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Original Research Article

Pattern of Serum Tumour Necrosis Factor, Interleukin 17 And 19, Levels in Young Adult Females with *Acne Vulgaris*

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Abstract

Acne is likely to be a genuine chronic inflammatory disease of pilosebaceous unit widely affecting adolescents and young adults. This study was aimed at evaluating the levels of tissue necrosis factor IL-17, IL-19 in female young adult of Imo State University with *Acne vulgaris*. The study was carried out in Owerri, Imo state. A total of one hundred young female adult was recruited for the study. The 100 subjects were divided into two groups, which were further grouped into mild, moderate and severe *Acne vulgaris* sufferers. Group 1 consists of 50 female subjects with *Acne vulgaris* while group 2 consists of 50 female subjects without *Acne vulgaris*. Five milliliters (5 ml) of blood was then collected into the vaccutainer tube with minimal stasis, the blood was allowed to clot at room temperature, and serum separated and harvested into clean dry well labeled sample bottles following centrifugation at 3000 rpm for 5 minutes. All reagents were commercially purchased and the manufacturer's standard operational procedures (SOPs) were strictly followed. The result of the test was analyzed using SPSS version 23. There was no significant difference (0.563) in the mean value of serum tissue necroses factor in female student with mild acne (111.33±46.58) pg/ml when compared to control (97.63±46.58) pg/ml.. The mean value of serum IL17 was significantly increased (0.000) in female student with mild acne (125.96±15.71) pg/ml when compared to control (27.23±9.57) pg/ml. The mean value of serum IL19 was significantly increased (0.000) in female student with mild acne (8.87±2.79) pg/ml when compared to control (3.16±1.74) pg/ml.. The mean value of serum TNF was significantly increased (0.015) in female student with moderate acne (143.25±4.24) pg/ml when compared to control (97.63±46.58) pg/ml. The mean value of serum IL17 was significantly increased (0.000) in female student with moderate acne (142.01±16.72) pg/ml when compared to control (27.23±9.57) pg/ml. The mean value of serum IL19 was significantly increased (0.000) in female student with moderate acne (15.11±3.16) pg/ml when compared to control (3.16±1.74) pg/ml. The mean value of serum TNF was significantly increased (0.000) in female student with severe acne (190.15±21.99) pg/ml when compared to control (97.63±46.58) pg/ml. The mean value of serum IL17 was significantly increased (0.000) in female student with severe acne (204.23±20.01) pg/ml when compared to control (27.23±9.57) pg/ml. The mean value of serum IL19 was significantly increased (0.000) in female student with severe acne (22.84±8.36) pg/ml when compared to control (3.16±1.74) pg/ml. There was a non significant positive correlation of TNF with IL17, and IL19 in female students with moderate acne (r=0.27, p=0.560; r=0.25, p=0.593 and r=0.30, p=0.514). There was a non significant negative correlation of TNF with IL17, IL19, total protein and albumin in female students with severe acne (r=-0.24, p=0.562; r=-0.21, p=0.618, r=-0.41, p=0.747 and r=-0.02, p=0.965). Acne vulgaris at different stages of severity in females is associated with significant increase in TNF-α, IL-17 and IL-19. These findings suggest that TNF-α, IL-17 and IL-19 could be used as a laboratory indicator to assess the severity of Acne vulgaris and its tendency to form scars, aiding in disease prognosis.

Keywords: tumour necrosis factor, interleukin 17 and 19, acne.

INTRODUCTION

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit typically affecting areas with a high density of hormonally-responsive sebaceous glands such as the face, neck, chest, upper back, and upper arms [1] Acne can present as non-inflammatory lesions, inflammatory lesions, or both and affecting mostly the face but also the back and chest [2]

Acne vulgaris is a multifactorial disorder of the pilosebaceous unit, resulting from sebum overproduction, follicular hyperkeratinization, inflammation, and bacterial colonization of hair follicles by Propionibacterium acnes. The sebaceous gland is controlled primarily by hormonal stimulation. In this way, the hormonal effect on sebum secretion is a key to the pathogenesis of acne [3]. During puberty, alteration of the sebum component, called dysseborrhea, stress, irritation, cosmetics, and potential dietary factors lead to the formation of acne lesions [4]. Changes in sebum secretion are considered to be an important factor of acne. In this way, increased sebum secretion can induce acne occurrence [5]. During puberty, in both sexes, Acne is often brought on by an increase in androgens such as testosterone. Excessive growth of propionibacteriumAcnes, which is normally present on the skin, is often involved [6]

Typical features of Acne include seborrhea (increased oil secretion), microcomedones, papules, pustules, nodules (large papules), and possibly scarring [7]. The appearance of Acne varies with skin colour. It may result in psychological and social problems. Some of the large nodules were previously called cysts and the term nodulocystic has been used to describe severe cases of inflammatory Acne.

