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Research Article

25-Hydroxyvitamin D Serum Levels Unrelated to Fasting Blood Glucose Levels of Premenopausal Women in Padang

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ABSTRACT

Low serum 25-Hydroxyvitamin D levels in premenopausal women result in the impaired release of insulin from the pancreas and reduce glucose tolerance which causes the body's metabolism to slow down resulting in weight gain leading to insulin resistance and resulting in diabetes mellitus (DM). The incidence of DM occurs at premenopausal ages compared to productive ages, the percentage of women experiencing diabetes is higher than men. This study aims to determine the relationship between 25-Hydroxyvitamin D serum levels and fasting blood glucose (FBG) levels of premenopausal women in Padang. Method: This study was conducted in the city of Padang, is observational, cross-sectional design. The study sample was 62 premenopausal women. Measurement of serum 25-Hydroxyvitamin D levels was measured by enzyme-linked immunosorbent assay and FBG levels were measured by the GOD-PAP method. Data were analyzed using the Pearson correlation test. Results: The average serum level of 25-Hydroxyvitamin D respondents was 30.96 ± 10.96 ng/ml. The average FBG level of respondents was 107.03 ± 13.74 mg/dl. There was no significant relationship between 25-Hydroxyvitamin D serum levels and FBG levels (r = - 0.038, p = 0.769). Conclusion: There is no significant relationship between 25-Hydroxyvitamin D serum levels and FBG levels of premenopausal women in Padang.

Keywords: 25-Hydroxyvitamin D serum levels, fasting blood glucose levels, premenopause

Introduction

Premenopause is a time when women have experienced a decrease in ovarian function in the production of estrogen. Estrogen decline occurs gradually, starting in the age range of 40-50 years (premenopause) [1]. Various conditions occur during premenopause caused by hormonal changes, these conditions include irregular menstruation, varying amounts of bleeding, and accompanying pain. One of the hormones that play a role in premenopause is estrogen. In premenopausal women the

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hormones estrogen and progesterone affect how the body's cells respond to insulin, changes in the body's hormone levels can trigger fluctuations in blood glucose levels which make blood glucose levels more difficult to predict, if blood glucose levels are not controlled, there is a risk of diabetes complications higher [3].

In premenopausal women, it is known that the hormone estrogen protects productive women against various cardiovascular diseases such as myocardial infarction or cerebral apoplexy [4]. The cause of the increased incidence of cardiovascular disease in women who have experienced estrogen deficiency is not entirely clear, one possibility is due to changes in glucose metabolism in the body, especially obstacles in the glucose transport process due to insensitivity of insulin receptors in every cell of the body. This situation is commonly referred to as insulin resistance which manifests as high blood glucose levels (hyperglycemia).

According to data from the International Diabetes Federation (IDF) in 2013, there were 382 million people in the world aged 20-79 years suffering from diabetes. Indonesia is the 7th country with the highest DM incidence [5]. Ministry of Health data from the 2018 Basic Health Research has seen an increase in the prevalence of DM in Indonesia from 6.9% in 2013 to 10.9% [6]. IDF data (2017) states that the estimated number of DM in Indonesia is estimated at 10 million, like conditions in the world, DM is now one of the biggest causes of death in Indonesia. The prevalence of DM in West Sumatra is 13% based on a doctor's diagnosis and 18% based on a doctor's diagnosis and symptoms. Data from RSUP Dr. M. Djamil showed that the number of DM sufferers increased every year in 2016 totaling 5900 people. If DM is not addressed, conditions like this can lead to decreased productivity, disability, and premature death [7].

Vitamin D has an important role both in glycemic control and even in reducing diabetes complications. The role of vitamin D in reducing blood glucose levels is still unclear, but the most likely mechanisms include 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 [8].

Vitamin D intake, food intake, and physical activity can affect a person's blood glucose levels. Food intake that can affect is the intake of carbohydrates, fats, proteins, and fiber. Restriction of carbohydrate intake has an effect on weight loss and blood glucose levels in people with type 2 diabetes. Administration of protein together with glucose has a synergistic effect on insulin compared to administration of glucose alone [9]. Excessive fat intake has the effect of reducing the amount of adiponectin which can reduce insulin sensitivity, whereas a study conducted in Japan showed that low plasma adiponectin is associated with insulin sensitivity [10]. Physical activity also affects a person's blood glucose levels, because of its effect on insulin sensitivity. Serum 25-Hydroxyvitamin D and calcium levels with fasting blood sugar levels in obese women aged 45-55 years, indicate that there is no relationship between consumption of foods containing vitamin D and fasting blood glucose levels in obese women aged 45-55 years [11].

