Investigation of Lipid Profile, Vitamin (A & B12), Zinc and Linoleic Acid In (Face & Shoulder) Acne Patients in Basrah Govern

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Abstract
Acne does not threaten life, but it is considered a painful and critical condition. It has been found that it is difficult to get rid of it. There are many causes of acne, with some being more certain than, other (Mahmood & Shipman, 2017). Acne is known as one of the most prevalent skin issues, as it occurs when the hair follicles under the skin become blocked. Sebum (oil that prevents drying of the skin), in addition to dead skin cells together contribute to closing the pores, which in turn leads to the spread of lesions or the so-called pimples (Traub, 2020). Aim: of this study is to investigate the lipid profile, vitamins, zinc and linoleic acid for acne patients, to evaluate their effect on acne and its severity. Results: In the Face acne patients: (HDL, vitamin A, vitamin B12, zinc and linolic acid) showed highly significant decrease comparing to the control group while (LDL) showed highly significant increase comparing to the control group. Probability ($P < 0.05$) was considered statistically significant. When comparing statistical results for females with males in the face acne: (BMI, HDL, vitamin B12) showed highly significant increase, while (LDL, Zinc & linoleic acid) showed highly significant decrease. In the Shoulder acne patients: (HDL, vitamin A, vitamin B12 & zinc) showed highly significant decrease comparing to the control group. When comparing statistical results for females with males in the shoulder acne: (cholesterol, HDL, vitamin A, vitamin B12) showed highly significant increase, while (zinc & linoleic acid) showed highly significant decrease. Using (ROC) curve for patients with shoulder acne: Females show: highly significant statistical behavior for (Vitamin A, zinc & linoleic acid), with high % of area under the curve and good characteristic of validity for all tests. For males: (HDL, vitamin A, vitamin B12, zinc & linoleic acid) shows highly significant statistical behavior with high % of area under the curve and good characteristic of validity for all test. Spearman's nonparametric statistical correlation coefficient for biomarkers, in all patients with (face & shoulder) acne, shows different correlations as showed in the tables. Conclusion: The obtained result concludes that: (Vitamin A, Vitamin B12, Zinc, and Linoleic Acid) have a severe effect on acne and its exacerbation. The use of (ROC) curve gave an evaluation of the ability and accuracy of some biomarkers in expressing acne severity, especially (vitamin A, zinc & linoleic acid). Abbreviations used: HDL: high density lipoprotein, LDL: low density lipoprotein, BMI: body mass index

Keywords: Face and shoulder acne, Lipid profile, vitamin (A & B12), zinc & linoleic acid.

1. Introduction

Skin is the largest organ in the human body, with a thickness of 2-3 mm and an average area of 30 square meters in adults. It serves as a physical and immune barrier that protects internal components from the influence of external factors, and limits infections and inflammation (Skowron et al., 2021). The skin forms a network of chemical, physical and microbiological barriers against external threats. It also contains keratinocytes, which are the most abundant cell type in the dermis. They form the first line of defences by sensing diseases through immune receptors. Then the antimicrobial response begins with the production of various cytokines and antimicrobial peptides (Chieosilapatham et al., 2021).

Acne is a skin infection that affects the entire world's population. It ranks as the eighth most common disease worldwide, with 645,499,139 affected worldwide. (Hapsari et al., 2022). It was estimated to affect about 50 million people in the U.S. About 85% of teenagers are affected by acne, but it can occur in any age group with many cases persisting into adulthood. (Zaenglein et al., 2016). Acne is a common and chronic skin disease involving blockage or inflammation of the sebaceous units and associated hair follicles. It most often affects the face, chest, and back (Tan & Bhate, 2015).

It is believed that the cause of acne is the contribution of four main factors

- Increased sebum secretion as a result of enlarged sebaceous glands.
- Clogging Pores due to the hyperkeratosis of the hair follicles, this prevents the shedding of keratinocytes naturally and leading to the accumulation of cellular debris and sebum.

