Assessment of Vitamin D Status in Egyption Boys Aged 2-10 Years

Thesis

Submitted for Partial Fulfillment at Master Degree in **Endocrinology & Metabolism**

$\mathcal{B}y$ Heba Fahd Abd El Shakour M.B.B.Ch

Supervised by

Prof. Dr. Raef Malak Botros

Professor of Internal Medicine Faculty of Medicine, Ain Shams University

Dr. Nancy Samir El Barbary

Professor of Pediatrics Faculty of Medicine, Ain Shams University

Dr. Ahmed Mohamed Bahaa El-Din

Lecturer of Internal Medicine Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2018



سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH**, the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Raef Malak Botros**, Professor of Internal Medicine Faculty of Medicine, Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.

I am also delighted to express my deepest gratitude and thanks to **Dr. Mancy Samir El Barbary**, Professor of Pediatrics Faculty of Medicine, Ain Shams University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.

I am deeply thankful to **Dr.** Ahmed Mohamed **Bahaa El-Din**, Lecturer of Internal Medicine Faculty of Medicine, Ain Shams University, for her great help, active participation and guidance.

Heba Fahd Abd El Shakour

List of Contents

Title	Page No.
List of Tables	5
List of Figures	7
List of Abbreviations	10
Introduction	1
Aim of the Work	15
Review of Literature	
Vitamin D	16
Vitamin D and Growth	36
 Vitamin D Deficiency and Related Diseases 	59
Subjects and Methods	88
Results	101
DISCUSSION	133
Summary and Conclusion	142
References	147
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Sources of vitamin D2 and vitamin 25 ng)	
Table (2):	Vitamin D and its metabolites	
Table (3):	Guidelines for dietary vitamin D	intake in
, ,	Australia and New Zealand	
Table (4):	Recommended dietary allowances (
	vitamin D in Canada	31
Table (5):	Recommended dietary allowances	(RDA) of
	vitamin D in united states	32
Table (6):	Tolerable Upper Intake Levels (ULs) for
	Vitamin D (Institute of Medicine (US	S)33
Table (7):	Description of the personal data	106
Table (8):	Biochemical results for the studied g	group 106
Table (9):	Distribution of the studied group a	as regard
	Vitamin D.	108
Table (10):	Distribution of the studied group a	
	age.	
Table (11):	Distribution of the studied group a	· ·
	nutrition	
Table (12):	Distribution of the studied group a	-
T 11 (10)	sun exposure.	
Table (13):	Distribution of the studied group a	-
7 11 (44)	social level.	
Table (14):	Demonstrate comparison between	
M-1-1- (15)	vitamin D as regard age group	
Table (15):	Demonstrate comparison between	
T-1-1- (10).	vitamin D as regard the diet	
Table (16):	Comparison between different vi	
Table (17):	level as regard sun exposure Comparison between levels of vitar	
1 anie (17):	regard social level	

List of Cables Cont...

Table No.	Title	Page No.
Table (18):	Comparison between the three vitamin D regarding age and ar measures data (weight, weight)	nthropometric
	length, length percentile and	_
Table (19):	Comparison between the three vitamin D regarding biochemica	ee groups of
	Total calcium, phospho	rus, ALK,
	Albumin, and corrected calci	ium) 121
Table (20):	Demonstrate comparison betwee with low and the group of high	0 1
	as regards vitamin D level	124
Table (21):	Demonstrate comparison betwee groups with different socio-econo	
	regards vitamin D status	125
Table (22):	Shows comparison between the	three groups
	with different age as regard vitar	
Table (23):	Demonstrates comparison betwee with diet rich and the group with	
	vitamin D as regards vitamin D	level 127
Table (24):	Spearman correlation between	n vitamin D
	(quantitative) with other variable	les 128
Table (25):	Multiple regression analys	sis between
	vitamin D and other parameters	s 132

