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Original Research Article

Evaluation of Serum Lipocalin-2 Levels and Their Association with Disease Severity in Patients with Acne Vulgaris: A Case-Control Study

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Abstract

Background: Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit characterized by follicular hyperkeratinization, increased sebum production, bacterial colonization, and immune activation. Lipocalin-2 (LCN2), also known as neutrophil gelatinase-associated lipocalin (NGAL), has emerged as a potential inflammatory biomarker in various dermatological and metabolic disorders.

Methods: This case-control study included 50 patients with acne vulgaris and 50 age- and gender-matched healthy controls. Acne severity was assessed using the Global Acne Grading System (GAGS). Serum Lipocalin-2 levels were measured using enzyme-linked immunosorbent assay (ELISA). Statistical analyses included independent samples t-test, one-way ANOVA, and Pearson's correlation coefficient.

Results: Serum Lipocalin-2 levels were significantly higher in patients with acne vulgaris compared with healthy controls (278.4 ± 198.6 ng/mL vs. 95.8 ± 61.3 ng/mL; $p<0.001$). Among acne patients, 32.0% had mild, 36.0% moderate, 22.0% severe, and 10.0% very severe disease. Mean Lipocalin-2 levels increased progressively with disease severity, ranging from 156.8 ± 72.4 ng/mL in mild acne to 521.4 ± 134.2 ng/mL in very severe acne ($p<0.001$). A significant positive correlation was observed between GAGS scores and serum Lipocalin-2 levels ($r=0.652$, $p<0.001$).

Conclusion: Serum Lipocalin-2 levels are significantly elevated in acne vulgaris and correlate positively with disease severity. Lipocalin-2 may serve as a useful biomarker for assessing inflammatory activity and severity in patients with acne vulgaris.

Keywords: Acne vulgaris; Lipocalin-2; Neutrophil gelatinase-associated lipocalin; NGAL; Biomarker; Inflammation; Global Acne Grading System.

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Introduction

Acne vulgaris is one of the most prevalent chronic inflammatory disorders of the skin, affecting a large proportion of adolescents and young adults worldwide. The condition primarily involves the pilosebaceous units and commonly affects areas rich in sebaceous glands, such as the face, chest, shoulders, and upper back. Clinically, acne vulgaris presents with a spectrum of lesions including comedones, papules, pustules, nodules, and cysts, which may lead to permanent scarring and significant psychosocial distress. Although acne is often considered a self-limiting condition, its impact on quality of life and emotional well-being makes it an important public health concern.[1], [2] The pathogenesis of acne vulgaris is multifactorial and complex. Several interrelated mechanisms contribute to disease development, including follicular hyperkeratinization, increased sebum production stimulated by androgens, colonization by Cutibacterium acnes (formerly Propionibacterium acnes), and activation of inflammatory pathways within the pilosebaceous unit. In addition, genetic predisposition, hormonal influences, immune dysregulation, and metabolic factors have been implicated in the initiation and progression of acne lesions. Recent evidence suggests that chronic low-grade inflammation plays a central role throughout the disease process rather than being merely a secondary event.[3] Increasing attention has been directed toward the role of

adipokines and inflammatory mediators in dermatological disorders. Among these molecules, Lipocalin-2 (LCN2), also known as neutrophil gelatinase-associated lipocalin (NGAL), has emerged as a potential biomarker of inflammation. Lipocalin-2 is a glycoprotein belonging to the lipocalin family and is produced by various cell types, including neutrophils, adipocytes, epithelial cells, and macrophages. It participates in numerous biological processes such as innate immunity, cellular differentiation, metabolic regulation, and inflammatory responses.[4], [5]

Studies have demonstrated that Lipocalin-2 expression is upregulated in response to inflammatory stimuli, including cytokines and bacterial products. Elevated circulating levels of Lipocalin-2 have been reported in several inflammatory and metabolic disorders, suggesting its involvement in immune-mediated tissue damage and chronic inflammation. Given the inflammatory nature of acne vulgaris, increased Lipocalin-2 levels may reflect disease activity and severity. Therefore, the present study was undertaken to evaluate serum Lipocalin-2 levels in patients with acne vulgaris and to explore its potential role as a biomarker associated with disease severity.

Materials and Methods

This comparative case-control study was conducted in the Departments of Biochemistry and Dermatology at M.G.M. Medical College and associated hospital, Indore, Madhya Pradesh, India. The study included 100 participants comprising 50 patients diagnosed with acne vulgaris and 50 age- and gender-matched healthy controls. Patients were recruited from the Dermatology Outpatient Department during the study period. Healthy volunteers without a history of acne or other inflammatory skin disorders served as controls.

Written informed consent was obtained from all participants prior to enrolment. The study protocol was approved by the Institutional Ethics Committee of M.G.M. Medical College, Indore, and was conducted in accordance with the ethical principles of the Declaration of Helsinki.

A detailed clinical history was obtained from all participants, including age, gender, duration of disease, family history of acne, treatment history, and associated medical conditions. Participants with systemic inflammatory diseases, diabetes mellitus, autoimmune disorders, active infections, pregnancy, or those receiving systemic anti-inflammatory or immunosuppressive medications were excluded from the study.

All participants underwent a complete general and dermatological examination. Body mass index (BMI) was calculated for each participant. In patients with acne vulgaris, disease severity was assessed using the Global Acne Grading System (GAGS). Based on GAGS scores, patients were categorized into mild, moderate, severe, and very severe acne groups.

