Vitamin D Levels in Schizophrenia

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ABSTRACT

Introduction: Studies have demonstrated that adult schizophrenia patients have lower vitamin D levels compared to the general population. Although there is a high prevalence of vitamin D deficiency in India, there is a scarcity in studies evaluating the role of vitamin D in schizophrenia. In this study we compared the levels of vitamin D of 50 schizophrenia patients with that of 50 age matched controls.

Material and methods: This study was conducted on patients attending the outpatient and inpatient wings of department of psychiatry of a tertiary care teaching hospital in Kochi, Kerala. This case control study was conducted from October 2012 to October 2014. The vitamin D levels of 50 (cases) patients diagnosed to have schizophrenia as per the International Classification of Disease, 10th revision; Diagnostic Criteria for Research (ICD-10-DCR) were compared to 50 age matched controls. The vitamin D levels were estimated from the venous blood samples by using ABBOT ARCHITECT i.

Results: In the present study among the patients diagnosed to have schizophrenia, 48% (24) had Vitamin D deficiency and in the control group 26% (13) had it. The difference was statistically significant (p-value **<0.001)**.

Conclusions: In this study the serum vitamin D levels are significantly lower in schizophrenia patients than in the controls. Further studies with larger random samples of schizophrenia patients are required to establish the result of this study.

Keywords: Vitamin D, Vitamin D deficiency, Schizophrenia.

INTRODUCTION

Schizophrenia is a chronic and severe psychiatric disorder. The lifetime prevalence of schizophrenia appears to be approximately 0.3%-0.7%, although there is reported variation across countries.[1] Schizophrenia can be very disabling. According to the National Mental Health Survey of India (2015-16), among the persons with mental illnesses, extreme disability was the highest among persons with schizophrenia and other psychotic disorders.[2]

There is extensive evidence for the hypothesis that schizophrenia is a neurodevelopmental disorder, resulting from genetic and environmental factors that lead to abnormalities in neural systems.[3] The effects of vitamin D insufficiency on central nervous system has been demonstrated by the fact that vitamin D deprived rats showed brain morphological changes like enlarged ventricles and thinner cortex, which are seen in brains of schizophrenia patients.[4] Low maternal vitamin D has been proposed to adversely affect the developing fetal brain, leaving the affected offspring at an increased risk of adult-onset schizophrenia.[5] Vitamin D deficiency acts to alter development, leading to neurodevelopmental disorders in many ways.[6]

Autoimmune mechanisms have also been implicated in the pathogenesis of schizophrenia. Multiple studies have elaborated on the various immunological aspects detected among patients with schizophrenia: namely, antibodies to neurotransmitter receptors and cytokines, the appearance of antinuclear antibodies in patients with schizophrenia, along with increased concentration of interleukin-3-producing CD5+ B cells.[7-11] Vitamin D has been shown to decrease the production of pro-inflammatory cytokines and increase the production of anti- inflammatory cytokines.[12] Similarly, vitamin D plays an important role in reducing oxidative stress and related damage.[13] Another evidence to the close relation of vitamin D to schizophrenia includes the association of schizophrenia with winter births, its greater frequency in dark-skinned migrants to cold climates, and the variation in incidence and prevalence of schizophrenia with latitude.[14,5]

Studies have demonstrated that adult schizophrenia patients have lower vitamin D levels compared to the general population.[15-22] Even though the current literature point towards the possible therapeutic benefits of vitamin D, very few studies have been reported from India. Also vitamin D deficiency prevails in epidemic proportions all over the Indian subcontinent, with a prevalence of 70%–100% in the general population.[23] In the present study the vitamin D levels of 50 patients diagnosed to have schizophrenia were compared with that of 50 age matched controls.

