

# Do Vitamin D Levels Correlate with Stroke Severity? Study on Patients with Ischemic Stroke

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## ABSTRACT

**Objective:** To assess the vitamin D levels among patients presenting with acute ischemic stroke and relationship of these levels with severity of stroke.

**Study Design:** Cross-sectional study

**Place and Duration of Study:** This study was conducted at the Department of medicine, Sheikh Khalifa Bin Zayed Al-Nyhan hospital Rawalakot, Eight months, from January 2020 to August 2020.

**Materials and Methods:** A total of 180 patients with ischemic stroke diagnosed by the consultant medical specialist on the basis of clinical and neuro-radiological findings were included in this study. Serum Vitamin D levels were assessed along with other baseline investigations among the study participants. Severity of stroke was assessed via National Institutes of Health Stroke Scale.

**Results:** Out of 180 patients of ischemic stroke included in the study 112 (62.2%) were male while 68 (37.8%) were female. On National Institutes of Health Stroke Scale, 98 (54.4%) had mild, 52 (28.8%) had mild to moderately severe, 20 (11.11%) had severe and 10 (5.56%) had very severe symptoms. 99 (55%) of the patients had Vitamin D levels within range while 81 (45%) had deficient vitamin levels. Statistical analysis revealed that presence of hypertension and vitamin D deficiency had a statistically significant relationship (p-value <0.05) with severity of acute ischemic stroke.

**Conclusion:** Vitamin D levels were found low in significant number of patients presenting with acute stroke. Patients with Vitamin D deficiency and diagnosis of hypertension were more at chance of having severe symptoms of stroke as compared to those without diagnosis of hypertension and vitamin d deficiency.

**Key Words:** Ischemic stroke; severity; vitamin D

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## INTRODUCTION

Cerebrovascular events make a huge chunk of patients who get admitted to all levels of health care facilities in developing countries.<sup>1</sup> Stroke is surely one of the most common cerebrovascular accident across the globe.<sup>2</sup> A lot of work has been done to look for the risk factors or consequences of such a devastating event which has a marked impact on quality of life of patients as well as care givers.<sup>3</sup> Multiple physical, endocrine and metabolic abnormalities have been related to stroke may be as a predisposing factor or as an after effect of the event.<sup>4</sup>

Vitamins though required in small amounts for the body; yet play a very significant role in maintaining homeostasis in the human body. Classically, Vitamin D has been linked with bone and skeletal functioning but recent research has highlighted that this nutrient has multiple functions for human body and deficiency may lead to multi-system problems.<sup>5</sup> Multiple extra renal and extra intestinal causes have also been linked with vitamin D deficiency and it has been emphasized that clinicians should manage the deficiency of this nutrient with a more holistic approach.<sup>6</sup>

Neurologist and researchers have tried to establish correlation between mortality and morbidity associated with stroke and vitamin D levels in other parts of the world. Wajda et al. from Poland published a study last year highlighting that more than 90% of the stroke patients had vitamin D deficiency or insufficiency. They concluded that severe vitamin D deficiency was related to increased mortality among the patients suffering from ischemic stroke.<sup>7</sup> Zhang et al. came up with similar findings among patients with acute ischemic stroke without diagnosis of hypertension and revealed that initially vitamin D levels were not associated with severity of stroke but at three month follow up these levels emerged as strong predictors of

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functional recovery among patients suffering from stroke.<sup>8</sup> Wei et al. in 2018 published a study on Chinese patients regarding Vitamin D deficiency in relation to the poor functional outcomes in non-diabetic patients with ischemic stroke. They came up with the findings that more than 50% patients had vitamin D deficiency by using levels of 20 ng/ml as cut off value. In multivariate analysis models, for vitamin D deficiency, the adjusted risk of poor functional outcomes and mortality was increased by 220% (odds ratio (OR): 3.2; 95% CI: 1.7-4.2, P<0.001) and 290% (OR: 3.9; 95% CI: 2.1-5.8, P<0.001), respectively. Vitamin D deficiency was associated with an increased risk of poor functional outcome events in their target population and they emphasized on future studies evaluating the role of vitamin D supplementation after acute ischemic stroke.<sup>9</sup> Rehabilitative services and tertiary prevention is a time consuming and expensive process. We need to find some easy to administer and cost effective way to reduce the severity and impact of stroke on the patients. Vitamin D deficiency has been a prevalent problem in our population and a recent study revealed that around half of our population may be at risk of this deficiency therefore we need to keep this important deficiency in mind when dealing with the patients of stroke. We planned this study with the rationale to assess the vitamin D levels among patients presenting with acute ischemic stroke and relationship of these levels with severity of stroke.

