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Serum vitamin D level in patients with schizophrenia: A community-based study

Sir,

Vitamin D deficiency during the developmental period is associated with increased risk for schizophrenia, probably due to altered neurogenesis and changes in dopamine transporter expression[1]. At the same time, there is no consensus on the association between vitamin D deficiency after the developmental period and schizophrenia, with some studies reporting lower serum vitamin D levels in patients compared to healthy individuals[2-5] and others finding no association[6-8]. Though vitamin D deficiency is prevalent in the general population in India[9,10], there are scant data on serum vitamin D level in patients with schizophrenia. The present study was therefore aimed to compare the serum vitamin D level in patients with schizophrenia with that in healthy individuals and also to study the effect of antipsychotic medication, smoking, body mass index (BMI) and sunlight exposure on the serum vitamin D level.

This study was conducted at the department of Psychiatry at the Institute of Mental Health and Neurosciences, Government Medical College, Kozhikode, Kerala, India. Data collection was done from March to May, 2019. The study group consisted of consecutively recruited patients with schizophrenia who attended the community clinics of the District Mental Health Programme (DMHP) in Kozhikode district during the study period. Patients of both sex with a clinical diagnosis of schizophrenia as per Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 diagnostic criteria[11], in the 18-75 yr age group, who were in remission of symptoms for a minimum period of six months and living in the community, were included in the study. Patients in acute episodes were not included. The control group consisted of individuals from the same locality with no physical or psychological disorders and matched for age and sex. Those with known metabolic disorders, liver diseases, kidney diseases, intellectual disability or substance dependence other than nicotine were excluded from the study. Those who were on vitamin D or calcium supplementation or drugs that affect vitamin D metabolism such as anti-epileptics, anti-tuberculosis, antiretroviral drugs and corticosteroids were also excluded.

Clinical history details, socio-demographic data and the nature of sunlight exposure were recorded in a proforma prepared for the study. The details of sunlight exposure were obtained by asking the individuals in the study and the control groups about the number of hours they spent outdoors during the daytime. Detailed physical examination was done. Height, weight and BMI were recorded. The sample size was estimated to be 68 in each group based on an effect size of four and an estimated standard deviation (SD) of 7.2 assuming 95 per cent confidence interval and 90 per cent power. The effect size was calculated by the difference in mean vitamin D level in patients with schizophrenia and in general Indian population, as reported in previous studies[12,13]. Informed written consent was obtained from all participants, and the study was approved by the Institutional Ethics Committee, Government Medical College, Kozhikode (GMCKKD/RP2017/IEC/199 dated 15 November 2017).

Five millilitres of peripheral venous blood was collected from both the cases and the controls and centrifuged at 2000 g for 15 min. The serum samples were stored at −80°C. Vitamin D was measured using chemiluminescent immunoassay (Beckman Coulter Immunoassay Systems #B24838, USA) with a Beckman Access 2 system (Beckman Coulter, USA)[14]. Serum 25(OH) vitamin D3 level <20 ng/ml was considered deficient while 21-29 ng/ml was considered insufficient[15].

Chi-squared test was used to compare categorical variables. Independent t test, Mann–Whitney U test and

analysis of variance were used to compare variables between groups as appropriate. All statistical tests were two-sided.

The study group included 74 patients with schizophrenia living in the community and the control group consisted of 72 healthy individuals from the same locality. The mean age of the patient group was 42.7±13 yr while that of the control group was 39.3±10.3 yr. There were 48 (64.9%) males and 26 (35.1%) females in the study group and 42 (58.3%) males and 30 (41.7%) females in the control group. There was no significant difference between the two groups in terms of age, gender, sunlight exposure, dietary habits and BMI.

The mean vitamin D level in the patient group was 16.25±5.5 ng/ml with vitamin deficiency and insufficiency in 56 (75.7%) and 17 (23%) patients, respectively and normal vitamin D level in one patient. The mean vitamin D level in the control group was 16.53±9.9 ng/ml, with vitamin deficiency and insufficiency in 55 (76.4%) and 14 (19.4%) persons, respectively, while four had normal vitamin D levels. There was no significant difference in the mean serum vitamin D levels between the study and the control groups.

