Interleukin 37 Levels in Relation to Serum Vitamin D Levels Among Ain Shams University Medical Students

Thesis

Submitted for Partial Fulfilment of Master Degree in Clinical Pathology

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2020

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. Randa Reda Mabrouk,*** *Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University for her 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 ***Prof. Dr. Afaf Abdelalim Mostafa,*** *Professor of Clinical Pathology, 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. Dina Aly Mohamed Aly Ragab,*** *Assistant Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her great help, active participation and guidance.*

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List of Abbreviations

Abbreviation	Full term
1,25(OH) D	1,25-hydroxyvitamin D
APCs	Antigen presenting cells
BFM	Body fat mass
BMI	Body mass index
CD	Crohn's disease
CRP	C-reactive protein
CT	Computed tomography
CXCL10	C-X-C motif chemokine 10
DC	Dendritic cell
DNA	Deoxyribonucleic acid
DXA	Dual-energy x-ray absorptiometry
ESR	Erythrocyte sedimentation rate
G‐ CSF	Granulocyte-colony-stimulating factor
GM‐ CSF	Granulocyte-macrophage colony-stimulating factor
HBeAg	Hepatitis B e antigen
HS	Highly significant
hsCRP	Highly sensitive c-reactive protein
IBD	Inflammatory bowel disease
IFN- γ	Interferon-γ
IL	Interleukin
IL1F7	IL-1 family member 7
IQR	Interquartile range
LPS	Lipopolysaccharide
M1	Classically-activated macrophages
M2	Alternatively-activated macrophages
MHC	Major histocompatibility
MRI	Magnetic resonance imaging

List of Abbreviations Cont...

Abb.	Full term
NAMES-ASU	Nutritional Assessment of Ain Shams University Medical Students
NF-kB	Nuclear factor kB
NK	Natural killer
NLRP3	NOD-like receptor family Pyrin Domain-Containing 3
NS	Non-significant
PAMPs	Pathogen associated molecular patterns
PBF	Percent body fat
PTH	Parathyroid hormone
RA	Rheumatoid arthritis
ROS	Reactive oxygen species
RXR	Retinoic X receptor
S	Significant
SiIL-37	Silencing IL-37
SLE	Systemic lupus erythematosus
SPSS	Statistical package for Social Science
STAT-3	Signal tranducer and activator of transcription 3
TGF- β1	Transforming growth factor β1
Th	T-helper
TLR	Toll like receptor
TNF	Tumor necrosis factor
T-reg	T-regulatory lymphocytes
UC	Ulcerative colitis
UVR	Ultraviolet rays
VDR	Vitamin D receptor
VDREs	Vitamin D response elements

INTRODUCTION

Interleukin (IL) -37, a newly discovered member of the IL-1 family, has been identified as a natural inhibitor of immune responses ***(Nold et al., 2010).***

Since its discovery, IL-37 has been studied extensively in immunological field. It has been established that IL-37 possesses anti-inflammatory characteristics both in innate immune response as well as in acquired immune responses by down regulating pro-inflammatory molecules ***(Ding et al., 2016).***

IL-37 has been found to play an important regulatory role in the development of a variety of inflammatory diseases, autoimmune diseases and tumors ***(Jia et al., 2018).***

Vitamin D refers to a group of fat-soluble secosteroid responsible for enhancing intestinal absorption of calcium, iron, magnesium, phosphate and zinc. In humans, the most important compounds in this group are vitamin D3 (also known as cholecalciferol) and vitamin D2 (ergocalciferol) ***(Norman, 2008)***.

Cholecalciferol and ergocalciferol can be ingested from the diet and from supplements. The body can also synthesize vitamin D in the skin, from cholesterol, when sun exposure is adequate ***(Dusso et al., 2005).***

While it was long held that vitamin D acted only at the intestine, kidney, and skeleton, and that its function was limited to calcium homeostasis, the possibility of extra skeletal effects has been considered for decades as a result of the discovery of the vitamin D receptor (VDR) in tissues that have no involvement in calcium homeostasis (e.g., skin, placenta, pancreas, breast, prostate, colon cells, and activated T cells). Discovery of the VDR in these tissues led to exploration of the roles and mechanisms of vitamin D function in each ***(Christakos et al., 2013)***.

Aim of the Work

The aim of this study is to determine the relation between the level of interleukin-37 and 25-hydroxy Vitamin D among Ain Shams University medical students.

VITAMIN D

Vitamin D is a fat-soluble secosteroid that is naturally present in very few foods and also available as a dietary supplement ***(Autier et al., 2014)***.

