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ORIGINAL ARTICLE

Correlation Between Vitamin D Levels and Schizophrenia and Its Symptom Profile: A Hospital Based Case-Control Study

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Abstract

Background: Vitamin D is a Neurosteroid hormone that plays a role in neuroprotection, neurotransmitter modulation, and neurodevelopment. The pathophysiology of schizophrenia and the intensity of related psychotic symptoms have been linked to its insufficiency. **Objectives:** The purpose of this study is to evaluate blood vitamin D levels between individuals with schizophrenia and age- and sex-matched healthy controls. Additionally, the Positive and Negative Syndrome Scale (PANSS) will be used to correlate vitamin D status with symptom profile. **Materials and Methods:** At a tertiary care teaching hospital in Tamil Nadu, India, this hospital based case-control study recruited 30 drug-naive patients with schizophrenia (diagnosed according to ICD-10 criteria) and 30 healthy, age- and sex-matched controls between the ages of 25 and 40 over the course of a year. Electrochemiluminescence immunoassay (ECLIA) was used to measure the amount of 25-hydroxyvitamin D in fasting serum. PANSS was used to gauge the severity of the symptoms. For statistical analysis, the chi-square test, independent-samples t-test, one-way ANOVA, and Pearson correlation were employed. **Results:** Compared to controls (19.57 ± 5.46 ng/mL; $t = 4.01$, $p = 0.001$), the mean blood vitamin D was considerably lower in cases (14.13 ± 5.03 ng/mL). Compared to 40.0% of controls, 83.3% of patients had inadequate or deficient vitamin D status ($\chi^2 = 12.08$, $p = 0.002$). Positive PANSS scores ($r = -0.465$, $p = 0.010$) and total PANSS scores ($r = -0.506$, $p = 0.001$) were significantly and negatively linked with vitamin D levels, but not negative PANSS ($r = -0.329$, $p = 0.076$) or general psychopathology scores ($r = -0.006$, $p = 0.976$). **Conclusion:** In this cohort, low blood vitamin D is linked to schizophrenia and corresponds with overall symptom severity and positive symptom load, but not with negative or general psychopathology symptoms. Patients with schizophrenia may benefit from routine metabolic evaluations that include vitamin D assessments, and treating deficiencies may help manage symptoms.

Keywords: Vitamin D, Schizophrenia, PANSS, Vitamin D deficiency, Case-control study, Psychosis

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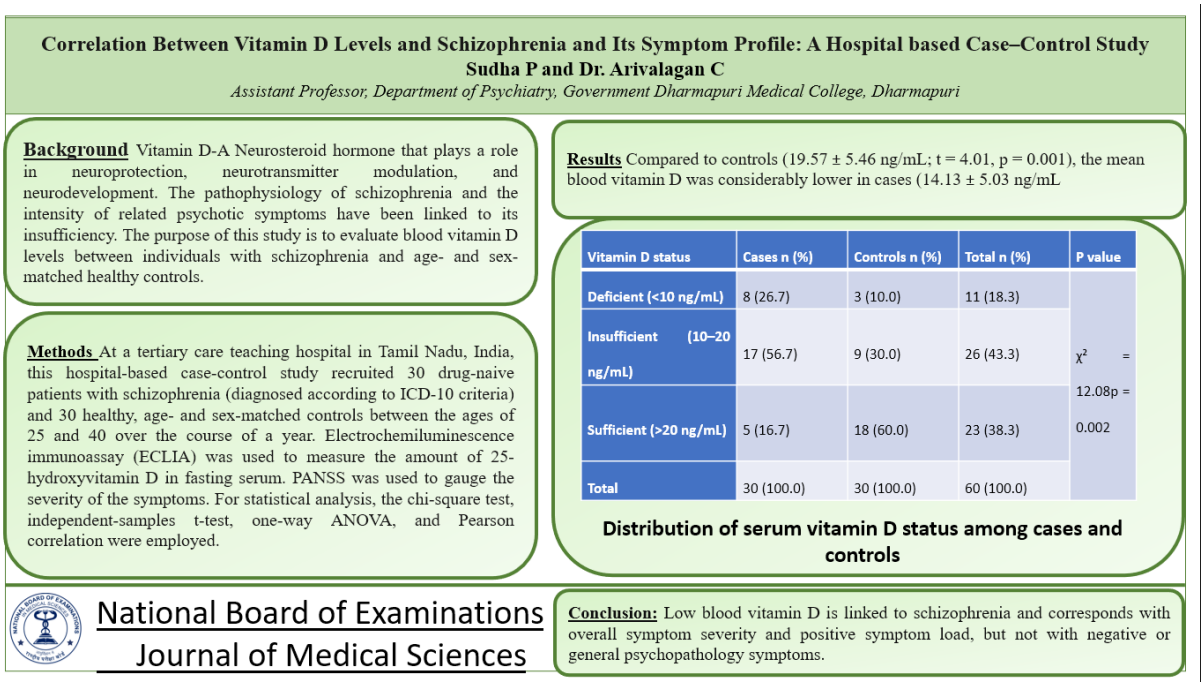
Graphical Abstract



