UNIVERSITY OF DIYALA
COLLEGE OF MEDICINE

THE EFFECT OF VITAMIN D DEFFICIENCY AMONG CHILDREN UNDER 10 YEARS

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ABSTRACT

Given the recent spate of reports of vitamin D deficiency, there is a need to reexamine our understanding of natural and other sources of vitamin D, as well as mechanisms whereby vitamin D synthesis and intake can be optimized, therefore our review pereformed and analysis of the 20 reviews was conducted. Also this study critically reviews renewed scientific interest in the sequelae of vitamin D deficiency, given the emerging evidence on the diverse biologic functions of vitamin D, besides its fundamental role in bone and mineral metabolism. For the past decade, the evidence in the medical literature pointing to a relationship between anemia risk and vitamin D deficiency has been accumulating. Despite the advances in unraveling the role of vitamin D in iron homeostasis, further research is still required to validate causality in the relationship between vitamin D deficiency and anemia, as well as to determine its optimal dosing, the ideal recipients for therapeutic intervention, and the preferred analogs to administer. Therefore ,Vitamin D research suggests it has a role in disorders other than bone metabolism, and the recommendations for sun exposure and vitamin D intake and possible caveats associated with these recommendations**..**

Keywords: Vitamin D, Childhood anemia ,Vitamin D deficiency, Sun exposure

CONTENTS

THE EFFECT OF VITAMIN D DEFFICIENCY AMONG CHILDREN UNDER 10 YEARS

LIST OF SYMBOLS AND ABBREVIATIONS

Description	Symbol
Baquba Teaching Hospital	BTH
Vitamin D deficiency	VDD
American Academy of Pediatrics	AAP
Vitamin D	25(OH)-D—25(OH)
Ultraviolet radiation	UVR
Parathyroid hormone	PTH
Alkaline phosphatase	ALP
Vitamin D–binding protein	DBP
Dihydroxy vitamin D	24,25(OH)2-D—24,25
Minimum erythema dose	MED
Monoclonal antibody	mAb
High-pressure liquidchromatography	HPLC
Sun protection factors	SPF
Parathyroid hormone	PTH
Pharmacokinetic/Pharmacodynamics.	PK/PD

CHAPTER 1

INTRODUCTION & GENERAL INFORMATION

During childhood and adolescence, vitamin D is important for calcium absorption and bone growth and accretion. In addition to skeletal effects, including maintenance of normal bone turnover, mineralization during adulthood, and prevention of rickets in children, vitamin D may confer protection against health problems such as type 1 diabetes mellitus, hypertension, multiple sclerosis, and cancer. There are growing data from studies of young adults, elderly persons, and youth in other countries that vitamin D deficiency is an unrecognized and prevalent health problem. Despite milk fortification in this country, subclinical vitamin D deficiency has been noted, with a high prevalence in adult medical inpatients, homebound elderly individuals, postmenopausal women presenting with hip fracture, and healthy young adults. Few data are available regarding the prevalence of this nutritional deficiency among healthy US children and adolescents. **(1)**

Building on data from the Third National Health and Nutrition Examination Survey, in which serum 25-hydroxyvitamin D (25OHD) levels were measured and vitamin D deficiency (25OHD level, _15 ng/mL [_37.5 nmol/L]) was found in 17% of southern adolescents during winter and 8% of northern teenagers during summer , and they examine the prevalence of hypovitaminosis D and secondary hyperparathyroidism in an adolescent cohort during each season, because parathyroid hormone (PTH) levels were not measured as part of the Third National Health and Nutrition Examination Survey.

To our knowledge, no previous studies have examined the prevalence of this problem in adolescent boys and girls in the United States across the 4 seasons. Adolescents in Boston are at increased risk for vitamin D deficiency because the high latitude precludes cutaneous vitamin synthesis during winter. Thus, we undertook the present study in our adolescent medicine clinic to determine the prevalence of vitamin D deficiency among an urban convenience sample of otherwise healthy teenagers. The researches test the hypothesis that vitamin D

deficiency (25OHD level,_15ng/mL) is prevalent among healthy adolescents, and determine whether a seasonal variation existed for serum 25OHD and PTH levels, testing the hypothesis that 25OHD levels would be lower and PTH levels higher during winter. In addition the factors within the adolescent lifestyle that represent predictors of hypovitaminosis D**..(1)**

There has been concern raised about a resurgence of vitamin D deficiency and rickets among infants and children, with reports emerging in the United States from Alaska ,Iowa, Nevada, California, North Carolina,Texas, and motherinfant pairs in Boston, among others. The prevalence of vitamin D deficiency in young children also appears to be high in other countries, including England, Greece, and Canada. One study from China found a 65.3% prevalence of vitamin D deficiency among 12- to 24-montholds, but few cases (3.7%) of radiographic or clinical rickets were noted. Previous studies suggest risk factors to be dark skin pigmentation and breastfeeding without supplementation.

