Evaluation of Serum Interleukin 36 in Egyptian Acne Vulgaris Patients versus Controls

Thesis

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Esraa Mahmoud Awaad

List of Contents

List of Tables

List of Figures

List of Figures

Fig. No.	Title	Page No.

List of Abbreviations

Abb.	Full term
ACTH	*Adrenocorticotrophic hormone*
AKT	*Protein kinase B*
ALA	*Aminolevulinic acid*
AMPs	*Antimicrobial peptides*
AP1	*Activator protein -1*
AR	*Androgen receptor*
BMLCS	*Bone marrow derived Langerhans cells*
CAH	*Congenital adrenal hyperplasia*
COCS	*Combined oral contraceptives*
CRH	*Corticotrophin releasing hormone*
CROSS	*Chemical reconstruction of skin scars*
DAMP	*Danger associated molecular pattern*
DC:	*Dendritic cell*
DHEA	*Dehydroepiandrosterone*
DHEAS	*Dehydroepiandrosterone sulfate*
DST	*Dexamethasone suppression test*
E2	*Estradiol*
FDA	*Food and drug administration*
FFA	*Free fatty acids*
FGF:	*Fibroblast growth factor*
FGFR2	*Fibroblast growth factor receptor 2*
Foxo1	*Factor fork head box O*
FSH	*Follicle Stimulating Hormone*
GA	*Glycolic acid*
GAGS	*Global acne grading system*
G-CSF	*Granulocyte- colony stimulating factor*
GPP	*Generalized pustular psoriasis*
HAIR-AN	*Hyperandroginism, insulin resistance, acanthosis nigricans*
HS	*Hidradenitis suppurativa*
HS	*Hidradenitis suppurativa*
HSD	*Hydroxysteroid dehydrogenase*
IGA	*Investigator global assessment*

List of Abbreviations cont...

Abb.	Full term
IGF	*Insulin growth factor*
IGFBP3	*Insuline growth factor binding protein 3*
IL	*Interleukin*
IL1RAcP	*IL-1receptor accessory protien*
JNK	*Janus kinase*
JS	*Jessner's solution*
LED	*Light emitting diode*
LH	*Luetenizing Hormone*
LPS	*Lipopolysaccharide*
MA	*Mandelic acid*
MAL	*Methyl ester of aminolevulinic acid*
MAPK	*Mitogen-activated protein kinase*
MMP	*Matrix metalloproteinase*
MNRF	*Microneediling radiofrequency*
MTZ	*Microthermal zone*
NF-κβ	*Nuclear factor-κβ*
NLRP3	*Nucleotide binding oligomerization domain like receptor*
OTC	*Over the counter medication*
P. acne:	*Propionibacterium acne*
PA	*Pyruvic acid*
PAC	*Pyoderma gangrenosum , acne, ulcerative colitis*
PAMP	*Pathogen associated molecular pattern*
PAPA	*Pyoderma gangrenosum, acne, pyogenic arthritis*
PAPASH	*Pyogenic arthritis, pyoderma gangrenosum, acne, hidradenitis suppurativa*
PASH	*Pyoderma gangrenosum, acne, hidraddenitis suppurativa*
PCO	*Polycyctic Ovary*
PDF	*Platelet derived growth factor*
PDL	*Pulsed dye laser*

List of Abbreviations cont...

Abb.	Full term
PDT	*Photodynamic therapy*
PG	*Pyoderma gangrenosum*
PI3K	*Phoshphoinsositide 3-kinase*
PIH	*Post inflammatory hyperpigmentation*
PPAR	*Peroxisome proliferator activator receptor*
PpIX	*Protoporphyrin IX*
PPP	*Palmoplantar psoriasis*
PRP	*Platelet rich plasma*
PRRS	*Pattern recognition receptors*
PsA	*Psoriatic arthritis*
PsAPASH	*Psoriatic arthritis, pyoderma gangrenosum, acne, hidraddenitis suppurativa*
Ra	*Receptor antagonist*
RF:	*Radiofrequency*
SA	*Salicylic acid*
SAHA	*Seborrhea, acne, hirsutism, androgenic alopecia*
SD	*Standard deviation*
SLE	*Systemic lupus erythematosus*
SNP	*Single nucleotide polymorphism*
SPSS	*Statistical package for social science*
T	*Testosterone*
TAU5	*Transcription activation unit 5*
TCA	*Trichloroacetic acid*
TGF	*Transforming growth factor*
TH	*T-helper*
TLR	*Toll like receptor*
TNF	*Tumor necrosis factor*
βHA	*β hydroxyl acids*

