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Relationship between vitamin D, vitamin C and blood glucose in patients with type 2 diabetes mellitus

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ABSTRAK

Latar Belakang: *Diabetes Melitus merupakan penyakit kronis yang terjadi ketika pankreas tidak lagi cukup dalam memproduksi insulin. Diabetes Melitus sebagai salah satu dari lima penyakit tidak menular yang menyebabkan kematian tertinggi sehingga diprioritaskan untuk pencegahan dan pengendaliannya. Beberapa penelitian vitamin D dan vitamin C menunjukkan kecendrungan variasi pro dan kontra dalam peningkatan sensitivitas insulin penderita Diabetes Melitus.*
Tujuan: *Mengetahui hubungan konsumsi vitamin D dan vitamin C dengan kadar glukosa darah pada pasien rawat jalan Diabetes Melitus tipe 2 Rumah Sakit Umum Daerah Harapan dan Doa Kota Bengkulu.*
Metode: *Desain penelitian observasional analitik dengan pendekatan cross sectional. Populasi penelitian adalah pasien diabetes melitus tipe 2. Sampel sebanyak 57 pasien dengan teknik purposive sampling. Analisis data menggunakan uji Korelasi.*
Hasil: *: Uji korelasi vitamin D dengan glukosa darah menunjukkan nilai p = 0,238, sedangkan vitamin C dengan kadar glukosa darah adalah nilai p = 0,000.*
Kesimpulan: *Tidak ada hubungan konsumsi vitamin D dengan kadar glukosa darah, namun ada hubungan konsumsi vitamin C dengan kadar glukosa darah pada pasien rawat jalan Diabetes Melitus tipe 2.*

KATA KUNCI*: diabetes melitus tipe 2; glukosa darah; vitamin C; vitamin D*

ABSTRACT

Background: *Diabetes mellitus is a chronic disease that occurs when the pancreas no longer produces enough insulin. Diabetes mellitus is one of the five non-communicable diseases with the highest mortality rate, therefore, its prevention and control are prioritized. Several studies on vitamin D and vitamin C have shown varying trends in improving insulin sensitivity in people with diabetes mellitus.*

Objectives: *To determine the relationship between vitamin D and vitamin C consumption and blood glucose levels in outpatients with type 2 diabetes mellitus at Harapan dan Doa Regional General Hospital, Bengkulu City.*

Methods: *The study design was an observational analytical study with a cross-sectional approach. The study population was patients with type 2 diabetes mellitus. A sample of 57 patients was selected using a purposive sampling technique. Data analysis used a correlation test.*

Results: *The correlation test for vitamin D and blood glucose showed a p-value of 0.238, while the correlation between vitamin C and blood glucose levels showed a p-value of 0.000.*

Conclusions: *There is no relationship between vitamin D consumption and blood glucose levels, but there is a relationship between vitamin C consumption and blood glucose levels in outpatients with type 2 diabetes mellitus.*

KEYWORD*: blood glucose; type 2 diabetes mellitus; vitamin D; vitamin C;*

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INTRODUCTION

The number of people with diabetes has increased from 200 million in 1990 to 830 million in 2022. This increase is more pronounced in low- and middle-income countries than in high-income countries. Diabetes complications can lead to blindness, kidney failure, heart attacks, strokes, and lower limb amputations. In 2021, data showed that more than 2 million deaths from diabetes and kidney disease were caused by diabetes. Furthermore, approximately 11% of cardiovascular deaths were attributable to diabetes (1). The prevalence of Diabetes Mellitus among adults aged 20 to 79 years worldwide in 2021 is 10.5% (536.6 million), increasing to 12.2% (783.2 million) by 2045. Globally >90% of all Diabetes cases are type 2, Diabetes Mellitus cases in Indonesia aged between 20 to 79 years are 19.5 million people which makes it the fifth most common disease in the world and causes 6.7 deaths, or 1 every 5 seconds in 2021 (2). Patients with Diabetes Mellitus in Indonesia based on gender are more women (1.8%) compared to men (1.2%), the most common age group is 55-64 (6.29%), and people with Diabetes Mellitus in Bengkulu Province based on doctor's diagnosis are 0.9% (3).

