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STUDY RELATIONSHIP BETWEEN LEVEL OF VITAMIN D AND ACUTE ISCHEMIC STROKE

General Medicine

Dr. Patel Parthkumar Pravinbhai	PG Resident, Dept. of General Medicine, National Institute of Medical Sciences, Jaipur; Rajasthan.
Dr. Rakesh Thakuriya	Professor, Dept. of General Medicine, National Institute of Medical Sciences, Jaipur; Rajasthan.
Dr. Vibha Patel	PG Resident, Dept. of Pathology, Gujarat Adani Institute of Medical Sciences, Bhuj, Gujarat.

ABSTRACT

Numerous documented risk factors for stroke exist, including smoking, diabetes mellitus, systemic hypertension, dyslipidaemia, and atrial fibrillation. Considered to be amongst the newest risk factors is vitamin D. Our major goal was to determine the levels of serum 25-hydroxyvitamin D in people who had previously experienced an ischemic stroke and how it linked to the severity of an acute ischemic stroke. **Methods:** The research was carried out at the NIMS Hospital in Jaipur, Rajasthan, in the neurology department. The investigation was conducted over a period of 18 months. 160 people participated in the research study. Patients have had to meet the individual stroke confirmation by brain CT/MRI as criteria for inclusion for the study protocol. Additionally, participants with any transitory incidents or a history of stroke were disqualified from the trial. **Result:** When compared to the overall mean value of controls, which was reported to be 21.663ng/ml, stroke patients exhibited a significant deficiency in vitamin D, with an average value of 13.54ng/ml. The patients under 50 were found to have substantially lower vitamin D levels. **Conclusion:** This research concluded that acute ischemic stroke patients had substantial vitamin D insufficiency. Therefore, having insufficient amounts of vitamin D could be a significant contributor to ischemic stroke.

KEYWORDS

Acute Ischemic Stroke, Vitamin D, Transient attacks.

INTRODUCTION

A stroke is described as an abrupt onset neurological deficit with a focal vascular cause. Stroke is the third leading cause of death in developed nations, behind heart disease and cancer, and is now widely recognized as the most prevalent preventable neurological condition that poses a serious risk of death. It significantly affects morbidity and mortality in both wealthy and developing nations [1]. Stroke has a major clinical and socioeconomic impact and is one of the most common causes of mortality and disability in the world. Its pathogenesis is varied, with modifiable risk factors including hypertension, diabetes mellitus, dyslipidaemia, sedentary behaviour, and smoking coexisting with unmodifiable risk factors like genetics, age, and sex [2].

As a result, the diagnosis of stroke must be supported by laboratory research, including brain imaging1. After heart disease and cancer, cerebrovascular disease is the third greatest cause of death in developed nations. It is also quickly becoming the most prevalent preventable neurological condition that can be fatal. Haemorrhagic stroke and ischemic stroke are two of the three main types of stroke. Haemorrhagic stroke occurs when a blood vessel bursts, causing blood to flood into the cerebral cavity, while ischemic stroke is caused by a blood vessel obstruction, which reduces the blood supply to the brain. The type of haemorrhagic stroke may be intracerebral haemorrhage or subarachnoid haemorrhage, depending on where the blood was spilled. Ischemic strokes account for 60–80% of all strokes. It significantly affects morbidity and mortality in both wealthy and poor nations. One of the fat-soluble steroid hormones, vitamin D regulates calcium and phosphate levels and maintains the health of the musculoskeletal system. In the presence of ultraviolet radiation, the epidermal layer of the skin produces vitamin D from 7-dehydrocholesterol. After then, it goes through two hydroxylation processes: inactive vitamin D is first converted to 25-hydroxyvitamin D in the liver, and then traditionally 1,25-dihydroxyvitamin D3 is produced in the kidney by 1-hydroxylase (CYP27B), which makes it biologically active. Macrophages, T cells, and neurons can also go through the second hydroxylation stage [3, 4]. On immune system performance and inflammation, vitamin D has a significant regulatory role [5]. . Numerous ailments, including problems with calcium metabolism, type 2 diabetes, autoimmune disorders, cardiovascular disease, stroke, multiple sclerosis, as well as various infectious diseases and malignancies, have been linked to low vitamin D levels [6, 7].