Genetics is estimated to be the cause of 80% of cases. The role of diet as a cause is unclear. However, cigarette smoking does increase the risk of developing Acne and worsens its severity [8]

Acne vulgaris is the most common skin condition affecting late adolescents worldwide. The prevalence of acne is said to be 85% in adults aged 12 to 25 years [10] Almost all teenagers between 15 and 17 years report having some degree of acne. Lower rates are reported in some rural societies. In 2010, Acne was estimated to affect 650 million people globally making it the 8th most common disease worldwide [11]. People may also be affected before and after puberty. Though it becomes less common in adulthood than adolescence, nearly half of the people in their twenties and thirties continue to have Acne. About 4% continue to have difficulties into their forties [12]

Treatment of acne significantly reduces symptoms of anxiety, depression and improves acne patients' quality of life. Many treatment options are available to improve the appearance of acne including life style changes, procedures and medications. Eating fewer simple carbohydrates like sugar may help to improve the condition [13] Topical benzoyl peroxide, salicylic acid, and azelaic acid are commonly used in treatments. While antibiotics and retinoid are available for both topical and oral administration in treatment of acne, resistance to antibiotics may develop [14]

Tumor necrosis factor (TNF) is a multifunctional cytokine that plays important roles in diverse cellular events such as cell survival, proliferation, differentiation, and death. As a pro-inflammatory cytokine, TNF is secreted by inflammatory cells, which may be involved in inflammation-associated carcinogenesis. Several single nucleotide polymorphisms (SNPs) in the *TNF* gene promoter have been identified, some of which may regulate *TNF* expression. One of these polymorphisms at position -308 (*TNF* -308 G/A) had been reported associated with regulation of *TNF* expression by, e.g., interfering with transcription factor binding sites or other regulatory elements [15]

Interleukins are secreted proteins that bind to their specific receptors and play a role in intercellular communication among leukocytes. IL-17A, also called IL-17 in some studies, is the founding member of this structurally distinct cytokine family. It binds as a homodimer or a heterodimer with IL-17F to its receptor, IL-17RA [16]. IL-17A is expressed by activated CD4+ TH17 cells (18), but its expression has also been detected in CD8+ T cells, γδ T cells, NK cells, and neutrophils. Consistent with the broad expression pattern of its receptor, IL-17A acts on a variety of cells, which respond by upregulating expression of proinflammatory cytokines, chemokines, and metalloproteases. By inducing cells to produce chemokines, IL-17A attracts neutrophils to mediate defenses against different pathogens. IL-17A and TH17 cells are involved in several inflammatory disorders [17]. IL-19 is expressed by LPS-stimulated monocytes, and low levels have been observed in B cells [18]

Mouse IL-19 stimulates production of IL-6 and TNF-α and induces apoptosis and production of reactive oxygen species in monocytes, indicating a role in proinflammatory responses. IL-19 might promote TH2 cell responses because it induces IL-4, IL-5, IL-10, and IL-13 expression by activated T cells [19]
Acne vulgaris (pimples) has been a major skin disease of teenagers in recent times affecting about 80-90% of the entire teenage population [20]. It is increasingly becoming clear that diet rich in fatty acids and unsaturated free fatty acids play a role in Acne pathogenesis. *Propionibacterium acnes*, a gram-positive anaerobic bacterium, is a member of the resident

