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ORIGINAL RESEARCH ARTICLE

SERUM VITAMIN-D, A NEUROIMMUNOMODULATOR IN SCHIZOPHRENIC PATIENTS: A STUDY AT UNIVERSITY OF ILORIN TEACHING HOSPITAL

Ishola Musbau AbdulAzeez[2], Adeoye Oyetunji Oyewopo[1] Kiblat Opeyemi Erinoso[1] Abiodun Felix Omolade[2], Jameel Omokunmi Yusuff [2], Uthman Akin Hamza[2], Medina Bukola Bello[2], Sikiru Abayomi Biliaminu[2], Adeyinka AbdulRazaq Akande[2], Adekunle Bashiru Okesina[2], Oluwabunmi IderaOluwa Nimata Buhari[3], David Olusegun Awoleye[4]

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[1]Department of Anatomy, University of Ilorin, Ilorin, Kwara State, Nigeria.

[2]Department of Chemical Pathology and Immunology, University of Ilorin, Ilorin, Kwara State, Nigeria.

[3]Department of Behavioral Science, University of Ilorin, Ilorin, Kwara State, Nigeria.

[4]Community Health department, Davest College of health Technology, Ekan, Kwara State, Nigeria

Correspondence author: Kiblat Opeyemi Erinoso, **Email**: kiblatopeyemierinoso@gmail.com

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Abstract

Introduction: Vitamin D interacts with various pathways implicated in schizophrenia pathogenesis and independently influences the nervous and immune systems, supporting its role as a neuroimmunomodulator.

Aim and Objective: This study assessed the relationship between serum vitamin D levels and the severity of schizophrenia and examined its correlation with disease progression in both first-episode and chronic schizophrenia patients.

Methodology: This hospital-based cross-sectional study, included 50 first-episode schizophrenia patients, 50 patients with chronic schizophrenia and 50 healthy controls. Data collection employed the use of structured questionnaires to obtain socio-demographic data and a symptom severity scale (Positive and Negative Syndrome Scale) to assess the severity of the disease. Participants' sera were obtained for serum vitamin D analysis.

Results: The serum Vitamin D level exhibited statistically significant and strong negative correlation with schizophrenia symptom severity among the first-episode schizophrenic group. Meanwhile, no statistically significant correlation was observed among the chronic schizophrenic participants.

Discussion: The study established a positive relationship between vitamin D deficiency and the severity of schizophrenia among the first-episode schizophrenic patients suggesting that vitamin D deficiency may contribute to the pathophysiology of schizophrenia and could be a modifiable risk factor for symptom management. The vitamin D levels in chronic schizophrenics could have been compensated for during the course of treatment due to family support, improved sun exposure, and diet.

Key Words: Vitamin D, Neuroimmunomodulator, Schizophrenia, nervous system.

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Introduction

Schizophrenia is a chronic and complex disorder with multiple mental and Behavioural abnormalities, characterized by disruptions in thought processes, perceptions, emotional responsiveness, and social interactions.[1] Schizophrenia symptoms are categorized as positive, negative, or cognitive impairments, with possible comorbid symptoms.[2] According to the Diagnostic and Statistical Manual of Mental Disorders (DSM V), two or more of the characteristic symptoms must be present for one month (or less if treated) and evidence of continuous impairment in social or occupational function for at least six months is required for the diagnosis.[2] The International Classification of Diseases (ICD-10), also requires that the symptoms must persist for one month, however, functional consequences are not specified.[3]

Schizophrenia affects people of all countries, regardless of race, age, gender and economic status.[4] About 20-30% of the Nigerian population is believed to suffer from mental disorders, a prevalence which corroborates the 2006 World Health Organization (WHO) survey report that about 20 million Nigerians suffer from mental illness with schizophrenia accounting for 52% of outpatient and 43% of inpatient mental illnesses treated in mental health facilities.[5]

The aetiology of schizophrenia is poorly understood, however, it is believed to be underlined by bio-psychosocial influences, including neuroanatomical abnormalities, genetic, environmental factors and neurochemical abnormalities.[1,6] Various theories including dopamine, glutamine and immune-related theory have been employed to elucidate the pathophysiology of the disease.[7] However, few of these theories have been explored in the pharmacological treatment of the disease.[8]

Interaction between nervous, endocrine and immune systems is termed neuroimmunomodulation, and this interaction involves neurosteroids, various cytokines, neurotransmitters, neuropeptides, protein kinases and calcium. Meanwhile, some vitamins and minerals have been identified as nervous system immunomodulators.[9,10]

Vitamin D is a neurosteroid hormone which has been reported to regulate multiple neuro-transmission pathways, including dopamine, serotonin, noradrenalin, and glutamine pathway.[11] The versatility of its action is believed to be due to the widespread distribution of its receptors in the brain and its neuronal functions which centers around the activation of several regulators and genes.[12] Study has shown that dendritic cells, macrophages, T cells, B cells, and other immune cells also express vitamin D receptors.[13]

