Original Article

Total Iron-Binding Capacity and Lactate Dehydrogenase Association with Acne Vulgaris in Adolescents and Young Adults: A Cross-Sectional Study

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ABSTRACT

Objective

The variation of iron status with the occurrence of acne vulgaris is not clarified and requires further investigation. Additionally, biochemical indicators such as magnesium, lactate, and lactate dehydrogenase activity (LDH) need to be adequately studied in acne patients. The aim of this study was to detect the association of acne vulgaris with iron parameters, gender, magnesium (Mg), lactate, and lactate dehydrogenase (LDH) in adolescents and young adults compared to a control group.

Material and methods

The study was conducted at the laboratory of Vin Private Hospital in Duhok, Iraq from March to November 2023. The study measured the levels of iron, unsaturated iron binding capacity (UIBC), Mg, lactate, and LDH in the serum samples of 200 individuals. The total iron-binding capacity (TIBC) and transferrin saturation (TS) were calculated mathematically. The study population consisted of 100 individuals diagnosed with acne vulgaris in the dermatology unit at Azadi Teaching Hospital, who were further subdivided into 28 mild, 44 moderate, and 28 severe cases, as well as 100 age- and sex-matched healthy controls selected from secondary schools and university students. Statistical analyses were performed using SPSS version 25 for Windows. A p-value less than 0.05 was considered statistically significant.

Results and discussion

Iron, TIBC, UIBC, Mg, and LDH levels were significantly increased in the patient group. Logistic regression analyses showed that TIBC and LDH associated with acne vulgaris, with odds ratios of 1.019 and 1.023, respectively. The areas under the ROC curves for TIBC and LDH were 0.808 (95% CI 0.745-0.871) and 0.829 (95% CI 0.771-0.888), respectively, which was statistically significant. The cutoff values for TIBC and LDH were 309.3 and 197.2, respectively. Multiple comparisons showed no significant differences in iron parameters, Mg, lactate, and LDH activity among the patient subgroups.

Conclusion

The abnormalities in iron status observed in patients with acne vulgaris, such as elevated total iron levels coupled with increased TIBC, along with elevated LDH, could serve as potential markers indicating the onset of acne vulgaris and concurrent hemolysis.

Keywords

Anemia; Iron Status; Lactate; Magnesium; Siderophores.

INTRODUCTION

The pathogenesis of acne vulgaris emerges as multifactorial and might involves androgen levels, dietary routines, oxidative and emotional stress, psychiatric morbidity, sebum production, and *Propionibacterium acnes (P. acnes)* [1,2]. P. acnes colonize the sebaceous glands, leading to inflammation and the development of inflamed lesions that attract immune cells[3-5]. As a result, follicular damage enhances the growth of other skin microflora species, such as *Klebsiella pneumoniae*, *Enterobacter spp*., *Staphylococcus epidermidis*, and *Streptococcus spp.* [6]. Acne vulgaris affects not only the skin; it has a negative social impact. A patient with acne vulgaris has less self-confidence and behaves poorly in social life [7]. A concomitant change in the levels of some biochemical factors with the onset of acne should be considered, specifically the alteration in iron levels due to its utilization by cells and microorganisms.

Iron as a trace element, is an essential nutrient for humans. It is crucial for several

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metalloproteinases as a cofactor for proceeding enzymatic reactions in the cell. About two-thirds of circulating iron is present in red blood cells. Leucocytes utilize some of the iron, while the remaining are transported by transferrin [8]. Transferrin is the main protein capable of transporting iron throughout the body by employing specific binding sites. The total iron-binding capacity (TIBC), also defined as transferrin iron-binding capacity, expresses the maximum possible amount of iron that can bind to transferrin if it exists. Similarly, the unsaturated iron-binding capacity (UIBC) assesses the transferrin unsaturated binding capacity to bind to iron or the amount of iron remaining for full saturation. Transferrin saturation (TS) measures how many binding sites in transferrin are occupied by iron [9].