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- Anaerobic bacterial colonization (known as Propionibacterium acnes).
- The rupture of the follicle will cause bacteria, lipids and fatty acids to leak into the dermis, and this causes an inflammatory response. Acne can be non-inflammatory (characterized by pustules) or inflammatory (characterized by papules and cysts), and acne can present as a combination of the two (Keri, J. E., 2022).

The areas covered with hair contain sebaceous glands, where these glands are connected to hair follicles at a rate of one gland per hair follicle or more. These glands provide about 90% of its surface lipids of the skin.

The sebaceous gland is an organ located in the dermis, and it is connected to the hair follicle through the excretory duct, the sebum is secreted through the excretory duct and along the hair root to the surface of the skin (Agarwal, S., & Krishnamurthy, K., 2022). Human skin contains sebaceous glands at a rate of 2.000.000, these glands are distributed at a density of approximately (400 - 900)/ cm2 on the face. Sebaceous gland secretes the sebum to increase the softness of the skin, hair and to protect the skin from external damage factors and dehydration. These cells also involved in the metabolism and lipid synthesis, so it is considered as a hormonal target and an endocrine organ (Hoover, E., Aslam, S., & Krishnamurthy, K., 2021). Human sebum contains composed of different types of lipid molecules: 57.5% triglycerides and fatty acids, wax esters 26% wax esters, squalene 12% and cholesterol (4.5%) (Lovászi et al., 2017).

Aim: Assessing the lipid profile, vitamins, zinc and essential unsaturated fatty acids (linoleic acid) for acne patients, then correlate these biomarkers with each other to see the effect of their levels on acne appearance and severity.

2. Research design and Methods

2.1 Research design

The biochemical study enrolled a representative sample of (240) participants, of whom (85) had a face acne, and (79) had acne shoulder with (76) as control group. The ages of the participants ranged between (17-35) years. The acne patients in the face and shoulder were also divided into subgroups (males & females). Age and gender were matched for all participants. The protocols for this study were approved by the College of Healthy and Medical Technologies in Basra and by the Ethical committee in the directorate of Health in Al-Basrah.

2.2 Sample Collection

Venous blood samples were collected from each participant in standardized vacuum gel tube, under standardized conditions. Serum was obtained and then stored at -20°C until the lab testing.

2.3 Methods

- Parameters were measured according to the following procedures:
- 1 - (lipids, vitamin B12 & zinc) by Cobas e 411 and Cobas c 311 automated analysers (fully automated quantitative testing system) using electroluminescence technology. The work steps were carried out according to the batch manufacturing procedures.
- 2- Vitamin A and linoleic acid levels were measured using ELISA technique, (Sandwich-ELISA as a method). Using spectrophotometer at a wavelength of 450 nm.

3. Results and Discussion

Acne is affected by biochemical factors related to the pilosebaceous unit such as, vitamins and elements necessary for skin health, genetic predisposition and lifestyle factors. Acne can affect hair follicles in other places of the body such as the back, chest and shoulders. where there is a higher density of hair follicles with a density of the glands that produce sweat and oil with which secrete sebum (Mahto, 2017). The damage caused by acne, varies according to the difference in the natural physiology of the skin of males and females. This study reviews the evaluation of the role of (lipid profile, vitamins, zinc & linoleic acid) in acne patients on (face & shoulder). Statistical evaluation of data was achieved by using SPSS version 25 (IBM, Chicago, Illinois, USA), using the independent test to compare the data of two different groups. ANOVA test were used when, the comparing within the same category. The P value ≤ 0.05 was considered statistically significant.

3.1 Presenting statistical comparison of biochemical markers for patients with acne in the (face & shoulder) compared to the control group as a total number.