Introduction

With a lifetime prevalence of roughly 1% worldwide and roughly 3 per 1000 people in India, schizophrenia is a severe, chronic psychiatric condition marked by disordered thought, perception, emotion, and conduct. It continues to be one of the major causes of disability worldwide [1]. Its aetiology is complex, with environmental exposures, neurodevelopmental insults, and genetic susceptibility all influencing the onset and progression of the illness.

Unlike other vitamins, vitamin D acts as a secosteroid hormone rather than a straightforward dietary supplement. Its receptors are widely expressed in the human brain in areas linked to schizophrenia, including the hippocampus, hypothalamus, substantia nigra, and prefrontal cortex [2]. It affects neurotrophic factor expression, dopaminergic neurotransmission, neurodevelopment, and neuroprotection from excitotoxic and oxidative damage. A number of neurobiological and behavioural traits associated with schizophrenia, such as altered dopaminergic ontogeny and poor social and cognitive behaviour, are replicated in animal models of embryonic vitamin D insufficiency [3].

Systematic reviews and meta-analyses have confirmed a significantly higher prevalence of vitamin D deficiency among patients with schizophrenia compared with healthy controls [4,5], and population-based studies have connected low neonatal vitamin D concentrations to an increased risk of schizophrenia in later life [3]. Even though the exact causal mechanism is still unknown, a recent narrative review commemorating two decades of research in this field concluded that the theory relating early-life vitamin D deficiency to schizophrenia risk remains biologically reasonable and continues to justify exploration [1]. Vitamin D supplementation has also been investigated

in early interventional research as a complement to conventional antipsychotic therapy [6].

Beyond illness risk, a number of research have looked at the relationship between vitamin D status and the profile and intensity of psychotic symptoms, which are often assessed using the Positive and Negative Syndrome Scale (PANSS) [7,8]. The results of various studies have been mixed, with some reporting significant negative correlations between vitamin D and positive, negative, or total PANSS scores and others finding no such correlation. This discrepancy may be due to variations in the length of the illness, exposure to antipsychotics, ethnicity, latitude, and assay methodology [5].

Aims and Objectives

The current study was conducted with the primary goal of comparing serum vitamin D levels between patients with schizophrenia and healthy controls, and the secondary goal of evaluating the correlation between vitamin D status and PANSS-rated symptom profile, due to the high prevalence of vitamin D deficiency in the general Indian population despite abundant ambient sunlight and the lack of Indian data specifically correlating vitamin D status with symptom profile in drug-naive schizophrenia.

Materials and Methods

Study design and setting

This was a hospital based case–control study conducted in the Department of Psychiatry of a government tertiary care teaching hospital in Salem, Tamil Nadu, India, over a one-year period (2017–2018), following approval by the Institutional Ethics and Research Committee.

