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EFFECT OF VITAMIN D LEVEL ON THE PROGNOSIS OF ISCHEMIC STROKE

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ABSTRACT Ischemic stroke (IS) accounts for 85% of overall stroke, and its pathophysiology is regulated by a combination of lifestyle, environmental and genetic risk factors. Vitamin D has garnered a lot of attention as a potential treatment for preventing IS. Due to its role in regulating the expression of neurotrophic factors and preserving the integrity of the blood-brain barrier, vitamin D is also neuroprotective. This study aims to ascertain whether vitamin D supplementation could enhance recovery of ischemic stroke. It was an observational cohort study. Routine laboratory tests were conducted in the hospital laboratory in consecutive patients with acute Ischemic Stroke admitted hospital. Follow-up data for subsequent ischemic strokes were obtained from hospital medical records, which were checked quarterly (3 & 6 months) during and after the entire observation period for the study subject. Outcome and severity were measured on mRS and NIHSS scale respectively. Total of 98 patients (59 males, 39 females) were assessed for various parameters on admission, discharge as well as at 6 months. Out of 98 patients, 91 had good outcome and 7 had poor outcome post stroke severity. This study concludes that patients with normal levels of Vit D on admission have shown better prognosis post ischemic stroke, rather than patients having Vit D deficiency.

KEYWORDS : Ischemic Stroke; Vitamin D; Good Outcome; Poor Outcome; NIHSS; mRS; GCS

INTRODUCTION

Stroke is the major leading cause of long-term disability and mortality globally. It has accounted for nearly 5.7 million deaths globally, and 87% of these deaths occur in low and middle-income countries. (1) Ischemic stroke (IS) accounts for 85% of overall stroke, and its pathophysiology is regulated by a combination of lifestyle, environmental and genetic risk factors. (2)

Vitamin D includes both cholecalciferol and ergocalciferols and is essential for maintaining the homeostasis of calcium and phosphates. It has garnered a lot of attention as potential treatment for preventing IS.(3) Due to its role in regulating the expression of neurotrophic factors and preserving the integrity of the blood-brain barrier, vitamin D is also neuroprotective. (1,2) It enhances synaptic plasticity, (4) reduces brain damage, lowers inflammatory response in ischemic/neurodegenerative disease (5) and reduces oxidative stress. (6) The association between vit D deficiency and stroke severity has been investigated in several studies. (7–11) Vit D may play a significant role in preventing neurological diseases like stroke. Thus, aim of this observational cohort study was to ascertain whether vitamin D supplementation could enhance recovery of ischemic stroke.

METHEDOLOGY

It was an observational cohort study. Routine laboratory tests were conducted in the hospital laboratory in consecutive patients with acute Ischemic Stroke admitted to the Stroke Unit, Department of Neurology at tertiary care hospital, India. Data concerning clinical status, comorbidities, medication, previous ischemic cerebrovascular episodes, cardiovascular risk factors, and laboratory parameter serum vit D level along with blood pressure (BP) were obtained from hospital medical files (routine work-up). Follow-up data for subsequent ischemic strokes were obtained from hospital medical records, which were checked quarterly (3 & 6 months) during and after the entire observation period for the study subject. Retrieval of data from medical reports was approved by the ethics Committee.

The diagnosis of acute IS was based on neurological examination and was supported with computed tomography (CT), after exclusion of other causes of acute neurological deficit (including haemorrhagic stroke), and in accordance with current guidelines.(12) Imaging studies were positive for ischemic changes typical for the acute phase of IS and correlated with clinical symptoms. The course of IS was evaluated based on the severity of neurological deficit in the NIHSS "National Institute of Health Stroke Scale" (13) and functional status at discharge using the modified Rankin scale (mRS).(14) Additional studies determined the probable mechanism of IS, according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification.(15) Patients with haemorrhagic stroke, history of cancer, apparent inflammation, and impairment in activities of daily living before the stroke (ADL less than 5 points in the Katz Index) were excluded from the analysis.Patients with post-schemic stroke who were admitted to a hospital and received Vit D for six weeks as an standard care and treatment. Further, all study subjects were followed up on three months and six months. Serum Vit D3 level including mRS and NIHSS scale were assessed on follow up.

