Section: Medicine

Original Research Article

STUDY ON VITAMIN D DEFICIENCY AND ITS CO-RELATION WITH SEVERITY OF STROKE AND CHANGES IN LIPID PARAMETERS

Moirangthem Ratankumar Singh[1], Abujam Indrajit Singh[2], Chingakham Arunkumar[3], Taskeen Fathima[4]

[1]*Associate Professor, Department of Medicine, Jawahar Lal Institute of Medical Sciences, Imphal, India.*
[2]*Assistant Professor, Department of Medicine, Jawahar Lal Institute of Medical Sciences, Imphal, India.*
[3]*Associate Professor, Department of Medicine, Jawahar Lal Institute of Medical Sciences, Imphal, India.*
[4]*SR Nephrology, SGPGI, Lucknow, India.*

Received *: 10/11/2025*
Received in revised form *: 23/12/2025*
Accepted *: 12/01/2026*

Corresponding Author:
Dr. Abujam Indrajit Singh,
Assistant Professor, Department of Medicine, Jawahar Lal Institute of Medical Sciences, Imphal, India.
Email: drgunalan86@gmail.com

DOI: 10.70034/ijmedph.2026.1.57

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (1); 320-325

ABSTRACT

Background: Vitamin D deficiency is highly prevalent in India and has been associated with increased risk of cardiovascular diseases including stroke. This study aimed to evaluate the relationship between serum vitamin D levels in cerebral stroke patients and assess its association with stroke severity, lipid profiles, and inflammatory markers.

Materials and Methods: A cross-sectional study was conducted on 118 stroke patients (both ischemic and hemorrhagic) at Jawaharlal Nehru Institute of Medical Sciences, Imphal, over a two-year period. Serum 25-hydroxyvitamin D levels were measured using chemiluminescence immunoassay. Lipid profiles (HDL, LDL, total cholesterol, triglycerides) and high-sensitivity C-reactive protein (hs-CRP) were evaluated. Stroke severity was assessed using the NIHSS scoring system.

Results: Only 24% of stroke patients had normal vitamin D levels (>30 ng/ml), while 39% had vitamin D insufficiency (21-29 ng/ml), 34% had deficiency (10-20 ng/ml), and 3% had severe deficiency (<10 ng/ml). The most common type of stroke was ischemic stroke involving the MCA territory (56.4%). Vitamin D deficiency was associated with higher BMI (mean 25 kg/m²), with severe deficiency observed at mean BMI of 26 kg/m². Patients with vitamin D deficiency showed trends toward higher mean LDL levels, lower HDL levels, higher triglyceride levels, and elevated hs-CRP levels (21-22 mg/L), though these correlations were not statistically significant ($p>0.05$).

Discussion: Our findings suggest that vitamin D status may influence stroke risk through both direct effects on endovascular function and inflammatory regulation, and indirect effects through modulation of established risk factors including hypertension, dyslipidemia, and insulin sensitivity. The high prevalence of vitamin D deficiency among stroke patients warrants consideration of vitamin D assessment in stroke prevention strategies. Study limitations include the small sample size, which likely contributed to the lack of statistical significance in observed correlations. Larger prospective studies are needed to further elucidate the complex relationship between vitamin D status, lipid profiles, inflammation, and stroke outcomes.

Keywords: Vitamin D deficiency, stroke, lipid profile, hs-CRP, NIHSS

INTRODUCTION

Vitamin D deficiency is widespread around the world and is a common issue in India.[1] The occurrence of Vitamin D deficiency varies between 70%-100% across different geographic areas, ethnicities, and socio-economic levels.[1] In addition to the welldocumented skeletal consequences of Vitamin D deficiency, numerous extra-skeletal correlations with Vitamin D deficiency have been identified. The link between a deficiency in 25-hydroxy Vitamin D (Vitamin D) and conditions such as atherosclerosis,[2]

myocardial infarction, and stroke has been documented.

