ORIGINAL RESEARCH REPORT

Clinical Profile of Type-1 Diabetes Pediatric Patients in Dr. Soetomo General Academic Hospital Surabaya: Correlation of Growth Status and Metabolic Control

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Article Info

Article history:
Received Aug 16, 2022
Revised Oct 5, 2022
Accepted Dec 6, 2022
Published Jan 10, 2022

Keywords:
Diabetes
Type-1 Diabetes Mellitus
Growth Status
HbA1c
Human & Disease

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ABSTRACT

Background: Type-1 diabetes mellitus (DM) is a chronic auto-immune disease characterizedby insulin insufficiency and resultant hyperglycemia caused by the destruction of insulin-producing beta cells in the pancreas. Metabolic control in type-1 DM affects the metabolism of patients, one of which is growth status, which is influenced by growth hormone. Improved growth rates can indicate stable HbA1c levels. However, whether growth is affected by the degree of diabetic control is still debatable. **Objective:** This study was conducted to determine whether the metabolic control correlates with growth status of children with type-1 diabetes in the Endocrine Polyclinic at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. **Material and Method:** Retrospective observational analysis with a cross-sectional method was conducted on 96 type-1 DM patients at Dr. Soetomo General Academic Hospital Surabaya, Indonesia. The analysis was carried out using Chi-Square test to determine whether there was a correlation. **Result:** From a total of 96 pediatric patients, the majority was male (54.1%), patients with high-risk metabolic control were 79.2%, and those with z-score normal category were 62.5%. The results indicated no significant correlation between growth status and metabolic control of pediatric patients, with Chi-Square test results showed p=0.421 (p>0.05). **Conclusion:** There was no significant correlation between growth status and metabolic control of type-1 diabetes pediatric patients at the Endocrine Polyclinic Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

How to cite:
Respati, G.D.P., Faizi, M., Pranoto, A., Andarsini, M.R. 2023. Clinical Profile of Type-1 Diabetes Pediatric Patients in Dr. Soetomo General Academic Hospital Surabaya: Correlation of Growth Status and Metabolic Control. Majalah Biomorfologi, 33(1): 7-13

Majalah Biomorfologi (Biomorphology Journal) p.ISSN:0215-8833, e.ISSN: 2716-0920
doi: 10.20473/ mbiom.v33i1. 2023.7-13

Highlights

1. Diabetes mellitus type 1 (DM) is a chronic autoimmune illness characterized by insulin insufficiency and hyperglycemia as a consequence.
2. Stable HbA1c levels may be indicative of improved growth rates.

BACKGROUND

Diabetes mellitus (DM) is a global issue whose incidence is rising globally. Mortality and morbidity due to microvascular and macrovascular problems are also more prevalent in diabetes (Romadhon., et al. 2019). Diabetes Mellitus may cause a variety of comorbidities, ranging from viral infections to metabolic disorders (Kaware., et al. 2022). Type 1 diabetes mellitus (DM) is a chronic autoimmune disease characterized by insulin deficiency and resultant hyperglycemia (DiMeglio, et al., 2018). The destruction of insulin-producing beta cells in the pancreas by an autoimmune process causes this chronic disease. The destruction of beta cells results in insulin insufficiency, and the patients will develop life-threatening hyperglycemia clinically manifested by weight loss, polyuria, and polydipsia (Simmons, 2015).

Good and optimal metabolic control can maintain normal development and growth and prevent complications (Adelita, et al., 2020). A good metabolic control will keep the blood glucose levels within normal limits or close to normal values without causing hypoglycemia. HbA1c parameter is considered the standard metabolic control parameter in DM (Van Loocke, et al., 2021). HbA1c value < 6.5% is the ideal lower goal that can be set as a standard in children, which can be achieved if the patients have no excessive hypoglycemia, impairment of quality of life, and undue burden of care or are in a honeymoon-state of type 1 diabetes. HbA1c values 7.5% are optimal in the majority of patients. HbA1c 7.5% - 9% is the suboptimal value in relatively controlled type 1 diabetes mellitus. HbA1C >9% is considered an as a high-risk condition which strongly associated with cardiovascular disease and mortality (Sherwani, et al., 2016; DiMeglio, et al., 2018). These criteria in children need to be adjusted according to age because the lowerthe HbA1c control, the higher the risk of hypoglycemia (Tridjaya, et al., 2021). To achieve these goals and objectives, the management component of type-1 diabetes consists of five pillars, including insulin administration, nutrition, exercise, and education, supported by self-monitoring. All of these components must be integrated (Adelita, et al., 2020). For this reason, research that discusses metabolic control of pediatric patients needs to be carried out to determine the factors influenced by metabolic control to prevent complications and maintain optimal child growth.

