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ORIGINAL ARTICLE

Association between Psychiatric Symptoms, Vitamin D serum level and Parental Stress in Children and Adolescents with Epilepsy

Lamis Ibrahim Ali[1], Alshaimaa Hatem Farhan[2], Eslam Elshafey[2*], Hemat Mostafa Elsayed[3], Enas Mohamed Ikram Sayed Badway[4], Mohamed Tarek Tawfik Al-Khatib[5], Hala Mohammed Amin[6]

[1] Psychiatry Department, Faculty of Human Medicine, Zagazig University, Zagazig, Egypt.
[2] Clinical Pathology Department, Al-Ahrar Teaching Hospital, General Organization for Teaching Hospitals and Institutes (GOTHI), Egypt
[3] Pediatrics Department, Al-Ahrar Teaching Hospital, General Organization for Teaching Hospitals and Institutes (GOTHI), Egypt
[4] Microbiology and Immunology Department, Al-Ahrar Teaching Hospital, General Organization for Teaching Hospitals and Institutes (GOTHI), Egypt
[5] Intern Doctor at Suad Kafafi University Hospital
[6] Pediatrics Department, Faculty of Human Medicine, Zagazig University, Zagazig, Egypt.

Corresponding author*: Eslam Elshafey
Email: eslamelshafeyelsaid245@gmail.com

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ABSTRACT:

Background: Cognitive impairment, vitamin D inadequacy, and psychiatric comorbidities are often linked to epilepsy in children and adolescents. Parental stress levels and quality of life can be greatly impacted by these factors. Although previous studies have examined how epilepsy affects behavior and cognition, little is known about how vitamin D functions in these relationships. So, we aimed to evaluate the relationship between vitamin D status, cognitive function, psychiatric symptoms, and parental stress in children and adolescents with epilepsy.

Methods: A cross-sectional study was conducted at the Al Ahrar Teaching Hospital, including 100 children and adolescents (aged 6–18 years) diagnosed with epilepsy. Participants underwent neurocognitive assessment using the Wechsler Intelligence Scale for Children (WISC-III) and behavioral evaluation via the Child Behavior Checklist (CBCL). Parental stress was assessed using the Parental Stress Index (PSI). Vitamin D levels were measured.

Results: 79% of subjects had vitamin D deficiency, with a mean level of 20.78 ± 10.63 ng/ml. Behavioral issues were far more common in the group that was vitamin D deficient. with higher total Problems, Anxiety/Depression, and ADHD Problems scores. Parental stress was also significantly higher in parents of vitamin D-deficient children, particularly in total stress and Difficult Child scores.

Conclusion: Vitamin D deficiency is prevalent among children with epilepsy and is associated with impaired cognitive function, increased psychiatric symptoms, and heightened parental stress.

Keywords: Pediatric Epilepsy; Vitamin D Deficiency; Cognitive Function; Psychiatric Symptoms; Parental Stress.

INTRODUCTION

Epilepsy, most prevalent in the first year of life, is one of the most prevalent long-term neurological conditions in children. Worldwide, more than 10 million children and teenagers under the age of 17 suffer with epilepsy; they make for approximately 25% of all patients suffering from epilepsy [1]. Children and adolescents with epilepsy are more likely than children in the general population to experience emotional and behavioral problems because of both psychosocial (the unpredictable clinical (the cause, age at onset of epilepsy, frequency, and severity of seizures) and psychological (the distressing nature of the seizures, the social stigma attached to epilepsy, and overprotective parental conduct) elements. These problems include concentration problems, behavioral problems, psychosis, sadness, and anxiety [2].

Family characteristics including socioeconomic level or mental health issues in other family members may also have an impact on the behavioral and emotional challenges faced by children with epilepsy [3]. Children with epilepsy are more prone than the general population to suffer from mental health issues, such as emotional and behavioral disorders, and the psychological weight of the condition can affect their quality of life, particularly if they have poor seizure control [4]. Numerous epidemiological studies that looked at the prevalence of psychopathological symptoms in children with epilepsy have concluded that the total risk for childhood psychopathology is between 21 and 60 percent. [5].

According to **Reilly et al.** [6], In population-based studies, depression was observed in 12–14% of children with epilepsy. A study carried out by **Williams et al**. [7] showed that mild-to-moderate anxiety symptoms were present in 23% of people with pediatric epilepsy. However, young people with epilepsy appear to have greater prevalence rates of anxiety and depression than children in the general pediatric population and children with other chronic medical conditions that do not affect the central nervous system. [8]. A recent population-based study of young people with epilepsy, aged 0–17, found that 43% of the participants had psychiatric or neurodevelopmental comorbidities. More severe forms of epilepsy were more often associated with the chance of developing psychiatric comorbidities, whereas even milder forms of epilepsy were burdened by emotional and behavioral difficulties. [9].