Vitamin D is a fat-soluble steroid hormone that plays a key role in maintaining calcium and phosphate balance as well as supporting musculoskeletal health. Vitamin D is produced from 7-dehydrocholesterol in the epidermal layer of the skin when exposed to ultraviolet light. Next, experience two hydroxylation processes: initially, inactive vitamin D undergoes hydroxylation in the liver, resulting in the formation of 25-hydroxyvitamin D, followed by the classic conversion in the kidney by 1-α-hydroxylase (CYP27B) to produce the biologically acti ve form 1,25-dihydroxyvitamin D3. The second hydroxylation process may also take place in macrophages, T cells, and neurons.[1,2]

Vitamin D plays a crucial role in regulating immune function and managing inflammation. Reduced vitamin D levels were linked to calcium metabolism disorders, type 2 diabetes mellitus, autoimmune conditions, cardiovascular issues, stroke, and multiple sclerosis.[4,5] Stroke ranks among the leading causes of mortality and disability globally, having a considerable clinical and socioeconomic effect. Its etiology is diverse, comprising unchangeable risk factors like genetics, age, and sex, alongside changeable risk factors such as hypertension, diabetes mellitus, dyslipidemia, inactivity, and smoking.[6] Acute stroke patients have been observed to have lower serum vitamin D levels than normal controls.[6,7]

Vitamin D is vital for the regulation of brain development, operation, and cerebrovascular health.[8] It has been associated with vasoprotective properties such as slowing atherosclerosis, enhancing endothelial function, inhibiting the renin–angiotensin– aldosterone system, which in turn lowers the risk of hypertension. Consequently, its lack may play a role in the onset of various illnesses, such as diabetes, hypertension, heart failure, ischemic heart conditions, and stroke.[9] In addition, lack of vitamin D affects vascular remodeling by regulating smooth muscle cell growth, inflammation, and blood clotting. These vascular alterations may ultimately lead to a stroke.[10] Nonetheless, various studies have indicated that a lack of vitamin D is a potential risk factor for stroke; the relationship between stroke severity and outcomes in relation to vitamin D levels has not been thoroughly investigated. The purpose of this research is to assess serum vitamin D levels in patients with cerebral strokes and to examine the relationship between vitamin D deficiency and the severity and outcomes of strokes.

The objective of our study is to assess serum vitamin D levels in patients with cerebral stroke (either ischemic or hemorrhagic) and to analyze the relationship between vitamin D deficiency and lipid profile concerning the incidence of stroke. To examine the impact of vitamin D on serum lipids in the Indian adult population, correlate serum vitamin D levels with stroke severity, and assess the vasoprotective role of vitamin D in lowering hs-CRP levels.

MATERIALS AND METHODS

This study was done at Jawaharlal nehru institute of medical sciences (JNIMS) Imphal, Manipur in all patients of stroke attending OPD, ATC, and stroke patients admitted in wards at department of Medicine of JNIMS for a period of two years as a cross sectional study in 118 stroke patients (both ischemic and hemorrhagic stroke) at JNIMS along with department of biochemistry, JNIMS Imphal. Patients with vitamin D and calcium supplementation, history of renal failure, with bone disease i.e. renal osteodystrophy were excluded from the study.

We considered Vitamin D levels more than 30 ng/ml as normal range, 21-29 ng/ml as insufficient, less than 20 ng/ml as deficiency and if less than 10 ng/ml considered as severe deficiency.

Ethical approval was taken from the institute ethics committee, JNIMS before the start of the study. The stroke patients were informed about the nature of the study. Patients who were willing to participate in this study were included after getting their written informed consent. Patients who fulfil the inclusion and exclusion criteria were enrolled in this study.

Detailed information was collected from the study population. Details of patient's age, duration of illness, history of initial symptoms, initial hospital visit, and clinical and radiological diagnosis of cerebral stroke were noted. A data collection form was prepared to note the name, age, sex, smoking, drug intake and other relevant history. The CT brain reports were noted.

Blood samples were taken at the time of admission to measure the serum levels of 25 hydroxy vitamin D level and lipid profile (HDL cholesterol, LDL cholesterol, total cholesterol and triglycerides) in stroke patients. Highly sensitive CRP levels were evaluated in stroke patients. Serum levels of 25 hydroxy vitamin D levels were measured by chemi luminescence immune assay technique. Lipid profile will be measured using enzymatic methods. Tests were done in single laboratory by the same person in order to avoid interpersonal error. CT Brain was also done in all patients

All statistical tests were performed using IBM SPSS Version 26 software. The data obtained were subjected to statistical analysis using descriptive statistical methods such as frequency, percentage, etc and analytical statistics such as Chi square test and all other compatible statistical techniques.

RESULTS

In our study of 118 patients, the most common age group is 61-70 years followed by 51-60 years. Majority cases were male (n=78) and rest were female (n=39) with a ratio of 2:1. In our study 77 of stroke patients were smoker and 4 were alcoholic, rest

had no habits associated. Around 51 patients were either obese or overweight.12 were underweight.