The results of the statistical analysis listed in table (1) shows the change in these biomarkers with the two types of acne as:

In face acne patients: (HDL, vitamin A, vitamin B12, zinc and linolic acid) showed highly significant decrease comparing to the control group, while (LDL) showed highly significant increase comparing to the control group.

In shoulder acne patients: (HDL, vitamin A, vitamin B12 & zinc) showed highly significant decrease comparing to the control group.

Lipid profile

Changes in the lipid profile are closely related to acne, as the increase in plasma cholesterol levels leads to an increase in androgen production, a factor in the appearance of acne. (Macedo et al., 2015).

When there is too much cholesterol in the bloodstream, it affects the skin and causes fatty deposits to form beneath the skin. Cholesterol can also clog the microscopic blood capillaries that feed the skin, cutting off oxygen transport (Jiang et al., 2015).

Vitamins: Are essential for metabolism and often work in tandem with enzymes and other cofactors.

Vitamin A

Vitamin A helps prevent cell damage by fighting free radicals, promoting healthy skin, slowing cell aging and decreasing the speed of cell shedding. It is expected to prevent acne formation by decreasing sebum (oil) production. (Srichairatanakool & Fucharoen, 2014).

Derivatives of vitamin A (retinoids), also promote the proliferation of keratinocytes. They are fat soluble so; they penetrate the stratum corneum and slightly into the dermis to reduce trans epidermal water loss. Vitamin A and its derivatives protect collagen from degradation in addition to inhibiting the activity of mineral proteins (Zizola et al., 2010).

Vitamin B12

All B's vitamins assist the body in converting food (carbohydrates) into the energy-producing fuel glucose. Vitamin B12 (cobalamin), is one of the most complex vitamins. It contains an organic molecule that surrounds the cobalt atom and is water soluble. The vitamin binds to the protein in the food we eat. Finally, it is better absorbed in the small intestine after being combined with a protein called intrinsic factor. (Etgen et al., 2011). This vitamin is very important for the nervous system to function dynamically and properly. It was found that taking vitamin B12 supplements in abundance affects the genes expressed by bacteria that live on the skin and are important to human physiology (Kang et al., 2015). A study found that, more vitamin B12 intake will increases its quantity on the skin of the face. This causes the bacteria (Propionibacterium acnes) to be produced on the face, which leads to inflammation and acne breakouts.

Zinc

The skin contains about 6% of the total zinc in the human body. The human needs a continuous supply of zinc because there is no storage depot for it and its movement through the different tissues is limited. In addition to its need for growth, metabolism and tissue repair. Zinc is an essential component of more than 300 mineral enzymes and more than 2,000 transcription factors important for regulating the metabolism of proteins and lipids (Faludi et al., 2014).

Due to zinc's anti-inflammatory characteristics, acne sufferers' bodies need it to experience less swelling and redness. Zinc can help lessen any leftover acne scars because it aids in wound healing as well. (Yee et al., 2020). Topical zinc may help eliminate acne-causing bacterium from the skin and lessen oil production (Bronsnick et al., 2014).

Zinc is involved in a very large number of enzymatic actions within the body. It is a natural inhibitor for dihydrotestosterone, and a reducer to the effect of androgens (DHT), as a result it reduces androgen receptors. As well as it reduces the excessive production of oily sebum in the skin Zinc, also reduces sebum stimulation in response to inflammation and stress. All studies indicated that zinc helps in stabilizing the life cycle of the cell. Other studies have also indicated that programmed cell death does not occur without zinc, and this in turn leads to abnormal accumulation of dying cells, especially in rapid growth stages during puberty.

Linoleic acid

Linoleic acid is an unsaturated fatty acid, have many physiological activities, it is also a component of the lipid barrier in the stratum corneum (the upper layer of the skin) along with cholesterol, ceramides and other fatty acids. Without its presence in these essential fats, the barrier will be weakened, then the weakened barrier will allow harmful things like bacteria and irritants to pass into the deeper layers of the skin, causing acne symptoms. (Yang et al., 2020).

