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Editorial

Vitamin D Supplementation: Still a Paradox!

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The classic work of Francis Glisson, a Cambridge physician, titled "De Rachitide" was published in Latin in 1650 and is still considered a treatise on rickets. Glisson was of the opinion that rickets was neither transmissible nor hereditary. His hypothesis regarding the association of age to the onset of rickets has remained time-tested [1].

A Scottish physician, Dr Palm, in 10 years of his stay in Japan noted that rickets was surprisingly absent and made a notable observation in 1890 on the incidence of rickets and its geographical distribution. Large towns and industrialised regions like Glasgow and Edinburgh in the UK had high prevalence of rickets alongside the coal mining regions of the country. Such cities were hazy and smoggy, and the air was filled with soot. Children in tropical countries were exposed to filth, poor sanitation and unsafe water and yet they didn't show symptoms of rickets, he noted. Other medical missions from areas in China, Mongolia, India, Morocco and Sri Lanka [erstwhile Ceylon] did not report rickets. Palm concluded that "the geography of rickets appears to involve the temperate latitudes of Europe: Germany, England, Holland, Belgium, France and northern Italy but southern Italy, southern Spain, Turkey and Greece with greater sunshine "enjoy a notable immunity from it" [2]. He suggested that exposure to abundant sunshine to toddlers in tropics was responsible for their protection against rickets. Palm recommended "systematic use of sun-baths as a preventive and therapeutic measure in rickets." However, Palm's observations and recommendations were ignored by the medical world [2].

Steenbock - a professor of biochemistry in 1916 began to expose rats, and their food to ultraviolet light after having worked on goats and finding that they were in positive calcium balance when kept in summer sun outdoors, but when kept indoors in the winter in the absence of sunlight, they went into negative calcium balance. He found that UV exposure of not only the rats but also their food could prevent or cure rickets. Industrial irradiation of milk to increase its antirachitic property was thus initiated [3].

Rickets and osteomalacia disappeared from most parts of the world by the middle of 20th century as a direct benefit from the knowledge of the anthracitic property of sun shine. On the other hand, the existence of subclinical deficiency of vitamin-D remained unidentified till a method was established for the estimation of 25(OH)D. Vitamin D insufficiency was first reported in literature from the UK. Three groups of scientists reported low levels of 25(OH)D in pregnant women who were Asian immigrants [4-6]. Vitamin D deficiency was attributed to inadequate sunlight exposure due to latitude of the country along with deficient dietary intake of the vitamin. Tropical countries such as India [7,8], Pakistan [9], Bangladesh [10], UAE [11], and even Africa [12] reported of vitamin D deficiency in males and females. There is no dearth of sunshine availability almost throughout the year in these countries. However, the role of various factors that determine the availability of UV radiation from solar exposure and the way environmental factors affect it, needs in-depth assessment.

Since the last 2 decades, perception of Vit-D has been created to be a kind of universal remedy for chronic health disorders such as cancer, cardiovascular disease, diabetes, bone health, cognition, and mental depression [13]. This has been created based on many of the findings that have been from observational studies, where a higher blood level of 25 (OH) D has been linked to a lower risk for these medical conditions. As such, such a correlation doesn't

prove causation, because other factors could co-exist [13]. Many randomised trials could not sufficiently prove the benefits of the protective role of Vit-D. Some other studies indicated that even meagre amounts of supplementation will meet the requirements for Vit-D for bone health and many other consequences related to Vit-D deficiency [13].

Vitamin D deficiency has been reported throughout the world in recent past. Reports have implicated vitamin D deficiency in calcium and bone metabolic disorders, as well as type I and II diabetes, rheumatoid arthritis, multiple sclerosis and hypertension [14-19]. Furthermore, vitamin D is known to play a role in the human response to antimicrobials [20].

More recently, the randomised trials of Vit-D, including the VITAL study [13], have generally not shown benefits in terms of reductions in the major health outcomes besides some exceptions that include a 22% reduction in autoimmune conditions (rheumatoid arthritis and psoriasis) and a 17% reduction in advanced (metastatic or fatal) cancers. Meta-analyses of some large-scale randomised studies pointed out towards reduction in advanced cancers, even with very small doses of vitamin D (400-800 IUs daily). The reduction in autoimmune diseases suggests that Vid-D may play a role in reducing inflammation. In recent years, it has been a matter of debate whether vitamin D is beneficial in reducing the severity of COVID illness, the need for hospitalisation, and long COVID [13]. Those results are awaited.

Amongst the practising physicians world-wide, the debate is whether to test and treat Vid-D deficiency or does this issue does not call for such attention because of ease of availability of sunshine. Small to moderate amounts of vitamin D are adequate and thus the healthy population may not need screening or supplements. On the other hand, it needs to be emphasized here that all sunshine does not lead to cutaneous synthesis of vitamin D. The radiation energies between 290 and 320 nm are considered effective for adequate response towards Vit-D synthesis [21]. Vitamin D3 production in the epidermis has a complex mechanism, thus the amount of solar exposure required for providing vitamin D adequate for the body's requirements varies in individuals and under different set of conditions. Many factors can affect adequate production of Vit-D in human skin and keep a person insufficiently low for Vit -D levels in spite of adequate sunlight exposure; such as the time of the day of exposure, the surface area of the skin exposed to sunlight, the amount of melanin pigment in the epidermis, the latitude at which the person resides though the year (UV radiation is most intense at the equator), the season, and environmental pollution [22]. Unrealistically long sunlight exposure times seem to be required to obtain recommended vitamin D doses through skin as a result of these confounding factors [23,24]. With increasing rates of identification of aggressive skin cancers in Australian population, such prolonged exposures can't be advocated without warning to the public about its perils [25].

The high-risk groups that do need supplementation include patients in long term care for example in nursing homes, those who are on restricted diets for medical reasons as well other who spend limited time in outdoor activities [13]. Vit-D supplementation may be reasonably important for patients with diagnosed osteomalacia and severe osteoporosis, malabsorption conditions such as Crohn's disease and celiac disease or after a gastric bypass surgery.

Conclusion

The exposure to sunlight in a large proportion of the human population seems to be inadequate for their daily requirement of Vit-D cutaneous synthesis, and therefore Vit-D deficiency is a global problem. A controlled multi-centric trial evaluating and investigating adequate oral supplementation as compared to timed exposure to sunlight under various environmental conditions might provide more insight into future recommendations to general population regarding best practices to avoid Vit-D deficiency.

In view of contrasting reports, the optimal recommendation to prevent and treat Vitamin D deficiency and its related symptoms would be either advocating fortified food and alternatively to perform blood sampling diagnostics and then prescribe appropriate supplementation. This is even more significant in view of a large proportion of human population living in precarious conditions where it is difficult to assess length and quality of exposure to natural sunlight.

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