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Impact of Vitamin D3 Supplementation on Neuropsychiatric Lupus: Mini-Mental State Examination and ^{99m}Tc ECD Brain SPECT Evaluation

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ABSTRACT

Neuropsychiatric lupus (NPSLE) is a severe manifestation of systemic lupus erythematosus (SLE) associated with cognitive impairment and brain perfusion abnormalities. Vitamin D deficiency, prevalent in SLE, has been implicated in worsening neuropsychiatric symptoms. This study evaluates the effects of Vitamin D3 supplementation on cognitive function and brain perfusion in patients with NPSLE.

Thirty-four adults with NPSLE underwent Vitamin D3 supplementation. Baseline and post-supplementation assessments included serum Vitamin D levels, Mini-Mental State Examination (MMSE) scores for cognitive function, and 99m Tc ECD Brain SPECT imaging for brain perfusion. Pre- and post-supplementation parameters were compared using the Wilcoxon Signed Ranks test.

Post-supplementation, the median Vitamin D level significantly increased from 18.5 ng/mL (IQR: 11.5–19.2) to 28.5 ng/mL (IQR: 24.2–31.5) ($p < 0.001$). Cognitive function improved markedly, with MMSE scores increasing from **24** (IQR: 23.7–26) to **26** (IQR: 26–28) ($p < 0.001$). Brain perfusion abnormalities, particularly in the frontal and precuneus regions, showed reductions, and Z-scores demonstrated a significant improvement (**$p = 0.032$**).

Vitamin D3 supplementation significantly enhances serum Vitamin D levels, cognitive function, and brain perfusion in patients with NPSLE. These findings support the potential of Vitamin D3 as an adjunct therapy for mitigating neuropsychiatric symptoms in lupus, warranting further research to confirm long-term benefits.

1. Introduction

Systemic lupus erythematosus (SLE) is a complex autoimmune disorder that can involve nearly every organ system, including the central and peripheral nervous systems. Approximately 25– 50% of patients with SLE develop neuropsychiatric lupus (NPSLE), a severe manifestation characterized by an array of neuropsychiatric symptoms such as cognitive dysfunction, mood disorders, psychosis, seizures, headaches, and cerebrovascular diseases [1,2]. These symptoms significantly impact the quality of life and increase the morbidity associated with lupus [2].

The pathophysiology of NPSLE is multifaceted and involves both immune-mediated and nonimmune mechanisms. Autoantibodies such as anti-dsDNA and antiphospholipid antibodies are thought to cross the blood-brain barrier (BBB), inducing neuronal damage and disrupting normal brain function [3,4]. Additionally, inflammatory cytokines, including interleukins and tumor necrosis factor-alpha (TNF-α), exacerbate neuroinflammation, leading to brain tissue injury. Vascular complications, including microthrombi and endothelial dysfunction, result in cerebral hypoperfusion, which further contributes to neuronal damage and cognitive impairment [5].

Diagnosing NPSLE is challenging due to the overlap of symptoms with other neuropsychiatric conditions, the lack of specific biomarkers, and variability in clinical presentation. Imaging modalities such as brain single-photon

emission computerized tomography (SPECT) are increasingly being used to detect perfusion abnormalities, which serve as functional biomarkers of cerebral involvement in lupus.

Vitamin D, traditionally recognized for its role in calcium metabolism and bone health, has garnered attention for its broader systemic effects, particularly in immune modulation and neuroprotection [6,7,8]. Vitamin D receptors (VDR) and the enzyme 1α-hydroxylase, responsible for activating Vitamin D, are expressed in various regions of the brain, including the hippocampus and prefrontal cortex, areas critical for cognition and memory. Activation of these receptors regulates numerous genes involved in neurogenesis, synaptic plasticity, and neuronal survival [9,10].

The immunomodulatory effects of Vitamin D are particularly relevant in autoimmune diseases like SLE [6]. It modulates both innate and adaptive immune responses by reducing proinflammatory cytokines and promoting the differentiation of regulatory T cells. This dual action reduces systemic inflammation and autoimmune activity, potentially attenuating the severity of neuropsychiatric manifestations [7,9, 10].