Linoleic acid help in treating acne and hair loss by inhibiting enzymes that convert testosterone into DHT. Linoleic acid also improves the receptors regulating sebum production and keratinocyte hyperactivity. It also, acts as an anti-inflammatory and protects the skin from damage caused by UV rays (Manosalva et al., 2020).

It was found that the lack of linoleic acid in the skin leads to the production of sebum in the sebaceous glands with oleic acid, the latter is irritating to the skin and promotes blockage that causes whiteheads and acne. Linoleic acid is also the building block for the production of skin ceramides, and its low levels in acne-prone patients result in insufficient ceramide production. This explains the lack of ceramides for people with acne (Ottaviani et al., 2010).

The statistical comparison of biochemical markers for the face acne group to their peers with shoulder acne showed: Highly significant decrease in (BMI & LDL), while (HDL, vitamin A, zinc & linoleic acid) showed highly significant increase when comparing the two acne affected groups.

Face acne group versus shoulder acne group as a total number of participants

Acne appears in different areas of the body due to the same factors, where the excessive activity of the sebaceous glands, dead skin cells and bacteria will cause inflammation and clogging the pores in adulthood (Kumar et al., 2016). Acne on the back, shoulders and chest is more severe and common than the face, because of the number of sebaceous glands and hair follicles in those places (Shannon, 2020). In addition to these standard factors, mechanical factors such as friction between skin, clothing, synthetic fabrics, and perspiration can provide an ideal environment for bacteria to thrive and lead to disease outbreaks (Mazhar et al., 2019).

The biochemical markers statistical comparison showed: highly significant decrease in (insulin,

cortisol & ACTH) for the face acne group to their shoulder acne peers.

3.2 Display statistical comparison for the biochemical markers in acne patients according to the gender for (face & shoulder) acne group.

The result of statistical comparison is showed in the table (2). Where, the type of disease was fixed and the gender was changed, in order to obtain conclusions that show the reflection of body physiology, skin type and the dominance of hormones for both sexes on the appearance, severity and persistence of acne. The statistical results for females relative to males, shows the following:

In Face acne: (BMI, HDL & vitamin B12) showed highly significant increase. While (LDL, Zinc &linoleic acid) showed highly significant decrease.

In shoulder acne: (BMI, HDL & vitamin B12) showed highly significant increase. While (LDL, Zinc &linoleic acid) showed highly significant decrease. The results obtained for the two cases of acne, show clear differences related to gender.

BMI, being overweight can increase acne. Researchers have found that women (but not men) with a BMI of over 25 are more likely to develop acne. Researchers have also suggested that obesity causes an increase in androgens that trigger acne. Where girls are affected more than boys. This may also cause psychological stress, which in turn leads to the release of stress hormones that exacerbate the problem (Sas & Reich, 2019).

Lipid profile, Nutritional factors influence the occurrence of acne. Evidence confirms that the output of the sebaceous gland changes due to nutritional manipulation. When the consumption of carbohydrates and dietary fats increases, the secretion of fats increases and a change in fat composition may occur, finally this will accelerate acne production (Kataria Arora et al., 2010).

It was found also that, increased levels of plasma cholesterol led to high production of androgens, which is one of the main factors predisposing to the appearance of acne.

Vitamin A, the importance of vitamin A, lies in encouraging skin cells to grow, regulating the amount of keratin produced and preventing dead skin cells from sticking to prevent clogging of hair follicles (Cherney, 2018). Since gender is a biological variable, it must be considered in immunological studies. Males differ from females in the immune response to foreign and self-antigens throughout life. Vitamin A is necessary to maintain a healthy reproductive system in both women and men (Klein & Flanagan, 2016).

Vitamin B12, one study indicated that men are more likely to be deficient in vitamin B12 than women. It was not explained through dietary habits or the effects of estrogen. Therefore, genetic differences play a key role in this difference (Margalit et al., 2018).