Inadequate dietary intake, malabsorption, or blood loss cause insufficient iron levels. The main consequence of iron deficiency is anemia. In some conditions, abnormally high iron levels result in iron overload, oxidative stress, which have direct etiologic relationships with a wide variety of tissue damage of skin problems such as psoriasis and dermatitis [10]. Even though iron deficiency and acne have been linked in earlier research, further research is needed to fully understand the connection between acne vulgaris and iron status. Previous study revealed that iron enhances bacterial growth in inflamed acne lesions, and cutaneous inflammation causes low iron concentrations, and moderate anemia rather than an iron-deficiency state. While other research did not find clear evidences to link nutritional anemia with acne. [11-13]. Additionally, elevated C-reactive protein levels are associated with the severity of acne vulgaris, but the impact of inflammation on the utilization of circulatory or cellular iron remains unclear [14].

However, the association between acne vulgaris and abnormality in iron status has yet to be elucidated and still needs work. Besides, some biochemical indicators should be adequately studied or reviewed in acne patients. Lactate dehydrogenase (LDH) is a biomarker for cell death or damage. It exists in the cytosol of all cells, enhancing glycolytic activity. LDH levels are high during cell apoptosis or other types of skin cell injury, such as necrosis and cancer [15,16]. Magnesium (Mg) is an activator of many enzymes and is associated with the progression of anemia in previous studies [17,18]. However, the associations between Mg and LDH levels and the development of acne vulgaris are still indistinct. More work is required to clarify the most effective biochemical factors in acne vulgaris that might help understand the underlying mechanism and identify potential targets for more effective treatments. The findings of the current study could have considerable clinical implications.

This study aimed to detect associations between the initiation or prevalence of acne vulgaris and selected parameters, such as iron parameters, Mg, lactate, and LDH activity levels, through measurement of these parameters in the sera of adolescents and young adults with acne vulgaris compared to controls.

MATERIALS AND METHODS

The current cross-sectional study was conducted in the laboratories of Vin Private Hospital and Azadi Teaching Hospital from March to November 2023. The study included two groups of adolescents and young adults of both genders: patients with acne vulgaris (mean age = 19.06±2.9), 45 males and 55 females, and healthy controls (mean age = 18.6±2.9), 50 males and 50 females. The patient group consisted of 100 visitors to the dermatology unit/Azadi teaching hospital who were diagnosed with acne vulgaris and were sub-grouped into 28 mild, 44 moderate, and 28 severe cases, based on the severity of acne vulgaris using the global acne grading system (GAGS) (Doshi, Zaheer, and Stiller, 1977). G*Power 3.1 was used to estimate the priori power analysis of the study (1-β error p), which was =0.94 (effect size d = 0.5, err prob = 0.05, two-tailed, t-test).

The healthy control group comprised 100 age- and sex-matched healthy individuals from secondary schools and university students. The control group reported that they did not have an acne history or current acne signs. In addition, they allowed for a quick scan of their faces, backs, chests, and shoulders. All participants replied to a questionnaire that included name, gender, age, weight, height, inherited disease, treatment, socioeconomic status, marital status, occupation, education level, and family history. The participants signed an informed consent before the study's initiation, and the procedures conformed to the Declaration of Helsinki. The work was approved by the Ethics Committee of the Directorate of Health of Duhok City Government (reference number: 15092021-9-3).

Inclusion and Exclusion Criteria

The inclusion criteria were patients diagnosed with

acne vulgaris and healthy individuals from adolescents and young adults of both genders who were willing to participate and provide informed consent.

Exclusion criteria for the study were participants with chronic illness or current medications (including acne medications), a history of skin disease other than acne vulgaris in the past six months, psychiatric illness, pregnancy, breastfeeding, or facial cosmetic surgery. In addition, participants were excluded if they had taken antibiotics or hormonal treatments for acne in the past three months, medications that could affect acne grading, or over-the-counter acne products in the past two weeks. Finally, participant was excluded if he had taken systemic or topical corticosteroids in the past month. Exclusion criteria were applied to both patients and controls to ensure that the study results were not affected by confounding factors.

Collection and Processing of Blood Samples

Venous blood samples were drawn from the participants into gel tubes. Furthermore, the sera were separated after venipuncture by centrifugation at 3500 rpm for 10 min. Then they were stored at -70^{oC} until ready for biochemical assay parameters.