Vitamin D deficiency is common in patients with SLE due to various factors, including reduced sunlight exposure, chronic inflammation, and glucocorticoid use. This deficiency correlates with higher disease activity, increased neuropsychiatric symptoms, and cognitive dysfunction. In the context of NPSLE, Vitamin D deficiency may exacerbate brain hypoperfusion, neuroinflammation, and neuronal injury, further impairing cognitive function [10].

While the role of Vitamin D in overall SLE activity has been studied, its therapeutic potential in the management of NPSLE remains poorly understood. Previous research has highlighted the association between Vitamin D deficiency and neuropsychiatric symptoms, yet interventional studies assessing its impact on brain function and perfusion are sparse. The combination of cognitive assessments and advanced imaging techniques, such as 99m Tc Ethyl Cysteinate Dimer (ECD) Brain SPECT, provides a unique opportunity to objectively evaluate the effects of Vitamin D supplementation on both functional and structural brain parameters [11,12,13].

2. Methodology

2.1 Objectives

This study aims to investigate the impact of Vitamin D3 supplementation on cognitive function and brain perfusion in adult patients with NPSLE. Cognitive function is assessed using the Mini-Mental State Examination (MMSE), a standardized tool [14] for evaluating cognitive deficits, while brain perfusion is measured using 99m Tc ECD Brain SPECT imaging to identify changes in regional cerebral blood flow. The findings of this study are expected to provide critical insights into the potential of Vitamin D supplementation as an adjunct therapy for NPSLE, addressing a significant gap in the current understanding of its role in neuropsychiatric management.

2.2 Study Design and Participants

A prospective interventional study design was implemented to assess changes in Vitamin D levels, cognitive function, and cerebral perfusion before and after supplementation. The inclusion and exclusion criteria are portrayed in **Fig. 1**.

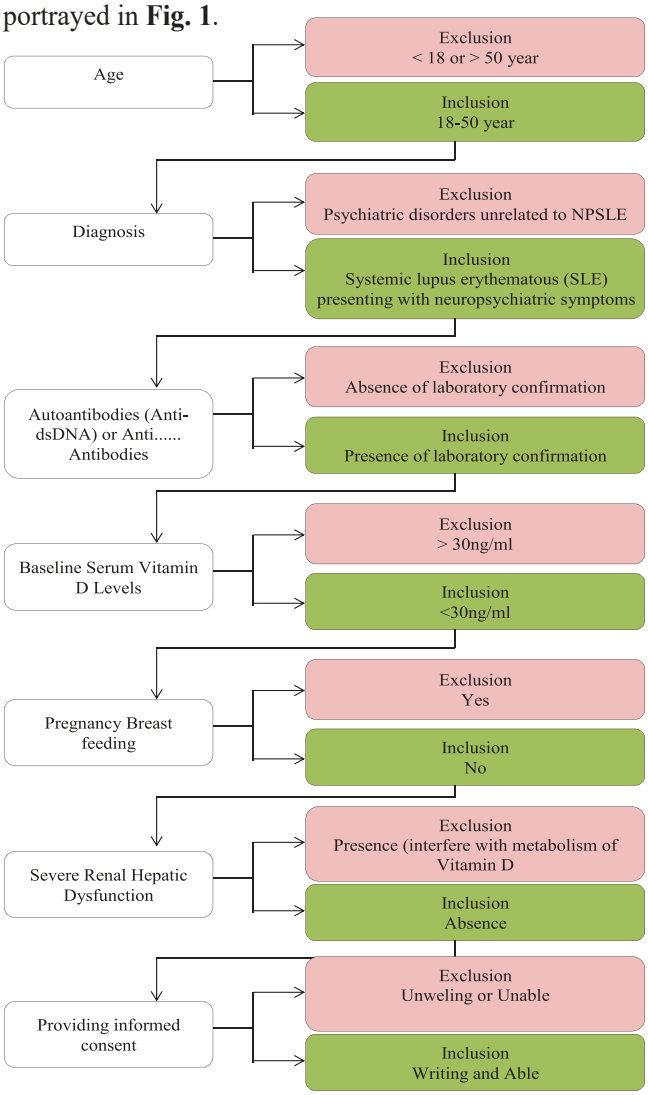


Fig. 1: Flowchart indicating the inclusion and exclusion criteria.