Therefore, one of the non-classic actions of vitamin D include various immunomodulatory effects subserved through the promotion of innate immunity and regulation of cell mediated and humoral immune cells.[14] These roles begin from the stage of brain development and continue throughout life through neuroimmunomodulation, regulation of growth factors, synaptogenesis, and neuronal outgrowth.[8] Interestingly, impairment of these functions have been linked to the pathogenesis of schizophrenia.[15,16]

Studies have shown that vitamin D also modulates the expression of Brain Derived Neurotropic factor (BDNF),[17,18] the most widely studied neurotrophin which is involved in the promotion of cellular and molecular functions related to neurotransmitter release. Meanwhile, a strong significant correlation between serum BDNF and the severity of schizophrenia has been established.[19,20]

The severity of schizophrenia has been identified as an important factor responsible for the high economic burden of the disease.[21] One of the tools for assessing the severity of schizophrenia is the Positive and Negative Syndrome Scale (PANSS), which probes three main symptom dimensions: positive symptoms, negative symptoms, and general psychopathology.[22] Positive symptoms are symptoms added to the experience of a person and include delusions, hallucinations, conceptual disorganization, excitement, grandiosity, suspiciousness, and hostility. Negative symptoms are features of the experience of a person that is “taken away,” and include emotional withdrawal, blunted affect, poor rapport, social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking.

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There are conflicting reports on the association between serum vitamin D and the severity of schizophrenia.[23,24] Similarly, findings on serum zinc which is known to have neuroimmunomodulatory effects like vitamin D have not been consistent.[25, 26] Most of these findings were reported in Caucasian populations, therefore, this study seeks to determine the relationship between severity of schizophrenia and serum level of vitamin D in our centre, a tertiary health facility in the North-Central Nigeria where much has not been done.

Method

This was a hospital-based descriptive cross-sectional study in which the participants included patient aged 18 to 50 years diagnosed with Schizophrenia as cases. The cases were further subgrouped into first-episode schizophrenics while the control group (age and sex-matched) were apparently healthy adults from the hospital community with neither chronic illness (e.g. renal, liver), nor endocrine disease.

The sample size was determined using Fisher's formula to yield a representative proportion. Fifty participants were recruited for each group: first-episode schizophrenia, chronic schizophrenia, and healthy controls.

All the participants in this research were consenting adults (18 – 50 years of age). The cases comprised patients attending the Behavioural Science Clinic, who were confirmed by a consultant Psychiatrist to satisfy diagnostic criteria for schizophrenia using the International Classification of Diseases (ICD-10) criteria.[3]

The criteria required either one symptom from (a) to (d) or at least two from (e) to (h) below which must have been present most of the time during a period of one month.

a) Thought echo, thought insertion or withdrawal and thought broadcasting.

b) Delusions of control, influence or passivity, clearly described body or limb movements, or specific thoughts, actions or sensations (delusional perceptions)

c) Hallucinatory voices giving a running commentary on the patient's behaviour or discussing the sufferer among themselves, or other type of hallucinatory voices coming from some part of the body.

d) Persistent delusions of other kinds that are impossible and not related to cultural background or ethnicity.

e) Persistent hallucinations in any modality, when accompanied by fleeting or half-formed delusions without clear mood content, or persistent overvalued ideas, or when occurring every day for weeks or months.

f) Breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech or neologism.

g) Catatonic behaviour, such as excitement, posturing, waxing flexibility, negativism and stupor.

h) Negative symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses (must not be due to depression or antipsychotic medications).

i) A significant and constant change in the overall quality of some aspects of personal behaviour, manifesting as loss of interest, aimlessness, idleness, a self-absorbed attitude and social withdrawal.

The first episode of schizophrenia included individuals with first manifestation of the disorder, meeting the defining ICD-10 diagnostic symptoms and time criteria as stated above.

The control group consisted of apparently healthy age and sex-matched adults from the hospital community.

Data Collection Procedure

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Schizophrenic patients attending clinics at the Science Department were recruited via random selection.

Written informed consent was obtained from these eligible participants or their caregiver where the participants were not competent to provide consent due to the prevailing clinical state.

Data was collected by administering questionnaires which were serially coded to provide anonymity.

This was achieved using Proforma (Appendix-C) as a tool which consisted of :

Section A: Socio-demographic characteristic

Section B: Participant's history

Section C: Positive and Negative Syndrome Scale (PANSS), an interview-based test which probes three main symptom dimensions: positive symptoms, negative symptoms, and general psychopathology, employs 30 items consisting of seven positive, seven negative and sixteen general psychopathology scales. Each item was rated with 1 to 7 points ranging from absent to extreme. The range for the positive and negative scales is 7 to 49, and the range for the general psychopathology scale is 16 to 112.

The total score obtained for each respondent was interpreted as mildly ill, moderately ill, markedly ill and severely ill corresponding to total PANSS scores of 58, 75, 95 and 116 respectively according to Clinical Global Impression Severity of illness.

