Evaluation of the impact of vitamin D on blood pressure in patients with diabetes mellitus

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Abstract

This study assessed the effects of vitamin D on blood pressure in individuals diagnosed with diabetes mellitus. Convenience sampling and a cross-sectional, analytical, quantitative approach were used. Blood samples were collected and analysed by a designated laboratory officer to measure vitamin D levels. Twenty-eight (70%) women, 18 (45%) housewives with a median age of 52 (36-60), median systole of 143.5 (102-180), and median diastole of 80 years (range, 59-110 years). Thirty-five (87.5%) had fasting blood glucose over 140 mg/dl, and 33 (82.5%) postprandial more than 100 mg/dl. The predictive validity test showed that a systole cut-off score of 160-179 yielded sensitivity, specificity, LR+, and LR– (81%, 67%, 2.4, and 0.3). Systole had a LR+ of 2.4 and was a moderate diagnostic test. Diastole cut-off score of 90-99 produced sensitivity, specificity, LR+, and LR– (84%, 67%, 2.5, and 0.2). The ROC for systole was AUC 0.65 (95% CI: 0.49-0.80) and diastole had AUC 0.67 (95% CI: 0.50-0.81). Patients with diabetes and hypertension were found to have vitamin D levels <30 ng/mL.

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Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterised by hyperglycaemia and elevated blood glucose levels beyond the normal range. DM is a significant health issue, and its prevalence is steadily increasing worldwide. According to the International Diabetes Federation (IDF), in 2021, there were 536.6 million individuals with DM worldwide, with a prevalence rate of 10.5.[1] DM has risen to become the seventh leading cause of death globally since 2013. In Indonesia, DM prevalence has shown an upward trend, as reported by Riskesdas (2018). In 2013, the prevalence was 6.9%, which grew to 8.5% in 2018.[2] According to the most recent data from the IDF for 2021, Indonesia has ranked fifth globally with a total of 19.5 million individuals affected with DM.[3]

Type 2 Diabetes Mellitus (T2DM) is a medical disorder characterised by a diminished ability to respond to insulin or impaired insulin activity in muscle and liver cells.[4] This leads to elevated blood sugar levels; pancreatic beta cells try to adjust for this by decreasing their function. Blood vitamin D levels also affect insulin synthesis in pancreatic beta cells. Vitamin D plays a crucial role in the functioning of pancreatic beta cells, as well as in insulin sensitivity and release, both through direct and indirect pathways.[5] Insufficient levels of vitamin D are linked to a higher likelihood of developing metabolic syndrome, a collection of risk factors for T2DM.[6] Vitamin D deficiency might indirectly affect insulin resistance by influencing aldosterone levels in the Renin-Angiotensin-Aldosterone System (RAAS). Angiotensin suppresses the action of insulin in blood vessels and muscles, leading to a disruption in the absorption of glucose and the fulfilment of energy requirements.[7] A research conducted by Shaheen in 2017 revealed that individuals with T2DM have deficient levels of vitamin D of <20 ng/mL. The statement above indicates that vitamin D may have a role in preventing T2DM in individuals who have not benefited from rigorous lifestyle changes.

Individuals with T2DM can develop vascular problems, including hypertension. Hypertension in individuals with DM results from high blood sugar levels, which might enhance the activation of the RAAS. Previous research has indicated a correlation between vitamin D levels and blood pressure in both individuals with and without DM. Elevated blood 25(OH)D levels are strongly linked to a reduced risk of cardiovascular disease in individuals with T2DM, regardless of genetic predisposition or variations in the Vitamin D Receptor (VDR) gene. Vitamin D has the ability to inhibit the gene responsible for producing renin, thus preventing the activation of renin-angiotensin-aldosterone and eventually preventing an increase in blood pressure.[9,10] In addition, vitamin D has the ability to block the production of COX-2 in the macula densa cells of the kidney. This prevents the conversion of arachidonic acid into prostaglandins, which ultimately leads to the inhibition of the renin gene.[9] An unhealthy lifestyle is a risk factor for hypertension in individuals with DM.[9] In the health service system, patients with DM with complications such as hypertension, as well as risk factors for complications such as the effect of vitamin D levels on DM and blood pressure, have not been widely studied in Indonesia.

Studies on the association between vitamin D levels, diabetes, and hypertension are lacking. Individuals unable to implement significant lifestyle changes may find it challenging to prevent this condition. Hence, vitamin D shows significant promise as a readily accessible, cost-effective, and secure means for lowering blood pressure. This study aimed to evaluate the sensitivity, specificity, and likelihood ratio of vitamin D on blood pressure in patients with DM.