It is not appropriate to solely attribute the psychiatric and behavioral comorbidities in these children to the chronic nature of the condition; rather, some elements connected to epilepsy, such as the underlying brain dysfunction, may be present [10]. It is believed that there are several intricate mechanisms behind the emergence of psychiatric comorbidities in epilepsy. Several theories can be put forth, albeit they are not entirely clear. The first is a hereditary risk that affects the development of common brain systems between psychiatric disorders and epilepsy. The second is that seizures themselves may contribute to inadequate limbic and frontocentral cortical networks [11].

Furthermore, it should be noted that epilepsy is more frequently linked to deficits in learning abilities, executive processes, social cognition, and cognitive profile, all of which may contribute to social and academic challenges. Last but not least, societal stigma may also make young individuals with epilepsy feel more emotionally burdened [12]. Some antiseizure medications (ASMs) appear to have a better tolerability profile than others; in general, a more positive emotional and behavioral profile is linked to better disease control and a decrease in seizures [1]. The clinical care of epilepsy is complicated by psychiatric comorbidities, emotional and behavioral issues, and a substantial burden on patients and their families [13]. Since chronic conditions in children, like diabetes, asthma, and autism, can generate stress for parents, having children with epilepsy, which is characterized by an unpredictable crisis onset, may result in treatment-related stress for their parents [14].

In particular, the stress that comes with raising children who have seizures fits the description of traumatic stress brought on by severe, recurrent, chronic, and unpredictable disorders. Furthermore, it has been demonstrated that the association The relationship between children's reported sad moods and their parents' psychological discomfort in children with chronic diseases is tempered by the uncertainty surrounding the child's illness. It may also affect children's health outcomes if it makes it more difficult to treat illness. [15]. According to a number of recent research, parents of children with serious chronic illnesses have higher levels of parental stress than the general population [16]. Numerous factors, including a recent epilepsy diagnosis, anxiety about medication side effects and seizure recurrence, and how seizures affect cognitive development, which can result in dysfunctional family dynamics and elevated parental stress [17]. With drug-resistant epilepsy, which affects 20–30% of people, parental stress might be especially high. Parents' stress levels can sometimes be exacerbated by psychiatric comorbidities, such as behavioral and mood issues in children with epilepsy, who also suffer sleep disruptions and social life impairment. The symptoms may progress to para-suicide or suicide. Psychiatric expertise is sometimes required [18].

There is proof that vitamin D deficiency has detrimental consequences on the body and mind. Mc Grath [19] was the first to propose that a vitamin D deficiency during pregnancy may act as a risk factor for the development of adult-onset schizophrenia. Moreover, it was proposed that a deficiency in vitamin D was the reason behind the high incidence of psychotic decompensations in immigrant communities [20].

Vitamin D is one of the several steroid hormones that signal through nuclear and membrane-associated receptors. When the skin is exposed to UVB rays, 7-dehydrocholesterol is converted into this substance. There are other types of vitamin D, but the one that occurs naturally in animals is vitamin D3. There is little concrete proof that vitamin D plays a part in epilepsy. Nonetheless, a number of indirect (ecological and epidemiological) lines of evidence, experimental data, and human interventional research point to a relationship between vitamin D and epilepsy [21].

METHODS

This cross-sectional study was conducted at was carried out at the Al-Ahrar Teaching Hospital, GOTHI, Egypt during the period from the beginning of February to the end of April 2025 on random sample of children and adolescents aged 6 to 18 who had received an epilepsy diagnosis at least six months before enrollment. The total sample size was 100. Written informed consent was acquired by the parents or legal guardians of all involved children and adolescents. The General Organization for Teaching Hospitals and Institutes' Research Ethical Committee gave its approval to the project (GOTHI: HAH00054-22/1/2025).

Inclusion criteria

1) According to the most recent International League Against Epilepsy (ILAE) guidelines (2017) [22], children and adolescents between the ages of 6 and 18 who have been diagnosed with epilepsy based on electroencephalogram (EEG) results and the typical clinical aspects of the symptoms.

2) Antiepileptic medication (AED)-treated children and adolescents.

3) No significant long-term neurological or medical disorders other than epilepsy.

Exclusion criteria

1) A history of central nervous system (CNS) illness or head trauma within the previous 12 months; 2) The existence of an intellectual handicap or pervasive developmental condition.

3) Current or recent (within the last six months) mental health therapy.

4) The incapacity to comprehend or adhere to the study protocols.

Participant Recruitment:

At the Pediatric Clinic, eligible patients and their parents were approached during their regular clinic visits. Those who consented to participate were enrolled after giving written informed consent after being briefed on the study's objectives and methods. Participants and their parents provided the following demographic and clinical information: age, gender, and socioeconomic status; age at onset of epilepsy; duration of epilepsy; types of seizures; current AED regimen; response to treatment; presence of comorbidities; and a family history of mental illnesses or epilepsy.