bacterial flora and mostly resides in pilosebaceous follicles. It has been known that the bacterium plays a critical role in the development of inflammatory acne vulgaris, which is the most common disease of human skin afflicting up to 80% of individuals through their lives [21]. In inflammatory acne lesions, the follicular epithelium is damaged and a dermal inflammation occurs. So far, several mechanisms of developing acne associated with *P. acnes* have been proposed. The mechanism for the onset of acne can generally be divided into two stages. The first stage is comedo formation, which is characterized by the initiation of inflammatory events before hyperproliferation of the follicular epithelia (microcomedo) [22]. The second stage is the occurrence of inflammation and disruption of follicular epithelia. It was widely accepted that inflammation in acne lesions may be induced by host immune reactions to *P. acnes*. Inflammation plays one of the main roles in the development of acne vulgaris. A research in vivo reported that a marked increase for tumor necrosis factor (*TNF*) gene transcripts was observed in acne lesions [23]. TNF is one of the main pro-inflammatory cytokines that play a central role in initiating and regulating the cytokine cascade during an inflammatory response. A number of case-control studies were conducted to investigate the association of tissue necrosis factor in acne vulgaris, however, these studies reported conflicting results which may be due to the limitations in sample size and different ethnic populations in the corresponding investigation.

There are few international studies investigating IL-17 and IL-19 concentration in acne patients. It was stated that there were changes in IL-17 and IL-19 concentration in *Acne vulgaris* patients at different stages of clinical severity. They suggested that IL-17 and IL-19 concentration levels may play a role in the pathophysiology of acne and be associated with its degree of clinical severity [24]. However, similar national-level studies on the link between IL-17 and IL-19 cytokines and acne or its severity are lacking. Therefore, this study primarily aims to examine the variation in IL-17 and IL-19 serum levels between *Acne vulgaris* patients. Due to paucity of information and the contradicting reports on serum, protease activated receptor, tissue necrosis factor, protein level and IL-17 and IL-19 in individuals with acne, this study is slated to investigate the levels of these parameters in subjects with *Acne vulgaris.*

MATERIALS AND METHODS

The study was carried out in Imo State University, Owerri, Imo state, Nigeria. Owerri is the capital of Imo State in Nigeria, set in the heart of Igboland. It is also the state's largest city. Owerri consists of three Local Government Areas including Owerri Municipal, Owerri North and Owerri West, it has an estimated population of about 401,873 as of 2006 census and is approximately 100 square kilometres (40 sq mi) in area. Owerri is bordered by the Otamiri River to the east and the Nworie River to the south

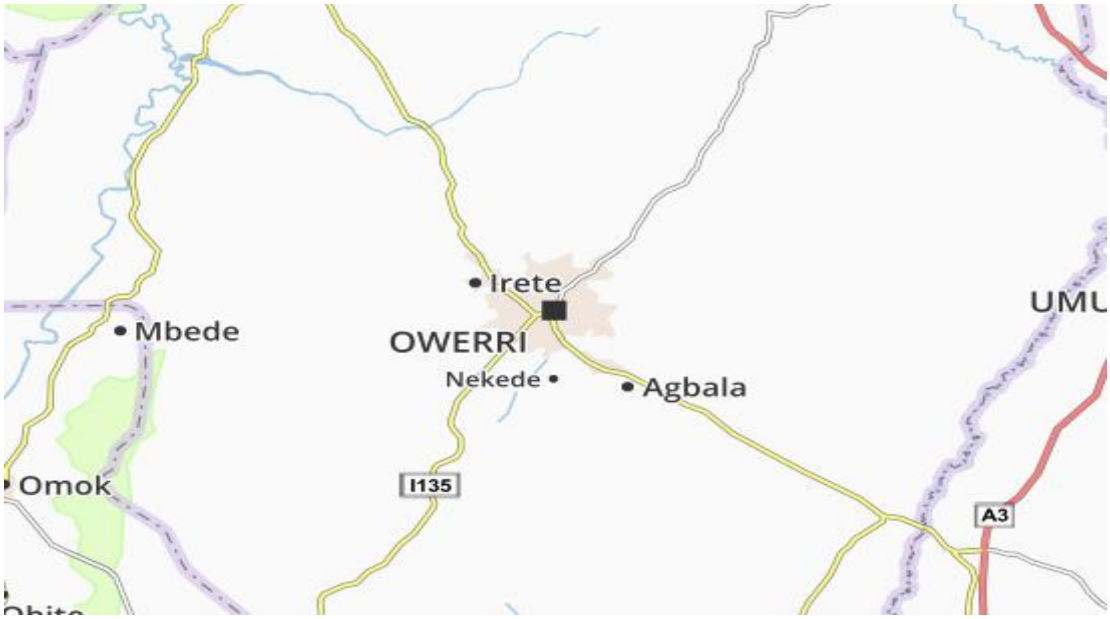

Fig 1: Map of Imo State

Ethics, Advocacy and Pre-Survey Contacts

A letter of introduction (Appendix I) from the Head of Department of Medical Laboratory Science, Imo State University was collected. The letter of introduction and research proposal was submitted to the dean of student affairs Imo State University for approval. On approval, informed consent was sought and obtained from the students before commencement of collection of samples. A structured questionnaire was employed in the study for the purpose of obtaining information regarding the participant history and demographic characteristics.

