

Reduction of Fructosamine Levels after Ramadan Fasting in Children with Type 1 Diabetes Mellitus

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ABSTRACT

Background: Ramadan fasting is one religious challenge for children with type 1 diabetes mellitus (T1DM) which required specific management and strict monitoring. Fructosamine, which reflects glycemic control within 2-3 weeks, is an ideal parameter of glycemic control in Ramadan fasting. This study aimed to analyzed the effect of Ramadan fasting on fructosamine level of children with T1DM.

Subjects and Method: This prospective cohort study included children aged under 18 years old diagnosed wit T1DM for >6 months at Dr. Soetomo Hospital, Surabaya, Indonesia in Ramadan 1438 H (May-June 2017). The independent variable from this study was Ramadhan fasting and the dependent variables were fructosamine and HbA1c. The sampling technique was total sampling. Forty-two children were included and devided into 27 children in the fasting and 15 children in the non-fasting group. Fructosamine and HbA1c levels were measured before, mid- and after Ramadan and the comparison between groups were analyzed using the independent T-test.

Results: The mean age of all the subjects was 8.95 (SD=3.2) years old, 47.6% were males. The mean (SD) HbA1c level of all the subjects was 10.42 (1.16) %. There was a mild reduction of mean fructosamine level after Ramadan in the fasting group. There was no significat differece I fructsamie level before (Mean= 556.8; SD= 180.39; p= 0.620), mid (Mean= 568.07; SD= 175.37; p= 0.520), and after Ramadhan between groups (Mean= 539.41; SD= 173.04; p= 0.410) respectively. The average fructosamine levels after Ramadan was positively and strongly related to HbA1c (r=0.69; p<0.001). There was no case of severe hypoglycemia and diabetic ketoacidosis in both groups.

Conclusion: There is a reduction of mean fructosamine level after Ramadan fasting in children with T1DM although it isn't statistically significant.

Keywords: type 1 diabetes, children, fasting, Ramadan, fructosamine

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BACKGROUND

The International Diabetes Federation (IDF) estimate that nearly 500,000 children under 15 years of age in the world have type 1

diabetes mellitus (T1DM) and find an increasing incidence of 2.8% per year (Patterson et al., 2014; Ziegler and Neu, 2018). Ramadan fasting is an obligatory

religious practice for all healthy adult Muslims. Although religion clearly states the exceptions of Ramadan fasting in people with a serious medical condition, many children and teenagers with T1DM are still doing this religious practice regarding their disease (Pathan et al., 2012; Sadikot et al., 2017; Beshyah et al., 2018).

According to The Epidemiology of Diabetes and Ramadan (EPIDIAR) study in 2001, there were about 43% patients with T1DM who fasted for a minimum of 15 days during Ramadan (Essa et al., 2019). The International Diabetes Federation (IDF) and Diabetes and Ramadan (DAR) International Alliance declared that patients with T1DM who fasted during Ramadan are classified as high-risk individuals (Arouj et al., 2010; Zabeen et al., 2014; Hawary et al., 2016; Ghouri et al., 2018). The risks facing these individuals are diabetic ketoacidosis and hypoglycemia (Ghouri et al., 2018; Jabbar et al., 2017; Alfadhli, 2018).

The commonly used parameters for metabolic control in patients with T1DM are daily plasma glucose, HbA1c and fructosamine. The American Diabetes Association (ADA) recommends HbA1c as an indicator of metabolic control which shows the complications of diabetes mellitus. HbA1c shows an average glucose level in a two-three months period (ADA, 2018). Meanwhile, fructosamine is a simple and fast method which reflects glycemic control of patients with T1DM within two to three weeks. Therefore, it is reliable to be used in Ramadan fasting setting (Hawary et al., 2016; Azad et al., 2012; Nansseu et al., 2015).

Studies regarding the safety of Ramadan fasting in children and teenagers with T1DM and its metabolic parameter are still limited. Some studies showed a variation of fructosamine level in children with T1DM who fast during Ramadan (Hawary et al., 2016; Rahim et al., 2011; Benbarka et al.,

2010). Therefore, this study aimed to analyze the effect of Ramadan fasting on fructosamine level of children with T1DM and the application of fructosamine as a parameter of glycemic control.

SUBJECT AND METHOD

1. Study Design

This prospective cohort study was conducted at the pediatric endocrinology outpatient clinic Dr. Soetomo Hospital Surabaya in Ramadan 1438 (May 27–June 24, 2017).

