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Biochemical Markers of Oxidative and Nitrosative Stress in Acne Vulgaris: Correlation With Disease Activity

Hani A. Al-Shobaili,[1†] Abdullateef A. Alzolibani,[1†] Ahmad A. Al Robaee,[1] Abdel-Raheim M.A. Meki,[2] and Zafar Rasheed[2*]

[1]Department of Dermatology, College of Medicine, Qassim University, Kingdom of Saudi Arabia
[2]Department of Medical Biochemistry, College of Medicine, Qassim University, Kingdom of Saudi Arabia

Background: Acne vulgaris is a multifactorial skin disorder of unknown etiology. Free radical-mediated reactions have been implicated but their role in eliciting this response and contributing to disease progress remains unexplored. This study was undertaken to investigate the status and contribution of oxidative/nitrosative stress in patients with acne vulgaris. *Methods:* Sera from 50 acne vulgaris with varying levels of disease activity (mild, moderate, and severe) according to the Global Acne Grading System (GAGS) and 40 age- and sex-matched controls were evaluated for serum levels of oxidative/nitrosative stress markers, including protein oxidation, lipid peroxidation and nitric oxide (NO), superoxide dismutase (SOD), and glutathione (GSH). *Results:* Serum analysis showed significantly higher levels of carbonyl contents, malondialdehyde (MDA) and NO, in acne patients compared with healthy controls ($P < 0.05$). Interestingly, not only there were an increased number of subjects positive for carbonyl contents, but also the levels of these oxidants were significantly increased with the increase of the disease activity ($P < 0.05$). In addition, a significant correlation was observed between the levels of carbonyl contents and the GAGS scores ($r = 0.341$, $r = 0.355$, and $r = 0.299$, respectively). Furthermore, sera from acne patients had lower levels of SOD and GSH compared with healthy control sera. *Conclusion:* These findings support an association between oxidative/nitrosative stress and acne. The stronger response observed in serum samples from patients with higher GAGS scores suggests that markers of oxidative/nitrosative stress may be useful in evaluating the progression of acne and in elucidating the mechanisms of disease pathogenesis. J. Clin. Lab. Anal. 27:45–52, 2013.

Key words: Acne vulgaris; biomarkers; protein oxidation; lipid peroxidation; nitration

INTRODUCTION

Acne vulgaris is one of the most prevalent skin conditions encountered by dermatologists (1). Despite technological advances and an increased degree of sophistication within experimental dermatology, the precise mechanisms of the acne process remain elusive (2). It is considered a multifactorial or complex disease of the pilosebaceous unit (3).

Excessive generation of reactive oxygen species (ROS) has the potential to initiate damage to proteins, lipids, and nucleic acids (4, 5). Antioxidant defense systems, such as superoxide dismutase (SOD) and glutathione (GSH) keep ROS production in check, thereby maintaining an appropriate cellular redox balance. Alterations in this redox balance resulting from elevated ROS levels and/or decreased antioxidant levels can lead to oxidative stress (6). Protein oxidation, which results in functional disruption, is not random but appears to be associated with increased oxidation in specific proteins (7). A number of studies indicate a strong role for increases in protein

[†]Authors contributed equally.

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*Correspondence to: Dr. Zafar Rasheed, College of Medicine, Qassim University, Kingdom of Saudi Arabia. E-mail: zafarrasheed@rocketmail.com

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oxidation as a primary cause of cellular dysfunction observed during aging and age-related neurodegenerative diseases (8) such as Alzheimer's disease, Parkinson's disease, and some other protein conformational diseases. Inhibition of a wide array of enzyme activities have been reported (9). Modification of structural protein can also lead to loss of function. As for example, fibrinogen on exposure to ROS loses its ability to form a solid clot (10). Oxidation of synovial fluid immunoglobulin causes aggregation and contributes to the etiology of rheumatoid arthritis (11). These disorders could be due to the formation of abnormal protein aggregates as a consequence of ROS damage. Lipid peroxidation, a process of oxidative degeneration of polyunsaturated fatty acids set into motion by ROS, leads to formation of highly reactive aldehydes, such as malondialdehyde (MDA) that can bind covalently to proteins and thus causes structural protein modifications and affects biologic functions (12). The skin is constantly exposed to oxidative injury induced by ROS generated both from endogenous sources and from external pro-oxidant stimuli (13). Free radical-mediated damage has been implicated in the pathogenesis of acne vulgaris (14–16). Like ROS, reactive nitrogen species (RNS) could also play a significant role in the pathogenesis of various diseases and has drawn significant attention in recent years (17, 18). Nitric oxide (NO) is one of the most important and widely studied RNS. The potential role of NO in disease pathogenesis lies largely in the extent of its production and generation of $O_2^{\cdot -}$, leading to formation of peroxynitrite ($ONOO^-$). $ONOO^-$ is a potent nitrating and oxidizing agent that induced modifications of endogenous proteins and nucleic acids, which disturbed the oxidative/nitrosative homeostasis (18).

