Vitamin D Status in Acute Ischemic Stroke: Relation To Initial Severity and Short-Term Outcome

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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 short-term outcome and the severity of stroke.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Medicine, Pak Emirates Military Hospital Rawalpindi Pakistan, from Dec 2019 to Feb 2021.

Methodology: A total of 300 patients with ischemic stroke diagnosed by the consultant medical specialist or neurologist 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 and short-term outcome was assessed by modified Rankin scale.

Results: Out of 300 patients of acute ischemic stroke, 183 (62.3%) were males while 117 (37.3%) were females. 151 (50.3%) of the patients had Vitamin D levels within range while 149 (49.7%) had deficient vitamin levels. On National Institutes of Health Stroke scale, 163 (54.3%) had mild, 87 (29%) had mild to moderately severe, 33 (11%) had severe and 17 (5.7%) had very severe symptoms. Statistical analysis revealed that short-term outcome and stroke severity had a statistically significant relationship (p-value <0.05) with Vitamin D deficiency among patients suffering from acute ischemic stroke.

Conclusion: Almost half of the patients presenting with acute ischemic stroke had vitamin D deficiency in our study. Those having vitamin D deficiency had more chances of having severe form of ischemic stroke and poor short-term outcome.

Keywords: Ischemic stroke, Outcome, Severity, Vitamin D.

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INTRODUCTION

Ischemic stroke is one of the commonly encountered non-communicable health condition which is associated with significant mortality and morbidity.[1] Multiple risk factors are associated with this condition making it a fairly common diagnosis in all the age groups in all parts of the world.[2] Post-stroke outcome and prognosis depend on number of factors related to patients' general health, management of acute stroke and circumstances after the stroke.[3] A lot of medical conditions have been closely related to stroke and patients suffering from these conditions need a close eye from treating physician for preventing the devastating consequences.[4] Traditionally, Vitamin D was thought to be relevant from skeletal system point of view but research over the years have revealed that this important nutrient is necessary for human body in number of ways.[5] Renal and intestinal causes were considered on top of the list while suspecting vitamin D deficiency but recent scientific data suggests that clinicians should manage this problem with a broader perspective.[6]

Work has been done in various parts of the world to look for the relationship of vitamin D status of patient and severity and outcome of stroke. Wajda *et al*, from Poland published a study in 2019 and concluded that severe vitamin D deficiency had significant relationship with increased mortality among the stroke patients.[7] Zhang *et al*, did not find any impact of Vitamin D levels on initial recovery but found a statistically significant relationship with the improvement from stroke after three months of treatment.[8] Wei *et al*, in 2018 published a study from China regarding association of functional outcome and vitamin D status in non-diabetic patients of stroke. They came up with the findings that more than half of the patients who suffered from stroke had vitamin D deficiency. They found that functional outcome was poor among those having vitamin D deficiency. They also had another important finding that mortality was also increased in those stroke patients who were having vitamin D deficiency.[9]

Post-stroke rehabilitation is always a challenge and is a complex multidisciplinary process. Predictors of good outcome if assessed early may yield better

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results in rehabilitative process. Vitamin D deficiency is not uncommon in our part of the world and a huge chunk of population was found deficient in this important and essential nutirent.[10] 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 short term outcome and severity of stroke.

METHODOLOGY

This cross-sectional study was conducted at the Medicine Department of Pak Emirates Military Hospital Rawalpindi between December 2019 to February 2021. World Health Organization sample size calculator was used for sample size was calculation, by taking the population prevalence of deficient vitamin D level in stroke as 13.6%.[11] Non-probability consecutive technique was used to gather the sample for the study. Acute ischemic stroke was diagnosed by consultant medical specialist/neurologist on the basis of clinical findings,[12] and plain CT scan brain done at the time of presentation.

Inclusion Criteria: Patients of both genders of age between 18 and 70 years presenting with acute ischemic stroke were included in the study.

Exclusion Criteria: Patients with a past or current history of skeletal abnormalities or rhematological conditions, patients who had cancer, or had past history of renal or autoimmune disease, or had a hemorrhagic stroke were excluded from the study. Patients already taking Vitamin D supplements prior to the onset of stroke or those who were lost to follow up and could not be assessed for short term outcome 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 co-efficients of variability below 7.8 and 6.5%, respectively. Levels <20 ng/ml were used as cut off value for vitamin D deficiency.[13] 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.[14]

Ethical approval for the study (via letter number A/28/EC/274/2021) was obtained from the Ethical Review Board Committee of the Pak Emirates Military Hospital, Rawalpindi. Subjects and their caregivers were provided with a detailed description of the study and were inducted into the study after the written informed consent. 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. Short-term outcome of stroke was assessed by using the Modified Rankin scale that ranges from level 0 depicting no symptoms at all to level 5 depicting severe disability requiring constant nursing support on bed.[15] It was assessed three months after the stroke had occurred.

Characteristics of participants and the distribution of the vitamin D levels were described by using the descriptive statistics. Relationship of age, gender, severity of stroke and short-term outcome with presence of Vitamin D deficiency was determined by applying the Pearson chi-square test keeping the *p*-values ≤0.05 as significant.

RESULTS

Out of 300 patients of acute ischemic stroke included in the study, 183 (62.3%) were males while 117 (37.7%) were females. 151 (50.3%) of the patients had Vitamin D levels within range while 149 (49.7%) had deficient vitamin levels. In Table-I the basic information regarding study participants was summarized.

