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Impact of Vitamin D3 Deficiency on Quality of Life in Epilepsy: A Call for Routine Screening and Intervention

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Abstract

Background The association between vitamin D3 levels and quality of life (QoL) in people with epilepsy on long-term antiseizure medications is an area of ongoing research. This study aims to assess serum vitamin D3 levels in people with epilepsy and evaluate the effects of supplementation on their QoL.

Methods A prospective study was conducted at a tertiary hospital from June 2021 to July 2022. People with epilepsy aged 12 to 45 years, receiving antiseizure medications for at least 1 year, were recruited. Baseline serum vitamin D3 levels were measured, and epilepsy diagnoses were confirmed according to the International League Against Epilepsy guidelines (2017). QoL was evaluated using the Quality of Life in Epilepsy Scale (QOLIE-31) for adults and the Quality of Life in Epilepsy for Adolescents Scale (QOLIE-48) for adolescents. Patients with vitamin D3 deficiencies received supplementation, and their QoL were reassessed at 3 and 6 months. Data were analyzed using *t*-tests, multiple logistic regression, and analysis of variance.

Results At baseline, the mean serum vitamin D3 level was 17.99 ± 6.77 ng/mL, increasing to 21.46 ± 2.91 ng/mL at 3 months and 24.41 ± 3.19 ng/mL at 6 months. Patients with vitamin D3 deficiency exhibited significantly lower scores across multiple domains of the Quality of Life Inventory (QOLIE-31 and QOLIE-48). A significant improvement was seen in most of the QOLIE scores and serum vitamin D3 levels after vitamin D3 supplementation.

Conclusion People with epilepsy on long-term antiseizure medications have vitamin D3 deficiency, which negatively impacts their QoL. Regular screening and supplementation are recommended for better management of epilepsy.

Keywords
- epilepsy
- vitamin D3
- quality of life
- antiseizure medication
- QOLIE-31
- QOLIE-48

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Introduction

Epilepsy, a chronic neurological condition characterized by recurrent seizures, affects millions worldwide.[1] While significant advancements have been made in epilepsy management, many patients continue to experience challenges related to seizure control and quality of life (QoL).[2] Various factors influence the QoL of epilepsy patients, including the choice of antiepileptic therapy and the disease duration.[3–5] The World Health Organization defines QoL as complete physical, mental, and social well-being.[3] Patients with generalized seizures often report poorer scores than those with partial seizures, while seizure-free individuals tend to have higher QoL scores. Seizure frequency is a significant determinant of low QoL.[4,5] People with epilepsy tend to have worse QoL than those without epilepsy, comparable to or lower than patients with other chronic diseases, and comparable to healthy individuals in well-controlled epilepsy patients.[6–8] In addition to seizure frequency and psychiatric comorbidities, serum vitamin D3 levels have also been shown to influence QoL in epilepsy patients.[9] Vitamin D3, a vital nutrient involved in various physiological processes, has emerged as a potential factor influencing epilepsy outcomes. Previous studies have consistently demonstrated a high prevalence of vitamin D3 deficiency in epilepsy patients.[9–12] This deficiency can be attributed to various factors, including reduced sun exposure, medication interactions, and underlying medical conditions. Research has also highlighted the potential impact of vitamin D3 on seizure frequency, cognitive function, and overall QoL in epilepsy patients.[10–12]

Antiepileptic drugs can affect vitamin D3 metabolism, lowering active vitamin D3 levels.[10–12] Vitamin D3 can regulate gene expression through a nuclear vitamin D3 receptor, a ligand-specific transcription factor activated by vitamin D3. This mechanism helps reduce the expression of proconvulsant cytokines and increase intestinal calcium uptake, ultimately decreasing neuronal excitability and preventing seizures.[13] In people with epilepsy, particularly those treated with enzyme-inducing antiepileptic drugs (AEDs), vitamin D3 levels are often compromised, leading to increased risks of osteoporosis and fractures.[12,14] The link between vitamin D3 deficiency and seizure control has garnered attention, suggesting that vitamin D3 supplementation may offer therapeutic benefits beyond bone health.