2. Population and Sample

Forty-two children aged under 18 years old diagnosed with T1DM for >6 months were included by total sampling technique. T1DM was diagnosed on the basis of the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines. Subjects divided into twenty-seven in the fasting and fifteen in the non-fasting group.

3. Study Variables

The independent variable in this study was Ramadan fasting. While, fructosamine is the dependent variable.

4. Operational Definition of Variables

Ramadan fasting is not eating and not drinking from dawn to sunset.

Fructosamine levels is hemoglobin that binds to glucose or hemo which functions to determine the amount of glucose in the blood for 2 – 3 weeks. HbA1C is the same as fructosamine levels but the measurement takes approximately 3 months.

DKA episodes is the frequency of DKA during Ramadan fasting. The severity of hypoglycemia is having low blood glucose levels that requires assistance from another person to treat.

5. Study Instruments

The outcome measures included the number of severe hypoglycemia and DKA episodes, fructosamine levels, and HbA1c level. Fructosamine and HbA1C levels were carried out from the blood venous samples then

examined in the laboratory using Cobas Integra, Roche diagnostic.

Ramadan fasting unit of measurement is fasting and non fasting group. The measurement of fructosamine levels ($\mu\text{mol/L}$) was carried out three times. First measurement was carried out two weeks before Ramadan, the second measurement was carried out two weeks mid-Ramadan and the third measurement was carried out two weeks after Ramadan. HbA1C level (%) was measured as a long-term parameter of metabolic control. HbA1C categorized into optimal ($\leq 8\%$) and poor ($\geq 8\%$) metabolic control. DKA episode measure by incidence. The severity hypoglycemia unit of measurement is happened and not happened.

The data scale of the variables fructosamine levels and HbA1C is continues. Variables Ramadan fasting, DKA episodes, and severe hypoglycemia the data scale is nominal.

6. Data Analysis

The nominal variables were compared using chi-square test. The fructosamine levels

between fasting and non-fasting group were compared using independent T-test. For all statistical analyzes, $p < 0.05$ was considered statistically significant and the confident interval was 95%.

7. Research Ethics

The study was approved by the ethics committee of health research, Dr. Soetomo Hospital, Surabaya, Indonesia (No.319/Panke.KKE/IV/2017). Informed consent was obtained from parents before the start of all the procedures.

RESULTS

1. Sample Characteristics

The mean age of all the subjects was 8.9 (SD= 3.2) years, 47.6% were male. The mean duration of illness was 44.88 (SD= 34.2) months. The demographic characteristics between both groups are presented in Table 1. All subjects with T1DM obtained a basal bolus insulin regimen with the mean on the daily dose of 1.05 (SD= 0.18) IU/ KgBW/day.

Table 1. Sample characteristics (categorical data)

Characteristics	Fasting group		Non-fasting group	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Gender				
Male	13	48.15	7	46.67
Female	14	51.85	8	53.33
Ethnicity				
Javanese	22	81.48	13	86.67
Madurese	5	18.52	2	13.33
Pubertal status				
Prepuberty	7	25.93	7	46.67
Puberty	20	74.07	8	53.33
Nutritional status				
Underweight	7	25.93	8	53.33
Normal	18	66.67	6	40.0
Overweight	2	7.40	1	6.67

2. Bivariate Analysis

Almost all of the subjects (95.2%) had poor level of metabolic control with a mean HbA1c 10.42% (SD= 1.16) . The mean HbA1c

levels in the fasting and non-fasting groups were 10.26% (SD= 1.09) and 10.71% (SD= 1.24), respectively. The mean level of fructosamine levels before, mid and after Rama-

dan between fasting and non-fasting group are shown in Table 2. There was a reduction of mean fructosamine level before, during, and after Ramadan in the fasting group although it wasn't statistically significant

($p=0.620$; $p=0.520$; $p=0.410$, respectively). The average fructosamine levels after Ramadan was positively and strongly related to HbA1c ($r=0.69$; $p<0.001$).

Table 2. Sample Characteristics (continuous data)

Variabel	Groups	Mean	SD	Min.	Max.
Age	Fasting group	13.55	2.93	5	18
	Non-fasting group	11.85	4.53	5	18
DKA episode	Fasting group	0.70	0.60	0	2
	Non-fasting group	1.0	0.756	0	2
Severe Hyoglycemia	Fasting group	0.02	0.01	0	1
	Non-fasting group	0.80	0.41	1	1
HbA1c	Fasting group	10.25	1.09	7.80	12.80
	Non-fasting group	10.71	1.24	8.20	12.30

Table 3. Mean average fructosamine fasting and non-fasting group (an analysis by independent T-test and One Way Anova test)