To date, reports have focused primarily on young infants compared with toddlers Thus, there appears to be less information available regarding variables that predispose young children to vitamin D deficiency as they wean to fortified milk and solid foods. In 2004, another study reported a high prevalence of vitamin D deficiency among otherwise healthy teenagers who were seen for primary care. It is recommended that, vitamin D deficiency (25-hydroxyvitaminD [25OHD] level,_20 ng/mL [to convert to nanomoles per liter, multiply by2.496]) is prevalent among healthy infants and toddlers to the same degree as among adolescents (ie, 42%), and 25OHD concentrations are lower and PTH levels are higher during winter, especially among those with darker skin pigmentation, as was seen among adolescents. Also, nutritional and lifestyle variables that represented predictors of vitamin D deficiency and 25OHD level, and breastfeeding without supplementation among infants, consumption of juice rather than milk in toddlers, dark skin pigmentation, and winter season would emerge as significant predictors of vitamin D deficiency.

This study reviewed the prevalence and risk factors associated with vitamin D deficiency in children .To determine the prevalence of vitamin D deficiency in healthy adolescents presenting for primary care. In addition to determine the

prevalence of vitamin D deficiency and to examine whether 25-hydroxyvitamin D (25OHD) concentration varies as a function of skin pigmentation, season, sun exposure, breastfeeding, and vitamin D supplementation, also to compare the prevalence of hypovitaminosis D and associated factors in schoolchildren and adolescents living in aregion of diyala province with other researches.

CHAPTER 2

LITERATURE REVIEW

Vitamin D is vital metabolically active compound that is either synthesized by the body using UVB light or absorbed via the digestive system from certain foods. The role of vitamin D is to facilitate calcium homeostasis. Deficiency of vitamin D is implicated in a great number of orthopaedic conditions, including SUFE, Perths, osteomalacia and fragility fractures.Vitamin D deficiency is very common in the UK due to diet, lifestyle, weather and our northern latitude. **(2)**

Vitamin D plays an important role in maintaining bone health through regulating calcium concentration in the body. The development of vitamin D deficiency is associated with deteriorating bone health**. (2)**

Vitamin D is a pro hormone that is essential for normal absorption of calcium from the gut, and deficiency of vitamin D is associated with rickets in growing children and osteomalacia in adults. Rickets is the failure of mineralization of growing bone and cartilage. Initial descriptions of rickets were provided by Daniel Whistler and Francis Glisson in England as early as the 17th century. At the turn of the 20th century, with industrialization, this disease became endemic until it was discovered that exposure to sunlight and cod liver oil could both prevent and treat rickets. Once vitamin D was identified and easy ways to supplement foods were developed, nutritional rickets almost disappeared from industrialized countries. However, there has been a reappearance of rickets from vitamin D deficiency in recent decades as a result of multiple factors. Dark-skinned infants who are exclusively breastfed and infants born to mothers who were vitamin D deficient through pregnancy seem to be at particularly high risk. However, rickets is also being reported in older children.
However, despite current guidelines for vitamin D supplementation, rickets continues to be reported. It is important to recognize that vitamin D is primarily made in the skin after exposure to ultraviolet radiation (UVR), and _10% is derived from dietary sources.**(3)**