Given the growing evidence supporting the role of vitamin D3 in epilepsy, this study aims to investigate the relationship between vitamin D3 levels and QoL in epilepsy patients receiving long-term antiseizure medications (ASMs). By examining the association between vitamin D3 status and QoL outcomes, this research seeks to contribute to a better understanding of the disease and inform the development of more comprehensive treatment strategies.

Methodology

This prospective study was conducted at the departments of psychiatry and neurology at a tertiary-level hospital in North India over 1 year, from June 1, 2021, to June 30, 2022. The study protocol received approval from the Institute's Ethical Committee XXXXXXXXX(XXXX/2K22p-TH/7535). Written informed consent was obtained from all adult participants and parents of children. Additionally, written assent was obtained from children aged 11 to 18 years.

The primary objectives of the study were to evaluate the serum level of vitamin D3 in people with epilepsy on long-term ASMs, assess their QoL, and evaluate the impact of oral vitamin D3 supplementation on the serum level of vitamin D3 and QoL. The inclusion criteria for the study were diagnosis of epilepsy (based on the International League Against Epilepsy guidelines)[15] and ASMs for more than 1 year, aged 12 to 45 years, and registered as outpatient or inpatient patients. People with epilepsy with severe medical ailments, on medications affecting bone metabolism and vitamin D3 levels, or taking calcium or vitamin D3 supplementation within the past 6 months were excluded.

The sample size ($n = 70$) was calculated using the population proportion method: $n = N^*X/(X + N - 1)$, where n is the sample size, N represents the population size, and X is the proportion estimate. Participants were selected through nonprobability sampling. The sociodemographic characteristics of the participants were meticulously collected using a standardized pro forma. This included their age, gender, marital status, occupation, educational attainment, family history of epilepsy or other neurological disorders, and socioeconomic status.[16] A comprehensive treatment history was collected, including details on the type, whether enzyme-inducing AEDs (EIAEDs), nonenzyme-inducing AEDs (NEIAEDs), frequency and duration of ASMs therapy, and any concomitant medications. Routine blood investigations included complete blood count, liver function tests, kidney function tests, electrolyte levels, and thyroid function tests to assess their overall health and rule out underlying medical conditions. Neuroimaging studies, such as computerized tomography or magnetic resonance imaging, identified any structural abnormalities in the brain. Electroencephalography was used to detect abnormal patterns associated with seizures. Based on the established criteria, the participants were carefully screened for eligibility to participate in the study. Those who met the inclusion criteria were selected and further assessed for their serum vitamin D3 levels and QoL.

Serum vitamin D3 levels were estimated using chemiluminescence principles on the Access 2 machine. Serum vitamin D3 levels were classified as deficient (< 29 ng/mL) or normal (> 30 ng/mL). Patients with deficient levels were provided with oral vitamin D3 supplementation until sufficient levels were reached, and serum levels were reassessed at 3 and 6 months.

Age-appropriate self-report measures were administered to evaluate the participants' QoL comprehensively. Adolescents aged 11 to 18 years completed the Quality of Life in Epilepsy for Adolescents Scale (QOLIE-48), while adults aged 19 to 45 years completed the Quality of Life in Epilepsy Scale (QOLIE-31).[17] The QOLIE-48 consists of two parts: general health and the effects of epilepsy and antiepileptic

medications.[18] The QOLIE-31 includes seven multi-item scales addressing emotional well-being, social functioning, energy/fatigue, cognitive functioning, seizure worry, medication effects, and overall QoL, along with a single item assessing overall health.[17] These instruments were available in vernacular (Punjabi) and used with the concerned authorities' permission.

Vitamin D3 Supplementation and Monitoring

People with epilepsy with vitamin D3 deficiency received oral vitamin D3 supplementation. A two-phase supplementation regimen was used: an intensive phase of 60,000 IU weekly for 6 weeks, followed by a maintenance phase of 600 to 1,000 IU daily for adolescents and 1,500 to 2,000 IU daily for adults.[19,20]

Statistical Analysis

The data of sociodemographic and other clinical variables was entered as a data matrix in Microsoft Excel. Data were described in terms of range: mean ± standard deviation, median, frequencies (number of cases), and relative frequencies (percentages). Group comparisons were performed using *t*-tests (independent or paired) for two groups and analysis of variance for multiple groups. Univariate analysis compared deficient and nondeficient groups. A multivariate logistic regression analysis was performed, controlling for age, sex, duration of epilepsy, number and type of ASMs, and socioeconomic status. Chi-square tests compared categorical data. Pearson's correlation analysis assessed the relationship between variables. All statistical calculations were done using the SPSS 26 version (Statistical Package for the Social Science, SPSS Inc., Chicago, Illinois, United States) statistical program for Microsoft Windows. A probability value (*p*-value) less than 0.05 was considered statistically significant.

