

Vitamin-D deficiency, the hidden pandemic in sunshine sufficient countries, exacerbating hypocalcaemia in a health worker undergoing thyroidectomy - a global perspective and review of literature

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Abstract

Introduction: Vitamin D deficiency (VDD) is common in young adults even in sunlight sufficient countries. It manifests with subtle and trivial symptoms that are often ignored. Nutritional deficiency due to improper dietary habits, poverty, long hours at work and study are factors. The lockdown during COVID has exacerbated the incidence. We had a patient with VDD who became symptomatic after routine thyroidectomy prompting our review into literature on the global health perspective of VDD.

Material and method: - A 21-year-old nursing student developed hypocalcaemia within 24 hours after a routine thyroidectomy. VDD was detected and patient improved after supplementation. Literature was reviewed from Pubmed database for the medical aspects of the problem, from Government archives like the Scientific Advisory Committee on Nutrition, ICMR etc for cause and medical archives including those of paediatric and general health for the impact of disease at the state, national and global level. A global health problem list was prepared and data was reviewed.

Discussion: Vitamin D is protective against respiratory infections due to viral aetiology including COVID. However, complete lockdown to prevent spread of COVID, online learning, and work from home culture has reduced sunlight exposure and increased incidence of VDD. Post thyroidectomy hypocalcaemia is common in VDD.

Conclusion: Since there is a high prevalence of asymptomatic VDD even in sunshine sufficient countries, it is recommended to screen all patients especially young adults for VDD during routine preoperative work up.

Introduction

Thyroidectomy, the operative removal of the thyroid gland, is a common procedure in most surgical centers across the world. Thyroidectomy is a safe procedure with very few complications. The most notable complications are injury to recurrent laryngeal and temporary or permanent hyperparathyroidism because of inadvertent removal or devascularisation of the parathyroid glands. The incidence of post-thyroidectomy hypocalcaemia has been reported to range from 0 to 45%^[1,2]. It usually manifests 48

to 72 hours after the surgery and is a cause for prolonged hospitalization & delay in discharge following thyroidectomy, especially in patients with severe symptoms^[3]. In benign thyroid diseases, Graves' disease is more commonly incriminated than multi-nodular goiter to develop post operative hypocalcaemia. However, experience of the surgical team, surgical skills and the surgeon's approach also have a significant role in reducing incidence, as well as in identifying and treating postoperative hypocalcaemia^[4]. Low Serum calcium, parathyroid

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hormone (PTH), and 25-hydroxy (25-OH) vitamin D levels prior to surgery increases the risk of post-op hypocalcemia (Fig 1)^[5].

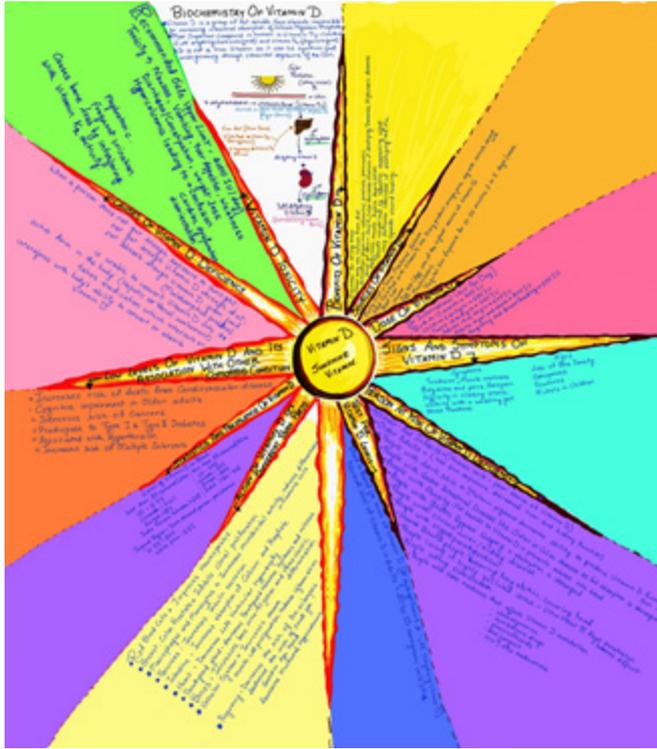


Fig 1 - Vitamin D - the sunshine vitamin. Biochemistry, pharmacology, causes, signs and symptoms of deficiency. (Illustration by Dr. Rajashree Menon, Author)

