Assessment of Vitamin D status in Healthy Egyptian Pre-pubertal Children

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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List of Abbreviations

Abb.	Full term
7-DHC	*7-dehydrocholesterol*
AAP	*American academy of pediatrics*
ALP	*Alkaline phosphatase*
ARI	*Acute respiratory infection*
BMI	*Body mass index*
CF	*Cystic fibrosis*
CFF	*Cystic fibrosis foundation*
CKD	*Chronic kidney disease*
DBP	*Vitamin D binding protein*
ELISA	*Enzyme-linked immune sorbent assay*
ESPGHAN	*European society for pediatric gastroentrology,*
GH	*Growth hormone*
ILGF1	*Insulin like growth factor 1*
IOM	*Institute of medicine*
KDOQI	*Kidney diseases outcomes quality initiative*
LD	*Linkage disequilibrium*
MED	*Minimal erythemal dose*
NHANES	*National health and nutrition examination survey*
OTC	*Over the counter*
P	*Phosphorus*
PES	*Pediatric endocrine society*
PTH	*Parathyroid hormone*
RCT	*Randomized controlled trial*
RFLPs	*Restriction fragment length polymorphisms*
SDS	*Standard deviation scores*
TMP	*Tetramethylbenzidine*
UTR	*Untranslated region*
UV	*Ultra violet*
VDR	*Vitamin D receptor*

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INTRODUCTION

Vitamin D is a fat-soluble vitamin that is naturally present in very few foods and available as a dietary supplement. It is also produced endogenously when ultraviolet rays from sunlight strike the skin and trigger vitamin D synthesis ***(Institute of Medicin, 2011).***

Vitamin D obtained from sun exposure, food, and supplements is biologically inert and must undergo two hydroxylations in the body for activation. The first occurs in the liver and converts vitamin D to 25-hydroxyvitamin D [25(OH)D], also known as calcidiol. The second occurs primarily in the kidney and forms the physiologically active 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], also known as calcitriol ***(Institute of Medicine, 2011).***

Vitamin D and its metabolites have a significant clinical role because of their inter- relationship with calcium homeostasis and bone metabolism. Vitamin D deficiency is common in infants who are dark skinned and exclusively breastfed beyond six months of age ***(Greer et al., 2006)***, particularly if there are additional risk factors such as lack of sun exposure ***(Binkley et al., 2007),*** maternal vitamin D deficiency during pregnancy or prematurity ***(Greer, 2001).*** Vitamin D deficiency is also common among children who use anticonvulsant or antiretroviral medications ***(Lehmann et al., 2000),*** or those with malabsorptive conditions ***(Pazianas et al., 2005).*** Subclinical vitamin D deficiency, as measured by low serum 25(OH)D, is very common ***(Forrest and Stuhldreher, 2001).***

Very few foods naturally contain vitamin D (fatty fish livers are the exception); dermal synthesis is the major natural source of the vitamin. Pre-vitamin D3 is synthesized nonenzymatically in skin from 7-dehydrocholesterol during exposure to the ultraviolet (UV) rays in sunlight. Previtamin D3 undergoes a temperature-dependent rearrangement to form vitamin D3 (cholecalciferol) ***(Haddad, 1992).*** The length of daily exposure required to obtain the sunlight equivalent of oral vitamin D supplementation is difficult to predict on an individual basis and varies with the skin type, latitude, season, and time of day ***(Binkley et al., 2007; Terushkin et al., 2010).*** Prolonged exposure of the skin to sunlight does not produce toxic amounts of vitamin D3 because of photoconversion of previtamin D3 and vitamin D3 to inactive metabolites (lumisterol, tachysterol, 5,6-transvitamin D, and suprasterol 1 and 2) ***(Holick et al., 1981; Holick, 2003).***

The plasma 1,25-dihydroxyvitamin D concentration is a function both of the availability of 25(OH)D and of the activities of the renal enzymes 1-alpha-hydroxylase and 24-alpha-hydroxylase ***(Christakos et al., 2010).***

The estimated adequate intake for infants up to 12 months is 400 international units (10 mcg) daily. The Lawson Wilkins Pediatric Endocrine Society also recommends supplementation with 400 international units daily of vitamin D beginning within days of birth for infants who are exclusively breast-fed ***(Misra et al., 2008)*****.**

Subclinical vitamin D deficiency may contribute to the burden of chronic diseases, particularly osteomalacia, osteoporosis, and decreased physical performance, and possibly cancer, cardiovascular disease, type 2 diabetes, and infectious and autoimmune disorders ***(Holick et al., 2011).***

AIM OF THE WORK

The study aims to:

- Evaluate 25OHD status in healthy pre-pubertal Egyptian children
- Estimate the frequency of vitamin D insufficiency and deficiency among them.
- Relate 25OHD to anthropometric parameters in those children.

Chapter 1

VITAMIN D

Background

Vitamin D compounds are fat soluble sterols which are essential for the absorption and utilization of calcium and phosphorus (in the form of inorganic phosphate) in the body to maintain normal calcification of the skeleton and bone mineralization ***(Shipkowski et al., 2018).***

Along with parathyroid hormone (PTH) the active form of vitamin D (25 – OHD) regulates serum calcium concentration by altering serum calcium and inorganic phosphate blood levels as needed. It maintains neuromuscular function and various other cellular processes, including the immune system and insulin production ***(Allgrove, 2015).***

Physiology

Our bodies obtain vitamin D in 2 different ways. The primary source of vitamin D_3 (cholecalciferol) comes from direct synthesis in our skin (>90%). Upon exposure to ultraviolet radiation, 7-dehydrocholesterol in our epidermal cells synthesizes vitamin D_3. The remainder of our need is typically obtained from dietary sources in either form, vitamin D_3 or vitamin D_2 (ergo-calciferol). Both forms undergo hydroxylation in the liver to create the storage form of vitamin

D, 25-hydroxy vitamin D (25(OH)-D, calcidiol, or calcifediol). Furthermore, in the kidneys, hydroxylation of calcidiol synthesizes the active metabolite, 1,25-dihydroxyvitamin D (1,25(OH)-D) (calcitriol) ***(Lee et al., 2013).***

Calcitriol is responsible for increasing calcium absorption, bone resorption, and decreasing renal calcium and phosphate excretion to maintain bone health ***(Bikle, 2014).***

The synthesis of calcitriol is mediated by PTH, serum phosphate concentration, and growth hormone, and may occur in non-renal sites, such as alveolar macrophages and osteoblasts ***(Hewison, 2012).***

Additionally, vitamin D has extraskeletal responsibilities, with vitamin D receptors in the small intestine, colon, osteoblasts, activated T and B lymphocytes, beta islet cells, and major organs (brain, heart, skin, gonads, prostate, breast, and mononuclear cells). The immunologic effects of vitamin D have stimulated great interest, but studies in these areas are currently limited in pediatric patients ***(Hewison, 2012).***