Results

Of the 85 individuals screened, 70 epilepsy patients were recruited and completed the study (►**Fig. 1**). This cohort consisted of 33 females and 37 males with a mean age of 28.70 ± 8.87 years. Generalized epilepsy was the most common type of epilepsy (74.3%), and 71.4% ($n = 50$) reported no seizures in the past year (►**Table 1**).

The mean serum vitamin D3 levels at baseline was 17.99 ± 6.77 ng/mL, with an increase observed at 3 months (21.46 ± 2.91 ng/mL) and 6 months (24.41 ± 3.19 ng/mL). At baseline, 44.3% ($n = 31$) of patients presented with vitamin D3 deficiency and were supplemented with vitamin D3. This intervention significantly improved vitamin D3 status, with the proportion of deficient patients decreasing to 22.9% ($n = 16$) at 3 months and 7.1% ($n = 5$) at 6 months.

►**Table 2A** presents the baseline QOLIE-31 scores for patients with and without vitamin D3 deficiency. Patients with vitamin D3 deficiency had significantly lower scores on emotional well-being, energy/fatigue, social functioning, and overall scores than those with normal vitamin D3 levels. However, the two groups had no significant differences in other domains.

The analysis of baseline QOLIE-48 scores in adolescent epilepsy patients revealed significant disparities between those with and without vitamin D3 deficiency. Adolescents with vitamin D3 deficiency reported significantly higher levels of epilepsy impact ($p = 0.013$), lower levels of social support ($p = 0.016$), and diminished school behavior (0.018). Overall, the QOLIE-48 summary score was significantly lower in adolescents with vitamin D3 deficiency ($p = 0.006$) (►**Table 2B**).

►**Table 3** presents the QOLIE-31 and QOLIE-48 scores for adult and adolescent epilepsy patients at baseline, 3 months,