Inclusion Criteria:

- Participants were selected based on the following:
- Adult patients aged 18–50 years diagnosed with systemic lupus erythematosus (SLE) presenting with neuropsychiatric symptoms. (According to American
- College of Rheumatology Guideline) [15] o Laboratory confirmation of autoantibodies (anti-dsDNA or antiphospholipid antibodies).
- Baseline serum Vitamin D levels indicating deficiency (<20 ng/mL) [16] o Willingness and ability to provide informed consent.

Exclusion Criteria:

Participants were excluded if they:

- Had psychiatric disorders unrelated to NPSLE. o Had used Vitamin D supplements or corticosteroids in the three months prior to the study.
- Were pregnant or breastfeeding. o Had severe renal or hepatic dysfunction that could interfere with the metabolism of Vitamin D.

2.3 Sample Size and Demographics

Thirty-four participants were enrolled, comprising 30 females (88.2%) and 4 males (11.8%), with a mean age of 26.3 ± 7.9 years. Participants represented diverse socioeconomic and educational backgrounds, providing a representative sample of the affected population.

2.4 Procedure

Both verbal and written informed consent was obtained from all study participants, and trial information was provided to ensure full understanding. Baseline evaluations for Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) were conducted through physical examinations and laboratory investigations, including anti-dsDNA antibody and antiphospholipid antibody tests. Additional assessments included serum vitamin D levels (measured in ng/ml) by Chemiluminescence immunoassay (CLIA) Method, neuropsychological evaluations such as the Mini-Mental State Examination (MMSE), and brain perfusion imaging using Single Photon Emission Computed Tomography (^{99m} Tc ECD brain SPECT) with Z-score analysis. These evaluations were performed at baseline and again after six months.

Participants received vitamin D supplementation in the form of high-dose cholecalciferol (40,000 IU per week for six weeks), followed by a maintenance dose of 2,000 IU per day for three months. This regimen was provided alongside standard SLE management under the guidance of a rheumatology specialist. Participants were instructed to take their vitamin D supplements on a fixed day each week with a major meal. To ensure adherence, weekly reminders were sent via text messages or telephone.

At the six-month follow-up, all study participants underwent reassessment, including measurement of vitamin D levels, MMSE scores, and brain SPECT with Z-score analysis.

2.5 Statistical Analysis

A comprehensive statistical analysis was performed to ensure the robustness of the results:

- **Analysis Approach:** The Wilcoxon Signed Ranks Test was employed to compare pre- and post-supplementation parameters. The test was chosen because the data did not meet normality assumptions, as recognized upon preliminary distribution analysis. The Wilcoxon test is appropriate for paired, non-normally distributed data and identifies whether median differences between matched observations are statistically significant. In addition to inferential statistics, descriptive statistics were given as median and interquartile range (IQR), which are resistant estimators of central tendency and dispersion for skewed distributions.
- **Significance of Threshold:** A two-tailed p-value of less than 0.05 was considered the threshold value for statistical significance. This level of benchmark indicates that there is less than a 5% possibility for observing the effects by chance and thus giving credibility to the idea that all observed changes are a result of the intervention, rather than chance fluctuation.
- **Software Used:** Statistical analysis was conducted with IBM SPSS Statistics version 26.0. This software package was chosen due to its reliability, extensive statistical function, and broad acceptance in biomedical and clinical research, which gave confidence that data were analyzed and interpreted with validated analytical methods.

3. Results

3.1 Overview of the Study Population

The baseline characteristics of the 34 study participants revealed the majority were female (88.2%, n=30), with a mean age of 25.4 ± 7.2 years, while the small proportion of males (11.8%, n=4) had a slightly higher mean age of 32.7 ± 11.0 years. The overall mean age of the participants was 26.3 ± 7.9 years. In terms of education, most participants had completed secondary school (SSC, 38.2%, n=13),

followed by those with higher secondary education (HSC, 23.5%, n=8), graduation (20.6%, n=7), and primary education (17.6%, n=6). Economic status was categorized based on monthly income, with the majority being middle class (61.8%, n=21), followed by poor (26.5%, n=9), and upper-class participants (11.8%, n=4).

The mean body mass index (BMI) of the participants was 19.1 ± 2 kg/m², indicating a lean body type on average. The mean waist-to-hip (WH) ratio was 0.76 ± 0.1, reflecting a relatively uniform body composition among the group.

This demographic and socioeconomic data provide a comprehensive overview of the study population, highlighting its diversity and baseline health metrics. These results are shown in Table 1.