Specimen Collection

Institutional ethical clearance was sought and obtained from the Ethics and Research Committee of the University of Ilorin Teaching Hospital. Two (2) mls of venous whole blood was obtained aseptically via venipuncture from the anterior cubital fossa of the forearm into a plain bottle. Serum was thereafter harvested for serum vitamin D analysis.

Specimen Analysis

Vitamin D was measured using the 25(OH) vitamin D ELISA kit (Calbiotech Inc, California, United States). The kit is a solid phase enzyme-linked immunoassay (ELISA), based on the principle of competitive binding. Anti-Vitamin D antibody-coated wells were incubated with Vitamin D standards, controls, samples, and Vitamin D-Biotin conjugate at room temperature for 90 minutes. During the incubation, a fixed amount of biotin-labelled vitamin D competes with the endogenous Vitamin D in the sample, standard, or quality control serum for a fixed number of binding sites on the anti-Vitamin D antibody. Following a wash step, bound Vitamin D-Biotin was detected with Streptavidin-HRP (horseradish peroxidase). Streptavidin-HRP conjugate immunologically bound to the well progressively decreased as the concentration of Vitamin D in the specimen increased.

Unbound Streptavidin-HRP conjugate was removed and the wells washed. After which, a solution of TMB (Tetramethyl Benzene) reagent was added and incubated at room temperature for 30 minutes, and this resulted in the development of blue colour. The colour development was stopped with the addition of a stop solution, and the absorbance measured spectrophotometrically at 450 nm. A standard curve was obtained by plotting the concentration of the standard versus the absorbance/optical density.

The colour intensity developed was inversely proportional to the of 25(OH) D in the sample. The assay measures both Vitamin D2 and D3. The concentration of vitamin D in the samples was determined by comparing the Optical Density (OD) of the samples to that of the standard curve.

Reference intervals for serum Vitamin D:

Severe deficiency <10ng/ml, Deficiency <20ng/ml, Insufficiency <30ng/ml, Sufficiency 30-44ng/ml, Toxicity >100ng/ml

Quality control: Levels 1 and 2 control samples of vitamin D were assayed with each batch of samples to validate the performance of the equipments, reagents, analytical method

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and personnel. The coefficient of variations of the levels 1 and 2 were 3.4% and 3.3% respectively.

The intra-assay and inter-assay coefficient of variations (CV) of serum vitamin D were 2.8% and 4.2% respectively.

Data Processing

The results of investigations and other data collected on the proforma were entered into a master sheet using numerical codes and subsequently cross-tabulated. The data was then entered into a computer. Data analysis was carried out using the SPSS software version 25. Tables and charts were used to report descriptive statistical analysis. Mean, standard deviation (SD), range and variance values were provided as appropriate. Categorical variables in different groups were compared, using the uncorrected chi-square test values; Yates's corrected chi-square or Fisher's exact test values for tables containing cells with less than five. Continuous variables were analyzed using a student's t-test, while multiple linear regression test was used to assess the relationships between the independent variables (schizophrenia symptom severity) and the dependent variables. Correlation analyses were performed with Pearson correlation co-efficient. The level of significance was established at a p-value of ≤ 0.05.

Results

Socio-demographic characteristics

There were 150 participants in the study, which consisted of 50 first episode schizophrenics, 50 chronic schizophrenics and 50 controls. In terms of age distribution for the purpose of this study, the participants generally were fairly distributed across three (3) different age groups, with 33.3% falling in the 18-30 age group, 32.7% in the 31-40 age group, and 34.0% in the 41-50 age group (Table 1). The control group had an average age of 32.50years (± 8.40), first episode schizophrenia group had average age of 32.94 years (±8.14). The difference in age between these groups was statistically not significant (p-value = 0.760). Additionally, Table 2 shows that the chronic schizophrenia group had an average age of 39.50 years (±7.13) compared to average age of 32.94 years (±8.14) among the first episode schizophrenia group. The difference in age between chronic schizophrenia group and first episode schizophrenia was statistically significant (p-value = 0.001).

Gender distribution showed slightly higher female representations (55.3%) compared to male representation (44.7%) among all participants. Similarly, female gender was higher among chronic schizophrenia (58.0%), and the first episode schizophrenic participants (54.0%) The employed category had a higher representation in the control group (80.0%) compared to first episode schizophrenia (76.0%) and chronic schizophrenia (66.0%). However, there was no statistically significant difference in employment status among the three groups (Table 1).

Schizophrenic participants' clinical history, diagnosis and treatment support

Concerning treatment responsibility, the families of the participants in both groups majorly took charge of their treatments, and no significant difference was observed between them (p-value = 0.400). Regarding the perception of support for their care, most participants in both groups considered the support received to be good. Although the chronic schizophrenia group showed a slightly higher percentage (84.0%) compared with (76.0%) in first episode schizophrenia, the difference between the groups was not statistically significant (p = 0.298). An important disparity was found in the family history of schizophrenia, with a significantly higher proportion of participants in the first episode schizophrenia group reporting a family history of the condition (24.0%) compared to the chronic schizophrenia group (2.0%) (p = 0.001). Both groups exhibited significant differences in the duration of diagnosis (p-value < 0.001) and treatment duration (p-value < 0.001). The majority of first

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episode schizophrenia participants had been diagnosed and receiving treatment for less than 1 year, while the chronic schizophrenia group had a higher percentage of individuals diagnosed and treated for more than 5 years. In terms of hospital admissions and the history of Electroconvulsive Therapy (ECT), no significant differences were observed between the two groups (p-value = 0.338). Notably, there was a significant disparity in the types of treatments received, with a larger proportion of participants in the chronic schizophrenia group receiving orthodox treatments (98.0%) compared to the first episode schizophrenia group (64.0%) (p-value < 0.001).