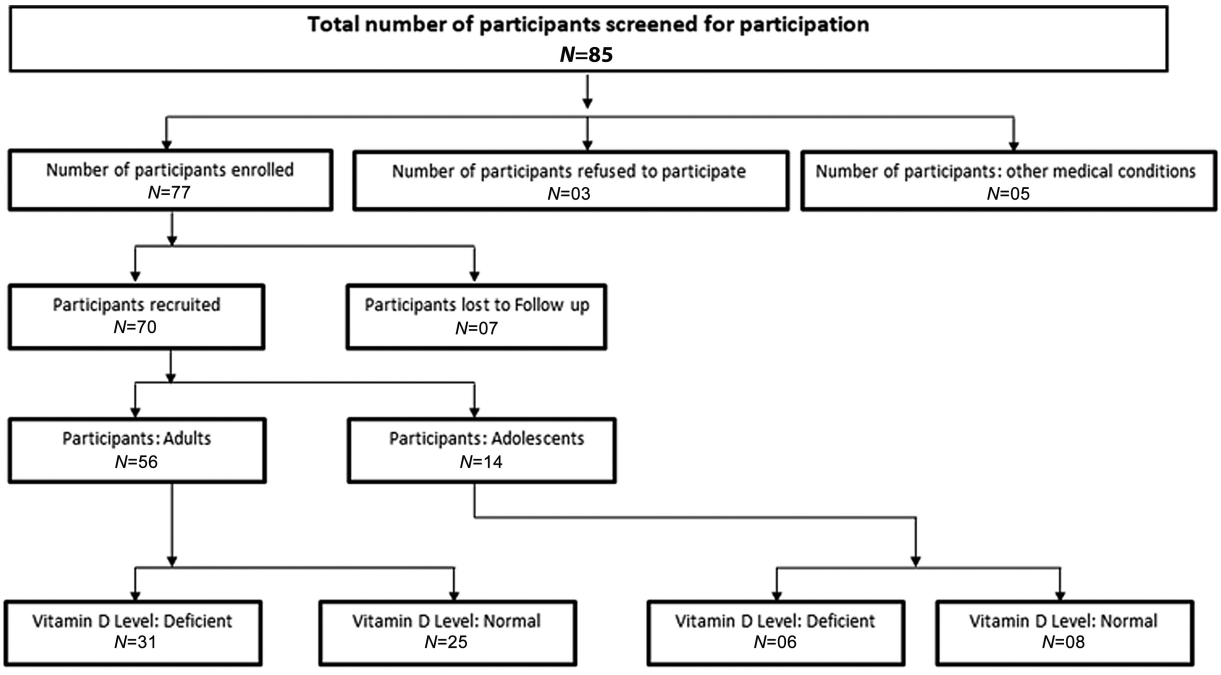

Fig. 1 Flowchart to depict participant recruitment process.

Table 1 Sociodemographic profile of the participants

Variable	Frequency (*n*)	Percent (%)
Age group (in years)		
11–20	15	21.4
21–30	22	31.4
31–40	27	38.6
41–50	6	8.6
Sex		
Female	33	47.1
Male	37	52.9
Education		
8th	7	10
9th	1	1.4
10th	20	28.6
12th	31	44.3
BA	11	15.7
Occupation		
Unemployed	6	8.6
Student	18	25.7
Housewife	21	30
Farmer	17	24.3
Shopkeeper	6	8.6
Dairy shop	1	1.4
Salesman	1	1.4
Frequency of seizures in past year		
Absent	50	71.4
Once	15	21.4
Twice	4	5.7
Thrice	1	1.4
Number of antiepileptic drugs		
Monotherapy	26	37.1
Dual therapy	35	50
Polytherapy	9	12.9
Antiepileptic drugs		
NEIAED	39	55.7
EIAED	18	25.7
NEIAED + EIAED	13	18.6
Compliance with treatment		
Not present	11	15.7
Present	59	84.3
Family history		
Absent	60	85.7
Present	10	14.3
Socioeconomic scale		
Upper middle	30	42.9
Lower middle	24	34.3
Upper lower	12	17.1
Lower	4	5.7
Type of epilepsy		
Generalized	52	74.3
Focal	13	18.6
Combined	5	7.1

Abbreviations: BA, Bachelor of Arts; EIAED, enzyme-inducing antiepileptic drug; NEIAED, nonenzyme-inducing antiepileptic drug.

and 6 months following vitamin D3 supplementation. Significant improvements were observed across all time points for most subscales. The overall QOLIE-31 score significantly improved from baseline to 3 months ($p = 0.001$) and from 3 to 6 months ($p = 0.000$) (►**Table 3A**). For QOLIE-48, significant improvements were observed across all time points for most subscales: epilepsy impact, attitude toward epilepsy, physical functioning, social support, and school behavior. The overall QOLIE-48 score significantly improved from baseline to 6 months ($p = 0.00$) (►**Table 3B**).

Patients on dual therapy had significantly lower baseline serum vitamin D3 levels (16.69 ± 7.17 ng/mL) than those on monotherapy (20.58 ± 5.61 ng/mL), and patients on polytherapy had the lowest baseline levels (15.56 ± 6.579 ng/mL) ($p = 0.041$). After 3 months of vitamin D3 supplementation, there were no significant differences in vitamin D3 levels between the three groups. At 6 months, patients on dual and polytherapy exhibited a significant increase in vitamin D3 levels compared with baseline ($p < 0.001$). Vitamin D3 supplementation can effectively improve vitamin D3 status in these patients, regardless of their ASMs regimen (►**Supplementary Table S1**, available in the online version only).

Patients on EIAEDs had significantly lower mean baseline vitamin D3 levels (14.61 ± 5.731 ng/mL) compared with those on NEIAEDs (19.28 ± 6.468 ng/mL) and combination therapy (18.77 ± 7.844 ng/mL) ($p = 0.046$). At 3 and 6 months, there was a trend toward higher vitamin D3 levels in patients on EIAEDs compared with the other groups, but the difference was not statistically significant ($p = 0.141$) (►**Supplementary Table S2**, available in the online version only). ►**Fig. 2** reveals a significant negative correlation between baseline vitamin D3 deficiency and the duration of epilepsy (Pearson's correlation coefficient = –0.474, $p < 0.001$).