Study Population/Sample Size

The study population was student of Imo State University, Owerri, who have *Acne vulgaris* and apparently healthy IMSU students without acne. A total of one hundred young female adult was recruited for the study. The 100 subjects were divided into two groups, which were further grouped into mild, moderate and severe *Acne vulgaris* sufferers. Group 1 consists of 50 female subjects with *Acne vulgaris* while group 2 consists of 50 female subjects without *Acne vulgaris*.

Selection Criteria

a. Inclusion criteria

The inclusion criteria are as follows:

(i) Subjects between the age range of 18-30 years.
(ii) Subjects who gave consent to participate in the study.
(iii) Subjects with no history of chronic viral infection and/or liver diseases (HBV, HCV, HIV, and alcohol consumption)
(iv) Subjects who are not on long-term drug regimen.
(v) Subjects students not taking contraceptive or any reproductive pill.

Exclusion criteria

(i) Subjects below the age of 18 years and above the age of 30 years of age.
(ii) Subjects who didn't give consent to participate in the study.
(iii) Subjects with history of chronic viral infection and/or liver diseases (HBV, HCV, HIV, and alcohol consumption).
(iv) Subjects who are on long-term drug regimen (especially oral contraceptives and reproductive pills).

Study Design

A case control study was carried out among young female adults. The test group comprises of 50 participants within the age range of 18-30years, while, the control group will comprise of 50 apparently healthy adult female students whose age matched with the test population.

A structured questionnaire was issued to them for the purpose of obtaining some information regarding their medical and demographic characteristics, in addition to their hospital records. Those who qualify to participate in the research were made to sign a written letter of consent.

Sample Collection

Blood samples was collected aseptically by venopuncture, using a 5ml sterile disposable syringe and needle from all the subjects and was dispensed into a labeled plain dry specimen container. The samples were centrifuged at 3,000pm for 5 minutes after clotting to separate and to obtain the serum. The sera were extracted using a Pasteur pipette and put into appropriate specimen container, and stored at -20^{o}C prior to use.

Laboratory Procedures

Determination of Serum Protease Activated Receptor, Serum Tissue Necrotic Factor and Serum Cytokines was done by standard method Serum concentrations of IL-17 and IL-19 were determined with the Human Cytokine/Chemokine Panel I Merck Millipore

Statistical Analysis

RESULT

Table 1: Comparison of Mean Value of TNF, IL17 and IL19, in Female Students with Acne

Parameter	Young Adult Female with Severe *Acne Vulgaris* n=20	Young Adult Female with Moderate *Acne Vulgaris* n=20	Young Adult Female with Mild *Acne Vulgaris*	f-value	p-value
TNF (pg/ml)	190.15±21.99	143.25±4.24	111.33±46.58	13.62	0.000
IL17 (pg/ml)	204.23±20.01	142.01±16.72	125.96±15.71	41.47	0.000
IL19 (pg/ml)	22.84±8.36	15.11±3.16	8.87±2.79	10.06	0.001

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

There was a significant difference (0.000) in the mean value of TNF in Female Students with Acne when compared using the Analysis of variance. There was a significant difference (0.000) in the mean value of IL-17 in Female Students with Acne when compared using the Analysis of variance. There was a significant difference (0.001) in the mean value of IL-19 in Female Students with Acne when compared using the Analysis of variance.

Table 2: Mean Value of TNF, IL17, and IL19, in Young Adult Female Student with Mild Acne Vs Control

Variable (Mean±SD)	Young Adult Female with Mild *Acne Vulgaris* n=10	Female Control n=50	t-value	p-value
TNF (pg/ml)	111.33±46.58	97.63±46.58	0.59	0.563
IL17 (pg/ml)	125.96±15.71	27.23±9.57	14.93	0.000
IL19 (pg/ml)	8.87±2.79	3.16±1.74	4.82	0.000

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

There was no significant difference (0.563) in the mean value of serum tissue necroses factor in female student with mild acne (111.33±46.58) pg/ml when compared to control (97.63±46.58) pg/ml. The mean value of serum IL17 was significantly increased (0.000) in female student with mild acne (125.96±15.71) pg/ml when compared to control (27.23±9.57) pg/ml. The mean value of serum IL19 was significantly increased (0.000) in female student with mild acne (8.87±2.79) pg/ml when compared to control (3.16±1.74) pg/ml.