The increasing prevalence of DM in Indonesian territory must of course be prevented. One way to prevent it is to know the factors that influence the occurrence of DM in the community. Based on previous studies, it is stated that sociodemography, behavioral, and lifestyle factors as well as clinical or mental conditions affect the incidence of DM. Therefore, this study was designed to determine the relationship between 25-Hydroxyvitamin D serum levels with FBG levels in premenopausal Minangkabau ethnicity women.

Methods

This research is a cross-sectional study of 62 premenopausal women in Padang aged 40-55 years. Subjects were selected by multistage random sampling. The inclusion criteria in this study were willing to enter the study by signing an informed consent, aged 40-55 years, Minangkabau ethnic, having menstrual disorders, and not using hormonal contraception. The exclusion criteria in this study were not coming and not being found when collecting

research data, in a menstruation cycle, not fasting for ± 8 hours (drinking water is allowed), suffering from chronic diseases such as DM, hypertension, cancers (obtained from anamnesis). The sample was collected in the working area of the Padang City Public Health Center. Venous blood was taken by health analyst in a 5cc cubital fossa then stored in a vacutainer. Blood samples will be examined for serum 25-Hydroxyvitamin D levels and FBG levels, which is examined at the Biomedical Laboratory and the Biochemistry Laboratory of the Faculty of Medicine, Andalas University, respectively.

Measurement of serum 25-Hydroxyvitamin D levels was carried out using an enzyme-linked immunosorbent assay. The optical density can be measured with spectrophotometry wavelengths at 450 nm.

FBG levels were carried out using the GOD-PAP method. The optical density can be measured with spectrophotometric wavelengths at 546 nm in 60 minutes.

This study was approved by the Research Ethics Committee, Faculty of Medicine, Andalas University (No. 279/KEP/FK/2017).

Data analysis was performed using univariate and bivariate methods. Univariate analysis was carried out descriptively and presented in the form of a frequency distribution table. Prior to the bivariate analysis, the Kolmogorov Smirnov normality test was carried out to see whether the data were normally distributed or not, and followed by the Pearson correlation test. Using the SPSS for Windows computer program. $p < 0.05$ was considered to be statistically significant.

Results and Discussion

Table 1. Average of Age, Body Weight, Height, Body Mass Index, 25-Hydroxyvitamin D serum levels, FBG levels

Variable	Mean ± SD	Minimum	Maximum
Age (years)	46.73 ± 4.03	40	54
Weight (kg)	62.02 ± 12.76	38.7	101.1
Height (cm)	151.16 ± 6.41	140	171
Body Mass Index (kg/m^2)	27.08 ± 4.99	17.91	43.76
25- Hydroxyvitamin D serum Levels (ng/ml)	30.96 ± 10.96	12.70	61.60
FBG Levels (mg/dl)	107.03 ± 13.74	91.7	156.2

This study shows the average of age of the respondents is 46.73 ± 4.03 years with a minimum age of 40 years and a maximum of 54 years. The average of bodyweight of the respondents was 62.02 ± 12.76 kg with a minimum value of 38.7 kg and a maximum value of 101.1 kg. The average of height of the respondents was 151.16 ± 6.41 cm with a minimum value of 140 cm and a maximum of 171 cm. The average of body mass index (BMI) of respondents was 27.08 ± 4.99 kg/m^2 with a minimum value of 17.91 kg/m^2 and a maximum value of 43.76 kg/m^2. The average of 25-Hydroxyvitamin D serum level was 30.96 ± 10.96 ng/ml with a minimum value of 12.70 ng/ml and a maximum value of 61.60 ng/ml. The average of FBG levels were 107.03 ± 13.74 mg/dl with a minimum value of 91.7 mg/dl and a maximum of 156.2 mg/dl (Table 1).

his study shows the average of age of premenopausal respondents is 46.73 ± 4.033 years with an age range of 40-55 years. The average of age of premenopausal women is 45-54 years. Premenopause is classified based on the criteria for Stage of Reproductive Aggregation Workshop (STRAW) with an age range of 40-55 years [12] [13]

The average of BMI in this study was 27.08 ± 4.99 kg/m^2. This study shows that the average BMI of premenopausal women of Minangkabau ethnicity in the city of Padang is obese because based on the BMI criteria of the Indonesian Ministry of Health obesity is defined if BMI is ≥ 27 kg/m^2 [14]. This result is in line with data from the Padang City Health Office 2017 which states that the number of obesity in the population aged ≥15 years in Padang City is 18.812. Of this total, 13.091 were

female. Obesity can be caused by various factors including an imbalance in energy intake, lack of physical activity, and genetic factors. In premenopausal women, obesity can also be caused by hormonal disturbances during this time [15].

