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The level of Vitamin D, serum Calcium, serum Phoshorous and Alkaline Phosphatase level in individuals with Stroke in Jharkhand.

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Aim And Objective: To study the level of Vitamin D, serum Calcium, serum Phoshorous and Alkaline Phosphatase level in individuals with Stroke in Jharkhand

I. Introduction

Stroke is one of the leading causes of death and disability in India. The estimated adjusted prevalence rate of stroke range,from 84 to 262/100,000 in rural and 334-424/ 100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population based studies .Stroke has a heterogeneous etiology, caused by modifiable and un-modifiable risk factors. It is becoming an important cause of premature death and disability in low-income and middle-income countries like India, largely driven by demographic changes and enhanced by the increasing prevalence of the key modifiable risk factors

Ever since its discovery vitamin D has been associated with mineral homeostasis and musculoskeletal health through its actions on intestine,bone and kidney.. Recent literatures describes the association between low level of vitamin D and cardiovascular disease, peripheral vascular disease diabetes, hypertension, multiple sclerosis, various cancers etc. Cerebrovascular disease (CVA), which has a similar pathophysiology like other macrovascular diseases, is an important cause of mortality and morbidity all over the world. Although various modifiable and non-modifiable factors are described to be etiologically related to CVA, little is known about the effect(s) of vitamin D on CVA. A poor vitamin D status is now recognized as a public health problem affecting almost every second person worldwide. Rates of vitamin D deficiency and cardiovascular disease increase with distance from the equator, with higher rates of ischemic heart disease noted in countries with lower levels of ultraviolet B exposure . Vitamin D levels have been shown to be seasonal, with higher levels in summer , and the rate of ischemic heart disease candisplay similar seasonal patterns.. Studies from India have uniformly pointed to low 25(OH) D levels in Indian population in all age groups and in all regions, despite plenty of sunshine. Indian epidemiological data also reveals high age- standardized prevalence and annual incidence rates of first- ever stroke in Indians as compared to non- Asian populations. Hence, it was interesting to explore the association between the two.

Materials And Methods - The study was approved by The Institutional Ethics Committee Rajendra Institute of Medical Sciences, Ranchi.
STUDY DESIGN: Cross sectional descriptive type.
PERIOD OF STUDY:
The period of study was from Sep 2015 to October 2016.

SAMPLE SIZE: 102
INCLUSION CRITERIA:
1. Should be a newly diagnosed stroke patient
2. Age .30-90 years.
3. Sex male or female.
4. Should readily agree to participate in the study with an informed consent.

EXCLUSION CRITERIA:

1. Non cooperative subjects.
2. . Any serious comorbid illness like septicaemia
3. . Cerebral malaria
4. Chronic liver disease
5. Meningitis
6. Chronic kidney disease
7. Known case of cerebral arterio-venous malformation

II. Results And Observations

The mean age was 57.9years. Age, body mass index were similar in distribution among cases and controls.

The mean serum vitamin D level in the stroke patients was m 21.27ng/ml and in the control group was28.45 ng/ml. Vitamin D deficiency was seen in (50)stroke patients and in% (27) of the control group (P value <0.001)..In case and control sufficient vitamin D present in 92.6%of control and 7.4% of hemorrhage. ,Insufficient vitamin D present in 52% of control and44%of hemorrhage and 4%of ischemic stroke, and low vitamin D 4% of control and4% of hemorrhage and 92% of ischemic stroke. p value is highly significant < 0.001.Mean of vitamin D in case is 21.27ng/ml and in control 28.77ng/ml and sd is 6.5.

