CORRELATION BETWEEN VITAMIN D DEFICIENCY AND FASTING BLOOD GLUCOSE LEVELS IN OBESE CHILDREN

Running Head: Vitamin D Deficiency and Fasting Blood Glucose

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Correlation Between Vitamin D Deficiency and Fasting Blood Glucose Levels in Obese Children

Abstract

Background: This study aimed to determine the correlation between vitamin D deficiency and hyperglycaemia in obese children.

Methods: This cross-sectional study was conducted from February - April 2020 with the subject of junior and senior high school students aged 11 to 17 years old who meet the obesity criteria. Measurement of vitamin D were 25 (OH) D levels were using Chemiluminescence Immune Assay method. Subjects were divided into 4 groups; vitamin D deficiency with hyperglycaemia, vitamin D deficiency without hyperglycaemia, normal vitamin D with hyperglycaemia, and normal vitamin D without hyperglycaemia.

Results: The frequency of hyperglycaemia in vitamin D deficiency group was 28 (54.9%), while in normal vitamin D group was 17 (37.8%). Statistical analysis showed no significant difference between the two groups with p = 0.093. There was a significant difference in the mean value of fasting blood glucose levels between the two groups with p = 0.031. The frequency of hyperglycaemia in vitamin D deficiency group was 54.9%, while in normal vitamin D group was 37.8%. Fasting blood glucose levels in obese children with vitamin D deficiency were lower than children with normal vitamin D deficiency. **Conclusion**: Fasting blood glucose levels had no clinical significance.

Keywords*:* Vitamin D deficiency; blood glucose; hyperglycaemia; child; obesity.

Introduction

Obesity and overweight are two terms that indicate there is excess in body weight, which occurs due to imbalance between the three energy components, they are food intake, energy expenditure and energy storage. Obesity is defined as a disorder or disease characterized by the accumulation of excess body fat tissue, which can cause health problems. Overweight is excess body weight compared to ideal body weight, which can be caused by accumulation of fat tissue or body mass.(1)

Childhood obesity is still remaining a complex and become a worldwide problem in both developed and developing countries. The causes are multifactorial, making it difficult to manage and if it is not immediately resolved, it will have the impact on the children's growth development, especially in psychosocial development. Moreover, obesity in childhood will have a high risk of becoming obese in adulthood, so that they will have the potential to experience various diseases and deaths, one of them is cardiovascular disease.(1)

The prevalence of obesity in children has increased sharply in the last 3 decades, not only in developed countries, but also in developing countries. Obesity in children will have the risk being obese when they grow into adults and they will have the potential to experience metabolic and cardiovascular diseases as well as degenerative diseases in the future, for example Type 2 diabetes, coronary heart disease, hypertension, etc.(1) The increase in the prevalence of obese children in the last 30 years has reached tripled and 17% occurs in children aged 2 to 19 years in the United States.(2) Early Initiation of Breastfeeding (EIBF) is a baby's natural process of breastfeeding by giving the baby the opportunity by finding and suckling to find the breast milk within first hour of life. This happened if after the birth, the baby is allowed to have skin contact with the mother's skin immediately (Sulistyaningsih et al., 2018).

Previous study reported that 98% of obese subjects had less vitamin D, 64% had deficiency and 34% had insufficiency consecutively.(3) This suggests that obesity itself is closely

related to vitamin D status. Several mechanisms can explain this, they are volumetric dilution, increased leptin, degradation theory, decreased vitamin D bioavailability and vitamin D sequestration in adipose tissue.

In obesity, chronic inflammation occurs which will lead to dysregulation of pancreatic B cells that affects insulin secretion and also insulin resistance, lead to an increase in blood glucose. The value of normal fasting blood sugar levels, but in the high range have the risk as an early stage of the prediabetes insulin resistance in children. Fasting blood glucose evaluation can help simple screening of obese In children who are at risk of developing insulin resistance to prevent type-2 diabetes in their future with intervention as early as possible.(3)

Increasing fasting blood glucose in obese children apart from obesity itself, is also associated with vitamin D deficiency that happened in obese children. The role of vitamin D in influencing blood sugar levels is still remain not well known. However, the most likely mechanisms including the role of vitamin D in the regulation of insulin synthesis and secretion in pancreatic β cells, increasing peripheral and hepatic glucose uptake, and inhibiting inflammation that often occurs in obesity.(4) The role of vitamin D in glucose metabolism has known due to the presence of a specific receptor for vitamin D (VDR) and the expression of the enzyme 1-α-hydroxylase in pancreatic β cells and peripheral tissues that are sensitive to insulin such as in muscle, liver and fat tissue.(5) However, research on the role of vitamin D in increasing levels of fasting blood glucose control, increasing insulin resistance in preventing the risk of type 2 diabetes is inconsistent. A number of studies have concluded that vitamin D supplementation can reduce insulin resistance and fasting blood glucose. Other studies have obtained conflicting results or identified no beneficial effect of vitamin D supplementation.(6)