Biochemical parameter (serum vitamin D) of the participants

The mean biochemical parameters of the participants, with data categorized into first episode schizophrenia, chronic schizophrenia, and control groups. Table 3 shows the average values and standard deviations for serum vitamin-D levels for each group.

Participants in the first episode schizophrenia group had lower average vitamin-D level of 23.42 ng/mL (±14.00), compared with those in the chronic schizophrenia group 26.44 ng/mL (±11.72), and the control group with 37.09 ng/mL (±8.36). The differences in vitamin-D levels were statistically significant (p-value < 0.001), There was also a significant difference in Vitamin-D levels between individuals with first episode schizophrenia and those with chronic schizophrenia (p-value = 0.033), highlighting variations in Vitamin-D status between individuals with first episode schizophrenia and those with chronic schizophrenia (Table 4).

Figures I and II present the relationship between PANS score and Vitamin D in First episode schizophrenia and chronic schizophrenia among the study subjects respectively. Each dot represents an individual subject used for the study. Regression lines and Pearson R- value are shown for correlations in each of the study group. The dotted lines are 95 % confidence band. p-value ≤0.05 were considered significant.

Discussion

The schizophrenic participants in this study consisted of first episode schizophrenics who recently developed the disease and were diagnosed in less than one year. The first episode schizophrenic participants in this study were significantly younger than those with the chronic disease. This strongly corroborates what is known about the onset and the course of schizophrenia that the disease typically begins in late adolescence or early adulthood.[1,28] In Nigeria, the age of onset of the disease is similar to what has been reported in the developed countries, however, delay in the pathway to care has been attributed to religious and sociocultural factors.[29] The mean age of first episode schizophrenia in this study was 32.94 years which was slightly higher than the widely reported mean onset age of the disease.[1,30,31] This largely supports the experience in Nigeria where most patients with mental illnesses would have sought spiritual help for their conditions before visiting the hospital thereby leading to late presentations.[28,32]

Ample evidence suggests that the incidence of schizophrenia is higher among men than women with a ratio of 1.4:1, although other reviews didn't find sex differences [33]. However, this study observed a slightly higher female representation among both groups of schizophrenia. This finding was a significant departure from a higher male incidence or no gender difference widely reported. The diverging finding of gender difference observed is likely to be connected to the report that men tend to conceal their symptoms, believing that seeking help for mental illnesses is a sign of weakness.[34] In addition, it was experienced in this study that all the potential participants who declined consent and/or opted out of the study at the stage of specimen collection were males.

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The interest is rapidly growing in exploring immune modulatory roles of vitamin D which is one of their prominent non-classical actions.[10,] This has been extended to various disease conditions including neuropsychiatric illnesses such as schizophrenia. The quest to explore the association between vitamin D and schizophrenia may not be out of place if we consider the fact that vitamin D in addition to its immune modulation, also modulates various neuronal pathways in the pathogenesis of schizophrenia.[10] Although, the exact mechanisms underlying the relationship between vitamin D and schizophrenia is not yet fully understood. However, it has been suggested that vitamin D deficiency may contribute to neuroinflammation, oxidative stress, and dysregulation of neurotransmitters, all of which are implicated in the pathophysiology of schizophrenia.[35] This study like other studies [23,24] demonstrated a notable decrease in vitamin D levels among individuals in both the first-episode schizophrenia group and the chronic schizophrenia group when compared to healthy control group. It further revealed significant variations in Vitamin-D status between individuals with first-episode schizophrenia and those with chronic schizophrenia. Notably, a much lower vitamin D status in the first episode disease observed in this study strongly suggests that its deficiency begins in the early stage of the disease and may be implicated in the pathophysiology of the disease. This finding aligns with some studies that reported that vitamin D deficiency may act as a risk factor for the development of schizophrenia.[16,35,36,37] It has been reported that vitamin D sufficient cells in vitro produced less inflammatory cytokines; TNF-α and IL-6 while vitamin D deficient cells released significantly higher titer of these cytokines implicated in the pathogenesis of schizophrenia.[38,39,40] Therefore, given the well-known anti-inflammatory actions of vitamin D, finding in this study seems to further corroborate the neuroprotective role of vitamin D.

