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Observation of Vitamin D Deficiency in newborn and its overcome by oral Vitamin D Supplements

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Abstract
Vitamin D is known to play an important role in bone metabolism through regulation of calcium and phosphate homeostasis and may also play an important role in immune system regulation. Vitamin D is produced by the body during exposure to sunlight, but is also found in oily fish, eggs and fortified food products. Infants are born with low vitamin D stores and are dependent on breast milk, sunlight or supplements as sources of vitamin D in the first few months of life. As the vitamin D content of breast milk is dependent on maternal vitamin D status and is often low, and sun exposure may be restricted for infants living at higher latitudes or for cultural or other reasons, infants are particularly vulnerable to vitamin D deficiency. Vitamin D deficiency in infants can lead to bone malformation (rickets), seizures and difficulty breathing. Current evidence suggests that vitamin D supplements may be effective in preventing rickets, particularly for infants and children who may be at higher risk due to limited sun exposure or those with darker skin pigmentation, however further research is needed before specific recommendations can be made. Hence the present study was planned for Observation of Vitamin D Deficiency in Newborn and Its Overcome by Oral Vitamin D Supplements.
The present study was planned in Department of Pediatrics, Government Medical College, Bettiah, West Champaran, Bihar. The 50 cases of the term new borns were delivered to our hospital were enrolled in the present study. The cord blood was collected in plane tube, serum separated and tested for serum vitamin D, calcium phosphorus and ALP by immune assay technique. The values are noted. Then the babies with the vitamin D deficiency/insufficiency were supplemented with single high dose of vitamin D 60000 IU orally. And followed up after 45 days with estimation of serum vitamin D, calcium phosphorus and ALP.
The data generated from the present study concludes that Most of our new borns, are born with vitamin D deficiency or insufficiency, and only a few babies have adequate serum vitamin D levels at birth. A single high dose of Oral vitamin D 60,000 IU is sufficient to normalise serum vitamin D levels with none developing hypervitaminosis.

Keywords: Vitamin D, deficient, supplement, newborn, etc

Introduction
Vitamin D is a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects. In humans, the most important compounds in this group are vitamin D3 (also known as cholecalciferol) and vitamin D2 (ergocalciferol) [1].
The major natural source of the vitamin is synthesis of cholecalciferol in the lower layers of epidermis skin through a chemical reaction that is dependent on sun exposure (specifically UVB radiation). Cholecalciferol and ergocalciferol can be ingested from the diet and from supplements. Only a few foods, such as the flesh of fatty fish, naturally contain significant amounts of vitamin D. In the U.S. and other countries, cow's milk and plant-derived milk substitutes are fortified with vitamin D, as are many breakfast cereals. Mushrooms exposed to ultraviolet light contribute useful amounts of vitamin D. Dietary recommendations typically assume that all of a person's vitamin D is taken by mouth, as sun exposure in the population is variable and recommendations about the amount of sun exposure that is safe are uncertain in view of the skin cancer risk [2].
Vitamin D from the diet, or from skin synthesis, is biologically inactive. A protein enzyme must hydroxylate it to convert it to the active form. This is done in the liver and in the kidneys. As vitamin D can be synthesized in adequate amounts by most mammals exposed to sufficient sunlight, it is not an essential dietary factor, although not technically a vitamin. Instead it could be considered a hormone, with activation of the vitamin D pro-hormone resulting in the active form, calcitriol, which then produces effects via a nuclear receptor in multiple locations [3].
Cholecalciferol is converted in the liver to calcifediol (25-hydroxycholecalciferol); ergocalciferol is converted to 25-hydroxyergocalciferol. These two vitamin D metabolites (called 25-hydroxyvitamin D or 25(OH)D) are measured in serum to determine a person's vitamin D status. Calcifediol is further hydroxylated by the kidneys to form calcitriol (also known as 1,25-dihydroxycholecalciferol), the biologically active form of vitamin D. Calcitriol circulates as a hormone in the blood, having a major role regulating the concentration of calcium and phosphate, and promoting the healthy growth and remodeling of bone. Calcitriol also has other effects, including some on cell growth, neuromuscular and immune functions, and reduction of inflammation [2].
Vitamin D has a significant role in calcium homeostasis and metabolism. Its discovery was due to effort to find the dietary substance lacking in children with rickets (the childhood form of osteomalacia). Vitamin D supplements are given to treat or to prevent osteomalacia and rickets. The

evidence for other health effects of vitamin D supplementation in the general population is inconsistent. The effect of vitamin D supplementation on mortality is not clear, with one meta-analysis finding a small decrease in mortality in elderly people, and another concluding no clear justification exists for recommending supplementation for preventing many diseases, and that further research of similar design is not needed in these areas [4].