Concerning those finding as said, another research is important and needed to be done to prove whether the increase in fasting blood glucose or hyperglycaemia that happened in

obesity can be obtained through the vitamin D deficiency pathway, which is in this case vitamin D deficiency is a part of obesity itself. By knowing the role of evaluating the levels of vitamin D and fasting blood glucose in children early, it can detect the presence of metabolic disorders, especially type 2 diabetes mellitus, thus prevent the incidence of cardiovascular disease in early childhood and can reduce mortality and morbidity associated with the incidence of hyperglycaemia. Considering the emergence of risk factors for increasing blood sugar levels happened at a younger age.(7,8)

Therefore, this study aimed to determine the association between vitamin D deficiency and the incidence of hyperglycaemia in obese children.

Materials and Methods

This analytical cross-sectional study was conducted from February - April 2020 in children aged 11 - 17 years who met the criteria for obesity. This study has been approved by Ethics committee of biomedical research on Human of Hasanuddin university, and written informed consent has been obtained from the parents of all children.

Children who met the inclusion criteria were given informed consent, weight and height were measured, and body mass index were assessed to determine the children with obesity. Children with a history of liver or kidney dysfunction, children with endocrinological disease, children with congenital syndrome, children in long term corticosteroid or other medication that can affect body weight were excluded.

Data collection methods

Subjects were chosen using multistage cluster random sampling method (total sampling). Body weight were measured using standardized CEBA digital body scale, while body heigh were measured using microtoise with accuracy 0.1 cm. Obesity were assessed using Body Mass Index (BMI) and classified based on CDC – NCHS growth chart for age > 2 years based on age and sex, children were classified as obese if the BMI is above 95

percentiles. Measurement of vitamin D were 25 (OH) D levels were using Chemiluminescence Immune Assay method. Subjects were divided into 4 groups; vitamin D deficiency with hyperglycaemia, vitamin D deficiency without hyperglycaemia, normal vitamin D with hyperglycaemia, and normal vitamin D without hyperglycaemia.

Data analysis

Data were analysed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Co., Armonk, NY, USA). Univariate analysis was used to describe the frequency, mean, standard deviation, range, and median value. Bivariate analysis was used to analyse the correlation between vitamin D deficiency and the incidence of hyperglycaemia.

Results

This study was including 96 obese children as subjects, 57 (59.4%) were male and 39 (40.6%) were female. In the group of obese children who experienced hyperglycaemia, the number of male children were 31 (54.4%), while female children were 14 (35.9%). Statistical analysis showed that there was no significant difference in the frequency of hyperglycaemia in obese children based on gender with p value = 0.075 ($p > 0.05$) (Table 1).

The frequency of hyperglycaemia in obese children with vitamin D deficiency were 28 (54.9%), whereas in obese children without vitamin D deficiency were 17 (37.8%). Statistical analysis showed that there was no significant difference in the incidence of hyperglycaemia between obese children with vitamin D deficiency and obese children without deficiency with p *value* = 0.093 ($p > 0.05$) (Table 2).

The mean value of fasting blood sugar levels in the obese group of children with vitamin D deficiency was 101.57 mg / dL, the median was 102.00 mg / dL and the range was 64-131 mg / dL. Whereas in the group without vitamin D deficiency, the mean value of fasting blood glucose was 98.27 mg / dL, the median was 87.00 mg / dL with a range of 23.00 - 213.00 mg / dL. The results of statistical analysis using the Mann Whitney test

showed that there was a significant difference in the mean value of fasting blood glucose levels between these two groups with a value of $p = 0.031$ ($p < 0.05$) (Table 3).

Based on the statistical analysis, the relationship between vitamin D levels and fasting blood glucose showed a negative correlation with p value = 0.035, which means that it was statistically significant but the strength of the correlation was weak, with r = -0.216 so make it has no clinical meaning (Table 4).

Discussion

This study found no statistical significance in the frequency of hyperglycaemia based on sex category, which means that sex category is not associated with the incidence of hyperglycaemia in obese children.