Type 2 diabetes mellitus has risk factors that are based on the interaction of genetic and metabolic factors. Diabetes Mellitus risk factors, some of which can be controlled such as obesity, physical activity, hypertension, dyslipidemia, high calorie diet, and smoking while those that cannot be controlled such as age, gender, ethnicity, race, genetics, history of giving birth to babies weighing >4000 grams, history of giving birth to babies with low birth weight <2500 grams (4). The mechanism of vitamin D in Diabetes Mellitus is that vitamin D has an effect on regulating insulin receptors and controlling fatty acid metabolism in adipose tissue and skeletal muscle, both of which play an important role in insulin sensitivity in people with Diabetes Mellitus. Vitamin D influences the regulation of insulin receptors and the control of fatty acid metabolism in adipose tissue and skeletal muscle, which are crucial for insulin sensitivity in individuals with Diabetes Mellitus. This is how vitamin D is involved in Diabetes Mellitus (5). The mechanism of vitamin C in type 2 diabetes mellitus with vitamin C consumption is insulin resistance and low insulin production is the cause of oxidative damage to β cells caused by excess ROS in the body resulting in fat

peroxidation. Ascorbic acid known as vitamin C is a water-soluble vitamin that acts as a powerful antioxidant that works by giving its electrons to fat radicals to end the chain reaction in the process of fat peroxidation (6). Based on previous research, 500 mg of vitamin C per day is considered sufficient to reduce blood glucose levels (7). Research shows vitamin D and glycaemic control are associated in patients with type 2 diabetes mellitus and identification of vitamin D response in the insulin promoter region triggers insulin gene production (5). Research shows the consumption of foods high in vitamin C and blood sugar levels shows there is a relationship between vitamin C consumption and blood glucose levels (8).

Initial survey with 10 respondents conducted in the Internal Poly room of Harapan and Doa Hospital, Bengkulu City. Vitamin D consumption of 10 respondents 10 of them were in the deficient category while vitamin C consumption of 10 respondents 5 of them were in the deficient category, and 5 of them had a good category. The average results obtained are as follows: average vitamin D consumption of 2.61 mcg/day, average vitamin C consumption of 63.4 mg/day. Of the 10 respondents with vitamin D and vitamin C consumption in the deficient category, 4 of them had a blood glucose level ≥200 mg/dl. Based on the description above, the results of previous studies that significantly link vitamin D and vitamin C consumption with blood glucose levels are still very few, so researchers are interested in conducting further research on the relationship between vitamin D and vitamin C consumption with blood glucose levels during outpatient Diabetes Mellitus type 2 patients at Harapan and Doa Hospital, Bengkulu City.

MATERIALS AND METHODS

This study used an analytic observational design with a cross-sectional research approach taken at the same time. The research was conducted in the inner poly room of Harapan and Dia Hospital, Bengkulu City. The study was conducted from February to March 2024 with the study population being type 2 Diabetes Mellitus patients aged 35-65 years at the age of male and female adult to pre-elderly with a total of 57 subjects who came to do outpatient treatment at Harapan and Doa Hospital, Bengkulu City. The subject to be taken in this study by purposive sampling determines the research subject with certain considerations which aim to make the data obtained more representative.

The types of data collected include primary data and secondary data: Primary data is data obtained directly from the subject consisting of subject identity, vitamin D consumption, vitamin C consumption obtained from subjects by recording directly using the Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) form. Subject identity consists of name, age, gender, body weight, results of blood glucose levels at baseline. Secondary data is data obtained from hospitals such as hospital descriptions, respondent identities, respondent disease histories. The data collection method consists of: vitamin D and vitamin C consumption by conducting a survey history interview of food consumption in the past month using the SQ-FFQ form. Calculate the food consumption score by summing up all the subject's scores based on the sum of the consumption column scores for each food ever consumed. Calculation of daily consumption. Daily consumption was calculated by multiplying the weight of each serving by the frequency of consumption. For example, daily consumption is known based on the result of multiplying the weight of each serving by the frequency of consumption, the result is then divided by the number of days (for example: subject A consumes biscuits (2x/month which means 40 grams x 2 = 80/30 = 2.6 grams/day) Data on the amount of food consumed can be analyzed for nutritional content using nutrisurvey (9). Age and gender were collected by conducting an interview using the respondent identity form. Body weight was collected by measuring the body weight of the subjects using a GEA ZT digital scale with an accuracy of 0.1 kg which was carried out by the researcher during the study.