When compared to healthy controls, acute stroke patients' serum vitamin D levels were shown to be low [8, 9]. The regulation of brain development, function, and cerebrovascular physiology depend on vitamin D [10]. It has been associated with the ability to prevent hypertension by reducing the progression of atherosclerosis, enhancing endothelial function, and suppressing the renin-angiotensin-aldosterone system. As a result, its lack may contribute to the onset of a number of illnesses, including as diabetes, hypertension, heart failure, ischemic heart disorders, and stroke [11]. Additionally, a vitamin D shortage affects vascular remodelling through regulating the proliferation of smooth muscle cells, inflammation, and thrombosis. Stroke may eventually result from these vascular alterations [12].

The results of various studies, however, indicated that vitamin D deficiency is a risk factor for stroke; yet, the relationship between the amount of vitamin D and the severity and outcome of a stroke has not been well studied. The purpose of this study is to investigate the serum vitamin D levels in cerebral stroke patients and determine whether a vitamin D deficit is associated with stroke severity and outcome [13].

MATERIAL AND METHODS

Study Design: This study is of the case-control variety.

Study Area: The study will be carried out at the National Institute of Medical Sciences and Research in Jaipur, Rajasthan, in the department of General Medicine.

Study Period: 1st January 2021 to 30th June 2022.

Time Frame: 18 months.

SELECTION CRITERIA OF PATIENTS:

Inclusion Criteria

1. Age 18 years and above.
2. Diagnosis of stroke is confirmed by CT/MRI Brain.
3. Patients presents within 48hr of onset of symptoms.
4. Willing to participate in the study.

Exclusion Criteria

1. History of Transient Attacks and prior stroke.
2. Patient of Haemorrhagic stroke.
3. Patient with history of malignancy.
4. Patient with known case of chronic kidney disease.
5. Patient with known case of coronary artery disease.
6. On drugs that affect Vitamin D metabolism (Anti epileptics,

Steroids, Rifampin).
7. Patient receiving Vitamin D supplementation.
8. Pregnant, lactating and menopausal females.

METHODOLOGY AND TECHNIQUE:

- This study is of the case-control variety. All indoor and outdoor patients who are 18 years of age or older and meet the inclusion and exclusion criteria in the department of General Medicine at the NATIONAL INSTITUTE OF MEDICAL SCIENCES & RESEARCH & HOSPITAL, JAIPUR, RAJASTHAN, participated in this study for a period of 18 months.
- All study participants will be required to provide written consent.
- In this hospital-based case-control study, a total of 160 people will be enrolled, of whom 80 patients will be selected as cases who were diagnosed with their first-ever ischemic stroke based on their CT or MRI report and admitted within 48 hours of the stroke in the General Medicine ward at the National Institute of Medical Sciences and Research, Jaipur, Rajasthan.
- The remaining 80 healthy, ambulatory patients who fulfil the criteria for age and sex will be enrolled and designated as the control group. On admission, the CANADIAN STROKE SCALE will be used to evaluate the initial stroke severity.
- Haemoglobin levels, random blood sugar levels, liver function tests, renal function tests, lipid profiles, and serum electrolytes are just a few of the routine laboratory tests that will be performed. Assay for serum 25-hydroxyvitamin D levels.

Following data will be recorded for each patient of acute stroke-
NCCT/MRI Brain

Serum 25-hydroxyVitamin D levels

Age, sex, history of Diabetes, Hypertension and smoking

Biochemical profile including: Haemoglobin levels, Blood Sugar Levels(random), Liver Function Tests, Renal Function Tests, Lipid Profile, Serum Electrolytes.

All the information will be collected on a pre-designed performa. After collecting the data, the appropriate statistical analysis will be performed using the licensed version of Statistical Package for Social Science 25 (SPSS-25) / Microsoft excel.

RESULT
This study included a total of 160 subjects out of which 80 were cases (acute ischaemic stroke) and 80 were controls.