Increased oxidative stress in acne vulgaris has been reported (15, 16). However, the potential role of oxidative/nitrosative stress, especially the consequences of oxidative modification of proteins, and the disturbances in oxidants–antioxidant systems in the disease progression remains unresolved. Therefore, we hypothesized that overproduction of reactive oxygen and nitrogen species (RONS) leads to a variety of RONS-mediated modifications of the endogenous proteins, such as increased formation of protein oxidative biomarker carbonyl contents, lipid peroxidative byproducts MDA, and nitrosative biomarker NO, which thus leads to oxidative and nitrosative stress in acne patients. To assess this hypothesis and establish a link between RONS and acne, we examined the levels of biochemical markers of oxidative/nitrosative stress in the sera of acne patients, and analyzed their relationship to the extent of disease activity (mild, moderate, and severe) according to the Global Acne Grading System (GAGS). Our results not only support an association between oxidative/nitrosative stress and acne, but also suggest that oxidative/nitrosative stress markers may be important in the evaluation of acne progression and in the elucidation of the mechanisms of disease pathogenesis.

PATIENTS AND METHODS

Human Subjects

The study group involved 50 patients (30 female and 20 male) with acne vulgaris, as defined by the GAGS criteria (19), and the mean age was 20.3 years. The GAGS score was determined using the disease activity and the patients were divided into the following three groups based on the lower vs. higher GAGS scores: (1) mild acne (2) moderate acne, and (3) severe acne. Patients did not receive any systemic or topical drug therapy for the last three months, did not have any additional systemic disease, had no history of systemic medication use, and had no smoking and other regular exercising habits except their daily activities. The control group comprised 40 healthy subjects (23 female and 17 male; mean age 19.3 years). The mean ages were not significantly different between the groups ($P > 0.05$). The racial/ethnic and sex compositions of the acne groups were comparable with those of the control group.

The study was approved by Local Ethical Committee, College of Medicine, Qassim University. Venous blood samples from the control subjects and acne patients were collected, and serum from individual subjects was stored in small aliquots at –20°C until analyzed further.

Assay for Protein Oxidation

Protein oxidation in acne patients was determined by carbonyl groups formation in the serum samples of acne patients and normal human subjects as previously described (20, 21) with slight modifications. Briefly, the reaction mixture containing 10 μl of serum samples, 0.5 ml of 10 mM 2,4-dinitrophenylhydrazine/2.5 M HCl was added and thoroughly mixed. After addition of 250 μM trichloroacetic acid (catalog # T6399, Sigma-Aldrich, St. Louis, Mo, USA; 20%) and centrifugation, the pellet was collected and washed three times with 1 ml ethanol:ethylacetate (1:1) mixture. The pellet was then dissolved in 1 ml of 6 M guanidine solution and incubated at 30°C for 15 min. After centrifugation, the supernatant was collected and the carbonyl contents were estimated from the absorbance at 370 nm using a molar absorption coefficient of 22,000 $M^{-1}cm^1$. Samples were spectrophotometrically analyzed against a blank of 1 ml of guanidine solution (6 M). Protein concentration was determined in the samples and carbonyl contents were expressed as nanomoles per milligram protein.

Assay for Lipid Peroxidation

Lipid peroxidation was determined in the sera of acne vulgaris patients and healthy controls by measuring the levels of lipid peroxidative end product MDA as described earlier (22). Briefly, 0.2 ml of serum was mixed with 1 ml of 20% trichloroacetic acid. To the mixture, 0.4 ml of 0.67% thiobarbituric acid (TBA) was added, shaken, and kept for 3 min in a boiling water bath. After cooling at room temperature, 1.6 ml of butanol was added and the mixture was shaken. Organic mixture was separated by centrifugation and its absorbance was measured at 532 nm.

