

# Study on Vitamin-D Levels in Acute Ischemic Stroke

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## Abstract

**Introduction:** Evidence suggests that Vitamin D deficiency is associated with an increased risk of ischemic stroke. Vitamin D is a neuroprotective prohormone, involved in the pathogenesis of cardiovascular disease. Recent studies have demonstrated the association between Vitamin D and stroke but the findings are inconsistent. In view of these discrepancies, we studied the association of Vitamin D levels with acute ischemic stroke using data from a population-based study.

**Aim:** The aim of the study was to evaluate the association between Vitamin D levels and acute ischemic stroke and assess the short-term outcome in these patients.

**Methodology:** A total of 50 acute ischemic stroke patients diagnosed with focal neurological signs or with acute infarct on CT brain were subjected to the study. Vitamin D levels in the range 30–100 ng/ml were defined normal, 10–30 ng/ml were defined insufficient, and <10 ng/ml were defined deficient.

**Results:** This prospective study included 50 patients of which 88% (44 patients) were male and 12% were female. A significant number of patients showed a deficiency in Vitamin D. There were no statistically significant differences regarding age and gender. No association was found between cholesterol and TGL with VIT D and there was no association between area of infarct with VIT D.

**Conclusion:** Vitamin D deficiency is an independent risk factor associated with the severity of cerebral ischemic stroke. Vitamin D supplementation should be used in the therapeutic management of cerebral stroke and screening for serum Vitamin D levels in routine investigations may identify the high-risk individuals and help in the prevention of serious disease events.

**Key words:** Cerebral ischemia, Inflammation, Ischemic, Stroke, Vitamin D

## INTRODUCTION

Vitamin D is associated with calcium and phosphate homeostasis and musculoskeletal health.

It is one of the fat-soluble steroid hormones and is synthesized in the presence of ultraviolet light from 7-dehydrocholesterol in the epidermal layer of the skin.<sup>[1,2]</sup> Vitamin D also has a regulatory effect on the immune function and inflammation.<sup>[3]</sup> Poor Vitamin D status is

a major public health problem that affects 30% of the patients worldwide. Many prospective studies have proved that a poor Vitamin D status can increase the risk of ischemic strokes.<sup>[4]</sup> The synthesis of Vitamin D requires two hydroxylation steps, the first being hydroxylation of inactive Vitamin D to 25-hydroxyvitamin D [25(OH) D] in the liver and then the conversion of 25-hydroxyvitamin D to biologically active form 1,25-dihydroxyvitamin D<sub>3</sub> in the kidney by 1- $\alpha$ -hydroxylase (CYP27B) activity. Meta-analytic studies have shown that a decreased concentration of plasma 25(OH)D has an increased risk of occurrence of symptomatic ischemic stroke.<sup>[5,6]</sup>

Acute ischemic stroke has a heterogeneous origin marked by the sudden onset of focal neurological deficits. It is the major cause of disability and mortality across the world and is associated with unmodifiable risk factors such as age, genetics, sex, and modifiable risk factors including hypertension,

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diabetes mellitus (DM), dyslipidemia, sedentary lifestyle, and smoking.<sup>[7]</sup> Studies by Tarcin *et al.* in 2009 say that Vitamin D deficiency (VDD) is associated with an increased prevalence of CVS risk factors and endothelial dysfunction and is an independent risk factor of acute ischemic stroke.<sup>[8]</sup> Turetsky *et al.* and Park *et al.* in 2015 demonstrated in their study that hypovitaminosis D was independently associated with larger ischemic infarct volume and poor outcome. Low Vitamin D levels were also associated with calcium metabolism disorders, type 2 diabetes mellitus, autoimmune diseases, cardiovascular disease, stroke, multiple sclerosis, and some infectious diseases and cancers.<sup>[9,10]</sup>

Indian studies have also pointed to low 25(OH)D levels in Indian population in all age groups and regions, despite plenty of sunshine. Hence, our study aims to explore the association of Vitamin D deficiency/insufficiency with ischemic stroke and its risk factors.

**Aim**

The aim of the study was to evaluate the association between Vitamin D levels and acute ischemic stroke and assess the short-term outcome in these patients.

**MATERIALS AND METHODS**

A total of 50 acute ischemic stroke patients diagnosed with focal neurological signs or with acute infarct on CT brain were subjected to the. Only patients with acute onset of stroke were included in the study. Patients with chronic kidney disease, history of transient ischemic attacks, prior stroke, DM, HTN, and CAD were excluded from the study. Demographic, epidemiological, and clinical data including traditional stroke risk factors and the use of any therapeutic drug were obtained using a standard questionnaire at the admission of the individuals. The study began after obtaining written informed consent from all individuals and the study protocol was approved by the Institutional Ethics Committee. Serum levels of 25-hydroxyvitamin D levels were measured by chemiluminescence immunoassay technique. Vitamin D levels in the range of 30–100 ng/ml were defined normal, 10–30 ng/ml were defined insufficient, and < 10 ng/ml were defined deficient. Dyslipidemia was defined by the presence of one or more than 1 of the abnormal serum lipid concentration: Total cholesterol ≥ 200 mg/dL and triglycerides > 150 mg/dL.