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MATERIAL AND METHODS

This study was conducted among patients attending the outpatient and inpatient wings of department of psychiatry of a tertiary care teaching hospital in Kochi, Kerala. This case control study was conducted from October 2012 to October 2014 (2 years) and was done as per the approval and guidelines of the Institutional Ethical Committee. Fifty cases and 50 controls were included in this study. The cases were patients aged between 15-80 years diagnosed to have schizophrenia as per the International Classification of Disease, 10th revision, Diagnostic Criteria for Research (ICD-10-DCR) by a psychiatrist. Patients with renal disease, liver disease, thyroid dysfunction and those on vitamin D therapy were excluded from the study. Fifty age matched healthy subjects were taken as control. An informed consent for the study was obtained from the patient and their relatives.

Sample size

Based on the figures available in the literature on Vitamin D and schizophrenia with 95% confidence level and 80% power, the calculated sample size was 32 cases and 32 controls.[15] In this study 50 cases and 50 controls were included. So the confidence level would be more than 95% and power more than 80%.

Procedure methodology

The parameters used for this study was levels of 25(OH) D and it was estimated by using ABBOT ARCHITECT i

Sample collection

The venous blood samples were obtained under aseptic precautions. Blood samples of patients meeting the above mentioned criteria which were ordered in the biochemistry laboratory for the determination of vitamin D in the above time period was taken for this study. The blood samples were stored at -20°C, till we collected enough samples for the Vitamin D assay.

Test method

Chemiluminnescence immunoassay

Principle

The architect 25-OH vitamin D assay is a delayed one step immunoassay including a sample pretreatment for the quantitative determination of vitamin D in human serum and plasma using CMIA TECHONLOGY (Chemiluminnescence immunoassay). Sample and pretreatment reagent are combined with assay diluent and paramagnetic antivitamin D Coated microparticles. After incubation abiotinylated vitamin D antiBiotinacridinium labeled conjugate complex is added to the reaction mixture and binds to un occupied binding sites of the antivitamin D coated microparticles. After washing, pretrigger and trigger solutions are added to the reaction mixture. The reasulting chemiluminescent reaction is measured as relative light unites. An indirect relationship exists between the amount of vitamin D in the sample and the relative light unites detected by the ARCHITECT I system optics.

Reference Range[24,25]

Vitamin D deficiency = <20ng/ml

Normal = >30 ng/ml

STATISTICAL ANALYSIS

Statistical analysis was done using IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, USA). For all the categorical variables data are as percentage or in frequency. Chi-square analysis was used for finding the association between two categorical variables. Odds Ratio was estimated for risk. Independent two sample t-test was applied to compare the mean age of the two groups. The p-value <0.05 were considered as statistically significant.

RESULT

Fifty patients diagnosed to have schizophrenia and 50 age matched controls were included in this case control study. The mean age of the controls was 39.24±15.001years and that of cases was 39.76±10.095years, also among the 50 controls 58% were males and in the group of cases 52% were males, the difference was not statistically significant (Table1).

In this study 48% (24) of the patients diagnosed to have schizophrenia and 26% (13) of the controls had Vitamin D deficiency. The difference was statistically significant. Also the odds ratio shows that the cases had 2.62 times

Variable	Category	Group				p-value
		Case		Control		
		No of cases	%	No of controls	%	
Sex	Male (55)	26	52%	29	58%	0.546
	Female(45)	24	48%	21	42%	
Mean age ± SD (in yrs)		Cases (50)		Controls(50)		0.839
		39.76 ±10.095		39.24±15.001		

Table-1: Comparison between cases and controls

Group	No	Vitamin D deficiency <20		OR	p-value
		No	%		
Control	50	13	26%	2.62	<0.001
Case (Schizophrenia)	50	24	48%		

Table-2: Association between schizophrenia and vitamin D deficiency

chance to develop Vitamin D deficiency than the controls. (Table2).

DISCUSSION

In this case control study we tried to investigate the association between low vitamin D levels and schizophrenia. The result of this study shows that among the 50 controls 58% were males and in the schizophrenia group 52% were males. Also the mean age of the controls was 39.24±15.001years and that of cases was 39.76±10.095years (Table1). So the two groups were demographically comparable.