STATISTICS

Quantitative variables were expressed as mean ± standard deviation (SD), whereas qualitative variables were expressed as frequencies and percentages. Comparison between patients and controls was performed using Student t test and association was found using chi-square test as deemed appropriate. p values ≤ 0.05 and ≤ 0.01 were considered significant and highly significant, respectively. Spearman correlation was performed to find correlation between vitamin D and NIHSS, GCS and mRS scores. We assessed vitamin D cut-off levels for poor stroke outcome in our study sample using the receiver-operating characteristic (ROC) analysis in figure2. All Statistical test including ROC curve analysis was performed using the STATA. 12.0.

RESULTS

Our sample population consisted of 98 patients (59 males, 39 females) who were assessed for various parameters on admission, discharge as well as at 6 months. At admission, they were evaluated for baseline characteristics such as age, gender, systolic and diastolic BP, hypertension, diabetes, Vit D levels and stroke severity using NIHSS, mRS and GCS scales. Outcome/prognosis was assessed using mRS scale after 6 months. Those with mRS scores 3 at 6 months were considered to have poor outcome. (16)

The age of the study population varied from 19-97 years (Mean age: 60.72±16.47 years). In this study, we have divided and compared the

sample population into two groups based on outcome. Out of 98 patients, 91 had good outcome and 7 had poor outcome shown in figure 1. It was found that the age, systolic BP and diastolic BP were comparable in both the groups at the time of admission. Also, Vit D levels and NIHSS were comparable in both the groups at the time of admission. Those with poor outcome had significantly worse GCS and mRS scores at the time of admission (p=0.0295 and p=0.0001 respectively) illustrated in table 1. Stroke severity and prognosis were analyzed showing in table 2 that mRS scores were significantly worse in poor outcome group at the time of discharge as well as after 6 months (p= 0.0000).

25-OH Vit D3 levels were further classified as deficiency<20 ng/ml, insufficiency 20-29 ng/ml, sufficiency ≥ 30 ng/ml.(3) Vitamin D levels at admission were found to be significantly associated with outcome (Chi^2 value= 7.21, p=0.0272). Relative risk of vit D deficiency with outcome was found to be 6.25 (p value =0.023, CI: 1.29 to 30.35) illustrated in table 3. Other factors such as age, hypertension and diabetes were not associated with outcome. Whereas, diabetes was found to be associated with Vit D level (p=009) and hypertension (p=0.02). Hypertension was associated with age (p=0.04). Vit D levels at admission and at 6 months had no association/correlation with severity of stroke (GCS, mRS or NIHSS scales). Outcome/mRS scores after 6 months had significant negative/positive correlation with GCS (p=0.001), NIHSS (p=0.0002) and MRS scores on admission (p=0.0000) as well as MRS scores on discharge (p=0.0000).

DISCUSSION

Vit D deficiency has been identified in literature studies as a separate risk factor for stroke, and greater the negative functional outcomes (short- and long-term) of IS severity get worse underlining the possible need for Vit D supplementation for stroke treatment.(17–20) The present study showed that patients with good outcome and poor outcome (based on mRS scores after 6 months) had significant difference in GCS scores at admission, mRS at admission and mRS at discharge. However, they had comparable Vit D levels at admission in the study population. Vit D levels at admission (deficiency<20 ng/ml, insufficiency 20-29 ng/ml, sufficiency ≥ 30 ng/ml) were significantly associated with outcome (p=0.02). Relative risk of vit D deficiency with poor outcome = 6.16 (P value =0.024) and Vit D levels on admission were not associated with severity of stroke (NIHSS). mRS scores after 6 months /outcome had significant correlation with GCS, NIHSS and mRS scores on admission as well as mRS scores on discharge. Our finding of diabetes and hypertension having significant association with Vit D is in line with a study that reported these diseases are major risk factors for lacunar stroke, the effects of vitamin D deficiency may explain this strong association with IS. (21)

A randomized control trial based on two group of IS found a highly significant (p=0.001) improvement in the stroke outcome after three months in patients who were supplemented with vit D.(22) A more population based cohort study reported, that lower vit D levels do not lead to a higher stroke risk but consequence for poor prognosis. It also suggests that severe Vit D deficiency was associated with stroke incident.(23)

However, Vit D mechanism against IS has yet to be fully understood and few neuroprotective mechanisms have been proposed such as; Vit D can promote the expression of insulin-like growth factor 1 (IGF-1) which has neuroprotective action and antithrombotic capability. (7,8,17,22,24) Although, diabetes may have some association with Vit D and stroke as a confounding variable too.(25,26) Impartial of age and functional ability, severe Vit D deficiency may an emerging, significant risk factor for prognosis and survival post IS. Vit D supplementation may be considered for prognosis and survival in stroke patients. (27)

The neuroprotective pathway and mechanism of Vit D in stroke onset is not studied in detail and has mixed evidence in previous studies. It can't be denied that Vit D plays a vital role in defense mechanism of neurons and better prognosis of IS and some other neurological disorders. This suggests it would be highly essential to monitor serum Vit D level in stroke patients as a supplement.