Measurements

The levels of iron, UIBC, Mg, lactate, and lactate dehydrogenase (LDH) were estimated using commercially available kits (Roche Diagnostics, Mannheim, Germany). The analyses were carried out according to the manufacturer's instructions using COBAS 6000 Hitachi Automatic Analyzer. Other biochemical parameters, TIBC and TS were calculated mathematically. TIBC is the sum of UIBC and iron level. TS is calculated by dividing the circulatory iron level by the TIBC.

Statistical Analysis

The normally distributed data were stated as means (±standard deviation, S.D.), while the abnormally distributed data were expressed as median (interquartile range, IQR). Independent-sample T-tests and Mann-Witney tests were performed to compare the two groups. Multiple logistic regression was performed to evaluate the association between influenced parameters and acne vulgaris. The receiver operating characteristic (ROC) curve was executed to analyze the predictive effect of TIBC and LDH on acne vulgaris. One-way ANOVA, Kruskal-Wallis, Welch tests, and post hoc multiple comparisons were performed to detect the significant differences between groups. The general linear model univariate analysis was performed to find the simple effect of gender on all disease levels. The SPSS software (version 25.0 for Windows) was used, and the p-value < 0.05 was statistically significant.

Ethical Clearance: The project was approved by the local ethical committee of the Directorate of Health of Duhok city Governate (reference number: 15092021-9-3).

RESULTS

The demographic and Anthropometric Measurements of Patients and Controls Groups

As seen in Table-1, T-test showed no significant difference in Age between patients and controls, and there was a significant increase in the body mass index (BMI) in patients group compared to control. The Chi-squire test showed significant differences in Socio-Economic states and education illiterate between patients and controls, the better economic status and more educated participants (university students) were in controls group. In addition, 58% of patients had a family history of acne vulgaris compared to 9% of controls. And there was no significant difference in marital status.

Table 1. Demographic and Anthropometric Characteristics of the Study Population

Parameters	Patient (n=100)	Controls (n=100)	p-value
Age (year) (mean±SD)	19.06±2.9	18.6±2.9	0.235 ^{T}
Gender male(female)	45(55)	50(50)	0.479 ^{S}
BMI (kg/m^2) (mean±SD) Male Female	21.98±2.9 21.5±2.7 22.4±3.1	20.7±3.3 20.3±3.3 21.1±3.3	0.005 ^{T*} 0.053 ^{T} 0.032 ^{T*}
Socio-Economic Status Moderate Good	 87 13	 71 29	0.006 ^{S*}
Marital status Single Married	 95 5	 89 11	0.118 ^{S}
Education illiterate primary intermediate University	 7 79 14	 7 48 45	<0.0001^{S*}
Family history Positive Negative	 58 42	 9 91	<0.001 ^{S*}

BMI-body mass index,^{T}- T-test, ^{S}- chi-square test;*-p-value <0.05 considered significant.

The Biochemical Measurements of Participated Patients with Age Matched Controls Groups

The independent t-test and Mann-Whitney test showed significant increases in UIBC, TIBC, iron, Mg, and LDH in the sera of patients compared with the sera of control, and no significant differences in the levels of other parameters, as shown in Table 2.

Table 2. The Biochemical Measurements of Patients Group and controls

Parameters (mean±SD)	Patients (n=100)	Controls (n=100)	p-value
Iron (µg/dL)	86.4.5±26.2	77.3±26.7	0.016*
male	91.5±28.04	84.8±24.4	0.22
female	82.2±23.9	69.8±27.1	0.014*
UIBC (µg/dL)	251.6±69	192±52.6	< 0.001*
male	234.5±72.6	175.7±32.8	< 0.001*
female	265.7±63.15	208.2±62.9	< 0.001*
TIBC (µg/dL)	338.04±60.8	269.3±50.2	< 0.001*
male	325.9±65.03	260.6±37.8	< 0.001*
female	347.9±55.7	278±59.3	< 0.001*
Transferrin saturation%	26.7±10.05	29.2±9.1	0.069
male	29.36±11.01	32.4±7.8	0.11
female	24.5±8.6	25.8±9.1	0.44
Mg (mmol/L)	0.82±0.05	0.77±0.07	< 0.001*
male	0.82±0.05	0.77±0.7	< 0.001*
female	0.81±0.04	0.77±0.07	< 0.001*
LDH (U/L)	251.8±50.3	184±52.4	< 0.001*
male	254.8±45.9	185.3±55.4	< 0.001*
female	249.4±53.9	183.8±49.8	< 0.001*
Lactate (mmol/L)	2.6±0.339	2.56±0.5	0.628
male	2.6±0.43	2.6±0.5	0.87
female	2.5±0.37	2.5±0.5	0.37

TIBC- total iron-binding capacity, UIBC- unsaturated iron-binding capacity, LDH- Lactate dehydrogenase,*-p-value <0.05 considered significant.

