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The low level of vitamin D3 among Type 1 Diabetes Mellitus (T1DM) children at Saiful Anwar General Hospital, Malang, Indonesia

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ABSTRACT

Background: The Type 1 Diabetes Melitus (T1DM) is a disease which is occurred because of autoimmune destruction in pancreas islet (insulin-producing ß cells). A Failure mechanism of immunoregulator causes inflammatory process in the islets and continue to damage the pancreatic β cell. Vitamin D deficiency may increase the risk of autoimmune diseases including type 1 diabetes mellitus. The aim of this study was to know the level of vitamin D in type 1 diabetes mellitus.

Methods: An observational analytic cross-sectional design was conducted among 40 T1DM subjects and 40 healthy controls aged between 10-18-year-old. They were not having local or systemic infection, nor liver and kidney disorders. Vitamin D levels were measured by the ELISA method (ng/ ml). Subjects' data were collected and processed by 2007 Microsoft Excel software, then analyzed with SPSS version 16.0 for Windows.

Results: Most of respondents in T1DM group were female (57.5%) and 15.94±1.00 years old for average age but not statistically significant compared with control group (p>0.05). There was a significant different of the mean level of vitamin D3 in the T1DM group (10.41 ± 2,20 ng/ml) compared with control group (18.41 ± 1.41 ng/ml) (p<0,05).

Conclusion: The level of vitamin D (25 (OH) D3) in the T1 DM group were significantly lower compared to the control group

Keywords: T1DM, Vitamin D, Children, Low Level

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INTRODUCTION

Vitamin D3 is a hormone (steroid) that primarily found in the skin. The exposure of ultraviolet B (UVB) radiation on the skin make the synthesis of vitamin D3 occurs. Not only from UVB exposure, but also, it can be supplied from diet (salmon fish) and supplement (drug). Some studies said that the vitamin D3 deficiency increased the risk of autoimmune diseases like Type 1 Diabetes Mellitus (T1DM).[1]

The cells within the immune system are affected by vitamin D3. So, it discourages generation and differentiation of B cell, and immunoglobulin secretion. Vitamin D3 also leads the suppression of T-cell regeneration and the converse of "Th1 to a Th2". Moreover, it affects the maturity of T-cell with a deviation away from the inflammatory Th17 phenotype and facilitates the T-regulatory cell induction. These effects lead to decrease the production of inflammatory cytokines (IL-21 and IL-17) and increased production of anti-inflammatory cytokines such as IL-10. Vitamin D3 also effect the dendritic cells (DCs) and monocytes. Not only, inhibits the production of inflammatory cytokines such as IL-12, IL-8, IL-6, IL-1 and TNFα, but also, inhibits DC maturation and differentiation.[2]

The deficiency of vitamin D3 level has been shown to be related in increasing the risk of myocardial infarction (MI), stroke, and total cardiovascular events. Furthermore, it has a beneficial effect against systemic conditions that enhanced atherosclerosis such as β-cell dysfunction, insulin resistance, RAAS, and dyslipidemia.[3,4]

Type 1 DM is still a multisystem disease and also a chronic disease which results from the noteworthy and progressive inability of β-cell pancreas to secrete insulin due to autoimmune process. Internationally, T1DM is increasing 2-5% per year In Europe, Australia, and Middle East.[5,6]

Indonesia is a tropical climate country with high sunlight exposure to help the skin produce Vitamin D3. With this fact and studies above, Indonesian children should have a lower risk of T1DM than children in non-tropical country. Moreover, this study was aimed to determine the vitamin D3 levels in T1DM children in Indonesia.

METHODS

A case-control study with two groups was designed in this research. The first group was the case group, with 40 children who was diagnosed with T1DM aged 10-18 year old (mean age 15.94 ± 1.00 years). The second group was 40 healthy children aged 10-18 year old (mean age 14.63± 1.00 years), without T1DM which was proven by negative result of GAD65. Both case and control groups have no systemic / sepsis infection, liver disorder, kidney dysfunction, malignancy / cancer, anemia with hemoglobin level less than 11 g / dL, take amlodipine, valsartan, statin therapy. All children were selected at endocrine polyclinic, Saiful Anwar general Hospital, Malang.

The subject was chosen by a maximum error (5%) and a 95% confidence interval. The P value of ≤0.05 provide statistically significant. The Examination of vitamin D3 levels was carried out in the Clinical Pathology Laboratory, Saiful Anwar Hospital, Malang. The sample was obtained in plasma form, stored at -20 ° C temperature. The examination was to prepare a polypropylene tube, one for the calibrator, controls and subjects respectively. The Biotin solution 25-D as much as 1 ml was added to all tubes, stirred for 10 seconds. Each dilution of the calibrator was added by 200 UL conjugate. After that, controls and samples were stored at sterile room. The plate was covered with plastic. And it was Incubated at 18-25 ° C for 2 hours. All plates were washed 3 times with a wash solution, 200 UL of the conjugate was added to the plate using a multichannel pipette. The plate was closed and wrapped with plastic, incubated at a temperature of 18-25 ° C for 30 minutes. After the incubation step, 200 UL TMB substrate was added to all wells, plates were closed and wrapped in plastic bags, incubated 18-25 ° C for 30 minutes, then as many as 100 UL stop solutions were added to all wells. The absorbance was measured at 450 nm using an ELISA reader in 30 minutes. Subjects' data were collected and processed by 2010 Microsoft Excel software, then analyzed with *SPSS 21.0* software.