Study population

Inclusion criteria

Individuals diagnosed with schizophrenia as per ICD-10 criteria, aged 25–40 years of either sex, willing to participate and to undergo blood investigation.

Exclusion criteria

Age <25 or >40 years; alcohol or substance dependence; organic brain disorder; metabolic disease affecting serum vitamin D concentration; prior vitamin D supplementation; inadequate sunlight exposure; and prior antipsychotic exposure (only drug-naive cases were enrolled).

Sample size and Sampling

A formal priori sample size calculation was not performed. The study included all eligible consecutive drug-naive patients with schizophrenia who fulfilled the inclusion and exclusion criteria and were recruited during the one-year study period, along with an equal number of age- and sex-matched healthy controls by convenience sampling. Thus, the final sample comprised 30 cases and 30 controls.

Tools

A semi-structured sociodemographic questionnaire (age, sex, education, marital status, height, weight, occupation, smoking status, skin colour, and daily sunlight exposure), an informed consent form, and the Positive and Negative Syndrome Scale (PANSS) were used.

PANSS assessment

The PANSS is a validated 30-item, 7-point rating instrument administered via a structured clinical interview of approximately 45 minutes, comprising a

positive scale (7 items), a negative scale (7 items), and a general psychopathology scale (16 items) [7]. Its reliability and validity in detecting change in schizophrenia symptom domains, including negative symptoms, have been established [8].

Blood collection and vitamin D estimation

In order to separate serum, 3–4 mL of fasting peripheral venous blood was obtained with informed consent, allowed to clot in tubes containing gel, then centrifuged at 4000 rpm for 10 minutes; samples that were hemolyzed or icteric were not included. The electrochemiluminescence immunoassay (ECLIA) method, which was selected for its analytical sensitivity, specificity, low reagent use, and quick turnaround, was used to measure serum 25-hydroxyvitamin D. In accordance with widely accepted clinical cut-offs for the Indian population, vitamin D level was classified as sufficient (>20 ng/mL), insufficient (10–20 ng/mL), or deficient (<10 ng/mL).

Statistical analysis

The chi-square test was used to compare categorical variables. The independent-samples t-test was used to compare the mean serum vitamin D levels between patients and controls. PANSS subscale scores were compared across vitamin D categories using one-way ANOVA, and the relationship between serum vitamin D level and PANSS domain scores was evaluated using Pearson's correlation coefficient. Statistical significance was defined as a p-value of less than 0.05.

Results

A total of 60 subjects were enrolled — 30 patients with schizophrenia (cases) and 30 age- and sex-matched healthy controls.

Sociodemographic profile

The majority of participants were aged between 25 and 35 years, with identical sex distribution in both groups (66.7% males and 33.3% females). Compared with controls, patients with schizophrenia more frequently had school-level education, were unemployed or engaged in manual occupations, and predominantly belonged to the lower-middle socioeconomic class. A family history of psychiatric illness was reported in 40.0% of cases, whereas none of the controls had a positive family history (Table 1).

Table 1. Sociodemographic characteristics of cases and controls (N = 60)