Sex distribution of patients of ischemic stroke case and control
Table.1: Showing Sex Distribution Of Patients Of Ischemic Stroke Case And Control

Gender	Case	Control
Male	46	51
Female	34	29

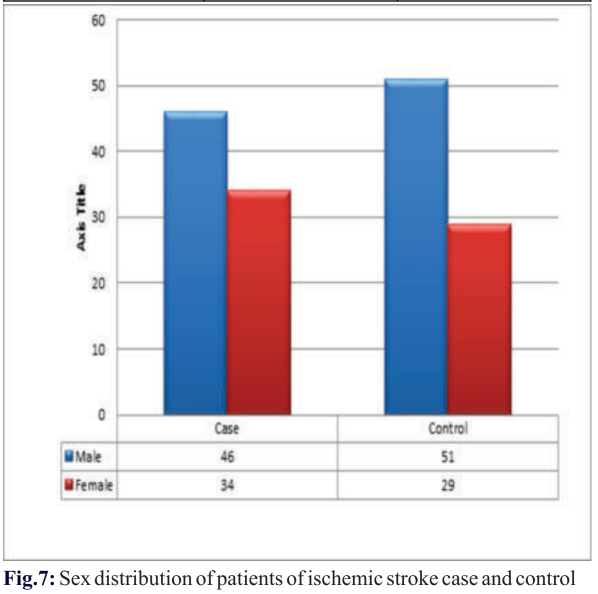

Fig.7: Sex distribution of patients of ischemic stroke case and control

Distribution And Representation Of Case And Control
Table.2: Showing Distribution And Representation Of Case And Control

	No. of patient	Percentage (%)
Case	80	50
Control	80	50
Total	160	100

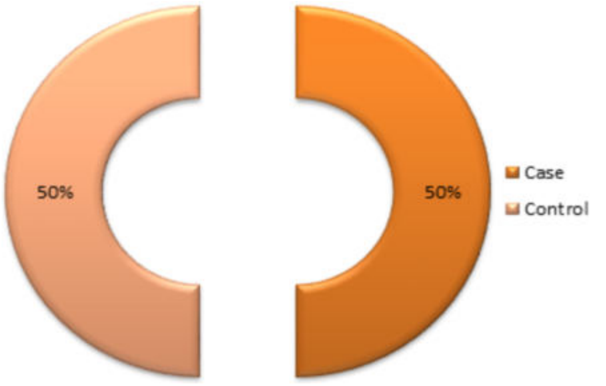

Fig.8: showing Distribution and representation of case and control

Age Wise Distribution Of Patients
Table.3: Showing Age Wise Distribution Of Patients

Age	Case	Control
20-30	20	11
30-50	24	17
50-70	28	25
70-90	08	27

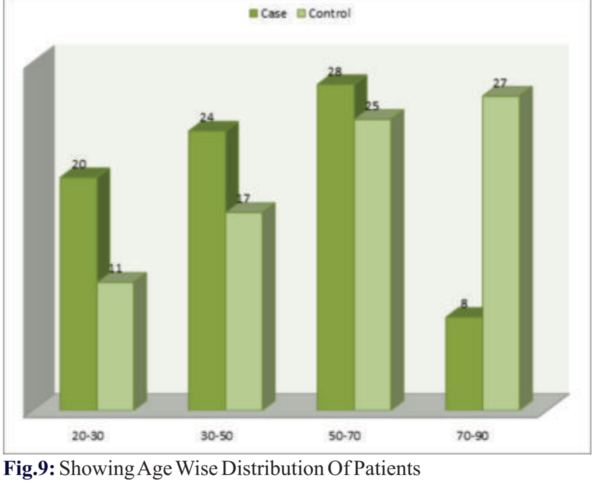

Fig.9: Showing Age Wise Distribution Of Patients

Cases And Controls With Respect To BMI
Table.4: Showing Cases And Controls With Respect To BMI