Variable	Fructosamine level ($\mu\text{mol/L}$)				p
	Fasting Group		Non-Fasting Group		
	Mean	SD	Mean	SD	
Pre Ramadan	556.89	180.39	530.53	128.13	0.620
Mid Ramadan	568.07	175.37	535.53	106.88	0.520
Post Ramadan	539.41	173.04	496.07	135.08	0.410

Table 4. Pearson Analysis Fructosamine Level and HbAc1

Variable	Significancy Value	Pearson Correlation
Fructosamine level and HbAc1	$P<0.001$	$r=0.69$

DISCUSSION

In this study, Ramadan fasting secured for children with T1DM. There was no case of severe hypoglycemia and diabetic keto-acidosis in the fasting group. The same study also concluded that fasting is generally safe for patients with T1DM, with possible breakfast if hypo/hyperglycemia arise (Deeb et al., 2017; Agha et al., 2017). Regarding of the used insulin regimen during Ramadan, there were cases of hypoglycemia events and diabetic ketoacidosis in a study by Hawary et al (2016). In this study, all subjects with T1DM obtained a basal bolus insulin regimen with an average daily dose with mean 1.05 (SD= 0.18) IU/KgBB/day. A study by Rahim et al showed that using the intensified insulin

therapy (glargine as basal insulin with insulin aspart before meals) in patients with T1DM who fast during Ramadan is safe under strict blood-glucose self-monitoring and close supervision (Rahim et al., 2011). Basal bolus and insulin pump are more recommended than split-mix as insulin regimen therapy in patients with T1DM who fast during Ramadan because of the lesser risk of hypoglycemia and hyperglycemia events (Pathan et al., 2012; Essa et al., 2019; Karamat et al., 2010).

Some studies showed a variation of fructosamine level in children with T1DM who fast during Ramadan (Hawary et al., 2016; Rahim et al., 2011; Benbarka et al., 2010). The average fructosamine level in this

study was higher compared to other study which showed the average pre-fasting and post-fasting fructosamine level of the patients were 419 (SD= 141.69) $\mu\text{mol/L}$ and 89.06 (SD= 19.59) $\mu\text{mol/L}$, respectively (Hawary et al., 2016). The average fructosamine level pre- and post- fasting in this study were above 500. This could be explained because the HbA1c level of the patients were quite high in this study, 10.26% (SD= 1.09) in the fasting group and 10.71% (SD= 1.24) in non-fasting group, respectively.

In this study, there was no significant reduction of fructosamine level before and after Ramadan in the fasting and non-fasting group. This finding is quite the contrary with a previous study that showed a significant correlation between the reduction of fructosamine level and number of fasting days (Hawary et al., 2016). Another study showed no significant difference in HbA1c and fructosamine levels between pre- Ramadan and end-of-Ramadan ($p=0.251$) (Rahim et al., 2011). Another study in 2010 showed a significant reduction in fructosamine levels after Ramadan in children with T1DM using insulin pump regimen (Benbarka et al., 2010).

HbA1c is known as an indicator for metabolic control which shows an average glucose level in two-three months period while fructosamine reflects glycemic control within two to three weeks (Hawary et al., 2016; ADA, 2018; Azad et al., 2012; Nansseu et al., 2015). In this study, the average fructosamine levels after Ramadan was positively and strongly related to HbA1c ($r= 0.69$; $p<0.001$). Other studies also showed the same correlation between fructosamine and HbA1c (Kang et al., 2015; Malmstrom et al., 2014). Therefore, fructosamine can also be used as a parameter of glycemic control as it is comparable with HbA1c. The reason of the absence of significant reduction in our study

was probably the lack of compliance to follow the recommended diet. Other than that, a tailored insulin regimen is compulsory for these patients. A study suggested using 70% pre- Ramadan insulin dose, divided as basal-bolus with 60:4 ratio (Afandi et al., 2017). Continuous insulin infusion can also be recommended as it provide more stable glucose level compared to multiple daily injection method (Alamoudi et al., 2018).

The limitation of our study is the small sample size. However, this study is the first study in Indonesia which compares the glycemic control of children with T1DM between fasting and non-fasting group. In conclusion, Ramadan fasting affects fructosamine level although it isn't statistically significant. Fructosamine is a simple and fast method which reflects glycemic control of patients with T1DM within two to three weeks. Therefore, it is reliable to be used in Ramadan fasting setting.

AUTHOR CONTRIBUTION

All authors made a significant contribution to the work reported, whether that is in the conception, study design execution, acquisition of data, analysis and interpretation or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for aspects of the work.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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