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Vitamin D Status in Small Vessel and Large Vessel Ischemic Stroke Patients: A Case–control Study

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Abstract

Background: Vitamin D insufficiency is a globally widespread issue. Recent studies have reported a high prevalence of Vitamin D deficiency in Middle-East countries. Studies have shown negative effects of Vitamin D deficiency on endothelium and related diseases such as ischemic brain stroke. Here, we assessed Vitamin D status in patients with different types of ischemic brain stroke and control group. **Materials and Methods:** Seventy-five patients (49.3% small vessel, 50.7% large vessel) and 75 controls, matched for age (68.01 ± 10.94 vs. 67.64 ± 10.24) and sex (42 male and 33 female) were recruited. 25(OH) D levels were measured by Chemiluminescence immunoassay. 25(OH) D status was considered as severely, moderately, or mildly deficient and normal with 25(OH) D levels of less than 5, 5-10, 10-16, and >16 ng/ml, respectively. **Results:** Mean ± standard error concentration of 25(OH) D in cases and controls were 17.7 ± 1.5 and 26.9 ± 1.6 ($P = 0.0001$), respectively. Mild, moderate, and severe Vitamin D deficiency were observed in 10.8%, 32.4%, 8.1% vs. 34.3%, 31.5%, 9.5% of small vessel and large vessel group, respectively. 21.7% of the controls were Vitamin D deficient. Vitamin D deficiency was significantly associated with higher risk for ischemic stroke, ($P = 0.000$, OR = 7.17, 95% confidence interval: 3.36–15.29). 25(OH) D levels were significantly higher in control group comparing to small vessel (26.9 ± 1.6 vs. 20.59 ± 2.6 $P < 0.05$) and large vessel (26.9 ± 1.6 vs. 13.4 ± 1.3 $P < 0.001$) stroke patients. Small vessel group had significantly higher levels of Vitamin D than large vessel ($P < 0.05$). **Conclusion:** Vitamin D deficiency significantly increases the risk of ischemic stroke, favoring the types with the pathogenesis of large vessel strokes.

Keywords: *25(OH) Vit D, 25-hydroxyvitamin D, stroke, small vessel, large vessel*

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Introduction

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Vitamin D is a micronutrient that can be either consumed or internally biosynthesized through direct exposure to sunlight.[1] Vitamin D deficiency has affected people worldwide with the prevalence of 30–50 among different populations with a higher rate in females.[2] Despite having abundant sun exposure, people living in the countries of the Middle East suffer from deficient or insufficient levels of Vitamin D.[3]

A growing body of evidence suggests that Vitamin D plays an important role in the cardiovascular well-being of individuals. Anti-inflammatory features and stimulating effects of Vitamin D on cellular repair are noticed in previous and ongoing studies.[4],[5] Other than aging, several risk factors such as chronic hypertension, atherosclerosis, and diabetes mellitus have been shown to be related to diminished vascular quality. It has been noted that Vitamin D is related to these risk factors aside from its independent effects on the vascular system.[6] Vitamin D also interacts with the calcium and bone homeostasis; a proper diet with enough Vitamin D protects against early-onset osteoporosis and bone diseases.[7]

Ischemic strokes are caused due to occlusion of blood flow to parts of the brain. Persistent acute hypoxic environment that follows damages the brain tissue permanently; these results in different levels of disability based on the extent of the damage to the central nervous system. Disturbance of blood flow may occur in major arterial branches or in distal arteries that affect smaller areas, dividing ischemic strokes into two subtypes; large vessel and small vessel strokes, respectively. Large vessel strokes, due to their bigger perfusion area, tend to be more severe; however, cardiovascular risk factors play the key part in both types of ischemic strokes.[8],[9] For the beneficial effects Vitamin D has on the cardiovascular system, its deficiency is proposed as a contributor to such ischemic events; therefore supplementation with Vitamin D counteracts this process.[10],[11],[12],[13]

Stroke patients often suffer from post stroke complications such as hip fractures and depression; these are also manageable with a properly regulated diet with enough Vitamin D to support patients' needs.[7]

There is conflict in the literature regarding the necessity of fortification with Vitamin D in at-risk groups.[14] We aimed in our study to investigate the presence and severity of Vitamin D deficiency among the two subtypes of ischemic stroke patients in comparison with otherwise matched controls and assess if there is any relation between the plasma levels of Vitamin D and incidence of small vessel or large vessel ischemic stroke.