CONCLUSION

This study concludes that patients with normal levels of Vit D on admission have shown better prognosis post ischemic stroke, rather than patients having Vit D deficiency. Based on the findings of this study, vitamin D supplementation might be a useful, affordable, and safe way to enhance prognosis and reduce the risk of stroke. Further, more robust design and large population clinical trial should be conducted, which may give more evident data to establish relation between Vit D and IS.

Table 1: Baseline characteristics of study

	Good outcome (n=91)	Poor outcome (n=7)	T value	P value
Age	60.84±18.48	59.28±19.69	0.21	0.83
Systolic BP	140.07±17.99	138.71±19.66	0.19	0.84
Diastolic BP	88.98±9.41	91.71±7.22	-0.74	0.45
Vit D at admission	33.51±21.31	19.85±14.57	1.66	0.10
GCS on admission	12.02±2.56	9.66±1.75	2.21	0.02
NIHSS on admission	17.75±8.41	23.50±6.18	-1.64	0.10
mRS at admission	2.93±1.05	4.57±0.78	-4.02	0.001

Table 2: Stroke severity and prognosis at discharge and after 6 months

	Good outcome (n=91)	Poor outcome (n=7)	t value	p value
mRS on discharge	1.69±0.96	3.5±0.84	-4.48	0.001
mRS at 6 months	1.17±0.69	3.72±1.11	-8.91	0.001
Vit D after 6 months	76.05±15.80	73.14±17.63	0.46	0.64

Table 3: Association of Vit D levels at admission with outcome

	Good outcome	Poor outcome	Total
Vit D levels adm (ng/ml)	MRS at 6 months <=2	MRS at 6 months >=3	
Deficiency <20	23	5	28
Insufficiency 20-29	23	0	23
Sufficiency >=30	45	2	47
Total	91	7	98

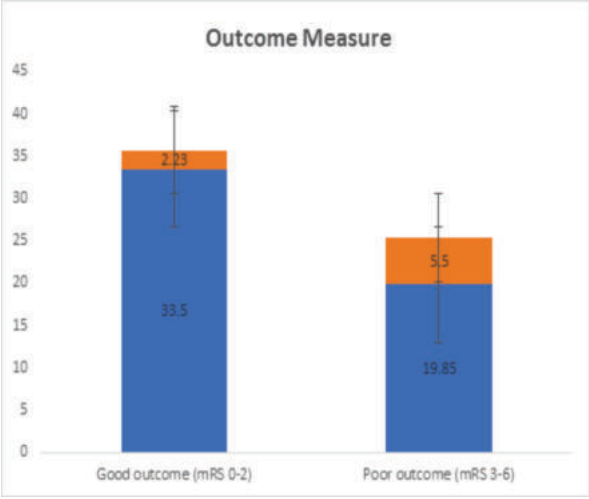

Figure 1. Study outcome measures based on mRS at 6 months

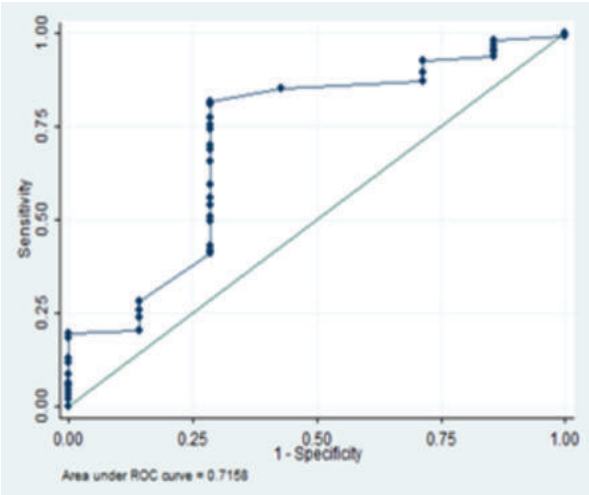

Figure 2. ROC curve for Vit D associated with good and poor outcome.

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