In this study among the patients diagnosed to have schizophrenia, 48% (24) had Vitamin D deficiency and in the control group 26% (13) had it. The difference was statistically significant. Also the odds ratio shows that the cases had 2.62 times chance to develop vitamin D deficiency than the controls. (Table2). Among the institutionalized schizophrenia patients there was 73% incidence of hypovitaminosis D according to a study by Agarwal SK (2013).[19] Some previous studies similar to the present study have showed that the serum vitamin D levels were lower in patients with schizophrenia as compared to healthy controls.[15-18] The sample size in the above mentioned studies are comparable with our study, except for the study by Hamidreza Jamilian et al.(2013) which included 100 schizophrenics and 100 healthy controls.[15-18] In a study by L.J. Norelli et al. (2010) serum vitamin D levels of 20 acute care (≤60 days) and 20 long-stay (≥6 months) adult public psychiatric hospital inpatients with schizophrenia-spectrum disorders, were compared to 20 normal controls, and the result showed that there was no significant differences in levels between the three groups.[26] In that study the proportion of female patients in all the three groups were lesser (acute care group-15%, long stay group-25% and control group-45%), and females sex is a known risk factor for vitamin D deficiency.[26]

A meta-analysis on vitamin D and psychosis reported a moderately significant reduction in the serum levels of vitamin D in schizophrenia patients compared to healthy controls and a trend for lower levels compared to other psychosis (Belvederi Murri et al.2013).[20] Findings from another meta-analysis on odds ratio found that vitamin D-deficient persons were 2.16 times (95% CI 1.32, 3.56) more likely to have schizophrenia than those with vitamin D sufficiency.[21] According to a recent systematic review and meta-analysis on first-episode psychosis deficits in vitamin D and folate previously observed in long-term schizophrenia appear to exist from illness onset, and are associated with worse symptomology.[22] The studies mentioned indicate the association between vitamin D deficiency and schizophrenia and support the results of our study, but studies with larger random samples of schizophrenia patients are required to substantiate the result of this study.

This case control study has some limitations as its sample size is small and no random sampling methods were used in it. Vitamin D deficiency in a schizophrenia patient may be secondary to their poor lifestyle and habits. It includes people attending a tertiary care teaching hospital, so it does not represent the general population.

CONCLUSION

Vitamin D deficiency is common but mostly undetected in India. In this study the serum vitamin D levels are significantly lower in schizophrenia patients than in the controls. Further case control studies with larger random samples of schizophrenia patients are required to establish the result of this study.

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REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013 May 22.
2. Gururaj G, Varghese M, Benegal V, Rao GN, Pathak K, Singh LK, Mehta RY, Ram D, Shibukumar TM, Kokane A, Singh RL. National mental health survey of India, 2015-16: Prevalence, patterns and outcomes. Bengaluru: NIMHANS. 2016.
3. William V. Bobo, The neurobiology of schizophrenia, in Allan Tasman(Ed.), Psychiatry, 4 (John Wiley & Sons Ltd.) 2015; 50:303-14.
4. Eyles D, Brown J, Mackay-Sim A, McGrath J, Feron F: Vitamin D3 and brain development. Neuroscience 2003;118:641–653.
5. McGrath J: Hypothesis- is low prenatal vitamin D a risk-modifying factor for schizophrenia? Schizophr. 1999;40:173–177
6. Berridge MJ. Vitamin D deficiency: infertility and neurodevelopmental diseases (attention deficit hyperactivity disorder, autism, and schizophrenia). American Journal of Physiology-Cell Physiology. 2017;314:C135-51.
7. Amital H, Shoenfeld Y: Autoimmunity and schizophrenia- an epiphenomenon or an etiology? Isr J Med Sci 1993;29:593-7.
8. Goldsmith CA, Rogers DP: The case for autoimmunity in the etiology of schizophrenia. Pharmacotherapy 2008; 28: 730-41.
9. Sirota P, Bogdanov I, Katzav A, Hershko R, Chapman J: Reduced anticardiolipinantibodies in first episode and chronic schizophrenia. Psychiatry Res 2006; 144:211-16.
10. Spivak B, Radwan M, Bartur P, Mester R, Weizman A: Antinuclear autoantibodies in chronic schizophrenia. Acta Psychiatr Scand 1995; 92: 266-9.
11. Strous RD, Shoenfeld Y: Schizophrenia, autoimmunity and immune system dysregulation- a comprehensive model updated and revisited. J Autoimmun 2006; 27: 71-80.
12. McCann JC, Ames BN: Is there convincing biological or behavioral evidence linking vitamin D deficiency to brain dysfunction? FASEB J 2008;22:982–1001.
13. Halicka HD, Zhao H, Li J, Traganos F, Studzinski GP, Darzynkiewicz Z: 539 Attenuation of constitutive DNA damage signaling by 1,25-dihydroxyvitamin D3. Aging (Albany NY) 2012; 4:270–278.
14. McGrath JJ, Eyles DW, Pedersen CB, Anderson C, Ko