Table-I: Characteristics of patients presenting with acute ischemic stroke.

Study Parameters	n (%)
Age (years)	
Mean ± SD	57.543 ± 9.797
Range (min-max)	38-65 years
Gender	
Male	187 (62.3%)
Female	117 (37.7%)
Presence of Vitamin D Deficiency	
Yes	149 (49.7%)
No	151 (50.3%)
Severity of Stroke	
Mild	163 (54.3%)
Mild to Moderately Severe	87 (29%)
Severe	33 (11%)
Very Severe	17 (5.7%)

On National Institutes of Health Stroke scale, 163 (54.3%) had mild, 87 (29%) had mild to moderately severe, 33 (11%) had severe and 17 (5.7%) had very severe symptoms. Statistical analysis revealed that short-term outcome and strove severity had a statistically significant relationship (*p*-value <0.05) with Vitamin D deficiency among patients suffering from acute ischemic stroke (Table-II).

DISCUSSION

Stroke medicine is an evolving specialty in Pakistan with neurologists or internal medicine experts looking after most of the cases for acute or long-term

Table-II: Association of independent variables with vitamin D status.

Socio Demographic Factors	Normal Vitamin D Levels	Vitamin D Deficiency	*p*-value
Age			
50 year or less	77 (50.9%)	68 (45.6%)	0.353
>50 years	74 (49.1%)	81 (54.4%)	
Gender			
Male	99 (65.6%)	84 (56.4%)	0.103
Female	52 (34.4%)	65 (43.6%)	
Severity of Stroke			
Mild	108 (71.5%)	55 (36.9%)	<0.001
Mild to moderate	32 (21.1%)	55 (36.9%)	
Severe	09 (5.9%)	24 (16.1%)	
Very severe	02 (1.3%)	15 (10.1%)	
Short Term Outcome (Levels of Modified Rankin Scale)			
Level 0,1,2	102 (67.5%)	72 (48.3%)	0.001
Level 3,4,5	49 (32.5%)	77 (51.7%)	

management. Rehabilitative services are also limited in bigger cities. Family and caregivers are usually responsible for rehabilitation of such patients. It therefore becomes very important for the treating team to identify the good and bad prognostic features among patients of stroke and inform the patients and caregivers accordingly. General health of the body and getting all the parameters within range really becomes important when a body is under enormous stress like after the stroke. Usually the team gets concerned about managing blood sugar levels, renal functions and blood pressure and few other relevant parameters may be neglected. We designed this study to assess the vitamin D levels among patients presenting with acute ischemic stroke and relationship of these levels with short-term outcome and severity of stroke.

Narasimhan *et al*,[16] performed a randomized controlled trial and observed the impact of vitamin D administration on short-term outcome in patients suffering from stroke. Functional outcome after three months was significantly better in those who were in vitamin D group as compared to those who were in placebo group.[15] Though ours was a cross-sectional study and we did not administer anything to reduce the severity of stroke or improve the functional outcome but our results were similar in a sense that those patients who had good vitamin D reserves had milder severity of stroke and better short term outcome.

Turetsky *et al*,[17] studied volume of stroke lesion on relevant neuro-imaging and its association with vitamin D levels among the patients suffering from acute ischemic stroke. According to their findings, serum vitamin D levels predicted the volume of stroke lesion in the study participants and patients with low levels of vitamin D had a higher volume stroke lesion and later poor short-term outcome.[17] Our results supported their findings in a way that clinical severity of stroke and three months' functional outcome was significantly associated with vitamin D levels of patients.

Another interesting study published in 2016 by Daumas *et al*,[18] found relationship of vitamin D levels and outcome after the acute ischemic stroke. They concluded that functional outcome was statistically significantly better among those with normal vitamin levels as compared to those patients with vitamin D deficiency.[18] Our results were quite similar to their results as almost half of our study participants had vitamin D deficiency and this deficiency emerged as predictor of more severe stroke symptomatology and poor short-term functional outcome.

Yarlagadda *et al*,[19] published a detailed review regarding the impact of vitamin D deficiency on incidence, severity and mortality of stroke. They also analyzed benefits of supplementation of vitamin D in patients suffering from stroke. They could not find the exact pathways related to neuroprotective and stroke recovery enhancing effects of vitamin D but their findings revealed that adequate Vitamin D levels were related to the reduced incidence, severity of stroke and good functional outcome. Our findings generated a baseline data and emphasized on role of vitamin D deficiency in predicting severity and short-term outcome of stroke.

LIMITATIONS OF STUDY

There were few limitations in this study. Our study design could not establish cause and effect relationship and we could not conclude that vitamin D deficiency lead to more severe stroke or poor short-term outcome. Control of DM and HTN etc. was not correlated with the outcome. Researchers in future can use better study design to establish the relationship accurately.

CONCLUSION

Almost half of the patients presenting with acute ischemic stroke had vitamin D deficiency in our study. Those having vitamin D deficiency had more chances of having severe form of ischemic stroke and poor short-term outcome.

Conflict of Interest: None.

Authors' Contribution

NS: Abstract introduction Methodology, discussion, statistical analysis, KMR: Methodology Discussion, SU: Statistical analysis, SK: Discussion, AH: Introduction.

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