	Normal	Overweight	Obese
Case	37	28	15
Control	47	27	06
Total	40	55	21

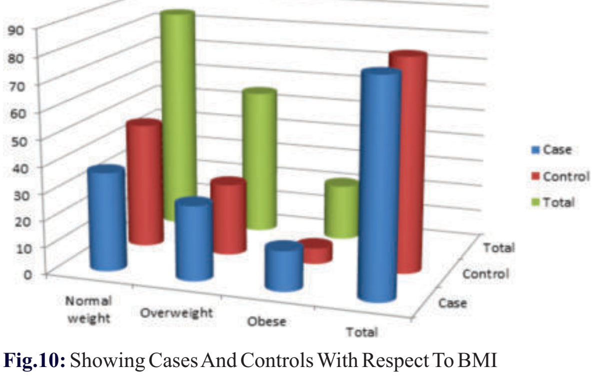

Fig.10: Showing Cases And Controls With Respect To BMI

Gender wise distribution of vit D level

Table.5: Showing Gender Wise Distribution Of Vit D Level

Gender	Normal Vit D level	Deficient Vit D level
Male	09	29
Female	06	56

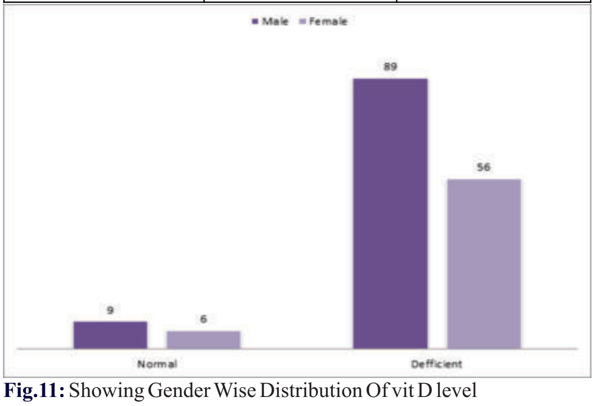

Fig.11: Showing Gender Wise Distribution Of vit D level

VITAMIN D STATUS IN THE STUDY POPULATION

Table.6:Showing Vitamin D Status In The Study Population

Group	Case	Control	Total
Normal	0	16	16
Insufficient	05	13	18
Deficient	75	51	126
Total	80	80	160

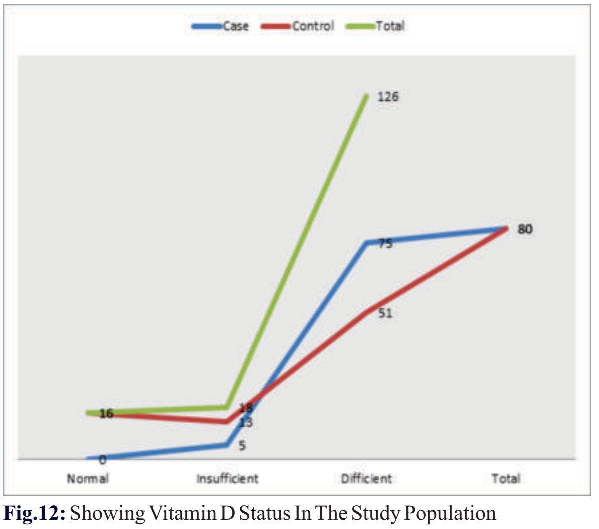

Fig.12: Showing Vitamin D Status In The Study Population

The Biochemical Parameters Of Case (Ischemic Stroke)

Table.7: Showing The Biochemical Parameters Of Case (Ischemic Stroke)

S.No.	Parameters	Mean±SD
1.	Age	47.46±19.11
2.	BMI	26.32±3.54
3.	LDL	132.14±30.20
4.	HDL	44.54±5.76
5.	TG	153.53±40.56
6.	TC	214.18±35.48
7.	Vit D	13.54±5.07

The Biochemical Parameters Of Control

Table.8: Showing The Biochemical Parameters Of Control

S.No.	Parameters	Mean±SD
1.	Age	57.65±20.04
2.	BMI	24.712±2.95
3.	LDL	119.45±28.44
4.	HDL	43.9375±6.21
5.	TG	151.8±58.02
6.	TC	191.5625±26.53
7.	Vit D	21.663±10.70

DISCUSSION

80 cases of acute ischemic stroke and 80 age- and sex-matched controls were included in our analysis of 160 patients. Our cases were chosen so that none of them had a history of stroke, coronary artery disease, chronic renal disease, systemic hypertension, or diabetes mellitus. This was done to find out if having low vitamin D levels could put people at risk for cerebrovascular accidents on their own. This case-control study included 160 patients with a mean age (47.46±19.11) of 64.27 years and 160 control subject with a mean age(57.65±20.04) of 64.65 years.

VITAMIN D & STROKE

According to a study by Tu WJ et al.[51], vitamin D levels were 10–18 ng/ml in stroke patients and 17–22 ng/ml in controls. While the prevalence was 100% in our investigation, Kenneth et al [49] discovered a 77% prevalence of Vitamin D insufficiency among stroke patients.

Studies by Pilzet al.[50], de Silva et al.[55], and LURIC study53 revealed that stroke patients had Vitamin D deficiency in 58%, 95%, and 92% of cases, respectively.

