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### RESEARCH ARTICLE

#### ISCHEMIC STROKE(CVA) AND VITAMIN-D LEVEL

Dr. Atanu Ghosh<sup>1</sup>, Dr. Pranabes Charaborti<sup>2</sup> and Dr. Bibhas Shil<sup>2</sup>

1. Associate Professor, Department of Medicine, Agartala Government Medical College(AGMC), GB Pant Hospital(GBPH), Kunjaban, Agartala, Tripura - 799006.
2. Senior Resident, Department of Medicine, Agartala Government Medical College(AGMC), GB Pant Hospital(GBPH), Kunjaban, Agartala, Tripura - 799006.

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#### Abstract

Vitamin D(25-hydroxyvitaminD), a neuroprotective prohormone, is associated with neurological disorders in particular ischemic stroke. In ischemic stroke patients lower than normal vitamin D level is more prevalent and number of male patients had low vitamin D as compared to number of female patients. Statistically significant, vitamin D in low level range was found in ischemic stroke with diabetes mellitus than patients with normal blood glucose level. Elevated CRP level was also found in those patients who had low vitamin D level. Compared to normotensive stroke patients, decreased value than normal vitamin D range were found in patients having hypertension. Ischemic stroke with associated dyslipidemia patients had low levels of vitamin D as compared to patients with normal lipid. Deficient levels of vitamin D were found mostly in age group more than 60 years.

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#### Introduction:-

Vitamin D(25-hydroxyvitaminD[25(OH)D]) (VTD), the “sunshine vitamin” is in recent days implicated with neurological disorders which includes important public health problem like stroke, though it is commonly known for bone metabolism and calcium homeostasis related disorders and findings from recent study, suggested that Vitamin D is a neuroprotective prohormone<sup>1,2</sup>.As reported by Peter Brøndum-Jacobsen et al., from Copenhagen city heart study, out of 10,170 individuals, in whom 25-hydroxy vitamin D measurement done, on 21 years follow up,1256 and 164 persons developed ischemic and hemorrhagic stroke respectively. Meta-analysis of ten studies on ischemic stroke, out of 56,384 participants there were 2,644 events. It was commented that stepwise decreasing plasma 25-hydroxy vitamin D concentrations were associated with stepwise increasing risk of ischemic stroke both as a function of seasonally adjusted percentile categories and as a function of clinical categories of 25-hydroxy vitamin D<sup>3</sup>.

In India reported prevalence rate of Vitamin D deficiency in general population is 70-100%, reaching an epidemic<sup>4,5</sup>.

Observation of relationship of VTD level, CRP(C-reactive protein) and ischemic CVA(cerebrovascular accident - stroke), Daniel Frizon Alfieri et al., from a study, reported the association of low levels of 25(OH)D and higher hsCRP, in regard to poor short-term outcome in acute ischemic stroke patients.It was suggested that the importance of VTD level, in the inflammatory response and ischemic event pathophysiology<sup>6</sup>.Framingham study by Natalia S Rost et al., commented that raised plasma CRP levels has significant predictability for the risk of future ischemic stroke and transient ischemic attack(TIA)<sup>7</sup> in elderly. Acute ischemic stroke leads to elevated CRP level, which is

**Corresponding Author:- Dr. Atanu Ghosh**

Address:- Associate Professor, Department of Medicine, Agartala Government Medical College(AGMC), GB Pant Hospital(GBPH), Kunjaban, Agartala, Tripura - 799006.

induced as an inflammatory response. Due to inflammatory reaction or tissue damage, elevated CRP level may be related to adverse outcome<sup>8</sup>. Genetically predicted serum 25(OH)D had an L-shaped association with serum CRP, where CRP level decreased sharply with increasing 25(OH)D concentration for participant within the deficiency range (25nmol/L) and levelled off at ~50nmol/L of 25(OH)D<sup>9</sup>.

### Materials and Methods:-

This study was done in a tertiary care medical institution in northeast India from February, 2021 to June, 2023. It is a non-blinded study. Both male and female ischemic CVA (Cerebrovascular accident- Stroke) patients were included in this study. One hundred five patients of age group of forty years to eighty-five years who were found to have ischemic stroke, were included in this study. Distribution of diabetes and hypertension also recorded among study patients. CRP level also measured in ischemic stroke patient included in this study. Vitamin D levels were estimated on Fluorescent Immunosorbent assay (CLIA) method and categorized on level basis, like sufficiency-(normal) 30 - 100ng/ml, insufficiency 10 -29.9ng/ml, deficiency <10ng/ml.