## MATERIALS AND METHODS

This cross sectional study was conducted at the medicine department of Sheikh Khalifa Bin Zayed Al-Nyhan hospital Rawalakot between January 2020 and August 2020. Sample size was calculated by using the WHO sample size calculator by using the population prevalence proportion of vitamin D levels in stroke as 13.6%.<sup>11</sup> Non probability consecutive technique was used to gather the sample for the study. Acute ischemic stroke was diagnosed by consultant medical specialist on the basis of clinical findings and plain CT scan brain done at the time of presentation.<sup>12</sup> Patients of both genders of age between 18 and 70 years presenting with acute ischemic stroke were included in the study. Exclusion criteria were the patients less than 18 years or more than 70 years of age or those who did not consent to or those with a past or current history of skeletal abnormalities or rheumatological conditions. Patients who had cancer or had past history of renal or autoimmune disease or had a hemorrhagic stroke were also excluded from the study. Patients already taking Vitamin d supplements prior to the onset of stroke were also not included in the study.

Vitamin D levels were assessed by an electrochemiluminescence method on a Cobas E411 analyzer (Roche Diagnostics GmbH, Mannheim, Germany) with inter-assay coefficients of variability

below 7.8 and 6.5%, respectively. Levels less than 20 ng/ml were used as cut off value for vitamin d deficiency.<sup>13</sup> Severity of stroke was assessed via National Institutes of Health Stroke Scale (NIHSS). Following classes were made on the basis of NIHSS score Mild <5, Mild to Moderately severe, severe 15-24 and very severe >25.<sup>14</sup>

Ethical approval for the study was obtained from the ethical review board committee of the Sheikh Khalifa Bin Zayed Al-Nyhan hospital Rawalakot/ Poonch medical college Rawalakot. Subjects and their caregivers were provided with a detailed description of the study and were inducted into the study after written informed consent. Subjects with confounding variables like presence of other neurological illness or rheumatological conditions were identified by detailed history taking and excluded from the study. Severity of stroke was assessed via National Institutes of Health Stroke Scale (NIHSS) by the treating physician. Serum Vitamin D levels were assessed from the laboratory of own hospital. Variables in the study included age, gender, Vitamin D levels and presence of hypertension. Characteristics of participants and the distribution of the severity of stroke were described by using the descriptive statistics. Chi-square was used to determine between-group variances in categorical correlates. Relationship of age, gender, presence of Vitamin D deficiency and presence of hypertension was assessed with the severity of stroke. All statistical analysis was performed using Statistics Package for Social Sciences version 23.0 (SPSS-23.0). Differences between groups were considered significant if p-values were  $\leq 0.05$ .

## RESULTS

**Table No.1. Characteristics of patients presenting with acute ischemic stroke N=180**

Age (years)	
Mean + SD	58.93 ±8.859
Range (min-max)	38 years-68 years
Gender	
Male	112 (62.2%)
Female	68 (37.8%)
Presence of Vitamin D deficiency	
Yes	81 (45%)
No	99 (55%)
Severity of stroke	
Mild	98 (54.5%)
Mild to moderately severe	52 (28.9%)
Severe	20 (11.1%)
Very severe	10 (5.6%)

Out of 180 patients of ischemic stroke included in the study 112 (62.2%) were male while 68 (37.8%) were female. Table I summarized the demographic profile of study participants. On National Institutes of Health Stroke Scale, 98 (54.4%) had mild, 52 (28.8%) had

mild to moderately severe, 20 (11.11%) had severe and 10 (5.56%) had very severe symptoms. 99 (55%) of the patients had Vitamin D levels within range while 81 (45%) had deficient vitamin levels. Statistical analysis

(person Chi-square test) revealed that presence of hypertension and vitamin D deficiency had a statistically significant relationship (p-value <0.05) with severity of acute ischemic stroke (Table 2).

