Assessment of monocyte to high density lipoprotein ratio and ischemia-modified albumin in acne vulgaris patients

Nermin Mamdouh Salem

Resident of Dermatology, Ministry of Health, Egypt, nerminmmdh@gmail.com

Soheir Abdelgaber Eltoukhy

Professor of Dermatology, Andrology and STDs, Mansoura Medical College.

Mohammed Mohammed El Sayed El Arman

Professor of clinical pathology, Mansoura Medical College

Sherief Refaat Ismail

Lecturer of Dermatology, Andrology & STDs Mansoura faculty of Medicine. Mansoura Medical College

Follow this and additional works at: https://mmj.mans.edu.eg/home

Part of the Medicine and Health Sciences Commons

Recommended Citation

ORIGINAL STUDY

Assessment of Monocyte to High-density Lipoprotein Ratio and Ischemia-modified Albumin in Acne Vulgaris Patients

Nermin M. Salem [a,*], Soheir A. Eltoukhy [b], Mohammed M. El Arman [c], Sherief R. Ismail [b]

[a] Dermatology, Ministry of Health, Dakahlia, Egypt
[b] Dermatology, Andrology and STDs, Mansoura Medical College, Dakahlia, Egypt
[c] Clinical Pathology, Mansoura Medical College, Dakahlia, Egypt

Abstract

Background: Acne vulgaris (AV) is a common, chronic, inflammatory lesion of the pilosebaceous unit. Oxidative stress plays an essential role about the pathogenesis of many dermatological conditions.

Aim: The aim of the present study is to assess Complete blood count (CBC) parameters and monocyte to high-density lipoprotein ratio (MHR) as indicators of inflammation, assess Ischaemia-modified albumin (IMA) as an indicator of oxidative stress in acne vulgaris patients, and to examine their relation to acne vulgaris severity.

Methods: This was a case−control study that included 48 acne vulgaris patients and 40 healthy individuals with age and sex-matched controls. Global acne grading scale (GAGS) was calculated. Complete blood count and the differential leukocytic count were done using a hematology auto analyzer five-part differential. High density lipoprotein (HDL) was estimated, MHR was calculated and serum IMA was measured.

Results: Serum IMA was significantly higher in acne vulgaris patients in comparison with control group. While MHR level did not differ significantly between case and controls. IMA revealed positive correlation with Global acne grading scale.

Conclusions: This result suggests that IMA accompanied by oxidative stress could have an essential role in AV pathogenesis and it is associated with disease severity.

Keywords: Acne vulgaris, Ischemia-modified albumin, Monocyte to high-density lipoprotein ratio

1. Introduction

Acne vulgaris (AV) is a self-limiting chronic inflammatory disorder of the pilosebaceous unit. It has been considered as a frequent cutaneous lesions that mainly affects the face but could also affect the arms, trunk, and back (Yan et al., 2018). AV happens due to hypersensitive reaction of the sebaceous glands to a normal level of androgens, worsened by *Propionibacterium acnes* (*P. acnes*) and inflammation (Motosko et al., 2019).

Oxidative stress plays an essential role in the context of AV pathogenesis as well as in several cutaneous lesions which include seborrheic dermatitis, vitiligo, lichen planus (LP), and psoriasis vulgaris (PV) (Savci et al., 2020).

Complete blood count (CBC) parameters could be utilized as diagnostic markers in terms of numerous diseases accompanied by inflammatory processes. Neutrophil lymphocyte ratio (NLR) is measured by utilizing hemogram parameters, and it was recorded that it could be utilized as an inflammatory marker in the context of several diseases in novel research (Wang et al., 2021; Asahina et al., 2017). CBC parameters have been considered as inflammation markers in cases with AV by utilizing

isotretinoin either before or after management (Tamer et al., 2019).

Monocyte high-density lipoprotein ratio represents the efficacy of monocytes which participate in systemic inflammation development and generation of free radicals, and the efficiency of HDL, which has anti-inflammatory and antioxidant actions on the cardiovascular (CV) system. Such data suggest that the monocyte to high-density lipoprotein ratio (MHR) could be used as a new prognostic inflammatory marker, that indicates oxidative stress, and inflammation in CV diseases (Usta et al., 2018).

High levels of Ischemia-modified albumin (IMA) are indicated to be accompanied by different dermatological lesions according to oxidative stress (generation of free radicals) such as vitiligo, PV, and Behçet's disease. However, studies analyzing IMA in acne vulgaris are limited (Omma et al., 2018). So, we aimed to assess CBC parameters and MHR as indicators of inflammation, assess serum IMA as indicator of oxidative stress and to examine their relation to acne vulgaris severity.