EFFECT OF VITAMIN D DEFICIENCY

Calcium and Phosphorus Metabolism and Bone In a vitamin D–sufficient state [25(OH)-D levels of _50 nmol/L (20 ng/mL)], net intestinal calcium absorption is up to 30%, although calcium absorption can reach 60% to 80% during periods of active growth. In a vitamin D–deficient state, intestinal calcium absorption is only 10% to 15% and there is a decrease in the total maximal reabsorption of phosphate. In conditions of vitamin D deficiency, low ionized calcium levels stimulate parathyroid hormone (PTH) secretion, which increases calcium reabsorption in renal tubules and increases 1-hydroxylase activity, which causes increased 1,25- dihydroxy vitamin D [1,25(OH)2-D] synthesis. Increased PTH levels also cause phosphorus loss in urine. Decreased levels of phosphorus (and also calcium) and decreased calcium*phosphorus product result in decreased bone mineralization. In addition, the low phosphorus levels cause a failure of the expected apoptosis of hypertrophied chondrocytes, with cellular "ballooning" and disorganization of the growth plate. Failure or delay of calcification of osteoid leads to osteomalacia in mature bones. Osteomalacia in immature bones is referred to as rickets. The term rickets also describes the abnormal organization of the cartilaginous growth plate and the accompanying impairment of cartilage mineralization. The clinical presentation of vitamin D–deficiency rickets includes symptoms and signs of bone deformity and/or pain and may be associated with hypocalcemia and associated clinical features. The disease can be divided into 3 stages . The first stage is characterized by osteopenia and subclinical or overt hypocalcemia (usually very transitory and, therefore, undocumented), which is followed in the second stage by rising levels of PTH. Increases in PTH levels cause calcium mobilization from bone and correction of hypocalcemia.

Demineralized collagen matrix is prone to hydration and swelling, which causes the periosteal covering to expand outward, and bone pain occurs, mediated by periosteal sensory pain fibers. In the final stage, bone changes become more severe, and hypocalcemia once again becomes evident. **(3)**

Skin

Keratinocytes express the vitamin D receptor, and when these cells are exposed to vitamin D, their growth is inhibited and they are stimulated to differentiate. This has led to the use of topical vitamin D analogs to treat psoriasis.

Immune Effects

Vitamin D modulates B- and T-lymphocyte function. Epidemiologic evidence exists of vitamin D deficiency being associated with autoimmune diseases such as type 1 diabetes and multiple sclerosis. One-year-old vitamin D–deficient children have been reported to be at a fourfold higher risk of developing type 1 diabetes than vitamin D–sufficient children. Also, the risk for multiple sclerosis is higher in people who live above 35°latitudes than in those who live below this latitude, and an inverse relationship has been reported between vitamin D concentrations and risk of multiple sclerosis. Data suggest that vitamin D sufficient states in the mother and infant may protect against type 1 diabetes and multiple sclerosis. Protective effects of vitamin D supplementation have also been demonstrated against rheumatoid arthritis and inflammatory bowel disease.

Cancer

Vitamin D concentrations of 75 nmol/L (30 mg/mL) keep cell growth in check and prevent cells from becoming autonomous and developing into unregulated cancer, and vitamin D deficiency has been related to breast, prostate, and colon cancer.

Psychiatric Conditions

Adequate vitamin D levels in pregnancy are associated with decreased risk of schizophrenia; conversely, low levels of sun exposure are associated with seasonal affective disorder and mood disturbances. It is unclear, however, whether it is decreased sun exposure or deficiency of vitamin D that is related to the latter conditions. Vitamin D sufficient states in the mother and infant are thought to be associated with a lower risk of bipolar disorder. Low maternal vitamin D levels may have an impact on fetal brain maturation, given that vitamin D is also involved in development and functioning of the nervous system**.(3)**

SOURCES OF VITAMIN D

Studies have indicated that most circulating vitamin D is synthesized from skin exposure to ultraviolet B (UV-B) radiation. Cutaneous Vitamin D Synthesis Vitamin D synthesis by the skin is the main source of this prohormone for most people. Vitamin D2 (ergocalciferol) is plant derived, whereas vitamin D3 (cholecalciferol) is synthesized by animals. The highest concentrations of 7-dehydrocholesterol are found in the stratum basale and stratum spinosum of the epidermis; thus, these layers have the greatest capability of previtamin D synthesis. Exposure to UV-B in the wavelengths of 290 to 315 nm initiates the synthesis of vitamin D by causing double bonds in the B ring of provitamin D to rearrange, which leads its B ring to open and, thus, converting it to the less rigid previtamin D. Previtamin D isomerizes to vitamin D and then is transferred to extracellular space and dermal capillaries, where it binds with vitamin D–binding protein (DBP). This binding ensures efficient conversion of previtamin D to vitamin D by shifting the equilibrium toward vitamin D. The complex of DBP with vitamin D is transported to the liver for 25-hydroxylation to 25(OH)-D (calcidiol). Although 25(OH)-D is 2 to 5 times as potent as vitamin D, it is not biologically active at physiologic concentrations. 25(OH)-D is released into the circulation and transported to the kidney bound to DBP for 1-hydroxylation to 1,25(OH)2-D and for 24-hydroxylation to 24,25-dihydroxy vitamin D [24,25(OH)2-D].1,25(OH)2-D (calcitriol) is the active form of vitamin D, whereas 24,25(OH)2-D has limited, if any, physiologic activity. Nuclear receptors for 1,25(OH)2-D are present in