Variable	Category	Cases n (%)	Controls n (%)	Total n (%)
Age (years)	25–30	13 (43.3)	11 (36.7)	24 (40.0)
	31–35	9 (30.0)	11 (36.7)	20 (33.3)
	36–40	8 (26.7)	8 (26.7)	16 (26.7)
Sex	Male	20 (66.7)	20 (66.7)	40 (66.7)
	Female	10 (33.3)	10 (33.3)	20 (33.3)
Education	Illiterate	3 (10.0)	3 (10.0)	6 (10.0)
	School level	23 (76.7)	16 (53.3)	39 (65.0)
	Undergraduate	4 (13.3)	11 (36.7)	15 (25.0)
Occupation	Unemployed	9 (30.0)	6 (20.0)	15 (25.0)
	Manual labourer	11 (36.7)	7 (23.3)	18 (30.0)
	Other (business/skilled /mason/painter/supervisor/tailor)	10 (33.3)	17 (56.7)	27 (45.0)
Marital status	Married	18 (60.0)	20 (66.7)	38 (63.3)
	Unmarried	9 (30.0)	8 (26.7)	17 (28.3)
	Separated	3 (10.0)	2 (6.7)	5 (8.3)
Socioeconomic status (Modified Kuppuswamy)	Lower middle	24 (80.0)	19 (63.3)	43 (71.7)
	Upper lower	4 (13.3)	5 (16.7)	9 (15.0)
	Upper middle	2 (6.7)	6 (20.0)	8 (13.3)
Family history of psychiatric illness	Present	12 (40.0)	0 (0.0)	12 (20.0)
	Absent	18 (60.0)	30 (100.0)	48 (80.0)

Note: Controls were recruited to have no family history of psychiatric illness

Serum vitamin D status

Vitamin D deficiency or insufficiency was observed in 83.3% (25/30) of patients with schizophrenia compared with 40.0% (12/30) of healthy controls. Conversely, sufficient vitamin D levels were present in only 16.7% of cases compared with 60.0% of controls. The distribution of vitamin D status differed significantly between the two groups (χ^2 = 12.08, p = 0.002) (Table 2).

Table 2. Distribution of serum vitamin D status among cases and controls

Vitamin D status	**Cases n (%)**	**Controls n (%)**	**Total n (%)**	P value
Deficient (<10 ng/mL)	8 (26.7)	3 (10.0)	11 (18.3)	χ^2 = 12.08 **p = 0.002***
Insufficient (10–20 ng/mL)	17 (56.7)	9 (30.0)	26 (43.3)	
Sufficient (>20 ng/mL)	5 (16.7)	18 (60.0)	23 (38.3)	
Total	**30 (100.0)**	**30 (100.0)**	**60 (100.0)**	

**Chi-square test; p < 0.05 -statistically significant.*

Mean serum vitamin D concentration was significantly lower among patients with schizophrenia than among controls (14.13 ± 5.03 vs. 19.57 ± 5.46 ng/mL; t = 4.01, p = 0.001) (Table 3).

Table 3. Mean serum vitamin D levels in cases and controls

Group	**N**	**Mean ± SD (ng/mL)**	**t**	**p**
Cases	30	14.13 ± 5.03	4.01	0.001**
Controls	30	19.57 ± 5.46		

**Independent t test; p < 0.05 -statistically significant.*

Vitamin D and PANSS symptom domains

Among patients with schizophrenia, positive symptom severity differed significantly across vitamin D categories (F = 5.262, p = 0.012). Participants with sufficient vitamin D levels demonstrated lower positive PANSS scores (15.60 ± 4.34) than those with deficient (22.63 ± 3.38) or insufficient (22.00 ± 4.44) vitamin D status. In contrast, negative symptom scores (F = 0.731, p = 0.491) and general psychopathology scores (F = 0.560, p = 0.578) did not vary significantly according to vitamin D status (Table 4).

Table 4. Serum vitamin D category and PANSS subscale scores in cases (N = 30)

Vitamin D category	**N**	**Positive PANSS Mean ± SD**	**Negative PANSS Mean ± SD**	**General PANSS Mean ± SD**
Deficient	8	22.63 ± 3.38	19.38 ± 7.44	32.13 ± 3.98
Insufficient	17	22.00 ± 4.44	17.12 ± 5.17	30.00 ± 4.60
Sufficient	5	15.60 ± 4.34	15.80 ± 2.05	31.00 ± 6.21
Total	**30**	**21.10 ± 4.75**	**17.50 ± 5.66***	**30.73 ± 4.65**
ANOVA F		5.262	0.731	0.56
p		0.012*	0.491	0.578

*One-way ANOVA across vitamin D categories; *p < 0.05.*

Pearson correlation analysis demonstrated a significant inverse correlation between serum vitamin D concentration and positive PANSS scores ($r = -0.465$, $p = 0.010$). No statistically significant correlations were observed between vitamin D levels and negative PANSS scores ($r = -0.329$, $p = 0.076$) or general psychopathology scores ($r = -0.006$, $p = 0.976$) (Table 6).