Vitamin D is obtained either through diet or supplements and plays a key role in calcium homeostasis. Exposure to sunlight for a short period every day is required for photolysis of 7-dehydrocholesterol to pre vitamin D₃ by ultra-violet (UV) B photons from sunlight (Fig 1)^[6,7]. Though easily available, a sedentary lifestyle, staying indoors, and eating junk food have increased the prevalence of Vitamin D deficiency (VDD) in the population, making it a global health problem. Symptoms may not manifest until late and if present, it is often dismissed as part of normal wear and tear of life. The symptoms include easy fatigability, dizziness, body pain, depression, and frequent infections due to reduced immunity. Children with VDD have a developmental delay, are lethargic and irritable, and with prolonged deficiency may develop rickets (Fig 1). If diagnosed early, treatment is simple oral replenishment of vitamin D^[8]. However, these trivial symptoms may need frequent hospital visits and often they are misdiagnosed or under diagnosed. These symptoms disturb the patient to such an extent that quality of life is affected and causes monetary loss to the patient in terms of loss of work and hospital expenses. This review of

literature was prompted by our experience with a young lady who underwent a routine thyroidectomy, presenting with symptomatic hypocalcemia on the first post-operative day which was diagnosed to be due to VDD.

Index patient report

A 21-year-old nursing student reported to our outpatient department with complaints of swelling in the front of neck for 9 months and a small lump in the left breast for 4 months. She had reported to a local hospital for evaluation, where an ultrasonography (USG) of the left breast showed a well-circumscribed solid hypoechoic lesion measuring 3.5 x 1.4 x 2.8 cm at 1-2 o'clock position and USG of the neck showed a well-circumscribed 1.9 x 1.4 x 2.8 cm nodule in the left lobe of thyroid without calcifications (TIRADS III). Since the parents were anxious about the breast lesion, she was brought to us for a second opinion and further management of both the lesions. On examination, there was a large multi-nodular goiter in the neck and a 4x3cm lump in the left breast, freely mobile within the breast tissue, suggestive of fibroadenoma. Her pre operative corrected calcium was 9.0mg/dL (normal 8.6 -10.2 mg/dl). Since there was a follicular lesion in the thyroid on fine needle aspiration which was suspicious and parents wanted a surgical option, a routine total thyroidectomy and excision of the lump in the left breast was done at the same sitting, to reduce their anxiety and overall cost. On post-operative day 1 (12 hours after surgery), the patient complained of perioral tingling and numbness along with severe paraesthesia in the upper limbs. Her corrected calcium at the time was 8.5 mg/dL. Since symptoms had occurred so early, we suspected that it could be due to metabolic response to major procedure. She was reassured. Our plan at the time was to observe for any other symptoms. By evening, <24 hours after surgery, she had worsening of symptoms. Chvostek's sign was positive. However, the corrected calcium sent at this time was 8.3 mg/dL. Since the patient had severe hypocalcemic symptoms, she was given a bolus dose of intravenous 10 ml of 10% calcium gluconate in 10 ml of 5% dextrose, given over 20 minutes. She was started on a treatment regimen of oral Calcium Carbonate + Vitamin D₃ (500+250IU/mg) 6th hourly and calcitriol (0.25 mcg) twice daily. She improved with this regimen temporarily but on second postoperative day, she had another episode of severe hypocalcemia and IV bolus had to be repeated. Since she had symptoms despite calcium correction, blood was taken for assessment of Parathyroid hormone (PTH) and 25OH Vitamin D. PTH was 11.12 pg/ml (15-65 pg/ml) and the Vitamin D level

was 13.55 ng/ml (deficiency <20 ng/ml). Addition of Vitamin D (Cholecalciferol (60000 IU) Capsule) to the calcium supplementation regimen markedly improved her symptoms. Vitamin D supplementation was continued as once a week regimen for 5 more weeks.