Table 2. Categorization of nutritional status based on BMI, Status of 25-Hydroxyvitamin D serum levels, FBG levels

Variable	Categorization	n = 62 (100%)	
		f	%
Nutritional status based on BMI	Very Thin (<17 kg/m^2)	-	-
	Skinny (17 - 18.4 kg/m^2)	1	1.6
	Normal (18.5 - 25.0 kg/m^2)	21	33.9
	Grease (25.1 - 27.0 kg/m^2)	14	22.6
	Obesity (> 27.0 kg/m^2)	26	41.9
25-Hydroxyvitamin D serum levels	Deficiency (<20 ng/ml)	9	14.5
	Insufficiency (21-29 ng/ml)	26	41.9
	Sufficiency (30-100 ng/ml)	27	43.5
FBG levels	Normal (≤ 100 mg/dl)	22	35.5
	Abnormal (> 100 mg/dl)	40	64.5

This study showed the nutritional status based on BMI at the obesity level (> 27.0 kg/m^2) as much as 41.9%. The serum level of 25-Hydroxyvitamin D at the level of deficiency (30-100 ng/ml) was 43.5%. abnormal FBG (> 100 mg/dl) as much as 64.5% (Table 2).

The serum levels of 25-Hydroxyvitamin D in premenopausal women in this study ranged from 12.70 to 61.60 ng/ml per day with a mean of 30.96 ± 10.96 ng/ml. This study showed that the average of serum 25-Hydroxyvitamin D levels of premenopausal women experienced vitamin D deficiency according to the classification by the Endocrine Society if serum 25-Hydroxyvitamin D levels were 30 – 100 ng/ml.16 This study shows that respondents who have vitamin D deficiency (25 (OH) D levels <20 ng/ml) are 14.5%, vitamin D insufficiency (25 (OH) D levels 21 - 29 ng/ml) are 41.9 %, vitamin D deficiency (25 (OH) D levels 30 - 100 ng/ml) was 43.5%. This study shows that serum 25-Hydroxyvitamin D levels at the level of insufficiency and deficiency are almost the same, only within 1.6% thus, the respondent's serum 25-Hydroxyvitamin D levels are overall in adequate condition.

This study showed higher results compared to previous studies, in 98 premenopausal women at Komfo Anokye Teaching Hospital, Kumasi, Ghana with average of serum 25-Hydroxyvitamin D levels 24.94 ± 4.55 ng/ml of the 98 respondents 41 people (35.7%) of them had vitamin D deficiency [16]. Other researchers also claimed similar results in 4347 respondents in the National Health and Nutrition Examination Survey (NHANES) with the average of 25-Hydroxyvitamin D serum level of 23.3 ± 9.4% in premenopausal women. The difference in results can be caused by differences in climate, sun exposure, race, culture, religion, and the method used in the measurement.

Other researchers also revealed lower results with the average of 25-Hydroxyvitamin D serum level of 27.79 ± 1.38 ng/ml. These results indicate that 41.9% of respondents had a deficiency, 39.8% of respondents had insufficiency and only 18.3 of respondents had vitamin D deficiency [17]. Another study in women aged 18-65 years in Medan obtained an average of serum 25-Hydroxyvitamin D level of 18.7 ± 7.0 ng/ml [18]. Various studies have shown that the prevalence of vitamin D insufficiency and deficiency in Indonesia is still high even though Indonesia is located in a tropical area with sufficient sun exposure throughout the year [19].

The ability to produce low vitamin D is influenced by various factors such as parathyroid hormone levels, low exposure to sunlight, wearing closed clothing (veil), low outdoor activity, and skin race/pigmentation. Women with low economic status due to vitamin D are obtained from foods that are low in vitamin D and supplements [20]. Less intake of dietary

sources of vitamin D, low milk consumption due to lactose intolerance [21]. Accumulation of fat under the skin can also reduce the bioavailability of vitamin D due to malabsorption and obesity, so BMI can affect serum 25-Hydroxyvitamin D levels.

