



## Correspondence

**Vitamin D: The silent rescuer from ischemic stroke**

Vitamin D, one of the fat-soluble vitamins, is recognized for its anti-atherogenic activities. Vitamin D is present abundantly not only in nature but also synthesized in the skin with the help of UV-B of sunlight. This can be found in a different form, though the active form is known as calcitriol [1,25 dihydroxy cholecalciferol [1,25(OH)<sub>2</sub>D<sub>3</sub>]. Calcitriol aids in calcium homeostasis, which is regulated by parathyroid hormone and nurtures bone and teeth formation. Besides this well-established action, a revolutionary discovery has been made. Vitamin D has a beneficiary effect on the cardiovascular system, particularly in lessening atherosclerosis, ischemic stroke, and MI. Calcitriol might accelerate vascular regeneration and repair, whereas deficiency has a deleterious effect on vascular endothelium [1].

Every year about 0.8 million people in developed countries face stroke attacks and 87% are ischemic strokes. Along with all known modifiable risk factors e.g.- a sedentary lifestyle, smoking, high fat, and alcohol intake, supplementary vitamin D could play an important role. Calcitriol, below the reference range, can result in stroke recurrence and mortality within 2 years [2].

Calcitriol has dominant immunomodulatory features-hampers T cell and B cell activity, T cell anergy. While the binding of vitamin D<sub>3</sub> upon its receptor, a significant reduction in pro-inflammatory mediators - IL-6, IL-1 $\beta$ , IL-23a, TGF- $\beta$ , and NADPH oxidase-2 occurs because of the neuroprotective function. This is evident that a single dose of 600000 IU of vitamin D<sub>3</sub> exerts neuronal protection by preventing reactive oxygen species damage and vasodilatation in moderate ischemia. The synergistic effect of vitamin A with vitamin D reduces serum IL-1 $\beta$  levels, resulting in a better outcome for ischemic stroke patients [3–6].

Distortion of the blood-brain barrier (BBB) and loss of structural integrity inspected after ischemic stroke. Vitamin D deficiency on top of distorted BBB activates inflammatory cascade and functional loss. Calcitriol commands synaptic structural protein synthesis, and calcium trafficking to mitigate damage, thus maintaining the structural conformation of BBB. Carotid bulb stenosis and calcification are occasionally associated with ischemic stroke due to *Fok I* and *TaqI* polymorphisms of the vitamin D receptor (VDR) gene [7–9].

Biomarkers of neuronal inflammation and integrity, organelle disruption, oxidative stress, and programmed cell death were assessed along with B cells, T cells, and additional immune cells. Systematic and immune disruptions are markedly visible in a vitaminD3 deficient state. Combined vitamin D and progesterone therapy revealed better consequences than single hormone therapy. Vitamin D is a recommended prognostic marker for ischemic stroke [10,11].

Appropriate interrelation between calcitriol into the cerebrovascular system is yet to be justified and unclogged, whether it is the reason or the marker of cardiovascular disorder. To demonstrate the connection, some reviews and analyses have been run to date. In 2018 systematic review and a meta-analysis revealed, vitamin D status in ischemic stroke

(relative risk = 2.45, 95% CI: 1.56–3.86), but not with hemorrhagic stroke (relative risk = 2.50, 95% CI: 0.87–7.15). Finally, provide the data that, diminished vitamin D status is linked with higher ischemic stroke risk. Vitamin D is found on a large scale in arterioles in comparison to large vessels. As a result, the incidence of stroke is higher in minor arteries. Calcitriol improves vessel tone by nitric oxide exposure on the endothelium [12–14].

Post-Stroke Depression affects about three fourth patients, where diminished blood vitamin D is reported. The rise of calcitriol could have a better cognitive and motor function outcome in rehabilitation [15].

While mild to moderate deficiency has a minor effect in stroke patients, intense vitamin D deficiency has an alarming association with post-ischemic stroke durability where boosting with vitamin supplementation might not be sufficient. [16].