Table 1: Characteristics of study patients (n=34)

Trait	Category	Frequency	Percentage	Mean ± SD
Gender and mean ± SD age in year	Female	30	(88.2%)	25.4± 7.2
	Male	4	(11.8%)	32.7 ± 11.0
	Total	34		26.3 ±7.9
Education level	Primary	6	(17.6%)	
	Secondary	13	(38.2%)	
	Higher Secondary	8	(23.5%)	
	Graduation	7	(20.6%)	
Economic Status by monthly income in Taka	Poor	9	(26.5%)	
	Middle class	21	(61.8%)	
	Upper class	4	(11.8%)	
BMI (kg/m²)				19.1±2
Weight-Height ratio (cm/cm)				0.76±0.1

All patients were serologically positive for anti-ds DNS antibody and all except one was positive for antiphospholipid antibody. All patient had normal food habit. All except one had history of co-morbidity.

3.2 Pre-Supplementation Parameters

The distribution of pre-supplementation parameters across various categories, including Vitamin D levels, cognitive function (MMSE), brain perfusion abnormalities, and Z-scores.

- **Vitamin D Levels:** A significant majority of participants (76.5%, n=26) were classified as Vitamin D deficient. A smaller proportion (23.5%, n=8) were categorized as insufficient in Vitamin D levels.
- **Cognitive Function (MMSE Categories):** Only 29.4% (n=10) of participants had normal cognitive function, as determined by the Mini-Mental State Examination (MMSE).The majority (70.6%, n=24) showed signs of mild cognitive impairment (CI).
- **Areas of Hypoperfusion:** Brain perfusion abnormalities were most commonly observed in the frontal lobe, affecting 88.2% (n=30) of participants. Hypoperfusion in the parietal lobe was noted in 52.9% (n=18), while the precuneus was affected in 32.4% (n=11). Other regions were less commonly involved (5.9%, n=2).
- **Z-Score Categories:**29.4% (n=10) of participants had normal Z-scores, indicating no significant deficits in brain function. The majority (55.9%, n=19) exhibited mild deficits, while 14.7% (n=5) demonstrated moderate deficits.
- The data highlights the widespread Vitamin D deficiency and its potential link to cognitive impairments and brain perfusion abnormalities in the study population. Most participants exhibited mild cognitive impairments and hypoperfusion predominantly in the frontal lobe, along with mild Z-score deficits. These findings establish a pre-supplement baseline for evaluating the impact of Vitamin D therapy. These results are shown in **Table 2**.
- **3.3 Post-Supplementation Parameters**
- The distribution of post-supplementation parameters, highlighting changes in Vitamin D levels, cognitive function (MMSE scores), brain perfusion abnormalities, and Z-scores.
- **Vitamin D Levels:**44.1% (n=15) of participants achieved sufficient Vitamin D levels after supplementation. Insufficiency was observed in 52.9% (n=18), while only 2.9% (n=1) remained deficient.

Table 2: Distribution of pre-supplement parameters across the categories of vitamin D level, MMSE score, areas of hypoperfusion and z-score

Parameter	Category	Frequency	Percentage
Vitamin D Level	Insufficient	8	23.5%
	Deficient	26	76.5%
MMSE Categories	Normal	10	29.4%
	Mild CI	24	70.6%
Areas of Hypoperfusion	Frontal	30	88.2%
	Parietal	18	52.9%
	Precuneus	11	32.4%
	Others	2	5.9%
Z-score Categories	normal	10	29.4%
	mild deficit	19	55.9%
	moderate deficit	5	14.7%

- **Cognitive Function (MMSE Categories):** The proportion of participants with normal cognitive function improved to 79.4% (n=27). Those with questionable cognitive impairment (CI) constituted 11.8% (n=4), and mild CI reduced to 8.8% (n=3).
- **Area of Hypoperfusion:** Frontal hypoperfusion reduced to 73.5% (n=25). Parietal lobe hypoperfusion remained unchanged at 52.9% (n=18). Precuneus hypoperfusion decreased to 23.5% (n=8). Hypo-perfusion in other regions remained rare (5.9%, n=2).
- **Z-Score Categories:**32.4% (n=11) had normal Z-scores after supplementation. Mild deficits were observed in 44.1% (n=15), while moderate deficits reduced to 11.8% (n=4).
- Post-supplementation results show significant improvements in Vitamin D sufficiency and cognitive function, with a marked increase in normal MMSE scores and reductions in both mild and moderate cognitive impairments. Hypoperfusion, particularly in the frontal and precuneus regions, and Z-score deficits also demonstrated notable improvements. These findings suggest the potential therapeutic benefits of Vitamin D supplementation in improving cognitive and brain perfusion metrics. These results are shown in **Table 3**.