Data were analyzed using univariate analysis and bivariate analysis. Univariate analysis is an analysis that is carried out for each variable in the research results to produce the distribution and percentage of each variable, these results are to determine the distribution and frequency of vitamin D and vitamin C consumption. Then bivariate analysis was used to determine the relationship between the variables of vitamin D

and vitamin C consumption (independent) with blood glucose levels during (dependent). Statistical test if p-value <0.05 then the calculation result reads, there is a relationship between the dependent variable and the independent variable in each ratio scale. Using bivariate analysis of correlation tests. Before this research was conducted, it had been submitted to Poltekkes Kemenkes Bengkulu for ethics for research eligibility and had been issued with a code of ethics No. KEPK.BKL/004/02/2024. There was an explanation before conducting the research by filling in the informed consent by the subject to request the subject's approval during the research.

RESULTS AND DISCUSSIONS

Description of Respondents

Description of respondents based on age and gender categories can be seen in the following table. Based on **Table 1**, the frequency of respondent characteristics based on the age of patients with type 2 diabetes mellitus was highest in the age group 61 to 65 years as many as 19 patients with a percentage of 33.3% while the lowest was in the age group 35 to 45 years as many as 3 patients with a percentage of 5.3%. Based on the gender of patients with type 2 diabetes mellitus, the highest number of women were 33 patients with a percentage of 57.9% compared to men as many as 24 patients with a percentage of 42.1%.

Table 1. Frequency distribution of diabetes mellitus patient characteristics

Characteristics	n	(%)
Age (years)		
35-40	3	5.3
41-45	3	5.3
46-50	7	12.3
51-55	14	24.6
56-60	11	19.3
61-65	19	33.3
Gender		
Male	24	42.1
Female	33	57.9

Associations between vitamin D and vitamin C consumption and real-time blood glucose levels

Frequency distribution of vitamin D, vitamin C and blood glucose levels in type 2 diabetes mellitus outpatients. Based on **Table 2**, the results of the distribution of vitamin D consumption, the average vitamin D consumption of respondents is 9.8 mcg with the lowest vitamin D consumption is 5 mcg and the highest vitamin D consumption is 19 mcg with a median of 10 and the average vitamin C consumption is 84.1 mg with the lowest vitamin C consumption of 36 mg and the highest vitamin C consumption is 132 mg. Meanwhile, the average blood glucose distribution obtained was 197 mg/dl with the lowest blood glucose level was 129 mg/dl and the highest blood glucose level was 250 mg/dL. Vitamin D consumption based on Recommended Dietary Allowance (RDA) recommended needs at the age of 9-70 years is 15 mcg / day. A total of 57 outpatients with type 2 diabetes mellitus at regional public hospital Harapan dan Doa Bengkulu City obtained the results of the distribution of vitamin D consumption on average was 9.8 mcg, this means indicating that there are still many patients in the deficit category, not meeting the needs of each individual. Sources of vitamin D nutrition in food and supplementation were used to calculate the vitamin D adequacy of each subject using the Nutrisurvey application.

Food sources of vitamin D that are often consumed in outpatients with type 2 diabetes mellitus at the Harapan and Doa Hospital, Bengkulu City are chicken eggs, mackerel, tuna, tofu, with an average frequency of 3x a week while the average food sources that are occasionally consumed in the last 1 month by patients are milkfish, margarine, butter, cheese, milk cream and vitamin D supplementation.