Vitamin D deficiency in schizophrenia has been consistently reported across the world regardless of the climatic location of the studies.[15,24,41] However, the argument on the association between serum vitamin D and the severity of schizophrenia remains unsettled.[23,24] In this study, a significant negative correlation between serum vitamin D levels and schizophrenia symptom severity was observed among the first-episode schizophrenic participants. Meanwhile, a negative but not significant correlation was found between serum vitamin D and the symptom severity among the chronic schizophrenic participants. Therefore, this study established a relationship between vitamin D deficiency and severe symptoms in the first-episode schizophrenia but not with symptoms severity among the chronic schizophrenia, suggesting that low vitamin D level in schizophrenia begins in the early stage of the disease and may be associated with aetiopathogenesis of schizophrenia. This finding is similar to what was observed in a Eurasian study.[65] Meanwhile, a similar study reported significant correlation between low levels of vitamin D and high severity of psychiatric symptoms in all stages of the disease.[23] Another study that limited the participants to chronic stable schizophrenia patients demonstrated a negative correlation but couldn't establish a significant relationship between vitamin D and the severity of symptoms.[42] This is similar to what was found among the chronic schizophrenic participants in this present study which can be attributed to the presence of less profound symptom severity among these participants. However, a study from south-west Nigeria revealed no association between vitamin D deficiency and the severity of schizophrenia symptoms.[24]

Antipsychotic medications have been reported to contribute to vitamin D deficiency due to possible hepatic enzyme-inducing effect similar to that of cytochrome P450 enzyme inducers.[43,44] However, the finding of lower mean serum vitamin D levels among the first-episode schizophrenia participants compared to the vitamin D levels among the

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chronic schizophrenia group who have been on antipsychotic drugs for a longer period in this study contradicts the claim. It was also revealed in this study that there were no significant differences between mean serum vitamin D levels among schizophrenic participants taking different antipsychotic medication classes. Therefore, vitamin D deficiency in schizophrenia cannot be attributed to the side effects of antipsychotic medications. Similarly, the degree of sunlight exposure is another factor that contributes to the vitamin D status in an individual, however, the participants in this study consisted of outpatients attending behavioural science clinics and healthy individuals who were equally not on admission, and thus had unhindered access to adequate sunlight exposure.

The course of the schizophrenia includes the acute stage, during which psychotic symptoms such as hallucinations and/or delusions develop presumably due to unregulated neurotransmitters, followed by the chronic stage which is characterized by lesser typical psychotic symptoms.[45] The severity of symptoms observed using the PANSS among the participants in this study were generally low compared to what was reported in another study.[41] This may not be surprising since the participants in the study were recruited from stable outpatients, not patients on admission or those in emergencies with acute symptom. However, it was observed in this study that the first-episode schizophrenia group had more severe symptoms than the chronic-episode schizophrenia group. The more pronounced symptoms observed among the first episode group cut across the three dimensions of symptoms including positive, negative and general psychopathologic symptoms. This may not be unexpected because the chronic schizophrenic participants were mostly patients on follow up clinic visits who might have had some of their symptoms relatively controlled. This finding underscores the ability of the current study to demonstrate the relationship between vitamin D and the severity of schizophrenia only among the first episode schizophrenia participants.

The novel discoveries of non-classical roles of vitamin D keep increasing. In addition to its role in the modulation of various neuronal pathways implicated in the pathogenesis of schizophrenia and other neuro-protective functions, vitamin D has been found to independently modulate BDNF.[12,21] Meanwhile, evidence gathered from some reviews has suggested that BDNF is relevant in the pathophysiology of schizophrenia and associated with psychotic symptomatology .[46]

Notably, the findings in this study revealed a strong positive correlation between serum levels of vitamin D among patients with first-episode schizophrenia, suggesting that vitamin D deficiency may be implicated among these participants. Therefore, vitamin D supplementation may be a promising option for ameliorating schizophrenia symptoms without conferring cardiovascular risks to the patients. Similar relationships have been reported in some other clinical conditions such as type 2 DM in which subsequent vitamin D supplementation significantly improved serum vitamin D and optimized serum BDNF levels.[47] Meanwhile, the common pathological feature to these conditions is increased inflammatory cytokines which has been linked to decrease in BDNF.[48,49] However, a study observed that vitamin D concentration positively affected neuregulin 1 (NRG1) among other neurotrophin in people with schizophrenia but not BDNF.[50]

Conclusion

It was concluded that vitamin D deficiency is prevalent among people with schizophrenia. The higher degree of vitamin D deficiency among first episode schizophrenia and chronic schizophrenia participants respectively, suggests that vitamin D is related to the early stage of the disease. The status of vitamin D as a neuromodulator was underscored by the direct link between vitamin D levels and

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BDNF; hence, the ability of BDNF to respond to neuroinflammation in schizophrenia depends on vitamin D sufficiency. The established relationship between vitamin D deficiency and the severity of schizophrenia among the first-episode schizophrenic patients suggesting that vitamin D deficiency may contribute to the pathophysiology of schizophrenia and could be a modifiable risk factor for symptom management. Therefore, vitamin D optimization in schizophrenia patients with severe symptoms may offer a supplementary route for quickly ameliorating schizophrenia symptoms with lesser side effects of antipsychotic medications.