Assay for Nitrosative Stress

Nitrosative stress in acne patients was determined by NO estimation using total nitrite assay in the serum samples of acne patients and normal human subjects as described previously (23). Briefly, serum samples were deproteinated using $ZnSO_4$ reagent and total nitrite was determined in the deproteinated serum samples by using Griess reagent (sulfanilamide 17 mM, *N*-(1-naphthyl) ethylene diamine dihydrochloride 0.4 mM, (w/v) 2.5% orthophosphoric acid in 0.1 M phosphate buffer). Absorbance of the reaction mixture was measured at 540 nm. Concentration of NO was determined using sodium nitrite (2.5–30 mM) as standard and the results were expressed as nanomoles per milliliter.

Antioxidants Assays

Determination of GSH

Levels of GSH were determined in the serum samples of acne patients and normal human subject as described elsewhere (24). Briefly, 100 ml of freshly thawed serum was pipetted into Eppendorf tube containing 200 ml of a 10% solution of tricholoroacetic acid, vortexed, and centrifuged at 4000 $\times$ *g* for 10 min at 10°C. To 200 ml of the supernatant, 700 ml of 400 mM Tris-HCl buffer, pH 8.9, was added followed by the addition of 100 ml of 2.5 mM DTNB (5.5-dithio-bis(2-nitrobenzoic acid)) dissolved in 40 mM Tris-HCl buffer pH 8.9. After 10 min at room temperature, the extinction of the samples was measured at 412 nm. Blank consisted of DTNB instead of serum; its extinction was subtracted from the test sample extinction before matching it with the standard curve. The concentration of GSH in the samples was read from a standard curve using different concentrations of GSH (1–10 mmol/ml).

Determination of SOD activity

Activity of antioxidant enzyme SOD in the serum samples of acne patients and normal human subject was determined as described earlier (25). Enzyme activity was detected by its ability to inhibit the autoxidation of epinephrine at pH 10.2. Each cuvette contained in a final volume of 3.0:0.50 ml of 1.8 mM epinephrine (freshly prepared); 0.50 ml of 0.6 mM ethylenediaminetertra acetic acid (EDTA); 0.50 ml of 0.30 M sodium carbonate, pH 10.2, and serum samples. The reaction was initiated by the addition of epinephrine, and an increase in absorbance was measured at 480 nm.

Statistical Analysis

All measurements were performed in duplicates and repeated at least two times using age- and sex-matched acne or control samples. Comparisons were performed by Origin 6.1 (Northampton, MA) and Graph Pad Prism-5 (San Diego, CA) statistical software's using one-way ANOVA followed by Tukey's post hoc analysis). Data correlations were performed using Spearman's rank correlation coefficient. *P* values less than 0.05 were considered significant. Values shown are mean $\pm$ standard error of the mean (SEM) unless stated otherwise.

RESULTS

Role of Protein Oxidation in the Progress of Acne Vulgaris

Protein oxidation typically results in an increase in carbonyl contents, therefore, increase in protein carbonyl content is considered to be a biomarker of protein oxidation (21). The data showed significant increase in serum protein carbonyl contents ($P < 0.05$) in 50 acne vulgaris patients compared with 40 normal subjects of the same age group. The average carbonyl contents ($\pm$SEM) in all studied subjects of acne serum proteins and normal human serum (NHS) proteins were 2.65 $\pm$ 0.13 and 2.06 $\pm$ 0.12 nmol/mg proteins, respectively (Fig. 1B). In addition, we have also determined the role of protein carbonylation in the progress of acne vulgaris. For that carbonyl contents, these were estimated in accordance with the disease activity in mild ($n = 20$), moderate ($n = 23$), and severe (7) acne patients. The average carbonyl contents ($\pm$SEM) in the patients sera with mild, moderate, and severe groups were 2.11 $\pm$ 0.10, 2.73 $\pm$ 0.15, and 3.10 $\pm$ 0.13 nmol/mg protein, respectively (Fig. 1A). Our results showed that carbonyl contents were significantly increased in moderate or severe patients as compared with healthy controls ($P < 0.05$), whereas mild acne patients showed no change in the carbonyl contents, when compared with normal human subjects ($P > 0.05$).

Effect of Lipid Peroxidation in the Progress of Acne Vulgaris

The degree of lipid peroxidation in the progress of acne vulgaris was analyzed by lipid peroxidative end products,