In view of VDD, we reviewed the history of the patient with her parents for dietary habits and sunlight exposure. The parents felt that their daughter used to be physically active and had adequate food when she was in their care at home. After she had joined her nursing course 5 years back, improper food habits at the college hostel may have contributed to her dietary deficiency. Long study periods and odd working hours may have contributed to an inadequate sunlight exposure. In the last 2 years, due to the COVID-19 pandemic, she had been restricted to her home and was continuing with online classes. She used to complain of easy fatigability, low scores in her exams, irritability, frequent back pain, and muscle cramps at night, that the parents attributed to her disinterest in studies and adolescent age. The histopathology of the thyroid specimen was reported as nodular hyperplasia with lymphocytic thyroiditis and the breast lesion was reported as a fibroadenoma.

The temporary hypocalcaemia due to hypoparathyroidism in this patient improved with oral calcium & vitamin D supplementation. She was slowly weaned off calcium over a period of 3 weeks, at which time her symptoms had completely disappeared. She was continued on her vitamin D supplementation for 2 more weeks.

Material and method

A global health problem list was initially prepared and the health problem was reviewed. Literature was reviewed from Pubmed database for the medical aspects of the problem including incidence, magnitude of the problem, causes, symptoms and treatment. The search parameters were "Vitamin D Deficiency", "Clinical features", "Diagnosis", "Vit-D", "COVID", "Nutritional deficiency", "geographic variation", "young adult", "post operative hypocalcaemia", "gender", "thyroidectomy". Boolean operatives "and" and "or" were used to improve the accuracy of the search. Each author was assigned to look at the data related to atleast two of these parameters, since there were more than 20000 search results. Important points on each of these parameters from the results and discussion sections of at least the first 10 results in the search were compiled as notes by each of the authors. Government archives of the Scientific Advisory Committee on Nutrition, the National Health Mission website, Ministry of Health and Family Welfare, Indian

Council of Medical Research and medical archives including those of paediatric and general health were then accessed for the impact of disease at the state, national and global level. A specific review of the literature was then made with search key health care worker being added. The compiled notes of each of the authors were then reviewed by the whole team for preparing the manuscript.

Global health problem list

- Vitamin D deficiency in India
- Vitamin D deficiency in young adults
- Pollution and vitamin D deficiency
- Vitamin D deficiency due to COVID-19 pandemic
- Vitamin D deficiency, COVID-19 pandemic and the health care workers/students
- Preoperative undiagnosed vitamin D deficiency in thyroidectomy
- Postoperative hypocalcaemia as result of undiagnosed vitamin D deficiency

Discussion

Vitamin D deficiency has become pandemic over the past few decades. The consequences of VDD are its effects on the musculoskeletal, neuro-cognitive and immune systems. It also leads to various cancers in the breast, colon, prostate, and pancreas^[9]. In India, VDD has been found commonly in inland regions and rural areas (71%); especially in the northern part of the country. Our region which is in the southernmost part of India, enjoys a tropical climate with adequate sunlight, and being on the costal belt provides some protection to VDD. The geographical location of Kerala and fish consumed in their diet by the local population may contribute to a low prevalence of VDD in our region. This has been proved in children^[10,11]. However, some studies have shown a remarkably high prevalence of VDD in perimenopausal women (89.1%) in the same region^[12]. There are similar studies from northern India and other parts of the world that show an increased prevalence of VDD. Greater than 20% of the population of India, Afghanistan, Tunisia, and Pakistan are reported to be severely vitamin D deficient^[13,14]. A change from an agrarian economy, rapid industrialisation, and sedentary lifestyle of the population in this region may have contributed to this condition. Advertisements and notifications by the government through audio-visual media, training the primary health care workers regarding sensitisation of the population to the cause, effect, prevention, and treatment of VDD will help to reduce the prevalence of the problem. In our population where cinema and cine-actors play a significant role in influencing the