Table 1: Baseline characteristics of study population

1- Age distribution	<50 yr	6%
	51-60 yr	27%
	61-70 yr	37%
	71-80 yr	21%
	>80 yr	9%
2- Sex distribution	Male	67%
	Female	33%
3- BMI	<20	6%
	21-25	27%
	25 -30	37%
	> 30	21%
4- Personal habits	Smoker	40%
	Alcoholic	5%
	No habits	55%

Table 2: NCCT Brain

NCCT BRAIN	NO OF PATIENTS	PERCENTAGE
Aca Territory Infarct	5	4.30%
Acute Ich At Left Basal Ganglia	9	7.70%
Acute Infarct In L Hemipontine Region	1	0.90%
Basal Ganglia Infarct	3	2.60%
Cardio Embolic Stroke	2	1.70%
Cerebellar Infarct	3	2.60%
Lacunar Infarct	10	8.50%
Mca Territory Infarct	66	56.40%
Pica Territory Infarct	1	0.90%
Pontine Infarct	4	3.40%
Right Thalamic Ich	1	0.90%
Thalamic Infarct	12	10.30%

In our studies CT findings, ischemic (thrombotic) stroke was most common type of stroke amongst patients of age group >45 years and the most commonly involved area was MCA territory followed by thalamic infarct. Lacunar infarct was seen in 10 patients, the severity of stroke was assessed using NIHSS scoring system at the time of presentation, with 36% of patients having NIHSS score >22, requiring admissions in our ICU. It was found that amongst these patients of severe stroke, 3 % of them had vitamin D levels < 10ng/ml, and the remaining having vitamin D levels < 30ng/ml.

In our study almost 89% of patients who presented with acute ischemic stroke were out of window period of 4.5hrs hence were not thromolysed and managed with dual anti platelet therapy and statins which is most common mode of treatment in stroke patients, 8 % of patients presented with acute hemorrhagic stroke and were managed with anti-edema measures and anti-hypertensives for optimal blood pressure control, 2% of patients presented with stroke of cardioembolic origin and were managed with anticoagulants ,1% of patients had underlying polycythemia vera and were managed with dual antiplatelet therapy with hydroxyurea.

Diabetes and hypertension was most common comorbidities seen among our patients of stroke followed by hypothyroidism.

Table 3: Vitamin D Levels

Vitamin D Levels	No of Patients	Percentage
MORE THAN 30	28	24%
21 TO 30	46	39%
10 TO 20	40	34%
LESS THAN 10	3	3%

Only 28 patients in our study was having normal Vitamin D levels. Rest of patients enrolled in the study had lower levels of Vitamin D, with 39% of patients having vitamin D insufficiency, 34% of patients having vitamin D deficiency, and 3% of patients having severe vitamin D deficiency.

There was not much significant correlation between age and vitamin D levels in our study, with vitamin D insufficiency and deficiency seen commonly in age group above 65years. In our study it was observed that vitamin D deficiency was observed with a BMI of 25kg/m2 and severe vitamin D deficiency observed with a BMI of 26 kg/m^2.

Vitamin D Levels and Lipid Profile

In our study it was observed that vitamin D deficiency was associated with a higher mean LDL level, with highest LDL levels associated with severe vitamin D deficiency. In our study as mean HDL

level decreases there is fall in Vitamin D level, but was statistically non-significant. In our study as mean triglycerides level increases there is fall in Vitamin D level, but was statistically non-significant.

In our study it was observed that there is fall in serum calcium levels there is lesser vitamin D levels, this association is statistically significant. In our study it was observed that the mean Hs CRP levels tends to increase in patients of stroke with vitamin D deficiency , with highest levels of CRP found in patients with severe vitamin D deficiency (<10nmol/l).

Table 4: Pearson Correlation

VITAMIN D	CORRELATION		
LDL	Pearson Correlation		-0.018
	Sig. (2-tailed)		0.849
HDL	Pearson Correlation		0.15
	Sig. (2-tailed)		0.108
TRIGLYCERIDES	Pearson Correlation		-0.045
	Sig. (2-tailed)		0.627
HS-CRP	Pearson Correlation		-0.112
	Sig. (2-tailed)		0.231

We also did Pearson correlation where LDL, Triglycerides and HS-CRP had negative correlation with Vitamin D levels, a trend towards highest levels of LDL, TG and Hs CRP was seen with severe vitamin D deficiency (ie <10 nmol/l) in our study. HDL had negative correlation. But these correlation was statistically non-significant, probably because of small sample size of our study.