We discovered that just 12% of the 100 patients who participated in the trial as a whole had normal levels of vitamin D. The remaining 88% had vitamin D levels below normal, with 21% suffering from a deficiency and 67% from an insufficiency. This high proportion of vitamin D deficiency in our study group mirrors the high prevalence of vitamin d deficiency in the Indian community, as was previously shown by Harinarayan et al [39], who found that between 50 and 90 percent of Indians were vitamin d deficient.

The average level of vitamin D in the control group was 23.03 ng/ml. This is comparable to the mean value of 24ng/ml among patients who appeared to be in good health as reported by the NHANES 2005–2006 survey [54].

In this study, we also examined the relationships between ischemic stroke and variables including gender, age, body mass index, smoking, LDL cholesterol, HDL cholesterol, total cholesterol, triglycerides, and infarct size. Statistical significance was not discovered for any other measure besides Body Mass Index. As a result, the majority of these confounding factors, which are also independent risk factors for stroke, could be safely disregarded.

In our study, we also examined the relationships between vitamin D and variables including gender, age, body mass index, smoking, LDL cholesterol, HDL cholesterol, total cholesterol, triglycerides, and infarct area.

VITAMIN D AND GENDER VARIATION

We found no conclusive correlation between gender distribution and vitamin D levels. Male case 09 and female case 06 both had normal levels of vitamin D. Male cases 29 and 56 both showed lower-than-normal levels of vitamin D.

In contrast, a research by Johnson et al. [47] found that men were significantly more likely than women to be vitamin D deficient.

CONCLUSION

Vitamin D insufficiency is linked to a wide range of disorders. This puts a heavy load on the neighbourhood. Therefore, the finding that a vitamin D shortage causes strokes is a significant scientific advance.

Patients with ischemic stroke in our study had noticeably low levels of vitamin D.

Due to the widespread prevalence of vitamin D insufficiency in our nation, these findings could have significant effects on public health. Vitamin D insufficiency is a risk factor that is simple to measure and treat.

The procedure is secure and economical. Therefore, it is necessary to raise awareness of this risk factor among the general public and to put into place recommendations for its diagnosis and treatment.

To further examine Vitamin D deficiency as a stroke risk factor and the benefits of Vitamin D supplementation on stroke prevention, large scale randomised control trials are required.