The impact of seizure frequency on QoL in people with epilepsy was assessed using QoL instruments, QOLIE-31 and QOLIE-48. A significant negative correlation ($r = -0.702$, $p < 0.01$) was observed at baseline, implying that higher QOLIE-31 scores correspond to fewer seizures. At 3 months, a mild correlation was observed ($r = -0.325$, $p < 0.05$), while no significant correlation was found at 6 months ($r = 0.15$, $p > 0.05$). However, no significant association was found between seizure frequency and total summary score for QOLIE-48 at any time point (►**Supplementary Table S3**, available in the online version only).

Table 2 Comparison of baseline QOLIE-31 scores (A) and QOLIE-48 scores (B) in adults and adolescents with and without vitamin D3 deficiency, respectively

A. Baseline QOLIE-31 (adults)	Serum vitamin D3 levels		*p*-Value
	Deficient ($n = 31$) Mean ± SD	Normal ($n = 25$) Mean ± SD	
Seizure worry	44.40 ± 10.83	48.07 ± 13.52	0.276
Overall quality of life	48.80 ± 9.27	52.58 ± 10.64	0.168
Emotional well-being	49.20 ± 9.54	55.65 ± 9.89	0.017
Energy/Fatigue	50.80 ± 12.56	63.23 ± 9.09	< 0.001
Cognitive functioning	53.20 ± 10.69	57.10 ± 11.01	0.188
Medication effect	57.20 ± 14.87	56.45 ± 10.82	0.828
Social function	52.40 ± 9.26	59.36 ± 8.54	0.005
Overall score	50.94 ± 6.41	56.71 ± 5.62	0.001
B. Baseline QOLIE-48 (adolescents)	**Deficient ($n = 06$) Mean ± SD**	**Normal ($n = 08$) Mean ± SD**	***p*-Value**
Epilepsy impact	45.00 ± 12.25	62.50 ± 10.35	0.013
Memory/Concentration	61.67 ± 9.83	66.25 ± 7.44	0.339
Attitude toward epilepsy	53.33 ± 15.06	62.50 ± 4.63	0.127
Physical functioning	56.67 ± 5.16	62.50 ± 7.07	0.115
Stigma	63.33 ± 10.33	61.25 ± 6.41	0.649
Social support	50.00 ± 8.94	66.25 ± 11.88	0.016
School behavior	45.00 ± 12.25	61.25 ± 9.91	0.018
Health perception	65.00 ± 5.48	68.75 ± 3.54	0.145
Total summary score	54.07 ± 6.29	63.10 ± 3.77	0.006

Abbreviations: QOLIE-31, Quality of Life in Epilepsy Scale; QOLIE-48, Quality of Life in Epilepsy for Adolescents Scale; SD, standard deviation.

Demographic characteristics were compared between vitamin D3-deficient and nondeficient groups using univariate analysis. Subsequently, a multivariate logistic regression model was employed to assess the association between vitamin D3 deficiency and various demographic and clinical factors. Although some variables exhibited potential associations, none reached statistical significance (►**Table 4**).

Discussion

People with epilepsy face a multitude of challenges that significantly impact their QoL, including seizure frequency, stigma, psychological factors, cognitive impairments, physical limitations, socioeconomic status, and medication side effects.[2] ASMs can lower vitamin D3 levels, leading to potential health issues such as bone problems, mood disorders, and cognitive impairments. These factors, along with other challenges faced by people with epilepsy, can significantly impact their QoL. Our findings highlight a high prevalence of vitamin D3 deficiency among people with epilepsy, particularly those on dual or polytherapy and those with longer durations. The administration of oral vitamin D3 supplementation resulted in a significant increase in serum vitamin D3 levels and corresponding improvements in QoL scores, as measured by the QOLIE-31 and QOLIE-48 scales, over 3 and 6 months.