30 tissues. Although specific intracellular binding proteins for 24,25(OH)2-D have been identified in healing bone tissue and cartilage at sites of fractures, a role in fracture healing has not yet been demonstrated**.(3)**

-Dietary Sources of Vitamin D

Natural Sources

Natural sources of vitamin D include oily fish such as salmon, mackerel, and sardines, cod liver oil, liver and organ meats (which, however, have a high cholesterol content), and egg yolks (which have a variable amount of vitamin D).

Note that the method used for cooking food can have significant effects on its vitamin D content. For example, frying fish reduces active vitamin D content by 50%, whereas baking does not affect the vitamin D content of fish. Also, with regards to fish, farm-raised fish may have higher vitamin D content than free-living fish. Table 3 describes the amount of vitamin D available in various foods. Unfortunately, most natural (unfortified) sources of vitamin D are not commonly consumed by children; therefore, fortifying food with vitamin D becomes important if there is inadequate sun exposure.

Supplements

Vitamin D supplements with 200 to 1000 IU per pill are available, as are preparations that provide much higher doses. Both vitamin D2 (ergocalciferol, plant derived) and D3 (cholecalciferol, animal derived) are used in supplements. Although traditionally D2 and D3 have been considered to be equipotent**.(3)**

CAUSES OF VITAMIN D DEFICIENCY

Decreased Vitamin D Synthesis

The important role of ultraviolet light in the UV-B range on cutaneous vitamin D synthesis was described in "CutaneousVitamin D Synthesis." The reemergence of vitamin D–deficiency rickets in northern Europe and North America is primarily associated with dark-skinned children on strict vegetarian diets, cult or fad diets, dark skinned infants exclusively breastfed beyond 3 to 6 months of age, premature infants, and infants born to vitamin D deficient mothers. Excessive use of sunscreen may also contribute to decreased cutaneous vitamin D synthesis.

Vitamin D Deficiency in Relation to Skin Pigmentation

Skin pigmentation determines the duration of sun exposure necessary to achieve a certain concentration of vitamin D. However, when UV-B exposure is not limited to a fixed amount of energy (of UV-B radiation) but is expressed as MED (the amount of UV-B required to produce slight pinkness of the skin), exposure to the equivalent MED of whole-body UV-B results in similar vitamin D levels. It should be noted that more UV-B is necessary to produce a MED in darker-skinned people; therefore, dark-skinned people require a longer duration of sun exposure than light-skinned people for a similar response.

Vitamin D Deficiency in Relation to Physical Agents Blocking UVR exposure, Clothing

The amount of skin that is exposed to the sun is important. Exposure of the whole body versus only the face, hands, and arms is associated with marked differences in vitamin D synthesis. For example, a fully clothed infant without a hat requires 4 times as much sun exposure as an infant in only a diaper to achieve similar 25(OH)-D concentrations. At least 20% of the body's surface should be exposed to UV-B for blood vitamin D concentrations to increase. Women and children in Saudi Arabia who wear traditional outfits, therefore, are at great risk for vitamin D deficiency. The nature of clothing is important, such that black wool is twice as effective in absorbing and thus preventing transmission of incident UV-B radiation to the skin as white cotton. In addition, more tightly woven fabric causes greater UV-B attenuation. In addition to clothing, the heat of the summer months in certain parts of the world leads to sun-avoidant behavior and, therefore, inadequate sunlight exposure.