awareness regarding social issues, this fact can be utilised to aid in improving the awareness about prevention and treatment of VDD. Indian council of medical research advocates an intake of 400 to 1000IU vitamin D for children less than one year and 600 to 1000 IU vitamin D for children up to 18 years of age^[15] [Fig 1]. The government of India runs a mid-day meal program for the children which aims at preventing malnutrition. Though the National Institute of Nutrition has given guidelines on the content and type of food to increase the availability of micronutrients like vitamin D, it is often not being followed as per the recommendation^[16]. It is felt that the dosage recommendation is inadequate for the Indian population since the dosages have been calculated for the western population^[15]. The condition can be rectified to a great extent if non-governmental organisations (NGO) can help or take over the mid-day meal programme^[17].

VDD is very common, especially in inland regions and rural areas and is believed to affect 70% population in India, being north of the Tropic of Cancer. Previous reports considered this problem to be rare in India. Though the children in central Kerala are exposed to sufficient sunlight they are found to have a subclinical deficiency of vitamin D^[18]. Since these children had no symptoms or signs suggestive of VDD, there was a recommendation to consider lower Vitamin D levels as normal for Indian children.

VDD has a major impact in young adults. Adolescence is an important period for building bone mass and bone mineral density requiring increased nutrition. A low bone mineral density at an early age leads to an increased risk of fracture and osteoporosis later in life. Vitamin D is pivotal for bone health as the active form improves calcium absorption from the intestine and promotes bone maturation^[19]. However, they are

preoccupied with studies, games and extracurricular activities keeping them away from food and sunlight. Many young women consciously avoid sunlight for cosmetic reasons or may not get adequate sunlight due to their dress codes^[20]. Often in India and other Asian countries, young women are forced to stay indoors by their parents or use a veil, for various social reasons.

In young adults, diet is often haphazard and incomplete, resulting in VDD that is often missed. Often the symptoms of VDD in these young adults are dismissed by their parents and care givers. It is attributed to their lack of interest in studies, rebellious behaviour, too much of play, and the condition worsens.

Vitamin D synthesis requires sunlight. Exposure to sunlight is low in population staying above the tropic of cancer and below the tropic of Capricorn and traditionally it was thought that the people living in tropical countries have adequate UV -B radiation to produce vitamin D^[21]. Though Holick et al suggested that exposure of the face and hands to a wavelength of UVB radiation between 290-370nm for about 30 minutes is adequate, even this may not be feasible for a young adult for reasons as described above^[22]. Migration of the population for work and education has also resulted in a reduced exposure to sunlight and a deficiency in diet due to dependence on restaurants and eateries once away from home. Increasing pollution levels have been proven to increase VDD in numerous studies^[23,24]. Air quality index in major cities across the world has worsened over the years, with India being the third worst affected country (Fig 2)^[25].

However, air quality is good in the rural areas. Our patient migrated from a coastal area to a temperate region for her nursing studies and had to subsist on infrequent, inadequate hostel food for the last 2 years.

