EVALUATION OF THE RELATIONSHIP BETWEEN ACNE VULGARIS AND THE SERUM LEVELS OF ZINC, COPPER, MAGNESIUM AND IRON

Thesis

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By

RANA GHALLAB MOHAMED
(M.B., B.Ch.)

Under Supervision of

PROF. DR. ZEINB ABD ELLATIF SHAHEEN
Professor of Dermatology
Faculty of Medicine, Cairo University

DR. MARWA FATHY HUSSEIN
Lecturer of Dermatology
Faculty of Medicine, Cairo University

PROF. DR. HALA GABR METWALLY
Professor of Clinical Pathology
Faculty of Medicine, Cairo University

FACULTY OF MEDICINE
CAIRO UNIVERSITY
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بسم الله الرحمن الرحيم

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ABSTRACT

Background: Acne is a chronic inflammatory disease of the pilosebaceous units with multifactorial pathogenesis. Nutritional factors such as vitamins and minerals may be involved in the pathogenesis of acne.

Objectives: The aim of the present study is to clarify a possible relation between acne vulgaris and serum levels of zinc, copper, magnesium and iron. This study aimed also to detect a possible effect of acne severity on the serum concentrations of zinc, copper, magnesium and iron.

Patients and methods: This study included 45 patients with acne vulgaris and 45 age and sex matched healthy controls. Acne patients were divided into three groups according to the severity of acne: Each group involved 15 patients (mild, moderate and severe). According to types of acne lesions, patients were classified into (mainly comedonal, mainly inflammatory and both comedonal and inflammatory). Clinical examination was done and estimation of serum zinc, copper, magnesium and iron using sphectrophotometric method.

Results: The serum iron was significantly lower in acne patients than in healthy controls. The serum zinc, copper and magnesium concentration in acne patients did not differ significantly from the healthy controls. Acne severity (mild, moderate and severe) didn't affect on the serum iron, zinc, copper or magnesium levels.

Conclusion: Serum iron level is lower in acne patients. So, iron may play a role in the pathogenesis of acne and further studies are needed to clarify such a relation. No significant difference in serum zinc, copper or magnesium levels between acne patients and healthy controls.

Keywords:
Acne vulgaris, zinc, copper, magnesium, iron.

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LIST OF ABBREVIATIONS

ANOVA	Analysis of variants
DcytB	Duodenal cytochrome B reductase
DHEA	Dehydroepiandrosterone
DHT	Dihydrotestosterone
DMT1	Divalent metal transporter 1
DNA	Deoxyribo nucleic acid
EFA	Essential fatty acid
Fe2+	Ferrous iron
Fe3+	Ferric iron
GH	Growth hormone
GSH	Glutathione
HCTR1	Human copper transport protein 1
ICAM-1	Intracellular adhesion molecule-1
IGF-I	Insulin-like growth factor-1
IL	Interleukin
IPL	Intense pulsed light
LFA-3	Leucocyte function associated antigen-3
mmol/L	Millimole per liter
MT	Metallothionein
MUFA	Monounsaturated fatty acid
Na- Mg	Sodium- magnesium
NK	Natural killer
P. acnes	Propionibacterium acnes
PAR-2	Proteaseactivated receptor-2
PPAR	Peroxisome proliferator-activated receptors
RARs	Retinoic acid receptors

RBCs	Red blood cells
RBP	Retinol binding protein
RDA	Recommended daily allowance
ROS	Reactive oxygen species
SD	standard deviation
SPSS	Statistical Package for the Social Science
Tf	Transferrin
TfR	Transferrin receptors
TLR	Toll-like receptor
TNF	tumor necrosis factors
UV	Ultraviolet
ω-3	omega-3
ω-6	omega-6

INTRODUCTION

Acne vulgaris is a common multifactorial inflammatory disease of the pilosebaceous unit affecting >80% of individuals at some time during their lives. Endogenous as well as exogenous factors, including increased sebum production, altered follicular keratinization, inflammation, and increased colonization by the anaerobic, Gram-positive commensal bacteriu , P. acnes underlie the pathogenesis of acne vulgaris **(Gupta *et al.*, 2015)**.

Acne is characterized by different types of lesions. The clinical lesions are: open, closed comedones, erythematous papules, pustules, nodules and different types of scars. It affects the regions rich in sebaceous glands (face, chest and upper back) **(Rocha *et al.*, 2014).**

The etiology of acne is not fully clarified but it is widely accepted that its pathogenesis is multifactorial. It includes abnormal follicular differentiation and increased cornification, enhanced sebaceous gland activity and hyperseborrhea, bacterial hypercolonization, as well as inflammation and immunological host reaction being the major contributors **(Zouboulis *et al.*, 2005).**

Specific dietary agents and certain supplements are known to enhance the health and appearance of the skin by improving immune function at the skin level and providing therapeutic bioactive agents that assist in the treatment of many skin conditions, such as psoriasis, eczema and acne **(Boelsma *et al.*, 2001).** Nutritional factors such as vitamins and minerals may be involved in the pathogenesis of acne **(Katzman and Logan, 2007).**

AIM OF THE WORK

The aim of this study is to clarify a possible relation between acne vulgaris and serum levels of zinc, copper, magnesium and iron and to detect a possible effect of acne severity on the serum concentrations of zinc, copper, magnesium and iron.

