EDITORIAL

Vitamin D and Its Myriad Disease Associations: Can the Heart be Left Behind?

Narayanan Parameswaran

Keywords: Children, Dilated cardiomyopathy, Vitamin D deficiency.
Indian Journal of Critical Care Medicine (2023): 10.5005/jp-journals-10071-24491

Department of Paediatrics, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

Corresponding Author: Narayanan Parameswaran, Department of Paediatrics, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India, Phone: +91 9443458850, e-mail: drnarayananp@gmail.com

How to cite this article: Parameswaran N. Vitamin D and Its Myriad Disease Associations: Can the Heart be Left Behind? Indian J Crit Care Med 2023;27(7):463–464.

Source of support: Nil

Conflict of interest: None

The effect of Vitamin-D deficiency (VDD) on the skeletal system is well-documented, and in children, nutritional rickets dramatically responds to vitamin-D supplementation. Since the early 2000s, the effect of VDD on other organ systems has been a matter of great interest, and numerous studies have shown associations between VDD and cardiovascular diseases, cancer, autoimmune diseases, infectious diseases, etc.[1] Being a vitamin that can be easily supplemented, the potential therapeutic implications of these associations, if found causal, are enormous. Though systematic reviews have not consistently supported these associations being causal, there is a strong perception among medical professionals that vitamin-D supplementation has potential benefits beyond the skeletal system.[1]

Physiologically, calcium has a vital role in cardiac muscle function, specifically in the binding of actin and myosin fibers, bringing about the contraction of the cardiac muscle fibers. Hence, it is possible that severe VDD can result in disturbances in calcium homeostasis and hence cardiac muscle function. There have been numerous case reports and case series on the possible association between VDD and dilated cardiomyopathy (DCM) in the literature both from the developed world and from the developing countries.[2–6] The common risk factors identified include exclusively breastfed infants with dark skin, not getting adequate exposure to sunlight, being born to mothers who are vitamin-D deficient themselves, and living in areas with a long winter.[2–4] Identifying a potentially reversible cause is very gratifying in a condition like DCM, which otherwise has a poor prognosis, often resulting in cardiac transplantation. But similar to the other reported associations of VDD, attributing causality for VDD in DCM is not always easy. This is primarily due to the reported high prevalence of VDD in the general population and the incomplete workup/characterization of DCM in most studies. There had been reports of infants with DCM thought to be due to VDD, which later turned out to be some other genetic condition.[7]

In this context, the retrospective study by Kumar S et al. in this issue of the journal brings to attention the potential association between VDD and DCM in Indian children.[8] They defined VDD as serum 25(OH)D_3 levels <20 ng/mL and found that over a period of 5 years (January 2017–December 2021), 50% of the children admitted with DCM ($n = 28$) in their PICU had VDD ($n = 14$), which is an interesting observation. The median age of the 14 children with VDD was 6 months and all were exclusively breastfed without any vitamin-D supplementation. Hypocalcemia was observed in 12 (86%) out of the 14 children and it is not clear whether anyone had radiographic evidence of rickets. Mechanical ventilation was required in 5 children (36%) and inotropes in 8 (57%). All children survived to discharge from hospital, none requiring ECMO. Out of the 14 children with VDD and DCM discharged on vitamin-D supplements, follow-up data were available for 10 children (71%) for a median duration of 10 months. All 10 children were asymptomatic and had normal left ventricular function by echocardiography on follow-up. Though the outcome of these children has been gratifying, attributing causation to these observed associations remains a challenge.

The reported prevalence of VDD in Indian children remains high. Previous publications from the authors' geographical location itself had reported a prevalence of 40% among apparently healthy children from the upper socioeconomic status.[9] Hence, it is not surprising that 50% of the children with DCM had VDD given the high prevalence of the same in the community. It is also noteworthy that none of the 14 children reported by Kumar S et al. had radiographic evidence of rickets. Hence, attributing causation of DCM to VDD is fraught with challenges. In the United Kingdom series by Maiya et al., who reported 16 children with VDD and DCM, all had radiographic features of rickets, suggesting that VDD may be the most probable cause of the cardiac dysfunction in their children.[2] It was noteworthy that 3 (19%) of them expired inspite of having a potentially treatable and reversible cause of cardiac dysfunction.[2]