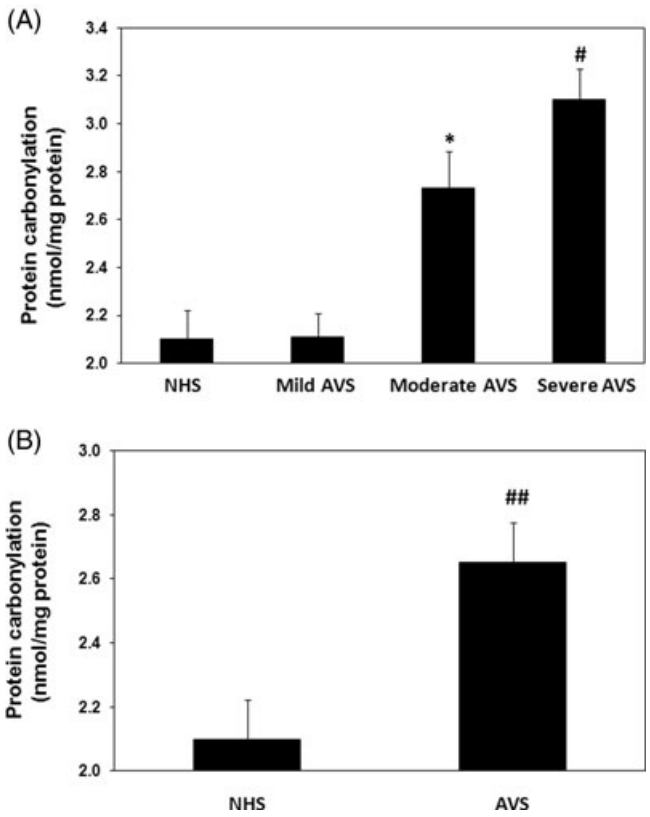

Fig. 1. Protein oxidation in acne vulgaris (AVS). (A) Levels of protein carbonyl contents in the sera of AVS patients with mild ($n = 20$), moderate ($n = 23$), and those with severe ($n = 7$) scores and in normal human sera (NHS, $n = 40$). $^{*}P < 0.01$ vs. mild AVS; $^{\#}P < 0.05$ vs. moderate AVS; $^{\#}P < 0.001$ vs. mild AVS. (B) Levels of protein carbonyl contents in the sera of all studied AVS patients ($n = 50$) and in NHS ($n = 40$). $^{\#\#}P < 0.001$ vs. NHS. Histograms show the mean ± SEM. Comparison analysis was performed using one-way ANOVA followed by Tukey's post hoc test.

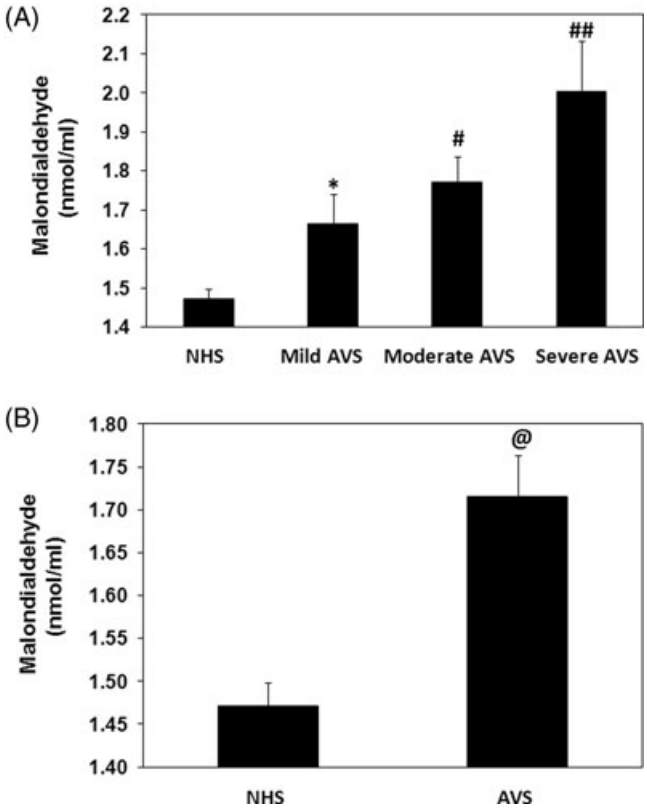

Fig. 2. Lipid peroxidation in acne vulgaris (AVS). (A) Levels of malondialdehyde (MDA) in the sera of AVS patients with mild ($n = 20$), moderate ($n = 23$), and severe ($n = 7$) scores and in normal human sera (NHS, $n = 40$). $^{*}P < 0.01$ vs. NHS; $^{\#}P < 0.05$ vs. mild AVS; $^{\#\#}P < 0.05$ vs. moderate AVS; $^{\#}P < 0.001$ vs. mild AVS. (B) Levels of MDA in the sera of all studied AVS patients ($n = 50$) and NHS ($n = 40$). $^{*}P < 0.01$ vs. NHS. Histograms show the mean ± SEM. Comparison analysis was performed using one-way ANOVA followed by Tukey's post hoc test.