The Child Behavior Checklist (CBCL) was used to assess children and adolescents who had emotional and behavioral problems. The self-report and parent-report were also available in Arabic [23]. The Parenting Stress Scale (PSS) was used to measure stress levels in parents related to their child's epilepsy and associated factors [24].Selected subtests from the Wechsler Intelligence Scale for Children (WISC) were administered to assess cognitive functioning [25].

Five ml of venous blood was withdrawn. The samples were sent to the lab for measurement of total vitamin D levels in the blood. Recombinant vitamin D binding protein is used in measurement of Vitamin D total competitive protein-binding test to measure 25-hydroxyvitamin D (25-OHD) by Roche Elecsys [26]. The electrochemiluminescence binding assay is intended for useon cobas e801 immunoassay analyzers. The values of vitamin D below 30 ng/mL indicating insufficiency and deficiency **[**27].

Statistical Methods

The data was imported and examined using the Statistical Package for the Social Sciences (SPSS) software, version 20.0. The chi-square test ($\chi 2$), Pearson correlation test, Mann-Whitney U-test, and Student's t-test were all employed. A p-value < 0.05 was considered statistically significant at the 95% confidence interval.

RESULTS

Based on age distribution, children with epilepsy were 13.86 ± 2.79 years old on average. 44% were female and 56% were male. The distribution of socioeconomic status was low (32%), high (32%), and intermediate (36%). 74% of people had no family history of epilepsy, whereas 26% had a positive family history. In terms of the length of epilepsy, the average was 2.89 ± 1.72 years. Regarding seizure type, 38% experienced focal seizures and 62% experienced generalized seizures. In terms of antiepileptic medication regimen, 44% were on monotherapy and 56% were on polytherapy. Neurophysiology and radiology studies showed that 68% of cases had normal EEG readings and 32% had abnormal EEGs. In terms of MRI results, all instances showed no abnormalities (100% normal MRI). The average vitamin D level was 20.78 ± 10.63 ng/ml. Just 21% of patients had normal levels, whilst 79% of cases were categorized as inadequate (Table 1). The mean full Scale IQ, Verbal IQ, and Performance IQ were 84.96 ± 5.22, 80.00 ± 5.26, and 81.12 ± 4.73, respectively, based on cognitive performance. The lowest cognitive indices were the Processing Speed Index (74.45 ± 5.07), the Verbal Comprehension Index (78.32 ± 4.17), the Perceptual Organization Index (81.37 ± 4.46), and the Freedom from Distractibility Index (77.95 ± 4.49) (Table 2).

Based on behavioral assessment, the average score for Total Problems was 62.51 ± 6.23, with higher scores for Social Problems (63.33 ± 4.06) and Somatic Complaints (63.57 ± 5.42). The mean score for internalizing problems was 60.87 ± 6.98, while the mean score for externalizing problems was lower at 56.94 ± 6.68. The scores for specific domains were 62.19 ± 5.99 for Attention Problems and 61.95 ± 5.84 for Anxiety/Depression. Interestingly, there was also an increase in conduct problems (56.41 ± 4.82), oppositional-defiant problems (58.00 ± 4.46), and ADHD problems (59.73 ±

4.80) (Table 3). The mean Total Stress score, as determined by the parental stress assessment, was 75.09 ± 12.53, suggesting that caregivers are under a lot of stress. Parent-Child Dysfunction had the highest mean score (79.78 ± 10.44) among the stress components, followed by Parental Distress (68.73 ± 11.54) and Difficult Child (72.70 ± 11.11). (Table 4).

Cognitive performance in connection to vitamin D levels showed that children with normal vitamin D had significantly higher Verbal Comprehension Index (80.24 ± 5.53, p=0.017) and Full-Scale IQ (87.62 ± 6.24, p=0.027) than children with insufficiency. There is a strong The considerably higher Perceptual Organization Index (83.71 ± 4.69, p=0.006), Freedom from Distractibility Index (82.48 ± 4.88, p=<0.001), and Processing Speed Index (77.81 ± 5.85, p=<0.001) all demonstrated an association between appropriate vitamin D levels and increased cognitive function in the normal vitamin D group. There were no discernible variations in either Performance IQ (p=0.338) or Verbal IQ (p=0.351) (Table 5). Children with vitamin D deficiency showed significantly higher Total Problems scores (64.39 ± 5.15, p=<0.001), Anxiety/Depression scores (63.61 ± 5.02, p=<0.001), and Somatic Complaints scores (64.77 ± 4.44, p=<0.001), indicating greater emotional distress, according to behavioral assessment in relation to vitamin D levels. Low vitamin D levels may be linked to issues with cognitive regulation, as deficient individuals also had significantly higher levels of Attention Problems (63.32 ± 5.77, p=<0.001) and ADHD Problems (61.14 ± 4.08, p=<0.001). The deficient group also had considerably higher levels of conduct problems (57.87 ± 3.98, p=<0.001) and aggressive behavior (60.89 ± 6.52, p=0.001). Both externalizing and internalizing problems were markedly increased; in deficient cases, externalizing problems (57.72 ± 5.95, p=0.023) and internalizing problems (61.82 ± 6.33, p=0.012) showed worse results. Additionally, scores for Withdrawn/Depressed and Thought Problems were considerably higher (p=0.011 and p=0.049, respectively). Neither Social Problems (p=0.587) nor Oppositional-Defiant Problems (p=0.495) showed any discernible differences (Table 6).