As the incidence of type 1 diabetes keeps rising over the year, concerns over this disease are constantly being raised, including impaired children's growth as a complication, especially in Indonesia, where impaired children's growth is a big concern (Pulungan, et al., 2019). However, whether growth is affected by the degree of diabetic control is still debatable, as shown in recent studies (Assar, et al., 2015; Asmasary, 2022).

In this study, the results of the measurement of the patient's HbA1c and growth rate were used as variables to be sought for each correlation. Based on the theory that the lower and more stable the patient's metabolic control (HbA1c) level, the better their growth status, we hypothesized that there was a correlation between metabolic control (HbA1c) and growth status, and the lower HbA1c, the better the growth control. Nutritional status is only presented in profiles, and no correlation test was carried out with the assumption that in type 1 DM the metabolism is mainly affected by growth hormone production, so in this study, the correlation test was more focused on growth status.

OBJECTIVE

This study was conducted to determine whether there was correlation between metabolic control, duration of type-1 diabetes, and the growth status of children with type-1 diabetes, especially in Indonesia as a developing country, to raise awareness and solutions related to this problem and as a clinical basis for further research concerning this problem related to children with type-1 diabetes mellitus.

MATERIAL AND METHOD

This study was a retrospective cohort observational study with a cross-sectional method. The results of the study were presented in the form of a proportion distribution table and a description of the respondent's characteristics data, insulin therapy administration, and metabolic control classification (HbA1C) based on CDC graphic indicators.

The data collection and processing of this study were carried out from May 1 to May 31, 2022, at the Endocrine Polyclinic, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. The inclusion criteria of this study were pediatric patients with type-1 DM at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, and patients' age of 2 – 18 years old. The exclusion criteria of this study were patients with incomplete data and patients who had just suffered from DM 1 with a duration of less than one month. Data of each patient was obtained from data center of Dr. Soetomo Hospital for the medical records. From the data collection process, there were 543 pediatric patients for the 2017-2022 period. A total of 96 pediatric patients were taken as a sample acording to the inclusion and exclusion criteria. All samples that met the inclusion criteria were treated with insulin therapy and the growth status was monitored, and then statistical tests were conducted to analyze the correlation between the variables studied.

RESULT

Patients

Data obtained from the results of medical records in each pediatric patient with Type 1 Diabetes Mellitus at the Endocrinology Polyclinic of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia are presented in Table 1.

Table 1. Patient's clinical profile

Respondents characteristic	Classification	Number of samples (n)	Percentage (%)
Gender	Female	45	45.9
	Male	51	54.1
Insulin Therapy	Given	96	100
HbA1C	Ideal (< 6.5)	3	3.1
	Optimal (<7.5)	6	6.3
	Suboptimal (7.5-9.0)	11	11.5
	High Risk (>9)	76	79.2
	Mean of HbA1c value: 11.07 Median of HbA1c value: 11.45		

This study was conducted on children aged 2-18 years. In this study, male patients were dominant as many as 52 people (54.1%) compared to female patients. In the results of the study, it was found that the majority of patient's metabolic control were at high risk, which was found in 76 children (79.2%) with a mean HbA1c value of 11.07 and median value of 11.45. All pediatric patients involved in this study received insulin therapy (100%).

Table 2. Nutritional and growth status profile

Respondents characteristic	Classification	Number of samples	Percentage (%)
Growth Status (height for age)	Short Stature (z-score < -3)	32	33.3%
	Normal (z-score ≥ -3)	60	62.5%
BMI	Good Nutritional Status	18	18.8%
	Malnutrition	65	67.7%
	Overweight	5	5.2%
	Obesity	8	8.3%

In the nutritional status and growth status of the patient's profile, there were 32 (33.3%) pediatric patients with short stature and 60 (62.5%) pediatric patients with normal stature according to their age as shown from to the measurement of their growth status. In regard with nutritional status, there were 18 (18.8%) pediatric patients with good nutrition, 65 (67.7%) pediatric patients with malnutrition, 5 (5.2%) pediatric patients with overweight conditions, and 8 (8.3 %) pediatric patients with obesity conditions. It should be noted that in this study, the nutritional status (BMI) of pediatric patients was not used in the follow-up correlation analysis and only shown in the status profile because this study

focused on the effect of type 1 diabetes mellitus in children as indicated by growth status (height per age). In contrast, the calculation in the nutritional status shown by BMI is the weight per height in square meters, where the body's weight is included in the analysis, thus the z-score does not concentrate on the development of children's bones exhibited in the child's height.

