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THE ASSOCIATION BETWEEN SERUM VITAMIN D LEVELS AND LIPID PROFILES AMONG PEOPLE WITH EPILEPSY

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ABSTRACT

Background and Purpose: Epilepsy, a neurological condition, is defined by the occurrence of unprovoked seizures on at least two occasions, with a minimum interval of 24 hours separating the initial and subsequent events. Individuals diagnosed with epilepsy frequently exhibit vitamin D deficiency, which influences various metabolic processes, including modifications to lipid profiles. Despite this, the precise relationship between serum vitamin D levels and lipid profiles continues to be a subject of ongoing investigation. This study aimed to examine the correlation between serum vitamin D concentration and lipid profiles. **Methods:** A cross-sectional study design was employed, encompassing 29 patients with epilepsy who were treated at the outpatient clinic of the Department of Neurology, Diponegoro National Hospital, Semarang. Participants were divided into two groups based on their serum vitamin D levels: the vitamin D deficiency group (n=9) and the vitamin D insufficiency group (n=20). Demographic and clinical information was gathered, vitamin D levels were measured using ELISA, and lipid profiles were assessed using spectrophotometry. A chi-square analysis was conducted to explore the relationship between serum vitamin D levels and lipid profiles in patients with epilepsy. **Results:** The average vitamin D concentration was 13.45 ± 5.74 ng/mL, with all participants showing deficient vitamin D. Examination of lipid profiles indicated mean values for total cholesterol at 183.76 ± 38.34 mg/dL, LDL cholesterol at 103.55 ± 34.92 mg/dL, HDL cholesterol at 48.72 ± 15.98 mg/dL, and triglycerides at 158.14 ± 104.48 mg/dL. Statistical analysis revealed that LDL levels were significantly elevated in the group with insufficient vitamin D ($p = 0.029$), while there were no significant differences in triglyceride, total cholesterol, or HDL levels. Statistical analysis revealed that LDL levels were significantly elevated in the group with insufficient vitamin D ($p = 0.029$), while there were no significant differences in triglyceride, total cholesterol, or HDL levels. **Conclusion:** There may be a link between low vitamin D levels and adverse LDL cholesterol levels; however, further research is required to confirm this.

Keywords:

Epilepsy,
Vitamin D,
Lipid profiles,
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INTRODUCTION

Epilepsy is a prevalent neurological condition characterized by repeated unprovoked seizures. ¹⁾ It affects people of all ages, genders, and ethnic backgrounds, with differences in prevalence,

incidence, risk factors, and mortality rates across various groups. ²⁾ Worldwide, approximately 50 million individuals are affected by epilepsy, ranking it among the most widespread neurological disorders. ³⁾ Epilepsy has a greater impact on low- and middle-



income countries (LMICs) due to increased exposure to risk factors, such as infections and limited access to healthcare.⁴⁾ Vitamin D is essential for bone health, immune function, and neurological processes in the body.⁵⁾ In people with epilepsy (PWE), vitamin D levels are particularly concerning because of the effects of antiepileptic drugs (AEDs), a heightened risk of bone disorders, and potential implications for seizure management.⁵⁾ Research indicates that 30–80% of PWE experience vitamin D deficiency or insufficiency due to various factors, including medication effects, reduced sunlight exposure, and lifestyle choices, increasing their risk of osteoporosis, osteomalacia, and fractures.^{5), 6), 7), 8), 9)} Unfortunately, there is a lack of extensive data on this issue in Indonesia. Hospital-based data from Jaeri et al. show that PWE have Vitamin D deficiency or insufficiency, but the study did not identify the factors contributing to the reduction of vitamin D.⁹⁾ Vitamin D is also vital in lipid metabolism, affecting cholesterol synthesis, transport, and storage.¹⁰⁾ Research suggests a possible connection between vitamin D levels and lipid profiles, although the findings are inconsistent.¹⁰⁾ Some studies have found that low vitamin D levels are linked to higher low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) levels and lower high-density lipoprotein cholesterol (HDL-C) levels.¹¹⁾ A meta-analysis supports this association, showing that individuals with vitamin D deficiency often have poorer lipid profiles than those with adequate vitamin D.¹¹⁾ However, observational studies cannot confirm whether low vitamin D directly causes dyslipidemia or whether impaired lipid metabolism leads to vitamin D deficiency.¹⁰⁾ Despite the increasing interest in the role of vitamin D in lipid metabolism, several research gaps persist. While some studies indicate a link between vitamin D deficiency and dyslipidemia, others report weak or non-significant associations between the two. Additionally, the direction of causality is still unclear,¹³⁾ and the precise molecular mechanisms by which vitamin D influences lipid metabolism are not fully understood.¹³⁾ In this study, we aimed to evaluate the relationship between serum vitamin D levels and lipid profiles, including total cholesterol (TC), LDL-C, HDL-C, and TG, to better understand the role of vitamin D in lipid metabolism.