P, Burne TH, Norgaard-Pedersen B, Hougaard DM, Mortensen PB. Neonatal vitamin D status and risk of schizophrenia: a population-based case-control study. Archives of general psychiatry. 2010;67:889-94

15. Dganit Itzhaky, Daniela Amital, Katya Gorden, Alisa Bogomolni P, Yoav Arnson,Howard Amital, Low Serum Vitamin D Concentrations in Patients with Schizophrenia IMAJ 2012;14:88-92.
16. Jamilian H, Bagherzadeh K, Nazeri Z, Hassanijirdehi M. Vitamin D, parathyroid hormone, serum calcium and phosphorus in patients with schizophrenia and major depression. International journal of psychiatry in clinical practice. 2013;17:30-4.
17. Schneider B, Weber B, Frensch A, Stein J, Fritze J. Vitamin D in schizophrenia, major depression and alcoholism. Journal of neural transmission. 2000;107:839-42.
18. Cha B, Shin YM, Kim YS, Kim BJ, Lee CS, Sohn JW, Park CS. P. 2. e. 021 Vitamin D deficiency in schizophrenia, bipolar disorder and major depressive disorder compared to healthy controls. European Neuropsychopharmacology. 2011(21):S429-30.
19. Agarwal SK. 1367–High incidence of vitamin d deficiency in patients with schizophrenia. European Psychiatry. 2013 Jan 1;28:1.
20. Belvederi Murri M, Respino M, Masotti M, Innamorati M, Mondelli V, Pariante C, Amore M: Vitamin D and psychosis- mini meta-analysis. Schizophr. 2013;150: 235–239.
21. Valipour G, Saneei P, Esmaillzadeh A. Serum vitamin D levels in relation to schizophrenia: a systematic review and meta-analysis of observational studies. The Journal of Clinical Endocrinology & Metabolism. 2014;99:3863-72.
22. Firth J, Carney R, Stubbs B, Teasdale SB, Vancampfort D, Ward PB, Berk M, Sarris J. Nutritional deficiencies and clinical correlates in first-episode psychosis: a systematic review and meta-analysis. Schizophrenia bulletin. 2017;44:1275-92.
23. Gupta A. Vitamin D deficiency in India: prevalence, causalities and interventions. Nutrients. 2014;6:729-75.
24. Carl A Burtis, Edward R Ashwood, David E. Brnus,TIETZ Fundamentals of clinical chemistry,sixth edition,38 (723-726)
25. Harinarayan CV, Joshi SR. Vitamin D status in India–its implications and remedial measures. JAPI. 2009;57:40-8.
26. Norelli LJ, Coates AD, Kovasznay BM. A comparison of 25-hydroxyvitamin D serum levels in acute and long-stay psychiatric inpatients: a preliminary investigation. e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism. 2010;5:e187-9.

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