Table 6. Pearson correlation between serum vitamin D level and PANSS domain scores

PANSS domain	**Pearson r**	**p**	**N**
Positive PANSS	−0.465	0.010*	30
Negative PANSS	−0.329	0.076	30
General psychopathology PANSS	−0.006	0.976	30

**p < 0.05-Statistically significant*

Discussion

In this cross-sectional case-control investigation, vitamin D status was inversely linked with both positive and total PANSS symptom scores, and drug-naive patients with schizophrenia had significantly lower serum vitamin D levels than age- and sex-matched healthy controls. These results are in line with a large body of research that connects schizophrenia with vitamin D deficiency.

Schizophrenia and vitamin D deficiency

The Study by Patel and Minajagi's, indicated a significant prevalence of vitamin D deficiency (49%) and insufficiency (42%) among psychiatric inpatients, is consistent with the finding of

lower mean blood vitamin D in cases compared to controls [9]. Our findings are also in line with the more recent meta-analysis by Zhu et al., which verified a significantly higher prevalence of vitamin D deficiency in patients with schizophrenia across observational studies published through 2020 [5], and the meta-analysis by Valipour et al., which found a strong correlation between vitamin D deficiency and schizophrenia [4]. Although the relative proportions of deficient versus insufficient status vary with cut-off values, latitude, and sun-exposure patterns across populations, in our cohort, 56.7% of cases fell into the insufficient category and 26.7% into the deficient category, together accounting for 83.3% of cases. This distribution is generally consistent with the high combined deficiency/insufficiency rates reported across recent case-control studies [9,10].

PANSS symptom domains and vitamin D

Yüksel et al. found a similar link between total vitamin D level and psychotic psychopathology [11], which is consistent with our study's strong negative correlation between vitamin D and positive PANSS score. Although a more recent Iranian case-control study confirmed lower vitamin D levels in schizophrenia overall, it also found no significant correlation between vitamin D and PANSS domain scores. Instead, it found a correlation between vitamin D and extrapyramidal side-effect severity [12]. This is in contrast to the report by Bulut et al., which found lower vitamin D associated with greater negative symptom severity [10]. Similar to Haddad et al. [13], we did not find a significant link between vitamin D and the general psychopathology score; however, Prasanty et al. reported a substantial negative correlation between vitamin D and the general psychopathology PANSS score [14]. The necessity for bigger, standardised multi-center research is highlighted by these discrepancies in the literature, which most likely reflect variations in sample size, illness chronicity, antipsychotic exposure, and rating instrument utilised [15,16].

Methodological factors

Similar to the enzyme-linked immunosorbent test used in similar studies classifying schizophrenia patients by illness severity, the ECLIA method for vitamin D quantification in this investigation offers high analytical sensitivity and specificity [17].

Correlates of Socio demographics

Our study found that over 40% of cases had a family history of mental illness, which is consistent with the acknowledged role that parental socioeconomic status and family history play in the risk of schizophrenia as reported in large population-based studies [18].

Recent evidence

The vitamin D-schizophrenia theory is still supported and improved by more current research. Both low and high newborn vitamin D concentrations were linked to an elevated risk of schizophrenia, according to large Danish population-based case-control research [3]. This suggests a U-shaped rather than a strictly linear association. The importance of vitamin D status in acute presentations of psychosis was reinforced by a cross-sectional study from a tertiary center in Iran that assessed vitamin D, parathyroid hormone, and C-reactive protein in acute psychotic episodes [19]. In terms of intervention, a double-blind randomised controlled trial

discovered that supplementing with both probiotics and vitamin D enhanced cognitive performance; nevertheless, the supplementation-induced decrease in PANSS score was not statistically significant [20]. Low neonatal vitamin D is positively correlated with later schizophrenia risk, and adult vitamin D deficiency is correlated with reduced grey matter volume, poorer bone health, and higher prevalence of metabolic syndrome in this population, according to a 2025 systematic review that synthesised evidence across maternal, neonatal, and adult life stages [16]. These findings further support the inclusion of vitamin D monitoring in routine psychiatric care.