vitD_new * Type of stroke Crosstabulation

			Type of stroke			
			No Stroke	Haemorrahage	Ischemic Stroke	Total
vitD_new	Sufficient	Count	25	2	0	27
		% within vitD_new	92.6%	7.4%	0.0%	100.0%
	Insufficient	Count	26	22	2	50
		% within vitD_new	52.0%	44.0%	4.0%	100.0%
	Low	Count	1	1	23	25
		% within vitD_new	4.0%	4.0%	92.0%	100.0%
Total		Count	52	25	25	102
		% within vitD_new	51.0%	24.5%	24.5%	100.0%

vitD_new * Type of stroke * Sex Crosstabulation

				Type of stroke			
Sex				No Stroke	Haemorrahage	Ischemic Stroke	Total
Female	vitD_new	Sufficient	Count	14	1	0	15
			% within	80.3%	15.7%	4.0%	100.0%
		Insufficient	Count	11	9	2	22
			% within	70.0%	20.9%	9.1%	100.0%
		Low	Count	0	0	15	15
			% within	0.0%	0.0%	100.0%	100.0%
	Total		Count	25	10	17	52
			% within	48.1%	19.2%	32.7%	100.0%
Male	vitD_new	Sufficient	Count	11	1	0	12
			% within	91.7%	8.3%	0.0%	100.0%
		Insufficient	Count	15	13	0	28
			% within	53.6%	46.4%	0.0%	100.0%
		Low	Count	1	1	8	10
			% within	10.0%	10.0%	80.0%	100.0%
	Total		Count	27	15	8	50
			% within	54.0%	30.0%	16.0%	100.0%
Total	vitD_new	Sufficient	Count	25	2	0	27
			% within	92.6%	7.4%	0.0%	100.0%
		Insufficient	Count	26	22	2	50
			% within	52.0%	44.0%	4.0%	100.0%
		Low	Count	1	1	23	25
			% within	4.0%	4.0%	92.0%	100.0%
	Total		Count	52	25	25	102
			% within	51.0%	24.5%	24.5%	100.0%

p=0.001(significant)

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
ca_r * condition	102	100.0%	0	0.0%	102	100.0%

ca_r * condition Crosstabulation

			condition		
			0	Case	Total
ca_r	1.1-1.4	Count	38	3	41
		% within ca_r	92.7%	7.3%	100.0%
	<1.1	Count	14	47	61
		% within ca_r	23.0%	77.0%	100.0%
Total		Count	52	50	102
		% within ca_r	51.0%	49.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	47.710[a]	1	.000		
Continuity Correction[b]	44.960	1	.000		
Likelihood Ratio	54.179	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	47.242	1	.000		
N of Valid Cases	102				

Ionized calcium mean in control is 1.1mmol/l and in case 0.86 mmol/l with sd.17.low ionized calcium in 77% of cases and 23% of control.Normal ionized calcium in 93% of control and7% of cases. p value is highly significant < 0.001

III. Discussion

Vitamin D acting through vitamin D receptor (VDR) leads to calcium and phosphate absorption from intestine, reabsorption of the same from kidney, suppression of parathyroid hormone secretion thus maintaining bone-mineral health[35].

At the cellular level presumably through VDR, vitamin D promotes cell differentiation and inhibits cell proliferation[40]. Similarly it influences proliferation of vascular smooth muscles along-with their migration and gene expression. It also influences elastogenesis and immunomodulation. All these are processes involved in the pathogenesis of atherosclerosis[41]Stefan Pilz, in his study[48]concluded that low levels of 25(OH)D and 1,25(OH)2D are independently predictive for fatal strokes, suggesting that vitamin D supplementation is a promising approach in the prevention of strokes. In line with the foundation works by Stefan Pilz and Kenneth E.S. Poole, our study has also found vitamin D deficiency to be highly prevalent in CVA patients. About 95% (36 of 38) of our study population was below sufficiency level for vitamin D. Poole et al[44] mentions that the half-life of 25(OH)vitamin D3 is approximately 3wks.

