

# The Impact of Vitamin D Deficiency and its Outcome Among Patients With Ischemic Stroke

Vitamin D  
Deficiency With  
Ischemic Stroke

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## ABSTRACT

**Objective:** To determine the Impact of Vitamin D Deficiency and Its Outcome among Patients with Ischemic Stroke

**Study Design:** The cross-sectional descriptive study

**Place and Duration of Study:** This study was conducted at the Liaquat University Hospital, Hyd from October, 2018 to March, 2019.

**Methods:** The vitamin D status of each of the 370 patients who had ischemic stroke was investigated, and the results included readmission within 30 days, length of stay, and mortality.

**Results:** The mean  $\pm$  SD for age (yrs) 57.72 $\pm$ 9.44, systolic blood pressure (mmHg) 160.94 $\pm$ 7.82, diastolic blood pressure (mmHg) 115.72 $\pm$ 11.74, duration of stroke (hrs) 41.95 $\pm$ 8.86, random blood sugar (mg/dL) 290.77 $\pm$ 18.95, fasting blood sugar (mg/dL) 150.84 $\pm$ 9.96, hospital stay duration (days) 19.00 $\pm$ 4.00 and vitamin D level (ng/ml) 12.76 $\pm$ 6.51. Regarding vitamin D status, the percentages for sufficient, deficient and insufficient were 99 (26.7%), 200 (54%), 71 (19.1%), respectively. However, there was statistical significance in the vitamin D status with regard to gender ( $p=0.02$ ), age ( $p<0.01$ ), hospital stay ( $p<0.01$ ), readmission ( $p<0.01$ ) and mortality ( $p<0.01$ ).

**Conclusion:** Ischemic stroke has been independently linked with vitamin D deficiency.

**Key Words:** Strokes, Cerebrovascular accident and Vitamin D.

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## INTRODUCTION

The ischemic cerebrovascular accident, caused by the blockage of the circulation of blood to the brain, continues to be a primary source of death and disability globally.<sup>1</sup> Recognizing and mitigating changeable danger indicators is essential for successful preventative and treatment measures.<sup>2</sup> Numerous studies have examined the correlation among vitamin D insufficiency and the occurrence, extent, and consequences of stroke caused by ischemia, underscoring the significance of sufficient vitamin D levels for cerebrovascular function.<sup>3,4</sup> Vitamin D, a lipid-soluble secosteroid, is essential for equilibrium of calcium and bone metabolism.<sup>5</sup> In addition to its traditional roles, recent data indicates that vitamin D has considerable neuroprotective abilities, affecting neuronal well-being and vascular stability.

As a result, vitamin D insufficiency has attracted interest as a potentially preventable risk factor for several neurological conditions; including stroke caused by ischemia.<sup>6</sup> A research in Egypt evaluated vitamin D levels in stroke individuals and investigated its correlation with initial severity and subsequent outcomes. The results indicated that those with stroke patients had markedly reduced blood vitamin D levels in comparison to healthy controls. Furthermore, vitamin D inadequacy and insufficiency were more frequent among patients. A strong negative connection existed between blood vitamin D levels and stroke scale (NIHSS) scores upon admittance and after seventy-two hours, suggesting that diminished vitamin D levels correlated with heightened stroke severity. Furthermore, diminished vitamin D levels were associated with worse results at discharge and after three months, indicating that vitamin D insufficiency is connected to suboptimal short-term rehabilitation in stroke due to ischemia patients.<sup>7</sup> A research in Ireland evaluated the frequency of vitamin D insufficiency in individuals over 50 years old who were hospitalized with acute stroke. The findings indicated that forty-four percent of the group had vitamin D deficiency, with levels falling below 50 nmol/L. The significant prevalence highlights the need for regular evaluation of vitamin D levels in individuals with stroke, as inadequacy may influence the likelihood of stroke and intensity.<sup>8</sup> The processes linking vitamin D deficiency