Stroke patients are clinically assessed for diagnosis and confirmed by Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI) of brain. Simple randomization of patients done on the basis of inclusion and exclusion criteria.

Approval of the institutional ethical committee was taken.

### Result:-

Out of 105 patients of ischemic (CVA) stroke, who were included in this study, 79 patients were found to have vitamin D (VTD) insufficient, whereas 08 patients were vitamin D deficient and normal vitamin D level recorded in 18 patients. This constitutes 75.2%, 7.6% and 17.1% in vitamin D insufficient, deficient and normal range patients respectively.

Among 105 patients, CRP values elevated, in 22 patients, normal in 83 patients. Out of elevated CRP level patients 17 patients were in the VTD insufficient group, 01 patients were in VTD deficient group.

In the study group 60 patients were found to have diabetes. In the diabetics 05 patients had normal VTD level, whereas 47 patients had insufficient range level and 08 patients had deficient VTD level. The p value is .002, which is statistically significant.

In our study we could find elevated level of CRP in VTD insufficient 17 patients and 1 deficient patient and 14 normal VTD patients, whereas CRP was normal in 62, 07 and 14 in the respective group.

In the hypertensive ischemic stroke group, 87 patients were hypertensive and among them 06 patients were in the VTD deficient group, 66 were in the insufficient range and 15 patients had normal level.

Out of 105 patients 81 patients were dyslipidemic. Number of patients in the dyslipidemic group VTD level were found to have normal, insufficient and deficient range were 11, 62 and 08 respectively.

As far as sex distribution is concerned among 71 male and 34 female study population, 08 female and 02 male were vitamin D deficient, 20 female and 59 male were in the insufficient range, normal level in 08 female and 10 male. (p value .008)

In our study we could find insufficient VTD level out of 105 patients, 17, 25 and 37 in 40-49 years, 50-59 years and >60 years age group and deficient level were 0, 7 and 1 patient in the previous mentioned age group where as normal level were 0, 3 and 15 in the previous mentioned age group, (Linear-by Linear Association df 1, Asymp. Sig. .005)

### Discussion:-

In Indian population Vitamin D (VTD) deficiency is extremely common and various study reports has implicated VTD with diseases involving neurological, cardiovascular, renal systems, and autoimmune, infectious, malignant diseases<sup>10,11,12,13</sup>. Increased prevalence of stroke, diabetes, high blood pressure, dyslipidemia is associated with low VTD level<sup>14</sup>.

Among ischemic CVA patients VTD level were normal in 17.1% patients whereas percentage of patients having deficient level and insufficient level were 7.6% and 75.2% respectively, which is consistent with the findings of Peter Brøndum-Jacobsen et al<sup>3</sup>, that increasing risk of symptomatic ischemic stroke when plasma VTD level is decreasing, but in our study more ischemic strokes were with the patients having VTD insufficient range rather than deficient range<sup>2</sup>. The Rotterdam study reported VTD, which is a neuroprotective prohormone, severe deficiency of which did show a significant association with stroke<sup>15</sup>. Near similar findings we could see from our study. Similar findings as revealed in our study regarding association of ischemic stroke with low level of VTD was also reported from meta-analysis by Ren Zhou, Mengying Wang et al. where they concluded with the remarks that lower VTD status was associated with increased risk of ischemic stroke<sup>16</sup>. But from our study findings we are not in agreement with the study by Anu Gupta et al., where they concluded with the remarks that Vitamin D deficiency has no association as far as ischemic stroke or its risk factors are concerned<sup>17</sup>.