Table 3: Mean Value of TNF, IL17, and IL19, in Young Adult Female Student with Moderate Acne Vs Control

Variable (Mean±SD)	Young Adult Female with Moderate *Acne Vulgaris* n=20	Female Control n=50	t-value	p-value
TNF (pg/ml)	143.25±4.24	97.63±46.58	2.79	0.015
IL17 (pg/ml)	142.01±16.72	27.23±9.57	16.61	0.000
IL19 (pg/ml)	15.11±3.16	3.16±1.74	6.24	0.000

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

The mean value of serum TNF was significantly increased (0.015) in female student with moderate acne (143.25±4.24) pg/ml when compared to control (97.63±46.58) pg/ml. The mean value of serum IL17 was significantly increased (0.000) in female student with moderate acne (142.01±16.72) pg/ml when compared to control (27.23±9.57) pg/ml. The mean value of serum IL19 was significantly increased (0.000) in female student with moderate acne (15.11±3.16) pg/ml when compared to control (3.16±1.74) pg/ml.

Table 4: Mean Value of TNF, IL17, IL19, in Young Adult Female Student with Severe Acne Vs Control

Variable (Mean±SD)	Young Adult Female with Severe *Acne Vulgaris* n=20	Female Control n=50	t-value	p-value
TNF (pg/ml)	190.15±21.99	97.63±46.58	2.79	0.000
IL17 (pg/ml)	204.23±20.01	27.23±9.57	16.61	0.000
IL19 (pg/ml)	22.84±8.36	3.16±1.74	6.24	0.000

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

The mean value of serum TNF was significantly increased (0.000) in female student with severe acne (190.15±21.99) pg/ml when compared to control (97.63±46.58) pg/ml. The mean value of serum IL17 was significantly increased (0.000) in female student with severe acne (204.23±20.01) pg/ml when compared to control (27.23±9.57) pg/ml. The mean value of serum IL19 was significantly increased (0.000) in female student with severe acne (22.84±8.36) pg/ml when compared to control (3.16±1.74) pg/ml.

Table 5: Mean Value of TNF, IL17, IL19, in Female Students with Moderate Acne Vs Female Students with Mild Acne

Variable (Mean±SD)	Young Adult Female with Moderate *Acne Vulgaris* n=20	Young Adult Female with Mild *Acne Vulgaris* n=10	t-value	p-value
TNF (pg/ml)	143.25±4.24	111.33±46.58	1.81	0.096
IL17 (pg/ml)	142.01±16.72	125.96±15.71	1.85	0.089
IL19 (pg/ml)	15.11±3.16	8.87±2.79	2.83	0.015

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

There was no significant difference (0.096) in the mean value of serum total TNF in female student with moderate acne (143.25±4.24) pg/ml when compared to female student with mild acne (111.33±46.58) pg/ml. There was no significant difference (0.089) in the mean value of IL-17 in female student with moderate acne (142.01±16.72) pg/ml when compared to female student with mild acne (125.96±15.71) pg/ml. The mean value of IL-19 was significantly increased (0.015) in female student with moderate acne (15.11±3.16) pg/ml when compared to female student with mild acne (8.87±2.79) pg/ml.

Table 6: Mean Value of TNF, IL17, IL19, in Female Students with Severe Acne Vs Female Students with Mild Acne

Variable (Mean±SD)	Young Adult Female with Severe *Acne Vulgaris* n=20	Young Adult Female with Mild *Acne Vulgaris* n=10	t-value	p-value
TNF (pg/ml)	190.15±21.99	111.33±46.58	4.29	0.001
IL17 (pg/ml)	204.23±20.01	125.96±15.71	8.33	0.000
IL19 (pg/ml)	22.84±8.36	8.87±2.79	4.19	0.001

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

The mean value of TNF was significantly increased (0.001) in female students with severe acne (190.15±21.99) pg/ml when compared to female students with mild Acne (111.33±46.58) pg/ml. The mean value of IL-17 was significantly increased (0.000) in female students with severe acne (204.23±20.01) pg/ml when compared to female students with mild Acne (125.96±15.71) pg/ml. The mean value of IL-19 was significantly increased (0.001) in female students with severe acne (22.84±8.36) pg/ml when compared to female students with mild Acne (8.87±2.79) pg/ml.

