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Research letter

Variable incidence of ketoacidosis in youth with type 1 diabetes onset during COVID-19 pandemic peaks in France

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During the 2020 coronavirus pandemic peak, several groups described a delay in the diagnosis of type 1 diabetes in youth, resulting in an increased rate of ketoacidosis (DKA) [1–5]. This probably reflects the fear of approaching medical services and the pandemic-related redistribution of healthcare resources [6]. After a year and half of Covid pandemic in Europe, its impact on access to healthcare services for an early diagnosis of type 1 diabetes should be assessed.

We examined the frequency and severity of DKA in youth at diagnosis of type 1 diabetes in France in the following timeframes of 2020 with respect to the same periods of the previous years (2017–2019): from 1 January to 31 December, only considering the months of lockdown/curfew or month-by-month.

Data were obtained from the national AJD Registry (*Aide aux Jeunes Diabétiques*), which collects records on type 1 diabetes onset in youth (0–15 years) from 164 pediatric centers in France (about 70% of national centers).

Ketoacidosis and severe DKA were defined according to the International Society for Pediatric and Adolescent Diabetes (ISPAD) recommendations [7]. The frequencies of DKA and severe DKA at diagnosis of type 1 diabetes in 2020 were compared with the ones in 2019, 2018, 2017. Rates of DKA and severe DKA during the 2020 lockdown periods in France from mid-March to mid-May (first lockdown) and from October to November (curfew and partial lockdown) were compared with the same periods of the previous years. Differences are presented as incidence rate ratio (IRR) with 95% confidence intervals (CIs). A two-sided $P < 0.05$ was considered statistically significant.

Between 1 January and 31 December 2020, a total of 2054 children were diagnosed with type 1 diabetes – higher than previous years (+9.1% vs 2019, $n = 1882$; +17.1% vs 2018, $n = 1754$; +16.0% vs 2017, $n = 1770$). Similarly to previous years, 52.5% were males (53.0% in 2019, 53.1% in 2018, 52.4% in 2017), 21.9% aged 0–4 years (21.7% in 2019, 21.7% in 2018, 23.4% in 2017), 35% 5–9 years (35.6% in 2019, 34.2% in 2018, 35.5% in 2017) and 43.1% 10–14 years (42.7% in 2019, 44.1% in 2018, 41.1% in 2017).

The proportion of children presenting with DKA was 48.7% ($n = 1000$) in 2020, 40.7% ($n = 765$) in 2019, 43.0% ($n = 754$) in 2018 and 41.1% ($n = 728$) in 2017. When compared with the previous years, the frequency of DKA was significantly higher in 2020 than in 2019 ($P < 0.001$), in 2018 ($P = 0.009$) and in 2017 ($P < 0.001$) (Table 1).

Similarly, the rate of severe DKA was higher in 2020, accounting for 18.5% of the cases compared to 13.2% in 2019 ($P < 0.001$), and 14.9% in 2018 ($P = 0.006$) and 11.8% in 2017 ($P < 0.001$).

During the first lockdown – mid-March to mid-May 2020 – the rate of youth with DKA was significantly higher compared with the same periods in 2019 (51.5% versus 38.0%, $P = 0.002$), in 2018 (51.5% versus 41.0%, $P = 0.024$), and in 2017 (51.5% versus 40.2%, $P = 0.014$). Similarly, the rate of severe DKA in the period was higher in 2020 than in 2019 (22.3% vs 12.0%, $P < 0.001$), in 2018 (22.3% vs 16.5%, $P = 0.005$) and in 2017 (22.3% vs 10.5%, $P < 0.001$).

Interestingly, when analyzed by month, the rate of presentation with severe DKA in 2020 compared to 2019 was higher in April (23.0% vs 17.4%, IRR 2.44 [95% CI, 1.30–4.77], $P = 0.003$), and in May (23.4% vs 7.4%, IRR 3.15 [1.55–7.08], $P < 0.001$), but also out of the lockdown period, in June (18.9% vs 10.0%, IRR 1.89 [0.96–3.94], $P = 0.04$) and in July (23.5% vs 9.3%, IRR 2.52 [1.27–5.45], $P = 0.004$).

