# Assessment of Serum Level of Vitamin D in Acne Vulgaris

Thesis
Submitted for Fulfillment of Master Degree (M.Sc.) in
Dermatology

By

### Mariam Maheeb Mohamed Elmahdy AbdelGhaffar

(M.B., B.Ch.)

**Under Supervision of** 

### Professor Dr. Amany Zaki El-Ramly, MD

Professor of Dermatology Faculty of Medicine, Cairo University

### Dr. Sara Bahaa El Din Mahmoud, MD

Lecturer of Dermatology Faculty of Medicine, Cairo University

### Professor Dr. Olfat Gamil Shaker, MD

Professor of Medical Biochemistry and Molecular Biology Faculty of Medicine, Cairo University

> Faculty of Medicine Cairo University 2016

## بسم الله الرحمن الرحيم

### **Contents**

Page
Acknowledgment I
Abstract II
List of abbreviations III
List of figures VI
List of tables VIII
Introduction and Aim of work 1
Review of literature 4
Chapter 1: Acne Vulgaris 4
Chapter 2: Pathogenesis of Acne 17
Chapter 3: Vitamin D
Patients and methods
Results 50
Discussion
Recommendations 70
<b>Summary71</b>
References
Arabic summary

### Acknowledgement

First and foremost, I thank GOD, the Most Merciful, for granting me the power to proceed and accomplish this work.

I owe my deepest gratitude to **Prof. Dr. Amany Zaki El-Ramly**, Professor of Dermatology, Faculty of Medicine, Cairo University, for giving me the honor of working under her supervision and providing me with an example of what a doctor, leader and teacher should be like. This work would not have been possible without her guidance, encouragement and continuous support.

I would like to acknowledge my profound gratitude to **Dr. Sara Bahaa El Din Mahmoud,** lecturer of Dermatology, Faculty of Medicine, Cairo University, for her valuable assistance, support and guidance during this work.

I would like to thank **Prof. Dr. Olfat Gamil Shaker**, Professor of Medical Biochemistry and Molecular Biology, Faculty of Medicine, Cairo University, for her support and cooperation.

Finally, I would like to thank my family for their great care, support and encouragement along this work and throughout my life.

Mariam Maheeb, 2016 **Abstract** 

**Background:** Acne is a chronic inflammatory disease of the pilosebaceous

units with multifactorial pathogenesis. Sebocytes were identified as

bioactive vitamin D-responsive target cells, suggesting a possible role for

vitamin D in the pathogenesis of acne.

Objectives: The aim of this study was to evaluate serum levels of 25-

hydroxy vitamin D (25 OH D) in a group of Egyptian patients with acne

vulgaris in comparison to controls, in order to shed more light on its possible

role in the pathogenesis and detect any relation between vitamin D and acne

severity.

**Patients and methods:** This study included 60 patients with acne vulgaris

and 60 age and sex matched healthy controls. Blood samples were taken

from all participants for the detection of serum 25 OH D levels by enzyme-

linked immunosorbent assay (ELISA).

**Results:** The present study revealed lower serum vitamin D levels in acne

patients in comparison to controls, however, the difference did not reach

statistical significance (p=0.226). In addition, the levels were lowest in

severe acne with no significant difference (p=0.127).

**Conclusion:** The present study revealed lower, although non-significant,

serum vitamin D levels in acne patients, suggesting a possible role for

vitamin D supplementation in acne treatment.