In our study we could find statistically significant findings of low level of VTD (p value .002), in diabetic patients presented with ischemic stroke, as compared to non-diabetics. Opinion by Scragg R et al., from NHANES III analysis, demonstrated that there was strong inverse association between levels 25(OH)D and diabetes prevalence, which has positive relevant findings with our study<sup>18</sup>. Meta-analysis and review done by Pittas et al., commented with the conclusion that the insufficient vitamin D and calcium appears to hinder glycemic control and supplementation of both may be necessary to optimize glucose metabolism<sup>19</sup>. Basir Ahmad Loway et al., commented from their study that vitamin D deficiency common in patients with type 2 DM<sup>20</sup>. Kayaniyil et al., came into conclusion, from their study, in regard to vitamin D, insulin resistance, beta cell function, that low vitamin D level may play significant role in the pathogenesis of T2DM (Type 2 Diabetes Mellitus). In accordance with such findings, from our analysis, high likely, that diabetes with ischemic stroke patient had low VTD as compared to non-diabetics<sup>21</sup>. Chiu KC et al., also gave opinion in regard to T2DM, VTD deficiency is related to insulin secretion, insulin resistance and  $\beta$ -cell dysfunction in the pancreas<sup>22</sup>.

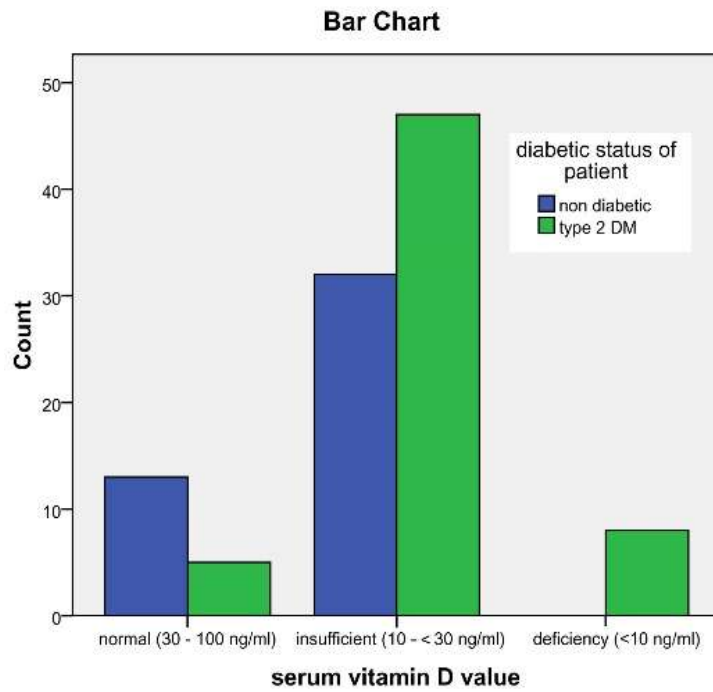
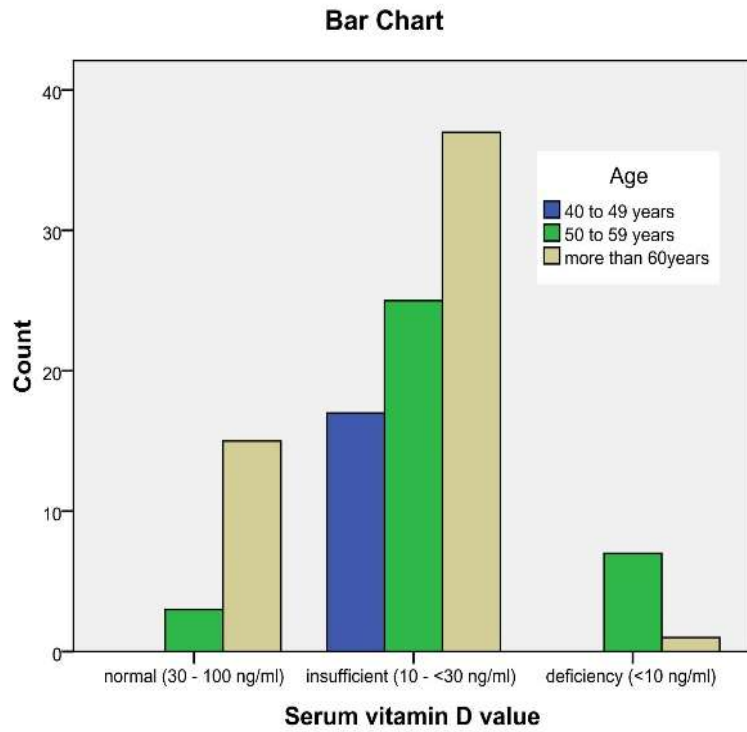
Number of male ischemic CVA patients with low VTD level were more as compared to the female counterpart (p value .008). Similar relevant conclusion drawn by Anita Subramanian et al., from a study, that severe vitamin D deficiency in Asian Indian with T2DM compared with non-diabetic patients and that more men with T2DM are affected with vitamin D deficiency than women<sup>23</sup>.

