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EDITORIAL

CAN WE REDEFINE VITAMIN D DEFICIENCY?

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Majority of the world population is vitamin D deficient based on its current definition for deficiency. But despite being deficient, most of the physiological and biochemical parameters related to vitamin D deficiency, namely serum calcium, alkaline phosphatase and serum parathyroid hormone (PTH) remains normal. Serum PTH should rise up as a physiological feedback in response to vitamin D low levels. But the inflection point of PTH occurs at much lower levels of vitamin D (15ng/dL) than at the currently defined cut-off for deficiency (20ng/dL). Can we redefine vitamin D deficiency taking into account the vitamin D-PTH coupled testing and considering the PTH rise/ inflection as the appropriate response to low vitamin D level?

Vitamin D, one of the fat-soluble vitamins is important not only for skeletal health but has role in every tissue of the body starting from biological level of cell growth, its proliferation and cell death to its immunological effects. Its role in various autoimmune, chronic organic and neuropsychiatric illnesses has been well postulated.[1-4]

Depending upon the degree of vitamin D deficiency, effects may range from enhanced bone turnover, bone loss and secondary hyperparathyroidism to rickets, osteomalacia and fractures.[5,6] Currently there is no consensus on the normal values of serum vitamin D levels. Moreover the normal value of vitamin D is different among various populations based on geography, race, and cultural factors.[7] These discrepancies in different studies have created a lot of concerns among the public which may cause a lot of physical and psychological impact on patients health while social and economic implications on health care systems.

Based on the current definitions for vitamin D deficiency; 28-100% of healthy adults and 70-100% of in-hospital patients have been labeled as vitamin D deficient, and is considered a pandemic.[8-11] Current literature about vitamin D has raised many questions and concerns; Is vitamin D deficiency really a pandemic? Is current reference range of vitamin D level of less than 20ng/dL a true representative of vitamin D deficiency? Can there be still vitamin D deficiency without any change in biochemical and physiological parameters of the body? Is there any role of vitamin D-Parathyroid hormone coupled testing in redefining vitamin D normal levels? Can the reference range for vitamin D be reconsidered and redefined based on population/ epidemiological studies?

Vitamin D, calcium and parathyroid hormones are interconnected physiologically, and they regulate each other's levels in the blood through feedback mechanisms. Thus, in the absence of primary parathyroid gland dysfunction, a fall in serum vitamin D levels stimulate the production of PTH. With progressively declining serum 25(OH)D levels, parathyroid glands are maximally stimulated through negative feedback and produce supra-physiological parathyroid hormone leading to secondary hyperparathyroidism.[12] This rise in PTH levels secondary to fall in vitamin D levels below the optimal level is used as a marker of vitamin D deficiency.[13] Mukhopadhyay, et al.[14] in his study reported only 9.1% patients to be vitamin D sufficient (>30ng/dL) and all other patients were either vitamin D insufficient (20-30ng/dL) or deficient (<20ng/dL). Similarly another study done on healthy individuals reported only 8.9% of participants to be vitamin D sufficient.[7] The inflection point at which serum PTH levels went up steeply was reported to be vitamin D levels less than 16.5ng/dL in the former and in the later study serum corrected calcium was reported normal while other bone related parameters namely alkaline phosphatase, serum phosphate levels didn't show any

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significant association with serum vitamin D levels.[7,14]

Thomas, et al.[15] in his study considered smaller increments of 5ng/dL in vitamin D levels and the inflection point was reported to be 15ng/dL below which PTH levels went steeply up. Another study which assessed PTH levels according to three sub categories of vitamin D levels concluded that PTH levels were highest in the group with vitamin D levels less than 10ng/dL and the lowest in group with vitamin D levels above 18ng/dL.[16] Current vitamin D deficiency is a major public health concern. But the question is, "Is it a true pandemic or mere an overestimation?" Is it still possible for all the physiological parameters to be in the normal range despite being vitamin D deficient? Can 15ng/dL or even lower level of vitamin D be taken as a new lower limit of normal based on the steep rise of PTH at this cut off as reported by most of the studies? Can the normal reference range for vitamin D levels be different for different populations/ regions?

Testing vitamin D levels coupled with measuring serum PTH levels may be the most reasonable way forward to redefine the lower limit of vitamin D keeping in view the steep rise in PTH levels as a physiologic feedback mechanism in response to the falling levels of vitamin D.

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CONFLICT OF INTEREST
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