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to heightened stroke severity and risk are complex. Vitamin D modulates inflammatory reactions, diminishes oxidative stress, as well as regulates endothelial function, all of which are crucial for cerebrovascular well-being.<sup>9</sup> A deficiency in vitamin D can result in dysfunctional endothelial cells, increased stiffness in the arteries, and a pro-inflammatory condition, consequently raising the likelihood of ischemic events. Additionally, vitamin D receptors are present in multiple parts of the brain, and their activation may provide neuroprotective benefits, such as enhancing neuronal survival and preventing excitotoxicity.<sup>10</sup>

The major warning factors for cerebral infarction include age and hypertension, which are associated with decreased serum vitamin D levels. The circulatory form of vitamin D is also associated with an independent risk of stroke in the future and plays a role in immunomodulation, immune system maintenance, and cell growth and differentiation in addition to maintaining calcium and bone homeostasis. Furthermore, a wide range of tissues, including endothelium, stimulated monocytes and T cells, astrocytes, cardiomyocytes, and neurons, express vitamin D receptors (VDR). Vitamin D deficiency significantly decreased the expression of interleukins and interferon gamma in ischemic brain cells, according to cytokine research

The development of CT scanning, a safe and noninvasive method for distinguishing among cerebral infarction and hemorrhage, has resulted in significant advancements in the examination of stroke patients.<sup>11</sup>

The association between vitamin D insufficiency and ischemic stroke was previously investigated across several groups. A research conducted in Iran investigated the relationship between blood vitamin D concentrations, stroke extent, and lesion volume. The results demonstrated that decreased vitamin D levels correlated with increased stroke severity and greater lesion sizes, indicating that low levels of vitamin D may intensify brain damage in individuals with ischemic stroke.<sup>12</sup> Growing data suggests a substantial correlation among vitamin D inadequacy and heightened risk, severity, and adverse consequences of ischemic stroke. Mitigating vitamin D insufficiency with lifestyle changes, food consumption, and supplementation might be a viable strategy for alleviating the incidence of ischemic stroke. This study assessed the amount of vitamin D present in ischemic stroke patients as well as the study's overall outcomes. It also offers insights for future research investigating whether taking vitamin D supplements can lower the incidence and mortality due to stroke.

## METHODS

Patients hospitalized with ischemic stroke at Liaquat University Hospital in Hyderabad from Oct-2018 to

March-2019 were enrolled and selected in this six-month cross-sectional descriptive research. Following informed permission and an initial examination of the inclusion criteria as all patients with a confirmed diagnosis of stroke by CT SCAN or MRI and regardless of gender, all patients were recruited in the research. A focused neurological dysfunction with a recent, abrupt start that is supported by an MRI or CT scan of the brain's hypodense region is known as a stroke.

Serum vitamin D levels below 20 ng/ml were deemed deficient, those between 29 and 20 ng/ml as insufficient, and those beyond 30 ng/ml as sufficient. As a result of the individuals' CVA and subsequent readmission owing to clinical deterioration in their health status, the outcome was assessed based on mortality in hospitals, length of stay, and readmission. The study's exclusion criteria included patients with brain tumors, seizures, paraparesis, hemorrhagic stroke, and those currently taking vitamin D supplements. The vitamin D level was investigated and evaluated following the diagnosis of an ischemic stroke using brain imaging, and the information was recorded on pre-made proforma. In addition to measuring blood pressure, blood sugar levels were also examined. The study's outcomes included length of stay, in-hospital mortality, and readmission of the participants within 30 days as whether individuals acquired evidence-based methods of severe stroke care. Patients also received proper follow-up visits every two weeks, and those subjects who did not follow up were excluded from the analysis.

For the analysis, SPSS version 21.00 was used. As qualitative data, the frequency (n) and proportions (%) of vitamin D insufficiency in ischemic stroke were computed. For each numerical variable, the mean, as well as the standard deviation ( $\pm$ SD), were computed. These included the blood pressure (mmHg), stroke length (hours), blood sugar level (mg/dl), hospital stay duration (days), and vitamin D level (ng/ml). Readmission, mortality, and length of hospital stay were examples of outcomes for which the data was categorical. For categorical variables, the chi-square test was used at 95% confidence intervals, with a p-value threshold of  $\leq 0.05$  indicating significance.