**Table No.2: Association of different variables with severity of stroke**

Socio demographic factors	Mild	Mild to moderately severe	Severe	Very severe	p-value
Age					
50 year or less	50 (51.1%)	24 (46.2%)	08 (40%)	08 (80%)	0.171
>50 years	48 (48.9%)	28 (53.8%)	12 (60%)	02 (20%)	
Gender					
Male	64 (65.3%)	32 (61.5%)	11 (55%)	05 (50%)	0.691
Female	34 (34.7%)	20 (38.5%)	09 (45%)	05 (50%)	
Vitamin D levels					
Absent	70 (71.4%)	20 (38.5%)	07 (35%)	02 (20%)	<0.001
Present	28 (28.6%)	32 (61.5%)	13 (65%)	08 (80%)	
Hypertension					
No	67 (68.7%)	30 (57.7%)	08 (40%)	03 (30%)	0.019
Yes	31 (31.3%)	22 (42.3%)	12 (60%)	07 (70%)	

## DISCUSSION

Human body had complex biochemical mechanism for maintenance of homeostasis especially at the time of physical or mental stress. Various types of vitamins though required in small quantity but have a vital role in proper functioning of different processes of human body. Cerebrovascular events like stroke pose a major stress to human body and is a big blow on homeostatic mechanism of the body. In this time of acute crisis, if any of the important nutrient is deficient it may add insult to the injury and make things difficult for the patient as well as the physician. We therefore planned this study to assess the vitamin D levels among patients presenting with acute ischemic stroke and relationship of these levels with severity of stroke at time of presentation at neurology unit of our tertiary care teaching hospital.

Narasimhan et al<sup>15</sup> did an interesting study which may be regarded as next step to the epidemiological data we have generated. They performed a randomized controlled trial to look for the efficacy of Vitamin D in predicting outcome after ischemic stroke. They concluded that there was a significant improvement in the stroke outcome after three months in those patients who were supplemented with vitamin D.<sup>15</sup> Ours was a basic cross-sectional study in this regard but supported findings of Narasimhan et al. in terms of deficient vitamin D levels clearly related to increased severity of stroke at the time of presentation.

Turetsky et al.<sup>16</sup> in 2015 studied this subject from another angle and emphasized on relationship of Vitamin D levels with volume of stroke lesion on neuro-radiological investigations. They concluded that lacunar infarct etiology, lower admission National

Institutes of Health Stroke Scale, and higher serum 25(OH)D concentration were associated with smaller infarct volumes (P < .05). The association of 25(OH)D with ischemic infarct volume was independent of other known predictors of the infarct extent (P = .001). Multivariable analyses showed that the risk for a poor 90-day outcome doubled with each 10-ng/mL decrease in serum 25(OH)D.<sup>16</sup> Our findings were similar in terms of National Institutes of Health Stroke Scale score and deficient vitamin D levels and hypertension predicted more severity of stroke.

Another similar study performed in France in 2016 by Daumas et al.<sup>17</sup> regarding correlation of vitamin D levels and functional outcomes after the stroke. They came up with the findings that the risk of functional impairment in patients with low 25(OH)D levels was greater than that in patients with higher 25(OH)D levels (odds ratio [OR] 2.10, 95% confidence interval [CI]: 1.35-3.27, P = .001). This association was still observed after adjustment for confounding variables (OR 1.70, 95% CI: 1.06-2.71, P = .027).<sup>17</sup> Results of our study supported their findings and vitamin D levels were strong predictor of severe symptomatology of acute ischemic stroke.

Yarlagadda et al.<sup>18</sup> in 2020 published a detailed review regarding effect of vitamin D deficiency on incidence, severity and mortality related to stroke and benefit if any of supplementation of vitamin D in such patients. They concluded that neuroprotective mechanisms by which vitamin D may be related to mitigate stroke onset and outcomes have yet to be fully studied, but researchers have proposed several pathways, including promotion of certain neuroprotective growth factors, reduction of arterial pressure through vasodilation, and inhibition of reactive oxygen species. There has been some evidence that vitamin D supplementation could

lower stroke risk and improve recovery, though outcomes can also be negligible or negative.<sup>18</sup> Our findings generated a baseline data and emphasized on role of vitamin D deficiency in predicting severity of stroke.

There were few limitations in our study. Assessing severity at time of presentation may not be very accurate measure of stroke severity and outcome. Long term follow up may yield better results in this regard.

## CONCLUSION

Vitamin D levels were found low in significant number of patients presenting with acute stroke. Patients with Vitamin D deficiency and diagnosis of hypertension were more at chance of having severe symptoms of stroke as compared to those without diagnosis of hypertension and vitamin d deficiency.

### Author's Contribution:

Concept & Design of Study: Sadia Hanif, Shazia Siddiq  
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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