RESEARCH LETTER

Ketoacidosis in Children and Adolescents With Newly Diagnosed Type 1 Diabetes During the COVID-19 Pandemic in Germany

During the coronavirus disease 2019 (COVID-19) pandemic, a significantly lower rate of health care use has been reported, potentially leading to delayed medical care.[1] Diabetic ketoacidosis is an acute life-threatening complication of a delayed diagnosis of type 1 diabetes.[2] We investigated the frequency of diabetic ketoacidosis in children and adolescents at diagnosis of type 1 diabetes in Germany during the first 2 months of the COVID-19 pandemic.

Methods | This study used data from the German Diabetes Prospective Follow-up Registry (DPV) of children and adolescents with the diagnosis of type 1 diabetes between March 13, 2020, when most kindergartens and schools were closed to reduce interpersonal contacts, through May 13, 2020. The DPV registry has a nationwide coverage of more than 90% of pediatric patients with type 1 diabetes.[3] Since 2018, 217 diabetes centers (hospitals and medical practices) have transferred information from pediatric patients with newly diagnosed type 1 diabetes.

Diabetic ketoacidosis was defined as a pH level less than 7.3 and/or bicarbonate level less than 15 mmol/L, and severe diabetic ketoacidosis as a pH level less than 7.1 and/or bicarbonate level less than 5 mmol/L.[2,3] The frequencies of diabetic ketoacidosis and severe diabetic ketoacidosis observed during the COVID-19 period were compared with the same periods in 2018 and 2019 using multivariable logistic regression, adjusting for age, sex, and immigrant background (defined as patient or at least 1 parent born outside Germany). Differences were presented as adjusted relative risks (aRRs) with 95% CIs. A 2-sided $P < .05$ was considered statistically significant. All analyses were performed with SAS version 9.4 (SAS Institute Inc). Informed consent for participation in the DPV registry was obtained from patients or their parents by verbal or written procedure, as approved by the responsible data protection officers at each center. The analysis of anonymized data was approved by the ethics committee of the University of Ulm.

Results | We obtained and analyzed data of 532 children and adolescents with newly diagnosed type 1 diabetes from March 13 through May 13, 2020, from 216 of 217 diabetes centers. The median age of the cohort was 9.9 years (interquartile range, 5.8-12.9 years; 61.5% male) (**Table 1**). Diabetic

Table 1. Characteristics of Pediatric Patients Newly Diagnosed With Type 1 Diabetes in Germany From March 13 Through May 13, 2020, During the COVID-19 Pandemic, and During the Same Period in 2019 and 2018

Characteristic	No. (%)		
	March 13 to May 13, 2020 (n = 532)	March 13 to May 13, 2019 (n = 503)	March 13 to May 13, 2018 (n = 456)
Age at diagnosis, median (IQR), y	9.9 (5.8-12.9)	9.1 (5.5-12.6)	9.7 (5.8-13.2)
Sex			
Male	327 (61.5)	263 (52.3)	254 (55.7)
Female	205 (38.5)	240 (47.7)	202 (44.3)
Age groups, y			
<6	135 (25.4)	147 (29.2)	120 (26.3)
6-11	232 (43.6)	211 (42.0)	186 (40.8)
12-18	165 (31.0)	145 (28.8)	150 (32.9)
Immigrant background[a]	147 (27.6)	127 (25.2)	115 (25.2)
Diabetic ketoacidosis[b]			
Age group, y			
All	238 (44.7)	123 (24.5)	110 (24.1)
<6	70 (51.9)	27 (18.4)	29 (24.2)
6-11	94 (40.5)	58 (27.5)	50 (26.9)
12-18	74 (44.8)	38 (26.2)	31 (20.7)
Severe diabetic ketoacidosis[b]			
Age group, y			
All	103 (19.4)	70 (13.9)	56 (12.3)
<6	33 (24.4)	18 (12.2)	14 (11.7)
6-11	44 (19.0)	30 (14.2)	25 (13.4)
12-18	26 (15.8)	22 (15.2)	17 (11.3)

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range.

[a] Immigrant background was defined as patient or at least 1 parent born outside Germany.

[b] Diabetic ketoacidosis: 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.

Table 2. Adjusted Relative Risk of Diabetic Ketoacidosis and Severe Diabetic Ketoacidosis at Diabetes Diagnosis From March 13 Through May 13, 2020, During the COVID-19 Pandemic, Compared With the Same Periods in 2019 and 2018

	COVID-19 period 2020 vs same period			
	2019		2018	
	aRR (95% CI)	*P* value	aRR (95% CI)	*P* value
Diabetic ketoacidosis[a]				
All patients[b]	1.84 (1.54-2.21)	<.001	1.85 (1.54-2.24)	<.001
Age groups, y[c]				
<6	2.75 (1.88-4.02)	<.001	2.12 (1.48-3.02)	<.001
6-11	1.51 (1.16-1.98)	.003	1.54 (1.16-2.04)	.003
12-18	1.73 (1.25-2.38)	<.001	2.15 (1.51-3.08)	<.001
Sex[d]				
Male	1.70 (1.34-2.16)	<.001	2.11 (1.61-2.76)	<.001
Female	2.01 (1.52-2.64)	<.001	1.63 (1.25-2.12)	<.001
Immigrant background[e]				
Yes	1.96 (1.42-2-71)	<.001	1.88 (1.36-2.60)	<.001
No	1.78 (1.43-2.22)	<.001	1.84 (1.46-2.31)	<.001
Severe diabetic ketoacidosis[a]				
All patients[b]	1.37 (1.04-1.81)	.03	1.55 (1.15-2.10)	.004
Age groups, y[c]				
<6	1.90 (1.12-3.23)	.02	2.06 (1.16-3.65)	.01
6-11	1.30 (0.85-1.99)	.23	1.37 (0.87-2.15)	.17
12-18	1.03 (0.61-1.75)	.90	1.39 (0.79-2.47)	.25
Sex[d]				
Male	1.16 (0.83-1.64)	.38	1.79 (1.19-2.70)	.006
Female	1.77 (1.10-2.83)	.02	1.31 (0.84-2.06)	.24
Immigrant background[e]				
Yes	1.57 (0.97-2.54)	.06	1.68 (1.01-2.77)	.04
No	1.26 (0.89-1.79)	.18	1.49 (1.03-2.17)	.04