Table 1. Characteristic of subjects

Characteristic of sample	Control (n=40)	Type 1 DM(n=40)	p-value
Male	19	17	0.758[a]
Female	21	23	0.758[a]
Age(years)	14.63±1.00	15.94±1.00	0.087[b]

*a. The correlation result was not significant with Chi-square test
*b. The compare mean result was not significant with Mann Whitney test.

Table 2. The mean of 25(OH)D3 level among subjects and controls

Variable	Subject		Control		*p*-value
	n	mean ± SD	n	mean ± SD	
25 $(OH)D_3$ (ng/ml)	40	10.41 ± 2,20	40	18.41 ± 1.41	0.000
Deficiency (<20 ng/ml)	37	9.68 ± 3.78	38	9.12 ± 4.40	
Insufficiency (21-29 ng/ml)	3	23.73 ± 3.50	2	27.54 ± 1.27	
Normal (>30 ng/ml)	0	-	0	-	

RESULTS

The result from first group consists of 40 children and the second group consist of 40 children who had been selected according to inclusion and exclusion criteria. The characteristic data were analyzed using Kolmogorov-Smirnov normality test. Unpaired t-test was used for normal transformed variable, and Mann Whitney test for unnormal transformed variables (Table 1).

Based in gender, this study found 19 boys and 21 girls in the control group. While in the subject group there were 17 boys and 23 girls. It appears that the distribution data by sex was not significantly different between the two groups (p=0.758). This explains that the selection of research samples from gender was evenly distributed. Likewise, the data based on the age (years) in the control group with the average 14.6053 years and in the T1DM with average 15.94 ±1.00 years. It appears that the distribution of the data based on the age is not significantly different (p=0.087). This explains that the taking or comparing of research samples based on the control group and T1DM obtained the age of children who have been homogeneous, because the distribution of the data on the age of the children is almost the same.

The mean of vitamin D3 level in the T1DM group was 10.41 lower than the mean level of vitamin D3 in the control group which was 18.41, and the sample was normally distributed with a significant value each group was higher than α 5%, with the p value is greater than α (0.278 > 0.050), which means that the vitamin D3 level in the T1 DM group was significant lower than the vitamin D3 level in the control group (Table 2).

DISCUSSION

Based on the gender, the male distribution compared to female in T1DM was fewer. This study has same results with Indonesia pediatric society which showed that the incidence ofT1DM was 0,00388 per 100,000 (male) and 0,00483 per 100,000 (female).[7] Oppositely, the reports of epidemiological data showed that T1DM was higher in male than Female.[6] These differences might be occurred due to randomized data selection.

Moreover, this study also found that T1DM group has 37 children with vitamin D3 deficiency, three children with vitamin D3 insufficiency, and no children with normal level of vitamin D3. While in control group, there were 38 children with vitamin D3 deficiency, two children with vitamin D3 insufficiency, and also there was no children with normal level of vitamin D3. Additionally, the mean (SD) of vitamin D3 level in T1DM group was 10.41(± 2,20) which was lower than control group, both groups have statistical different (p=0,00). Our results is similar to the result of study done by Penna et al, in 2000 which said that vitamin D3 was lower in T1DM compared to normal children.[7]

To date, T1DM patients have done regular follow up at endocrine polyclinic Saiful Anwar Hospital. The follow up give them advice about T1DM, its complications, and the benefit of vitamin D3. Additionally, a research by Subandiyah[8] said, vitamin D3 can be regulating inflammation factors in which also playing role in T1DM phatomecanism. Moreover, endocrine polyclinic Saiful Anwar Hospital also give them advice to do appropriate sun exposure and give advice about the source of vitamin D3 in food. Applying sunscreen which used as sun protection may reduce vitamin D3 synthesis in the skin by more than 95%. Many factors can affect the vitamin D3 status, including skin color, clothing, latitude, season, time spent outdoors, weight status, medications, and some medical conditions which were not included in our research.[9]

CONCLUSION

Based on the results the vitamin D3 level in T1DM group was significantly lower than the control group.

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CONFLICT OF INTEREST

No conflict of interest regarding the publication of this article.

RESEARCH ETHIC

This research has been conducted an ethics test and accepted by the research ethics team at dr. Saiful Anwar Malang.

AUTHOR CONTRIBUTION

All authors contributed to the process of this research

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