Table 2. Vitamin D and vitamin C consumption in type 2 diabetes mellitus outpatients

Variable	n	Mean ±SD	Median	Min	Max
Vitamin D (mcg)	57	9.8 ± 2.8	10	5	19
Vitamin C (mg)	57	84.1 ± 24	81	36	132
Blood glucose (mg/dl)	57	197 ± 35.9	188	129	250

Vitamin D has many benefits for the body, one of which is for Diabetes Mellitus patients. Vitamin D fulfillment can have an effect in regulating the insulin receptor gene and controlling fatty acid metabolism in adipose tissue and skeletal muscle, both of which play an important role in insulin sensitivity in people with Diabetes Mellitus (5). In a meta-analysis, vitamin D supplementation reduced the risk of type 2 diabetes mellitus in individuals with prediabetes by 11% (10).

Vitamin C consumption based on Recommended Dietary Allowance (RDA) recommended needs are 70-90 mg / day. A total of 57 outpatients with type 2 diabetes mellitus at Harapan and Doa Hospital Bengkulu Cityobtained the results of the distribution of vitamin C consumption on average was 84.1 mcg, this means that the average patient has met the vitamin C consumption needs of each individual in the good category. Food sources of vitamin C that are often consumed in outpatients with type 2 diabetes mellitus at the Harapan and Doa Hospital, Bengkulu City are carrots, cassava leaves, mustard greens, watercress, bananas, papaya, watermelon and oranges, with an average frequency of 4-6x weeks while the average food sources that are occasionally consumed in the last 1 month by patients are capri beans, genjer red beans, waluh pumpkin, durian, mustard greens, soursop, guava, salak, avocado, CDR and other supplements. Vitamin C has many benefits in the body, one of which is in Diabetes Mellitus patients. Vitamin C is an organic compound that the body needs in small amounts to support metabolic processes and functions as an antioxidant. In addition to being an antioxidant, vitamin C also significantly reduces the harmful effects of reactive species, such as reactive oxygen, which can damage macromolecules such as lipids, DNA, and proteins through oxidative reactions associated with chronic diseases (11).

Relationship between vitamin D and vitamin C consumption and blood glucose levels

Correlation test results of vitamin D and Vitamin C consumption with blood glucose levels in type 2 diabetes mellitus outpatients. Results obtained from statistical tests, namely vitamin D consumption and blood glucose levels with a p value = 0.238 which indicates that there is no significant relationship between vitamin D consumption and blood glucose levels during outpatient Diabetes Mellitus type 2.

Table 3. Relationship between vitamin D and vitamin C consumption and blood glucose levels in type 2 diabetes mellitus patients

Variable	*r*	*p value*
Vitamin D (mcg) vs. Blood glucose (mg/dl)	-0.159	0.238
Vitamin C (mcg) vs. Blood glucose (mg/dl)	- 0.449	0.000*

Using The Correlation Test.

Vitamin D consumption data was collected using the Semi Quantitative Food Frequency Questionnaire (SQ-FFQ) form. It was found that vitamin D consumption of 49 subjects (86%) was in the deficit category of needs and 8 subjects (14%) in the good category. On average, patients with high blood glucose levels rarely consumed sea fish, eggs, tofu, margarine, butter, cream cheese, milk, and vitamin D supplementation. Foods that are often consumed by patients are chicken eggs, chicken egg yolks, sardines, mackerel, tofu with a frequency of ≥ 1x/day to 3x/week, while salmon, margarine, butter, milk, and supplements containing vitamin D are rarely consumed at a frequency of 1-2 x/week to ≥ 1x/month. The results of the research conducted are in line with the research of Zakiyah et al (2023) on the relationship between carbohydrate intake,

fiber, vitamin D with blood glucose levels of Diabetes Mellitus inpatients, stating that there is no relationship between vitamin D intake and blood glucose levels (p = 1.000; OR = 1.09; 95% CI: 0.242-4.936). In line with the research conducted because in the results of this study the average patient has a low level of vitamin D consumption. Therefore, the level of vitamin D consumption does not show a significant relationship with blood glucose levels, patients who have higher vitamin D consumption compared to other patients but glucose levels remain in the abnormal category, the average vitamin D consumption of respondents is also small, namely 9.8 mcg per day which is still less than the recommended adequacy of 15-20 mcg per day (12).