There is renewed interest in vitamin D synthesis, metabolism, and action. The two principal driving forces for heightened interest can be traced to: 1) the worsening world-wide trend of vitamin D insufficiency and 2) new knowledge regarding the nonhormonal, intracrine, and paracrine actions of 1-hydroxylated vitamin D ***(Adams and Hewison, 2010).***

In humans, the most important cmpounds in this group are vitamin D2 (ergocalciferol)and vitamin D3 (cholecalciferol). Ergocalciferol and cholecalciferol can be ingested from the diet and from supplements ***(Nair and Maseeh, 2012).***

Vitamin D is a fat-soluble vitamin that is synthesized in the skin in response to sunlight exposure and then converted in the liver to 25-hydroxyvitamin, which is mainly transformed by the kidneys in 1,25-dihydroxyvitamin D also known as calcitriol ***(Langlois et al., 2018).***

I. Sources of Vitamin D

Vitamin D may come from three potential sources: nutritional sources, ultraviolet B-dependent endogenous production and supplements. In humans, vitamin D is mainly

synthesized in the skin after exposure to ultraviolet B whereas only a minor part is derived from dietary sources ***(Prietl et al., 2013).***

A. Food

Very few natural, non-fortified products such as fatty fish (salmon, mackerel, sardines, cod liver oil) or some types of mushrooms (Shiitake), especially if sundried, contain relevant amounts of one of the two major forms of vitamin D (cholecalciferol or ergocalciferol) ***(Prietl et al., 2013).***

B. Sun exposure

Most people meet at least some of their vitamin D needs through exposure to sunlight. Ultraviolet rays (UVR) with a wavelength of 290–320 nanometers penetrate uncovered skin and convert cutaneous 7-dehydrocholesterol to previtamin D_3, which in turn becomes vitamin D_3. Because any excess previtamin D_3 or vitamin D_3 is destroyed by sunlight, excessive exposure to sunlight does not cause vitamin D_3 intoxication ***(Fernandes et al., 2014) (Fig.1).***

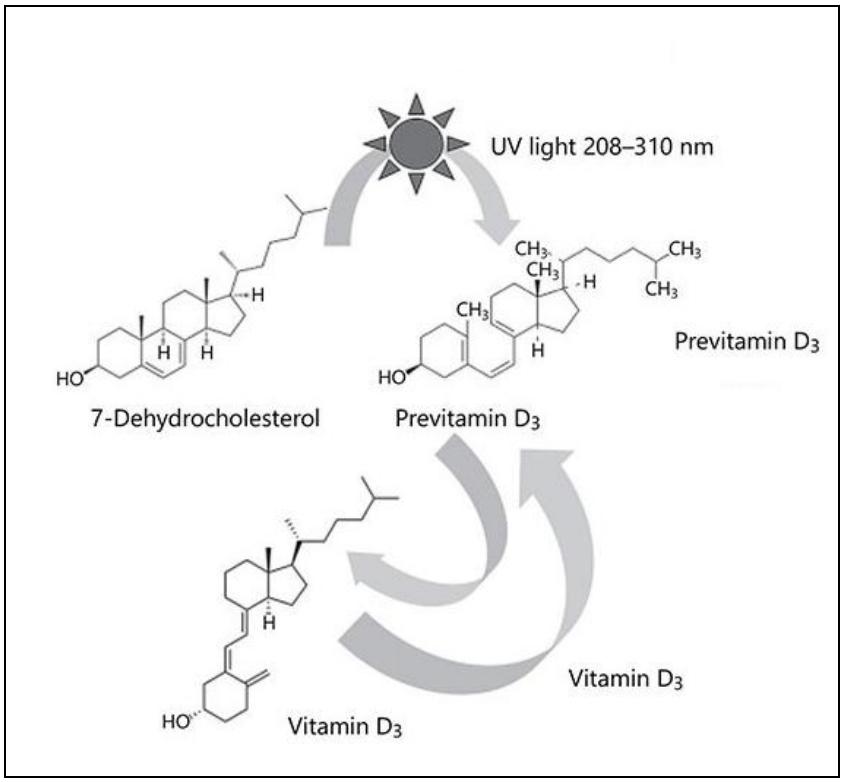

Figure (1): Photobiogenesis of vitamin D ***(Langlois et al., 2018)*.**

C. Dietary supplements

In supplements and fortified foods such as milk and orange juice, vitamin D is available in both forms, D_2 (ergocalciferol) and D_3 (cholecalciferol) ***(de Boer, 2010).***

Some countries like the United States and Canada fortify staple products such as dairy products with vitamin D. Thus, vitamin D dietary intake of an individual is highly dependent on nutritional habits, and the country's fortification strategy (***Tripkovic et al., 2012).***