# Assessment of Serum Interleukin-19 in Acne Vulgaris Patients of Different Clinical Severities

*Thesis*

*Submitted for Partial Fulfillment of Master Degree*
*in* ***Dermatology, Venereology and Andrology***

*Presented By*

***Moustafa Adel Abdelrazik Deif***
*M.B. B.CH.*

*Under Supervision of*

**Prof. Dr. Hanan Mohamed Saleh**
*Professor of Dermatology, Venereology and Andrology*
*Faculty of Medicine - Ain Shams University*

**Dr. Rania Mahmoud Elhusseiny**
*Lecturer of Dermatology, Venereology and Andrology*
*Faculty of Medicine - Ain Shams University*

*Faculty of Medicine*
*Ain Shams University*
*2019*


بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللهِ عَلَيْكَ
عَظِيمًا
صدق الله العظيم
سورة النساء آية (١١٣)

# Acknowledgments

*First and foremost, I feel always indebted to* ***Allah*** *the Most Beneficent and Merciful.*

*I wish to express my deepest thanks, gratitude and appreciation to* ***Prof. Dr. Hanan Mohamed Saleh****, Professor of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, kind guidance, valuable instructions and generous help.*

*Special thanks are due to* ***Dr. Rania Mahmoud Elhusseiny****, Lecturer of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, for her sincere efforts, fruitful encouragement.*

Moustafa Adel Abdelrazik Deif

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# List of Abbreviations

| Abb. | Full term |
|---|---|
| *°C* | *Celsius Degree* |
| *AAD* | *American Academy of Dermatology* |
| *ANOVA* | *Analysis of Variance* |
| *AR* | *Androgen Receptors* |
| *AV* | *Acne Vulgaris* |
| *BP* | *Benzoyl Peroxide* |
| *C* | *Carbon* |
| *CD* | *Cluster of differentiation* |
| *CHS* | *Contact Hypersenstivity* |
| *Co2* | *Carbon Dioxide* |
| *COC* | *Combined oral contraceptives* |
| *D* | *Dalton* |
| *DHEA* | *Dehydroepiandrosterone* |
| *DHEA-S* | *Dehydroepiandrosterone sulphate* |
| *DHT* | *Dihydrotestosterone* |
| *EASI* | *Eczema area and severity index* |
| *EGF* | *Epidermal Growth Factor* |
| *ELISA* | *Enzyme-Linked Immunosorbent Assay* |
| *Er* | *Erbium* |
| *FDA* | *Food and Drug Adminstration* |
| *Fig* | *Figure* |
| *GAGS* | *Global Acne Grading System* |
| *GEA* | *Global Evaluation Acne* |
| *GM-CSF* | *Granulocyte macrophage colony-stimulating factor* |
| *HIV* | *Human Immunodefeciency Virus* |
| *HRP* | *Horse Reddish Peroxidase* |
| *HS* | *Highly significant* |

# List of Abbreviations cont...

| Abb. | Full term |
|---|---|
| *IL* | *Interleukin* |
| *IL-1* | *Interleukin-1 Beta* |
| *IL-10R1* | *Interleuki-10 Receptor 1* |
| *IL-10R2* | *Interleuki-10 Receptor 2* |
| *IL-20R1* | *Interleuki-20 Receptor 1* |
| *IL-20R2* | *Interleuki-20 Receptor 2* |
| *IL-20Rα* | *Interleukin-20 Receptor Alpha Subunit* |
| *IL-20Rβ* | *Interleukin-20 Receptor Beta Subunit* |
| *IL-22R1* | *Interleukin-22 Receptor 1* |
| *INF* | *Interferon* |
| *IPL* | *Intense Pulse Light* |
| *KTP* | *Potassium titanyl phosphate* |
| *LASER* | *Light Amplification by Stimulated Emission of Radiation* |
| *LPS* | *Lipopolysaccharide* |
| *mAbs* | *Monoclonal antibodies* |
| *MMPs* | *Matrix metalloproteases* |
| *mRNA* | *Messenger ribonucleic acid* |
| *Nd:YAG* | *Neodymium-doped Yttrium Aluminum Garnet* |
| *NFκB* | *Nuclear Factor Kappa Beta* |
| *ng/L* | *Nanogram per Litre* |
| *NK* | *Natural killer* |
| *Nm* | *Nanometer* |
| *NS* | *Non-significant* |
| *OD* | *Optical Density* |
| *P value* | *Calculated Propability* |
| *P.acnes* | *Propionibacterium acne* |

# List of Abbreviations cont...

| Abb. | Full term |
|---|---|
| *PASI* | *Psoriasis activity and severity index* |
| *PBMCs* | *Peripheral blood mononuclear cells* |
| *PCOS* | *Poly cystic ovary syndrome* |
| *PDL* | *Pulsed Dye Laser* |
| *PDT* | *Photodynamic Therapy* |
| *PIH* | *Post inflammatory hyperpigmentation* |
| *QOL* | *Quality of life* |
| *RA* | *Rheumatoid Arthritis* |
| *ROC Curve* | *Receiver operating characteristic Curve* |
| *Rpm* | *Revolutions per minute* |
| *S.aureus* | *Staph aureus* |
| *SAHA* | *Seborrhoea-acne-hirsutism-androgenetic alopecia syndrome* |
| *SD* | *Standard deviation* |
| *Sig.* | *Significance* |
| *STAT6* | *Signal transducer and activator of transcription 6* |
| *T2DM* | *Type 2 Diabetes Milletus* |
| *Th* | *T helper cell* |
| *TLR2* | *Toll like receptor 2* |
| *TLR4* | *Toll like receptor 4* |
| *TNF α* | *Tumor Necrosis Factor Alpha* |
| *YAG* | *Yttrium Aluminum Garnet* |
| *γδT* | *Gamma Delta T cell* |
| *μl* | *MicroLitre* |