Zinc is a cofactor for antioxidant enzymes and helps build muscle and repair damage. In addition to building healthy cells and promoting skin health, zinc is important in the synthesis of the main protein that makes up hair - keratin. Men need zinc more than women. Zinc deficiency often leads to low testosterone levels, which leads to fatigue and loss of muscle mass. Zinc also promotes prostate health. A study also found that higher intakes reduce the risk of prostate cancer in men (Sauer et al., 2020).

Linoleic Acid, it has recently been shown that polyunsaturated linoleic fatty acids are beneficial for various diseases and have functions in cell membranes as building blocks for human development and optimal health. Linoleic acids help reduce fat mass from the abdomen or buttocks and prevent bone loss for both sexes. These acids are also gaining momentum in alleviating deadly diseases such as atherosclerosis, cancer and diabetes (Lohner et al., 2013).

3.3 Display Receiver-operating characteristic (ROC) curve analysis for all shoulder acne patients as a (males & females).

due to the difference physiological state of women and men body, in terms of different ratios of hormones, number of sebaceous glands, and density of body hair. ROC curve will assess the good characteristics of validity for the tests with face and shoulder acne and for both genders, as shown in table able (5).

In Females' group: (Vitamin A, zinc & linoleic acid), shows highly significant statistical behavior with high percentage of the area under the curve rang (79% - 97%), and good characteristic of the validity for all of the test, except (Sensitivity % & NPV) for zinc and linoleic acid.

In Males' group: (HDL, Vitamin A, Vitamin B12, zinc & linoleic acid), shows highly significant statistical behavior with high percentage of the area under the curve rang (74% - 99.8%), and good characteristic of the validity for all of the test.

♦ When the biochemical marker shows, high statistically significant behavior with a high percentage of the area under the curve, and a good validity characteristic for all tests (% sensitivity, % specificity, PPV & NPV). This biochemical marker will be confirming the disease. Whereas, if the biochemical marker shows, non-significant statistical behavior with high percentage of the area under the curve or good validity to some tests. That means, auxiliary evidence is needed to prove the presence of the disease.

3.4 Display Spearman's Statistical Correlations for Biomarkers With Each Other in patients having acne in (face & shoulder)

Correlation is defined as a bivariate analysis that measures the relationship between two variables in terms of the strength of the association and the direction of the relationship (Schober & Schwarte, 2018).

The study included verifying a set of biomarkers that are directly related to the presence of acne, whether in the face, back and shoulders.

3.4.1 Presentation of Spearman's nonparametric statistical correlation coefficient for biomarkers in all patients with facial acne