Materials and Methods

This study employed a cross-sectional, quantitative analytical research method. This study was conducted in the outpatient clinic of Tanjung Pura University Teaching Hospital using convenience sampling. Participants diagnosed with DM and hypertension, those aged <60 years without comorbidities, including kidney failure, heart failure, or stroke, and those receiving regular outpatient therapy were included in this study. A designated laboratory officer was responsible for collecting and analysing blood samples exclusively for vitamin D examinations. The serum vitamin D (25[OH]D) levels of patients were examined using the Chemiluminescent Microparticle Immunoassay method with reagents from Architect at the Prodia Pontianak Clinical Laboratory; samples were taken from patients who underwent examination and routine follow-up at the polyclinic of the Tanjungpura University Teaching Hospital. The primary researcher collected demographic data, and blood pressure was measured using the Health Questionnaire to collect information on history, hypertension, and diabetes. A digital monitor from OMRON (model HEM-7113) was used for the blood pressure measurements.

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Statistical analysis

Descriptive analysis was used for the characteristic data. Sensitivity and specificity are the two fundamental measurements used to estimate the diagnostic accuracy of a test.[11] Sensitivity refers to a test's capacity to accurately identify the presence of a disease, while specificity refers to a test's ability to correctly rule out the condition in individuals who do not have it. The sensitivity was calculated as the ratio of true positives to the sum of true positives and false negatives, whereas the specificity was calculated as the ratio of true negatives to the sum of true negatives and false positives. The Likelihood Ratio (LR) is calculated as the ratio of the probability of obtaining a positive test result in patients with the disease to the probability of obtaining the same test result in patients without the condition. In other words, LR is a measure of how sensitive compared to (100 - specificity). The magnitude of LR indicates the level of certainty of a positive diagnosis. An LR = 1 indicated an equal likelihood of test results in patients with and without the disease. LR >1 indicates a higher likelihood of the test result in patients with the disease, while LR <1 indicates a higher likelihood of the test result in patients without the disease.[11] Also, we analysed vitamin D[12,13] and blood pressure categories[13] with the concordance statistic (c-statistic) or Receiver Operator Characteristic (ROC) curve area.[14] The statistical analysis used a significance level of $p < 0.05$. Exploratory statistical analyses were performed using the MedCalc Statistical Software version 22.009 (MedCalc Software bvba, Ostend, Belgium).

Results

The baseline characteristics of the patients are illustrated in Table 1. Twenty-eight (70%) were female, 18 (45%) were housewives. The median age was 52 (36–60) years, the median systole was 143.5 (102–180), and the median diastole was 80 (59–110). Thirty-five (87.5 %) were fasting blood glucose (>140 mg/dl) and 33 (82.5%) postprandial blood glucose (>100 mg/dl).

The sensitivities, specificities, and LR were calculated for the systole scores and ranged from <120 to >180 mmHg (Table 2). The predictive validity test indicated that a systole cut-off score of 160–179 produced the sensitivity, specificity, LR+, and LR– (81%, 67%, 2.4, and 0.3, respectively). Systole was found to be a small-to-moderate diagnostic test with a PLR of 2.4. While diastole cut-off score of 90–99 produced the sensitivity, specificity, LR+ and LR– (84%, 67%, 2.5, and 0.2, respectively). In Figure 1, sensitivity was plotted *vs.* 1-specificity for each possible score of the systole to generate the ROC; AUC 0.65 (95% CI: 0.49–0.80). While diastole: AUC 0.67 (95% CI: 0.50–0.81).

Table 1. Characteristic of participants.

Variable	
Sex n (%)	
Male	12 (30)
Female	28 (70)
Occupation n (%)	
Public servant	10 (25)
Private	12 (30)
Housewife	18 (45)
Age, median (min-max) years	52 (36-60)
Systole, median (min-max) mmHg	143.5 (102-180)
Diastole, median (min-max) mmHg	80 (59-110)
Fasting blood glucose n (%)	
<140 mg/dl	5 (12.5)
>140 mg/dl	35 (87.5)
Postprandial blood glucose n (%)	
<100 mg/dl	7 (17.5)
>100 mg/dl	33 (82.5)
Vitamin D, median (min-max)	18.4 (4.6-54.2)