DISCUSSION

Vitamin D deficiency is very common in India and studies have shown the association of vitamin D deficiency with cardiovascular disease and stroke. Vitamin D deficiency is associated with increased prevalence of diabetes, hypertension, dyslipidemia and stroke. In our study conducted at JNIMS 118 patients who met the inclusion and exclusion criteria were admitted in medicine wards /ICU during the study period.

In our study, majority of the patients were in the age group of 61 – 70 years followed by 51- 60 years, of which 67 % (n – 78) were male and 33 % (n- 39) were female patients, in the ratio of 2: 1. The most common type of stroke was thrombotic (ischemic stroke) involving the MCA territory, followed by thalamic infarct.

Patients who met the eligibility criteria were enrolled, out of 118 stroke patients 77 were smokers and 4 were alcoholic, remaining had no risk factors, with smoking being the most common risk factor associated with stroke which is consistent with the study conducted by Amelia K. Boehme, Charles Esenwa, et al.[11] In our study it was observed that vitamin D deficiency was commonly associated with a BMI of 25kg/m2 and severe vitamin D deficiency observed with a BMI of 26 kg/m^2. In same review on the link between obesity and low circulating 25-hydroxyvitamin D concentrations it was found that obesity was associated with low circulating levels of vitamin D.11 One potential mechanism by which obesity could contribute to low serum 25-hydroxyvitamin D is adipose sequestration of vitamin D. There is evidence that vitamin D may regulate adipose tissue mass, differentiation and metabolism in ways that might contribute to obesity. Additional research is needed to elucidate the multifaceted factors underlying the association between low circulating 25-hydroxyvitamin D and obesity.

Majority of patients enrolled in our study were elderly, smokers, hypertensive and obese which are common modifiable risk factors associated with stroke, in our study it was found that these risk factors were also associated with vitamin D deficiency which in turn contributes to increased risk of stroke.

In this study it was found that vitamin D deficiency is associated with higher mean LDL levels, with highest LDL levels found in patients with severe vitamin D deficiency (ie <10 ng/ml). An elevated low-density lipoprotein cholesterol (LDL-C) level is a risk factor for cardiovascular disease, including ischemic stroke.1 For patients with a history of ischemic stroke, an elevated LDL-C level is associated with an increased risk of subsequent major cardiovascular events. In a meta analysis of Randomised controlled trials published by Meng Lee, et al, it was found that benefits and risks of more intensive LDL-Cholesterol lowering statin based therapies for recurrent stroke risk reduction might be more favorable than the benefits and risks of less intensive LDL cholesterol lowering statin based therapies, especially for patients with evidence of atherosclerosis.

In a systematic review and meta analysis conducted by Huang, X., Yang, Y., Jiang, Y.
et al.[13] Association between vitamin D deficiency and lipid profiles in overweight and obese adults, which enrolled 7952 adults with overweight it was found that vitamin D deficiency was related to an increased level of LDL. HDL level was inversely associated with the vitamin D deficiency status, the results of which have been consistent with our study.

In our study it was found that the mean HDL levels tend to fall and mean LDL and triglyceride levels tend to increase with vitamin D deficiency, however this correlation was not statistically significant in our study (p value- 0.189 for HDL, P- 0.416 for TG, P-0.201 for LDL), this could be explained by a small

sample size of our study and the characteristics of the study population enrolled in this study, hence further studies are needed to establish the significance of this observation.

The most common co morbidities associated with stroke in our study was hypertension (30.5%) and diabetes (29%) followed by hypothyroidism seen in 7.5% of stroke patients. There is accumulating evidence between vitamin D deficiency and blood pressure. Worldwide studies have also demonstrated such an association. In a cross- sectional study of 833 Caucasian males in Uppsala (central Sweden), a threefold higher prevalence of confirmed hypertension was found in participants with 25(OH) D levels < 37.5 nmol/L11, the findings of which are consistent with our study.

