CoV-2 infection and new onset diabetes.

Strengths and limitations

As a major strength, our study uniquely captures highly granular data on children with diabetes presenting to EDs affliated to the PERUKI network representing emergency care facilities from the entirety of the UK and Ireland. The large number of sites involved provides assurance that our results are reflective of actual patterns nationally. Paucity of testing for SARS-CoV-2 antibodies may have led to an underestimation of the impact of the virus on the reported outcomes. Due to missing data on deprivation and ethnicity, and it's not being missing at random, multivariable modelling was not undertaken. The DIMPLES study is a retrospective study; all characteristics of study participants could not be captured. Each centre has a defined geographical area and population providing a near 100% of new-onset diabetes from that area being captured. Population movement can still cause an occasional patient with new onset diabetes to be missed; similarly, a new onset diabetes from another area can be picked up; however, population movement during the pandemic was restricted.

CONCLUSIONS

The causes of paediatric diabetes are complex and can result from several pathogenic processes; however, given the high incidence of new onset diabetes and the incidence and severity of DKA, it is possible that SARS-CoV-2 may have a role as an accelerator or precipitator in a genetically predisposed child. Prospective studies, a priori designed, are needed to help us understand the role of SARS-CoV-2 in the pathogenesis of new onset diabetes. This is important, given the higher observed incidence and DKA severity noted in the pandemic.

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Correction notice This paper has been amended since it was first published. Some typographical errors were introduced in the headers for table 1 and these have now been removed.

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