Discussion

Characteristic of participants

The study's sex characteristics revealed that the number of women was 70% higher. These results are not the same as those of other researchers who reported that there were no differences between sexes and women who suffer from T2DM.[15] This discrepancy could be attributed to small sample sizes. The job characteristics revealed that 45% of the patients were housewives. The results of this study are the same as those of other studies in which individuals who did not work were at risk of developing DM.[16] Occupational factors influence the major risk of developing DM. Working with light physical activity will cause a lack of energy burning by the body, so excess energy in the body will be stored in the form of fat, which results in obesity, a risk factor for DM.[17] The median age was 52 years, and the results of this study are consistent with other studies showing that patients with DM are generally aged >40 years and have a tendency to experience a risk of vascular disorders. Blood sugar results revealed that most patients undergoing outpatient treatment or follow-up treatment (80%) had uncontrolled blood sugar levels. This shows that patients who undergo routine follow-up DM treatment are still less aware of the impact of the risk of complications that may occur to them. Therefore, it is crucial for service providers to deliver comprehensive and multidisciplinary services optimally. Patients with DM require comprehensive and multidisciplinary care to prevent complications.[19,20] This study found that the median systole was 143.5 mmHG, and it can be concluded that patients with DM are at risk of developing hypertension.

Sensitivity, specificity, and likelihood ratio

Our study found that individuals with DM with a systolic blood pressure level between 160 and 179 have a sensitivity of 81% and a specificity of 67% in relation to vitamin D levels below and above 30 ng/mL (Table 3). Nevertheless, this categorisation failed to accurately assess the vitamin D levels <30 ng/mL, underestimating it by only 19%. Furthermore, the accuracy of this categorisation was 67%. It inaccurately predicted the lack of good results for vitamin D levels of 30 ng/mL by 23%. This study demonstrated high sensitivity; however, our classification showed low specificity and was associated with a substantial false-positive rate. A precise test yields a low number of false-positive results. This study also showed equivalent levels of sensitivity and specificity in diastolic blood pressure tests for vitamin D levels at or over 30 ng/mL. Individuals in this study who had vitamin D levels <30 ng/mL, both systolic and diastolic blood pressure, and were classified as having hypertension also exhibited LR values of >1, indicating the presence of positive illnesses.[11]

Our study confirmed previous study findings indicating a substantial correlation between decreased vitamin D levels and those diseased with both DM and hypertension.[15] Literature review studies indicate that there is an ongoing disagreement over the correlation between a decline in vitamin D levels and the occurrence of hypertension.[16] It was concluded that hypertension can occur owing to many factors. Our study found that the median age of the participants was 52 years. This finding aligns with prior systematic literature reviews and meta-analysis, which have reported a substantial difference in age groups, namely those over 50.[17] There is empirical data indicating that the incidence of hypertension rises in correlation with advancing age. As individuals age, their capacity to absorb and metabolise vitamin D diminishes, leading to vitamin D deficiency. Vitamin D3 supplementation in those aged >50 years with low vitamin D levels will lead to a considerable drop in systolic blood pressure once their vitamin D levels return to normal.[17]

In patients with DM, there is an increasing number of studies indicating a substantial association between vitamin D deficiency and decreased insulin secretion in both animal models and humans.[18] Multiple studies have revealed that a deficiency in vitamin D can lead to the onset of insulin resistance and subsequently non-insulin dependent diabetes mellitus via disrupting insulin sen-

Table 2. Sensitivity, specificity, and likelihood ratio for systole score (n =40).

Criterion	Sensitivity	Specificity	LR+	LR–
<120	0	100		1.0
120-129	16	67	0.5	1.3
130-139	27	67	0.8	1.1
140-159	41	67	1.2	0.9
160-179*	81	67	2.4	0.3
>180	97	33	1.5	0.1

Table 3. Sensitivity, specificity, and likelihood ratio diastole score (n =40).