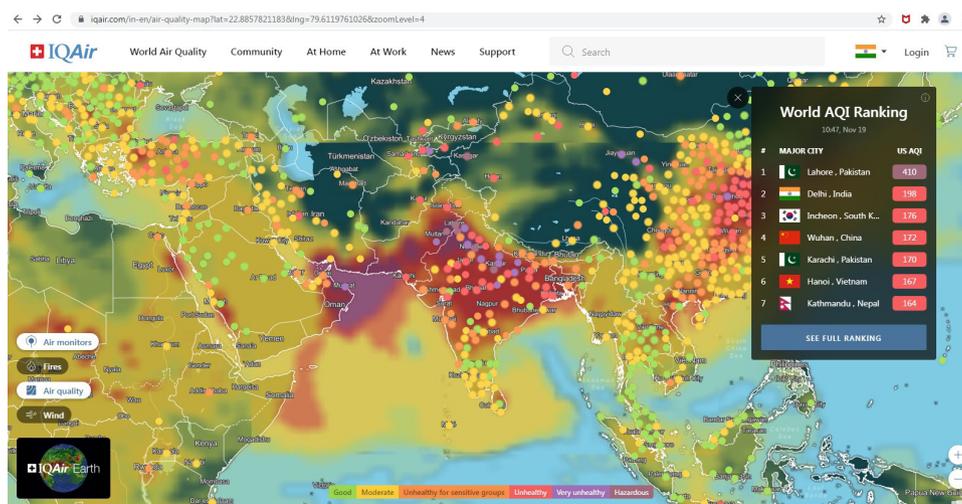


Fig -2 - Air Quality Index (Source - <https://www.iqair.com/in-en/india>)

The protective role of vitamin D supplementation against harbouring viral respiratory infection has been reported by numerous studies. There is also an increased risk of progression and death from viral infections like Human immunodeficiency virus, due to increased inflammation, immune activation and activated monocytes in patients with VDD^[26]. An updated review from the Scientific Advisory Committee on Nutrition (SACN 2020) suggested that low-dose vitamin D supplementation (400 IU/day) is beneficial in lowering the risk of acute respiratory tract infections^[27].

The COVID-19 pandemic has caused most countries in the world to keep their population under lockdown to prevent spread of the disease and exposed them to the effects of lack of exposure to sunshine. VDD has been associated with increased severity of lung involvement due to an altered inflammatory response^[28,29]. Many health advisories at the beginning of the pandemic recommended Vitamin D supplementation in affected individuals as prophylaxis and many people availed this vitamin over the counter. In those countries with deficiency in vitamin D, COVID-19 related morbidity and mortality was found to be high^[30]. Advisory from the health authority to screen for VDD and include Vitamin D in the treatment regimen of common viral fevers including COVID would help improve management.

There is a high prevalence of VDD in the health care workers especially in students, compared to other professionals associated with healthcare. Long work hours, improper sleep, improper timing, and quality of diet have rendered this group susceptible for many nutritional disorders^[31]. Our patient, a nursing student, affected by this problem is an adolescent from a lower socioeconomic stratum of society, with poor eating habits and dietary deficiency. She had VDD but these symptoms were missed due to similarity with problems of adolescence and was unmasked at thyroidectomy.

Post thyroidectomy hypocalcaemia may be temporary or permanent and is a common cause for delay in hospital discharge. It is due to low circulating parathyroid hormone because of damage to the parathyroid glands, their vascular supply, or inadvertent removal. Several studies have reported the effect of vitamin D supplementation in the prevention of post-thyroidectomy hypocalcaemia and found its impact on reducing the incidence and severity of the condition. Serum 25(OH)D has even been suggested as a marker of postoperative hypocalcaemia and can be used as a routine screening test during work up for thyroidectomy^[32,33,34].

We have started to routinely screen all patients for VDD as part of the pre-operative workup. We have found that nearly 80% of patients have asymptomatic /subclinical VDD. A prospective randomised comparative study is presently underway to study effect of Vitamin supplementation given to patients with VDD, preoperatively versus post operatively, in reducing the symptomatic effects of post op hypocalcaemia.

Figure 1 gives details regarding benefits, sources, actions on organs, dose, toxicity of vitamin D and also the clinical features and risk factors in deficiency states.

Learning Points

- VDD is common even in sunlight sufficient countries and the prevalence rates are much higher than previously thought.
- Adolescents are commonly affected by VDD. Early and more aggressive screening can identify and alleviate many health & psychological problems attributable to VDD.
- Symptoms of hypocalcaemia appears much earlier following thyroidectomy in patients having VDD.
- It is suggested to screen asymptomatic patients coming for routine procedures for VDD

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