MDA. Our data showed that MDA levels were significantly increased with the increase of the disease activity ($P < 0.05$). The average MDA levels (±SEM) in the patients sera with mild ($n = 20$), moderate ($n = 23$), or severe ($n = 07$) groups were 1.66 ± 0.01, 1.77 ± 0.07, and 2.00 ± 0.13 nmol/ml, respectively (Fig. 2A). Our results also demonstrated that MDA level was significantly high in acne vulgaris patients when compared with normal human subjects ($P < 0.05$). The average MDA (±SEM) in the sera of acne patients and normal human subjects was 1.72 ± 0.05 and 1.47 ± 0.03 nmol/ml, respectively (Fig. 2B).

Effect of Nitrosative Stress in Acne Vulgaris Progress

Nitrosative stress in acne patients was demonstrated by the estimation of NO using nitrite assays in the sera of studied subjects. Our data showed that NO level was significantly increased with the increase of the acne activity ($P < 0.05$). The average NO levels (±SEM) in the patients sera with mild ($n = 20$), moderate ($n = 23$), or severe ($n = 07$) groups were 5.92 ± 0.37, 8.31 ± 0.91 and 10.80 ± 1.59 nmol/ml, respectively (Fig. 3A). Our results also demonstrated that NO level was significantly high in acne patients when compared with normal human subjects ($P < 0.05$). The average NO (±SEM) in the sera of acne patients (50 independent assays) and normal human subjects (40 independent assays) was 1.72 ± 0.05 and 1.47 ± 0.03 nmol/ml, respectively (Fig. 3B).

Effect of Antioxidant System in the Progress of Acne Vulgaris

To validate our hypothesis that oxidative stress may be involved in acne vulgaris, we assessed the antioxidant

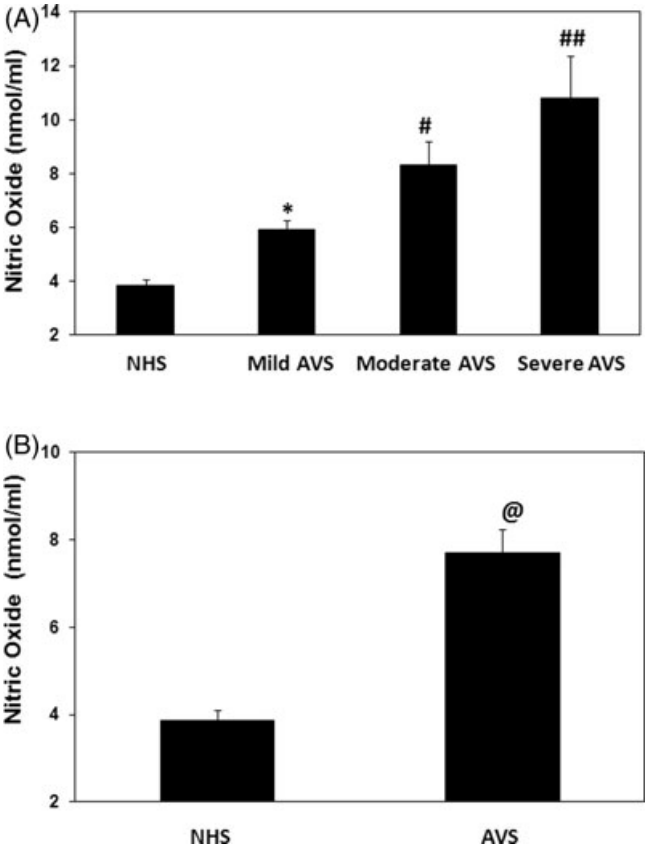

Fig. 3. Nitric oxide in acne vulgaris (AVS). (A) Levels of nitric oxide in the sera of AVS patients with mild ($n = 20$), moderate ($n = 23$), and those with severe ($n = 7$) scores and in normal human sera (NHS, $n = 40$). $^{*}P < 0.05$ vs. NHS; $^{\#}P < 0.05$ vs. mild AVS; $^{\#\#}P < 0.05$ vs. severe AVS. (B) Levels of nitric oxide in the sera of all studied AVS patients ($n = 50$) and NHS ($n = 40$). $^{@}P < 0.01$ vs. NHS. Each bar shows the mean ± SEM. Comparison analysis was performed using one-way ANOVA followed by Tukey's post hoc test.