Criterion	Sensitivity	Specificity	LR+	LR–
<80	0	100		1
80-84	49	67	1.5	0.8
85-89	68	67	2.0	0.5
90-99*	84	67	2.5	0.2
100-109	92	0	0.9	
>110	97	0	0.9	

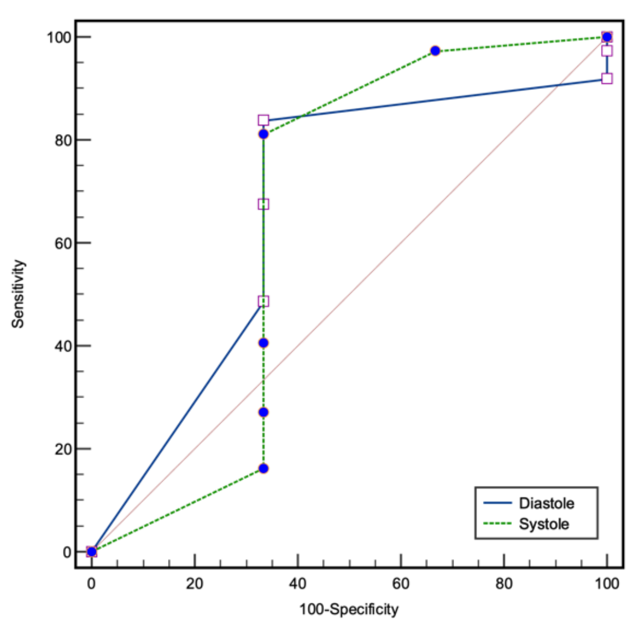

Figure 1. The receiver operator characteristic curve of the systole and diastole for vitamin D level (n 40). Systole: AUC 0.65 (95% CI: 0.49-0.80) and Diastole: AUC 0.67 (95% CI: 0.50-0.81).

sitivity and/or β-cell activity. Vitamin D3 has a hypotensive effect on patients with hypertension but is not useful for non-hypertensive patients.[18]

Nevertheless, our study found that individuals with diabetes and hypertension experienced a decline in vitamin D levels. In this study, it is imperative to explore additional factors, such as cholesterol levels, sun exposure, dietary issues, and other variables, in addition to age and diabetes, which may contribute to the situation. This study has the potential to aid in the prevention of additional problems in individuals with both diabetes and hypertension. Individuals with diabetes may encounter a weakened immune system,[19] hence it may be advisable to consider vitamin D supplements as a preventive measure against potential consequences.[20] In the meta-analysis conducted by Golzarand, it was shown that interventions lasting <6 months, with an average daily dosage >800IU/d, and daily doses were more beneficial in decreasing blood pressure.[21] While there is no consensus agreement on the necessity of vitamin D supplementation for enhancing health outcomes in the general population, administering doses between 600 and 4000 IU/day may be considered to elevate 25(OH)D levels near 50 ng/mL, potentially improving insulin resistance and related conditions.[22,23] Another study in Indonesia recommended maintaining serum vitamin D levels >20 ng/mL for patients with DM.[24] High-dose vitamin D supplementation of 300,000–500,000 IU has been shown to be safe and does not cause toxicity.[25] However, in Indonesia, there is a lack of standardised vitamin D administration for individuals diagnosed with DM and hypertension. Consequently, further investigation is required to confirm these results.

Implication in clinical practice

Our study showed that individuals with DM and hypertension were at an increased risk of developing decreased vitamin D levels. To prevent the worsening of conditions caused by vitamin D deficiency, such as the risk of metabolic syndrome, which includes increased blood pressure, high triglycerides, high low-density lipoprotein, increased waist circumference, and increased fasting glucose, this will be considered a warning in the healthcare system for patients with DM and hypertension.[22] In Indonesia, owing to the lack of standardisation in administering vitamin D to patients with DM and hypertension, these patients require additional vitamin D and monitoring of serum vitamin D levels following treatment.

Study limitations

The primary limitations of this study were its use of a cross-sectional methodology instead of a prospective (follow-up) approach, the absence of a standardised sample size pertaining to this specific topic, and the failure to investigate other factors associated with vitamin D insufficiency. The results of this study revealed that the AUC was 0.67, indicating that the diagnostic evaluation of vitamin D levels in patients with DM and hypertension was not particularly robust, which aligns with the LR findings. Consequently, additional research with extensive samples and multicentre facilities is required to generalise these results. Additional research on the impact of vitamin D dosage in individuals with DM and hypertension is essential, given the prevalence of vitamin D insufficiency identified in the current study.

Conclusions

Our study indicated that individuals with DM and hypertension had a drop in vitamin D, with a threshold score of systolic blood pressure of 160–179 mmHg, sensitivity of 81%, specificity of 67%, and likelihood ratio of 2.4. The threshold score for diastolic blood pressure was 90–99 mmHg, with 84% sensitivity, 67% specificity, and a likelihood ratio of 2.5. Consequently, individuals with DM should consistently assess their serum vitamin D levels for early identification of problems.

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