Caregivers of children with vitamin D deficiency reported significantly higher Total Stress scores (76.51 ± 11.68, p=0.030), indicating greater overall burden, based on parental stress levels in connection to vitamin D status. Parents of children with vitamin D deficiency had more emotional strain, as evidenced by the extremely significant Parental Distress score (70.56 ± 10.51, p=0.002). The deficient group had substantially higher Parent-Child Dysfunction ratings (80.94 ± 9.69, p=0.034) in relation to parent-child relations. Notably, Difficult Child scores (75.11 ± 10.12, p=<0.001) were also highly significant (Table 7).

Correlation analysis revealed a strong positive relationship between vitamin D levels and cognitive performance, specifically the Freedom from Distractibility Index (p<0.001), Full Scale IQ (p<0.001), and Perceptual Organization Index (p<0.001). This suggests that higher vitamin D levels are associated with higher cognitive scores. Anxiety/Depression (p<0.001), ADHD Problems (p<0.001), and Total Problems (p<0.001) all exhibited significant negative relationships with behavioral outcomes, indicating that higher mental symptoms are linked to lower vitamin D levels (Table 1 Supplementary). Regarding parental stress, Difficult Child (p<0.001) and Parental Distress (p<0.001) demonstrated significant inverse correlations, indicating a greater caregiver burden associated with vitamin D insufficiency. Age (p=0.143), age at beginning of epilepsy (p=0.698), and duration of epilepsy (p=0.753) did not significantly correlate (Table 1 supplementary).

Table (1); Baseline data and vitamin D leveles in the studied group

Parameter	Category	Epilepsy (n=100)
Age (years)	Mean ± SD	13.86 ± 2.79
	Median (IQR)	12.00 (9.00-18.00)
Gender	Male	56 (56.0%)
	Female	44 (44.0%)
Socioeconomic Status	Middle	36 (36.0%)
	High	32 (32.0%)
	Low	32 (32.0%)
Family History of Epilepsy	No	74 (74.0%)
	Yes	26 (26.0%)
Duration of Epilepsy (years)	Mean ± SD	2.89 ± 1.72
	Median (IQR)	3.00 (1.00-4.00)
Seizure Types	Generalized	62 (62.0%)
	Focal	38 (38.0%)
Antiepileptic Drug Regimen	Polytherapy	56 (56.0%)
	Monotherapy	44 (44.0%)
EEG Abnormalities	No	68 (68.0%)
	Yes	32 (32.0%)
MRI Abnormalities	No	100 (100.0%)
Vitamin D Levels (ng/ml)	Mean ± SD	20.78 ± 10.63
Vitamin D	Deficient	79 (79.0%)
	Normal	21 (21.0%)

IQR: Interquartile Range, SD: Standard Deviation.

Table (2); Cognitive Performance (WISC-III) in the studied group

Parameter	Category	Epilepsy (n=100)
WISC-III - Full Scale IQ	Mean ± SD	84.96 ± 5.22
	Median (IQR)	84.00 (81.00-88.00)
WISC-III - Verbal IQ	Mean ± SD	80.00 ± 5.26
	Median (IQR)	80.00 (77.00-83.00)
WISC-III - Performance IQ	Mean ± SD	81.12 ± 4.73
	Median (IQR)	82.00 (78.00-84.25)
WISC-III - Verbal Comprehension Index	Mean ± SD	78.32 ± 4.17
	Median (IQR)	78.00 (76.00-81.00)
WISC-III - Perceptual Organization Index	Mean ± SD	81.37 ± 4.46
	Median (IQR)	81.00 (78.00-85.00)
WISC-III - Freedom from Distractibility Index	Mean ± SD	77.95 ± 4.49
	Median (IQR)	77.00 (75.00-80.25)
WISC-III - Processing Speed Index	Mean ± SD	74.45 ± 5.07
	Median (IQR)	74.00 (71.00-79.00)

WISC-III: Wechsler Intelligence Scale for Children - Third Edition, SD: Standard Deviation.