Materials and Methods

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Study design

We conducted a case–control study from March 2011 to March 2012. Cases, (small vessel and large vessel strokes) were chosen from the patients admitted to the Neurology Department, in Alzahra Hospital, in Isfahan, Iran (32_390 North, 51_430 East, and 1475 m above sea). All cases were first-ever stroke patients and were grouped as a small vessel or large vessel cases based on the imaging studies and a neurologist's opinion. Age- and sex-matched controls were also recruited. Use of Vitamin D supplements or other drugs with known effect on serum Vitamin D levels, history of liver and kidney disorders and presence of a rheumatologic or gastrointestinal disease were defined as exclusion criteria. Informed consents were taken from all participants or their medical proxy. The study was approved by the Committee of Ethics in Research at the Isfahan University of Medical Sciences.

Data collection

Demographic data included age and gender of the participants. Five milliliters of venous blood were obtained from all participants. Serum content was extracted using a routine centrifuge method and kept frozen at −70°C. All Serum samples were measured for 25-hydroxy vitamin D, using Chemiluminescence immune assay kit (“25 OH Vitamin D total assay-Diasorin Liason”) by LIAISON ® analyzer. After the primary data collection, Vitamin D levels further than three standard deviations from the sample's mean were double checked to minimize laboratory misreads.

Data analysis

Statistical Package of Social Science software (SPSS version 18.0, Chicago, IL, USA) was used to analyze the data. Mann–Whitney U-test was used for quantitative variables between two groups and Kruskal–Wallis test was used to compare mean of 25(OH) D between multiple groups since our data was not normally distributed. The relation between Vitamin D status (mild, moderate, or severe deficiency) and different categorized variables, (age, sex, case–control) were established using Chi-square test and calculation of odds ratio (OR) (confidence interval [CI] = 95%). Sample size achieved 80% of the statistical power. A two-tailed $P < 0.05$ was considered statistically significant.

Results

During 12 months, 75 stroke patients (37 with small vessel stroke and 38 with large vessel stroke) were enrolled in the study; also 75 controls, matched for age (68.01 ± 10.94 vs. 67.64 ± 10.24) and sex (42 male and 33 female in each group) were recruited. There was no significant difference between the cases and controls regarding the age ($P = 0.83$). The age was not significantly different between the case groups as well ($P = 0.71$). Out of the enrolled patients, 49.3% were diagnosed with small vessel stroke and 50.7% had large vessel stroke; the demographic data are presented in [Table 1].

Table 1: Demographic data

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Based on previous national studies, we defined Vitamin D deficiency as severe, moderate, or mild with 25(OH) D levels of [15] Vitamin D deficiency was observed in (76.3%) of the large vessel stroke group, followed by the small vessel strokes (51.4%); in the controls only 21.7% of the participants were Vitamin D deficient. [Table 2] presents the severity of Vitamin D deficiency among our sample.

Table 2: Vitamin D status

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The mean ± standard error (SE) concentration of Vitamin D in cases and controls were 17.7 ± 1.5 and 26.9 ± 1.6, respectively with the Vitamin D levels significantly higher in the control group ($P = 0.000$). The mean ± SE of Vitamin D was also significantly higher in the controls than Vitamin D in each of the small vessel or the large vessel stroke groups; when compared, the small vessel stroke patients had significantly higher levels of Vitamin D than large vessel stroke patients. The data is presented in [Table 3].

Table 3: Vitamin D status among the cases and controls

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Vitamin D deficiency was associated with significantly higher risk for development of ischemic stroke in patients comparing to the controls, ($P = 0.000$, OR = 7.17, 95% CI: 3.36–15.29). The OR for the development of small vessel stroke due to Vitamin D deficiency was 4.37 ($P = 0.001$, 95% CI: 1.8–10.4); while among large vessel stroke patients, the OR was calculated to be 13.4 ($P = 0.000$, 95% CI: 5.03–36.02). This difference remained significant after the data was adjusted between cases and controls for other cardiovascular risk factors.

Discussion

Our observations indicated that there is a significant relation between Vitamin D deficiency and the two types of ischemic stroke.

Our cases were first-ever stroke patients; the mean age of our cases was relatively high. As a dietary pattern, lifestyle, and metabolic states vary between different age groups a similar comparison in a younger sample could lead into different results; however, based on a national study, Vitamin D deficiency is prevalent across all age groups in the Iranian population with various severities.[15] Comparison of the results to a matched control group minimized the effects of the age-related shift in metabolic patterns and Vitamin D status.