Association Between Clinical Parameters and Acne in Participants.

Multiple logistic regression (ENTER) was performed to find influenced biochemical parameters that might be associated with the development of acne in participants. Patient and control were used as categorical-dependents variables. In contrast, TIBC, LDH, gender, and BMI were independent variables. UIBC, Mg, lactate, iron, and TS were excluded because they violated logistic regression assumptions. The Nagelkerke R Square was 57.6, and the percentage of prediction was 82.5%. The results showed that for every one unit increase of LDH, the odds of acne vulgaris increase by 2.3% (p-values <0.001). And for every one-unit increase in TIBC, the odds of acne vulgaris increase by 1.9% (p-value <0.001). There are no significant differences in odds ratios of Age, BMI, and gender; the p-values were more than 0.05, as seen in Table 3.

The predictive values of TIBC and LDH for acne disease in all participant.

ROC curve was performed to find the predictive values of TIBC and LDH for acne disease in all participants. When TIBC and HDL were used as predictors, the areas under the curve (AUC) were 0.808(95% CI 0.745-0.871),0.829(95% CI 0.771 -0.888), respectively, as shown in Fig. 1. Meanwhile, the sensitivity and specificity for TIBC (sensitivity 75%, specificity 82%) and for LDH (sensitivity 90%, specificity 67%) were evaluated. The AUC of TIBC and LDH were significantly more than the area of 0.5 (p-values <0.0001). The cutoff values for the TIBC and for the LDH were 309.3 and 197.2 respectively.

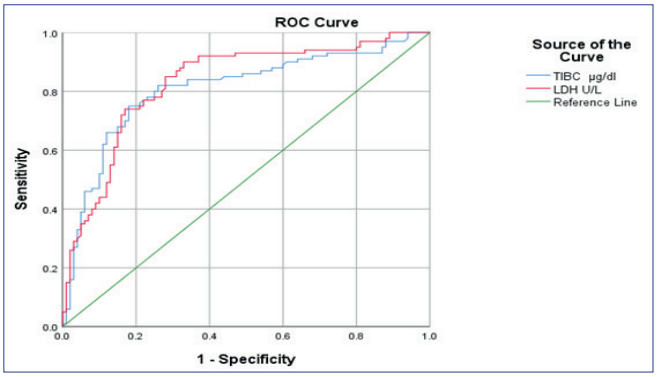

Figure 1. Receiver Operating Characteristic (ROC) Curve and Corresponding Areas Under the Curve (AUC) of TIBC and LDH for Predicting Acne Vulgaris.

Multiple Comparisons Between Types of Acne and Control Groups

One-way ANOVA, Kruskal-Wallis, welch tests, and multiple comparisons were performed to detect the significant differences between groups, including mild, moderate, severe, and control. The result showed significant differences in the TIBC, UIBC, Mg, and LDH levels between the control group and all acne Vulgaris groups (p-values<0.01). A significant difference was in iron levels between control and severe groups (p-value<0.05); this difference appears in

Table 3. Association Between the Selected Parameters and Acne in Participants

Variables	B	S.E	Wald test	p-value	OR	95% C.I.	
						Lower	Upper
TIBC	0.019	0.004	27.88	$1.2*10^{-8*}$	1.019	1.012	1.026
LDH	0.022	0.004	31.86	$1.6*10^{-8*}$	1.023	1.015	1.031
Gender	-0.002	.408	0.00001	0.996	0.998	0.448	2.222
BMI	-0.129	.066	3.8	0.51	0.879	0.773	1.000
Age	0.073	.074	0.952	0.329	1.075	.929	1.244

Patients and controls groups served as a categorical variable, the controls group was used as a reference, BMI- body mass index, TIBC- total iron-binding capacity, LDH- Lactate dehydrogenase, B- beta, S.E- standard error,*-p-value<0.05 considered significant.