Table 1: Socio demographics of the participants

Variable	Categories	Control	First episode schizophrenia	Chronic schizophrenia	Total	Pearson Chi-Square	df	P-value
Age	18-30	22(44.0%)	22(44.0%)	6(12.0%)	50(33.3%)	28.100[a]	4	0.010
	31-40	17(34.0%)	17(34.0%)	15(30.0%)	49(32.7%)			
	41-50	11(22.0%)	11(22.0%)	29(58.0%)	51(34.0%)			
Gender	Male	23(46.0%)	23(46.0%)	21(42.0%)	67(44.7%)	1.498[a]	2	0.473
	Female	27(54.0%)	27(54.0%)	29(58.0%)	83(55.3%)			
Tribe	Yoruba	48(96.0%)	48(96.0%)	47(94.0%)	143(95.3%)	4.014[a]	4	0.404
	Hausa	0(0.0%)	2(4.0%)	1(2.0%)	3(2.0%)			
	Igbo	2(4.0%)	0(0.0%)	2(4.0%)	4(2.7%)			
Participant's Occupational status	Employed	40(80.0%)	38(76.0%)	33(66.0%)	111(74.0%)	4.456[a]	2	0.108
	Unemployed	10(20.0%)	12(24.0%)	17(34.0%)	39(26.0%)			

Table 2: Participants' mean age comparison between groups

Group	Variable	Mean ±SD	p-value
First episode	Age	32.94 ±8.14	0.760
Control		32.50± 8.40	
Chronic schizophrenia	Age	39.50±7.13	0.001
Control		32.50±8.40	
First episode	Age	32.94 ±8.14	0.001
Chronic schizophrenia		39.50±7.13	

Table 3 Mean biochemical parameters of first episode schizophrenia, chronic schizophrenia and control participants

Variable	First episode schizophrenia	Chronic schizophrenia	Control	P-value
Vitamin-D	23.42±14.00	26.44±11.72	37.09±8.36	0.001

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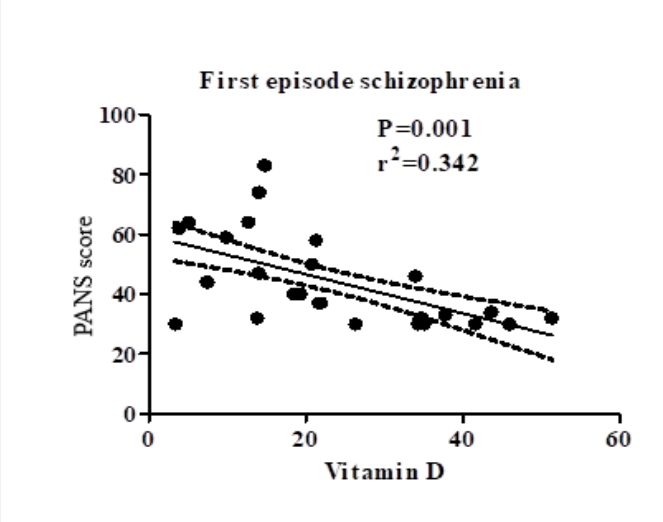
Table 4: Mean biochemical parameters of first episode schizophrenia, chronic schizophrenia and control participants

Variable	Groups		p-value
	First Episode schizophrenia	Control	
Vitamin D	23.42±14.00	37.09±8.36	0.001
	Chronic schizophrenia	Control	
Vitamin D	26.44±11.72	37.09±8.36	0.001
	First Episode	Chronic schizophrenia	
Vitamin D	23.42±14.00	26.44±11.72	0.033

Figure 1:
Scatter graph of the correlation between serum vitamin D levels and Symptoms severity among the first episode schizophrenic participants.



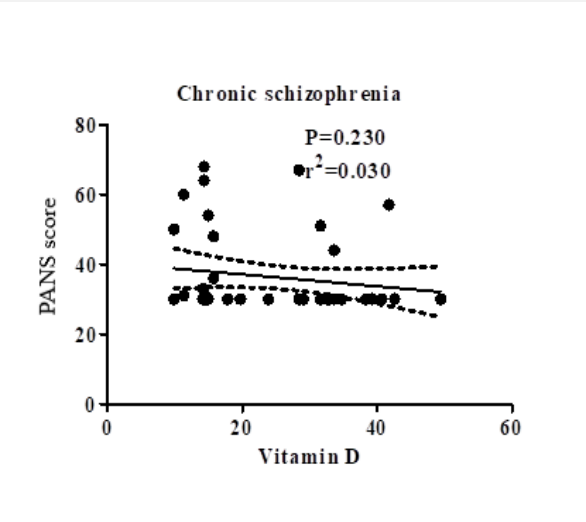


Figure 2: Scatter graph of the correlation between serum vitamin D Levels and symptoms severity among the chronic schizophrenic participants.