While the exact mechanisms underlying the relationship between vitamin D3 deficiency and QoL remain unclear, potential pathways include its critical roles in calcium absorption, immune function, and neurotransmitter regulation, with deficiencies linked to altered serotonin and dopamine levels that affect mood and cognition.[21] As seen in earlier studies, our study showed that 35/70 (50%) patients were on dual ASMs.[22,23] However, another study reported a higher prevalence of polytherapy, suggesting potential variations in treatment practices or patient characteristics.[24] Patients on dual therapy and those taking EIAEDs had lower baseline vitamin D3 levels. Previous studies have reported inconsistent associations between specific ASMs and vitamin D3 deficiency.[25–27] The precise duration of ASM treatment required to induce vitamin D3 deficiency remains unclear

At baseline, the QOLIE-31 assessment revealed that seizure worry was the least concerning issue among participants, while energy and fatigue were the most significant concerns. The overall QoL score (54.14 ± 6.60) aligned with a previous study.[28] However, our results differ from those of another study, where the effects of medication and energy/fatigue were reported as the lowest concerns.[29] These discrepancies may be attributed to cultural beliefs, socioeconomic factors, and geographical locations. Three months after the intervention, participants experienced

Table 3 Comparison of QOLIE-31 (A) and QOLIE-48 (B) scores at baseline, 3 months, and 6 months after vitamin D3 supplementation in adults and adolescents, respectively

A. QOLIE-31 Score (adults)	Baseline (mean ± SD)	3 mo (mean ± SD)	6 mo (mean ± SD)	*p*-Value (A)	*p*-Value (B)	*p*-Value (C)
Seizure worry	46.43 ± 12.42	54.82 ± 12.36	69.29 ± 3.22	< 0.001	< 0.001	< 0.001
Overall quality of life	50.89 ± 10.14	56.25 ± 11.84	69.46 ± 4.01	0.002	0.000	0.000
Emotional well-being	52.77 ± 10.18	58.21 ± 12.08	65.89 ± 7.08	0.001	< 0.001	< 0.001
Energy/Fatigue	57.68 ± 12.36	61.79 ± 12.52	74.46 ± 5.37	0.003	0.000	0.000
Cognitive functioning	55.36 ± 10.95	57.32 ± 10.18	65.71 ± 5.68	0.17	0.000	0.000
Medication effect	56.79 ± 12.66	60.36 ± 12.20	66.43 ± 5.54	0.001	0.000	0.000
Social function	56.25 ± 9.45	58.04 ± 9.99	66.61 ± 5.81	0.007	0.000	0.000
Overall score	54.14 ± 6.60	57.88 ± 7.91	67.81 ± 3.08	0.001	0.000	0.000
B. QOLIE-48 Score (adolescents)	**Baseline (mean ± SD)**	**3 mo (mean ± SD)**	**6 mo (mean ± SD)**	***p*-Value (A)[a]**	***p*-Value (B)[a]**	***p*-Value (C)[a]**
Epilepsy impact	55.00 ± 14.01	57.14 ± 13.83	62.14 ± 10.51	0.38	0.013	0.012
Memory/Concentration	64.29 ± 8.52	67.86 ± 5.79	66.43 ± 4.97	0.18	0.165	0.336
Attitude toward epilepsy	58.57 ± 10.99	63.57 ± 11.51	65.71 ± 7.56	0.05	0.19	0.01
Physical functioning	60.00 ± 6.79	66.43 ± 6.33	67.86 ± 5.79	0.01	0.16	0.00
Stigma	62.14 ± 8.02	64.29 ± 6.46	65.71 ± 6.46	0.19	0.16	0.05
Social support	59.29 ± 13.28	67.14 ± 6.11	67.12 ± 6.10	0.00	1	0.01
School behavior	54.29 ± 13.42	62.14 ± 10.51	69.29 ± 4.75	0.04	0.00	0.00
Health perception	67.14 ± 4.69	67.10 ± 4.29	68.57 ± 3.63	1	0.16	0.15
Total summary score	59.23 ± 6.66	62.44 ± 5.12	64.85 ± 4.25	0.02	0.15	0.00

Abbreviations: QOLIE-31, Quality of Life in Epilepsy Scale; QOLIE-48, Quality of Life in Epilepsy for Adolescents Scale; SD, standard deviation.
[a]A = Baseline and 3rd month, B = 3rd month and 6th month, C = 6th month and baseline.

