

Deficiency Serum Vitamin 25 (OH) D Levels Increase Risk Factors of Poor Quality Sleep in Resident at Sanglah Hospital

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ABSTRACT

Introduction/aim: Serum vitamin D level, estimated as 25(OH) D, is related to an increase in number of physiological mechanisms of sleep. The circadian period of the sleep can be deferred with sun exposure and vitamin D supplementation. The mechanism of lower vitamin D level causing sleep disturbances is unknown, several possible mechanisms have been proposed. Receptors of vitamin D are commonly found in most human tissues, including central nervous system. Low level of vitamin D is related with an increased risk of sleep problems, such as low sleep quality, short sleep length and excessive drowsiness. This study aims to

Methods: This study is an analytical study with a case-control design in resident St. Sanglah Hospital from July-September 2021

Result: A total of 54 subjects were divided into case and control groups, age 25-35 years. From the statistical analysis using SPSS program on bivariate analysis with Chi-square obtained OR 12.6 (95% Confidence Interval=3.4-46.0; $p < 0,001$). Multivariate analysis showed that cortisol serum had P-value $< 0,001$

Conclusion: Deficiency serum vitamin 25(OH) D levels increase risk factors of poor quality sleep thirteen times in resident at Sanglah hospital

Keywords: poor sleep quality, resident, vitamin 25 (OH) D, young people

INTRODUCTION

Sleep is one-third part of our lifetime that has critical advantages in our daily routine. Normal sleep duration is a fundamental factor for metabolism and general wellbeing. According to The National Sleep Foundation, adults are suggested to get 7-8 hours of sleep each day; even though sleep needs vary by age and sexual orientation. Lacking or extreme sleep span is related to different physical or psychological instabilities, like obesity, diabetes, hypertension, metabolic disorder, depression, and other mental illnesses. Lately, sleep problems have turned into a worldwide epidemic. However, numerous people including medical staff, are ignorant of their side effects.[1] Sleep span is mostly impacted by circadian rhythm, and levels of melatonin controlled by light exposure will affect the circadian rhythm. Therefore, sun exposure plays a fundamental part in determining sleep time.[2]

Vitamin D is a fundamental supplement known to be a fundamental part in the development and bone wellbeing of the human body. Vitamin D can be acquired from food as ergocalciferol (nutrient D2) or generated in the skin as cholecalciferol (nutrient D3) by the activity of ultraviolet (UV) light.[3] Vitamin D is a novel fat-solvent nutrient acquired from food intake or incorporated through UVB radiation. It is assumed that the best indicator of vitamin D

level in the body is 25-hydroxyvitamin D. Serum 25-hydroxyvitamin D level may be influenced by several factors such as lifestyle, insufficient sun exposure, and skin tone. Vitamin D insufficiency is common; the benefit of vitamin D related with cardiovascular sickness, infectious disease, and sleep issues is getting more attention given the lack of study on this matter.[1]

Serum vitamin D level, estimated as 25(OH) D, is related to an increase in number of physiological mechanisms of sleep. The circadian period of the sleep can be deferred with sun exposure and vitamin D supplementation. At last, serum vitamin D level is associated to daytime lethargy, and epidemiological examinations have shown that nutrient D level is related to mid-point of sleep, sustained sleep, and sleep length in grown-ups.[2] Several investigations reported that the receptors of vitamin D are expressed in brain areas that manage sleep-wake cycles, such as hypothalamus. This proof proposes that higher vitamin D level decreases the risk of sleep disturbances.[1]

METHOD AND PROCEDURES

This study is an analytic observational study with a case-control design to determine that deficiency serum vitamin 25(OH) D levels increase risk factors of poor quality sleep in resident at Sanglah hospital. We collected the data from resident Neurology at Sanglah General Hospital Denpasar from July to September 2021. We collected the samples serum vitamin 25(OH) D from the subjects in laboratories every afternoon after finished the job as resident. Deficiency vitamin D if

the level serum vitamin 25(OH) D total < 20 ng/ml. The sleep quality of the samples was assessed using the PSQI questionnaire. Permission ethics in this study from the ethics commission research of the Faculty of Medicine, Udayana University/Sanglah Central General Hospital Denpasar.