REFERENCES

1. MacCabe JH. Clinical Handbook of Schizophrenia. Edited by Kim T. Mueser & Dilip V. Jeste, Guildfor Press.2008: 117-118.
2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-V-TR). 5th ed. Arlington, VA: American Psychiatric Press; 2013.
3. ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva. World Health Organization. 1992.
4. Esan OB, Ojagbemi A, Gureje OYE. Epidemiology of schizophrenia – An update with a focus on developing countries. Int Rev Psychiatry.2012;24(5):387-392.
5. WHO-AIMS Report on Mental Health System in Nigeria, WHO and Ministry of Health, Ibadan, Nigeria, 2006.
6. Padmanabhan J, Keshavan MS. Pathophysiology of Schizophrenia Pathophysiology of Schizophrenia. 2014:35-51.
7. Murray AJ, Rogers JC, Zia M, Haq U, Liddle PF, Upthegrove R, et al. Oxidative Stress and the Pathophysiology and Symptom Profile of Schizophrenia Spectrum Disorders. Front. Psychiatry. 2021; 12:1–16.

E- ISSN: 2720 – 765X

ORIGINAL RESEARCH ARTICLE

8. Adebisi YA, Umah JO, Olaoye OC, Alaran AJ, Sina-odunsi AB. Assessment of Health Budgetary Allocation and Expenditure Toward Achieving Universal Health Coverage in Nigeria. Int. J Health Life Sci. 2020; 6(2)
9. K. Dhama, M. Kesavan, K. Karthik, Amarpal, R. Tiwari, Lakshimi T. et al. Neuroimmunomodulation Countering Various Diseases, Disorders,Infections, Stress and Aging. International Journal of pharmacology. 2015;11: 76-79
10. Eyles D, Fe F. Vitamin D, a neuro-immunomodulator : Implications for neurodegenerative and autoimmune diseases. J. Psyneuen. 2009: 265-277.
11. Okasha TA, Sabry WM, Hashim MA, Abdeen MS, Abdelhamid AM. Vitamin D serum level in major depressive disorder and schizophrenia. Middle East Current Psychiatry. 2020.
12. Abreu DAF De, Eyles D, Fã F. Vitamin D, a neuro-immunomodulator : Implications for neurodegenerative and autoimmune diseases. Psychoneuroendocrinology [Internet]. 2018;
13. Lang PO, Aspinall R. Can We Translate Vitamin D Immunomodulating Effect on Innate and Adaptive Immunity to Vaccine Response? 2015; 25:2044–2060.
14. Zhao R, Zhang W, Ma C, Zhao Y, Xiong R, Wang H. Immunomodulatory Function of Vitamin D and Its Role in Autoimmune Thyroid Disease. Front. Immunol. 2021; 12:1–6.
15. Cui X, Mcgrath JJ, Burne THJ, Eyles DW. Vitamin D and schizophrenia : 20 years on. Mol Psychiatry. 2021;3.
16. McGrath J.J, Eyles D.W, Pedersen C.B, Anderson C., Pauline K., Burne T.H. et al. Neonatal Vitamin D Status and Risk of Schizophrenia. Arch Gen Psychiatry. 2010;67(9):889-894.
17. Eyles DW. Vitamin D : Brain and Behavior. JBMR Plus. 2021;5(1):1–12.
18. Pochwat BB, Nowak G, Szewczyk B. Relationship between Zinc (Zn2+) and Glutamate Receptors in the Processes Underlying Neurodegeneration. Neural Plast. 2015; 2015:591563.
19. Hendriati D, Effendy E, Amin MM, Camellia V, Husada MS. Brain-Derived Neurotropic Factor Serum Level and Severity Symptom of Bataknese Male Patients with Schizophrenia in North Sumatera, Indonesia. Maced J Med Sci. 2019;7(12):1957–1961.
20. Singh, S.; Roy, D.; Marzouk, T.; Zhang, J.P. Peripheral Blood Levels of Brain-Derived Neurotrophic Factor in Patients with First Episode Psychosis: A Systematic Review and Meta-Analysis. Brain Sci. 2022, 12, 414.
21. Brink V Den, Salize HJ, Mccabe R, Bullenkamp J. Cost of treatment of schizophrenia in six European countries Cost of Treatment of Schizophrenia in Six European Countries. Schizophr Res.2009;111(1-3):70-77.
22. Kay S.R, Opjer L.A. Lindernmayer J.P. The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia. Schizophr Bull.1987; 13(2):261-276.
23. Coentre R, Canelas I. Symptomatic Correlates of Vitamin D Deficiency in First-Episode Psychosis. Psychiatry J. 2019; 2019:7839287.
24. Akinlade KS. Vitamin D levels in Different severity groups of schizophrenia. Front. Psychiatry 2017; 8:1–6.
25. Uddin SMN, Hossain MK. Effect of antioxidant, malondialdehyde, macro-mineral and trace element serum concentrations in Bangladeshi patients with schizophrenia : A case-control study. Health Sci Rep. 2021 ;(12):1–7.
26. Sharma SK, Sood S, Sharma A, Gupta ID. Estimation of serum zinc and copper levels patients with schizophrenia : a preliminary study. Sri Lanka Journal of Psychiatry. 2014;5(1):14–17.
27. Charan J, Biswas T. Review Article How to Calculate Sample Size for Different Study Designs in Medical Research ? 2013;35(2).
28. Mental Health in Nigeria; Survey Conducted by Africa Polling Institute and Epi AFRIC Report. January. 2020.
29. Adeosun II, Adegbohun AA, Adewumi TA, Jeje OO. The Pathways to the First Contact with Mental Health Services among Patients with Schizophrenia in Lagos , Nigeria. Schizophrenia Research and Treatment. 2013(11):769161.
30. Oloniniyi IO, Akinsulore A, Aloba OO, Mapayi BM, Oginni OA, Makanjuola R. Economic cost of schizophrenia in a Nigerian teaching hospital. J Neurosci Rural Pract 2019; 10:39-47.
31. Hdfner H, Maurer K, Loffler W, Heiden W Der, Hambrecht M, Lutter FS. Modeling the Early Course of Schizophrenia. Schizophr Bull. 2003;29(2)325–340.
32. Abiodun OA. Pathways to Mental Health Care in Nigeria. Psychiatr Serv.1995;46(8):823–826.
33. Aleman A, Kahn RS, Selten JP. Sex differences in the risk of schizophrenia: evidence from meta-analysis. Arch Gen Psychiatry. 2003;60(6):565-571.