2. Patients and methods

This was a case–control study comprised 48 patients complaining from acne vulgaris. Additionally, 40 healthy subjects of matched age and sex were included as a control group. Patients receiving systemic therapy in the previous 3 month and topical AV treatment in the past 30 days were ruled out.

2.1. Methods

All cases were subjected to the next:

(1) Complete history taking and complete general and cutaneous examination.
(2) Global acne grading system (GAGS) score calculation (Shahbag, 2017) (Table 1).

Table 1. Global acne grading system (GAGS).

Area	Factors
Forehead	2
Right cheek	2
Left cheek	2
Nose	1
Chin	1
Chest and upper back	3

All types are given a value according to severity: no lesions = 0, comedones = 1, papules = 2, pustules = 3 and nodules = 4. The score for each area (local score) is measured by utilizing the formula: local score = factor x grade (0–4). The global score is consisting of the local outcomes: 1-18-mild degree, 19-30-moderate degree, 31-38-severe degree, and above 39-acne with a very severe.

Laboratory work: Venous blood sample was acquired from each participant for

(1) Complete blood count and differential leukocytic count.
(2) Determination of HDL.
(3) MHR was calculated.
(4) IMA level was determined by ELISA.

2.2. Statistical analysis

Data were analyzed by IBM SPSS Corp. Released 2013 (IBM SPSS Statistics for Windows, Version-22). Qualitative data were expressed as numbers and percentages. Quantitative data were expressed as medians concerning non-normal distribution of data and means, SD concerning normal distribution of data following assessing the normal distribution of data by Kolmogrov–Smirnov test. Significant results were judged at the (0.05) level.

3. Results

The current study was carried out on 48 acne vulgaris cases. Their mean age was 20.3 ± 5.1 years. They were 19 males (39.6 %) and 29 females (60.4 %). In addition to 40 healthy control subjects of matched age and gender. Median GAGS was 25, ranged from 9 to 57; 20.8 % had mild, 41.7 % had moderate, 18.8 % had severe and 18.8 % had very severe GAGS (Table 2). IMA showed significantly higher concentration in acne vulgaris patients when compared with control group (median = 89.5 vs. 58, respectively, $P < 0.001$). While MHR level did not differ significantly among cases and controls (Table 3). IMA showed gradual increasing median level associated significantly with increased disease severity (Table 4). Although MHR showed gradual increasing median level associated with increased disease severity, this

Table 2. Acne vulgaris grades among studied cases.

	Acne Vulgaris	
	$n = 48$	
GAGS		
Median, range	25	9–57
Mild (1–18)		
No, %	10	20.8 %
Moderate (19–30)		
No, %	20	41.7 %
Severe (31–38)		
No, %	9	18.8 %
Very severe (<39)		
No, %	9	18.8 %

GAGS, Global Acne grading scale.

Table 3. Comparison of Ischaemia-modified albumin and monocyte to high-density lipoprotein ratio among studied groups.

	Control	Acne Vulgaris	P
	n = 40	n = 48	
	median (min−max)	median (min−max)	
IMA (ng/ml)	58 (17−86)	89.5 (41−413)	<0.001
MHR	0.0107 (0.003−0.026)	0.0113 (0.003−0.047)	0.263

Numerical data are expressed as median and range, compared by Mann−Whitney test.

Table 4. Comparison of Ischaemia-modified albumin according to acne vulgaris grades.

Grades	IMA	P
	median (min−max)	
Mild	54.5 (41−120)	P1<0.001 P2 = 0.001 P3<0.001 P4<0.001
Moderate	74 (50−93)	
Severe	96 (89−142)	
Very severe	225 (120−413)	

P1, comparison between all grades.
P2, comparison between mild and moderate.
P3, comparison between moderate and severe.
P4, comparison between severe and very severe.

Table 5. Comparison of monocyte to high-density lipoprotein ratio according to acne vulgaris grades.

Grades	MHR	P
	median (min−max)	
Mild	0.00977 (0.007−0.018)	0.648
Moderate	0.01087 (0.006−0.028)	
Severe	0.01133 (0.003−0.047)	
Very severe	0.01539 (0.007−0.04)	

Numerical data are expressed as median and range, compared by Kruskal Walls test.

increase in median MHR level did not differ significantly between acne grades (Table 5). GAGS showed significant positive correlation with IMA, but not with MHR (Table 6).