Vitamin D status is affected by various factors among the different population, such as racial ethnicity, cultural backgrounds and lifestyle, geographical situations, and economic status.[16] These differences between populations call for a regional standardization the data. We defined the normal and deficient cut-off point values of Vitamin D based on a prior study in the Iranian population. While in several studies, Vitamin D level lower than 30 ng/ml is considered insufficient,[14] we considered participants with Vitamin D levels higher than 16 ng/ml as sufficient.

Another point of difference between the studies regarding Vitamin D is the measurement tools. While we used a chemiluminescence assay in our study, other methods such as radioimmunoassay and enzyme-linked immune sorbent assay are also used in other studies. Differences in the quality and precision of the measurement tools, sensitivity, and specificity of each method, and reliability of laboratories potentially alter the final results. The discrepancies between the findings may be based on the use of several different measurement methods.[17] Laboratory-related mismeasurements were minimized by double checking the outlying data.

Since the prevalence of the subtypes of ischemic stroke was irrelevant to our study, we recruited an equal number of each subtype in our study and formed their groups separately. Regardless of its severity, the highest percentage of Vitamin D deficiency was observed in the large vessel stroke group. Controls had the least percentage of Vitamin D deficiency. Interestingly, most of severe Vitamin D deficiency cases were also observed in the large vessel group as well. Mean of Vitamin D in the large vessel group was below the accepted cut-off point for sufficient Vitamin D but in the other two

groups the mean of Vitamin D was over 16 ng/ml and significantly higher than that of large vessel strokes. This indicates that lower levels of Vitamin D are associated with involvement of larger vessels in terms of ischemic events.

In contrast to our findings, Gupta *et al*., declared in their study that Vitamin D deficiency was not associated with ischemic strokes; however, their frame of reference was different from ours. They chose 30 ng/ml as the cut-off point for sufficient Vitamin D; as the majority of the sample is considered Vitamin D deficient in a population with high prevalence of Vitamin D deficiency, regional cut-off points are best indicated to distinguish better different severities of the Vitamin D insufficiency.[14]

In another study, Wang *et al*. said that Vitamin D level is a reliable predictor for severity of symptoms at admission and prognosis of functional outcome.[10] In the same way, Chaudhuri *et al*. declared that the effect of Vitamin D deficiency on ischemic stroke is independent and associated with atherosclerosis of large vessels and embolic strokes.[18] We observed that in large vessel strokes, Vitamin D had lower mean levels.

Although the small vessel patients had sufficient mean of Vitamin D levels, it was significantly lower than the controls. This is interesting because sufficient levels of Vitamin D are defined as cut-off points, yet even when Vitamin D levels are adequate, higher levels show beneficial features. It suggests that Vitamin D deficiency has a step-wise effect on the cardiovascular system. This is what Brondum-Jacobsen *et al*., reported in their meta-analysis; they have claimed that an increase is observed in the risk for development of symptomatic ischemic stroke as Vitamin D level decreases.[12]

We showed in our results that Vitamin D deficiency had increased the risk of ischemic stroke by nearly 7-fold in our patients. In comparison to the controls, there was a 13-fold increase in the risk of large vessel stroke; comparing to the 4.37-fold increase in the small vessel group. This confirms our previous statement that Vitamin D deficiency is associated with ischemic strokes in the brain with a higher risk for large vessel events. Sun *et al*., suggested that when combined with several other studies, their results revealed a 1.52-fold increase in the risk of stroke because of Vitamin D deficiency. [13]

The enrolled samples in our study were limited. Considering the variability of Vitamin D levels in our population, larger sample presumably achieves a more accurate estimation of the observed effects; however, we tried to match our controls from the same population and backgrounds to avoid detection of accidental differences. It is suggestible that randomized clinical trials with blinding of the groups be conducted to investigate further the effects of Vitamin D on ischemic strokes. We did not take the seasonal difference in the Vitamin D levels into account, but patients and controls were enrolled in the study at the same time to minimize the seasonal effect.

Conclusion

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Our results showed that there is a relation between Vitamin D and development of ischemic strokes. Large vessel strokes were associated with more severe Vitamin D deficiency in comparison with small vessel strokes. We also showed that even with insufficient levels, protective effects of Vitamin D increases at higher concentrations.

