Event Rates and Risk Factors for the Development of Diabetic Ketoacidosis in Adult Patients With Type 1 Diabetes: Analysis From the DPV Registry Based on 46,966 Patients

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Hannes Kalscheuer,[1] Jochen Seufert,[2] Stefanie Lanzinger,[3,4] Joachim Rosenbauer,[4,5] Wolfram Karges,[6] Dominik Bergis,[7] Julia K. Mader,[8] Stefan Zimny,[9] Sebastian M. Schmid,[1,4] Michael Hummel,[10] Wolfgang Kerner,[11] and Reinhard W. Holl,[3,4] on behalf of the DPV Initiative

Diabetic ketoacidosis (DKA) is a life-threatening complication of type 1 diabetes mellitus (T1DM) that results from absolute insulin deficiency and is marked by acidosis, ketosis, and hyperglycemia (1). Therefore, prevention of DKA is one goal in T1DM care, but recent data indicate increased incidence (2).

For adult patients, only limited data are available on rates and risk factors for development of DKA, and this complication remains epidemiologically poorly characterized. The Diabetes Prospective Follow-up Registry (DPV) has followed patients with diabetes from 1995. Data for this study were collected from 2000 to 2016. Inclusion criteria were diagnosis of T1DM, age at diabetes onset ≥6 months, patient age at follow-up ≥18 years, and diabetes duration ≥1 year to exclude DKA at manifestation. DKA was defined as serum pH <7.3, and rates of DKA were analyzed based on a Poisson regression model accounting for overdisperson stratified by sex, age, diabetes duration, HbA_{1c}, treatment regimen, size of diabetes center, and migration background, i.e., whether the patient or one or both parents were born outside the countries of the registry. A diabetes center that treated ≥50 adult patients with T1DM in the year 2016 was considered large.

In total, 46,966 patients were included in this study (average age 38.5 years [median 21.2], 47.6% female). The median HbA_{1c} was 7.7% (61 mmol/mol), median diabetes duration was 13.6 years, and 58.3% of the patients were treated in large diabetes centers.

On average, 2.5 DKA-related hospital admissions per 100 patient-years (PY) were observed (95% CI 2.1–3.0). The rate was highest in patients aged 18–30 years (4.03/100 PY) and gradually declined with increasing age (Fig. 1*A*). No significant differences between males (2.46/100 PY) and females (2.59/100 PY) were found (Fig. 1*B*). Individuals with a migration background had significantly higher hospitalization rates than nonmigrants (3.40/100 PY vs. 2.47/100 PY; $P < 0.05$) (Fig. 1*C*). Diabetes duration ≤2 years or >20 years was associated with lower DKA rates (2.03 and 1.62/100 PY, respectively) in comparison with diabetes duration between 5 and 10 years (Fig. 1*D*). Patients with HbA_{1c} levels <7% (53 mmol/mol) had significantly fewer DKA admissions than patients with HbA_{1c} ≥9% (75 mmol/mol) (0.88/100 PY vs. 6.04/100 PY; $P < 0.001$) (Fig. 1*E*).

Regarding therapy, use of an insulin pump (continuous subcutaneous insulin infusion [CSII]) was not associated with higher DKA rates (Fig. 1*F*), while patients aged 31–50 years on CSII showed lower rates than patients using multiple daily injections (2.21 vs. 3.12/100 PY; adjusted $P < 0.05$) (Fig. 1*G*). Treatment in a large center was associated with lower DKA-related hospital admissions (Fig. 1*H*).

The overall DKA rate was lower than in a previous DPV analysis of patients

[1]*Department of Endocrinology, Diabetes and Metabolism, University of Lübeck, Lübeck, Germany*
[2]*Division of Endocrinology and Diabetology, Department of Medicine II, Medical Center, Faculty of Medicine, University of Freiburg, Freiburg, Germany*
[3]*Institute for Epidemiology and Medical Biometry, ZIBMT, University of Ulm, Ulm, Germany*
[4]*German Center for Diabetes Research (DZD), München-Neuherberg, Germany*
[5]*Institute for Biometrics and Epidemiology, German Diabetes Center, Leibniz Institute for Diabetes Research at Heinrich Heine University, Düsseldorf, Germany*
[6]*Section of Endocrinology and Diabetology, RWTH Aachen University, Aachen, Germany*
[7]*Department of Internal Medicine 1, Goethe University Hospital, Frankfurt, Germany*
[8]*Division of Endocrinology and Diabetology, Medical University of Graz, Graz, Austria*
[9]*Department of General Internal Medicine, Endocrinology and Diabetology, Helios Clinic Schwerin, Schwerin, Germany*
[10]*Specialized Diabetes Practice, Rosenheim, Germany*
[11]*Diabetes Center Karlsburg, Karlsburg, Germany*

Corresponding author: Hannes Kalscheuer, hannes.kalscheuer@uksh.de

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H.K. and J.S. contributed equally to this work.