The results of the research conducted are in line with the research of Rochmah et al (2017) on the relationship between vitamin D and calcium intake with fasting blood glucose levels of obese women stating there is no relationship between vitamin D and calcium intake with fasting blood glucose levels (p = 0.295). In line with the research conducted because in the results of this study all patients had vitamin D consumption in the deficient category while fasting blood glucose levels were mostly in the normal category which caused a lack of variation in the data, in addition, in the research conducted some subjects had not experienced menopause, so there was still estrogen production which had a protective effect on blood glucose levels (13).

The mechanism of vitamin D with blood glucose levels is that vitamin D can affect pancreatic beta cell function directly through the vitamin D receptor (VDR) found on these cells. Activation of VDR can increase the expression of genes involved in insulin production, thus increasing insulin secretion. Vitamin D plays a role in increasing insulin sensitivity in body tissues such as muscle and liver. This makes the body more efficient in using insulin to transport glucose from the blood into cells, thereby reducing blood glucose levels. Vitamin D helps in the regulation of calcium in the body. Calcium is important for the normal functioning of pancreatic beta cells and insulin secretion. Maintaining calcium balance, vitamin D can support optimal insulin production and secretion. Vitamin D has anti-inflammatory properties that can reduce chronic inflammation. Chronic inflammation is often associated with insulin resistance and type 2 diabetes. By reducing inflammation, vitamin D may help improve insulin sensitivity and lower the risk of diabetes. Vitamin D treatment could be more effective in patients under 50 years, as these populations possibly have fewer metabolic disorders. Overall, multiple mechanisms provide a foundation for ongoing interest among researchers in the clinical field to explore the potential roles of vitamin D supplements in enhancing glucose metabolism and lowering the risk of T2DM (14). Vitamin D may decrease blood glucose by increasing insulin sensitivity, glucose uptake of peripheral tissues, and glycogen synthesis in liver. Also, response elements to VD in human insulin promoters may activate insulin gene transcription (15). vitamin D supplementation can improve the glucose and lipid metabolism in T2DM patients with IR. We believe this is mainly because vitamin D can improve IR and insulin sensitivity, posing a positive effect on glucose metabolism. By increasing the expression of insulin receptor and promoting glucose transport, vitamin D is helpful to reduce blood glucose level and alleviate the glucose metabolic disorder in T2DM patients (16). Vitamin D, a hormone-like substance, has been proven to boost the production of insulin in the human body when everything is working as it should, and it also helps maintain a healthy level of glucose in the body (17). Vitamin D had a clinical positive impact on glucose level, particularly on hemoglobin A1c (HbA1c) reduction, alleviation of diabetic neuropathy and nephropathy symptoms, and hyperglycemia induced-oxidative stress on the retinal cells (18).

Vitamin D is known to have an important role in calcium and phosphate metabolism and immune function. Research shows that Vitamin D deficiency can contribute to insulin resistance, which is one of the main causes of type 2 diabetes (19). Research shows consuming vitamin D >500 IU / day reduces the risk of diabetes mellitus by 13%. other studies show vitamin D consumption >800 IU / day has a 33% lower risk of experiencing type 2 DM complications (10). The active form of vitamin D, 1,25-OHD, binds to vitamin D receptors and pancreatic beta cells, which stimulates insulin

receptors to increase insulin sensitivity and pancreatic beta cell resistance, thereby reducing proinflammatory cytokines and resulting in lower blood glucose levels (20). The results of a meta-analysis study showed that In patients with type 2 diabetes mellitus who have a history of vitamin D deficiency, vitamin D supplementation can result in lower blood sugar and HbA1C levels (21). The results of a similar study showed no relationship between vitamin D and blood sugar in type 2 diabetes patients, but the opposite was true for type 1 diabetes (22).