25 OH vitamin D levels was tested in all patients of stroke using chemi luminescence assay, in our study the mean vitamin D level was 23.34ng/ml, only 28 patients in our study were having normal Vitamin D levels. Rest of patients enrolled in the study had lower levels of Vitamin D, with 39% of patients having vitamin D insufficiency, 34% of patients having vitamin D deficiency, and 3% of patients having severe vitamin D deficiency, based on the observations made in our study majority of the patients with stroke had vitamin D insufficiency followed by vitamin D deficiency. Our study population was small but our findings are consistent with similar previous studies such as, Lana Fani, et al,[14] were an association was found between vitamin D deficiency and prevalent stroke, but only severe vitamin D deficiency was associated with incident stroke. Another Danish study with comparable follow-up times found an increased stroke risk in individuals aged 20 to 100 years with serum 25(OH) Vitamin D. values < 25nmol/l compared with that of >50nmol/l, the findings of which are consistent with our study.

Recent years have witnessed tremendous strides in our understanding of risk factors and prevention of stroke. The major modifiable risk factors of stroke is HTN, DM, Smoking, and Dyslipidemia. These modifiable risk factors have also independently shown an association with vitamin D deficiency, which intern is associated with an increased stroke risk, as per the studies conducted in the past. Direct and indirect effects of vitamin D have been proposed for pathophysiological pathways leading to stroke.[15] Directly, vitamin D is involved in maintaining endovascular function,[16-18] and regulating inflammatory activity within vascular walls.[19] Indirectly, vitamin D is involved in regulating renin production through the Renin-Angiotensin-Aldosterone system-pathway, thereby attenuating hypertension.[20] Although hypertension and atherosclerosis are important factors in the pathophysiology of stroke,[21] other established cardiovascular risk factors have also been linked to vitamin D status, such as serum lipid status and insulin sensitivity.[22,23] Indeed, any association within our data became statistically nonsignificant after adjustment for any of these risk factors, possibly because of the small sample size which is the limitation of our study.

In order to study the association between vitamin D deficiency and stroke with Hs CRP, we tested the stroke patients enrolled in our study for hs-CRP, where we found that stroke patients with vitamin D deficiency were associated with a higher mean CRP levels of 21-22mg/L. Levels of inflammatory biomarkers have been associated with increased risk of stroke, just as they have been associated with risk of other cardiovascular diseases and allcause mortality. C-reactive protein, measured using a high-sensitivity assay (hsCRP), is one marker that has been particularly well studied. hsCRP has become the inflammatory marker of choice in the clinical setting because of its consistent association with cardiovascular events, long half-life, and stability when stored frozen for prolonged periods of time.

A meta-analysis of 54 prospective cohort studies, including a total of >160309 individuals, found a modest association between hsCRP levels and ischemic stroke (relative risk per SD increase in the log CRP concentration 1.27; 95% CI, 1.15–1.40).24 Similar results were obtained in a meta-analysis of 12 observational studies of hsCRP and stroke risk. The findings of our study has been consistent with the previous studies, however the correlation between vitamin D deficiency and hs-CRP levels is statistically non -significant in our study (p value-0.154), due to the small sample size of our study.

CONCLUSION

This study demonstrates a significant association between vitamin D deficiency and stroke, with only 24% of stroke patients presenting with normal vitamin D levels while 76% showed insufficiency or deficiency. The findings suggest that vitamin D status may play an important role in stroke risk and outcomes through multiple pathways.

Our observations revealed that vitamin D deficiency was more common in patients with higher BMI, which aligns with previous research on vitamin D sequestration in adipose tissue. Additionally, patients with vitamin D deficiency showed higher mean LDL levels and lower HDL levels, though these correlations did not reach statistical significance possibly due to the limited sample size of 118 patients.

The study also found that common stroke risk factors—hypertension (30.5%), diabetes (29%), and smoking—frequently coexisted with vitamin D deficiency. Furthermore, elevated hs-CRP levels (21-22 mg/L) were observed in vitamin D-deficient stroke patients, suggesting a potential inflammatory link, though this correlation was also statistically non-significant.

While our study adds to the growing body of evidence connecting vitamin D deficiency with cardiovascular risk factors and stroke, the limitations

of sample size prevented some associations from reaching statistical significance. The findings suggest both direct effects of vitamin D on endovascular function and inflammatory regulation, and indirect effects through modulation of established risk factors like hypertension, dyslipidemia, and insulin sensitivity.

These results emphasize the potential importance of vitamin D assessment and supplementation in stroke prevention strategies, particularly among individuals with established risk factors. Larger prospective studies are needed to further elucidate the complex relationship between vitamin D status, lipid profiles, inflammation, and stroke outcomes.

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