Abbreviations: aRR, adjusted relative risk; COVID-19, coronavirus disease 2019.

[a] Diabetic ketoacidosis: 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.

[b] Adjusted for age at diabetes onset, sex, and immigrant background.

[c] Adjusted for sex and immigrant background.

[d] Adjusted for age at diabetes onset and immigrant background.

[e] Adjusted for age at diabetes onset and sex. Immigrant background was defined as patient or at least 1 parent born outside Germany.

ketoacidosis was present in 238 patients (44.7%) and severe ketoacidosis in 103 patients (19.4%) (Table 1). During the COVID-19 period in 2020, the frequency of diabetic ketoacidosis was significantly higher compared with the 2 previous years (44.7% in 2020 vs 24.5% in 2019; aRR, 1.84 [95% CI, 1.54-2.21]; $P < .001$; vs 24.1% in 2018; aRR, 1.85 [95% CI, 1.54-2.24]; $P < .001$). The incidence of severe diabetic ketoacidosis was also significantly higher compared with the previous years (19.4% in 2020 vs 13.9% in 2019; aRR, 1.37 [95% CI, 1.04-1.81]; $P = .03$; vs 12.3% in 2018; aRR, 1.55 [95% CI, 1.15-2.10]; $P = .004$) (**Table 2**). Children younger than 6 years had the highest risk for diabetic ketoacidosis (51.9% in 2020 vs 18.4% in 2019; aRR, 2.75 [95% CI, 1.88-4.02]; $P < .001$; vs 24.2% in 2018; aRR, 2.12 [95% CI, 1.48-3.02]; $P < .001$) and severe diabetic ketoacidosis (24.4% in 2020 vs 12.2% in 2019; aRR, 1.90 [95% CI, 1.12-3.23]; $P = .02$; vs 11.7% in 2018; aRR, 2.06 [95% CI, 1.16-3.65]; $P = .01$) during the COVID-19 pandemic (Table 2).

Discussion | This study found a significant increase in diabetic ketoacidosis and severe ketoacidosis at diabetes diagnosis in children and adolescents during the COVID-19 pandemic in Germany. Underlying causes may be multifactorial and reflect reduced medical services, fear of approaching the health care system, and more complex psychosocial factors.[1,4]

Limitations of this study include that the individual socioeconomic status and a family history of diabetes were not available.

Further research into the possible causes of the increase in diabetic ketoacidosis during the COVID-19 pandemic and interventions to reduce diabetic ketoacidosis, such as public and health care clinician education or β-cell antibody screening, is required.

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Accepted for Publication: July 8, 2020.

Published Online: July 20, 2020. doi:10.1001/jama.2020.13445

Author Contributions: Dr Holl had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Kamrath and Mönkemöller contributed equally to this work.
Concept and design: Kamrath, Mönkemöller, Holl.
Acquisition, analysis, or interpretation of data: All authors.
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Conflict of Interest Disclosures: Dr Mönkemöller reported receiving personal fees from Medtronic outside the submitted work. Dr Biester reported receiving personal fees from Medtronic, Sanofi, Ypsomed, Novo Nordisk, AstraZeneca, DexCom, and Roche outside the submitted work. No other disclosures were reported.

Funding/Support: The German Diabetes Prospective Follow-up Registry (DPV) is supported through the German Federal Ministry for Education and Research within the German Center for Diabetes Research (DZD, grant 82DZD14A02). Further financial support was received by the German Robert Koch Institute (RKI, diabetes surveillance) and the German Diabetes Association (DDG).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank Katharina Fink (Institute of Epidemiology and Medical Biometry [ZIBMT], Ulm University, Ulm, Germany), Klemens Raile, MD, PhD (Department of Pediatric Endocrinology and Diabetology, Charité, University Medicine Berlin, Germany), and Angeliki Pappa, MD (Department of Pediatrics, University Hospital RWTH Aachen, Aachen, Germany), for their contribution to this work for methodology (Ms Fink), data analysis (Ms Fink), data collection (Drs Raile and Pappa), scientific discussion of the results (Ms Fink and Drs Raile and Pappa), and editing of the manuscript (Ms Fink and Drs Raile and Pappa). Andreas Hungele and Ramona Ranz developed the DPV software, Esther Bollow aggregated the DPV data, and Alexander Eckert, MSc, helped with the analysis (all clinical data managers, Ulm University). We thank Marianne Rohrer (Homburg) for language editing. None of the persons named received compensation for their contributions. We thank all centers participating in the DPV initiative (a list is available at www.d-p-v.eu).

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