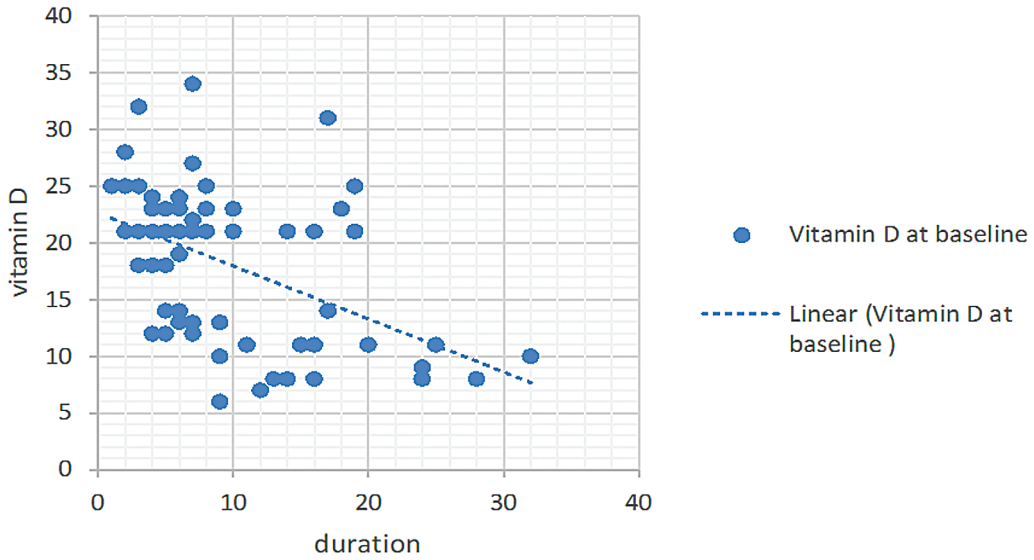

Fig. 2 Correlation between baseline serum vitamin D3 levels and duration of epilepsy.

Table 4 Multiple logistic regression analysis to predict vitamin D3 deficiency in participants

Variable		OR	95% CI	*p*-Value
Sex	Male	Reference		
	Female	0.074	0.005–1.229	0.069
Age groups (in years)	11–20	Reference		
	21–30	1.565	0.153–16.039	0.706
	31–40	0.472	0.057–3.910	0.487
	41–50	5.868	0.038–897.82	0.491
Education	8th	Reference		
	9th	0.000	0.000	1.000
	10th	0.260	0.002–30.132	0.579
	12th	1.475	0.019–117.62	0.862
	BA	0.039	0.000–35.024	0.350
Religion	Hindu	Reference		
	Sikh	0.631	0.036–11.155	0.753
SES	Upper middle	Reference		
	Lower middle	8.752	0.980–78.139	0.052
	Upper lower	2.368	0.175–32.082	0.517
	Lower	1.214	0.010–145.65	0.937
Frequency of seizures	Absent	Reference		
	Once	5.989	0.194–184.61	0.306
	Twice	22.063	0.084–576.6	0.276
	Thrice	39.985	0.000–681.0	1.000
No. of epileptic drugs	Monotherapy	Reference		
	Dual therapy	4.160	0.503–34.412	0.186
	Polytherapy	14.87	0.000–52.61	0.999
Type of drug	NEIAED	Reference		
	EIAED	7.084	0.797–2.982	0.079
	NEIAED + EIAED	0.000	0.000–0.000	0.999

(*Continued*)

Table 4 (*Continued*)

Variable		OR	95% CI	*p*-Value
Compliance	Not Present	Reference		
	Present	0.621	0.050–7.777	0.712
Family history of epilepsy	Absent	Reference		
	Present	0.454	0.036–5.788	0.544
Type of epilepsy	Generalized	Reference		
	Focal	0.228	0.016–3.309	0.279
	Combined	109.43	0.056–120.02	0.224

Abbreviations: BA, Bachelor of Arts; CI, confidence interval; EIAED, enzyme-inducing antiepileptic drug; NEIAED, nonenzyme-inducing antiepileptic drug; OR, odds ratio; SES, socioeconomic status.

improvements in all QOLIE-31 domains, which were sustained at the 6-month follow-up. The observed improvements in QoL over time can be attributed to the vitamin D3 supplementation provided to participants.

