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Risk Factors for Diabetic Ketoacidosis in Children with Type 1 Diabetes Mellitus: A Single-center, Cross-sectional Study in Indonesia

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Abstract

Background: Diabetic ketoacidosis (DKA), the leading cause of mortality in childhood with diabetes mellitus (DM). Identification of risk factors for DKA in children with type 1 DM (T1DM), can aid in reducing the incidence of DKA.

Objective: To determine risk factors for DKA in children with T1DM.

Methods: This was a single-centre, cross-sectional study of patients aged 0–16 years diagnosed with T1DM who were hospitalised in or visited Dr. Soetomo General Hospital in Surabaya between January 2016 and June 2021. Data on sex, age, parental educational background, parental occupation, parental age, family history of DM and DKA frequency were collected, and statistical analyses using the SPSS software.

Results: The risk of DKA was higher in children with working mothers (OR 9.3, 95%; CI 2.168–40.182, $p = 0.003$). Significant correlation between maternal age younger than 40 years and DKA frequency (OR 1.73, 95%; CI 8.684–3.478, $p = 0.000$). The highest frequency of DKA was observed in children with low parental educational level, whereas there was no correlation between age at diagnosis and parental educational level with DKA.

Conclusion: Young maternal age and working mothers might be associated with increased frequency of DKA in children with T1DM.

Keywords: diabetic ketoacidosis; type 1 diabetes mellitus; risk factor; parental age; occupation

Introduction

Approximately 26 per 100,000 children are diagnosed with type 1 diabetes mellitus (T1DM)

every year, with the rate continually increasing approximately 4% per year. Despite the increased life expectancy associated with the improvements

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in diabetes care, the mortality rate remains higher in children with T1DM than in the general population and the leading cause of death is diabetic ketoacidosis (DKA). Globally, the incidence of DKA at presentation varies, ranging from 13% to 80%.¹ Children presenting with DKA are at higher risk for life-threatening complications including cerebral oedema, cerebral ischaemia and hypoxic brain injury. These patients are also more likely to require admission to an intensive care unit, which contributes to greater healthcare spending.^{2,3}

It is unclear why only some children present with DKA. Furthermore, whether the development of DKA is a consequence of delayed diagnosis and treatment or a reflection of a particularly aggressive form of diabetes remains unknown. Therefore, identification of factors associated with DKA at diagnosis and understanding the relative importance of delayed diagnosis and treatment are important for the advancement of our understanding of DKA and for the development of patient-, professional- and population-based interventions to reduce the rate of children presenting with DKA.⁴

The factors associated with DKA in children can be categorised into individual factors (age, sex, ethnicity, family history of diabetes, body mass index and parental consanguinity), family factors (parental education, family structure, health insurance status, rural versus urban residence, family income, parental employment and social status), physician-related factors (delayed diagnosis, diagnostic error, number of medical consultations before diagnosis, delayed treatment and presence of a structured diabetes care team) and disease-related factors (duration of symptoms, pattern and frequency of symptoms and preceding infection or febrile illness).⁵ In a study examining the association of parental educational level with DKA prevalence, Sadauskaite-Kuehne et. al. found that the DKA prevalence was higher in Lithuanian children than in Swedish children (21.3% vs. 7.3%, $P < 00001$) and that younger age at the time of diagnosis and low maternal educational level influenced DKA in Lithuanian children.⁶

Materials and Methods

This was a cross-sectional study including children diagnosed with T1DM based on the

International Society for Pediatric and Adolescent Diabetes guidelines. Patients with T1DM aged 0–16 years who were hospitalised in or visited the Pediatric Endocrinology Outpatient Clinic at Dr. Soetomo General Hospital in Surabaya between January 1, 2016 and June 30, 2021 were included, and patients with incomplete medical records during recruitment were excluded. A total 50 patients signed informed consent and joined the study. Data for the study were obtained from the medical records of the Pediatric Endocrinology Outpatient Clinic and from interviews with the parents of inpatients.

Data Analysis

All statistical analyses were performed using SPSS version 21. Univariate analyses were performed to determine frequency of variables, and chi-squared test (Fisher's exact test) was performed to analyse the association between independent and dependent variables. Multivariate logistic regression analysis was performed to analyse risk factors that affect in DKA in children. The results were reported as odd ratios (ORs) with 95% confidence intervals (CIs). A p value of <0.05 was considered to indicate statistical significance.

Results and Discussion

The baseline characteristics of 50 patients with T1DM included in the study are summarised in Table 1. Briefly, the male/female ratio was 1:1.5, 32 patients experienced at least one DKA episode, and 6 patients experienced DKA more than once.