1. LDL, showed highly significant difference and highly important positive correlation with cholesterol, while shows highly significant difference and low negative correlation with HDL
2. In a similar recent study conducted to assess the lipid profile of acne sufferers. The study included (45) participants and a control group of a same number. The results of the study showed significant statistical increase for both biomarkers (cholesterol & LDL) together in a positive correlation (Sobhan et al., 2020).
3. Vitamin A showed highly significant difference and good positive correlation with (HDL). Many functions are conferred on HDL through its ability to enhance the flow of cholesterol through molecules including carotenoids and vitamins. Based on HDL's ability to interact with nearly all cells and to transport and deliver lipid-soluble compounds.
4. vitamin B12, showed highly significant difference and moderate positive correlation with (HDL), while showed low positive correlation with (vitamin A).
5. Some epidemiological studies have shown an association between vitamin (B12) and metabolic syndrome. It has been observed that mothers with low levels of vitamin (B12) may give birth to children with excess fat accumulation (Boachie et al., 2020).
6. Zinc showed highly significant difference and moderate positive correlation with (HDL), while shows high positive correlation with vitamin (A). As well as, showed low positive correlation with (vitamin B12).
7. Zinc supplementation studies have reported that taking zinc leads to increased plasma HDL levels and decreased TC and LDL levels (Faludi et al., 2014).
8. ❍zinc is one of the vital antioxidants, and its deficiency limits the body's ability to transfer vitamin A from the liver to the tissues. This confirms the positive correlation between them. Moreover, zinc helps the body's proteins to convert vitamin A into the usable retinol. Other studies have shown that, retinol-A compounds are able to kill acne-causing bacteria. (Eren et al., 2013)
9. **Linoleic acid,** showed highly significant statistical difference and many different correlations with (BMI, cholesterol, vitamin A, vitamin B12 & zinc) and as the following:
10. Linoleic acid showed low negative correlation with (BMI), low positive correlation with cholesterol, low positive correlation with (vitamin A & vitamin B12) and a good positive correlation with zinc.
11. Conjugated linoleic acid (CLA) is an anti-obesity agent, and recent research in humans indicates that linoleic acid reduces weight gain by modulating the properties of lipid metabolism, resulting in reduced obesity (Lehnen et al., 2015).
12. It was found that the metabolism and absorption of vitamin A correlated with fat. It has been observed that linoleic acid is a fatty acid that increases retinol levels in tissues, and this may be due to the ways in which vitamin A and lipids are metabolized (Carta et al., 2014) This confirms the positive correlation between them under this study.
13. Linoleic acid is the basic building block for ceramides production in human skin. Its low levels in the sebum of acne patients are insufficient to produce ceramides. This in turn leads to a weakening of the skin barrier associated with follicular hyperkeratosis, as well as an increased risk of acne (Balić et al., 2020).
14. **Zinc,** have crucial roles in growth, metabolism, immune and neurological functions. So, many physiological functions are affected by zinc deficiency. Zinc and essential fatty acids are involved in the regulation of gene transcription and the regulation of some metabolic pathways (Monteiro et al., 2021).

3.4.2 Presentation of Spearman's nonparametric statistical correlation coefficient for biomarkers in all patients with shoulder acne.

Acne in different areas of the body is a common problem. An estimated 10% of people have acne problems at some point in their life. While acne begins during puberty, it is now more common in adults. The chest, shoulders and upper arms are common sites for infection. Overactive sebaceous glands, bacteria and dead skin cells lead to acne (Shannon, 2020). This is shown in table (5).

Cholesterol showed high significant difference and good positive correlation with (LDL), and low positive correlation with (HDL).

Vitamin A showed high significant difference and low positive correlation with cholesterol, and good positive correlation with (HDL).

Vitamin B12, showed high significant difference and low positive correlation with cholesterol, and moderate positive correlation with (HDL & vitamin A).

Zinc showed high significant difference and low positive correlation with (HDL, vitamin A & vitamin B12).

Linoleic acid, showed high significant difference and low positive correlation with (HDL), and moderate positive correlation with vitamin A.

4. Conclusions

Through the different statistical treatments of the biochemical markers associated with acne and the

lipid unit. It was found that, some biochemical markers such as, (vitamin A, vitamin B12, zinc and linoleic acid) have a severe impact on acne and its exacerbation. Therefore, we concluded that they should be included in subsequent studies.

- Through the different statistical treatments of the biochemical markers associated with acne and the lipid unit. It was found that, some biochemical markers such as, (vitamin A, vitamin B12, zinc and linoleic acid) have a severe impact on acne and its exacerbation. Therefore, we concluded that they should be included in subsequent studies.
- To obtain, conclusions showing the reflection of body physiology, skin type for both genders on the appearance, severity and persistence of acne. Statistical study was performed for patients with acne on the face (comparing males with females). It was found that, (HDL, vitamin A, vitamin B12, zinc & linoleic acid) showed high significant statistical behavior. This evidence indicates that acne is linked to important factors other than stress and genetics, namely the lipid profile, vitamins and mineral. This opens new horizons for linking acne to diet.
- By using the receiver operating characteristic (ROC) curve to assess the ability and accuracy of biomarkers in expressing disease severity (in face acne patients), it was found that:
  - (Vitamin A, zinc & linoleic acid), showed good test characteristic for females. In the same way (HDL, vitamin A, vitamin B12, zinc & linoleic acid) shows good test characteristic for males.
- From Spearman's statistical correlations, it was observed that there were positive and negative significant correlations between these indicators, confirming their link to the mechanics of getting acne.