Vitamin D deficiency, or hypovitaminosis D, most commonly results from inadequate sunlight exposure (in particular sunlight with adequate ultraviolet B rays). Vitamin D deficiency can also be caused by inadequate nutritional intake of vitamin D, disorders limiting vitamin D absorption, and conditions impairing vitamin D conversion into active metabolites—including certain liver, kidney, and hereditary disorders. Deficiency impairs bone mineralization, leading to bone softening diseases such as rickets in children. It can also worsen osteomalacia and osteoporosis in adults, leading to an increased risk of bone fractures. Muscle weakness is also a common symptom of vitamin D deficiency, further increasing the risk of fall and bone fractures in adults [5].

Ultraviolet B rays from sunlight is a large source of vitamin D. Fatty fish such as salmon, herring, and mackerel are also sources of vitamin D. Milk is often fortified with vitamin D and sometimes bread, juices, and other dairy products are fortified with vitamin D as well. Many multivitamins now contain vitamin D in different amounts [5]. Vitamin D deficiencies are often caused by decreased exposure of the skin to sunlight. People with a darker pigment of skin or increased amounts of melanin in their skin may have decreased production of Vitamin D. Melanin absorbs ultraviolet B radiation from the sun and reduces vitamin D production. Sunscreen can also reduce vitamin D production. Medications may speed up the metabolism of vitamin D, causing a deficiency. Some types of liver diseases and kidney diseases can decrease vitamin D production leading to a deficiency. The liver is required to transform vitamin D into 25-hydroxyvitamin D. This is an inactive metabolite of vitamin D but is a necessary precursor (building block) to create the active form of vitamin D [6].

In liver disease, the 25-hydroxyvitamin D may not be formed, leading to a vitamin D deficiency. The kidneys are responsible for converting 25-hydroxyvitamin D to 1, 25-hydroxyvitamin D. This is the active form of vitamin D in the body. Kidney disease often prevents 1, 25-hydroxyvitamin D from being formed, leading to a vitamin D deficiency. Intestinal conditions that result in malabsorption of nutrients may also contribute to vitamin D deficiency by decreasing the amount of vitamin D absorbed via diet. In addition, a vitamin D deficiency may lead to decreased absorption of calcium by the intestines, resulting in increased production of osteoclasts that may break down a person's bone matrix. In states of hypocalcemia, calcium will leave the bones and may give rise to secondary hyperparathyroidism, which is a response by the body to increase serum calcium levels. The body does this by increasing uptake of calcium by the kidneys and continuing to take calcium away from the bones. If prolonged, this may lead to osteoporosis in adults and rickets in children [7].

The serum concentration of 25(OH)D is typically used to determine vitamin D status. Most vitamin D is converted to 25(OH)D in the serum, giving an accurate picture of vitamin D status. The level of serum 1,25(OH)D is not usually used to determine vitamin D status because it often is regulated by other hormones in the body such as parathyroid hormone. The levels of 1,25(OH)D can remain normal even when a person may be vitamin D deficient. Serum level of 25(OH)D is the laboratory test ordered to indicate whether or not a person has vitamin D deficiency or insufficiency. It is also considered reasonable to treat at-risk persons with vitamin D supplementation without checking the level of 25(OH)D in the serum, as vitamin D toxicity has only been rarely reported to occur [8].

Levels of 25(OH)D that are consistently above 200 ng/mL (500 nmol/L) are thought to be potentially toxic, although data from humans are sparse.[citation needed] Vitamin D toxicity usually results from taking supplements in excess. Hypercalcemia is often the cause of symptoms, [9] and levels of 25(OH) D above 150 ng/mL (375 nmol/L) are usually found, although in some cases 25(OH)D levels may appear to be normal. Periodic measurement of serum calcium in individuals receiving large doses of vitamin D is recommended.

In the United States and Canada as of 2016, the amount of vitamin D recommended is 400 IU per day for children, 600 IU per day for adults, and 800 IU per day for people over age 70. The Canadian Paediatric Society recommends that pregnant or breastfeeding women consider taking 2000 IU/day, that all babies who are exclusively breastfed receive a supplement of 400 IU/day, and that babies living north of 55°N get 800 IU/day from October to April [10].

Treating vitamin D deficiency depends on the severity of the deficit. Treatment involves an initial high-dosage treatment phase until the required serum levels are reached, followed by the maintenance of the acquired levels. The lower the 25(OH)D serum concentration is before treatment, the higher is the dosage that is needed in order to quickly reach an acceptable serum level [11]. The initial high-dosage treatment can be given on a daily or weekly basis or can be given in form of one or several single doses (also known as stoss therapy, from the German word "Stoßen" meaning to push) [12]. Therapy prescriptions vary, and there is no consensus yet on how best to arrive at an optimum serum level. While there is evidence that vitamin D3 raises 25(OH)D blood levels more effectively than vitamin D2, other evidence indicates that D2 and D3 are equal for maintaining 25(OH)D status [11].