CHAPTER ONE

ACNE VULGARIS

Acne vulgaris is a chronic inflammatory disorder of sebaceous follicles, found primarily on the face and upper trunk (chest and back), characterized by the formation of comedones, erythematous papules, pustules and less frequently by nodules or pseudocysts **(Williams *et al.*, 2012).**

Epidemiology of acne vulgaris:

Acne is known as an extremely common condition, affecting almost 80% of adolescents and young adults aged 11 to 30 years. However, rates of prevalence in the range of 41.7% to 93.3% were reported in different countries with populations aged 12 to 18 years **(Uslu *et al.*, 2008).**

Acne is one of the most frequently encountered conditions in all of dermatology and primary care practice. Even in its mild form, acne can have lingering impacts on mental health (e.g., anxiety and depression), as well as on social interactions, self-confidence, self-esteem, and employment opportunities **(Valerie, 2004).**

Pathogenesis of acne vulgaris:

Acne vulgaris is a multifactorial, spontaneously resolving pleomorphic skin disease, characterized by a variety of non-inflamed and inflamed skin lesions **(Wilcox *et al.*, 2007).**

The etiology of acne is not yet fully clarified but it is widely accepted that its pathogenesis is multifactorial as shown in **Fig. (1)** with abnormal follicular differentiation and increased cornification, enhanced sebaceous gland activity and hyperseborrhea, bacterial hypercolonization, as well as inflammation and immunological host reaction being the major contributors **(Zouboulis *et al.*, 2005).**

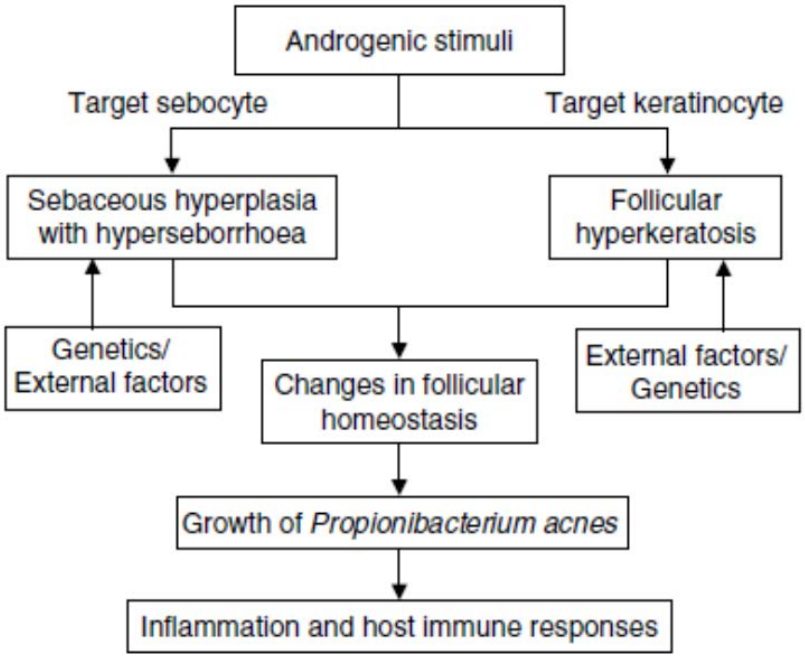

Figure (1): A proposed overall theory for acne pathogenesis **(Gollnick, 2003)**

1. Sebum Production and Cell Differentiation:

Increased sebum excretion, alteration of lipid composition and the oxidant/antioxidant ratio characteristic of the skin surface lipids are major concurrent events associated with the development of acne (**Zouboulis, 2004)**. Seborrhea is not considered to be the only responsible factor for the development of acne. Sebum interferes with the process of follicular keratinization in the pilosebaceous unit, which may cause pore blockage and formation of acne **(Kurokawa *et al.*, 2009)**.

The composition of the produced lipids is also of great importance. Lower essential fatty acid levels were found in wax esters in twins with acne rather than in twins with no acne (**Stewart, 1992)**. Low levels of linoleic acid have been observed in skin surface lipids of acne patients **(Downing *et al.*, 1986).**

Another hallmark of sebum in acne patients is the presence of lipoperoxides, mainly due to the peroxidation of squalene and a decrease in the level of vitamin E, the major sebum antioxidant **(Ottaviani *et al.*, 2006)**. Both lipoperoxides and monounsaturated fatty acid (MUFA) are capable of inducing alteration in keratinocyte proliferation and differentiation. Also peroxides are capable of inducing production of pro-inflammatory cytokines and activation of peroxisome proliferator-activated receptors (PPARs), which are molecules that regulate lipogenesis during adipocyte differentiation **(Ottaviani *et al.*, 2006)**.