Sunscreen

Sunscreen absorbs UV-B and some UV-A light and prevents it from reaching and entering the skin. A sunscreen with a sun protection factor (SPF) can decrease vitamin D3 synthetic capacity by 95%, and SPF can decrease it by 98%. In adults who apply sunscreen properly (2 mg/cm2), the amount of vitamin D3 produced is decreased 95%. However, the effect of sunscreens on vitamin D production may also be affected by geography, with adequate vitamin D production despite sunscreen application in areas of excessive sunlight exposure, lower vitamin D levels in people using SPF sunscreens than in those not using sunscreen; however, these lower levels were not sufficient to cause PTH level elevations. For adequate vitamin D synthesis, exposure to the midday sun (between 1000 and 1500 hours) for 10 to 15 minutes in the spring, summer, and fall is considered sufficient for light-skinned people, providing 25% of the MED. After this extent of exposure, application of a sunscreen with an SPF of 15 is recommended to prevent damaging effects of chronic excessive exposure to sunlight.

Shade

Increased urbanization and increased time spent indoors at work may lead to decreased time spent outdoors and, therefore, decreased vitamin D synthesis, even in light-skinned populations. Shade reduces the amount of solar radiation by 60%, and windowpane glass blocks UVR. Research showed a third of students at Boston University who stayed indoors for long periods and always wore sun protection were vitamin D insufficient [25(OH)-D levels 50 nmol/L (20 ng/mL)] at the end of winter. Similarly, disabled children and children who stay indoors may not receive a summertime boost in vitamin D levels.

Vitamin D Deficiency in Relation to Geography

Latitude and Season

Vitamin D deficiency rickets is more commonly reported in white children from the northern than the southern United States. This is attributed to a decrease in incident UVR with increasing latitude, because the oblique angle at which sunlight reaches the atmosphere leads to a greater path being traversed through the atmosphere and ozone layer, with greater resultant scatter and absorption of UVR. Similarly, in the winter months, the rays of the sun enter the atmosphere at an oblique angle, UV-B photons have to pass through a greater distance of the atmosphere, and more UV-B photons are efficiently absorbed by ozone.Therefor , fewer photons per unit area strike the earth. Above 37° north latitude, in the winter months, the number of UV-B photons reaching the earth's atmosphere is decreased by 80% to 100%, and as a consequence, little vitamin D3 is produced in the skin.56 A minimum amount of UV-B is necessary for vitamin Dproduction, and this may not be reached at a latitude of above 40° in winter even with prolonged sun exposure .There are, therefore, 4 to 5 months in winter when vitamin D cannot be produced from UV-B in places such as Boston (42.5° north).Vitamin D levels reach their nadir in February and March in the northern hemisphere. Children of all ages are more susceptible to low vitamin D levels during the winter compared with the summer months. A report from Iowa (41° north) indicated that during winter, 78% of un supplemented breastfed infants of different skin pigmentations had 25(OH)-D levels of _27.5 nmol/L (11 ng/mL), as

opposed to only 1% of such infants during summer. Infants with florid rickets are known to first present in the late winter or early spring at 6 to 12 months of age with hypocalcemia and associated clinical features, often frank tetany or convulsions, also known as “spring tetany.” In Edmonton, Alberta, Canada (52° north), the prevalence of 25(OH)-D levels of _40 nmol/L (18 ng/mL) at the end of winter was 22% and 8% in boys and girls 2 to 8 years old and 69% and 35% in boys and girls 9 to 16 years old, respectively. Summertime vitamin D levels are usually adequate.Therefore, in northern latitudes, despite sun exposure during summer, vitamin D supplementation may be necessary to maintain optimal vitamin D levels during winter.

Cloud Cover, Air Pollution, and Altitude

Cloud cover, increasing water vapor, and industrial pollution can reduce the amount of UV-B that reaches the earth’s surface, and industrial pollution has been associated with a greater prevalence of vitamin D–deficiency rickets. In contrast, higher altitudes (as in the Rocky Mountains) are associated with greater UVR because of the thinner atmosphere and lower stratospheric ozone, thus protecting against vitamin D deficiency even in otherwise northern latitudes. Decreased Nutritional Intake of Vitamin D Lower intake of vitamin D–fortified foods, particularly milk and fortified cereals, may result in vitamin D–deficiency rickets in certain populations, particularly in dark-skinned people who live in higher latitudes and in the winter months. The decreased intake may be from choice or from necessity in societies poor enough to be unable to afford these foods. Reduced intake of fortified milk is common among adolescents and young women of childbearing age, which results in decreased vitamin D concentrations in blood. Maternal Vitamin D Status, Prematurity, and Exclusive Breastfeeding.