Table (3); Child Behavior Checklist (CBCL) in the studied group

Parameter	Category	Epilepsy (n=100)
CBCL - Total Problems	Mean ± SD	62.51 ± 6.23
	Median (IQR)	62.00 (57.75-67.00)
CBCL - Internalizing Problems	Mean ± SD	60.87 ± 6.98
	Median (IQR)	61.00 (55.00-66.00)
CBCL - Externalizing Problems	Mean ± SD	56.94 ± 6.68
	Median (IQR)	57.00 (52.75-61.00)
CBCL - Anxiety/Depression	Mean ± SD	61.95 ± 5.84
	Median (IQR)	62.00 (58.00-66.00)
CBCL - Withdrawn/Depressed	Mean ± SD	61.52 ± 4.36
	Median (IQR)	62.00 (58.00-64.00)
CBCL - Somatic Complaints	Mean ± SD	63.57 ± 5.42
	Median (IQR)	64.00 (61.00-67.00)
CBCL - Social Problems	Mean ± SD	63.33 ± 4.06
	Median (IQR)	63.00 (60.00-66.00)
CBCL - Thought Problems	Mean ± SD	58.50 ± 4.34
	Median (IQR)	58.00 (55.00-61.25)
CBCL - Attention Problems	Mean ± SD	62.19 ± 5.99
	Median (IQR)	62.00 (58.00-66.00)
CBCL - Aggressive Behavior	Mean ± SD	59.50 ± 7.70
	Median (IQR)	60.00 (55.00-64.00)
CBCL - ADHD Problems	Mean ± SD	59.73 ± 4.80
	Median (IQR)	59.00 (56.00-64.00)
CBCL - Oppositional-Defiant Problems	Mean ± SD	58.00 ± 4.46
	Median (IQR)	58.00 (55.00-61.00)
CBCL - Conduct Problems	Mean ± SD	56.41 ± 4.82
	Median (IQR)	56.50 (53.00-59.25)

CBCL: Child Behavior Checklist, ADHD: Attention-Deficit/Hyperactivity Disorder, SD: Standard Deviation.

Table (4); Parental Stress Index (PSI) in the studied group

Parameter	Category	Epilepsy (n=100)
PSI - Total Stress	Mean ± SD	75.09 ± 12.53
	Median (IQR)	75.50 (64.75-84.25)
PSI - Parental Distress	Mean ± SD	68.73 ± 11.54
	Median (IQR)	69.00 (61.00-76.00)
PSI - Parent-Child Dysfunction	Mean ± SD	79.78 ± 10.44
	Median (IQR)	79.00 (73.00-85.00)
PSI - Difficult Child	Mean ± SD	72.70 ± 11.11
	Median (IQR)	73.50 (65.75-79.00)

PSI: Parental Stress Index, SD: Standard Deviation.

Table (5); Cognitive Performance (WISC-III) according to vitamin D level

Parameter	Category	Deficient (n=79)	Normal (n=21)	p-value	Significance
WISC-III - Full Scale IQ	Mean ± SD	84.25 ± 4.71	87.62 ± 6.24	0.027	S
	Median (IQR)	84.00 (81.00-88.00)	87.00 (83.00-94.00)		
WISC-III - Verbal IQ	Mean ± SD	79.53 ± 4.45	81.76 ± 7.44	0.351	NS
	Median (IQR)	80.00 (77.00-82.00)	79.00 (77.00-90.00)		
WISC-III - Performance IQ	Mean ± SD	81.00 ± 4.40	81.57 ± 5.90	0.338	NS
	Median (IQR)	82.00 (78.00-84.00)	84.00 (76.00-86.00)		
WISC-III - Verbal Comprehension Index	Mean ± SD	77.81 ± 3.60	80.24 ± 5.53	0.017	S
	Median (IQR)	78.00 (75.50-80.00)	80.00 (76.00-86.00)		
WISC-III - Perceptual Organization Index	Mean ± SD	80.75 ± 4.21	83.71 ± 4.69	0.006	HS
	Median (IQR)	80.00 (78.00-83.00)	85.00 (81.00-86.00)		
WISC-III - Freedom from Distractibility Index	Mean ± SD	76.75 ± 3.54	82.48 ± 4.88	< 0.001	HS
	Median (IQR)	76.00 (75.00-79.00)	84.00 (79.00-86.00)		
WISC-III - Processing Speed Index	Mean ± SD	73.56 ± 4.47	77.81 ± 5.85	< 0.001	HS
	Median (IQR)	73.00 (70.50-77.00)	80.00 (76.00-82.00)		

WISC-III: Wechsler Intelligence Scale for Children - Third Edition, SD: Standard Deviation, IQR: Interquartile Range, S: Significant, HS: Highly Significant, NS: Not Significant.