## RESULTS

A total of 370 ischemic stroke patients had their vitamin D status assessed; Table 1 shows the mean  $\pm$  SD for all quantitative variables, while Table 2 displays the frequency and proportions for age, gender, and vitamin D status. The number and percentages of those with vitamin D status that were deficient, insufficient, and sufficient were 200 (54%), 71 (19.1%), and 99 (26.7%), respectively. Table 3-6 shows that the vitamin D status was statistically significant in terms of sex ( $p=0.02$ ), hospitalization ( $p<0.01$ ), death ( $p<0.01$ ), and readmission ( $p<0.01$ ).

**Table No. 1: The Descriptive Statistics of the Study Population**

Quantitative variables	Mean ±SD
Age (yrs)	57.72±9.44
Systolic blood pressure (mmHg)	160.94±7.82
Diastolic blood pressure (mmHg)	115.72±11.74
Duration of stroke (hrs)	41.95±8.86
Random blood sugar (mg/dL)	290.77±18.95
Fasting blood sugar (mg/dL)	150.84±9.96
Hospital stay duration (days)	19.00±4.00
Vitamin D level (ng/ml)	12.76±6.51

**Table No. 2: The Frequency and Percentage for Age, Gender and Vitamin D Status of the Population**

AGE (yrs)	Frequency (n=370)	Percent (%)
20-30	33	8.9
30-40	62	16.8
40-50	69	18.6
50-60	91	24.6
60+	115	31.1
<b>GENDER</b>		
Male	245	66.2
Female	125	33.8
<b>Vitamin D Status</b>		
Sufficient	122	32.9
Deficient	145	39.1
Insufficient	103	27.8

**Table No. 3: The Vitamin D Status in Accordance to Gender**

		VITAMIN D STATUS			Total
		Sufficient	Deficient	Insufficient	
Gender	Male	89	97	59	245
		73.0%	66.9%	57.3%	66.2%
	Female	33	48	44	125
		27.0%	33.1%	42.7%	33.8%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

\*P-value: 0.04

**Table No. 4: The Vitamin D Status and Hospitalization**

		VITAMIN D STATUS			Total
		Sufficient	Deficient	Insufficient	
HOSPITAL	<14	11	52	84	147

STAY	days	9.0%	35.9%	81.6%	39.7%
	>14 days	111	93	19	223
		91.0%	64.1%	18.4%	60.3%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

\*P-value: <0.01

**Table No. 5: The Vitamin D Status and Mortality**

		VITAMIN D STATUS			Total
		Sufficient	Deficient	Insufficient	
Mortality	Yes	18	31	6	55
		14.8%	21.4%	5.8%	14.9%
	No	104	114	97	315
		85.2%	78.6%	94.2%	85.1%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

\*P-value: <0.01

**Table 06: The Vitamin D Status And Readmission**

		VITAMIN D STATUS			Total
		Sufficient	Deficient	Insufficient	
Readmission	Yes	89	48	15	152
		73.0%	33.1%	14.6%	41.1%
	No	33	97	88	218
		27.0%	66.9%	85.4%	58.9%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

\*P-value: <0.01

## DISCUSSION

A significant cause of death and disability worldwide, stroke is also on the rise in nations with low or middle incomes. Vitamin D has a major role in immunological, cardiac, and cerebrovascular physiological control and has gained recognition as a potential risk factor for heart diseases because of its potential for vasoprotection.<sup>13</sup>