Vitamin D Deficiency Resulting From Prematurity

Prematurely born infants have a shorter duration in which to accumulate vitamin D stores from transplacental transfer from the mother and also have a higher requirement for vitamin D than term infants. Therefore, they are more likely to be vitamin D deficient. They have been reported to be more likely to have enamel

defects in both primary and permanent teeth, because vitamin D sufficiency is necessary for normal fetal tooth development.

Vitamin D Deficiency Resulting From Exclusive Breastfeeding

We have previously indicated that, assuming an average consumption of 750 mL/day, exclusive breastfeeding without sun exposure would provide only 11 to 38 IU/day of vitamin D. It is important to note that the vitamin D content of breast milk varies on the basis of skin color, with lower vitamin D concentrations in breast milk of black compared with white women. Therefore, breastfed infants need to obtain additional vitamin D through either sun exposure or supplementation . Thus, breastfed infants need to obtain additional vitamin D through supplementation or adequate sun exposure.

PREVENTION AND TREATMENT OF NUTRITIONAL VITAMIN D–DEFICIENCY RICKETS

Prevention

-Exposure to Sunlight (Cutaneous Vitamin D Synthesis From Solar UV-B Exposure)

-Fortification of Food With Vitamin D

-Use of Supplements

The essential physiology of vitamin D involves the sequential hydroxylation of cholecalciferol in the liver and the kidney, leading to the formation of 25-hydroxyvitamin D (25[OH]D), and 1,25(OH)D, respectively, the latter being the hormonally active form of the vitamin. Serum 25(OH)D level is the best indicator to evaluate total vitamin D status in the body, as the metabolite is the main circulating form**.** **(3)**

Noncalcemic actions of vitamin D

The noncalcemic actions of vitamin D have been grouped into three major effects: control of hormone secretion, modulation of immune function, and control of cellular proliferation and differentiation. This classification is not clear-cut, because the effects of calcitriol on any given tissue overlap with actions from any of the three groupings. Generally, calcitriol has the following actions: it

blocks parathyroid hormone (PTH) elaboration, but aids insulin secretion; it inhibits adaptive immunity, but supports innate immunity; and it hinders cell proliferation, but induces cell differentiation.

Effects of vitamin D on insulin secretion

The association of vitamin D with insulin resistance or abnormal glucose metabolism has attracted scientific attention recently. With respect to insulin secretion, the stimulatory effect of calcitriol is well established, although the mechanism of action is not yet resolved. Nevertheless, a study conducted

with a murine model shows that VDRs and calbindin- D28k are located in pancreatic cells, while other studies suggest that calbindin-D28k (a calcium-buffering protein in pancreatic cells) not only regulates depolarization-stimulated insulin secretion but also protects against cytokine mediated ablation of cells. Evidence from observational human studies, and interventional human studies further indicates that vitamin D deficiency may contribute to increased risk of type 2 diabetes mellitus (T2DM) **.(4)**

Vitamin D deficiency management

The evidence suggests that VD supplementation in clinical disorders at risk for VDD and VD3 doses between 400 and 1000 IU may be enough to maintain these values; however, if that is not the case, the dose should be adjusted whenever possible and 25(OH)D levels should be checked until reaching optimal levels. It has been suggested that children with 25(OH) D levels < 25 nmol/L should be referred to a specialized team for their assessment and management.**(5)**

Vitamin D, recently coined as the D hormone, is a pleiotropic steroid hormone that has multiple biological ects. Most notably, it plays an integral function in the regulation of calcium and phosphorus homeostasis, and thus has a vital role in bone health. Emerging evidence suggests further extra-skeletal physiological actions, but clinical consequences are still debatable. Hypo vitaminosis D, or low serum levels of 25-hydroxyvitamin D (25OHD), is widespread in both adults and children around the world . The most common determinants of deficiency include

limited sunlight exposure, diseases that cause malabsorption (i.e., celiac disease, cystic fibrosis), diet, obesity, and altered metabolism secondary to some medications . Hypertension, or elevated blood pressure (BP), is a well-recognized risk factor for both cardiovascular and renal diseases in addition to a vast array of diseases contributing significantly to**..** mortality. Specifically, childhood hypertension poses a considerable public health challenge and is associated with essential hypertension in adults and detrimental cardiovascular events .