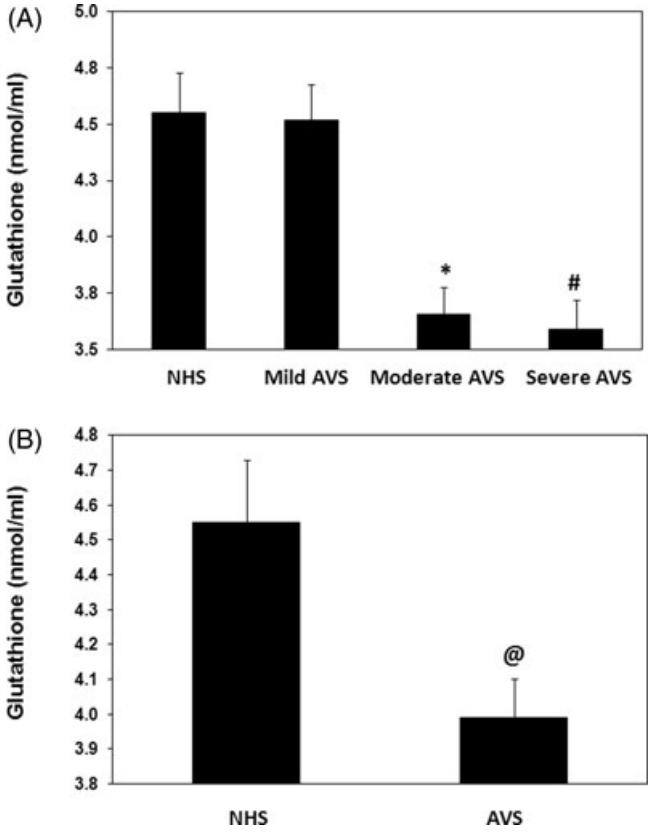

Fig. 4. Antioxidant glutathione in acne vulgaris (AVS). (A) Levels of glutathione (GSH) in the sera of AVS mild scores ($n = 20$), moderate scores ($n = 23$), and those with severe scores ($n = 7$) and in normal human sera (NHS, $n = 40$). $^{*}P < 0.001$ vs. mild AVS; $^{\#}P < 0.001$ vs. mild AVS. (B) Levels of GSH in the sera of all studied AVS patients ($n = 50$) and NHS ($n = 40$). $^{@}P < 0.05$ vs. NHS. Histograms show the mean ± SEM. Comparison analysis was performed using one-way ANOVA followed by Tukey's post hoc test.

potential with the following parameters in patient's sera as a function of disease activity.

Correlation of GSH with disease activity

As evident from Figure 4A, the levels of serum GSH were significantly reduced in mild or severe acne patients compared with normal subjects of the same age group ($P < 0.05$). The average GSH levels (±SEM) in mild and severe acne patients were 3.65 ± 0.12 and 3.59 ± 0.33 nmol/ml, respectively, whereas the average GSH (±SEM) in normal human controls was 4.55 ± 0.18 nmol/ml. Our results also demonstrated that mild acne patients showed insignificant decreased in the serum GSH when compared with normal human subjects ($P > 0.05$). As far as GSH level in all studied acne cases was concerned, our data showed that GSH level was significantly reduced in acne patients when compared with normal human subjects ($P < 0.05$). The average GSH (±SEM) in the sera of acne patients (50 independent assays) and normal human subjects (40 independent assays) was 3.99 ± 0.11 and 4.55 ± 0.18 nmol/ml, respectively (Fig. 4B).

Disease progress related decrease of SOD activity

To provide further support to our hypothesis and assess the week antioxidant system of acne patients, activity of SOD was determined in the serum samples of studied subjects. As shown in Figure 5A, SOD activity was significantly decreased with the increase of the acne activity ($P < 0.05$). The average SOD activity (±SEM) in the patient's sera with mild ($n = 20$), moderate ($n = 23$), or severe ($n = 07$) groups was 37.38 ± 0.48, 36.75 ± 0.27 and 35.67 ± 0.32 kU/l, respectively (Fig. 3A). Our results also demonstrated that SOD activity was significantly reduced in acne patients when compared with normal human subjects ($P < 0.05$). The average SOD activity (±SEM) in the