REFERENCES

1. Narayan, M., & Singh, S. K. (2018). Study of association between serum ferritin and prognosis of patients in acute ischemic and haemorrhagic stroke. *IOSR Journal of Dental and Medical Sciences*, *17*, 46-56.
2. Chaudhuri, J. R., Mridula, K. R., Alladi, S., Anamika, A., Umamahesh, M., Balaraju, B., ...&Bandaru, V. S. (2014). Serum 25-hydroxyvitamin D deficiency in ischemic stroke and subtypes in Indian patients. *Journal of stroke*, *16*(1), 44.
3. Holick, M. F. (2007). Vitamin D deficiency. *New England journal of medicine*, *357*(3), 266-281.
4. Lugg, S. T., Howells, P. A., &Thickett, D. R. (2015). Optimal vitamin D supplementation levels for cardiovascular disease protection. *Disease Markers*, *2015*.
5. Ayele, B. A., Wuhib, M. Z., Zenebe, B. G., &Metaferia, G. Z. (2021). Serum Vitamin D Level among Multiple Sclerosis Patients in the Tropics: Experience from a Private Clinic in Addis Ababa, Ethiopia. *Ethiopian Journal of Health Sciences*, *31*(3).
6. Wacker, M., &Holick, M. F. (2013). Vitamin D—effects on skeletal and extraskeletal health and the need for supplementation. *Nutrients*, *5*(1), 111-148.
7. Selim, F. O., Fahmi, R. M., Ali, A. E., Raafat, N., &Elsaid, A. F. (2019). Serum vitamin D levels in acute stroke patients. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, *55*(1), 1-8.
8. Chaudhuri, J. R., Mridula, K. R., Alladi, S., Anamika, A., Umamahesh, M., Balaraju, B., ...&Bandaru, V. S. (2014). Serum 25-hydroxyvitamin D deficiency in ischemic stroke and subtypes in Indian patients. *Journal of stroke*, *16*(1), 44.
9. Alfieri, D. F., Lehmann, M. F., Oliveira, S. R., Flauzino, T., Delongui, F., de Araújo, M. C. M., &Reiche, E. M. V. (2017). Vitamin D deficiency is associated with acute ischemic stroke, C-reactive protein, and short-term outcome. *Metabolic brain disease*, *32*(2), 493-502.
10. Eyles, D. W., Liu, P. Y., Josh, P., & Cui, X. (2014). Intracellular distribution of the vitamin D receptor in the brain: comparison with classic target tissues and redistribution with development. *Neuroscience*, *268*, 1-9.
11. Carvalho, L. S. F., &Sposito, A. C. (2015). Vitamin D for the prevention of cardiovascular disease: are we ready for that?. *Atherosclerosis*, *241*(2), 729-740.
12. Thapa, L., Shrestha, A., Pradhan, M., Bhandari, T. R., Shrestha, S., Poudel, R. S., ...&Poudel, R. (2014). Status of vitamin D and its association with stroke risk factors in patients with acute ischemic stroke in a tertiary care hospital. *Journal of the Nepal Medical Association*, *52*(195), 935-939.
13. Selim, F. O., Fahmi, R. M., Ali, A. E., Raafat, N., &Elsaid, A. F. (2019). Serum vitamin D levels in acute stroke patients. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, *55*(1), 1-8.
14. BalaVignesh, S. (2015). *A Study on Serum Vitamin D Levels in Acute Ischaemic Stroke* (Doctoral dissertation, Kilpauk Medical College, Chennai).
15. Pedelty, L., Gorelick, P., Torbey, M. T., &Selim, M. H. (2007). Stroke risk factors: impact and management. *The Stroke Book*.
16. Kanyal, N. (2015). The science of ischemic stroke: pathophysiology & pharmacological treatment. *International Journal of Pharma Research & Review*, *4*(10), 65-84.
17. Xing, C., Arai, K., Lo, E. H., &Hommel, M. (2012). Pathophysiologic cascades in ischemic stroke. *International Journal of Stroke*, *7*(5), 378-385.
18. Muir, K. W., & Lees, K. R. (1998). Dose optimization of intravenous magnesium sulfate after acute stroke. *Stroke*, *29*(5), 918-923.
19. www.whvc.com
20. www.ajnr.org
21. Bayır, A., Ak, A., Kara, H., &Şahin, T. K. (2009). Serum and cerebrospinal fluid magnesium levels, Glasgow Coma Scores, and in-hospital mortality in patients with acute stroke. *Biological trace element research*, *130*(1), 7-12.
22. Amighi, J., Sabeti, S., Schlager, O., Mlekusch, W., Exner, M., Lalouschek, W., ...& Schillinger, M. (2004). Low serum magnesium predicts neurological events in patients with advanced atherosclerosis. *Stroke*, *35*(1), 22-27.
23. Deluca, H. F., &Cantorna, M. T. (2001). Vitamin D: Its role and uses in immunology *The FASEB journal*, *15*(14), 2579-2585.
24. Holick, M. F. (2002). Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. *Current Opinion in Endocrinology, Diabetes and Obesity*, *9*(1), 87-98.