The frequency of hyperglycaemia in obese children with vitamin D deficiency and obese children without vitamin D deficiency showed no significant difference. In contrast, a cross-sectional study involving 3577 adolescents who participated in the 2001-2004 NHANES study concluded that there was an association between vitamin D deficiency with hyperglycaemia, hypertension and metabolic syndrome.(9)

Vitamin D receptors have been identified to be present in most human tissues, including smooth muscle, pancreatic β cells and epithelial cells as well as a various of immune system cells including those are associated with diabetes mellitus and glucose hemostasis. Multiple sites of VDR expression underlie the multiple effects of vitamin D and provide the basis for the mechanism of the association between vitamin D deficiency and number of disorders, including cardiovascular disease, metabolic syndrome, diabetes mellitus and insulin resistance characterized by elevated blood glucose levels.(10) The role of vitamin D through vitamin D receptors on pancreatic β cells by activating 1α hydroxylase in pancreatic β cells. Therefore, vitamin D deficiency conditions can affect the release of insulin from the pancreas

and reduce glucose tolerance and lead to conditions of hyperglycaemia and insulin resistance.(11)

In this study, 37.8% of obese children were not deficient in vitamin D but already had hyperglycaemia. This finding proves that there are other pathways besides vitamin D deficiency that cause an increase in fasting blood glucose in obese children. Probably, this finding also cause why there was no significant difference in the incidence of hyperglycaemia between obese children with vitamin D deficiency and without vitamin D deficiency in this study. We have known that, the mechanism of increasing blood glucose in obesity is not only through the vitamin D deficiency pathway, but obesity itself can cause hyperglycaemia through chronic inflammatory mechanism even though without going the vitamin D deficiency pathway.

This study was also included 23 (45.1%) children with vitamin D deficiency, but had not yet experienced hyperglycaemia, this is probably because in this study the degree of obesity was not analysed or how long the study subjects were obese and also it was not known how long the child has been in vitamin D deficiency. So, it might be the degree and duration of suffering from obesity and experiencing vitamin D deficiency has not significantly causing metabolic disorders, refers to increase in blood glucose (hyperglycaemia) in these cases. However, the process will be continued, so it is very important to monitor the levels of vitamin D and blood glucose and the most important is to treat the obesity from an early age.

The results of a statistical test of fasting blood glucose levels in this study showed a significant difference between the group of obese children with vitamin D deficiency and without vitamin D deficiency. This is similar to a previous study from Johnson et al.(12) which found that children with Vitamin D deficiency had higher fasting plasma glucose levels. From the results of this study, it appears that although in statistical analysis there is no significant relationship between hyperglycaemia and vitamin D deficiency, but in the analysis

of fasting blood glucose levels, it appears that there has been a trend towards a significant increase in fasting blood glucose levels in obese children with vitamin D deficiency compared to those without Vitamin D deficiency. Thus, it can be concluded that vitamin D deficiency also plays a role in increasing fasting blood glucose levels in obese children, aside from the mechanism that caused the obesity itself.

The Spearman correlation statistical analysis test in the study showed a negative correlation between levels of vitamin D and fasting blood glucose, but the strength of the correlation was weak ($r = -0.216$) so it was not clinically significant. This is consistent with the results of study by Johnson et al.(12) which found 25 (OH) D levels were inversely correlated with fasting plasma glucose levels. Another study also showed a negative correlation between vitamin D levels and fasting blood glucose levels in obese children in Sri Lanka.(13)

The strength of this study was it reflects the health conditions of children with middle and upper economic status in Makassar, especially in terms of obesity and its effect on vitamin D deficiency and hyperglycaemia. The subjects also reflect puberty age, so there is no need for an analysis of pubertal status to assess its association with hyperglycaemia.

The limitation of this study is that there was no analysis of the degree of obesity, the duration of those who are in vitamin D deficiency and then which of these as said happened first, whether vitamin D deficiency or hyperglycaemia. Therefore, it is important to monitor vitamin D levels and fasting blood glucose levels in every obese child even though they have not yet experienced vitamin D deficiency or hyperglycaemia, because the root of why both things as said happened is due to obesity itself. This is important to prevent and treat early the incidence of vitamin D deficiency and hyperglycaemia that can be found in obese children so that the complications such as metabolic syndrome can be prevented.

Conclusion

Fasting blood glucose levels were correlated with vitamin D levels in obese children, but the strength of the correlation was weak so that it had no clinical significance. It is very important to carry out the early screening to check the levels of vitamin D and fasting blood glucose to prevent the risk of metabolic and cardiovascular diseases.

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