The case inclusion criteria in this study were: (1) All resident signed informed consent (2) 25-35 years old. The exclusion criteria were: (1) Resident with moderate-severe depression, moderate-severe anxiety, obesity (BMI>30), history of using hypnotic drugs, stimulants, and alcohol in the last 30 days. We analyzed the data statistically using SPSS version 23 for Windows.

RESULT

The study involved 54 resident subjects who met the eligibility criteria, grouped into groups with poor sleep quality (27 subjects) and good sleep quality (27 subjects).

The sample characteristics assessed in this study included gender, age, marital status, level serum 25(OH) D, at **table 1**.

Table 1: Characteristics of Subjects Based on Research Groups

Variable	Case	Control
	n (%)	n (%)
Average age (years)	28.2 (25-35)	28.7 (25-35)
Gender	Man	9 (33%)
	Female	18 (67%)
Marital status	Married	11 (41%)
	Not married	18 (67%)
Serum 25(OH)D level (mean)	25.0 (12.7-38.7)	18.9 (17.1-20.0)

The correlation between serum vitamin 25(OH) D total levels and risk factors for poor sleep quality in the resident with bivariate analysis showed the results in **table 2**.

Table 2: Bivariate Analysis of serum vitamin 25(OH)D total levels as a risk factor for poor sleep quality in the resident

Variable	Case n (%)	Control n (%)	OR	95% CI	p*
Serum vitamin 25(OH)D total levels	Normal	7 (26%)	12.6	3.4-46.0	<0.001†
	Deficiency	20 (74%)			

† significant * Chi-Square

Based on the bivariate analysis using the Chi-square test, there was a significant relationship between deficiency serum vitamin 25(OH)D total levels as a risk factor for poor sleep quality in the resident with

OR=12.6 (95% CI=3,4-46.0; p<0.001). Deficiency serum vitamin 25(OH) D total levels have an increased risk of experiencing a poor sleep quality 12.6 times

compared to the resident with normal vitamin 25(OH) D total

Other factors that also affect the risk of poor sleep quality in resident including

gender, age, marital status which will be analyzed multivariate with the results obtained in **table 3**.

Table 3: Multivariate Logistic Regression Analysis

Characteristic	Adjusted OR	CI 95%	P (value)
Step 1			
Vitamin 25(OH)D total level	15.5	3.6-66.0	<0.001
Gender	0.5	0.7-1.0	0.306
Married	0.5	0.7-0.6	0.426
Age	0.8		0.934
Step 2			
Vitamin 25(OH)D total level	15.4	3.7-62.7	<0.001
Gender	0.5	0.1-1.9	0.302
Married	0.6	0.1-2.3	0.418
Step 3			
Vitamin 25(OH)D total level	14.6	3.7-57	<0.001
Gender	0.4	0.2-1.6	0.207
Step 4			
Vitamin 25(OH)D total level	12.6	3.4-46.0	<0.001

Based on multivariate analysis results, it was found that deficiency serum vitamin 25(OH)D total levels as a risk factor for poor sleep quality in the resident with OR=12.6 (95% CI=3,4-46.0; p<0.001) as independent risk factors for poor sleep quality in resident is statistically significant.

DISCUSSION

Serum 25-Hydroxyvitamin D or 25(OH) D plays a part in calcium and phosphate metabolism for maintenance of normal musculoskeletal condition. Ongoing clinical investigations have shown that 25(OH) D may be associated with persistent metabolic disorders. Receptors of the 25(OH) D are available in most cells of the body and generate a variety of symptoms because of the chemical like impacts of 25(OH) D. Low level of vitamin D is frequently overlooked as it tends to cause no symptoms. UV beams exogenously trigger the generation of 25(OH)D, and it can be acquired by food consumptions. Discrepancies in 25(OH)D bioavailability have been accounted for relying upon the structure, activation pathway involved, and route of administration. Nowadays, it is not easy to get sufficient exposure to the sun due to more indoor activities.[2]