1. INTRODUCTION

Acne is a multifactorial inflammatory disease affecting the pilosebaceous follicles of the skin. The current understanding of acne pathogenesis is continuously evolving. Key pathogenic factors that play an important role in the development of acne are follicular hyperkeratinization, microbial colonization with *Propionibacterium acnes*, sebum production, and complex inflammatory mechanisms involving both innate and acquired immunity. In addition, studies have suggested that neuroendocrine regulatory mechanisms, diet, and genetic and nongenetic factors all may contribute to the multifactorial process of acne pathogenesis ***(Zaenglein et al., 2016).***

Interleukin (IL)-36 sub-family members are new cytokines of IL-1 family that include IL-36α, IL-36β, IL-36γ, and IL-36 receptor antagonist (Ra). IL-36 cytokines are mainly expressed in keratinocytes and monocytes/macrophages and play an important role in the modulation of T helper (Th) 1 and Th17 immune responses. Since IL-36 cytokines are mainly expressed in epithelial cells, particularly in keratinocytes, they have been predominantly studied in skin diseases ***(Gresnigt and van de Veerdonk, 2013).***

It has been reported that an imbalance in IL-1 family agonist and antagonist functions could play an important role in cutaneous inflammation and in the phenotype of skin damage;

in particular, genetic deficiency of IL-36Ra may lead to an autoinfammatory condition which primarily manifests as a severe form of pustular psoriasis. Therefore, IL-36 cytokines have been studied in other two important infammatory skin disorders, such as acne and hidradenitis suppurativa ***(Di Caprio et al., 2017).***

2. AIM OF THE WORK

The aim of this study is to compare the level of serum IL36 in acne vulgaris patients versus controls and to find out any possible correlation between its serum level and severity of acne vulgaris.

3. Review of Literature

3.1. Chapter 1: Acne Vulgaris

Acne vulgaris is a chronic multifactorial, pleomorphic inflammatory skin disease of the pilosebaceous units which is characterized by formation of comedones and micro-comedones, erythematous papules and pustules. Nodules and pseudocysts are less common, and scarring occurs in some cases ***(Layton, 2010).***

Studies suggest that the emotional impact of acne is comparable to that experienced by patients with systemic diseases, like diabetes and epilepsy. In conjunction with the considerable personal burden experienced by patients with acne, acne vulgaris also accounts for substantial societal and health care burden ***(Dawson et al., 2012)***.

3.1.1. **Epidemiology:**

3.1.1.1. **Prevalence**

Acne is estimated to affect 9·4% of the global population, making it the eighth most prevalent disease worldwid***e (Tan and Bhat, 2015)***.

3.1.1.2. **Age:**

Acne vulgaris is the most frequently diagnosed dermatosis in patients between 11 and 30 ***(Bergler, 2014).*** Acne

is most prevalent during the teenage years affecting over 80% of adolescents ***(Tan and Bhat, 2015). Karciauskiene et al. (2014)*** reported that the age of onset of acne is becoming earlier with 42% of those aged 7–9 years and 76% of those aged 10–12 years having acne**.** This earlier onset of acne might be due to puberty occurring at an earlier age ***(Bhate and Williams, 2013).***

Although perceived as a teenage disease, acne may persist into adulthood ***(Collier et al., 2008).*** One population study in Germany found that 64% of those aged 20 to 29 years and 43% of those aged 30 to 39 years had visible acne ***(Schafer et al., 2001)***.

3.1.1.3. **Sex:**

Acne is more prevalent in girls at younger age ranges, with increasing prevalence in boys as they reach puberty. Male subjects also tend to have more severe acne. Following the teenage years, the prevalence in women again tends to be higher than in men ***(KokuAksu et al., 2012).***

3.1.1.4. **Race:**

The prevalence of clinical acne varied with ethnicity: African Americans, Hispanics, Asians, Caucasians and Continental Indian women, at 37%, 32%, 30%, 24% and 23% respectively ***(Perkins et al., 2011)***.There are special populations in which the absence of acne may be instructive regarding pathogenesis as no acne was observed in two