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Table (1): Statistical analysis of biomarkers for patients with (face & shoulder) acne compared to the control group as a total number, using Post hoc analysis of ANOVA

Biomarker	Control (76)n(mean±SD)	Face Acne (85)n(mean ±SD)	Shoulder Acne (79)n(mean ±SD)	*P*- value*		
				Face AcnenVsnControl	Shoulder Acne Vs Control	Face Acne Vs Shoulder Acne
BMI	23.95 ± 3.17	24.77 ± 2.83	23.51 ± 3.15	0.239	0.753	0.025 ↓
cholesterol	160.12 ± 23.97	177.50 ± 117.10	154.49 ± 32.47	0.293	0.882	0.113
LDL	99.42 ± 16.79	122.50 ± 44.39	109.20 ± 29.91	0.0001 ↑	0.184	0.030 ↓
HDL	69.27 ± 7.72	52.31 ± 13.98	58.04 ± 13.82	0.0001 ↓	0.0001 ↓	0.009 ↑
Vit. A	19.86 ± 3.95	7.33 ± 4.64	9.56 ± 3.67	0.0001 ↓	0.0001 ↓	0.002 ↑
Vit. B12	419.32 ± 141.35	325.65 ± 130.80	320.34 ± 120.64	0.0001 ↓	0.0001 ↓	0.991
Zinc	106.86 ± 27.42	63.14 ± 17.57	79.19 ± 31.43	0.0001 ↓	0.0001 ↓	0.0001 ↑
Linol. Acid	5.51 ± 5.43	3.12 ± 2.29	6.43 ± 1.90	0.0001 ↓	0.279	0.0001↑
The probability ($P < 0.05$) was considered statistically significant.						

Table (2): Statistical analysis of biomarkers according to acne patient groups in (males & females), using Mann Whitney's test.

Diseased Group						
Face Acne			Biomarker	Shoulder Acne		
P value*	Gender			Gender		P value*
	Female (43) (mean±SD)	Male (42) (mean±SD)		Male (40) (mean±SD)	Female (39)(mean±SD)	
0.008	25.57 ± 2.85	23.96 ± 2.60	BMI	22.90 ± 2.53	24.14 ± 3.60	0.079
0.876	179.47 ± 156.91	175.48 ± 53.54	cholesterol	144.86 ± 31.47	164.36 ± 30.82	0.007
0.003	108.83 ± 35.87	136.49 ± 48.18	LDL	106.81 ± 27.39	111.65 ± 32.47	0.475
0.0001	59.03 ± 14.20	45.42 ± 9.90	HDL	52.19 ± 15.29	64.04 ± 8.89	0.0001
0.369	7.78 ± 3.81	6.87 ± 5.36	Vit. A	7.47 ± 2.78	11.72 ± 3.21	0.0001
0.007	362.91 ± 157.54	287.50 ± 81.74	Vit. B12	281.38 ± 61.46	360.30 ± 150.86	0.003
0.006	58.07 ± 15.60	68.33 ± 18.13	Zinc	96.10 ± 33.31	61.85 ± 16.71	0.0001
0.0001	1.14 ± 0.48	5.15 ± 1.48	Linol. Acid	6.95 ± 1.90	5.90 ± 1.77	0.013

The area under the curve in the range of 60% will be considered as the influencer, as will the rest of the data (Sensitivity %, Specificity %, PPV & NPV). Cells related to the biomarkers that have non-significant statistical relationship, but at the same time possess (60% or more) of the test-validity characteristics, will be indicated in grey

The study considered the value of the correlation coefficient within the limits:

1. (0.61) and more as a highly important

indicator for the relationship between the binary variable.
2. (0.50.-0.60) good indicator for the relationship between binary variables.
3. (0.36-0.50) moderately indicator for the relationship between binary variables.
4. (0.20 -0.35) low indicator for the relationship between binary variables

Table (6): Receiver-operating characteristic (ROC) curve analysis of biomarkers for all shoulder acne patients according to the gender, the age is in the range (17-33).