25. Davis, M., & Barer, D. (1999). Neuroprotection in acute ischaemic stroke. II: Clinical potential. *Vascular Medicine*, *4*(3), 149-163.
26. Kidd, P. M. (2009). Integrated brain restoration after ischemic stroke--medical management, risk factors, nutrients, and other interventions for managing inflammation and enhancing brain plasticity. *Alternative Medicine Review*, *14*(1).
27. Holick, M. F. (2007). Vitamin D deficiency. *New England journal of medicine*, *357*(3), 266-281.
28. Davis, M., & Barer, D. (1999). Neuroprotection in acute ischaemic stroke. II: Clinical potential. *Vascular Medicine*, *4*(3), 149-163.
29. Meloni, B. P., Campbell, K., Zhu, H., &Knuckey, N. W. (2009). In search of clinical neuroprotection after brain ischemia: the case for mild hypothermia (35 C) and magnesium. *Stroke*, *40*(6), 2236-2240.
30. Dyker, A. G., Edwards, K. R., Fayad, P. B., Hormes, J. T., & Lees, K. R. (1999). Safety and tolerability study of aptiganel hydrochloride in patients with an acute ischemic stroke. *Stroke*, *30*(10), 2038-2042.
31. Amighi, J., Sabeti, S., Schlager, O., Mlekusch, W., Exner, M., Lalouschek, W., ...& Schillinger, M. (2004). Low serum magnesium predicts neurological events in patients with advanced atherosclerosis. *Stroke*, *35*(1), 22-27.
32. Davis, M., & Barer, D. (1999). Neuroprotection in acute ischaemic stroke. II: Clinical potential. *Vascular Medicine*, *4*(3), 149-163.
33. Holick, M. F. (2002). Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. *Current Opinion in Endocrinology, Diabetes and Obesity*, *9*(1), 87-98.
34. Davis, M., & Barer, D. (1999). Neuroprotection in acute ischaemic stroke. II: Clinical potential. *Vascular Medicine*, *4*(3), 149-163.
35. Bayır, A., Ak, A., Kara, H., &Şahin, T. K. (2009). Serum and cerebrospinal fluid magnesium levels, Glasgow Coma Scores, and in-hospital mortality in patients with acute stroke. *Biological trace element research*, *130*(1), 7-12.
36. Kaur, J., Arora, S., Singh, B., Thakur, L. C., Gambhir, J., &Prabhu, K. M. (2011). Role of oxidative stress in pathophysiology of transient ischemic attack and stroke. *Int J Biol Med Res*, *2*(3), 611-615.
37. Holick, M. F. (2007). Vitamin D deficiency. *New England journal of medicine*, *357*(3), 266-281.
38. Kimball, S. M., Lee, J., &Vieth, R. (2017). Sunbeds with UVB radiation can produce physiological levels of serum 25-Hydroxyvitamin D in healthy volunteers. *Dermato-endocrinology*, *9*(1), e1375635.
39. Dawson-Hughes, B., Heaney, R. P., Holick, M. F., Lips, P., Meunier, P. J., &Vieth, R. (2005). Estimates of optimal vitamin D status. *Osteoporosis international*, *16*(7), 713-716.
40. https://www.physiopedia.com/Stroke_Medical_Management
41. Acharya, D., Sekhar, S., Mishra, D., Padhy, D., Kumari, R., &Malini, D. D. S. (2022). A RANDOMISED CONTROL TRIAL ON EFFECT OF VITAMIN D IN STROKE IN A TERTIARY CARE HOSPITAL OF SOUTHERN ODISHA. *European Journal of Molecular & Clinical Medicine*, *9*(7), 838-847.
42. Deluca, H. F., &Cantorna, M. T. (2001). Vitamin D: Its role and uses in immunology 1. *The FASEB journal*, *15*(14), 2579-2585.
43. Holick, M. F. (2002). Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. *Current Opinion in Endocrinology, Diabetes and Obesity*, *9*(1), 87-98.
44. Gupta, A. (2014). Vitamin D deficiency in India: prevalence, causalities and interventions. *Nutrients*, *6*(2), 729-775.
45. Harinarayan, C. V., Ramalakshmi, T., &Venkataprasad, U. (2004). High prevalence of low dietary calcium and low vitamin D status in healthy south Indians. *Asia Pacific journal of clinical nutrition*, *13*(4).
46. Harinarayan, C. V., Ramalakshmi, T., Prasad, U. V., Sudhakar, D., Srinivasarao, P. V., Sarma, K. V., & Kumar, E. G. T. (2007). High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. *The American journal of clinical nutrition*, *85*(4), 1062-1067.
47. Harinarayan, C. V., Ramalakshmi, T., Prasad, U. V., &Sudhakar, D. (2008). Vitamin D status in Andhra Pradesh: a population based study. *Indian Journal of Medical Research*, *127*(3), 211.
48. Harinarayan, C. V., & Joshi, S. R. (2009). Vitamin D status in India--its implications and remedial measures. *JAPI*, *57*, 40-8.