Strengths and Limitations

Strengths

A significant confounding factor observed in many previous investigations was eliminated because all individuals were antipsychotic-naive. Standardised ICD-10 criteria were used to make the diagnosis, the validated PANSS instrument was used to measure the severity of symptoms, other potential causes of vitamin D deficiency were ruled out, and vitamin D was estimated using a particular, sensitive biochemical approach (ECLIA).

Limitations

Because this was a single-center study with a small sample size not formally estimated (n = 30 per group), statistical power and generalisability are limited, especially for subgroup analysis. Seasonal differences in dietary consumption, outdoor physical activity, and vitamin D production were not extensively recorded. Because of the case-control approach, randomisation was not appropriate. Although participants with inadequate sunlight exposure and metabolic disorders affecting vitamin D metabolism were excluded, residual confounding from factors such as body mass index, dietary vitamin D intake, physical activity, smoking status, socioeconomic differences, and variations in actual sunlight exposure could not be completely eliminated, as these variables were not quantitatively adjusted for in the analysis. Therefore, the observed associations should be interpreted with appropriate caution.

Conclusion

Antipsychotic-naive schizophrenia patients had significantly lower serum vitamin D levels than healthy controls, and there was an inverse relationship between vitamin D status and both positive and total PANSS symptom scores, but not negative or overall psychopathology scores. These results lend credence to the idea that schizophrenia and, more especially, positive-symptom load are linked to vitamin D insufficiency. The fact that none of the vitamin D-deficient individuals—cases or controls—showed obvious clinical signs of deficiency highlights the value of biochemical screening as opposed to depending solely on clinical suspicion. From the standpoint of public health, detecting and treating vitamin D deficiency is an easy, safe, and affordable intervention that may be helpful in lowering the morbidity linked to schizophrenia; however, this needs to be confirmed by sufficiently powered randomised controlled trials.

Recommendations for future research

To confirm the association between vitamin D insufficiency and the symptom profile of schizophrenia across a range of populations and latitudes, larger, multi-center investigations are required.

Additionally, interventional research is needed to determine whether vitamin D administration affects the course of symptoms and whether there is a causal association between vitamin D and schizophrenia.

Statements and declarations

Ethics approval

This study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrolment.

Conflict of interest

The authors declare no conflict of interest.