Table 7: Mean Value of TNF, IL17, IL19, in Female Students with Severe Acne Vs Female Students with Moderate Acne

Variable (Mean±SD)	Young Adult Female with Severe *Acne Vulgaris* n=20	Young Adult Female with Moderate *Acne Vulgaris* n=20	t-value	p-value
TNF (pg/ml)	190.15±21.99	143.25±4.24	5.52	0.000
IL17 (pg/ml)	204.23±20.01	142.01±16.72	6.48	0.000
IL19 (pg/ml)	22.84±8.36	15.11±3.16	2.12	0.054

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

The mean value of TNF was significantly increased (0.000) in female students with severe acne (190.15±21.99) pg/ml when compared to female students with moderate Acne (143.25±4.24) pg/ml. The mean value of IL-17 was significantly increased (0.000) in female students with severe acne (204.23±20.01) pg/ml when compared to female students with moderate Acne (142.01±16.72) pg/ml. There was no significant difference (0.054) in the mean value of IL-19 in female student with severe acne (22.84±8.36) pg/ml when compared to female student with moderate acne (15.11±3.16) mg/dl.

Table 8: Correlation of TNF with IL17, IL19, in Female Students with Mild Acne

Variable	n	R	p-value
IL17 (pg/ml)	10	-0.43	0.338
IL19 (pg/ml)	10	0.59	0.161

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

There was a non significant negative correlation of TNF with IL17, in female students with mild acne (r=-0.43, p=0.338; r=-0.22,). There was a non significant positive correlation of TNF with IL19 in female students with mild acne (r=0.59, p=0.161).

Table 9: Correlation of TNF with IL17, IL19, in Female Students with Moderate Acne

Variable	n	R	p-value
IL17 (pg/ml)	20	0.27	0.560
IL19 (pg/ml)	20	0.25	0.593

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

There was a non significant positive correlation of TNF with IL17, IL19 and albumin in female students with moderate acne (r=0.27, p=0.560; r=0.25, p=0.593 and r=0.30, p=0.514).

Table 10: Correlation of TNF with IL17, IL19, in Female Students with Severe Acne

Variable	n	r	p-value
IL17 (pg/ml)	20	-0.24	0.562
IL19 (pg/ml)	20	-0.21	0.618

KEY:

TNF: Tissue Necroses Factor

IL17: Interleukin 17

IL19: Interleukin 19

P<0.05: Significant

P>0.05: Not Significant

There was a non significant negative correlation of TNF with IL17, IL19, in female students with severe acne (r=-0.24, p=0.562; r=-0.21, p=0.618.

Discussion

It is suggested that *Acne vulgaris* is likely to be a genuine chronic inflammatory disease of pilosebaceous unit widely affecting adolescents and young adults [5]. Proinflammatory cytokines such as TNF-α, IL-17 and IL-19 were considered the main responsible mediators of inflammatory acne. It has been shown that acnes stimulate cytokine production from lymphocytes, monocytes, and keratinocytes [23]

In the present study, there was no significant difference in the mean value of serum alpha tissue necroses factor in female student with mild acne when compared to control, but there was a significant increase in the mean value of TNF-α in female student with mild acne when compared to control. Tumor necrosis factor-α is the main proinflammatory cytokine that plays a central role in initiating and regulating the cytokine cascade during an inflammatory response [10].It is well known that TNF-α plays an important role in the pathogenesis of acne as well as in other inflammatory skin diseases [24]. Factors affecting its production may possibly influence the degree of inflammatory response and hence may account for the clinical severity of acne. The observed elevations of TNF-α serum levels were significantly

correlated with disease severity. The result of this study is in agreement with the study carried out by [25] who reported that TNF-α serum concentrations are increased in various inflammatory skin condition. The results of this study also concur with those obtained by [26] who also stated that changes in TNF-α in females with acne is due to the alterations in the immune system state occurring in Acne vulgaris condition. In his study, they further assumed that monocytes isolated from acne patients' peripheral blood had poorer ability to respond to lipopolysaccharide (LPS) stimulation, as manifested in the production and secretion of TNF-α (and IL-6), than monocytes isolated from healthy people. A study carried out by [27] reported that TNF-α polymorphisms and serum levels are not associated with acne type, but they further stated that the sample size might be the reason behind the non significant difference in the level of TNF-α in females with Acne.