Correlation between metabolic control and growth status

Table 3. The correlation test result of metabolic control and growth status

Metabolic Control (HbA1c)	Growth status			Chi-square result
	Short	Normal	Tall	
	N	n	n	
Ideal	0	3	0	0.421
Optimal	1	5	0	
Suboptimal	2	9	0	
High Risk	29	43	4	

As many as 43 pediatric patients (44.79%) in this study had high-risk metabolic control with normal growth status, while 29 pediatric patients (30.21%) had high-risk metabolic control with short stature. Therefore, there was no significant correlation between growth status and metabolic control of pediatric patients at the Endocrine Polyclinic Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, as indicated by the Chi-Square results $p = 0.421$ ($p>0.05$).

DISCUSSION

A systematic review of 54 studies on the incidence of Type 1 Diabetes Mellitus revealed that males experience Type 1 Diabetes 1.47 times more than females (Pérez Bedoya, et al., 2022). In contrast, Rianti's study (2017) found that the majority of respondents who experienced Type 1 DM were female as many as 37 people (62%) (Rianti, 2017). Meanwhile, in 2018 there was also a study which found that most children with type 1 DM aged 1-18 years, who were treated at Dr. Saiful Anwar Hospital Malang, were mostly female, consisting of 16 people (57%) (Indriyani, 2018). In addition, in a recent study the majority of Type 1 Diabetes was also experienced by females aged >12-19 years as many as 21 people (67.7%) (Kusumastuty, et al., 2021). Risk factors for diabetes mellitus in children 0-18 years old increased by 700% over ten years (from 2009-2018) (Indonesian Pediatric Society, 2018). Boys and girls can experience Type 1 diabetes. The risk of having Type-1 DM among the children is higher if they have family members who suffer from diabetes mellitus.

A total of 96 patients at the Endocrine Polyclinic Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, were examined for HbA1C to see the glycemic condition in pediatric patients and to see changes in therapy during the previous 8-12 weeks. The HbA1C value based on DCCT is expressed in percent (%). The degree of HbA1C control based on ISPAD and IDF was divided into four categories, Ideal (<6.5%), Optimal (<7.5%), Suboptimal (7.5-9.0%), and High Risk (>9.0%). From the results of the study, it was found that as many as 76 pediatric patients (79.2%) had high-risk HbA1C and 11 pediatric patients (11.5%) in suboptimal category. Kayirangwa, et al (2018) said that 41.2% of the patients had HbA1C levels >10% (Kayirangwa, et al., 2018). In addition, it was also found that the group of adolescents who had Type 1 DM and ADHD had poor metabolic control (HbA1C > 8.4%). The study from Pulungan (2021) showed that as many as 79.1% (34 children) have an HbA1C category >8.5% or a suboptimal type (Pulungan, 2021).

HbA1C levels monitoring in pediatric patients with Type 1 DM in this study was carried out 3-6 times in 1 year. Almost all of the patients involved in this study showed a significant increase in HbA1C levels and exhibited high-risk HbA1C levels. Monitoring of HbA1C levels was adjusted to achieve values as close to normal as possible (Tuomilehto, 2013). HbA1C levels tend to be high because children with Type 1 DM have experienced glucose intolerance due to impaired insulin function (Ray, et al., 2015). Insulin resistance is closely related to clinical conditions of hypertriglyceridemia and hypertension, high levels of C-reactive protein, and low HDL cholesterol, which tend to be experienced by obese children (Tagi, et al., 2019). This study also showed that as many as five children were overweight, and

eight children were obese. According to research in 2016, there are differences in HbA1C levels experienced by stunted obese children with small non-obesity groups, and HbA1C levels tend to be higher in obese children (Luthfiah & Sulchan, 2016).