At baseline, adolescents with epilepsy demonstrated moderate to good QoL scores across all domains of the QOLIE-48. Our findings are consistent with previous studies reporting relatively good QoL scores in adolescents with epilepsy.[30,31] However, our study observed lower scores in patients on long-term ASMs, particularly in the epilepsy impact and attitude toward epilepsy domains. While significant improvements were observed in other subscore domains after vitamin D3 supplementation, the limited improvement in the epilepsy impact and attitude toward epilepsy suggests that these areas may require additional attention. Statistically significant improvements were noted in various QOLIE-31 and QOLIE-48 parameters, similar to other reports indicating that patients receiving vitamin D3 supplementation experienced substantial improvements in their QoL.[32] People with epilepsy had low baseline vitamin D3 levels, but these levels increased significantly at 3 and 6 months, consistent with findings from a larger patient group.[26] Hypovitaminosis D has been identified as an independent risk factor for total mortality in the general population, highlighting the importance of addressing vitamin D3 deficiency as part of comprehensive health care strategies.[33]

At baseline, people with epilepsy had a positive correlation between lower seizure frequency and higher QoL scores and 3 months postintervention. However, this association attenuated at 6 months. Conversely, the QOLIE-48 did not reveal any significant correlation between seizure frequency and QoL scores at any time point. People with epilepsy suffer from poor QoL as a result of frequent seizures, cognitive dysfunction, and a high risk of psychiatric comorbidities.[32] Factors beyond seizure frequency, such as medication effects and disease duration, may exert a more substantial influence on QoL in people with epilepsy.[34] Vitamin D3 supplementation in drug-resistant epilepsy significantly reduces seizure frequency and improves comorbid conditions and QoL.[35] Univariate analysis suggested associations between vitamin D3 deficiency and demographic/clinical factors. However, multivariate analysis did not confirm these findings. Age may be a significant factor, with older children at higher risk due to lifestyle changes or increased vitamin D needs.[36] Other factors (medication duration, underlying health conditions, mobility, body mass index) did not significantly impact vitamin D levels.[36]

The goals of epilepsy treatment extend beyond mere seizure control and to reduce the overall impact of the condition and the side effects of ASMs on patients' daily lives. While this study provides valuable insights into the relationship between vitamin D3 deficiency and QoL in people with epilepsy, it is subject to certain limitations. The relatively small sample size and short follow-up period may limit the generalizability of the findings. Self-reported measures and the potential influence of cultural, socioeconomic, nutritional, and psychosocial factors may also affect the results. Additionally, the study did not account for other health conditions, lifestyle factors, or medications participants may have been taking, which could confound the findings. Despite these limitations, the study's strengths include its prospective design, comprehensive assessment, clinical relevance, longitudinal follow-up, and the potential for improved patient outcomes.

The findings of this study highlight the need for routine vitamin D3 screening for people with epilepsy, especially those on long-term ASMs. Future studies with extended durations are warranted to investigate the long-term clinical implications of vitamin D3 supplementation, particularly in relation to seizure control. Moreover, challenges such as adherence to supplementation regimens, costs, and access to health care may arise. To overcome these barriers, health care providers should focus on patient education, offer affordable supplementation options, and integrate vitamin D3 screening and supplementation into routine clinical practice.[25] This comprehensive approach can enhance patient outcomes and improve the overall management of epilepsy.

Conclusion

This study demonstrates a strong association between vitamin D3 deficiency and reduced QoL in people with epilepsy, emphasizing the need for routine screening and

supplementation, especially for those on long-term ASMs. The positive impact of supplementation on vitamin D3 levels and QoL suggests its potential as a valuable intervention in epilepsy management.

Note

The authors declare that this manuscript is based on original work and has not been published in whole or part, in any print or electronic media, nor is it under consideration for publication elsewhere, except as an abstract of conference proceedings.

Statement by Corresponding Author

As the corresponding author of this manuscript, I confirm that no person who has contributed substantially to its production has been excluded from authorship.

Authors' Contributions

S.S., P.D., and I.P.: conceptualized the study design; I.P.: was responsible for the data collection and analysis; S.S. and P.D.: supervised the data collection and analysis; I.P.: prepared the first draft of the study; S.S., D.G., and A.N.: revised the manuscript. All authors approved the final manuscript.

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Conflict of Interest

All authors declare no conflict of interest. No financial relationships or affiliations exist that could have influenced this study's conduct, outcome, or publication. A formal ICMJE conflict-of-interest form has been completed and submitted for each author.

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