METHODS

This observational analytic study involved twenty-nine epilepsy patients who were consecutively recruited from the neurology outpatient department at Diponegoro National Hospital between March and August 2024. Participants were required to meet the following criteria: 1) adults aged 18–65 years with a diagnosis of epilepsy; 2) no vitamin D supplementation in the previous six months; and 3) no use of lipid-lowering drugs or conditions impacting lipid metabolism. The exclusion criteria were as follows: 1) chronic kidney disease, liver disease, or endocrine disorders (including parathyroid hormone issues) and 2) the use of medications known to affect vitamin D metabolism, such as corticosteroids and certain antiepileptic drugs. The sample size was determined using a formula for correlation study.

Demographic information, including age, sex, and anthropometric data such as body mass index (BMI), lifestyle factors, and history of previous diseases such as diabetes mellitus (DM), hypertension, and cardiovascular disease, were gathered from medical records. Venous blood samples were collected from the median cubital vein for laboratory tests. Serum 25-hydroxyvitamin D (25(OH)D) levels were measured using ELISA at the Gangguan Akibat Kekurangan Yodium (GAKY) Laboratory, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia. Serum 25(OH)D concentrations were categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥ 30 ng/mL). Lipid profiles, including TC, LDL-C, HDL-C, and TG levels, were assessed using enzymatic colorimetric techniques.

Data analyses were performed using SPSS for Windows (version 23). Initially, descriptive analyses were performed to characterize the participant attributes, with continuous variables expressed as mean \pm SD and categorical variables as proportions. Subgroup analyses stratified by vitamin D status were performed on demographic and clinical variables. The association between serum vitamin D levels and lipid profiles (TC, LDL-C, HDL-C, and TG) was examined using Fisher's exact test.

This investigation synthesizes the outcomes of three studies. The study protocols were sanctioned by the Local Research Ethics Committee, and ethical approval was obtained from the Health Research



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Ethical Committee RSUP Dr. Kariadi, Semarang, Indonesia, with the following ethical clearance numbers: 007/EC/KEPK/FK-UNDIP/I/2024, 289/EC/KEPK/FK-UNDIP/IX/2024, and 515/EC/KEPK/FK-UNDIP/IX/2024. Informed

RESULTS

Participant Characteristics

Table 1 presents the participants' characteristics. The mean age was 32.03 ± 12.56 years, with an age range spanning from 18 to 56 years; furthermore, a greater proportion of the sample was male (62.1% male, 37.9% female).

Table 1. Demographic Characteristics

Characteristics	Frequency	%	Mean \pm SD	Median (min – max)
Age (Years)			$32,03 \pm 12,56$	27 (18 – 56)
Gender				
Male	18	62,1		
Female	11	37,9		
Anthropometry				
Underweight	2	6,9		
Normal	14	48,3		
Overweight	5	17,2		
Obesity	8	27,5		
Duration of ASM				
> 2 years	17	58,6		
≤ 2 years	12	41,4		
Type of ASM				
Single	10	34,5		
Combination	19	65,5		
TC				
> 200 mg/dL	7	24,1		
≤ 200 mg/dL	22	75,9		
LDL-C				
> 130 mg/dL	8	27,6		
≤ 130 mg/dL	21	72,4		
HDL-C				
≥ 35 mg/dL	23	79,3		
< 35mg/dL	6	20,7		
TG				
> 150 mg/dL	11	37,9		
≤ 150 mg/dL	18	62,1		
25 (OH)D				
Deficient	9	31,0		
Insufficient	20	69,0		

The average body mass index (BMI) was 23.11 ± 4.18 kg/m², with values ranging from 16.0–33.9 kg/m². Most participants (93.1%) had a BMI that fell within the normal to obese range, whereas 6.9% were classified as underweight. None of the participants reported alcohol consumption, smoking, or taking other medications, including those for lowering lipids. Furthermore, there were no reported cases of diabetes

mellitus, dyslipidemia, or adherence to special diets by the participants.