Among children and adolescents, obese children with low levels of vitamin D showed increased odds for hypertension, even after adjusting for body mass index and body fat . **(6)**

There are growing data from studies of young adults, elderly persons, and youth in other countries that vitamin D deficiency is an unrecognized and prevalent health problem. Despite milk fortification in this country, subclinical vitamin D deficiency has been noted, with a high prevalence in adult medical inpatients, homebound elderly individuals, postmenopausal women presenting with hip fracture, and healthy young adults. Few data are available regarding the prevalence of this nutritional deficiency among healthy US children and adolescents. **(7)**

There has been concern raised about a resurgence of vitamin D deficiency and rickets among infants and children, with reports emerging in the United States from Alaska, Iowa, Nevada, California, North Carolina,Texas, and motherinfant pairs in Boston, among others. The prevalence of vitamin D deficiency in young children also appears to be high in other countries, including England,Greece, and Canada .To date, reports have focused primarily on young infants compared with toddlers. Thus, there appears to be less information available regarding variables that predispose young children to vitamin D deficiency as they wean to fortified milk and solid foods…**(8)**

Given the recent spate of reports of vitamin D deficiency, there is a need to reexamine our understanding of natural and other sources of vitamin D, as well as mechanisms whereby vitamin D synthesis and intake can be optimized. therefore the recommendations for sun exposure and vitamin D intake and possible caveats associated with these recommendations.**((9)**

Vitamin D plays an essential role in maintaining bone health through regulating calcium concentrations in the body. The development of vitamin D deficiency is associated with deteriorating bone health and in severe cases, hypocalcemia, rickets, and osteomalacia in children and adults. Those at greatest risk of vitamin D deficiency include patients with chronic illnesses**.(10)**

There are not many natural food items that contain vitamin D, therefore the amount of time in sunlight is the important source of vitamin D2). Vitamin D deficiency can result in skeletal diseases, such as rickets and osteomalacia). In addition, vitamin D receptors exist in the endocrine glands and cardiovascular tissues, and take part in the differentiation of cell, and the production of various cytokines and interleukins, which, taken together, means that they are relevant in metabolic syndromes, diabetes, autoimmune diseases, and cardiovascular diseases). Moreover, respiratory infections, food allergies, and asthma are known to increase with vitamin D deficiency, and there are also reports that menarche starts earlier in vitamin D deficient girls. The known risk factors associated with vitamin D deficiency are skin pigmentation, older age, lesser sunlight exposure, lower intake of vitamin D rich food or supplements, and higher body mass index (BMI). Recently, vitamin D deficiency has become very common in both adults and children, due to a lack of exposure to sunlight, which is model of treatment.(**11)**

Studies in 2003, the American Academy of Pediatrics (AAP) recommended a vitamin D supplement for breastfed infants who do not consume at least 500 mL of a vitamin D–fortified formula/beverage14 and non breastfed infants who do not consume _500 mL of vitamin D–fortified beverages. The supplementation should start during the first 2 months of life and continue throughout childhood and adolescence. The rationale for this timing is that vitamin D stores in the newborn, which are obtained through transplacental passage from the vitamin D–replete mother, should last for at least 8 weeks after delivery given that the half-life of serum 25(OH)-vitamin D [25(OH)-D] is _2 to 3 weeks.In a term infant born to a vitamin D–replete mother, the supply of vitamin D may last even longer (8–12 weeks) given the storage of vitamin D in fat. **(12)**

Vitamin D is important for bone and muscles health. It helps the body absorb calcium and phosphate from food, which are important for healthy and strong bones. Only a few food (some types of fish) naturally contain vitamin D, and it is hard to get enough vitamin D, and it is hard to get enough vitamin D from food alone, but most people only get about a quarter or even less of their vitamin D needs from food. Most vitamin D is made in the skin when it is exposed to the sun**.(13)**

The deficiency of vitamin D may develop from nutritional deficiencies, malabsorption , enzyme-inducing medications, and many other etiologies. It may present as hypocalcemia before bone demineralization at periods of increased growth velocity (infancy and adolescence) because the increased calcium demand of the body cannot be met**.(14)**