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Molecular structure of vitamins D2 a	nd D3 17
Figure (2):	Vitamin D metabolism pathway	19
Figure (3):	Vitamin D-binding protein	22
Figure (4):	Vitamin D3 synthesis, activation	
	catabolism	24
Figure (5):	Widening of wrist	44
Figure (6):	Signs and symptoms of rickets	
Figure (7):	Wrist X ray showing changes in	
	Mainly cupping is seen here	
Figure (8):	Chest X ray showing changes con	
	with rickets	
Figure (9):	Radiograph of 4-years old girl	
J	depicts bowing of the legs caused by l	
Figure (10):	Proposed mechanism for vitami	•
3	influence on the development	
	progression of autoimmunity	
Figure (11):	Percentage of vitamin D level amo	
	studied group	-
Figure (12):	Shows age distribution of the studied	
	as regards age	
Figure (13):	Shows percentage of diet rich in vit D	
5 , ,	the studied group.	
Figure (14):	Shows percentage of duration of	
	exposure in the studied group	
Figure (15):	Percentage of social status distr	
5 , /	among the studied group	
Figure (16):	Comparison between vitamin D le	
3 - \ -/-	different age groups	
Figure (17):	Comparison between different le	
3 - \ - / -	vitamin D deficiency as regards its	
	in diet	

List of Figures Cont...

Fig. No.	Title	Page No.
Figure (18):	Comparison between different vitamin D deficiency as regreexposure.	ards Sun
Figure (19):	Comparison between different vitamin D deficiency as reg exposure.	levels of ards sun
Figure (20):	Demonstrates that there is difference between levels of vitathe group studied as regard haem	significant amin D in
Figure (21):	Demonstrate that there is difference between level of vitamis studied group as regard tot	significant n D in the al serum
Figure (22):	calcium. Demonstrate that there is difference between level of vitami studied group as regard phosphatase.	significant n D in the alkaline
Figure (23):	Demonstrate that there is difference between levels of vitathe studied group as regard serum	significant amin D in
Figure (24):	Demonstrate that there is difference between levels of vita regard corrected calcium	min D as
Figure (25):	Demonstrate that there is a difference between levels of vita regard sun exposure	min D as 124
Figure (26):	Demonstrates that there is no a difference between the three gr different socio-economic levels a	oups with as regards
Figure (27):	Demonstrates that there is no difference between the different three age groups and vitamin D le	significant ce in the

List of Figures Cont...

Fig. No.	Title	Page N	lo.
Figure (28):	Demonstrates that There is sig difference between the two group		
	different diet as regard vitamin D st	atus	127
Figure (29):	Correlation between vitamin	D and	
	haemoglobin		129
Figure (30):	Correlation between vitamin D ar calcium.		129
Figure (31):	Correlation between vitamin D and	alkaline	
C	phosphatase		130
Figure (32):	Correlation between vitamin albumin.	D and	
Figure (33):	Correlation between vitamin		
_	corrected calcium.		131



List of Abbreviations

Full term Abb. AITDs Autoimmune thyroid diseases AMPs Antimicrobial peptides aPL..... Against cell membrane phospholipids APS Anti-phospholipid syndrome BCG Bromocresol green Ca..... Calcium COPD...... Chronic obstructive pulmonary disease CT Calcitonin CVD Cardiovascular disease DEXA...... Dual energy X-ray absorptiometry DNA...... Deoxribonuclic-acid DRIP Vitamin D receptor interacting protein complex ECLAM European Consensus Lupus Activity Measurement EDTA..... Ethylenediaminetetraacetic acid ELISA..... Enzyme-Linked Immunosorbent Assay FEV1..... forced expiratory volume in 1 HT...... Hashimoto's thyroiditis IBD..... Inflammatory bowel disease IL-6 Interleukin-6 INF- γ Interferon IU......International unit MCTD Mixed connective tissue disease MS...... Multiple sclerosis MT...... Mycobacterium tuberculosis NAFLD Non-alcoholic fatty liver disease OCPC Ortho-cresolphthalein complexone PTH..... Parathyroid hormone RA Ruhmatiod arthritis RCTs Randomized controlled trials RDA Recommended dietary allowances RNP Anti- ribonucleo protein

List of Abbreviations Cont...