Vitamin D deficiency is considered to be the most common nutritional deficiency [31] and also one of the most common undiagnosed medical conditions in the world. Vitamin D has evolved into a hormone that is active throughout the body not only to regulate calcium and bone metabolism but also to reduce the risk of chronic diseases including auto immune diseases, malignancies, cardiovascular and infectious diseases. It has been estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency [14]. Though majority of population in India lives in areas receiving ample sunlight throughout the year, vitamin D deficiency is very common in all the age groups and both the sexes across the country [15-17].

Over the last two decades, understanding of vitamin D synthesis and its function has changed remarkably. This led us to re-examine the traditional concepts and current recommendations for vitamin D supplementation, sun light exposure and revised management strategies for deficiency. In this review, we discuss the current knowledge on diagnosis, prevention and treatment of vitamin D deficiency.

Vitamin D is known to play an important role in bone metabolism through regulation of calcium and phosphate homeostasis and may also play an important role in immune system regulation. Vitamin D is produced by the body during exposure to sunlight, but is also found in oily fish, eggs and fortified food products. Infants are born with low vitamin D stores and are dependent on breast milk, sunlight or supplements as sources of vitamin D in the first few months of life. As the vitamin D content of breast milk is dependent on maternal vitamin D status and is often low, and sun exposure may be restricted for infants living at higher latitudes or for cultural or other reasons, infants are particularly vulnerable to vitamin D deficiency. Vitamin D deficiency in infants can lead to bone malformation (rickets), seizures and difficulty breathing. Current evidence suggests that vitamin D supplements may be effective in preventing rickets, particularly for infants and children who may be at higher risk due to limited sun exposure or those with darker skin pigmentation, however further research is needed before specific recommendations can be made.Hence the present study was planned for Observation of Vitamin D Deficiency in Newborn and Its Overcome by Oral Vitamin D Supplements.

Methodology

The present study was planned in Department of Pediatrics, Government Medical College, Bettiah, West Champaran, Bihar. The 50 cases of the term new borns were delivered to our hospital were enrolled in the present study.The cord blood was collected in plane tube, serum separated and tested for serum vitamin D, calcium phosphorus and ALP by immune assay technique. The values are noted. Then the babies with the vitamin D deficiency/insufficiency were supplemented with single high dose of vitamin D 60000 IU orally. And followed up after 45 days with estimation of serum vitamin D, calcium phosphorus and ALP.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results & Discussion

A recent institute of medicine (IOM) report defines "inadequate vitamin D" when serum concentrations of 1,25(OH)D are <20 ng/ml [10]. A recent task force of the Endocrine Society defines vitamin D "deficiency" as a 25(OH) D value below 20 ng/ml, "insufficiency" as a 25(OH) D value between 20 and 30 ng/ml, and recommended target of treatment should be to achieve a 25(OH) D above 30 ng/ml [18]. To date, specific range for neonates is not available.

Vitamin D inadequacy and deficiency are global problems, and their prevalence is high even in developed and sunny countries [19]. The prevalence of vitamin D insufficiency is increasing globally. Although the reason for the increase in vitamin D deficiency is unclear, a combination of a change in lifestyle, liberal use of sunscreens in some parts of the world, adoption of covered attire in some societies and global environmental pollution might have contributed to the widespread increase in vitamin D deficiency [20]. Risk factors for vitamin D deficiency and rickets in early life include breastfeeding without vitamin D supplementation, dark skin pigmentation, race, season, latitude and maternal vitamin D deficiency [21].

There is a high prevalence of vitamin D deficiency in pregnant and lactating mothers especially nonwestern immigrants in countries at higher latitude. Evidence from observational studies shows higher rates of preeclampsia, gestational diabetes, bacterial vaginosis, preterm birth and cesarean section in women with low vitamin D levels; all of which have potentially adverse effects on the neonate. However, other studies found no associations with the same outcomes. [22] Contradictory results can be explained by methodological, genetic, ethnic and racial differences as well as latitude of residence and season.

The relationship between maternal vitamin D status and fetal birth weight has been studied in randomized controlled trials (RCTs) and a number of observational studies with mixed results. The presence of multiple confounding factors such as, maternal nutritional status, calcium and phosphorus intake, prepregnant body mass index and socioeconomic status could explain the inconsistent findings. There is a strong correlation between maternal and infant cord blood 25(OH) D concentrations. However, in utero, skeletal mineralization is primarily independent of maternal vitamin D status; consequently, the blood calcium, calciotropic hormones and skeleton are normal at birth in the offspring of mothers who are severely vitamin D deficient. [No systemic studies have examined the effect of maternal vitamin D status on neonatal skeletal mineral content. Only few studies [23-25] reported contradictory results. Therefore, the importance of maternal vitamin D status to fetal skeletal development is not sufficiently investigated.