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34. Porsche D, Jr SJG. The Crisis in Male Mental Health : A Call to Action. Am J Mens Health. 2020;14(4):1557988320936504.
35. Koc E, Meier U. Vitamin-D Deficiency As a Potential Environmental Risk Factor in Multiple Sclerosis, Schizophrenia, and Autism. Front Psychiatry. 2017;8:47.
36. Sotodeh-asl N, Tamadon M, Malek F, Zahmatkesh M. Vitamin D deficiency and psychological disorders. J Parathyr. 2014;2(1):21–25.
37. Chiang M, Natarajan R, Fan X. Vitamin D in schizophrenia : a clinical review. 2016;19(1):17–20.
38. Upthegrove R, Khandakar GM. Cytokines, Oxidative Stress and Cellular Markers of Inflammation in Schizophrenia. Curr Top Behav Neurosci. 2020;44:49-66.
39. Ym M, Mostafa M, Elwasify M, Hm Y, Nm O. Vitamins & Minerals. 2017;6(1):1–15.
40. Zhang Y, Leung DYM, Richers BN, Liu Y, Remigio LK. Vitamin D Inhibits Monocyte/macrophage Pro-inflammatory Cytokine Production by Targeting Mitogen-Activated Protein Kinase Phosphatase 1 J Immunol. 2012;188(5): 2127–2135.
41. Yüksel RN, Altunsoy N, Tikir B, Külük MC, Unal K. Correlation between total vitamin D levels and psychotic psychopathology in patients with schizophrenia : therapeutic implications for add-on vitamin D augmentation. 2014;268–275.
42. Sheikhmoonesi F, Zarghami M, Mamashli S, Yazdani J. Effectiveness of Vitamin D Supplement Therapy in Chronic Stable Schizophrenic Male Patients : A Randomized Controlled Trial. 2016;15:941–950.
43. Urichuk L, Prior TI, Dursun S, Baker G. Metabolism of Atypical Antipsychotics : Involvement of Cytochrome P450 Enzymes and Relevance for Drug-Drug Interactions. Curr Drug Metab. 2008;9(5)410–418.
44. Uwe Gröber & Klaus Kisters. Influence of drugs on vitamin D and calcium metabolism. Dermato-Endocrinology, 2012;4:2, 158-166.
45. Kim M. Understanding the Etiology and Treatment Approaches of Schizophrenia : Theoretical Perspectives and Their Critique. Open Journal of Psychiatry 2016;253–261.
46. Nurjono M, Lee J, Chong S. A Review of Brain-derived Neurotrophic Factor as a Candidate Biomarker in Schizophrenia. Clin Psychopharmacol Neurosci. 2012;10(2):61–70.
47. Alqudah M, Khanfar M, Alfaqih MA, Shboul OAL, Ghazi DOAA, Datt ALU, et al. Correlation between vitamin D and serum brain derived neurotropic factor levels in type 2 diabetes mellitus patients. Biomed Rep. 2022;16(6):54.
48. Upthegrove R, Khandakar GM. Cytokines, Oxidative Stress and Cellular Markers of Inflammation in Schizophrenia. Curr Top Behav Neurosci. 2020;44:49-66.
49. Fond G, Lançon C, Auquier P, Boyer L. C-Reactive Protein as a Peripheral Biomarker in Schizophrenia . An Updated Systematic Review. Front Psychiatry. 2018;9:392. Peitl V, Silić A, Orlović I, Vidrih B, Crnković D, Karlović D. Vitamin D and Neurotrophin Levels and Their Impact on the Symptoms of Schizophrenia.Neuropsychobiology. 2020;79(3): 179-185.

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