Furthermore, vitamin D deficiency influences vascular remodeling by regulating inflammation, thrombosis, and smooth muscle proliferation. Furthermore, too much parathyroid hormone promotes myocyte hypertrophy and vascular remodeling, whereas too little vitamin D results in secondary hyperparathyroidism.<sup>14</sup> The instability of atherosclerotic plaques may be exacerbated by the pro-inflammatory cytokine parathyroid hormone-related protein (PTHrP). Although these circulatory changes are ultimately what cause stroke, a lack of food has been connected to a number of neurological disorders.<sup>15</sup> Two risk factors that may raise the chance of any kind of stroke are diabetes and high blood pressure. However, high blood pressure might lead to erroneous findings in the systems

for scoring and bias the analysis to favor bleeding. The former study's findings indicated that having a male gender was linked to terrible consequences while the mortality was distributed rather equally across all age categories in the prior research.<sup>16</sup> One factor that negatively affects stroke outcomes is aging. This is due to the fact that secondary problems are much too common as individual's age. The in-hospital mortality rate was previously greater when comparing the present research to other worldwide studies.<sup>17</sup> For those who have had an ischemic stroke, serum vitamin D levels are considered to be a very good prognostic indicator. The blood 25-OH D test demonstrated the overall production of vitamin D from both internal and external sources, including exposure to UVB rays and consumption of a range of food types. It is still unclear what pathophysiology underlies atherosclerosis and vitamin D deficiency. A prior research found that vitamin D inhibits the renin-angiotensin system, which in turn regulates blood pressure.<sup>18</sup> According to a different research, a lack of vitamin D may assist lower arterial hypertension and prevent blood vessel thrombosis.<sup>19</sup> Prior studies confirmed that vitamin D deficiency was previously substantially linked to increased carotid plaque development and intimal media thickness in the general population.<sup>20</sup> Modifications to the intimal media, arterial hypertension, inhibition of the renin-angiotensin system in two instances, and changes in thrombotic nations are some of the reasons that have raised the risk of CVA. Additionally, appropriate monitoring has shown a link between atherogenic dyslipidemia and a lack of vitamin D and known to be linked to dyslipidemia. It was shown that stroke patients with low 25(OH) D levels at admission were more likely to die, have a poor early functional result, and have a severe stroke. Blood 25(OH) D levels in individuals with acute ischemic stroke are predictive of both the extent of harm at admission and the favorable functional outcome. The stroke patients often have low nutritional D values, which have been associated with an elevated risk of cardiovascular events in the future. However, they discovered that oral vitamin D supplementation temporarily enhanced endothelial features but did not reduce blood strain in stroke patients whose baseline blood pressure was appropriately controlled.<sup>21</sup> Vitamin D deficiencies reduce neuroprotective chemicals like Insulin Growth Factor-1 (IGF-1) and dysregulates the inflammatory response. Clinical recovery may be enhanced by vitamin D's potential to promote modifications in neuroplastic characteristics. Because it can pass across the blood-talent barrier and because the brain has Vitamin D Receptors (VDR), nutritional vitamin D also has antithrombotic and neuroprotective properties. Genetic polymorphisms in the VDR gene may put people who are vitamin D deficient at higher risk for

stroke. Vitamin-D insufficiency may also be associated with acute stroke or its general risk factors, as shown by the perfect correlation between low 25(OH) D stages and the likelihood of acute ischemic stroke in patients who arrive at our tertiary care hospital. There is more proof of acute ischemic stroke, and low vitamin D levels are a risk factor for deadly strokes on their own. Vitamin D supplementation is a prospective stroke prevention approach since insufficient vitamin D may be a sign of increased co-morbidity and is directly associated to stroke and paralysis.<sup>22</sup> Therefore, the clinicians should identify patients who have the highest risk of repeat stroke and mortality by looking at functional outcomes, survival, and recurrence rates

## CONCLUSION

The study observed an independent correlation between vitamin D deficiency and ischemic stroke patients. Assessing the level of vitamin D in individuals with ischemic stroke is crucial. Given the large number of stroke patients that present to our local hospitals, local information on the subjects is highly necessary. To validate these results and ascertain whether vitamin D supplements could increase stroke patients' survival more multidisciplinary and multicenter research is required.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Beenish Memon, Mumtaz Ali Lakho
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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