It is recommended, for babies up to 1 year of age daily allowance (RDA) is 400 IU (10µg). For children and adults aged 1-40 years the RDAis 600 IU(15µg).**(15)**

In addition to its contribution to bone metabolism, vitamin D seems to fulfill a broad spectrum of biological functions which justifies the interest in monitoring its body content**.(16)**

Another study explained that, if women don't get enough vitamin D during pregnancy, their children are at greater risk of developing rickets later in childhood, also delayed motor development, muscle weakness, aches and pains, and fractures . This risk is reduced if children get enough vitamin D after birth, as well as in adults the deficiency in adults has been linked to some cancers, heart disease and diabetes**.(17)**

Also, children need sun light on their skin for their bodies to make vitamin D, they got about 80% of their vitamin D in this way, and this depends on a bit on your skin colour. People with naturally very dark skin need 3-6 times more sun to make vitamin D than the amount fair-skinned people need**.(17)**

Available studies suggest that vitamin D supplementation is known to both prevent and treat rickets, also by improving living conditions including sun light

exposure, as childhood is a period of great bone development and therefore, attention to the vitamin D needed to optimize bone health in childhood is imperative **.(18)**

It is concluded that, the great importance of vitamin D is the moderation of calcium (Ca) and Phosphorus(P) homeostasis as well as the absorption of Ca, vitamin D has two different forms vitamin D2 which exist in food (plants) and D3 (cholecalciferol)which is produced by the following the path 7-dehydrocholesterol- previtamin D-vitamin D3 in the skiun upon ultraviolet B(UVB) sun exposure and at skin temperature.**(19)**

Also there is enough evidence that the deficiency of vitamin D may lead to skeletal and non skeletal disease, both children and adolescents seem to be in high risk of low vitamin D status especially during winter, Having a diet higher in calcium and vitamin D as well as oral supplementation with vitamin D may be necessary for children and adolescents not only in the absence of sun exposure in winter time but also in preventing other diseases such as diabetes type 1, cancer, and cardiovascular disease. Further researches is needed in order to identify the optimal dietary recommendation needed begging from pregnancy in order to prevent vitamin D deficiency**.(19,20)**

CHAPTER 3

CONCLUSIONS AND RECOMMENDATIONS

Vitamin D deficiency was present among children (aged 6-12 years) and adolescents all over the world, particularly during winter, although the problem seems to be common across sex, season, and ethnicity. Suboptimal vitamin D status is common among otherwise healthy young children. Predictors of vitamin D status vary in infants vs toddlers, information that is important to consider in the care of these young patients. The increasing numbers of reports of rickets in many industrialized nations are related to the practice of exclusive breastfeeding without concomitant vitamin D supplementation in other countries, decreased UV-B exposure (particularly in dark-skinned people), and the excessive use of sunscreen. Recommendations for vitamin D supplementation in breastfed infants should take into account skin pigmentation and geography. Recommendations for fortification of commonly used foods with vitamin D are necessary in keeping with various cultural norms of food intake and geography. In addition, current recommendations of sun exposure and vitamin D supplementation are limited because of a paucity of studies in children. Several body functions may be affected by VD deficiency: bone, glucose, and acute immune metabolism, autoimmunity, etc.; VD nuclear receptors may also be involved. Certain clinical disorders associated with VDD include obesity, prematurity, breastfeeding, intestinal malabsorption syndromes, and use of anticonvulsant agents, together with lifestyle conditions, body-covering clothing, living at extreme latitudes, low consumption of food sources, and little exposure to the sun. More studies are necessary in children using standard assays to determine safe levels of sun exposure and resultant vitamin D levels, as well as the 25(OH)-D levels below which pathologic changes begin. A low threshold for assessing vitamin D sufficiency in infants, children, and adolescents is recommended given the growing knowledge about effects of vitamin D not only on bone mineral metabolism but also on the immune system and in preventing various kinds of cancer. Data indicate greater health care costs from diseases

related to vitamin D deficiency than from those caused by excessive exposure to UVR, indicating the need for a reexamination of recommendations for sun-avoidant behavior, including the use of sunscreens , also The recommendation is to prevent VDD in risk conditions(so future studies are required to clarify VD's role in non-bone parameters in children and adolescents. The recommendation is to prevent and detect VDD in an early manner in the case of risk conditions. and to maintain 25(OH)D serum levels > 75 nmol/L.

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