The results obtained from statistical tests, namely vitamin C consumption and blood glucose levels with a p value = 0.000 which indicates that there is a significant relationship between vitamin C consumption and blood glucose levels at any time with a value of r = -0.449 indicating that the two variables, namely vitamin C consumption with blood glucose levels, have a correlation with a moderate degree of correlation and a negative relationship form indicating the higher the consumption of vitamin C or the fulfilment of vitamin C needs, the lower the glucose in the blood in patients with type 2 diabetes mellitus. In line with research by Hannah Marcus (2021) An additional 80 participants (16%) could likewise be diagnosed with pre-diabetes, leaving 231 participants (46.2%) with normal blood glucose levels according to all four indicators used (i.e. fasting, post prandial, and random blood glucose, and HbA1C). there is no statistically significant association between vitamin D status and HbA1C (p ¼ 0.07) (23). In line with Mansour S Almetwazi's 2017 study. The analysis sample consists of 802 respondents without missing values for all the variables. The result shows that a small but insignificant, increase in odds (11%) of having uncontrolled diabetes exists in patients with a vitamin D deficiency after adjustment for control variables (24)

The results of vitamin C consumption taken using the *Semi Quantitative Food Frequency Questionaire* (SQ-FFQ) form, obtained data on vitamin C consumption of patients less than the average needs tend to have higher blood glucose levels, indicating patients rarely consume vegetables and fruits. Foods that are often consumed by patients are papaya, orange, pear, banana, carrots, spinach with a frequency of often ≥ 1x / day up to 3x / week and foods that are rarely consumed such as beans, moringa leaves, katuk leaves, cassava leaves, long beans, genjer, walnut pumpkin, while in fruit namely guava, mango, pineapple, soursop, avocado, sapodilla with a frequency of rarely 1-2 x / week up to ≥ 1x / month.

The research conducted is in line with based on the results of the fisher's exact test p value of 0.004 <0.05 which shows there is a significant relationship between vitamin C consumption and blood glucose levels with an OR value of 12.714 (8). The results of the study were conducted in line with using the spearman rank correlation test, the test results showed a p value of 0.021 <0.05 which means that there is a relationship between consumption of food sources of vitamin C with blood sugar levels with linear R2 0.166. This is because vitamin C can increase insulin sensitivity and can reduce blood glucose levels because of the way vitamin C works by reducing glucose toxicity and contributing to the prevention of a decrease in beta cell mass and the amount of insulin. The role in lowering blood glucose, vitamin C plays a role in modulating the action of insulin in people with Diabetes Mellitus in non-oxidative glucose metabolism (25).

The mechanism of vitamin C in type 2 Diabetes Mellitus with vitamin C consumption can reduce blood glucose levels and improve insulin sensitivity. In Diabetes Mellitus, vitamin C affects the effects of insulin, especially non-oxidative glucose, and reduces glucose toxicity while helping to prevent loss of beta cell mass and increase insulin levels (6). Vitamin C can help prevent complications of type 2 diabetes mellitus by inhibiting sorbitol production. Sorbitol is a byproduct of glucose metabolism that will accumulate in cells and play a role in the development of neuropathy. Giving vitamin C 1000-3000 mg/day to patients with Diabetes Mellitus can reduce sorbitol production (26). Vitamin C supplementation significantly improves serum parameters such as fasting blood sugar (FBS) and hemoglobin A1c (HbA1C), which are also indicators of glycemic control. Vitamin C's antioxidant properties may play a key role in helping manage diabetes and reducing oxidative stress (27). This meta-analysis aimed to investigate the effects of vitamin C

supplementation on glycemic profile in patients with T2DM. The results showed a significant decrease in serum levels of HbA1c, fasting insulin, and FBG in (28).

CONCLUSIONS AND RECOMMENDATIONS

Based on the results of the study and discussion of vitamin D and vitamin C consumption of patients with diabetes mellitus, almost all vitamin D consumption is in the deficit category while vitamin C consumption is only part of the patients in the deficit category. There is no significant relationship between vitamin D consumption and blood glucose levels and there is a significant relationship between vitamin C consumption and blood glucose levels in type 2 diabetes mellitus patients.

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