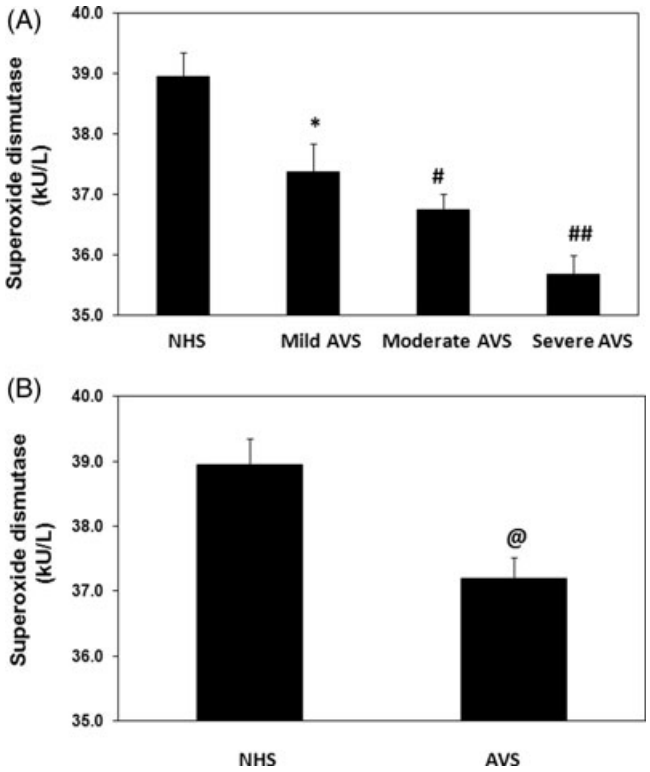

Fig. 5. Activity of superoxide dismutase (SOD) in acne vulgaris (AVS). (A) Activity of antioxidant enzyme SOD in the sera of AVS patients with mild ($n = 20$), moderate ($n = 23$), and severe ($n = 07$) scores and normal human sera (NHS, $n = 40$). $^{*}P < 0.05$ vs. NHS; $^{\#}P < 0.05$ vs. mild AVS; $^{\#\#}P < 0.05$ vs. moderate AVS. (B) Activity of SOD in the sera of all studied AVS patients ($n = 50$) and NHS ($n = 40$). $^{@}P < 0.05$ vs. NHS. Each bar shows the mean ± SEM. Comparison analysis was performed using one-way ANOVA followed by Tukey's post hoc test.

sera of acne patients (50 independent assays) and normal human subjects (40 independent assays) was 37.19 ± 0.33 and 38.95 ± 0.40 nmol/ml, respectively (Fig. 5B).

DISCUSSION

Acne vulgaris is a skin disease caused by the changes in pilosebaceous units. It is common in adolescence and may proceed into adulthood, affecting roughly 33% of people aged between 15 and 44 years (26). Despite the research, the etiology and pathogenesis of acne is not completely understood and a single, primary cause that has not been identified (2, 27). A few previous studies have proposed the role of oxidative stress in the aetiopathogenesis of acne (14–16). The generation of ROS by neutrophils resulting in tissue injury is proposed to be responsible for one of the pathogenic conditions in acne vulgaris, and inhibition of ROS production has been reported to be of therapeutic benefit (28, 29). In the present study, we have demonstrated for the very first time that the roles of biochemical markers of protein oxidation, lipid peroxidation, or nitrosative stress in the progress of acne vulgaris.

The oxidative modification of proteins, lipids, and nucleic acids has been implicated in the etiology of numerous disorders and diseases (30–33). Oxidatively modified serum proteins can serve as important in vivo biomarkers of oxidative stress. Proteins are better candidates in detecting oxidative stress, due to the accessibility of serum protein for sampling, their relatively long half-lives, and their well-defined biochemical pathways. Since extracellular fluids contain only small amounts of antioxidant enzymes, it has been proposed that the major extracellular antioxidants are proteins (34). The in vitro oxidation of amino acid residues leads to protein degradation, aggregation, and crosslinking. In contrast, significant evidence for the presence of ROS-mediated protein damage in vivo and its possible clinical significance is not currently available. The oxidation of a protein typically results in an increase in carbonyl contents. This increase is due to the oxidation of Lys, Arg, Pro, or other amino acid residues. In short, protein carbonyl groups are the biomarker of oxidative stress (21). In human plasma, all amino acids in the protein are susceptible to oxidative modification by oxidants such as hydroxyl radicals and hypochlorous acid (21). Present data showed total serum protein carbonyl contents were significantly increased ($P < 0.05$) in acne vulgaris patients as compared to normal subjects. Our data pointed out that mainly serum protein carbonyl contents were significantly increased in moderate or severe acne patients as compared with the total serum protein present in normal human subjects, whereas mild acne patients showed negligible increase in the carbonyl contents as compared with healthy controls ($P > 0.05$). This data clearly indicated that serum proteins in acne patients were oxidatively modified and this oxidative modification may have a role in disease progression.