Among the 14 children reported by Kumar S et al. in this issue of the journal, 10 (71%) were followed up for a median duration of 10 months, and all of them showed improvement during follow-up with vitamin-D supplementation, which could suggest a possibility of VDD being the underlying cause of the DCM. But it is well known that many children with DCM can improve over time, especially the post-viral myocarditis group and those with other potentially reversible causes like beriberi, selenium deficiency, tachyarrhythmias, etc.[10] Hence, establishing VDD and documenting

improvement over time with vitamin-D supplementation, though suggestive, is not sufficient to prove causation of VDD in DCM, unless all other potentially reversible causes are ruled out. Additional information, if available, would have been useful in the report by Kumar S et al. Appropriate workup to rule out common viruses and other causes of myocarditis would have helped in ruling out causes of DCM, which can improve over time. Moreover, it is not clear what was the outcome of the other 14 children with DCM who did not have VDD. It will be interesting to know their etiology and cardiac status on follow-up. If a significant proportion of the 14 children without any evidence of VDD also did well on follow-up, it could be an indirect evidence that other potentially reversible causes that were not identified could be the major etiological factors in this group of 28 children with DCM.

Though the attribution of causality for VDD is challenging, the message from the data of Kumar S et al. is clear. We should make every effort to identify potentially reversible causes in all infants and children presenting with DCM, VDD being one of them. The presence of radiographic evidence of rickets and low ionized calcium levels in an exclusively breastfed child not receiving vitamin D supplementation could be suggestive. Relying solely on low $25(OH)D_3$ levels without considering the clinical setting may be misleading. It is always prudent to work up for viral myocarditis and other treatable causes like tachyarrhythmia, coronary anomalies (ALCAPA), etc., based on the clinical situation. Finally, follow-up over several months may answer many questions like any other chronic illness.

Orcid

Narayanan Parameswaran https://orcid.org/0000-0002-8297-5789

References

1. Theodoratou E, Tzoulaki I, Zgaga L, Ioannidis JP. Vitamin D and multiple health outcomes: Umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. BMJ 2014;348:2035. DOI: 10.1136/bmj.g2035.
2. Maiya S, Sullivan I, Allgrove J, Yates R, Malone M, Brain C, et al. Hypocalcaemia and vitamin D deficiency: An important, but preventable, cause of life-threatening infant heart failure. Heart 2008;94(5):581–584. DOI: 10.1136/hrt.2007.119792.
3. Jammal Addin MB, Young D, McCarrison S, Hunter L. Dilated cardiomyopathy in a national paediatric population. Eur J Pediatr 2019;178:1229–1235. DOI: 10.1007/s00431-019-03404-w.
4. Hunter L, Ferguson R, McDevitt H. Vitamin D deficiency cardiomyopathy in Scotland: A retrospective review of the last decade. Arch Dis Child 2020;105(9):853–856. DOI: 10.1136/archdischild-2019-317794.
5. Brown J, Nunez S, Russell M, Spurney C. Hypocalcemic rickets and dilated cardiomyopathy: Case reports and review of literature. Pediatr Cardiol 2009;30(6):818–823. DOI: 10.1007/s00246-009-9444-z.
6. Gupta P, Tomar M, Radhakrishnan S, Shrivastava S. Hypocalcemic cardiomyopathy presenting as cardiogenic shock. Ann Pediatr Cardiol 2011;4:152–155. DOI: 10.4103/0974-2069.84655.
7. Yeşilbaş O, Epçaçan S. Occurrence of nutritional hypocalcaemic rickets-related dilated cardiomyopathy in a child with concomitant rickets and infantile-onset Pompe disease. Cardiol Young 2019;29(3):425–427. DOI: 10.1017/S1047951118002287.
8. Surjeet Kumar, Manjinder Singh Randhawa, Suresh Kumar Angurana, Karthi Nallasamy, Arun Bansal, Manoj Rohit Kumar, et al. Clinical profile, intensive care needs, and outcome of children with dilated cardiomyopathy associated with vitamin D deficiency: A 5-year PICU experience. Indian J Crit Care Med 2023;27(7):510–514.
9. Angurana SK, Angurana RS, Mahajan G, Kumar N, Mahajan V. Prevalence of vitamin D deficiency in apparently healthy children in north India. J Pediatr Endocrinol Metab 2014;27(11–12):1151–1156. DOI: 10.1515/jpem-2013-0387.
10. Jain P, Jain A, Khan DN, Kumar M. Human parvovirus B19 associated dilated cardiomyopathy. BMJ Case Rep 2013;2013:bcr2013010410. DOI: 10.1136/bcr-2013-010410.