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Conflicts of interest

There are no conflicts of interest.

References

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1. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-81. Back to cited text no. 1 [PUBMED]
2. Hovsepian S, Amini M, Aminorroaya A, Amini P, Iraj B. Prevalence of Vitamin D deficiency among adult population of Isfahan City, Iran. J Health Popul Nutr 2011;29:149-55. Back to cited text no. 2 [PUBMED]
3. Mytton J, Frater AP, Oakley G, Murphy E, Barber MJ, Jahfar S. Vitamin D deficiency in multicultural primary care: A case series of 299 patients. Br J Gen Pract 2007;57:577-9. Back to cited text no. 3 [PUBMED]
4. Adorini L, Penna G. Control of autoimmune diseases by the Vitamin D endocrine system. Nat Clin Pract Rheumatol 2008;4:404-12. Back to cited text no. 4 [PUBMED]
5. Talmor Y, Golan E, Benchetrit S, Bernheim J, Klein O, Green J, *et al.* Calcitriol blunts the deleterious impact of advanced glycation end products on endothelial cells. Am J Physiol Renal Physiol 2008;294:F1059-64. Back to cited text no. 5 [PUBMED]
6. Drechsler C, Pilz S, Obermayer-Pietsch B, Verduijn M, Tomaschitz A, Krane V, *et al.* Vitamin D deficiency is associated with sudden cardiac death, combined cardiovascular events, and mortality in haemodialysis patients. Eur Heart J 2010;31:2253-61. Back to cited text no. 6 [PUBMED]
7. Sato Y. Immobilization and hip fracture. Clin Calcium 2006;16:1991-98. Back to cited text no. 7

[PUBMED]
8. Caplan LR. Lacunar infarction and small vessel disease: Pathology and pathophysiology. J Stroke 2015;17:2-6. Back to cited text no. 8
[PUBMED]
9. Kim BJ, Kim JS. Ischemic stroke subtype classification: An asian viewpoint. J Stroke 2014;16:8-17. Back to cited text no. 9
[PUBMED]
10. Wang Y, Ji H, Tong Y, Zhang ZB. Prognostic value of serum 25-hydroxyvitamin D in patients with stroke. Neurochem Res 2014;39:1332-7. Back to cited text no. 10
[PUBMED]
11. Chaudhuri JR, Mridula KR, Alladi S, Anamika A, Umamahesh M, Balaraju B, *et al.* Serum 25-hydroxyvitamin d deficiency in ischemic stroke and subtypes in Indian patients. J Stroke 2014;16:44-50. Back to cited text no. 11
[PUBMED]
12. Brøndum-Jacobsen P, Nordestgaard BG, Schnohr P, Benn M. 25-hydroxyvitamin D and symptomatic ischemic stroke: An original study and meta-analysis. Ann Neurol 2013;73:38-47. Back to cited text no. 12
13. Sun Q, Pan A, Hu FB, Manson JE, Rexrode KM. 25-Hydroxyvitamin D levels and the risk of stroke: A prospective study and meta-analysis. Stroke 2012;43:1470-7. Back to cited text no. 13
[PUBMED]
14. Gupta A, Prabhakar S, Modi M, Bhadada SK, Lal V, Khurana D. Vitamin D status and risk of ischemic stroke in North Indian patients. Indian J Endocrinol Metab 2014;18:721-5. Back to cited text no. 14
[PUBMED]
15. Moradzadeh K, Larijani B, Keshtkar A, Hossein-Nezhad A, Rajabian R, Nabipour I, *et al*. Normative values of Vitamin D among Iranian population: A population based study. Int J Osteoporos Metab Disord 2008;1:8-15. Back to cited text no. 15
16. Rosen CJ. Clinical practice. Vitamin D insufficiency. N Engl J Med 2011;364:248-54. Back to cited text no. 16
[PUBMED]
17. Wallace AM, Gibson S, de la Hunty A, Lamberg-Allardt C, Ashwell M. Measurement of 25-hydroxyvitamin D in the clinical laboratory: Current procedures, performance characteristics and limitations. Steroids 2010;75:477-88. Back to cited text no. 17
[PUBMED]
18. Chowdhury R, Stevens S, Ward H, Chowdhury S, Sajjad A, Franco OH. Circulating Vitamin D, calcium and risk of cerebrovascular disease: A systematic review and meta-analysis. Eur J Epidemiol 2012;27:581-91. Back to cited text no. 18
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