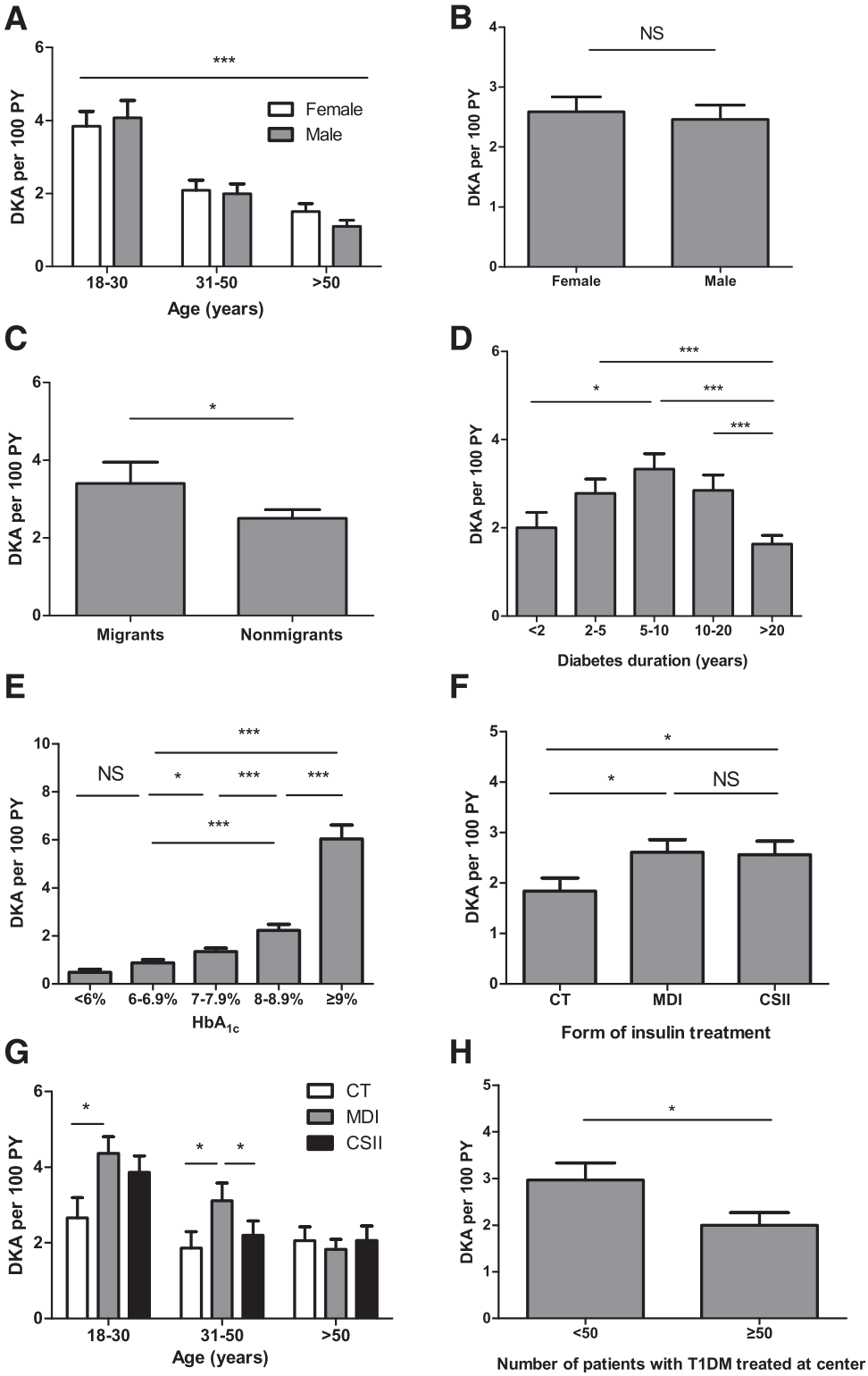

Figure 1—Adjusted rates of hospital admission for DKA. Rates per 100 PY with 95% CI were adjusted for age (*A*), sex (*B*), migration background (*C*), diabetes duration (*D*), HbA_{1c} (*E*), treatment regimen (*F*), age and treatment regimen (*G*), and size of diabetes center (*H*). CT, conventional insulin therapy; MDI, multiple daily injections; NS, not significant. *$P < 0.05$; ***$P < 0.001$.

that were ≤20 years old (3). While glycemic control in children and adolescents with T1DM can be more challenging, parents of children with T1DM may be less reluctant to visit the emergency room than the adult patient. In both adults and children, poor metabolic control was the strongest predictor of hospital admission due to DKA. This might be explained by suboptimal diabetes treatment and/or inadequate patient adherence possibly because of

poor patient education and/or other factors. In contrast to the findings in younger patients (3), the DKA rate was not higher in females, possibly demonstrating that omitting insulin injections in order to lose weight might be less prevalent in adult patients. Migrants showed increased risk for DKA, possibly due to lower household income, a separate DKA risk factor (4). Furthermore, diabetes education may be insufficient because of cultural and/or language barriers.

CSII was not associated with higher DKA rates, which stands in contrast to older studies (5). This may be attributable to technological advances in current CSII and catheter technology as well as improved patient education. In this study, patients were rarely equipped with glucose sensors; therefore, the increased use of continuous glucose monitoring since 2016 might further reduce DKA rates, especially in patients with CSII. Conventional insulin therapy is not considered a standard treatment of T1DM. Since DKA rates are low, it is a safe option for patients that need the simplest possible therapy, e.g., bedridden or mentally restricted patients.

One strength of this study is its population-based multicenter database, permitting analysis of demographic and treatment variables. Limitations are its observational design, which precludes detection of causal associations, and possible reporting biases due to the structure of the registry.

In conclusion, the results of this study identify patients with T1DM at risk for DKA (high HbA_{1c}, diabetes duration 5–10 years, migrants, age 30 years and younger) in real-life diabetes care. These at-risk individuals may need specific attention since structured diabetes education has been demonstrated to specifically reduce and prevent this acute complication.

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