The current study reveals that the mean value of serum IL-17 was significantly increased in female student at the different stages of acne (mild, moderate and severe) when compared to controls. The higher serum IL-17 levels are likely due to a spill-over of increased IL-17 secretion at the disease site. The high levels in serum resulting from a disease localized to a small area of skin is reflective of the quantum of this cytokine produced at one site and emphasizes its important role in the pathogenesis of acne. Further, it is noted that a significant rise in IL-17 levels with increasing grade of acne was in concordance with results of [8] lending further support to the association. However, this finding was contrary to the findings of [28] who did not find any significant difference in serum IL-17 levels between patients of mild and moderate acne. Further in this study, acne patients with severe lesions had significantly higher mean levels of IL-17 which is indicative of the severity of acne at this site. Also, higher IL-17 levels are induced by *P. acnes* strain isolated from acne lesions (PA) than healthy skin (PH) [29]. Further, it was documented that sebocytes functionally interact with *P. acnes* in inducing maturation of dendritic cells which result in preferential priming of Th17 cells in response to P. acnes. This probably signifies the predominant role of IL-17 in the inflammatory stages or progression of acne [30].

It can be seen from the present study that the mean value of serum IL19 was significantly increased in female student with mild, moderate and severe acne when compared to control. Additionally, IL-19 levels significantly differed between mild, moderate, and severe AV patients, with changes being proportional to the degree of clinical severity. The IL-19 human genetic locus is located on human chromosome 1q32, and this locus has a strong link to IL-10 as part of a gene cluster [31]. When exposed to proinflammatory stimuli, monocytes and epithelial cells produce IL-19. In turn, IL-19 amplifies the proinflammatory nature by creating a positive feedback loop, encouraging these cells to further amplify their response. As soon as they are stimulated in the inflammatory process, they will continuously produce the cytokine [32]. Several other studies have assessed IL-19 concentration levels, and the role of IL-19 in the pathogenesis of other inflammatory skin diseases, such as psoriasis and atopic dermatitis, was established in previous studies [32] who were the first to investigate IL-19 levels in patients with AV of varying severity, found results similar to ours. They demonstrated a statistically significant difference in IL-19 concentration between mild and severe cases, as well as between moderate and severe cases. However, in contrast to this finding, they did not observe a significant difference between mild and moderate cases [33]. The results showed significant differences not only between mild and severe and moderate and severe cases but also between mild and moderate cases, a finding also confirmed by another study [34]. This suggests that higher concentrations of IL-19 are associated with more severe inflammation. This is in line with findings by [35] who demonstrated that the production of the proinflammatory cytokine IL-19 mainly depends on cells involved in the inflammatory microenvironment, implying that severe inflammation correlates with higher levels of IL-19 [36]. Similarly, the findings are consistent with those of [37] who estimated IL-19 levels in patients with another inflammatory skin disorder, psoriasis, highlighting that disease severity is reflected in increased levels of proinflammatory cytokines. In the study carried out by [24] the median IL-19 serum concentration among cases of different severity and controls was lower than that found by [28] However, variations in IL-19 concentrations have been reported in similar studies, which could be attributed to racial differences or the use of different experimental kits by different investigators.

And lastly there was a non significant correlation between TNF-α with IL-17, IL-19, total protein and albumin level. The result clearly shows that the level of TNF-α cannot be used to predict the level of IL-17, IL-19, level in female patient with mild, moderate and severe acne. The result of this study is in concordance with the study carried out by [32] who also assessed the level of TNF-α with IL-17, IL-19, in acne, psoriasis and atopic dermatitis patients correlating the cytokine level with disease severity. Using severity indices for both conditions, they found a non significant correlation between the serum level of TNF-α with IL-17, IL-19, and disease severity in acne vulgaris condition [38]

Conclusion

Acne vulgaris at different stages of severity in females is associated with significant increase in TNF-α, IL-17 and IL-19. Total protein and albumin are not altered in female's patient with various grades of acne condition. These findings suggest that TNF-α, IL-17 and IL-19 could be used as a laboratory indicator to assess the severity of Acne vulgaris and its tendency to form scars, aiding in disease prognosis.

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