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References

1. Cui X, Gooch H, Petty A, McGrath JJ, Eyles D. Vitamin D and schizophrenia: 20 years on. Mol Psychiatry. 2021;26(7):2708–20.
2. Kesby JP, Cui X, Burne THJ, Eyles DW. Altered dopamine ontogeny in the developmentally vitamin D deficient rat and its relevance to schizophrenia. Front Cell Neurosci. 2013;7:111.
3. Albiñana C, Boelt SG, Cohen AS, Zhu Z, Musliner KL, Vilhjálmsson BJ, et al. Developmental exposure to vitamin D deficiency and subsequent risk of schizophrenia. Schizophr Res. 2022;247:26–32.
4. Valipour G, Saneei P, Esmaillzadeh A. Serum vitamin D levels in relation to schizophrenia: a systematic review and meta-analysis of observational studies. J Clin Endocrinol Metab. 2014;99(10):3863–72.
5. Zhu JL, Luo WW, Cheng X, Li Y, Zhang QZ, Peng WX. Vitamin D deficiency and schizophrenia in adults: a systematic review and meta-analysis of observational studies. Psychiatry Res. 2020;288:112959.
6. Ghaderi A, Banafshe HR, Mirhosseini N, Moradi M, Karimi MA, Mehrzad F, et al. Clinical and metabolic response to vitamin D plus probiotic in schizophrenia patients. BMC Psychiatry. 2019;19(1):77.
7. Kay SR, Opler LA, Lindenmayer JP. Reliability and validity of the positive and negative syndrome scale for schizophrenics. Psychiatry Res. 1988;23(1):99–110.
8. Edgar CJ, Blaettler T, Bugarski-Kirola D, Le Scouiller S, Garibaldi GM, Marder SR. Reliability, validity and ability to detect change of the PANSS negative symptom factor score in outpatients with schizophrenia on select antipsychotics and with prominent negative or disorganized thought symptoms. Psychiatry Res. 2014;218(1–2):219–24.
9. Patel D, Minajagi M. Prevalence of vitamin D deficiency in adult patients admitted to a psychiatric hospital. BJPsych Bull. 2018;42(3):123–6.
10. Bulut SD, Bulut S, Atalan DG, Berkol T, Gürçay E, Türker T, et al. The relationship between symptom severity and low vitamin D levels in patients with schizophrenia. PLoS One. 2016;11(10):e0165284.
11. Yüksel RN, Altunsoy N, Tikir B, Cingi Külük M, Unal K, Goka S, et al. Correlation between total vitamin

D levels and psychotic psychopathology in patients with schizophrenia: therapeutic implications for add-on vitamin D augmentation. Ther Adv Psychopharmacol. 2014;4(6):268–75.

12. Shahini N, Mousavi Zade Jazayeri SM, Jahanshahi R, Charkazi A. Relationship of serum homocysteine and vitamin D with positive, negative, and extrapyramidal symptoms in schizophrenia: a case–control study in Iran. BMC Psychiatry. 2022;22(1):681.
13. Haddad C, Zoghbi M, Hallit S, Bou Assi T, Hashim M, Nabout R. Vitamin D levels in Lebanese patients with schizophrenia: a case-control study. Ann Nutr Disord Ther. 2017;4(1):1041.
14. Prasanty N, Amin MM, Effendy E, Simbolon MJ. Low vitamin D serum level increases symptom severity in schizophrenic patients measured by Positive and Negative Symptoms Scale (PANSS) in Batak Tribe Sumatera Utara, Medan-Indonesia. Bali Med J. 2018;7(1):249–54.
15. Chiang M, Natarajan R, Fan X. Vitamin D in schizophrenia: a clinical review. Evid Based Ment Health. 2016;19(1):6–9.
16. Mosiołek J, Mosiołek B, Szulc A. Vitamin D as a modifiable risk factor in schizophrenia: a systematic review. Biomolecules. 2025;15(8):1094.
17. Akinlade KS, Olaniyan OA, Lasebikan VO, Rahamon SK. Vitamin D levels in different severity groups of schizophrenia. Front Psychiatry. 2017;8:105.
18. Agerbo E, Sullivan PF, Vilhjálmsson BJ, Pedersen CB, Mors O, Børglum AD, et al. Polygenic risk score, parental socioeconomic status, family history of psychiatric disorders, and the risk for schizophrenia: a Danish population-based study and meta-analysis. JAMA Psychiatry. 2015;72(7):635–41.
19. Arya S, Kamyab A, Sanatkar SA, Pourmehdiardebili M, Ebrahimi A, Kamyab P, et al. Evaluating the association of vitamin D3, parathyroid hormone, and C-reactive protein serum levels in patients with an acute psychotic episode: a cross-sectional study in a tertiary centre in Iran. BMC Psychiatry. 2023;23(1):724.
20. Mohammadi A, Sadighi G, Nazeri Astaneh A, Tajabadi-Ebrahimi M, Dejam T. Co-administration of probiotic and vitamin D significantly improves cognitive function in schizophrenic patients: a double-blinded randomized controlled trial. Neuropsychopharmacol Rep. 2024;44(2):556–65.