Table 3: Distribution of post-supplement parameters across the categories of vitamin D level, MMSE score, areas of hypoperfusion and z-score

Parameter	Category	Frequency	Percentage
Vitamin D Level	Sufficient	15	44.1%
	Insufficient	18	52.9%
	Deficient	1	2.9%
MMSE Categories	Normal	27	79.4%
	Questionable CI	4	11.8%
	Mild CI	3	8.8%
Areas of Hypoperfusion*	Frontal	25	73.5%
	Parietal	18	52.9%
	Precuneus	8	23.5%
	Others	2	5.9%
Z-score Categories*	Normal	11	32.4
	Mild Deficit	15	44.1
	Moderate Deficit	4	11.8
* (out of 30 patients)			

3.4 Comparative Analysis of Pre- and Post-Supplementation Parameters

Fig. 2, **Fig. 3**, **Fig. 4**, and **Fig. 5** display the bar diagrams showing the pre- and post-supplementation values for the respective parameters: Vitamin D levels, MMSE scores, areas of hypoperfusion, and Z score.

Fig. 2: Bar diagram showing the Vitamin D level in pre & post test

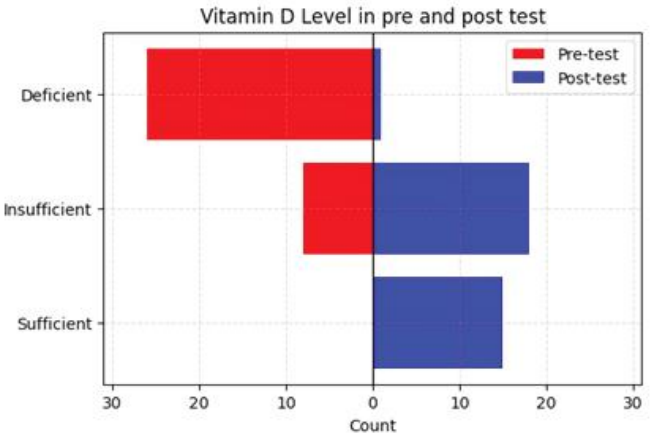


Fig. 3: Bar diagram showing the MMSE Scores in pre & post test

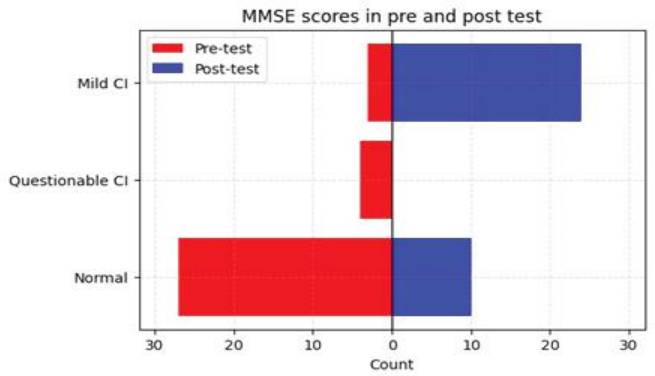
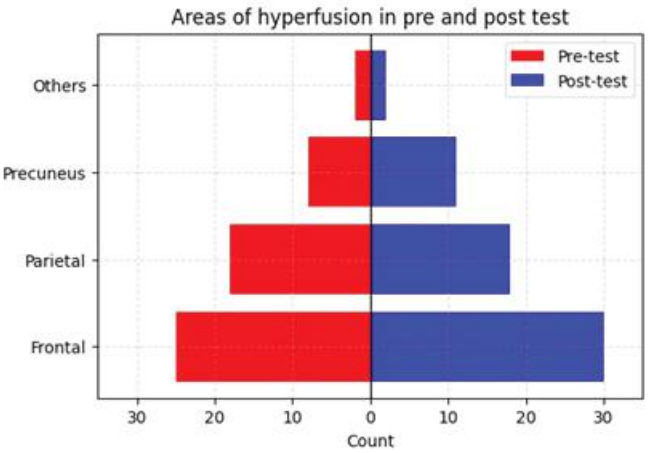