Aging factor or age is directly related to decreased serum 25-Hydroxyvitamin D levels which cause impaired absorp-tion of vitamin D in the intestine and decreased concentrations of vitamin D precursors that are normally stored in the skin. So it experiences a decrease in its capacity to synthesize vitamin D in the skin when exposed to ultraviolet-B (UVB) radiation. It is also associated with levels of follicle-stimulating hormone (FSH), which is a biomarker of the ovarian reserve by showing a decrease in primordial follicles and triggering acceleration leading to menopause [22]. In addition, decreased estrogen can suppress the activity of vitamin 1-alpha hydroxylase-D, which plays an important role in activating vitamin D and its receptors (VDR).

FBG levels premenopausal women in this study ranged from 91.7 to 156.2 mg/dl per day with the average 107.03 ± 13.74 mg/dl. This study shows that the average of FBG of premenopausal women has increased glucose. The data of this study showed that respondents who experienced high or above normal FBG (> 100 mg/dl) were 67.7% and normal FBG (≤100 mg/dl) was 32.3%.

In theory, changes in the body's hormone levels can trigger fluctuations in blood glucose levels. This can affect the sensitivity of the body's cells to insulin. So that menopause symptoms can worsen blood glucose levels making it difficult to predict. If blood glucose levels are not controlled, there is a higher risk of diabetes complications [3]. DM is defined as a chronic disease characterized by an increase in blood glucose levels equal to or more than 200 mg/dl and fasting blood glucose levels above or equal to 126 mg/dl.

Other researchers revealed that 28 people (60.9%) of respondents who were premenopausal experienced high FBG levels 115 mg/dl with a range of 80-125 mg/dl. High blood glucose levels are a heterogeneous group of disorders characterized by high blood glucose levels or hyperglycemia [23].

Women were 1.4-2.3 times more likely to suffer from high blood glucose levels, from 38 female respondents, mostly 31 people aged 40 years or who were in the premenopausal period [24]. During premenopause the hormone estrogen decreases which results in increased insulin resistance and can lead to type 2 DM.

The factors that can increase blood glucose include: lack of exercise, consuming large amounts of food, increased stress, emotional levels, consumption of steroid-containing drugs, and increasing body weight with age [25].

Relationship between serum 25-Hydroxyvitamin D levels and FBG levels

This study showed no relationship between vitamin D and FBG levels (r = - 0.038, p = 0.769). The relationship between serum 25-Hydroxyvitamin D levels and FBG levels are clearly shown in the scatter plot below.

Correlation analysis in this study showed a negative (r = -0.038) and insignificant (p = 0.769) correlation between serum 25-Hydroxyvitamin D levels and FBG levels (Fig. 1). These results indicate that an increase in serum 25-Hydroxyvitamin D levels is not followed by an increase in FBG levels.

This study showed a correlation between 25-Hydroxyvitamin D serum levels and FBG levels with a weak and negative pattern (r = -0.038, p = 0.769). The high 25-Hydroxyvitamin D serum levels in our study were not followed by high FBG levels. The theory suggests that high 25-Hydroxyvitamin D serum levels are associated with FBG levels. Our results differ from the theory because the average respondent (41.9%) with nutritional status is obese (BMI> 27.0 kg/m^2). People with higher BMIs have lower 25-Hydroxyvitamin D serum levels due to the absorption of fat-soluble vitamin D and stored in body fat stores for later use. The greater the volume of adipose tissue, the greater the likelihood of vitamin D being trapped, thus vitamin D will be low in serum [26] [27].

Other studies also report similar results that the average of 25-Hydroxyvitamin D serum level is 4.1 ± 2.2349. Age and blood glucose levels were negatively correlated (r = -0.137, p = 0.245) [11]. The study concluded that there is no association between vitamin D intake and high FBG levels because vitamin D does not directly affect FBG levels, but affects serum vitamin D first, in which serum vitamin D can increase insulin sensitivity [10].