**RESULTS**

This prospective study included 50 patients of which 88% (44 patients) were male and 12% were female. This indicates that the risk of occurrence of stroke is significantly associated with male sex but there is association with Vitamin D [Figure 1].

Most of the patients were of the age group >61 years (34%) and 15 patients (30%) belonged to the age group of 41–50 years. Only 6 patients (12%) were <40 years of age. There were no statistically significant differences regarding age [Figure 2]. According to the area of infarct, 34 patients (68%) had infarct in the middle cerebral artery (MCA), 6 cases (12%) in anterior cerebral artery (ACA), and 10 cases (20%) in posterior cerebral artery (PCA). The most common site of occurrence of infarct is the MCA but there was no association between area of infarct and Vitamin D [Figure 3]. The mean total cholesterol level was 212.34 mg/dL with a SD of 38.92 and the mean triglyceride level was 160.24 mg/dL with a SD of 42.24 [Figure 4]. Dyslipidemia was not associated with Vitamin D levels and stroke occurrence according to our study findings. Vitamin D levels were normal in 6 cases (12%), insufficient in 32 cases (64%), and deficient in 12 cases (24%) in our study [Figure 5]. This indicates that insufficient levels of Vitamin D can increase the risk of acute ischemic stroke.

**DISCUSSION**

Ischemic stroke has a clinical and socioeconomic effect on death and disability around the world. The etiology of