Acutely reduced 25OHD attributable to a decline in hormone synthesis or existing stores (largely found in body fat) seems unlikely because there was no relationship between serum 25(OH)D and time between stroke and 25(OH)D sampling. So it seems likely that this deficiency has been present from before the stroke. The mean level of vitamin D in our study (20.01 ng/ml) was higher than what Stefan Pilz found (27.5 nmol/L or 11.01 ng/ml) despite higher percentage of females (38.1% to 28.94%) in his study. Several explanations seem likely. Mean age of LURIC study stroke patients was 69.3yrs (64-76yrs) whereas our CVA patients had a mean age 60.55yrs (35-85yrs) .Thus age 268 could be a confounding factor. Percentage of diabetics in LURIC study

stroke patients was 50% compared to 26.3% in our CVA patients. As diabetics have a lower mean vitamin D level this may have confounding effect as well. Adding to these is the higher sun exposure in jharkhand as it is at lower latitude than Germany where LURIC study was performed. Also because of hot and humid weather people of jharkhand prefer wearing loose fitting clothes with higher percentage of exposed body part which further increase the sun exposure and hence the subsequent vitamin D level. Despite finding lower vitamin D level in our CVA patients we must also keep in mind Indian people are especially prone to develop vitamin D deficiency because of dietary inadequacy (Khadilkar AV[49]) , vegetarian diet, genetic factors (Awumey et.al[51]), cultural beliefs, repeated unplanned pregnancies, growing urbanization, pollution (Babu et.al[50]) as is described by DrVikram Londhey[52]in his article 'Vitamin D deficiency , Indian scenario'.

However 50% of our study population had low serum calcium level. Mean ionized calcium of our study is lower (0.86mmol/l, range 1.1to1.4) than the lowest value found by Stefan Pilz (mean 2.33 mmol/L, i.e. 9.32mg/dl, range 2.24-2.43 mmol/L, i.e. 8.96-9.72 mg/dl).

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. Vitamin D level was also compared between male hypertensive or non-hypertensive and male diabetic or non-diabetic CVA patients, similar comparison was done for female CVA patients as well. Urban CVA patients was divided into hypertensive or non-hypertensive subgroups and diabetic or nondiabetic subgroups for comparison of their vitamin levels. Two major types of CVA patients, intra-cerebral hemorrhage (ICH) and infarct were divided into hypertensive or non-hypertensive and diabetic or non-diabetic group. Except between male diabetic or non-diabetic subgroup none of these comparisons yielded significant result. This means vitamin D level is low irrespective of the blood pressure or diabetes status. We propose further studies to be done on vitamin D, parathormone, calcium and phosphate levels in acute stroke patients to make any further comments.

In our study, we found a significant association between 25- hydroxyvitamin D deficiency and ischemic stroke and established an independent association. Similar results have been found from the western part of the world.2,3,23-26 25 A recent study showed low 25-hydroxyvitamin D was significantly associated with increasing intimal media thickness and carotid plaques in individuals.27 We also found a significant association of 25-hyroxyvitamin D deficiency with cardioembolic stroke. Several studies have shown a strong association of vitamin D deficiency with cardiovascular disease.28-30 Giovannucci et al.[46] demonstrated low levels of 25-hydroxyvitamin D as a high risk factor for myocardial infarction. Lower 25-hydroxyvitamin D concentration was shown to be an independent risk factors for atherosclerosis, coronary calcification and cardiovascular death. However some studies have found no association between vitamin D and cardiovascular disease.

In our study we also observed significantly higher proportion of stroke patients with elevated levels of alkaline phosphatase and decreased phosphate levels compared with control subjects. This is advocated by Nibet et al.[57] and Preece et al.[58]

IV. Conclusion

This study established that deficiency of 25-hydroxyvitamin D had an independent association withstroke. Among stroke patient ischemic stroke was associated with low25-hydroxyvitamin D and haemorrhageic stroke with insufficient25-hydroxyvitamin D level. Vitamin D deficiency in stroke patient manifeseted as low calcium and low phosphate and high ALP. A single serum measurement of this compound could be a useful marker in epidemiologic studies.However it is equally insufficient in age, sex matched controlpopulation. The role of vitamin D deficiency as a direct causative factor of stroke has to be established for advocating vitamin D usage for stroke prevention. Large scale interventional studies are required to confirm these findings.

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