Enlargement of the sebaceous glands and increased production of sebum is stimulated by the increasing production of androgens at puberty, mainly testosterone which is converted to the more active dihydrotestosterone (DHT) by the enzyme type I 5α-reductaseas shown in **Fig. (2).** This more active androgen then stimulates increased sebum production **(Cunliffe and Gollnick, 2001)**. So increased sebum production seen in patients with acne is primarily as a result of individual increased sebaceous gland sensitivity to androgen (end-organ hyper response hypothesis) **(Henze *et al.*, 1998)**, increased circulating levels of androgen (**Davis, 1999)** or increased type I 5α-reductase activity **(Thiboutot *et al.*, 1995).** Androgen hormones have been implicated as the initial triggering factor on comedones **(Zouboulis *et al.*, 2005).**

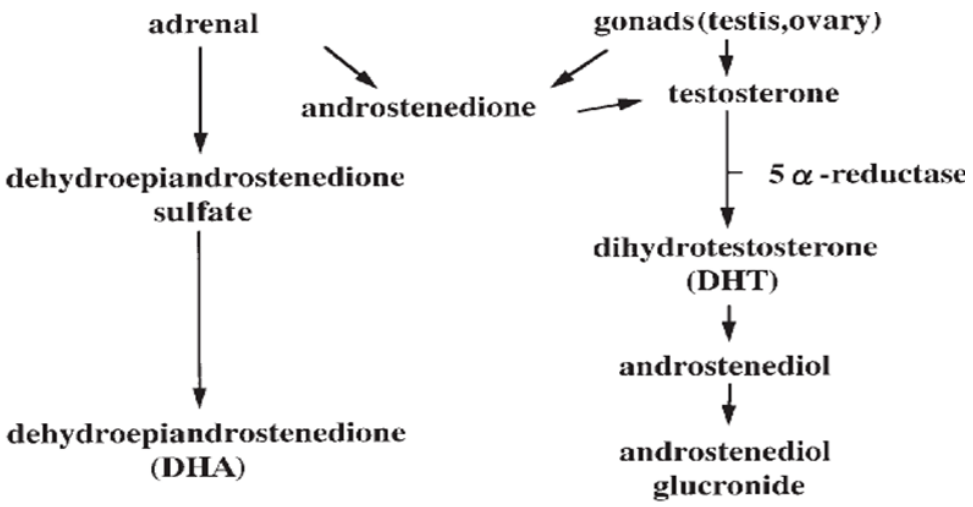

Figure (2): Metabolic pathways of androgen and 5α-reductase
(Masahiko and Masaaki, 2001)

Acne cannot develop without the sebocyte differentiation and proliferation that occurs under androgen stimulation. This may be mediated by interaction of androgens with PPARs, as shown in **Fig. (3) (Zouboulis *et al.*, 2005 & Makrantonaki *et al.*, 2011).**

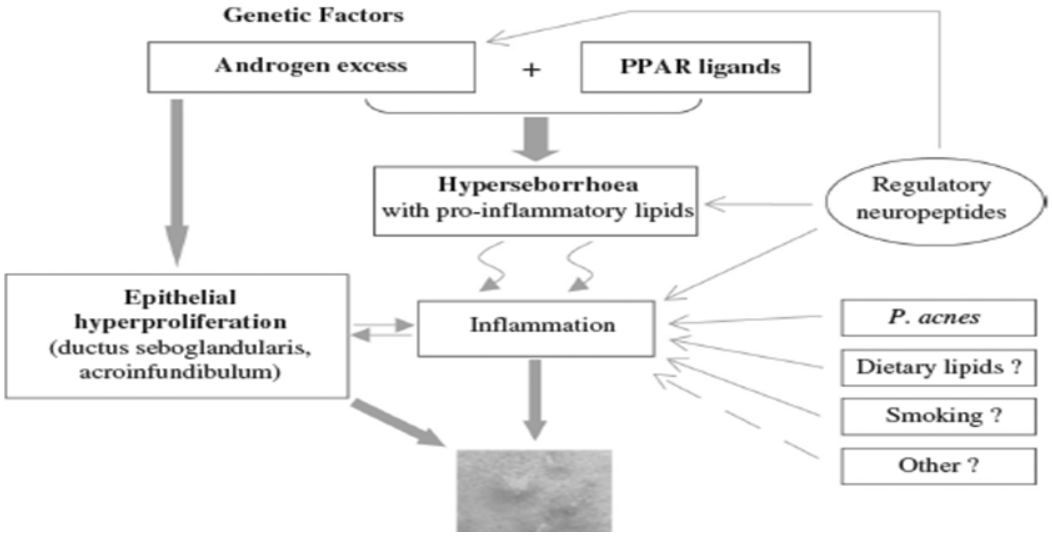

Fig. (3): Other aspects of acne pathogenesis **(Zouboulis *et al.*, 2005)**