Resident activities in 70% at indoor place so sun exposure lower than others who works outside. In contrast to previous studies which stated that vitamin D levels

were lower in the younger age group who spend more time indoor and tend to use sunscreen.[4] In an investigation led by Choi Ji Ho et al. concerning impact of low sun exposure and other risk factors in vitamin D insufficiency found sun exposure and vitamin D level had strong relationship which is the effect of 25 (OH)D activation pathway as indicated by past investigations. [2] Other than homeostasis of the bone, vitamin D is involved in several physiological mechanisms such as sleep, immunity, and others. Though the mechanism of lower vitamin D level causing sleep disturbances is unknown, several possible mechanisms have been proposed. Receptors of vitamin D are commonly found in most human tissues, including central nervous system.[1]

1. Relationship between sleep duration and serum 25-Hydroxyvitamin D level

In a research same with conducted by Choi Ji Ho et al. in 2020, it was discovered that there was no remarkable difference between vitamin D level and sleep duration in a person exposed to adequate daylight. However, in the subject that rarely get sun exposure, it was discovered that people with lower level of 25(OH)D had excessive sleep length, even when the confounding factors were already controlled. Previous research has shown that lower vitamin D level was associated with

shorter sleep duration, although the data were limited by age and the sun exposure and other factors were not controlled. In spite of the fact that vitamin D supplementation has been accounted for increased sleep quality, its effect on sleep span has not been studied.[2]

Vitamin D deficiency can indirectly affect sleep length and quality by increasing the risk of chronic nonspecific musculoskeletal pain, indirectly affecting sleep quality and sleep duration. The finding of delayed sleep time by nearly one hour in a person with low level of vitamin D may explain that vitamin D level functions as one of the modulators of the circadian rhythm. In line with this, previous studies have reported that supplementation with high dose vitamin D negatively affects melatonin production. This effect will indirectly affect the circadian rhythm. Vitamin D can also directly impact vitamin D receptors in the suprachiasmatic nucleus, which is the central circadian clock in the brain.[3]

Low serum vitamin D level is associated with longer sleep duration in people with low sun exposure. Hence, if a locality has low sun exposure, sufficient level of vitamin D will be required for normal sleep duration. Investigation of the connection between serum vitamin D level and sleep span in the extraordinary sun openness bunch didn't track down any huge distinction between nutrient D status in the normal sleep group and sleep-deprived group. Nevertheless, the oversleeping group had lower 25(OH) D levels significantly, compared to the normal sleep group, even after confounding variables are controlled. [2]

The correlation between vitamin D level, exposure to sun, and sleep span showed that, after adjusted for demographic, physical, lifestyle, and sociodemographic variables, vitamin D level alone have no effect on sleep duration, although in different factors, including sun exposure and sleep span, there were significant relationship. Based on sleep duration, in

subjects with low sun exposure, there was statistical differences on 25(OH)D level. Compared to the normal sleep span, subjects with low sun exposure and excessive sleep span had lower 25(OH) D level. Individual with limited sun exposure had to keep adequate vitamin D level to get adequate sleep duration for wellbeing.[2]

Vitamin D supplementation treatments in adult have shown improvements in sleep span and other measures of sleep quality. A recent study by Yong et al. hypothesized that vitamin D deficiency may have long term impacts on sleep span. They found that patients with low cord blood vitamin D levels at birth had reduced risk of sleep length of less than 10.5 hours/night in the preschool years between the ages of 2 and 5-6 years.[3]

2. The Correlation of Vitamin D Deficiency with Sleep Quality

A remarkable correlation was found between deficiency of serum vitamin D level and reduced sleep quality. A study from Jung et al. found that the treatment of sleep disorder in workers can be done by regularly checking the levels of serum vitamin D, and giving vitamin D to subjects who suffer from deficiency of serum vitamin D, to further improve sleep quality. [4] Low level of vitamin D was not related with sleep stage, periodic limb movement and arousal index. Vitamin D deficiency was correlated with almost 60 minutes of delayed sleep. There was also a tendency for these patients to wake up later, however this difference was not statistically significant.[3]