Table 1: Basic Characteristics

Characteristics	No. of Cases
Term gestation	50
Birth weight > 2500 grams	2
Breast feeding up to 6 month	45
Complementary feed rich in calcium (ragi)	32
Milk intake (>200 ml per day)	49
Oily fish intake	14
Sunlight exposure > 30 minutes/day	22

Table 2: Status of Vitamin D

Characteristics	No. of Cases
Normal	14
Deficient	11
Insufficient	26
Total	50

Table 3: Serum Vitamin D level after supplement

Characteristics	No. of Cases
Normal	49
Deficient	1
Insufficient	0
Total	50

Cranney *et al*. [26] summarized the published trials on the effect of vitamin D supplementation on circulating 25(OH) D concentrations. Interestingly, the daily doses of vitamin D2 used in all of these trials were < 400 IU [27]. Zeghoud *et al*. Administered either 200,000 IU once at birth or 100,000 IU vitamin D3 at birth, 3 and 6 months [28]. They later compared daily doses of 500 IU versus 1000 IU. Another trial demonstrated a dose-response relationship infants receiving daily vitamin D2 of 100, 200 and 400 IU. Authors suggested that 200 IU of vitamin D2 may not be enough to

prevent vitamin D deficiency in some infants residing at northern latitudes. Consistent dose-response to vitamin D supplementation is noted across trials, however infants who are vitamin D deficient may respond differently and require higher doses of vitamin D. [27]

More recently, Siafarikas *et al*. [29] and Holmlund-Suila *et al*. [30] performed RCTs to investigate vitamin D status in breastfed, term infants with measurement of calcium homeostasis and bone health. Siafarikas *et al* [29] studied "low doses" of vitamin D supplementation, 250 versus 500 IU/day, Holmlund-Suila *et al* [30] evaluated the effects of "high doses" of vitamin D supplementation with three dose groups (400, 1200 and 1600 IU/day) to identify the dose that ensures 25(OH) D status of at least 32 ng/ml without evidence of toxicity. In both studies, no vitamin D toxicity and no difference in markers of calcium homeostasis or bone health were appreciated among doses. Siafarikas *et al* [29] concluded that 250 IU/day is adequate for breastfed infants and the Holmlund-Suila *et al* [30] concluded that vitamin D supplementation up to 1600 IU/day safely maintains vitamin D sufficiency. Until more conclusive results are available, the AAP.Recommendation to provide 400 IU/day to all infants remains generally safe and efficacious in preventing rickets.

The most important factor determining the vitamin D status in infancy is the maternal vitamin D status [31] Though practically difficult, all pregnant women should have their 25(OH) D levels checked during the first trimester of pregnancy. If they are deficient they should be treated with 3000-5000 IU until 25(OH)D is more than >20 ng/dL followed by 400 IU /daily [32]

Routine vitamin D supplementation to all the pregnant women is controversial [33] Administration of high dose of vitamin D (400-6400 IU) daily to breast feeding mothers increases the anti-rachitic activity of breastmilk [34-35] without causing hypervitaminosis in the mother.

Preterm infants should be supplemented from birth with 400-800 IU/day because of inadequate transfer of maternal vitamin D stores and issues associated with prematurity such as poor feeding, gastrointestinal difficulties impairing absorption and sometimes liver and kidney impairment. Consideration for universal supplementation particularly in breastfed infants has been suggested [36].

The preparations available in India are; Vitamin D3 – as oral drops 400 IU/mL; Syrup 400 IU/5mL; and Tablets as 1000 and 2000 IU in blister packing and also as sachet in powder form with each sachet containing 60000 IU of vitamin D3.

Supplementation in newborn period: For infants who are exclusively breastfed a minimum daily intake of 400 IU/day should be initiated within a few days after birth. Since most of the infant formulas contain 400 IU/L, infants who are on formula feeds also need supplementation unless they consume more than 1000 mL of formula per day.

Toddlers and adolescents: Children who are dark skinned, veiled, exposed to reduced sun light or who have underlying medical condition should receive 400 IU daily to prevent vitamin D deficiency.

Considering the increased prevalence of vitamin D deficiency and the confusion about supplementation and treatment of vitamin D deficiency for various age groups, the IAP has put forth recommendations for prevention and treatment of vitamin D and calcium deficiency. The recommendations are in line with other international organizations. As a long term policy, fortifying everyday staple foods, which will be consumed by the at-risk segments of the population, with calcium and vitamin D is the solution to the problem.

Conclusion

The data generated from the present study concludes that Most of our new borns, are born with vitamin D deficiency or insufficiency, and only a few babies have adequate serum vitamin D levels at birth.A single high dose of Oral vitamin D 60,000 IU is sufficient to normalise serum vitamin D levels with none developing hypervitaminosis.

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