(1) Regression analysis was conducted to predict higher grades of AV, using age, sex, CBC parameters, HDL, IMA, and MHR as covariates. Higher IMA was considered as risk predictor of higher acne vulgaris grades (Table 7).

Table 6. Correlations of Ischaemia-modified albumin and monocyte to high-density lipoprotein ratio with Global Acne grading scale among all studied cases.

	GAGS	
	rs	P
IMA(ng/ml)	0.825	<0.001
MHR	0.088	0.552

rs, correlation coefficient.

Table 7. Regression analysis for prediction of higher grades.

	P	OR (95 % CI)
Age	0.317	1.078 (0.914−1.147)
Sex	0.153	0.633 (0.338−1.185)
BMI (Body Mass Index)	0.263	1.045 (0.968−1.128)
ANC (Absolute Neutrophilic Count)	0.566	1.046 (0.896−1.222)
ALC (Absolute Lymphocytic Count)	0.554	1.189 (0.67−2.109)
Monocytes (%)	0.356	2.201 (0.963−8.320)
Platelets (10^9/L)	0.271	0.996 (0.992−1.012)
NLR (Neutrophil Lymphocyte Ratio)	0.285	1.157 (0.886−1.511)
HDL(mg/dl).	0.393	1.015 (0.981−1.050)
PLR (Platelet Lymphocyte Ratio)	0.253	0.991 (0.981−1.003)
MLR (Monocyte Lymphocyte Ratio)	0.154	2.179 (0.747−6.35)
IMA(ng/ml)		
	<0.001	1.035 (1.02−1.050)
MHR	0.280	3.783 (0.981−11.560)

(2) Receiver operating characteristic curve of IMA, MHR was performed for evaluation of diagnostic validity of these markers. IMA had moderate accuracy, Area under the curve (AUC = 0.827). At best cut off value of 65.5, sensitivity was 75 % (i.e. 75 % are true positive among studied cases), specificity was 70 % (i.e. 70 % are true negative among studied controls), PPV was 75 % (75 % are true positive among all positive results), NPV was 70 % (i.e. 70 % are true negative among all negative results), accuracy was 72.7 % (i.e. 72.7 % are true positive and negative results among all studied subjects).

(3) While MHR showed low accuracy (AUC = 0.570). At best cut off value of 0.011, sensitivity was 52.1 % (i.e. 52.1 % are true positive among studied cases), specificity was 55 % (i.e. 55 % are true negative among studied controls), PPV was 58.1 % (58.1 % are true positive among all positive results), NPV was 48.9 % (i.e. 48.9 % are true negative among all negative results), accuracy was 53.4 % (i.e. 53.4 % are true positive and negative results among all studied subjects) (Table 8).

Table 8. Validity of Ischaemia-modified albumin, monocyte to high-density lipoprotein ratio, combined markers for discrimination between acne vulgaris cases and control groups.

	IMA	MHR	IMA + MHR
AUC	0.827	0.570	0.881
Cut off	65.5	0.011	−
Sensitivity (%)	75	52.1	79.2
Specificity (%)	70	55	70
PPV (%)	75	58.1	76
NPV (%)	70	48.9	73.7
Accuracy (%)	72.7	53.4	75

4. Discussion

AV is a chronic inflammatory disease which demonstrates polymorphic lesions (comedone, papule, pustule, nodule, cyst, and scar) (Bhate and Williams, 2013).

Although the etiopathogenesis of AV is not totally identified, Four primary factors have a role in terms of AV pathogenesis. Such factors are increase in sebum formation, abnormalities in follicular keratinization, bacterial proliferation, and inflammatory process (Önder and Ozturk, 2020).

P. acnes play an essential role in the formation of free radicals (Grange et al., 2009) and the inflammatory responses (Kistowska et al., 2014) in keratinocytes, as a result encouraging cell proliferation and migration (Jahns et al., 2015), that enhance the progression of acne vulgaris (Das and Reynolds, 2014).

In addition, free radicals could be generated from the damage of follicular epithelium, that might participate in the development of inflammation in disease pathogenesis (Briganti and Picardo, 2003). Oxidative stress is recorded to have a main role in acne initiation and progression (Wong et al., 2016). IMA is a novel biochemical marker. It is accompanied by ischaemia, inflammation, and oxidative stress (Karatas et al., 2014).