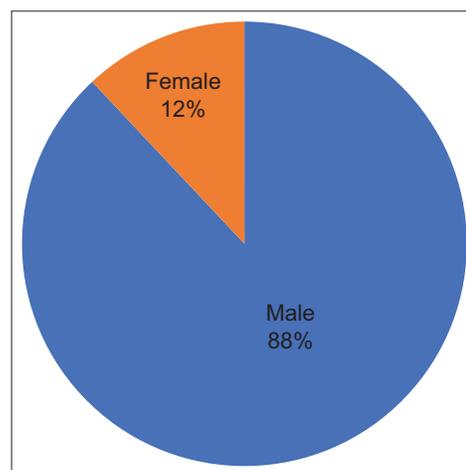


Figure 1: Sex distribution

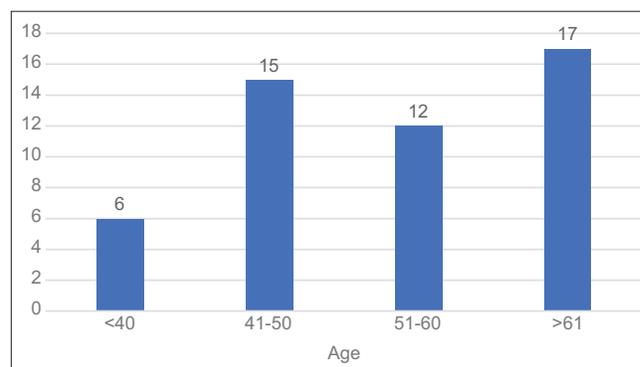


Figure 2: Age distribution

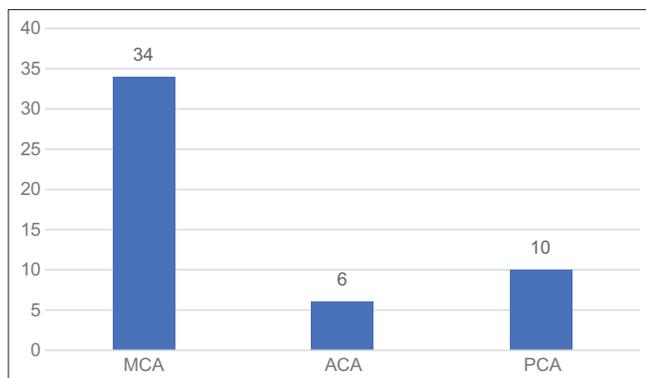


Figure 3: Distribution of area of infarct

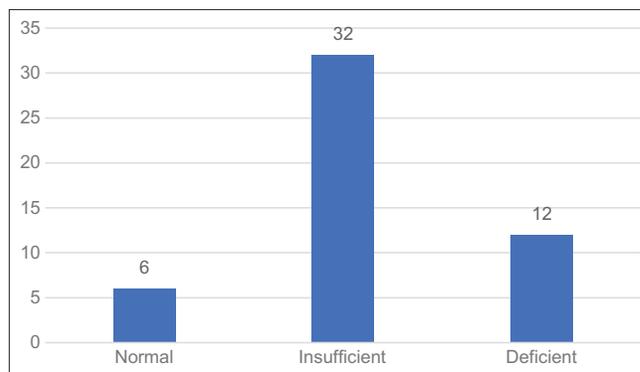


Figure 5: Distribution of vitamin D

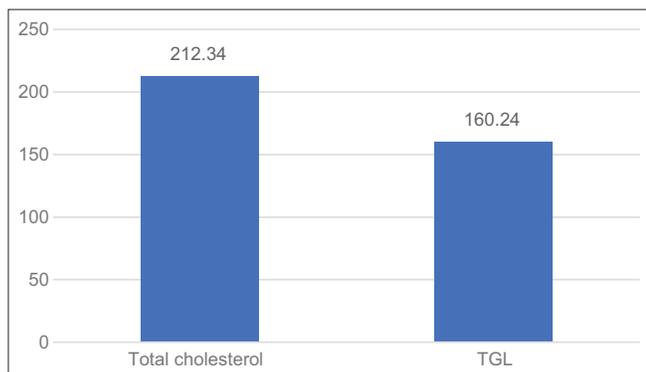


Figure 4: Distribution of lipid levels

ischemic stroke is heterogeneous and factors such as age, sex, genetics, hypertension, diabetes, sedentary lifestyle, and smoking may increase the risk of disease occurrence.<sup>[11]</sup> Studies have demonstrated the association between low levels of Vitamin D and acute stroke in patients.<sup>[12,13]</sup> Vitamin D has a vasoprotective potential and can slow down atherosclerosis, promote endothelial function, and reduce hypertension by suppressing the renin–angiotensin–aldosterone system. It is also linked to brain development and function and regulation of cerebrovascular physiology and a deficiency may lead to stroke and brain-related disorders.<sup>[14]</sup> In addition, Vitamin D also modulates smooth muscle cell proliferation, inflammation, and thrombosis and this vascular remodeling can result in stroke.

In the current study, there was no significant association between age group and gender with Vitamin D and no association was also found between the area of infarct and Vitamin D. Studies by Ponda and Zittermann *et al.* demonstrated in their study that Vitamin D deficiency was associated with dyslipidemia among stroke patients.<sup>[15,16]</sup> However, in our study, we did not find any association between TGL and cholesterol levels. A significant number (64%) of study patients (32 patients) had insufficient levels of Vitamin D in our study and 24% had Vitamin D deficiency. This result is in agreement with the other study

findings and Vitamin D can be used as an independent marker of acute ischemic stroke. Studies by Pilz *et al.* in 2008 and Sun *et al.* in 2013 showed that low levels of 25(OH)D are consistent with ischemic stroke.<sup>[17]</sup> Poole *et al.*, in his study, found that 34 of 44 patients (77%) with stroke had low serum 25(OH)D levels (< 50 nmol/L) which were substantially lower than healthy elderly subjects.<sup>[18]</sup>

The results from our analyses suggest that low Vitamin D serum levels are a consequence of stroke. Limited Vitamin D production in the affected group may be because of reduced exposure to sunlight and quality of diet. The study findings of Brian *et al.* say that any benefit of Vitamin D supplementation is too mild to have an impact on stroke risk, unless the individuals are already severely Vitamin D deficient, as rightfully suggested by the VITAL trial investigators.<sup>[19]</sup> There are two proposed pathophysiological pathways leading to stroke: Vitamin D is involved in maintaining endothelial function directly and an indirect pathway where it regulates renin production through the renin–angiotensin–aldosterone system pathway, thereby attenuating hypertension. Hypertension and atherosclerosis are in general risk factors in stroke development but our study results did not link to TGL and total cholesterol levels. The main finding of the present study is that VDD can be considered as an independent marker associated with acute ischemic stroke.

The limitations of the study are the small sample size and failure to assess the levels of Vitamin D overtime to make sure if the levels remained stable. The exact dose of Vitamin D administration as a supplement in stroke patients was also not assessed.

## CONCLUSION

Vitamin D deficiency is an independent risk factor associated with the severity of cerebral ischemic stroke according to our study results. The results suggest that Vitamin D supplementation should be used in the

therapeutic management of cerebral stroke. Further prospective studies are needed to establish the appropriate therapeutic dose of Vitamin D in stroke patients. Screening for serum Vitamin D levels in routine investigations may identify the high-risk individuals and help in the prevention of serious disease events.

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