Many factors can affect sleep quality, and deficiency of serum vitamin D is one of them. A research conducted in Korea by Jung et al. demonstrated that serum vitamin D deficiency was related with sleep quality and other factors. Based on these outcomes, the working environment may control sleep problem by performing routine serum vitamin D tests along with proper treatment to prevent sleep issues.[4]

3. Different Factors Affecting Vitamin D

Different factors have been associated with a significant increase in serum vitamin D levels, including routine exercise, smoking, alcohol consumption, marital status and examination season. Through exposure to ultraviolet, practice helps the making of vitamin D in the skin. It can be concluded that the subject who practiced at least three times a week had more exposure to sun, resulting in higher levels of vitamin D. In addition, smoking and alcohol intake can influence parathyroid hormone, which affect calcium absorption, and eventually lead to vitamin D deficiency. From June to August, which are the summer months, serum vitamin D levels were at peak, with average level of 16.87 ng/mL. The lowest levels were found in winter months from December to February, with an intermediate level of 11.54 ng/mL. These outcomes are also consistent with past investigations showing that in winter, lower serum vitamin D levels are found, due to production of vitamin D in the skin rely upon the amount of sun exposure.[4]

Vitamin D is additionally connected with the event of Obstructive Sleep Apnea Syndrome (OSAS). The connection between low level of vitamin D and OSAS is mediated by a complex mechanism and several confounding factors. When clinically indicated, screening of vitamin D levels among OSAS patients are suggested to be performed, due to the fact that low level of vitamin D is common among them. On comorbidities related with OSAS, like cardiovascular problem, the good effects of vitamin D should be thought of, particularly in the relatively limited cost of vitamin D supplementation.[5]

4. Connection between Deficiency of Vitamin D and Sleep Disorders

The mechanism by which vitamin D influences sleep is not fully understood. Animal studies have shown that receptors of vitamin D in brain areas were associated with sleep regulation, such as the hypothalamus, raphe nuclei and midbrain

grey matter, suggesting the importance of vitamin D in sleep regulation. Deficiency of vitamin D can directly affect sleep by acting on these sleep-regulating centre.[3]

In population, low level of vitamin D is associated with increased risk of sleep disorder. Further subgroup analysis showed that serum vitamin D level <20 ng/mL might contribute to the increasing risk of sleep problem. The relationship between deficiency of vitamin D and sleep distraction including bad sleep quality, short sleep span, and drowsiness, revealed that levels of serum 25(OH)D are inversely connected with increased sleep disturbance. [6] and same with this case.

The connection between serum vitamin D levels and sleep problems can be reciprocal. Sleep disturbances can lead to reduced vitamin D level by affecting the duration of sunlight exposure, vitamin D metabolism or even absorption. There are many components related with vitamin D and various aspects of the sleep schedule. External factors affect sleep time, and intrinsic factors assess sleep duration and sleep efficiency. Vitamin D might play a part in a child's sleep, especially the duration and efficiency. Furthermore, vitamin D may likewise play a part in circadian rhythms.[7]

Chronic and non specific clinical pain may be a marker for low level of vitamin D. Deficiency of vitamin D is quite common in patients who complain intractable pain with uncertain causes. People with chronic pain are at risk for low sleep quality and short sleep length. High level of pain sensation was related with lack of sleep and related with increased IL-6 level. Pain score, sleep quality, and different parts of Quality of Life can be enhanced significantly following supplementation of vitamin D.[7-9]

Low level of vitamin D can increase the possibility that lead to autoimmune diseases and respiratory infections. Vitamin D might play a part in immunomodulation by changing immune regulation, reducing inflammatory factors, along with those that

modulate sleep, like tumor necrosis factor (TNF-a), prostaglandin D2, and cytokines. Patients with OSAS had more elevated levels of lipocalin-type PGD synthase compared to patients without OSAS. This shows that low level of vitamin D can also control symptoms of frequent awakening from sleep which is commonly associated with sleep disorders.[4,10]

CONCLUSION

Deficiency serum vitamin 25(OH) D levels increase risk factors of poor quality sleep thirteen times in resident at sanglah hospital

Informed Consent and Patient Details: The authors declare that this case report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

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