Regarding serum IMA, the present study revealed that IMA level was elevated in acne vulgaris patients in comparison with controls. In addition, it showed gradual increasing median level associated significantly with increased disease severity. This denotes that serum IMA could have a role with regard to AV pathogenesis. Moreover, measuring the serum level of IMA could be helpful in evaluating AV severity and progression.

In line with our study, Ebrahim et al. (2020) demonstrated that AV group was associated with a significant increase in IMA in comparison with the control group. Increased IMA value was significantly accompanied by increased AV grades. In the same line, Akyurek et al. (Tunçez Akyürek et al., 2020) recorded that IMA values were accompanied by a significant increase among cases with AV compared with normal subjects and its level demonstrated a positive correlation with the disease severity. They have recorded that IMA accompanied by ischaemia and oxidative stress could have an essential role with regard to AV etiopathogenesis. Similar to our result, Gürel et al. (Gürel et al., 2019) have demonstrated that the average IMA level was elevated in AV cases. However on contrast to our finding they found no significant differences in serum IMA levels among the AV subgroups according to acne vulgaris severity. This may be explained by potential participation of compensatory mechanisms.

CBC parameters could be utilized as diagnosis biomarkers for several diseases related with inflammatory processes (Asahina et al., 2017; Akarsu and Dikker, 2019). NLR, PLR, and MLR were recognized as predictors of systemic inflammation and poor prognosis in several diseases (Asahina et al., 2017; Imtiaz et al., 2012; Feng et al., 2016). Of notes, these ratios are of great stability compared with the individual cell counts and aren't influenced by clinical situations which alter the individual cell counts (Asahina et al., 2017). In the previous researches, NLR, PLR, and MLR were evaluated in the context of diabetes, acute coronary syndrome, ulcerative colitis, tuberculosis, haptic cirrhosis, systemic inflammation, and in certain malignant tumours to detect prognosis (Fu et al., 2015; Huang et al., 2015; Özer et al., 2015). Previous study showed that CRP, MHR, NLR, and MLR were increased among cases with PV compared with the control group (Aktaş Karabay et al., 2020).

The present study revealed that cases and controls showed no significant differences regarding ANC, ALC, AMC, platelet count, HDL, PLR, and MLR.

In line with our finding, Sobhan et al. (2020) demonstrated that there was no statistical significant difference between cases with AV and the control group as regards plasma lipids including TG, LDL, and HDL. On the contrast to our study, Turkmen et al. (2020) showed that AV cases were associated with a significant increase in neutrophil, NLR ratio and HDL.

Monocyte HDL ratio has been considered as a novel inflammatory marker nowadays utilized in the context of CV diseases (Usta et al., 2018).

In our study, we found that MHR level did not differ significantly among cases and controls. Also, it showed gradual increasing median level associated with increased disease severity, this increase in median MHR level did not differ significantly between acne grades. In accordance with the current study, Turkmen et al. (2020) did not found significant changes regarding MHR in Acne Vulgaris.

Of note, this is the first research assessing MHR and IMA all together in Acne vulgaris patients. The present study revealed that the combination MHR and IMA increased the performance characteristics compared with MHR or IMA alone.

In conclusion, Serum IMA level could be considered as a predictor of AV susceptibility, activity and severity. However, MHR is not correlated to the pathogenesis of acne vulgaris.

Publication ethical statement

All patients gave their informed consent for inclusion before they participated in this study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by IRB (MS.21.07.1574).

Conflicts of interest

None declared.

Acknowledgements

References

Akarsu, M., Dikker, O., 2019. The neutrophil lymphocyte rate and mpv relationship with helicobacter pyloripositivity. Dicle. Med. J. 46, 201–207.

Aktaş Karabay, E., Demir, D., Aksu Çerman, A., 2020. Evaluation of monocyte to high-density lipoprotein ratio, lymphocytes, monocytes, and platelets in psoriasis. An. Bras. Dermatol. 95, 40–45.

Asahina, A., et al., 2017. Neutrophil–lymphocyte ratio, platelet–lymphocyte ratio and mean platelet volume in Japanese patients with psoriasis and psoriatic arthritis: response to therapy with biologics. J. Dermatol. 44, 1112–1121.

Bhate, K., Williams, H., 2013. Epidemiology of acne vulgaris. Br. J. Dermatol. 168, 474–485.

Briganti, S., Picardo, M., 2003. Antioxidant activity, lipid peroxidation and skin diseases. New J. Eur. Acad. Dermatol. Venereol. 17, 663–669.