Table 4. The Multiple Comparisons Between Types of Acne Vulgaris Groups and Control Group.

Variables	Mild [a]	Moderate [b]	Sever [c]	Control	p-value
Total number of cases (male/female)	28(7/21)	44(18/26)	28(20/8)	100(50/50)	
BMI(Kg/m^2)	21.0±3.3	20.9±3.5	20.1±3.0	21.9±2.9	0.026
Iron (µg/dL) male female	79.2±25.7 89.3±30.7 75.8±23.8	85.03±24.8 89.1±26.6 82.2±23.5	86.2(43.45) 84.5(50.5) 99.03±19.7	77.3±26.7 c 84.8±24.4 69.8 ± 27.1 c	0.035 0.766 0.013
UIBC (µg/dL) male female	264.5±73.8 274 ±67.0 261.3±77.3	264(57.8) 241.2 ±74.7 265.5(58)	237.3±72.2 214 ±69.1 293.9±44.7	192(47) abc 172.5(28.5) ab 188.5(17.5) abc	$1*10^{-9}$ $5*10^{-5}$ $2*10^{-5}$
TIBC (µg/dL) male female	343.7±59.7 363.3±37.8 337.1±58.9	337.6±58.8 330.3 ± 68.8 342.7±51.6	332.7±66.4 309 ±59.1 373.2(81.1)	269.3±50.2 abc 260.6 ±37.8 abc 278.0±59.8 abc	$9*10^{-14}$ $4.4*10^{-5}$ $1*10^{-9}$
TS% male female	24.4±10.1 25.3 ±9.7 24.08±10.4	25.9±8.5 28.0±8.7 24.56±8.17	26(13.51) 27.09(19) 25.38±5.2	29.1(11.2) 30.3(8.7) 25.8±9.06	0.025 0.12 0.872
Mg (mmol/L) male female	0.83±0.04 0.87(0.05) 0.82±0.03	0.81±0.05 0.8 ±0.05 0.82±0.057	0.83(0.05) 0.84(0.05) 0.81±0.03	0.76(0.08) abc 0.76 (0.08) ac 0.77±0.078 ab	$2.5*10^{-8}$ $2*10^{-5}$ 0.008
LDH (U/L) male female	237.3±56.5 234.7 ±34 238.2±63.0	264.5(47.3) 250 ±53.1 260.5±47.9	259.33±42.8 265.9 ±42.1 242.7±45.1	176(54) abc 176(52.2) bc 177.3(53.8) ab	$1.5*10^{-14}$ $1.3*10^{-7}$ $2.9*10^{-7}$

BMI- body mass index, UIBC- unsaturated iron-binding capacity, TIBC- total iron-binding capacity, LDH- lactate dehydrogenase, Mg- magnesium, TS- transferrin saturation, c- significant difference between control and severe, b- significant difference between control and moderate, a- significant difference between control and mild. p-value <0.05 considered significant.

females, not males. In females, a significant decrease in TIBC and UIBC was in control compared to acne groups (p-value<0.05). Also, LDH levels decreased significantly in the control group compared to the mild and moderate groups. In males, there is a significant decrease in UIBC levels in the control group compared to the mild and moderate groups. Similarly, the level of TIBC decreased significantly in the control group compared to the mild, moderate, and severe groups. Mg levels were significantly reduced in the control group compared to the mild and moderate groups. In contrast, LDH levels decreased in the control group compared to moderate and severe groups, as shown in Table 4.

The Simple Effect of Gender on the Levels of the TIBC and LDH within Types of Acne Vulgaris.

The general linear model univariate analysis was performed to detect the simple effect of gender within types of acne Vulgaris. The results showed no significant differences in LDH levels between males and females in all groups (p-value<0.05). In addition, there are no significant differences in TIBC levels between males and females in mild, moderate, and control groups. In contrast, there is a significant difference between males and females in severe groups, as shown in Table 5 and Fig. 2.