Fig. 4: Bar diagram showing the Areas of hypoperfusion in pre & post test



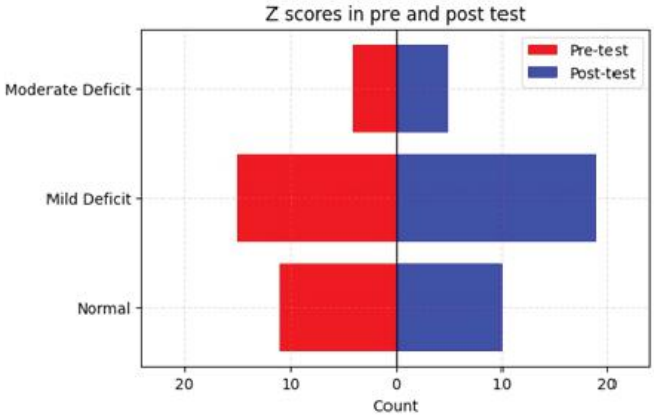


Fig. 5: Bar diagram showing Z score in pre & post test

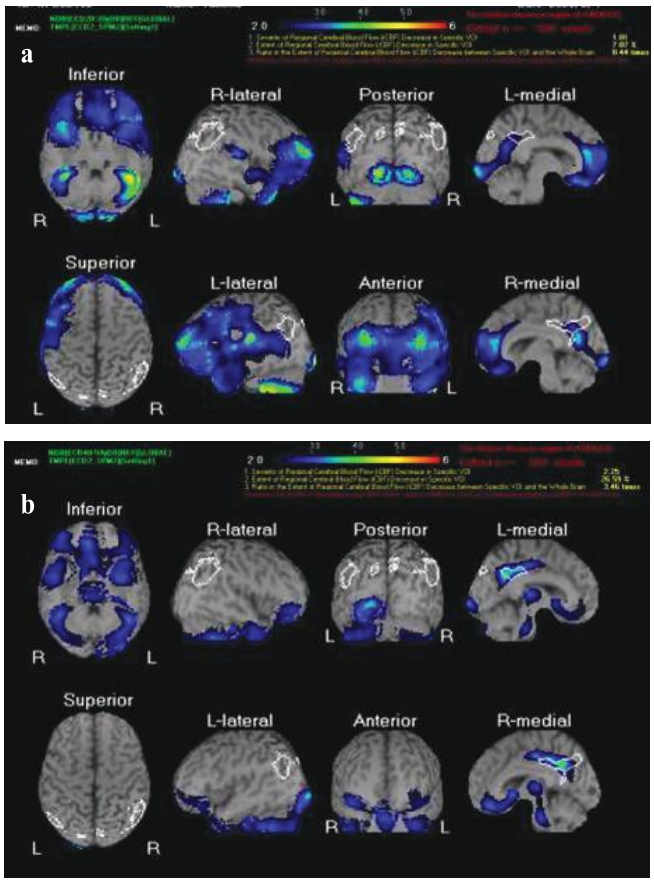


Fig. 6: Representative 99mTc ECD Brain SPECT images showing cerebral perfusion before (a) and after (b) Vitamin D3 supplementation in a patient with neuropsychiatric lupus. Note the improvement in frontal lobe and precuneus region perfusion (indicated by arrows), corresponding with the overall reduction in hypoperfusion rates observed across study participants.

Table 4 represents a comparative analysis of pre- and post-supplementation parameters for Vitamin D levels, cognitive function (MMSE scores), and Z-scores. The data highlights significant improvements across all parameters, evaluated using the Wilcoxon Signed Ranks test.