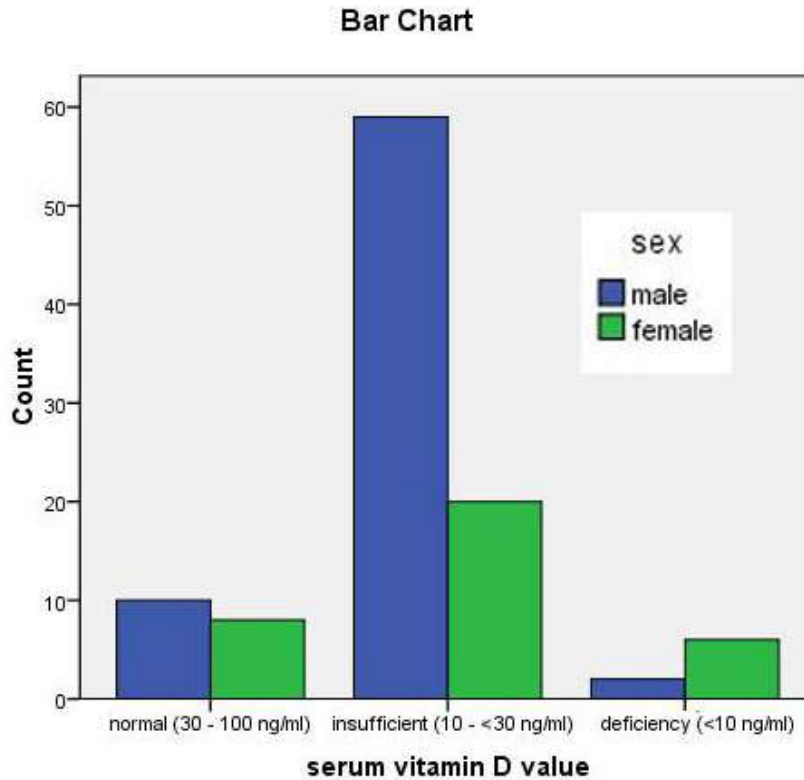
When patients were suffering from chronic disease, Hypertension, associated with cardiovascular complications, it was appeared that VTD levels in the body indirectly modulated blood pressure<sup>24</sup>. John P Forman et al. from a study reported regarding the inverse relationship between plasma 25(OH)D levels and risk of incident hypertension<sup>25</sup>. In our study we also got low level of VTD level in hypertensive ischemic stroke patients as compared to normotensive patients.

In ischemic stroke patients, VTD level were more in age group of more than 60 years and then among 50 to 59 years. From the literature it was reported as an inverse relationship between VTD levels and 1 year mortality for ischemic stroke patient younger than 75 years of age and after adjusting for other risk factors, although the association between death and VTD deficiency was no longer observed for patients aged more than 75 years<sup>26</sup>.

In regard to low VTD and dyslipidemia, studies from China among 3788 adults, it was concluded that serum 25(OH)D was inversely correlated with LDL cholesterol and triglyceride level and positively correlated with HDL cholesterol level<sup>27</sup>. We got similar findings in our study, that the number of patients having dyslipidemia were more with low level of VTD, as compared to normal VTD level (Likelihood ratio .038, Linear by Linear association .026).

Charts, Tables, Bars.





Serum Vitamin D value	Diabetic Status of Patient		Total
	Non-Diabetic	Type 2 DM	
Normal (30 - 100 ng/ml)	13	5	18
insufficient (10 - <30ng/ml)	32	47	79
Deficiency (<10 ng/ml)	0	8	8
Total	45	60	105

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	12.516a	2	.002
Likelihood Ratio	15.489	2	.000
Linear-by-Linear Association	12.262	1	.000
N of Valid Cases	105		

**Conclusion:-**

Low VTD level is more prevalent in ischemic stroke patients and more so in male patients compared to female patients. Diabetic patients when presented with ischemic CVA, the number of patients with low VTD level outnumbered the non-diabetic patients. Ischemic stroke patients with hypertension, dyslipidemia and high CRP level found to have decreased than normal VTD level in comparison to normotensive normolipemic patients. Further studies with large number of patients are required to establish these findings more rigidly.

**Conflict of Interest :**

Nil.

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