Table 1: Baseline characteristics of the patients with T1DM included in the study

| Variable | N = 50 |
|----------------------|--------|
| Sex | |
| Female | 30 |
| Male | 20 |
| Family history of DM | |
| Yes | 4 |
| No | 46 |

| Variable | N = 50 |
|----------------------------------|--------|
| DKA | |
| Yes | 32 |
| Never | 18 |
| Sex of patients experiencing DKA | |
| Female | 14 |
| Male | 18 |
| Socioeconomic status | |
| Low | 10 |
| Moderate | 40 |
| Maternal occupation | |
| Working | 25 |
| Nonworking | 25 |
| DKA frequency | |
| Once | 26 |
| More than once | 6 |
| Parent age (years) | |
| - Father | 1. |
| 20-40 | 22 |
| 40-60 | 27 |
| >60 | 1 |
| - Mother | 2. |
| 20-40 | 33 |
| 40-60 | 17 |
| >60 | 0 |
| Parental educational level | |
| - Father | 3. |
| Elementary school | 9 |
| Junior high school | 6 |
| Senior high school | 26 |
| Academic | 9 |
| - Mother | |
| Elementary | 10 |
| Junior high school | 10 |
| Senior high school | 22 |
| Academic | 8 |

Bivariate analysis revealed that there was an association between working mothers and DKA (OR 9.33, 95% CI 2.168- to 40.182, $p = 0.003$), indicating an increased DKA risk among children with working mothers.

Multivariate analysis revealed significant correlation between maternal age below 40 years and DKA frequency (OR 1.73, 95% CI 8.684-3.478, $p = 0.000$). The highest DKA frequency was among the patients with low parental educational level. However, there was no statistically significant correlation between parental educational level and DKA.

The present study, which aimed to provide updated information on potential factors associated with the development of DKA, revealed a number of key findings: parental occupation, sex, family history of DM, DKA frequency, socioeconomic status and parental educational level.

First, we found that parental occupation was association with the risk of DKA in children with T1DM. Specifically, children with working mothers were at higher risk of DKA. The signs and symptoms suggesting DKA might have been recognised earlier in the children with nonworking mothers included in the study. Two studies examined the effect of parental employment on the frequency of DKA. A study in Sweden found that the risk of DKA was higher in children with nonworking mothers (OR 4.8, 95% CI 1.8-13.1), whereas another study in Lithuania reported that the paternal employment status did not have an effect on the rate of DKA (OR 1.17, 95% CI 0.53-2.57).⁴

In the present study, the educational level was senior high school in majority of the fathers and mothers of the children who experienced DKA (52% and 44%, respectively). Several studies reported that higher parental educational level was a protective factor in DKA.^{6,7,8} As suggested in other studies, better parental educational level may aid in the improvement of metabolic regulation in children with T1DM.⁹

The current study cohort was predominantly composed of female children with T1DM, whereas DKA developed predominantly in male children,

with a male/female ratio of 1.3:1. A systematic review of 21 studies revealed that sex did not have an effect on the frequency of DKA in 20 studies and that only one study including 2121 subjects reported a small, albeit statistically significant, increase in the frequency of DKA in female patients (OR 1.30, 95% CI 1.07–1.58, $p = 0.0079$).⁴

In the current study, only four patients had a family history of type 2 DM and none of the patients had a family history of T1DM. Azab et. al. stated that a positive family history of T1DM was associated with increased T1DM risk among relatives.¹¹ These results are in contrast with the study by Roche et. al. who described the abrupt onset of T1DM and the absence of family history.¹²

Numerous studies demonstrated that younger age was associated with increased DKA risk at onset. In some studies, most of the patients with newly diagnosed T1DM and DKA were younger than two years of age,¹³ which may be due to the lower efficacy to control metabolic deterioration and/or low speech ability in expressing issues in younger children.⁷ In contrast, only 6 (12%) patients with T1DM who were 5 years of age or younger experienced DKA.

One major study limitation of the present study is the small sample size because of the lower rates of T1DM in Asian populations compared with Caucasian populations; therefore, the current study findings might not be representative of other populations.

Conclusion

The present single-center, cross-sectional study in Indonesia has identified several factors associated with DKA in children with T1DM, which might be considered as important targets to reduce the incidence of DKA at diagnosis in Indonesia, especially East Java. The risk of DKA was influenced by local culture. Young and poor children were disproportionately affected, although DKA occurred even in children from affluent and well-educated families.

Increased public awareness and greater medical alertness concerning the symptoms and signs of DKA are warranted. Additionally, improved access to care may additionally reduce the severity and cost of initial T1DM treatment in children.

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Ethical clearance: We sought approval of this research from the Clinical Research Unit of Dr. Soetomo General Hospital Surabaya, Indonesia, as our Ethical Committee Review Board. The ethical clearance was issued by the Clinical Research Unit of Dr. Soetomo General Hospital Surabaya (number 1023/KEPK/III/ 2019).

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