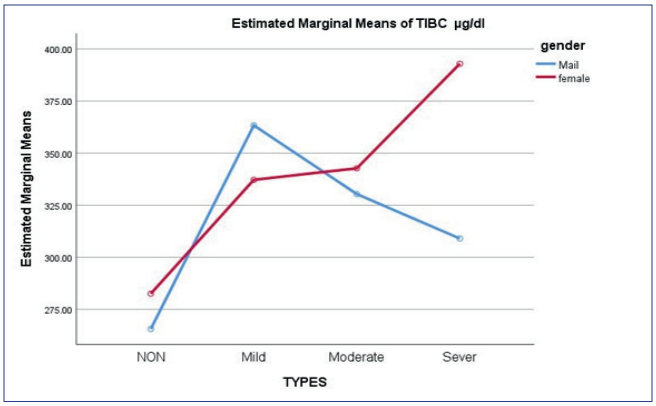

Figure 2. Gender's Effect on the Levels of TIBC within Types of Acne Vulgaris

Correlations of Magnesium with Iron Status and the Selected Parameters in Patient and Control.

Spearman correlation was conducted to find the correlation of Mg with the selected parameter. The results showed a significant correlation with the iron in patient group (correlation coefficient =0.197, p-value=0.05) and a significant correlation with lactate in the control group (correlation coefficient=0.437, p-value=$5*10^{-5}$). No correlations were found with other parameters in both groups.

DISCUSSION

In the current study, the control group matched the patients' group by age and had similar male-to-female percentages. The logistic regression analysis clearly showed that age, BMI, and gender have no association with acne vulgaris; the odds ratios were 1.075, 0.879, and 0.998, respectively. Besides, the participants are adolescents and young adults, and the expectation is low iron levels in both genders, particularly in females, due to the menstrual cycle.

The comparisons between acne vulgaris's patients and controls showed significant increases in iron, TIBC, UIBC, Mg, and LDH levels and a nonsignificant decrease in TS by about 8.56% in the patients compared to controls. Iron is vital for human immunity and bacterial growth. It is necessary to enhance lymphocytes' activity and proliferation. In acne vulgaris patients, P. Acnes' antigen indirectly causes an increase in iron uptake by lymphocytes and other leucocyte cells by stimulating the immune response [8]. Furthermore, iron as a cofactor activates enzymatic reactions, such as those controlled by catalase, superoxide dismutase, and DNA synthesis in both human cells and bacteria. This makes iron an essential element for the growth and metabolism of bacteria [19]. In addition to *P. Acnes*, other isolated bacteria from acne lesions, such as *Klebsiella pneumoniae, Enterobacter spp., Staphylococcus epidermidis*, and *Streptococcus spp*., might cause an alteration in TIBC, UIBC, and transferrin saturation. All these species share releasing siderophores, a virulence factor that acquires iron from the protein of the host environment by active transport to allow the proliferation of the infecting organism[20].

Siderophores have a higher affinity for ferric ions than transferrin; they gain iron by employing their chelating structure in the protein-iron complex, especially transferrin, which reduces its saturation [21]. The point is that the circulating iron levels significantly increase in patients than in the control group. At the same time, the significant increases in the TIBC, UIBC, and a decrease in TS percentage refer to the iron deficiency that bacterial siderophores might cause.

Plasma LDH activity levels have been known as an indicator of cell damage that is caused by several diseases, including cutaneous inflammations such as

Table 5. The Simple Effect of Gender on the Levels of the TIBC within Types of Acne Vulgaris.

Univariate Tests							
Dependent Variable	TYPES		Sum of Squares	df	Mean Square	F	p-value
TIBC (µg/dL)	control	Contrast	7624.258	1	7624.258	2.609	0.108
		Error	560972.997	192	2921.734		
	mild	Contrast	3595.038	1	3595.038	1.23	0.269
		Error	560972.997	192	2921.734		
	moderate	Contrast	1626.79	1	1626.79	0.557	0.456
		Error	560972.997	192	2921.734		
	severe	Contrast	40230.769	1	40230.77	13.769	<0.0001*
		Error	560972.997	192	2921.734		

TIBC- total iron-binding capacity, *- p-value< 0.05 is considered statistically significant.