Gender (In Shoulder acne)												
Male (40)							Female (39)					
NPV	PPV	Specificity %	Sensitivity %	P- value (AUC =0.05)	Area under the curve	Biomarker	Area under the curve	P- value (AUC =0.05)	Sensitivity %	Specificity %	PPV	NPV
55	95	99	18	0.406	0.445	BMI	0.461	0.555	35	55	44	46
50	54	94	7	0.0001	0.247	cholesterol	0.583	0.210	1	99	50	50
50	50	98	2	0.07	0.494	LDL	0.617	0.075	7	99	88	52
88	100	100	87	0.0001	0.930	HDL	0.600	0.130	30	98	94	58
97	98	98	97	0.0001	0.998	Vit. A	0.971	0.0001	97	94	94	97
97	96	96	97	0.0001	0.955	Vit. B12	0.545	0.494	2	99	50	50
77	99	99	70	0.0001	0.781	Zinc	0.893	0.0001	30	97	91	58
67	64	60	75	0.0001	0.743	Linol. Acid	0.798	0.0001	28	99	97	58

Table (4): Nonparametric Spearman's statistical correlation coefficient for biomarkers in all face acne patients.

Bio-markers	Variable	cholesterol	LDL	HDL	Vitamin A	Vitamin B12	Zinc	Linoleic acid
BMI	r Value	- 0.086	- 0.037	- 0.146	- 0.061	- 0.127	- 0.166	- 0.215
	P Value	0.277	0.643	0.065	0.442	0.107	0.035	0.006
cholesterol	r Value		0.632	0.080	0.071	0.032	0.110	0.223
	P Value		0.0001	0.314	0.369	0.686	0.167	0.004
LDL	r Value			- 0.226	- 0.171	- 0.194	0.002	0.105
	P Value			0.004	0.030	0.014	0.980	0.183
HDL	r Value				0.540	0.476	0.450	0.114
	P Value				0.0001	0.0001	0.0001	0.150
Vitamin A	r Value					0.342	0.685	0.339
	P Value					0.0001	0.0001	0.0001
Vitamin B12	r Value						0.301	0.216
	P Value						0.0001	0.006
Zinc	r Value							0.505
	P Value							0.0001

Table (5): Nonparametric Spearman's statistical correlation coefficient for biomarkers in all shoulder acne patients.

Bio-markers	Variable	cholesterol	LDL	HDL	Vitamin A	VitaminB12	Zinc	Linoleic acid
BMI	r Value	0.041	-0.084	0.055	0.151	-0.108	-0.061	-0.204
	P Value	0.612	0.300	0.500	0.061	0.180	0.447	0.011
cholesterol	r Value		0.558*	0.326	0.236	0.305	0.004	-0.013
	P Value		0.0001	0.0001	0.003	0.0001	0.958	0.874
LDL	r Value			0.041	-0.055	0.101	0.030	0.035
	P Value			0.611	0.499	0.211	0.708	0.664
HDL	r Value				0.516*	0.361	0.203	0.213
	P Value				0.0001	0.0001	0.011	0.008
Vitamin A	r Value					0.386	0.278	0.435
	P Value					0.0001	0.0001	0.0001
Vitamin B12	r Value						0.206	-0.035
	P Value						0.010	0.665
Zinc	r Value							0.063
	***P* Value**							**0.434**

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