49. Kho, A. T., Sharma, S., Qiu, W., Gaedigk, R., Klanderman, B., Niu, S., ...&Tantisira, K. G. (2013). Vitamin D related genes in lung development and asthma pathogenesis. *BMC medical genomics*, *6*(1), 1-9.
50. Pilz, S., Dobnig, H., Fischer, J. E., Wellnitz, B., Seelhorst, U., Boehm, B. O., &März, W. (2008). Low vitamin D levels predict stroke in patients referred to coronary angiography. *Stroke*, *39*(9), 2611-2613.
51. Tu, W. J., Zhao, S. J., Xu, D. J., & Chen, H. (2014). Serum 25-hydroxyvitamin D predicts the short-term outcomes of Chinese patients with acute ischaemic stroke. *Clinical Science*, *126*(5), 339-346.
52. Thomas, G. N., ó Hartaigh, B., Bosch, J. A., Pilz, S., Loerbroks, A., Kleber, M. E., ... &März, W. (2012). Vitamin D levels predict all-cause and cardiovascular disease mortality in subjects with the metabolic syndrome: the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study. *Diabetes care*, *35*(5), 1158-1164.
53. BalaVignesh, S. (2015). *A Study on Serum Vitamin D Levels in Acute Ischaemic Stroke* (Doctoral dissertation, Kilpauk Medical College, Chennai).
54. Ramachandran, A., Snehalatha, C., Kapur, A., Vijay, V., Mohan, V., Das, A. K., ...& Nair, J. D. (2001). High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. *Diabetologia*, *44*(9), 1094-1101.
55. Wild, S., Roglic, G., Green, A., Sicree, R., & King, H. (2004). Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes care*, *27*(5), 1047-1053.
56. Hurst, E. A., Homer, N. Z., &Mellanby, R. J. (2020). Vitamin D metabolism and profiling in veterinary species. *Metabolites*, *10*(9), 371.
57. Emile Millerot-Serrurot, Nathalie Bertrand, ClaudeMossiat, PhilippeFaure, Annepriget Tessier, Neurochemistry International.2015.35:456
58. Clancy N, Onwuneme C, Carroll A, McCarthy R, McKenna MJ, Murphy N, et al. Vitamin D and neonatal immune function. J MaternFetal Neonatal Med. 2013;26:639.
59. Wacker M, Holick MF. Vitamin D effects on skeletal and extraskeletal health and the need for supplementation. Nutrients. 2013;5:111.
60. Fahmi RM, Lotfy SM, Mohamed WS, Elsaid AF, Murad MH, Abdulmoneem G. Vitamin D levels in patients with multiple sclerosis. Egypt J NeurolPsychiatrNeurosurg. 2014;51:145.
61. Chaudhuri JR, Mridula KR, Alladi S, Umamahesh M, Balaraju B, Swath A, et al. Serum 25- hydroxyvitamin D deficiency in ischemic stroke and subtypes in Indian patients. J STROKE. 2014;16:44.
62. Alfieri DF, Lehmann MF, Oliveira SR, Flauzino T, Delongui F, de Araújo MC, et al. Vitamin D deficiency is associated with acute ischemic stroke, C- reactive protein, and short-term outcome. Metab Brain Dis. 2017;32:493.
63. Eyles DW, Liu PY, Josh P, Cui X. Intracellular distribution of the vitamin D receptor in the brain: comparison with classic target tissues and redistribution with development. Neuroscience. 2014;268:1.
64. Carvalho LS, Sposito AC. Vitamin D for the prevention of cardiovascular disease: are we ready for that? Atherosclerosis. 2015;241:729.
65. Thapa L, Pokhrel B, Shrestha A, Pradhan M, Bhandari TR, Shrestha S, et al. Status of vitamin D and its association with stroke risk factors in patients with acute ischemic stroke in a tertiary care hospital. J Nepal Med Assoc. 2014;52:935.
66. Kenneth E. S. Poole, Nigel Loveridge, Peter J. Barker, David J.Halsall, Collette Rose, Jonathan Reev,et al. Reduced Vitamin D in Acute Stroke; stroke AHA journal.2016;34:656
67. Stefan Pilz, MD;HaraldDobnig, MD;Joachim E. Fischer, MD;BrittaWellnitz, LLD; Ursula Seelhorst, ety al. Low Vitamin D Levels Predict Stroke in Patients Referred to Coronary Angiography 2012;23:345
68. Tu WJ1 , Zhao SJ, Xu DJ, Chen H.; Serum 25-hydroxyvitamin D predicts the short-term outcomes of Chinese patients with acute ischaemic stroke.2014;35:435
69. Thomas GN1 , O Hartaigh B, Bosch JA, Pilz S, Loerbroks A, Kleber ME, et al. Vitamin D levels predict all-cause and cardiovascular disease mortality in subjects with the metabolic syndrome: the Ludwigshafen Risk and Cardiovascular Health (LURIC) Study.2015;45:657
70. Deidre A De Silva1 ; Loreto P Talabucon1 ; Ebonne Y Ng1 ; Eng King Tan1 ; TienYin Wong2 et al. Vitamin D Levels Are Lower In Acute Ischemic Stroke Patients Compared To Matched Controls.2012;43:23