Furthermore, effective studies and trials can provide data in the future about the integral relationship between the cerebrovascular system and vitamin D. Vitamin D could be an effortless treatment protocol to lessen the physical and psychological burden on ischemic patients.

**Ethical approval**

It is not necessary.

**Please state any sources of funding for your research**

None.

**Author contribution**

All authors equally contributed to the analysis and writing of the paper.

**Registration of research studies**

Name of the registry: Not applicable.

Unique Identifying number or registration ID: Not applicable.

Hyperlink to your specific registration (must be publicly accessible and will be checked): Not applicable.

**Guarantor**

Safinaz Khan.

Department of Biochemistry and Molecular Biology.

Sir Salimullah Medical College, Dhaka.

Email: [safinazkhan23@gmail.com](mailto:safinazkhan23@gmail.com).

<https://doi.org/10.1016/j.amsu.2022.103751>

Received 27 March 2022; Received in revised form 8 May 2022; Accepted 8 May 2022

Available online 11 May 2022

2049-0801/© 2022 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Consent

Not applicable.

## Conflicts of interest

None.

## References

- [1] Y.H. Chan, C.M. Schooling, J. Zhao, S.L. Au Yeung, J.J. Hai, G.N. Thomas, K. K. Cheng, C.Q. Jiang, Y.K. Wong, K.W. Au, C.S. Tang, C. Cheung, A. Xu, P.C. Sham, T.H. Lam, K.S. Lam, H.F. Tse, Mendelian randomization focused analysis of vitamin D on the secondary prevention of ischemic stroke, *Stroke* 52 (12) (2021) 3926–3937, <https://doi.org/10.1161/STROKEAHA.120.032634>.
- [2] H. Qiu, M. Wang, D. Mi, J. Zhao, W. Tu, Q. Liu, Vitamin D status and the risk of recurrent stroke and mortality in ischemic stroke patients: data from a 24-month follow-up study in China, *J. Nutr. Health Aging* 21 (7) (2017) 766–771, <https://doi.org/10.1007/s12603-016-0821-z>.
- [3] M.A. Evans, H.A. Kim, Y.H. Ling, S. Uong, A. Vinh, T.M. De Silva, T.V. Arumugam, A.N. Clarkson, G.R. Zosky, G.R. Drummond, B. Broughton, C.G. Sobey, Vitamin D<sub>3</sub> supplementation reduces subsequent brain injury and inflammation associated with ischemic stroke, *NeuroMolecular Med.* 20 (1) (2018) 147–159, <https://doi.org/10.1007/s12017-018-8484-z>.
- [4] A. Kadri, H. Sjahrir, R. Juwita Sembiring, M. Ichwan, Combination of vitamin A and D supplementation for ischemic stroke: effects on interleukin-1 $\beta$  and clinical outcome, *Med. Glas. : Off. Pub. Med. Assoc. Zenica-Doboj Canton Bosnia Herzegovina* 17 (2) (2020) 425–432, <https://doi.org/10.17392/1137-20>.
- [5] K. Yarlagadda, N. Ma, S. Doré, Vitamin D and stroke: effects on incidence, severity, and outcome and the potential benefits of supplementation, *Front. Neurol.* 11 (2020) 384, <https://doi.org/10.3389/fneur.2020.00384>.
- [6] O. Hesami, S. Iranshahi, S.Z. Shahamati, M. Sistanizd, E. Pourheidar, R. Hassanpour, The evaluation of the neuroprotective effect of a single high-dose vitamin D<sub>3</sub> in patients with moderate ischemic stroke, *Stroke Res. Treat.* (2022), 8955660, <https://doi.org/10.1155/2022/8955660>, 2022.