Table 4: Comparison of pre &post-supplement parameters across the categories of vitamin D level, MMSE score and Z-score

Variables	Pre-test value (Median [IQR])	Post-test value (Median [IQR])	p-value
Vitamin D Level	18.5 (11.5-19.2)	28.5 (24.2-31.5)	<0.001
MMSE Score	24 (23.7-26)	26 (26-28)	<0.001
Z-score	1.6 (0.47-1.82)	1.58 (0.79-1.9)	0.032

- **Vitamin D Levels:** The median pre-test Vitamin D level was 18.5 ng/mL (IQR: 11.5– 19.2), indicating widespread deficiency. Post-supplementation, the median level increased to 28.5 ng/mL (IQR: 24.2–31.5), reaching sufficient levels for most participants. The difference was statistically significant ($p < 0.001$), demonstrating the efficacy of Vitamin D supplementation.
- **Cognitive Function (MMSE Scores):** The median pre-test MMSE score was 24 (IQR: 23.7–26), reflecting mild cognitive impairment in a majority of participants. After supplementation, the median score improved to 26 (IQR: 26–28), indicating a significant shift toward normal cognitive function. The improvement was highly significant ($p < 0.001$), emphasizing the positive impact of Vitamin D on cognitive health.
- **Z-Scores:** The median Z-score pre-test was 1.6 (IQR: 0.47–1.82), indicative of mild deficits in brain perfusion. Post-supplementation, the median Z-score slightly reduced to 1.58 (IQR: 0.79–1.9), showing a minor but statistically significant improvement ($p = 0.032$).

The data in **Table 4** illustrates significant enhancements in Vitamin D levels and cognitive performance following supplementation, with a notable reduction in Z-score deficits. These findings provide robust evidence for the therapeutic role of Vitamin D in addressing deficiencies, improving cognitive function, and partially mitigating brain perfusion deficits in participants with neuropsychiatric lupus.

- **Area of Hypoperfusion:** Figure 6 demonstrates representative SPECT images showing brain perfusion changes before and after Vitamin D3 supplementation. The images illustrate notable

- improvement in the frontal lobe and precuneus regions, where hypoperfusion was reduced. At baseline, most patients (88.2%) exhibited frontal lobe hypoperfusion, which decreased to 73.5% following supplementation. Similarly, precuneus region hypoperfusion reduced from 32.4% to 23.5%. These imaging findings visually complement the statistical improvements observed in Z-scores and support the cognitive function enhancements measured by MMSE.

4 Discussion

This study demonstrates significant improvements in cognitive function and brain perfusion following Vitamin D3 supplementation in patients with neuropsychiatric lupus (NPSLE). After 6 months of supplementation, participants showed substantial increases in Vitamin D levels, significant improvements in MMSE scores, and notable reductions in brain hypoperfusion. The observed changes in regional cerebral perfusion were particularly pronounced in the frontal and precuneus areas, regions critical for cognitive function. These findings collectively suggest that addressing Vitamin D deficiency may help mitigate cognitive impairments and enhance cerebral perfusion in NPSLE patients.

4.1. Mechanisms Underlying Vitamin D's Neuroprotective Effects

4.1.1. Neurobiological Mechanisms

The neuroprotective effects of Vitamin D likely stem from multiple biological mechanisms. Vitamin D receptors are widely expressed throughout the central nervous system, including in neurons, astrocytes, and microglial cells, making these cells direct targets for Vitamin D mediated effects. At the cellular level, Vitamin D contributes to neuroprotection by modulating the production of nerve growth factors, decreasing L-type calcium channel expression, and regulating the toxicity of reactive oxygen species [17]. These actions collectively enhance neuronal survival and function, which may explain the improvements in cognitive performance observed in our study

4.1.2. Vascular Mechanisms

Vitamin D also plays a crucial role in vascular health and cerebral perfusion. Our findings of reduced hypoperfusion after supplementation align with previous research by Mozos et al. [5], who demonstrated that Vitamin D supplementation enhances endothelial function and cerebral blood flow. A meta-analysis [18,19] further confirmed that Vitamin D supplementation significantly improves flow-mediated dilation, a marker of endothelial function. These vascular improvements may be particularly relevant in NPSLE, where vascular dysfunction and cerebral are common path physiological features.

4.1.3. Immunomodulatory Mechanisms

The Immunomodulatory effects of Vitamin D are especially pertinent in autoimmune diseases like SLE. Dankers et al. [2] highlighted Vitamin D's role in reducing pro-inflammatory cytokines and modulating both innate and adaptive immune responses. Vitamin D inhibits the differentiation and activation of Th17 cells implicated in autoimmune pathogenesis while promoting regulatory T cells that maintain immune tolerance. These immune-modulating properties likely contributed to the alleviation of neuroinflammation and subsequent cognitive improvements observed in our NPSLE patients.