Das, S., Reynolds, R.V., 2014. Recent advances in acne pathogenesis: implications for therapy. Am. J. Clin. Dermatol. 15, 479–488.

Ebrahim, A., et al., 2020. Ischemic modified albumin as A biomarker in predicting oxidative stress in patients with acne vulgaris. Benha J. Appl. Sci. 5 (8), 205–209.

Feng, F., et al., 2016. Combination of PLR, MLR, MWR, and tumor size could significantly increase the prognostic value for gastrointestinal stromal tumors. Medicine 95, 14.

Fu, H., et al., 2015. Neutrophil-and platelet-to-lymphocyte ratios are correlated with disease activity in rheumatoid arthritis. Clin. Lab. 61, 269–273.

Grange, P.A., et al., 2009. Production of superoxide anions by keratinocytes initiates P. Acnes-induced inflammation of the skin. PLoS Pathog. 5, e1000527.

Gürel, G., et al., 2019. Evaluation of ischemia-modified albumin levels in acne vulgaris patients. Turkderm 53, 84–87.

Huang, W., et al., 2015. Neutrophil–lymphocyte ratio is a reliable predictive marker for early-stage diabetic nephropathy. Clin. Endocrinol. 82, 229–233.

Imtiaz, F., et al., 2012. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. Int. Arch. Med. 5, 1–6.

Jahns, A.C., et al., 2015. Propionibacterium species and follicular keratinocyte activation in acneic and normal skin. Br. J. Dermatol. 172, 981–987.

Karatas, Z., et al., 2014. Increased ischaemia-modified albumin is associated with inflammation in acute rheumatic fever. Cardiol. Young 24, 430.

Kistowska, M., et al., 2014. IL-1β drives inflammatory responses to propionibacterium acnes in vitro and in vivo. J. Invest. Dermatol. 134, 677–685.

Motosko, C., et al., 2019. Acne: a side-effect of masculinizing hormonal therapy in transgender patients. Br. J. Dermatol. 180, 26–30.

Özer, S., et al., 2015. Simple markers for subclinical inflammation in patients with Familial Mediterranean Fever. Med. Sci. Monit. İnt Med. J. Exp. Clin. Res. 21, 298.

Önder, S., Ozturk, M., 2020. Can monocyte/HDL show inflammatory activity of isotretinoin treatment in acne patients? Cutan. Ocul. Toxicol. 39, 111–114.

Omma, A., et al., 2018. Serum calprotectin and ischemia modified albumin levels as markers of disease activity in Behçet's disease. Adv. Dermatol. Allergol./Post. Dermatol. Alergol. 35, 609–613.

Savci, U., et al., 2020. Ischemia-modified albumin as a possible marker of oxidative stress in patients with telogen effluvium. An. Bras. Dermatol. 95, 447–451.

Shahbag, D., 2017. Evaluation of severity in patients of acne vulgaris by global acne grading system in Bangladesh. Clin. Pathol. 1, 105–110.

Sobhan, M., Seif Rabiei, M.A., Amerifar, M., 2020. Correlation between lipid profile and acne vulgaris. Clin. Cosmet. Invest. Dermatol. 67–71.

Tamer, F., Yuksel, M.E., Avcı, E., 2019. Is mean platelet volume an inflammatory marker in acne patients treated with isotretinoin? Acta Dermatovenerologica Alpina Pannonica et Adriatica 28 (2), 12–25.

Tunçez Akyürek, F., et al., 2020. Assessment of ADMA, IMA, and vitamin A and E levels in patients with acne vulgaris. J. Cosmet. Dermatol. 19, 3408–3413.

Turkmen, D., Altunisik, N., Sener, S., 2020. Investigation of monocyte HDL ratio as an indicator of inflammation and complete blood count parameters in patients with acne vulgaris. Int. J. Clin. Pract. 74, e13639.

Usta, A., et al., 2018. The monocyte counts to HDL cholesterol ratio in obese and lean patients with polycystic ovary syndrome. Reprod. Biol. Endocrinol. 16, 1–8.

Wang, W.-M., et al., 2021. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and other hematological parameters in psoriasis patients. BMC Immunol. 22, 1–7.

Wong, A., et al., 2016. Oxidative stress in acne vulgaris. J. Clin. Dermatol. Ther. 3, 020.

Yan, H.M., et al., 2018. Gut microbiota alterations in moderate to severe acne vulgaris patients. J. Dermatol. 45, 1166–1171.