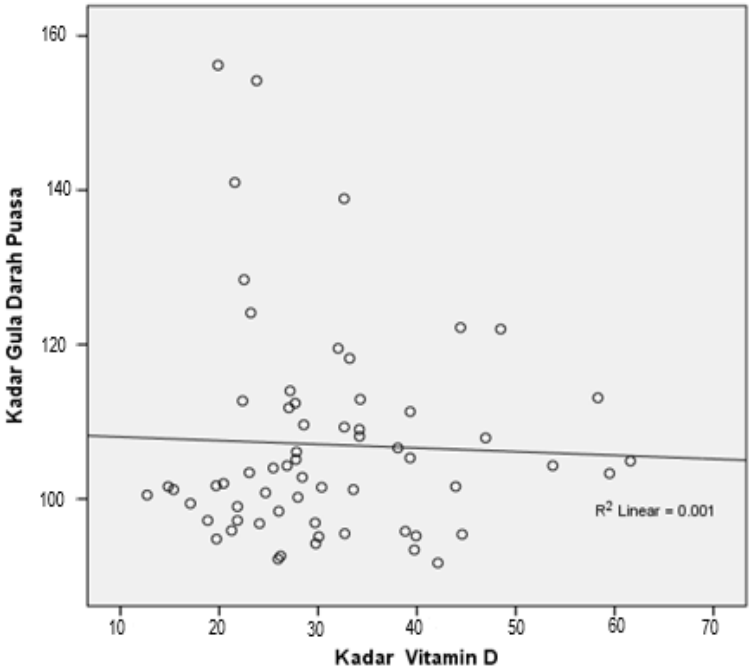

Figure 1. Log Correlation of serum 25-Hydroxyvitamin D levels with FBG levels

There were no significant differences between controlled blood glucose levels and uncontrolled blood glucose levels. There was no significant difference between 25-Hydroxyvitamin D serum levels in premenopause who experienced controlled type 2 diabetes was found (22.94 ± 6.18) higher than those with controlled type 2 diabetes (20.99 ± 6.47) with p-value = 0.310 [28].

Previous researchers also demonstrated a significant association between vitamin D and glycemic control, suggesting that vitamin D improves insulin sensitivity and improves pancreatic beta-cell function. This cross-sectional study, involving 680 Brazilian women aged 35-74 years, aimed to evaluate the possible association between vitamin D deficiency and increased glycemia. Of the women interviewed 24 (3.4%) taking vitamin D supplements was negatively associated with high blood glucose levels [29].

Other studies showed that 25-Hydroxyvitamin D serum levels were inversely related to FBG levels to age, sex, and body mass index (BMI). A negative correlation between serum 25-Hydroxyvitamin D level and degree of adiposity induced by BMI [30]. The previous study revealed that there was a significant negative correlation between serum 25-Hydroxyvitamin D levels and FBG levels [31].

Adequate serum vitamin D protects pancreatic beta cells and aids insulin synthesis and secretion [32]. Thus increasing the insulin response to an increase in blood glucose. This is related to the role of vitamin D in increasing blood glucose levels [33]. Vitamin D supplements do not affect controlling blood glucose levels. Rather, glucose secretion and insulin sensitivity are by regulating extracellular calcium (Ca^{2+}) concentration and flux through β cell membranes in insulin target tissue [10] [34].

Other researchers also report similar results on the role of vitamin D which was not related to the concentration of FBG secretion levels [35]. Similar findings were also reported in

a study of 380 Malay adults (mean age 48.5 years) there was no correlation between 25 (OH) D FBG levels [20] [36].

It is known that vitamin D deficiency in people with high FBG levels or DM in many countries, it's just that the prevalence and mean value are different which can be caused by differences in geographic location, race, skin color, genetics, BMI, culture and a diet rich in vitamin D. Non-diabetic vitamin D deficiency in Indonesia has a mean serum value of 25-Hydroxyvitamin D of 15.57 ng/ml in addition to taking into account Indonesia's high culture of wearing hijab and other sun protectors.

Conclusion

The average serum level of 25-Hydroxyvitamin D in premenopausal Minangkabau ethnicity women was 30.96 ± 10.96 ng/ml, this value indicates that the average 25-Hydroxyvitamin D serum level is at a level of deficiency. The average FBG level in premenopausal Minangkabau ethnicity women was 107.03 ± 13.74 mg/dl, this value shows that the average of FBG level is abnormal. There is no relationship between 25-Hydroxyvitamin D serum levels and FBG levels in premenopausal Minangkabau ethnicity women.

Statistically, in this study, it was stated that there was no correlation between 25-hydroxyvitamin D levels and FBG levels, but in theory and other researchers reported a relationship between the consumption of foods containing vitamin D sources in controlling blood glucose levels. Thus, we suggest increasing health promotion and preventive efforts through health services such as counseling on the importance of consuming food sources of vitamin D and the importance of maintaining normal blood sugar levels.

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