necrosis and atopic dermatitis. LDH is released from the cytosol of damaged cells into the bloodstream, raising its levels [15,16]. A recent study suggested the convenience of LDH levels to evaluate the damage in respiratory cells or monitor treatment response in patients with COVID-19 [21,22]. However, the current study showed significantly elevated levels of LDH in patients with acne vulgaris compared with the control. The high levels of LDH serve as a connecting point between oxidative stress and acne vulgaris. Studies showed high malonaldehyde levels and low total antioxidant status in patients with acne vulgaris compared with controls [24-26]. The reactive oxygen species attack cell membranes through oxidative stress and initiate lipid peroxidation [27,28]. On the other hand, Capoor M.N. et al. Showed the hemolytic activity of *P. Acnes* in tissue samples of patients with intervertebral disc degeneration [29]. Whether hemolysis is induced by oxidative stress and/or *p. Acnes*, the worn-out cell components release into the blood, including protein, hemes, and minerals. In the same context, Mg is one of the most abundant intracellular minerals. The levels of plasma Mg were higher in patients with polycystic ovarian syndrome suffering from acne than in polycystic ovarian syndrome patients without acne [30]. Also, plasma levels of Mg were increased in patients with hemolysis [31]. Similarly, the current study showed a significant elevation in Mg levels in patients with acne vulgaris with a positive correlation to iron in the patients' group. This correlation indicates hemolysis.

The logistic regression model showed that the TIBC and LDH, among other parameters, are significantly associated with acne vulgaris; the odds ratios were 1.019 and 1.023, respectively. In addition, the ROC curve showed that TIBC and LDH are potential predictors of acne vulgaris with 75% and 90% sensitivity and 82% and 67% specificity, respectively. These results revealed that the inflammation-inducing acne vulgaris significantly increases TIBC by increasing the number of unsaturated sites in transferrin. Moreover, the high level of LDH in the patients' group suggests LDH is a potential indicator of cell damage.

To the best of the authors' knowledge, this is the first work that showed the probability of predicting acne vulgaris development by the TIBC and LDH. It also revealed an increase in iron demand in patients with acne vulgaris compared to the control, which might be caused by bacterial iron acquisition and oxidative stress. The current study observations might explain the association between iron deficiency anemia and acne vulgaris in previous studies [10-12].

Furthermore, the results showed no significant differences in TIBC and LDH among mild, moderate, and severe groups. Instead, the levels of TIBC and LDH rose significantly in all types of acne groups compared to the control group, suggesting that the demand for iron and the damage to cells start in the early stages of the disease as earlier signs.

In addition, gender differences only appeared in the

levels of the TIBC in the severe group. This difference may be due to the menstrual cycle, which adds another burden to decreasing iron levels caused by bacterial siderophores. Thus, the unsaturated sites in transferrin increase in females compared to males.

Generally, the study examined the link between acne vulgaris and iron, TIBC, UIBC, Mg, and LDH levels in adolescents and young adults. Patients with acne vulgaris exhibited significantly elevated levels of iron, TIBC, UIBC, Mg, and LDH compared to the control group. Elevated LDH levels, which signal cell damage, and abnormal iron status may indicate the influence of other factors not included in the scope of the current study, such as oxidative stress and bacterial iron acquisition. The current findings may inspire future work to understand the mechanism and etiology. TIBC and LDH are potential predictors of the development of acne vulgaris.

CONCLUSION

This study demonstrated that high TIBC and LDH levels predict the occurrence of acne vulgaris. In addition, the rise in LDH as a sign of cell damage and high iron levels correlated with high Mg levels might indicate slight hemolysis in acne vulgaris patients. Abnormal iron status represented by low levels of transferrin saturation with high iron levels in acne patients may indicate the influence of other factors, such as iron binding to bacterial siderophores, leucocyte iron uptake, and oxidative stress, which might stimulate future research. Early detection of abnormalities in iron status and LDH levels in acne patients reflects the therapeutic benefits of these findings.

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Authors' Declaration

-Conflicts of Interest: None.

-We hereby confirm that all the Figures and Tables in the manuscript are ours.

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Authors' Contribution Statement

Hamza M.A., Mosa A.A. and Khalaf M.Y. contributed to the design and implementation of the research. Hamza M.A. Statistically analysed the results, drafted tables and figurs. Hamza M.A., Mosa A.A. and Khalaf M.Y contributed to the writing of the manuscript and aproved the final version.

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