Table (6); Child Behavior Checklist (CBCL) according to vitamin D level

Parameter	Category	Deficient (n=79)	Normal (n=21)	p-value	Significance
CBCL - Total Problems	Mean ± SD	64.39 ± 5.15	55.43 ± 4.70	<0.001	HS
	Median (IQR)	64.00 (61.00-67.50)	56.00 (53.00-57.00)		
CBCL - Internalizing Problems	Mean ± SD	61.82 ± 6.33	57.29 ± 8.22	0.012	S
	Median (IQR)	61.00 (56.50-66.50)	55.00 (50.00-62.00)		
CBCL - Externalizing Problems	Mean ± SD	57.72 ± 5.95	54.00 ± 8.45	0.023	S
	Median (IQR)	57.00 (53.00-61.00)	55.00 (47.00-60.00)		

Parameter	Category	Deficient (n=79)	Normal (n=21)	p-value	Significance
CBCL - Anxiety/Depression	Mean ± SD	63.61 ± 5.02	55.71 ± 4.34	<0.001	HS
	Median (IQR)	63.00 (61.00-66.50)	55.00 (54.00-57.00)		
CBCL - Withdrawn/Depressed	Mean ± SD	61.94 ± 3.87	59.95 ± 5.69	0.049	S
	Median (IQR)	63.00 (58.00-64.50)	60.00 (55.00-64.00)		
CBCL - Somatic Complaints	Mean ± SD	64.77 ± 4.44	59.05 ± 6.45	<0.001	HS
	Median (IQR)	65.00 (61.50-67.50)	60.00 (53.00-63.00)		
CBCL - Social Problems	Mean ± SD	63.35 ± 4.02	63.24 ± 4.31	0.587	NS
	Median (IQR)	63.00 (61.00-66.00)	63.00 (59.00-67.00)		
CBCL - Thought Problems	Mean ± SD	59.06 ± 4.29	56.38 ± 3.96	0.011	S
	Median (IQR)	59.00 (56.00-62.00)	58.00 (54.00-58.00)		
CBCL - Attention Problems	Mean ± SD	63.32 ± 5.77	57.95 ± 4.88	<0.001	HS
	Median (IQR)	62.00 (60.00-66.50)	56.00 (56.00-58.00)		
CBCL - Aggressive Behavior	Mean ± SD	60.89 ± 6.52	54.29 ± 9.58	0.001	HS
	Median (IQR)	61.00 (57.00-64.50)	54.00 (46.00-59.00)		
CBCL - ADHD Problems	Mean ± SD	61.14 ± 4.08	54.43 ± 3.40	<0.001	HS
	Median (IQR)	61.00 (58.00-64.00)	54.00 (53.00-55.00)		
CBCL - Oppositional-Defiant Problems	Mean ± SD	58.13 ± 4.72	57.52 ± 3.36	0.495	NS
	Median (IQR)	58.00 (54.50-62.00)	58.00 (56.00-59.00)		
CBCL - Conduct Problems	Mean ± SD	57.87 ± 3.98	50.90 ± 3.60	<0.001	HS
	Median (IQR)	58.00 (55.00-60.00)	51.00 (50.00-52.00)		

CBCL: Child Behavior Checklist, ADHD: Attention-Deficit/Hyperactivity Disorder, SD: Standard Deviation, IQR: Interquartile Range, HS: Highly Significant, S: Significant, NS: Not Significant.

Table (7); Parental Stress Index (PSI) according to vitamin D level

Parameter	Category	Deficient (n=79)	Normal (n=21)	p-value	Significance
PSI - Total Stress	Mean ± SD	76.51 ± 11.68	69.76 ± 14.41	0.030	S
	Median (IQR)	76.00 (66.00-84.50)	63.00 (58.00-82.00)		
PSI - Parental Distress	Mean ± SD	70.56 ± 10.51	61.86 ± 12.87	0.002	HS
	Median (IQR)	72.00 (62.00-76.50)	63.00 (50.00-69.00)		
PSI - Parent-Child Dysfunction	Mean ± SD	80.94 ± 9.69	75.43 ± 12.16	0.034	S
	Median (IQR)	79.00 (75.00-88.00)	74.00 (68.00-82.00)		
PSI - Difficult Child	Mean ± SD	75.11 ± 10.12	63.62 ± 10.08	<0.001	HS
	Median (IQR)	75.00 (68.50-81.00)	61.00 (59.00-66.00)		

PSI: Parental Stress Index, SD: Standard Deviation, IQR: Interquartile Range, HS: Highly Significant, S: Significant.