Treatment with first- and second-generation antipsychotics, clozapine and trihexyphenidyl had no significant influence on serum vitamin D levels in patients with schizophrenia. The antipsychotics prescribed included haloperidol, trifluoperazine, risperidone and olanzapine in addition to clozapine.

Male patients had a higher mean serum vitamin D level compared to female patients, but the difference was not significant. The effect of age, gender, BMI, smoking, diet and sunlight exposure in patients with schizophrenia is shown in the Table.

Antipsychotic-naive schizophrenia patients had a mean serum vitamin D level of 14.5 ng/ml with 83 per cent of them having vitamin D deficiency in a study by Shivakumar *et al*[12] on the association between serum vitamin D level and hippocampal grey matter volume in patients with schizophrenia. In our sample, more than three-fourth of patients with schizophrenia as well as healthy individuals had vitamin D deficiency. The reported mean serum 25(OH) vitamin D3 levels in the general population in India range from 14 to 15 ng/ml with more than 80 per cent of the population having vitamin D deficiency[9,13,16,17]. The mean serum vitamin D levels in patients and healthy individuals in our study were consistent with the earlier studies, and the low levels of vitamin D in patients with schizophrenia could be a reflection of the vitamin D status of the general population.

Our findings were in concordance with the findings of two randomized controlled trials: one from Iran[8] and the other from Israel[18] which found no change in symptom profile after vitamin D supplementation in patients with schizophrenia. A two-sample bidirectional Mendelian randomization also showed no causal relation between the vitamin D levels and schizophrenia[19]. On the other hand, many authors had reported increased vitamin D deficiency in patients with psychosis and schizophrenia[2-5]. A systematic review and meta-analysis concluded that patients with schizophrenia were at increased risk of vitamin D deficiency, even though there was no evidence that vitamin D deficiency adversely affects adult brain health[20].

No difference in the serum vitamin D levels was found in patients receiving different types of antipsychotics even though it is postulated that antipsychotic medications may lower the serum level of 25(OH) vitamin D3, through their action on 7-dehydrocholesterol reductase, and contribute to osteoporosis in patients with schizophrenia[21]. Previous studies had reported comparable findings[22]. In our sample, patients with higher BMI had lower serum levels of vitamin D even though there was no linear relationship. Association between low serum vitamin D level and obesity has been reported previously[23,24].

One limitation of the present study was that we could not study the relationship between symptom severity and serum vitamin D level or the role of vitamin D in acute episodes of schizophrenia since the sample consisted of patients in remission living in the community. Furthermore, the sample size was small considering the high prevalence of vitamin D deficiency in the general population.

In conclusion, no significant difference was found in the serum vitamin D levels in patients with schizophrenia and the control group and hence further studies are required to ascertain whether vitamin D deficiency is a risk factor or cause for worsening of the symptoms in schizophrenia.

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Table. Serum vitamin D level in relation to age, gender, body mass index, smoking, diet and sunlight exposure in patients with schizophrenia

Independent variable	Vitamin D level (ng/ml); mean±SD	Test statistic	*P*
Age (yr)			
18-35	15.6±4.4	F (2, 71)=0.3	0.75
35-55	16.7±6.2		
>55	16.6±5.9		
Gender			
Male	17.1±5.7	t (72)=1.8	0.07
Female	14.7±4.8		
BMI (kg/m^2)			
<18.5	15.8±6.4	F (2, 71)=206.9	0.03
18.5-24.9	17.9±5.7		
>25	14.4±4.4		
Nicotine			
Dependent	19.2±7.2	U=227.5, Z=−1.5	0.14
Absent	15.8±5.1		
Diet			
Non-vegetarian	16.6±5.5	U=114, Z=−1.8	0.75
Vegetarian	17.6±1.3		
Sunlight exposure (h)			
<1	15.7±5.2	F (2, 71)=1.5	0.23
1-3	18.8±7.1		
>3	16.5±4.5		

SD, standard deviation; BMI, body mass index

***Conflicts of Interest*:** None.

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