During the second national lockdown in October-November 2020, the rate of DKA and severe DKA were similar to the same period of the previous years (Table 1).

This study confirmed the increased rate of DKA and severe DKA in youth at onset of type 1 diabetes in 2020 compared to the previous years. Analysis of monthly rates reported an increase of DKA cases during the first pandemic peak and concomitant lockdown (mid-March to mid-May), as previously described [1–4]. Our data highlighted a persistent increase in the DKA rate in June and July, although Covid-19 incidence decreased. This suggests that the delayed diagnosis may be due to the fear of accessing medical units more than to a reduction in clinical services related to the national restrictions.

Moreover, this study did not find an increased DKA rate during the second pandemic peak (October-November), although no specific national campaign was run to encourage families not to delay medical consultations for their children after the first lockdown. One possible explanation is reduced fear of families for approaching healthcare services or, possibly, better accessibility to routine visits. These results are in line with national data previously published and are supported by the strenght of the national registry and the annual incidence rates [8]. Limitations of this study include the lack of socio-demographics and Covid-19 infectious data for youths for the periods of interest. Further research to better define the causes for the increased DKA rates during the pandemic is needed for a future implementation of prompt diagnostic programs.

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Table 1
Incidence relative risk (IRR) of diabetic ketoacidosis (DKA) and severe diabetic ketoacidosis at the onset of type 1 diabetes in the pediatric population (0–15 years) during the whole year 2020 and during the national lockdown periods compared to the same periods in 2019, 2018 and 2017.

1 January 2020 to 31 December 2020 vs same periodIRR (95% CI)						
	2019	*P* value	2018	*P* value	2017	*P* value
DKA	1.19 (1.08–1.31)	<0.001	1.13 (1.02–1.24)	0.009	1.18 (1.07–1.30)	<0.001
Severe DKA	1.40 (1.19–1.65)	<0.001	1.24 (1.06–1.46)	0.006	1.57 (1.32–1.87)	<0.001
15 March 2020 to 15 May 2020 vs same period IRR (95% CI)						
	2019	*P* value	2018	*P* value	2017	*P* value
DKA	1.35 (1.11–1.65)	0.002	1.25 (1.02–1.54)	0.024	1.28 (1.04–1.57)	0.014
Severe DKA	1.85 (1.33–2.60)	<0.001	1.35 (0.98–1.86)	0.005	2.13 (1.47–3.12)	<0.001
1 October 2020 to 31 November 2020 vs same period IRR (95% CI)						
	2019	*P* value	2018	*P* value	2017	*P* value
DKA	1.0 (0.78–1.27)	1.00	1.07 (0.83–1.38)	0.57	1.00 (0.79–1.29)	0.95
Severe DKA	1.25 (0.80–1.94)	0.29	1.25 (0.80–1.97)	0.30	1.46 (0.92–2.35)	0.09

Legend.
Abbreviations: IRR, incidence relative risk; DKA, diabetic ketoacidosis.
Diabetic ketoacidosis (DKA): pH level <7.3 and/or serum bicarbonate level <15 mmol/L; severe diabetic ketoacidosis: pH level <7.1 and/or serum bicarbonate level <5 mmol/L.

Authors' contribution

Conceptualization: DL, CC and JB - Data curation: CC JD and DL - Formal Analysys: JD and EG - Project administration: CC - Software: EG, DL - Methodology: CC and JB - Validation: JB and CC - Writing - original draft: JD and EG - Writing - review and editing: JB, MK, CC - Supervision: JB. C.C. and J.B. are guarantors of this work and, as such, had full access to all the data in the study and take the responsibility for the integrity of the data and the accurancy of the data analysis.

Appendix supplementary material

Supplementary materials (Appendix) associated with this article can be found at http://www.scincedirect.com at doi . . .

Declaration of Competing Interest

No potential conflicts of interest relevant to this article were reported.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.diabet.2022.101322.