Table 1 supplementary; Correlation between vitamin D and study parameters

	Pearson Correlation Coefficient	P-Value of Pearson Correlation
Age (years)	-0.147	0.143
Age at Epilepsy Onset (years)	0.039	0.698
Duration of Epilepsy (years)	0.032	0.753
WISC-III - Full Scale IQ	0.588	<0.001*
WISC-III - Verbal IQ	0.481	<0.001*
WISC-III - Performance IQ	0.320	<0.001*
WISC-III - Verbal Comprehension Index	0.456	<0.001*
WISC-III - Perceptual Organization Index	0.550	<0.001*
WISC-III - Freedom from Distractibility Index	0.703	<0.001*
WISC-III - Processing Speed Index	0.527	<0.001*
CBCL - Total Problems	-0.768	<0.001*
CBCL - Internalizing Problems	-0.507	<0.001*
CBCL - Externalizing Problems	-0.434	<0.001*

	Pearson Correlation Coefficient	P-Value of Pearson Correlation
PSI - Total Stress	-0.399	<0.001*
PSI - Parental Distress	-0.503	<0.001*
PSI - Parent-Child Dysfunction	-0.421	<0.001*
PSI - Difficult Child	-0.558	<0.001*
CBCL - Anxiety/Depression	-0.682	<0.001*
CBCL - Withdrawn/Depressed	-0.378	<0.001*
CBCL - Somatic Complaints	-0.460	<0.001*
CBCL - Social Problems	-0.249	0.012*
CBCL - Thought Problems	-0.511	<0.001*
CBCL - Attention Problems	-0.557	<0.001*
CBCL - Aggressive Behavior	-0.549	<0.001*
CBCL - ADHD Problems	-0.742	<0.001*
CBCL - Oppositional-Defiant Problems	-0.365	<0.001*
CBCL - Conduct Problems	-0.747	<0.001*

WISC-III: Wechsler Intelligence Scale for Children - Third Edition, CBCL: Child Behavior Checklist, PSI: Parental Stress Index, SD: Standard Deviation, HS: Highly Significant, S: Significant.

DISCUSSION

In this study 56% of the children with epilepsy were male, and their average age was 13.86 ± 2.79 years. The age distributions in juvenile epilepsy populations described by **Serra-Pinheiro et al. [28]** and other earlier investigations are consistent with this demographic profile. The psychiatrist saw patients between the ages of 10 and 14 the most frequently. This gender-specific expression is in line with a study by **Alfstad et al. [29]** found that boys with epilepsy had higher rates of hyperactivity and difficulty with peer relationships, while girls had more emotional problems.

This study found that vitamin D insufficiency was significantly more common in children with epilepsy (79%) with a mean level of 20.78 ± 10.63 ng/ml. This is significantly more than the rates found in the general pediatric population by **Miftah et al. [30],** who found that 42% of Ethiopian pediatric epilepsy patients taking antiepileptic medications had a lack of vitamin D. The following were identified as significant risk factors for vitamin D deficiency: age, female sex, polytherapy, and non-ambulation.

According to **Elmazny et al. [31],** this rate is consistent with findings from earlier research in Egypt on young people with idiopathic generalized epilepsy who have just received a diagnosis. Forty percent of the patients in this

study had vitamin D deficiency, and 38 percent had vitamin D insufficiency.

Sarhan et al. [32] They sought to assess how anti-seizure drugs (ASMs) affected the levels of Sclerostin, a biomarker of bone turnover in children with epilepsy, and vitamin D. They discovered that vitamin D deficiency affected 53.3% of children with epilepsy. They found that when both vitamin D deficiency and insufficiency are considered as hypovitaminosis D, more than two-thirds of children with epilepsy have vitamin D deficiency, despite Egypt's tropical climate.

According to a meta-analysis by **Junges et al. [33],** Vitamin D deficiency was found in 33% of epileptic children using enzyme-inducer ASMs. while children receiving non-enzyme inducers had a 24% prevalence. The study by **Muskens et al. [34]** was to ascertain the prevalence of vitamin D3 deficiency in children diagnosed with psychiatric conditions, including internalizing disorders (anxiety and mood disorders) and children with ASD. Their results showed that 77.4% of respondents were vitamin D3 deficient. (<50 nmol/L). Furthermore, vitamin D3 deficiency was present in 79.5% of the children with internalizing problems and 75.9% of the children with ASD.

Vitamin D deficiency may be an independent component rather than a side effect of chronic illness or therapy, as evidenced by the lack of link seen in this study between vitamin D levels and patients' age, the duration of their epilepsy, or the age at which it first appeared.

This is in line with the findings of **Sarhan et al. [32],** who also pointed out that patients' ages and serum vitamin D levels seem to be negatively correlated. According to **Siddiqee et al. [35] and McGillivray et al. [36],** vitamin D levels showed a significant decline in the younger age group. However, the participants in these trials were ages ranging from newborns to five years old. However, according to **Baek et al. [37],** Age is one of the most important variables affecting serum vitamin D levels.