- [7] S. Won, I. Sayeed, B.L. Peterson, B. Wali, J.S. Kahn, D.G. Stein, Vitamin D prevents hypoxia/reoxygenation-induced blood-brain barrier disruption via vitamin D receptor-mediated NF- $\kappa$ B signaling pathways, *PLoS One* 10 (3) (2015), e0122821, <https://doi.org/10.1371/journal.pone.0122821>.
- [8] I. Sayeed, N. Turan, D.G. Stein, B. Wali, Vitamin D deficiency increases blood-brain barrier dysfunction after ischemic stroke in male rats, *Exp. Neurol.* 312 (2019) 63–71, <https://doi.org/10.1016/j.expneurol.2018.11.005>.
- [9] F. Foroughinia, N. Morovati, A. Safari, M. Dianatpour, I. Jamhiri, S.T. Heydari, S. Hooshmandi, A. Borhani-Haghighi, Association between FokI and TaqI polymorphisms of vitamin D receptor gene with the severity of stenosis and calcification in carotid bulb in patients with ischemic stroke, *J. Clin. Neurosci. : Off. J. Neurosur. Soc. Australasia* 97 (2022) 115–120, <https://doi.org/10.1016/j.jocn.2022.01.009>. Advance online publication.
- [10] A. Siniscalchi, P. Lochner, S. Anticoli, D. Chirchiglia, G. De Sarro, L. Gallelli, What is the current role for vitamin D and the risk of stroke? *Curr. Neurovascular Res.* 16 (2) (2019) 178–183, <https://doi.org/10.2174/1567202616666190412152948>.
- [11] S. Yousuf, F. Atif, C. Espinosa-Garcia, W. Harris, N. Turan, D.G. Stein, Stroke-Induced peripheral immune dysfunction in vitamin D-deficient conditions: modulation by progesterone and vitamin D, *Mol. Neurobiol.* 58 (3) (2021) 950–963, <https://doi.org/10.1007/s12035-020-02129-4>.
- [12] F. Saponaro, C. Marocci, R. Zucchi, Vitamin D status and cardiovascular outcome, *J. Endocrinol. Invest.* 42 (11) (2019) 1285–1290, <https://doi.org/10.1007/s40618-019-01057-y>.
- [13] N. Manouchehri, M. Vakil-Asadollahi, A. Zandifar, F. Rasmani, M. Saadatnia, Vitamin D status in small vessel and large vessel ischemic stroke patients: a case-control study, *Adv. Biomed. Res.* 6 (2017) 146, <https://doi.org/10.4103/2277-9175.219411>.
- [14] M. Torrisi, L. Bonanno, C. Formica, F.A. Arcadi, D. Cardile, V. Cimino, P. Bramanti, E. Morini, The role of rehabilitation and vitamin D supplementation on motor and psychological outcomes in poststroke patients, *Medicine* 100 (45) (2021), e27747, <https://doi.org/10.1097/MD.00000000000027747>.
- [15] J. Wajda, M. Świat, A.J. Owczarek, A. Brzozowska, M. Olszanecka-Glinianowicz, J. Chudek, Severity of vitamin D deficiency predicts mortality in ischemic stroke patients, *Dis. Markers* (2019), 3652894, <https://doi.org/10.1155/2019/3652894>, 2019.

Safinaz Khan\*

Department of Biochemistry and Molecular Biology, Sir Salimullah Medical College, Dhaka, Bangladesh

Md Moshir Rahman

Department of Neurosurgery, Holy Family Red Crescent Medical College, Dhaka, Bangladesh

E-mail address: [dr.tutul@yahoo.com](mailto:dr.tutul@yahoo.com).

A.H.M. Ataulah

Medical Officer, Sher-E-Bangla Medical College Hospital, Barishal, Bangladesh

E-mail address: [ataullah\\_cox@yahoo.com](mailto:ataullah_cox@yahoo.com).

Rubaya Rashid

Masters of Public Health, North South University, Bangladesh

E-mail address: [rubaya.rashid@northsouth.edu](mailto:rubaya.rashid@northsouth.edu).

\* Corresponding author.

E-mail address: [safinazkhan23@gmail.com](mailto:safinazkhan23@gmail.com) (S. Khan).