Regarding treatment, the average duration of anti-seizure medication (ASM) use was 55.31 ± 71.28 months, ranging from 6 to 348 months. Most participants (65.5%) were on combination therapy, while 34.5% were on a single ASM regimen.

Lipid profile analysis showed a total cholesterol (TC) level of 183.76 ± 38.34 mg/dL, with values ranging from 121 to 310 mg/dL. The low-density lipoprotein cholesterol (LDL-C) level was 103.55 ± 34.92 mg/dL, high-density lipoprotein cholesterol (HDL-C) level was 48.72 ± 15.98 mg/dL, and triglyceride (TG) level was 158.14 ± 104.48 mg/dL. Table 2 shows the distribution of the full lipid profiles based on vitamin D levels. The analysis of vitamin D showed an average 25(OH)D level of 13.45 ± 5.74 ng/mL. All participants had vitamin D deficiency, defined as less than 20 ng/mL. This widespread deficiency could be due to the long-term use of ASM, insufficient sunlight, and a poor diet.

Table 2. Lipid profiles and serum vitamin D levels

Variable	Mean \pm SD	Median (min – max)
TC	$183,76 \pm 38,34$	185 (121 – 310)
LDL-C	$103,55 \pm 34,92$	96 (37 – 201)
HDL-C	$48,72 \pm 15,98$	50 (18 – 82)
TG	$158,14 \pm 104,48$	111 (52 – 403)
25(OH)D	$13,45 \pm 5,74$	12 (3 – 29)

Relationship Between Serum Vitamin D Levels and Participant Characteristics

Before examining our main goal, we examined the relationship between demographic factors and serum vitamin D levels (Table 3). The results showed that sex was the only significant factor affecting vitamin D levels, with females more likely to be deficient than males.

Table 3. Association of demographic characteristics and serum vitamin D levels

Characteristics	Serum 25(OH)D levels		p
	Deficient	Insufficient	
Age (Years)	$26,89 \pm 9,88$	$34,35 \pm 13,16$	0,089
Gender			
Male	2 (22,2%)	16 (80%)	0,010
Female	7 (77,8%)	4 (20%)	
BMI (Kg/m2)	$22,04 \pm 4,42$	$23,59 \pm 4,09$	0,346
Anthropometry			
Underweight	2 (22,2%)	0 (0%)	0,337
Normal	4 (44,4%)	10 (50%)	
Overweight	0 (0%)	5 (25%)	
Obesity	3 (33,3%)	5 (25%)	
Duration of ASM	$54,22 \pm 4,698$	$55,80 \pm 80,98$	0,539



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Characteristics	Serum 25(OH)D levels		p
	Deficient	Insufficient	
> 2 years	6 (66,7%)	11 (55%)	0,694
≤ 2 years	3 (33,3%)	9 (45%)	
Type of ASM			1,000
Single	3 (33,3%)	7 (35%)	
Combination	6 (66,7%)	13 (65%)	

Conversely, age, body mass index (BMI), lifestyle factors, and ASM use did not significantly affect vitamin D concentrations.

Table 4 presents the correlation between serum vitamin D levels and lipid profiles in the cohort of patients with epilepsy. Specifically, the subgroup with insufficient vitamin D levels exhibited significantly elevated LDL-C levels (P = 0.029). Nevertheless, no statistically significant disparities were observed in other lipid parameters, including triglycerides (TG), total cholesterol (TC), and HDL-C levels, across the vitamin D groups. These observations imply a potential association between diminished vitamin D levels and adverse LDL-C levels, necessitating further investigation.