Significant correlations between vitamin D levels and cognitive performance were found in our investigation. Across several cognitive areas, children with normal vitamin D levels showed significantly superior scores, especially in the Processing Speed Index (77.81 ± 5.85 vs. 73.56 ± 4.47, $p<0.001$) and Freedom from Distractibility Index (82.48 ± 4.88 vs. 76.75 ± 3.54, $p<0.001$).

These results are consistent with those of **De Marzio et al. [38],** who examined the metabolic role of vitamin D in the neurodevelopment of youngsters. The metabolic networks associated with the metabolism of fatty acids, linoleic acid, and tryptophan —all of which are essential for brain function—were discovered to be altered in response to low vitamin D levels. The cognitive deficits seen in children with vitamin D deficiency may be caused by these metabolic alterations.

Higher maternal vitamin D levels during pregnancy were associated with better brain development and higher IQ scores in infants, according to another study that Seattle infants's Hospital highlighted in 2020. According to this, getting enough vitamin D throughout crucial stages of brain development may improve cognitive function for a long time **[39].**

On the other hand, **Chowdhury et al. [40]** found no evidence of a significant correlation link early childhood vitamin D levels and cognitive development. The study suggests that early-life low vitamin D levels could not have a significant impact on inhibiting cognitive development and linear growth.

In a similar vein, **Mutua et al. [41]** found no proof linking five-year-old Ugandan children's cognitive and motor results to their earlier vitamin D status. This work contributes to the body of research indicating that a number of factors, including genetic, The relationship between vitamin D and cognitive performance may be influenced by environmental and dietary factors. Children with vitamin D insufficiency had considerably higher problem ratings, particularly in the areas of ADHD problems, according to the CBCL data (61.14 ± 4.08 vs.

54.43 ± 3.40, p<0.001), Anxiety/Depression (63.61 ± 5.02 vs. 55.71 ± 4.34, p<0.001), and Total Problems (64.39 ± 5.15 vs. 55.43 ± 4.70, p<0.001). A possible involvement of vitamin D in behavioral regulation is suggested by the high negative association (r=-0.768 for Total Problems) between vitamin D levels and behavioral issues.

These results build on earlier research by **Robinson et al. [42],** who, although their study was aimed at the general population, discovered links between low vitamin D and behavioral issues in adolescents. The study by **Omanakuttan et al. [43],** which found a connection between poor seizure control and higher psychiatric morbidity among teenagers with epilepsy, supports this conclusion. Effective seizure management is crucial for reducing psychiatric comorbidities in this population, according to the study.

In order to gauge the stress levels of their parents, **Operto et al. [1]** sought to determine whether Children and teenagers with epilepsy had behavioral and emotional issues. Their results showed that the statistical comparison showed that the group with epilepsy scored significantly higher than the controls on nearly every CBCL scale ($p < 0.05$). The DSM-IV axis I disorders were more common in children with recent onset epilepsy than in controls, according to a 2007 study by Jones et al. In addition to depressive disorders (22.6 vs. 4%, $p = 0.01$) and ADHD (26.4 vs. 10%, $p = 0.01$), they also had anxiety disorders (35.8 vs. 22%, $p < 0.05$). were also noticeably higher. These issues were present in 45% of children with epilepsy prior to the onset of the first seizure, which may indicate the impact of unidentified antecedent neurobiological variables.

The strong correlation between parental stress levels and children's vitamin D status was one of the study's key findings. Higher Total Stress ratings (76.51 ± 11.68 vs. 69.76 ± 14.41, p=0.030) and especially higher Difficult Child scores (75.11 ± 10.12 vs. 63.62 ± 10.08, p<0.001) were observed in parents of kids who didn't get enough vitamin D. Given the robust correlation observed between parental stress markers and vitamin D levels, it seems plausible that vitamin D status may have an indirect effect on family dynamics by influencing how children behave and function.

This is consistent with studies by **Hattangadi et al. [44],** which discovered that stress levels are higher among parents of children who have mental health issues. These findings support **Klotz et al. [45],** which discovered that the stress levels of parents of children with epilepsy are significantly greater than those of the general population. The results of the study point to a complicated interaction between parental stress, behavioral outcomes, cognitive function, and vitamin D levels in children with epilepsy. Strong relationships between vitamin D levels and several areas (cognitive, behavioral, and parental stress) raise the possibility that vitamin D may be more important in the treatment of pediatric epilepsy than previously thought.

CONCLUSIONS

Vitamin D insufficiency is common in children with epilepsy, which is linked to increased mental symptoms, decreased cognitive function, and elevated parental stress. These results emphasize the significance of keeping an eye on vitamin D levels and taking supplements into account as part of an all-encompassing treatment plan for children with epilepsy. The possible advantages of vitamin D supplementation on behavioral and cognitive results in this population require more long-term research**.**

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