SLE Systemic lupus erythrmatosis SPSS ... Statistical package for Social Science SS ... Sjogren's syndrome SSc ... Systemic sclerosis TGF-βl ... Transforming growth factor-βl TIDDM ... Type1diabtis mellitus TNF-α ... Tumor necrosis factor alpha TNF-α ... Tumor necrosis factor- α UCTD ... Undifferentiated connective tissue disease ULs ... Upper Intake Levels UVB ... Ultraviolet B VDBP ... Vitamin D-binding protein VDREs ... Vitamin D response elements

INTRODUCTION

Itamin D is a potent steroid hormone that have important physiological actions. Apart from its role in mineral homeostasis it has many extra-skeletal actions, as most of tissues and cells in the body have vitamin D receptors. Several of these cells posess the enzymatic machinery to convert the primary circulating form of vitamin D, 25 – hydoxy vitamin D, to the active form: 1,25 – dihydroxy vitamin D (*Holick*, 2007).

As regards skeletal health, vitamin D is essential in regulation of calcium homeostasis and bone metabolism. On the other hand, vitamin D plays an important role to decrease risk of many chornic illnesses. These include cancers e.g. colorected cancer (Joan et al., 2007), autoimmure diseases e.g., Rheumatoid arthritis (Munger et al., 2006) infections diseases, cardiovascular diseases (Wang et al., 2008), schizophrenia and Alzheimer diseases.

Humans get vitamin D mainly from exposure of the skin to solar ultra violet B radiation (uVB; 290-315 nm) and from dietary intake. The solar ultravidolet radiation penetrates the skin and converts 7 – dehydorxy cholesterol to pre-vitamin D3 (Holick, 2007).

Vitamin D deficiency is common because of lack of appreciation that sun exposure is the major source of vitamin D for most humans. In countries of the Middle East the common



use of concealing clothing where the skin is shielded from the sun reduces the skin's ability to synthesize vitamin D in response to sunlight exposure.

Vitamin D deficiency causes Rickets in children and Osteomalacia in Adults. It also precipitates and exacerbates osteopenia, osteoporosis and fractures in adult (*Holick*, 2008).

A circulating level of 25-hydroxyvitamin D of >30 ng/ml is required to maximize vitamin D beneficial effects for health. In the absence of adequate sun exposure, at least 800-1000 IU vitamin D₃ / day needed to achieve this in children and adults (Holick, 2007).

Some people are more at risk of vitamin D deficiency and so are recommended to take vitamin supplements routinely, these include all pregnant and breast feeding women, all infants and young children aged 6 month to 5 years, people aged 65 years and over and people who are not exposed to much sun (Holick, 2006). Adoctor may also recommended routine supplements for certain people with darker skin and for people with certain gut, liver, or kidney diseases (Ravithadhani et al., *2012*).

Vitamin D deficiency is a worldwide health problem, spanning many countries and including all ages (Hossein-Nezhad and Holick, 2013).



High prevelance of vitamin D insufficiency in healthy children and adolescent has been reported worldwide in the past few years. Studies in India found that hypovitaminosis D was seen in 95% of apparently healthy adolescents. Other studies reported prevelance of vitamin D deficiency as 59.4% in Turkey, 78% in France, 42.5% in Beijing, 47% in Greece (Rajakumar et al., *2005*).

In recent studies about the prevelance of vitamin D deficiency in Egypt reveal that: the rate of hypovitaminosis in adult between (20-60) years is 77% (Marawan, 2013), infertile females between (20-50) years is 80% in Cairo (*Matar*, 2011) and 70% in port-Foud (ElDawoody, 2011), and in old age between (60-70) years the rate is more than 50% (Salem, 2011) and 90% in those over 75 years (Salem, 2011).

AIM OF THE WORK

e aim to determine the status of vitamin D deficiency/sufficiency in a sample of Egyption male children in the age period 2-10 years living in greater Cairo region.