Table 4. Association of serum vitamin D levels and lipid profiles among people with epilepsy

Lipid profiles	Serum 25(OH)D Levels				p
	Deficient		Insufficient		
	n	%	n	%	
TC					0,273
> 200	1	11,1	6	30	
≤ 200	8	88,9	14	70	
LDL-C					0,029*
> 130	0	0	8	40	
≤ 130	9	100	12	60	
HDL-C					0,375
≥ 35	8	88,9	15	75	
< 35	1	11,1	5	25	
TG					0,053
> 150	1	11,1	10	50	
≤ 150	8	88,9	10	50	

DISCUSSION

Prior investigations have thoroughly established the prevalence of vitamin D deficiency among patients with epilepsy and its metabolic consequences, specifically concerning lipid profiles.^{7, 8, 9)} Vitamin D, a crucial nutrient, is indispensable for regulating calcium levels and preserving bone integrity.⁶⁾ Furthermore, recent studies have suggested a potential role for vitamin D in lipid metabolism, particularly in blood lipid concentrations.^{10, 11)} However, the relationship between serum vitamin D levels and lipid profiles remains a subject of ongoing discussion. Some studies

have proposed that vitamin D supplementation can improve lipid profiles, whereas others have found no substantial impact.¹⁴⁾ This discrepancy has been addressed through meta-analyses and randomized controlled trials (RCTs) that examined the effects of vitamin D on total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

This study explored the correlation between serum vitamin D concentrations and lipid profiles in individuals with epilepsy (PWE), thereby offering significant perspectives on this association. The findings revealed that all participants exhibited low vitamin D levels, with 31% classified as deficient and 69% as insufficient. These observations align with prior research suggesting that patients with epilepsy are susceptible to vitamin D deficiency, potentially stemming from extended antiepileptic medication (ASM) use, restricted sun exposure, and possible dietary inadequacies.

Vitamin D Deficiency and Demographic Variables

The analysis demonstrated that among the demographic variables, sex emerged as the only statistically significant predictor of vitamin D levels (p = 0.010), with women displaying a greater propensity for deficiency relative to men. This disparity may be explained by several factors, including lifestyle habits, diminished sun exposure, and hormonal variations that affect vitamin D metabolism.

In contrast, vitamin D levels were significantly associated with age, BMI, and ASM duration or type. These findings suggest that while ASM use is a known risk factor for vitamin D deficiency, its effects may be modulated by individual metabolic differences and lifestyle factors.^{7, 15)}

Vitamin D and Lipid Profiles

The investigation revealed a significant correlation between vitamin D levels and LDL-C; specifically, individuals with insufficient vitamin D exhibited elevated LDL-C levels compared with those with a deficiency. This finding aligns with previous studies, indicating that vitamin D may influence lipid metabolism, particularly in the regulation of LDL-C levels.¹⁶⁾ Conversely, other lipid parameters,



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including TC, HDL-C, and TG, were not significantly associated with vitamin D levels.

While prior research has established a correlation between vitamin D deficiency and dyslipidemia, characterized by increased LDL-C and TG concentrations alongside decreased HDL-C levels, our results demonstrated statistical significance only for LDL-C.¹²⁾ This discrepancy may be attributable to factors such as a limited sample size, the presence of potential confounding variables, or individual variations in lipid metabolism within the population of people with epilepsy (PWE). Furthermore, factors such as dietary patterns, genetic predispositions, and the specific type of antiepileptic medication (ASM) employed could influence lipid profiles, underscoring the need for further investigation.¹⁵⁾ These findings underscore the critical need to monitor vitamin D levels in PWE, especially those undergoing prolonged ASM treatment. The observed association between vitamin D and LDL-C suggests that maintaining adequate vitamin D levels through supplementation, dietary modifications, and increased sun exposure may benefit lipid metabolism and cardiovascular well-being in PWE.¹⁵⁾

Further investigation employing larger sample sizes and interventional methodologies is essential to definitively ascertain causality and elucidate the underlying mechanisms of this relationship.

Limitations and Prospective Research

This study was subject to several constraints, including a restricted sample size and cross-sectional design, which limited the capacity to infer causal connections. Additionally, factors such as dietary patterns, physical activity levels, and genetic predispositions influencing lipid metabolism were not assessed comprehensively. These limitations highlight the need for subsequent studies involving more extensive participant cohorts. Future studies should investigate the potential benefits of vitamin D supplementation in improving the lipid profiles of individuals with epilepsy.

CONCLUSION

In summary, our investigation revealed a significant correlation between vitamin D concentrations and LDL-C, whereas no analogous relationship was observed with other lipid parameters.

Notably, all participants presented with deficient vitamin D levels, with a more pronounced prevalence of deficiency among female participants. These findings emphasize the need for further research on the influence of vitamin D on lipid metabolism in PWE and the importance of developing appropriate clinical interventions to improve overall health outcomes.

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