# INTRODUCTION

Acne Vulgaris (AV) is a common chronic inflammatory disorder of the pilosebaceous unit among adolescents and young adults. It affects about 27% of early adolescents and up to 93% of late adolescents. Typical sites for acne include the face, chest and upper back with the appearance of comedones. Inflamed lesions are characterized by red papules, pustules and often by a subcutaneous abscess. Scarring, sometimes keloid formation, can occur even after the inflammation settles ***(AL-Hammadi et al., 2016).***

Acne vulgaris has a multifactorial pathogenesis, of which the key factor is genetics**.** Acne develops as a result of an interplay between the following four factors: (1) follicular epidermal hyperproliferation with subsequent plugging of the follicle, (2) excess sebum production, (3) the presence and activity of the commensal bacteria Propionibacterium acnes, and (4) inflammation ***(Thiboutot et al., 2009).***

It was stated that inflammation continues to happen in early stage and late stage of acne vulgaris; therefore, the inflammation does have a central role in the formation of both inflammatory and non inflammatory lesions in acne vulgaris ***(Rico, 2013).***

Interleukin (IL)-19 is a member of the IL-10 family of cytokines which includes IL-10, IL-19, IL-20, IL-22, IL-24 and IL-

26. This cytokine is produced by a variety of immune and non-immune cells such as monocytes, macrophages, B cells, endothelial and epithelial cells. IL-19 exerts its biological effects through the IL-20R1/IL-20R2 receptor complex ***(Sabat, 2010).*** Also IL-19 was shown to induce TNF- α and IL-6 production by mouse monocytes, while it increased IL-10 and decreased TNF- α in human peripheral blood mononuclear cells (PBMCs) ***(Jordan et al., 2005).***

It has been reported that IL-19 can promote T-helper2 (Th2) response, which is associated with a wide variety of allergic (i.e., asthma and atopic dermatitis), type 1 diabetes, and cardiovascular disease. Moreover, IL-19 have indispensable functions in many inflammatory diseases such as Rheumatoid Arthritis, Psoriasis, Atopic Dermatitis, Contact Hypersenstivity, and Acne Vulgaris ***(Li et al., 2017).***

The inflammation in acne vulgaris is linked with *P. acnes* which stimulates keratinocytes through the Toll-like receptors (TLRs) to produce proinflammatory cytokines. An example of proinflammatory cytokines that are already known is interleukin-1$\beta$ ***(Grange et al., 2010).*** IL-1$\beta$ could induce expression of IL-19 in keratinocytes both in vitro and in vivo ***(Kunz et al., 2006).***

***Mochtar et al. (2018)*** reported that there are differences in serum levels of IL-19 in acne vulgaris patients with different severities. They concluded that IL-19 might have a potential role in the pathogenesis of Acne vulgaris in correlation to its severity.

# Aim of the Work

The aim of this work is to measure serum levels of Interleukin 19 in acne vulgaris patients with different severities, and compare it with healthy controls, in order to further understand the role of Interleukin 19 in the etiopathogenesis of acne vulgaris and correlating it with acne vulgaris severity.

# Chapter 1

# ACNE VULGARIS

Acne Vulgaris (AV) is a common chronic inflammatory disorder of the pilosebaceous unit among adolescents and young adults ***(Knutsen-Larson et al., 2012)***.

**Epidemiology of Acne Vulgaris:**

Estimates of acne prevalence vary substantially given the absence of a universally accepted diagnostic or grading schema. Additionally, estimates continue to change as the prevalence of acne decreases secondary to improved treatment modalities. Acne vulgaris affects approximately 650 million people globally or around 9.4% of the population ***(Dawson and Dellavalle, 2013).***

- **Age of onset:**

Although all ages may be affected, acne vulgaris is primarily a disorder of adolescence ***(Layton, 2010).*** The average age of onset of acne is 11 years in girls and 12 years in boys. Acne is increasing in children of younger ages, with the appearance of acne in patients as young as 8 or 9 years of age. This trend toward earlier development of acne is thought to be related to the decreasing age of onset of puberty ***(Friedlander et al., 2010).***

- ***Sex***

Acne is marginally found in females more than males (9.8% versus 9.0%) ***(Dawson and Dellavalle, 2013).*** However, it is more common in males in adolescence and early adulthood, which is a trend that reverses with increasing age ***(Bhate and Williams, 2013).***

- ***Ethinic Groups***

Other factors impacting acne prevalence and severity include ethnicity and genetic propensity. It affects people of all ethnic groups ***(Bhate and Williams, 2013).***

- ***Affected Sites***

The face is most commonly affected site in 99% of cases, followed by the back in 60% of cases and the chest in 15% of cases ***(Layton, 2010).***

**Natural Course of Acne vulgaris:**

Acne has been defined as chronic disease, as for many patients, acne is characterized by a prolonged course, a pattern of recurrence or relapse, manifestation as acute outbreaks or slow onset, and a psychologic and social impact that affects the individual's quality of life ***(Zouboulis et al., 2014).***

It persists in nearly half of affected people into their twenties and thirties and a smaller group continue to have