Lipid peroxidation is another important parameter and a hallmark of the oxidative stress. MDA, an end product of lipid peroxidation induced by ROS and is considered to be the suitable biomarker for the determination of lipid peroxidation (35). Increased lipid peroxidation has previously been detected in acne vulgaris patients (12), but the significance of lipid peroxidation with disease activity or in the initiation or development of acne remains largely unexplored. In this study, when the acne patients were divided into three groups on their GAGS scores, such as mild, moderate, and severe acne groups, all the groups showed higher serum levels of MDA than were observed in healthy controls, but the levels were much greater in the groups with higher GAGS scores as MDA levels: control < mild < moderate < severe. This clearly suggests an ongoing involvement of lipid peroxidation in acne patients. In contrast to this, it also indicates that there is a close association between lipid peroxidation and disease activity,

i.e. the greater the lipid peroxidation stress, the higher the acne activity.

NO is a diffusible messenger known to display a variety of physiological functions, including vasorelaxation, bronchodilator, inhibition of platelet aggregation, and neurotransmission. Additionally, it appears to be involved in the macrophage-dependent killing of intracellular parasites and possibly cancer cells, indicating the potential of this free radical to mediate cytotoxic and pathological effects. When produced in excess, NO can have a multitude of potentially toxic effects, which are highly dependent on its concentration and the particular microenvironment in which it is produced (36). NO has been reported to inhibit mitochondrial respiration and ribonucleotide reductase and to damage DNA (37) and bring about protein modification (38). There is a increasing evidence that NO may be involved in the pathogenesis of various diseases including acne vulgaris (15). Serum nitrite/nitrate level, which is an index of NO production, was well reported to correlate with disease activity in various diseases (38). Therefore, we hypothesized that increased serum level of NO thus presents another important potential mechanism in the pathogenesis of acne vulgaris and it may be correlated with disease activity. Our results provide evidences that NO level was significantly increased with the increase of the acne activity in patient groups with mild, moderate, or severe as NO: control < mild < moderate < severe acne patients. The increased levels of NO observed in the acne patients in the present study provide solid evidence of the involvement of nitrosative stress in the progress acne vulgaris.

Humans have both enzymatic and nonenzymatic antioxidant defense systems. SOD, a major enzyme and first line of defense against oxygen-derived free radicals, controls ROS production by catalyzing the dismutation of the $O_2^{\cdot -}$ into hydrogen peroxide (H_2O_2), which is further converted into water by catalase, and thereby, an appropriate cellular redox balance is maintained. Alterations in this normal balance, as a result of elevated ROS production and/or decreased antioxidant levels, can lead to a state of oxidative stress (39). Another important well-known parameter for antioxidant defense system is GSH. GSH together with its related enzymes, comprises a system that maintains the intracellular reducing environment and acts as primary defense against excessive generation of harmful ROS (40). The oxygen radical scavenging activity of GSH directly facilitates ROS neutralization and the repair of ROS-induced damage (40). In addition to its antioxidant activity, GSH has many physiological functions including detoxification of xenobiotics, modulation of redox-regulated signal transduction, regulation of cell proliferation, and immune responses (41). Now, it is well established that GSH deficiency contributes to oxidative stress, which plays a key role in various pathological conditions (40, 41).

The enhanced protein oxidation, lipid peroxidation, and nitration observed in acne patients in this study drew our attention to evaluating the SOD activity and serum GSH levels in these subjects. Clearly, the SOD activity or GSH levels was significantly lower in the acne patients as compared with the healthy controls, but the groups of patients with severe or moderate acne showing even greater reductions in the SOD activity or GSH levels in comparison with acne patients with mild disease activity. The decreased serum activities of SOD or GSH levels suggest that the antioxidant balance is compromised in acne that may lead to increased ROS levels and, thus, contribute to increased oxidative stress. In addition, these findings also indicate that oxidative stress is increased in acne vulgaris and is associated with increased disease activity.

CONCLUSIONS

Our results clearly show significant increases in oxidative/nitrosative stress in acne patients, suggesting there is an imbalance between RONS production and antioxidant defense mechanisms in acne vulgaris. In this study, the increased levels of protein carbonylation and lipid peroxidation observed in the acne patients also suggest that oxidative modification of endogenous proteins. More importantly, the results of this study, for the first time, provide evidence of a strong association between serum levels of protein oxidation, lipid peroxidation or NO, and acne disease activity, suggesting that oxidative/nitrosative stress markers may be useful in evaluating acne disease activity, and would therefore be helpful for predicting the progression of the disease.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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