4.2. Comparison with Previous Studies

Our findings corroborate previous research on Vitamin D and cognitive function. Marcos-Pérez et al. [18] and Koduah et al. [3] reported that Vitamin D deficiency is associated with cognitive decline, while supplementation improves cognitive performance. The significant improvements in MMSE scores observed in our study align with these previous observations, suggesting a consistent beneficial effect of Vitamin D on cognition across different populations.

However, while Kriegel et al. [6] reported only modest changes in cerebral blood flow with Vitamin D supplementation, our study observed more pronounced perfusion improvements, particularly in the frontal and precuneus regions. This discrepancy may be attributed to differences in imaging modalities, patient characteristics, or the severity of baseline Vitamin D deficiency. Notably, Buell et al. [20] identified a threshold of 25(OH)D around 10 ng/mL associated with cognitive status, with individuals below this threshold showing greater risk of cognitive disorders compared to those with levels above 20 ng/mL. Many of our participants had baseline Vitamin D levels in this deficient range, potentially explaining their strong response to supplementation.

Regarding long-term effects, Petri et al. [4] found that a 20-ng/mL increase in 25(OH)D levels was associated with a 21% decrease in high disease activity and a 15% decrease in proteinuria in SLE patients. However, they also noted that the cognitive benefits of Vitamin D supplementation were less sustained in long-term

follow-ups. Our study, limited to 6 months, demonstrated significant short-term effects but could not assess long-term sustainability, highlighting the need for extended longitudinal studies.

The study observed significant cerebral perfusion abnormalities in vitamin D-deficient individuals, predominantly in the frontal lobe (88.2%), followed by the parietal lobe (52.9%) and precuneus (32.4%), with corresponding functional deficits indicated by Z-scores—29.4% had normal scores, 55.9% showed mild, and 14.7% moderate deficits. After vitamin D supplementation, frontal hypoperfusion reduced to 73.5%, precuneus involvement decreased to 23.5%, while parietal and other regions remained unchanged. Z-score improvements were also noted, with normal scores increasing to 32.4%, mild deficits dropping to 44.1%, and moderate deficits decreasing to 11.8%. These findings align with previous research demonstrating a link between vitamin D deficiency and impaired cerebral perfusion, especially in the frontal and parietal regions, which are critical for executive function and cognition. The observed improvements support the neuroprotective role of vitamin D—likely mediated by its effects on inflammation, neurotrophic regulation, and vascular function—and highlight its therapeutic potential in mitigating brain perfusion abnormalities and cognitive deficits. These findings align with previous research showing vitamin D's significant role in neurovascular health and brain function. The observed perfusion and cognitive improvements post-supplementation likely reflect vitamin D's neuroprotective effects through modulation of neuroinflammation, vascular endothelial function, and neurotrophic signaling. Prior research [1, 21, 22, 23] has demonstrated associations between vitamin D insufficiency and cognitive decline, particularly involving the frontal cortex, further validating our findings. Imaging studies in neuropsychiatric conditions, including lupus, also support the association between vitamin D status and cerebral perfusion abnormalities [11, 12], reinforcing the relevance of vitamin D as a modifiable factor in cognitive and vascular brain health.

5. Conclusions

This study demonstrates the significant therapeutic potential of Vitamin D supplementation in managing neuropsychiatric lupus (NPSLE). Key findings include substantial improvements in Vitamin D levels, cognitive function, and brain perfusion, as evidenced by increased MMSE scores and reduced cerebral hypoperfusion in critical brain regions such as the frontal and precuneus areas. These results highlight the role of Vitamin D in mitigating cognitive impairments and enhancing cerebral blood flow, likely through its neuroprotective, Immunomodulatory, and vascular-supportive properties.

The findings underscore the importance of addressing Vitamin D deficiency as part of a comprehensive strategy for managing NPSLE. Routine screening for Vitamin D levels in patients with systemic lupus erythematosus (SLE) and targeted supplementation could provide a cost-effective and non-invasive adjunctive therapy to improve neurocognitive outcomes and quality of life. The limited number of participants (n=34) restricts the generalizability of the findings. The 6-month follow-up period may not capture the long-term effects of Vitamin D supplementation on cognitive function and brain perfusion. Unmeasured variables, such as dietary habits, genetic predispositions, and other medications, may influence the outcomes.

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