**Keywords:** Acne vulgaris- Vitamin D.

Ш

### List of abbreviations

**1,25** (**OH**)<sub>2</sub> **D**:1,25-dihydroxy vitamin D

**25 OH D:** 25-hydroxy vitamin D

**5α-DHT**: 5α-dihydrotestosterone

**AAS:** androgenic anabolic steroids

**AR**: Androgen receptor

**CAMP:** cathelicidin antimicrobial peptide

**COX**: Cyclooxygenase

**CRH:** Corticotropin releasing hormone

**DHEA:** dehydroepiandrosterone

**EGF**: Epidermal growth factor

**ELISA:** enzyme-linked immunosorbent assay

**FGF**: Fibroblast growth factor

FOXO1: Forkhead box protein O1

**FSH:** follicle stimulating hormone

**GH**: Growth hormone

**H\betaD:** human  $\beta$  defensin

**IGF-I**: Insulin-like growth factor-I

IL: Interleukin

**IOM**: Institute of Medicine

LH: luteinizing hormone

LOX: Lipooxygenase

MAPK: mitogen-activated protein kinase

**MMPs:** matrix metalloproteinases

**NF-κB**: Nuclear factor kappa B

**P. acnes**: Propionibacterium acnes

**PAMPs:** pathogen-associated molecular patterns

**PAR- 2**: Protease-activated receptor-2

**PCOS:** polycystic ovary syndrome

**PCR:** polymerase chain reaction

**PIH:** Post-inflammatory hyperpigmentation

**POMC**: Proopiomelanocortin

**PPARs**: Peroxisome proliferator activated receptors

**PRRs:** pattern recognition receptors

PTH: parathyroid hormone

**RXR:** retinoid X receptor

**SD:** standard deviation

**SZA:** Solar zenith angles.

**TGF-β:** transforming growth factor beta

**TLRs**: Toll-like receptors

**TNF-**  $\alpha$ : Tumour necrosis factor-  $\alpha$ 

**Tregs:** T regulatory cells

**UV**: Ultraviolet

**VD2**: vitamin D2

**VD3**: vitamin D3

**VDR:** vitamin D receptor

**VDREs**: vitamin D response elements

**ω-3**: omega-3

**ω-6**: omega-6

### List of figures

- Figure (1): Modern aspects of the pathogenesis of acne. (p20)
- Figure (2): Mechanism of hyperkeratinization. (p23)
- Figure (3): Innate Immune Response in Acne. (p25)
- Figure (4): P. acnes effect on innate immunity. (p28)
- Figure (5): The different sources and forms of vitamin D. (p35)
- Figure (6): Effects of Vitamin D on the Immune system. (p39)
- Figure (7): Severity of acne vulgaris in patients included in the study. (p51)
- Figure (8): Comparison between male and female acne vulgaris patients regarding serum vitamin D level. (p53)
- Figure (9): Comparison between patients with mild, moderate and severe acne regarding serum vitamin D level. (p56)
- Figure (10): Comparison between male and female controls regarding serum vitamin D. (p57)
- Figure (11): Vitamin D status in male and female controls. (p58)
- Figure (12): Comparison between controls with adequate and those with inadequate sun exposure regarding vitamin D status. (p60)
- Figure (13): Comparison between acne vulgaris patients and controls regarding sun exposure. (p61)
- Figure (14): Comparison between acne vulgaris patients and controls regarding serum vitamin D. (p62)

Figure (15): Comparison between acne vulgaris patients and controls regarding vitamin D status. (p63)

### List of tables

- Table (1): Targets of acne treatments. (p12)
- **Table (2): Treatment algorithm for acne. (p16)**
- Table (3): Clinical and laboratory data of the studied groups. (p52)
- Table (4): Comparison between male and female acne vulgaris patients regarding serum vitamin D level. (p53)
- Table (5): Comparison between male and female acne vulgaris patients regarding vitamin D status. (p54)
- Table (6): Comparison between acne vulgaris patients with adequate and those with inadequate sun exposure regarding serum vitamin D level. (p54)
- Table (7): Comparison between acne vulgaris patients with adequate and those with inadequate sun exposure regarding vitamin D status. (p55)
- Table (8): Comparison between patients with mild, moderate and severe acne regarding serum vitamin D level. (p55)
- Table (9): Comparison between acne vulgaris patients with mild, moderate and severe acne regarding vitamin D status. (p56)
- Table (10): Comparison between male and female controls regarding serum vitamin D. (p57)
- Table (11): Comparison between male and female controls regarding vitamin D status. (p58)
- Table (12): Comparison between controls with adequate and those with inadequate sun exposure regarding serum vitamin D level. (p59)

Table (13): Comparison between controls with adequate and those with inadequate sun exposure regarding vitamin D status. (p59)

Table (14): Comparison between acne vulgaris patients and controls regarding sun exposure. (p60)

Table (15): Comparison between acne vulgaris patients and controls regarding serum vitamin D. (p61)

Table (16): Comparison between AV patients and controls regarding vitamin D status. (p62)

Table (17): Correlation between the duration of the disease and serum vitamin D of acne vulgaris patients. (p63)

# Introduction and Aim of the Work

### **Introduction**

Acne vulgaris is a chronic multifactorial pleomorphic inflammatory, exclusively human disease of the sebaceous gland follicles located on the face, chest, shoulders and back, where they are most common (Wilcox et al., 2007).

Acne vulgaris is characterized by seborrhoea, the formation of comedones, erythematous papules and pustules, less frequently by nodules, deep pustules, or pseudocysts and, in some patients, is accompanied by scarring (Adityan et al., 2009).

Acne is a multifactorial disease involving alterations in the pattern of keratinization within pilosebaseous follicles, resulting in comedo formation, increased sebum production, the proliferation of Propionibacterium (P.) acnes and peri-follicular inflammation. P. acnes has-been shown to stimulate the production of inflammatory cytokines such as interleukin-8 (IL-8), tumour necrosis factor-  $\alpha$  (TNF- $\alpha$ ) and IL-1 $\beta$  in acne patients (Agak et al., 2014).

Vitamin D is a steroid hormone synthesized in the epidermal keratinocytes under influence of ultraviolet- B (UV-B) light (290-315 nm) or acquired in the diet and dietary supplements (**Bouillon et al.**, **2008**).

Sebocytes were identified as bioactive vitamin D-responsive target cells, suggesting a possible role for vitamin D in acne (**Reichrath et al., 2007**).

In addition, the active form of vitamin D, 1,25-dihydroxy vitamin D (1,25 (OH)<sub>2</sub> D), has multiple effects on innate and adaptive immune responses through its varied effects on T and B lymphocytes, macrophages and dendritic cells, all of which express vitamin D receptors (**Kim et al, 2007**, **Adorini and Penna, 2008**). As such, the impact of vitamin D on human physiology and disease is broad and there is wide interest in the role of this hormone in many areas of medicine (**Gorman et al, 2007**).

The relation between vitamin D level and acne vulgaris and whether vitamin D supplementation helps in the treatment of acne vulgaris represent an attractive area of research.