The growth status of children can be seen from the growth curve. The CDC curve is a reference that describes how children grow at a certain time and place. In this study, the growth status of pediatric patients was observed using the 2000 CDC curve by monitoring the results of the z-score of the indicators of height for age of children with Type1 DM at the Endocrine Polycliniclinic Dr. Soetomo General Academic Hospital Surabaya, Indonesia.

Based on the results of the study, it was found that 32 pediatric patients (33.3%) were stunted (short), 60 children (62.5%) were normal, and four children (4.2%) grew tall. This was similar to Rianti's study (2017) study that the prevalence of stunting and diabetes mellitus occurred in 21 children out of 60 respondents, with a percentage of 35% (Rianti, 2017). However, it is different from the study of Luthfiah & Sulchan, (2016) that there were only two stunted and obese adolescents (10%) who had diabetes mellitus.

Children's condition of growth status is not only seen at once monitoring time, especially for children with special conditions such as stunting, as shown from the results of the z- score on the z-score of height per age indicator. Stunting occurs in children because there is a previous long term nutritional deficiency that last during the first 1000 days of life. The causes of stunting also vary, such as being influenced by factors of parenting, coverage, quality of health services, the environment, and food security. This is supported by Kayirangwa, et al (2018) study on the prevalence of stunted children under five years of age in Rwanda, Africa, which showed a correlation between glucose monitoring, insulin therapy, and sociodemographic conditions of families with stunted children and Type 1 DM. Families of stunted children who suffer from Type 1 DM tend to have low economic status and have significant challenges in the cost of treatment, hospitalization, mileage, and adequate food availability to support the health of their children with Type 1 DM and stunting (Kayirangwa, et al., 2018).

In addition, children with slow growth status, stunted and undernourished or malnourished, are influenced by insufficient calorie intake from daily food. Malnutrition often causes children to become underweight and slow in gaining height. Malnutrition reduces the level of Insulin Growth Factor-1 (IGF-1), which reduces sensitivity to growth hormones in children.

Chi-Square test to determine whether or not there is a correlation between HbA1C metabolic control and the growth status of children with type 1 diabetes. Chi-Square p= 0.421 (p>0.05) showed no correlation between HbA1c and growth status in children with type 1 diabetes. A previous study showed that HbA1C and height had a negative correlation in children with Type 1 diabetes, especially in those with low metabolic control (Aljuhani, et al., 2018). Poor metabolic control can reduce growth in height. This was evidenced in a cohort study in Mexico in 2016 that 50% of respondents experienced failure to thrive (Assar, et al., 2015). However, it was different from the latest study in 2022 that there was a significant correlation between HbA1c and HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) in obese children with a p-value = 0.012 (Asmasary, 2022). The higher the HbA1C level, the higher the risk of insulin resistance in obese children. Bone development and growth associated with height gain in children are influenced by the duration of diabetes mellitus, age at onset, corticosteroid treatment, malnutrition, decreased physical activity, and pro-inflammatory cytokines. In addition, it is also influenced by fibroblast growth factors, bone morphogenic proteins, and peptides related to parathyroid hormone (Santi, et al., 2019).

Strength and limitations

Nutritional status is only reported in profiles, and no correlation test was conducted based on the idea that type 1 diabetes metabolism is mostly influenced by growth hormone production. Thus, the correlation test in this research was more focused on growth status. Further research is necessary to measure IGF-1 levels to determine the correlation with bone growth that affects children's height.

CONCLUSION

There was no significant correlation between growth status and metabolic control of pediatric patients at the Endocrine Polyclinic, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. The observed growth status of pediatric patients indicates that other factors may influence growth status more than the metabolic control, which requires further research in the future. The management

of pediatric patients with type 1 diabetes mellitus needs to consider many other factors besides metabolic control to avoid stunting.

Acknowledgment
Special Thanks to the Department of Pediatrics, Airlangga University, Surabaya, Indonesia

Conflict of Interest
All authors have no conflict of interest.

Ethic Consideration
This research has been approved by the ethical committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, with ethics number 1335/105/4/III/2022.

Funding Disclosure
This research was done using a personal fund, no external source of funding was used.

Author Contribution
All authors have contributed to all processes in this research, including preparation, data gathering, analysis, drafting, and approval for publication of this manuscript.

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