References

[1] Rabbone I, Schiaffini R, Cherubini V, Maffeis C, Scaramuzza A, Diabetes Study Group of the Italian Society for Pediatric Endocrinology and Diabetes. Has COVID-19 delayed the diagnosis and worsened the presentation of type 1 diabetes in children? Diabetes Care 2020;43:2870–2.
[2] Kamrath C, Mönkemöller K, Biester T, Rohrer TR, Warncke K, et al. Ketoacidosis in children and adolescents with newly diagnosed type 1 diabetes during the COVID-19 pandemic in Germany. JAMA 2020;324:801–4.
[3] Unsworth R, Wallace S, Oliver NS, Yeung S, Kshirsagar A, Naidu H, et al. New-onset type 1 diabetes in children during COVID-19: multicenter regional findings in the U.K. Diabetes Care 2020;43:e170–1.
[4] Ho J, Rosolowsky E, Pacaud D, Huang C, Lemay JA, Brockman N, et al. Diabetic ketoacidosis at type 1 diabetes diagnosis in children during the COVID-19 pandemic. Pediatr Diabetes 2021;22:552–7 Epub 2021 Mar 27PMID: 33745226PMCID: PMC8251027. doi: 10.1111/pedi.13205.
[5] Dżygało K, Nowaczyk J, Szwilling A, Kowalska A. Increased frequency of severe diabetic ketoacidosis at type 1 diabetes onset among children during COVID-19 pandemic lockdown: an observational cohort study. Pediatr Endocrinol Diabetes Metab 2020;26:167–75 EnglishPMID: 33554490. doi: 10.5114/pedm.2020.101003.
[6] Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. Lancet Child Adolesc Health 2020;4:e10–1 Epub 2020 Apr 9PMID: 32278365PMCID: PMC7146704. doi: 10.1016/S2352-4642(20)30108-5.
[7] Wolfsdorf JI, Glaser N, Agus M, Fritsch M, Hanas R, Rewers A, et al. ISPAD Clinical Practice Consensus Guidelines 2018: diabetic ketoacidosis and the hyperglycemic hyperosmolar state. Pediatr Diabetes 2018;19(Suppl 27):155–77.
[8] Piffaretti C, Mandereau-Bruno L, Guilmin-Crepon S, Choleau C, Coutant R, Fosse-Edorh S. Trends in childhood type 1 diabetes incidence in France, 2010-2015. Diabetes Res Clin Pract 2019;149:200–7 Epub 2018 Nov 12PMID: 30439385. doi: 10.1016/j.diabres.2018.11.005.

Juliette Delpeut
Service de pédiatrie, CHRU Brest, Brest, France

Elisa Giani
Department of Biomedical Sciences, Humanitas University, via Rita Levi Montalcini 4, Pieve Emanuele, Milan 20090, Italy
Service d'endocrinologie gynécologie et diabétologie pédiatrique, APHP centre, Hôpital Necker Enfants Malades, Paris, France
INSERM U1016, Institut Cochin, Paris, France

Dalila Louet
Aide aux Jeunes Diabétiques, 38 rue Eugène Oudiné, Paris 75013, France

Marc de Kerdanet
Aide aux Jeunes Diabétiques, 38 rue Eugène Oudiné, Paris 75013, France
Pediatric Endocrinology Unit, University Hospital, Rennes, France

Carine Choleau
Aide aux Jeunes Diabétiques, 38 rue Eugène Oudiné, Paris 75013, France

Jacques Beltrand*
the AJD Study Group (see appendix on line)
Service d'endocrinologie gynécologie et diabétologie pédiatrique, APHP centre, Hôpital Necker Enfants Malades, Paris, France
INSERM U1016, Institut Cochin, Paris, France
Aide aux Jeunes Diabétiques, 38 rue Eugène Oudiné, Paris 75013, France
UFR de Médecine, Université de Paris, Paris, France

*Corresponding author at: APHP Centre, Hôpital Necker Enfants Malades, Université de Paris, 149 rue de Sèvres, Paris 75015, France.
E-mail address: jacques.beltrand@aphp.fr (J. Beltrand).

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