After an overnight fast, approximately 5 mL of venous blood was collected from each participant under aseptic conditions. Blood samples were allowed to clot at room temperature and were subsequently centrifuged at 3000 rpm for 10 minutes to obtain serum. The separated serum was aliquoted into labeled Eppendorf tubes and stored at −20°C until analysis.

Serum Lipocalin-2 levels were measured using a commercially available Human Lipocalin-2 (NGAL) Enzyme-Linked Immunosorbent Assay (ELISA) kit according to the manufacturer's instructions. All samples were analyzed in duplicate, and strict quality control measures were maintained throughout the assay procedure.

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons between two groups were performed using the independent samples t-test, while comparisons among acne severity groups were performed using one-way analysis of variance (ANOVA) followed by post hoc analysis where appropriate. Correlations were assessed using Pearson's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 100 participants were enrolled in the study, including 50 patients with acne vulgaris and 50 age- and gender-matched healthy controls. There were no statistically significant differences between the two groups with respect to age, gender distribution, or body mass index (BMI), indicating good baseline comparability (Table 1). Serum Lipocalin-2 levels were significantly higher in patients with acne vulgaris compared with healthy controls (278.4 ± 198.6 ng/mL vs. 95.8 ± 61.3 ng/mL, $p<0.001$) (Table 2).

Based on the Global Acne Grading System (GAGS), 16 (32.0%) patients had mild acne, 18 (36.0%) had moderate acne, 11 (22.0%) had severe acne, and 5 (10.0%) had very severe acne (Table 3). A progressive increase in serum Lipocalin-2 levels was observed with increasing disease severity. Mean Lipocalin-2 concentrations increased from 156.8 ± 72.4 ng/mL in patients with mild acne to 248.5 ± 96.3 ng/mL, 382.7 ± 118.5 ng/mL, and 521.4 ± 134.2 ng/mL in patients with moderate, severe, and very severe acne,

respectively. This trend was statistically significant (ANOVA, p<0.001) (Table 4).

Pearson correlation analysis revealed a significant positive correlation between GAGS score and serum Lipocalin-2 levels (r=0.652, p<0.001), indicating that higher Lipocalin-2 concentrations were associated with greater acne severity (Table 5).

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Variable		Acne Vulgaris (n=50)	Controls (n=50)	p-value
Age (years)		21.6 ± 3.8	21.1 ± 3.5	0.48 [a]
Gender	Male, n (%)	24 (48.0)	24 (48.0)	1.000 [b]
	Female, n (%)	26 (52.0)	26 (52.0)	
BMI (kg/m²)		22.3 ± 2.7	21.9 ± 2.5	0.44 [a]
Independent Student's t-test; Chi-square test. p<0.05 considered statistically significant.				

Table 2: Comparison of Serum Lipocalin-2 Levels between Acne Vulgaris Patients and Healthy Controls

Parameter	Acne Vulgaris (n=50)	Controls (n=50)	p-value
Serum Lipocalin-2 (ng/mL)	278.4 ± 198.6	95.8 ± 61.3	<0.001
Independent Student's t-test. p<0.05 considered statistically significant.			

Table 3: Distribution of Acne Severity among Patients with Acne Vulgaris (n=50)

Acne Severity (GAGS)	Number of Patients	Percentage (%)
Mild	16	32.0
Moderate	18	36.0
Severe	11	22.0
Very Severe	5	10.0
Total	**50**	**100.0**

Table 4: Serum Lipocalin-2 Levels According to Acne Severity

Acne Severity	n	Serum Lipocalin-2 (ng/mL) Mean ± SD	p-value
Mild	16	156.8 ± 72.4	**<0.001**
Moderate	18	248.5 ± 96.3	
Severe	11	382.7 ± 118.5	
Very Severe	5	521.4 ± 134.2	
One-way ANOVA. p<0.05 considered statistically significant.			

Table 5: Correlation between Acne Severity and Serum Lipocalin-2 Levels

Variable	Correlation Coefficient (r)	p-value
GAGS Score vs Serum Lipocalin-2	0.652	<0.001
Pearson's correlation analysis. p<0.05 considered statistically significant.		

Discussion

Acne vulgaris is a multifactorial inflammatory disorder of the pilosebaceous unit in which follicular hyperkeratinization, increased sebum production, Cutibacterium acnes colonization, and dysregulated immune responses interact to produce characteristic lesions. In recent years, increasing attention has been directed toward the role of inflammatory adipokines and immune mediators in acne pathogenesis. Lipocalin-2 (LCN2), also known as neutrophil gelatinase-associated lipocalin (NGAL), has emerged as a potential biomarker linking inflammation, innate immunity, and metabolic dysfunction.

In the present study, serum Lipocalin-2 levels were significantly higher in patients with acne vulgaris compared with healthy controls (278.4 ± 198.6 ng/mL vs. 95.8 ± 61.3 ng/mL, p<0.001). Furthermore, Lipocalin-2 concentrations increased progressively with disease severity, and a significant positive correlation was observed between serum Lipocalin-2 levels and GAGS scores (r=0.652, p<0.001). These findings suggest that Lipocalin-2 is closely associated with both the presence and severity of acne vulgaris.

Our findings are in agreement with the work of Sorour et al., who reported significantly elevated serum Lipocalin-2 levels among acne patients compared with healthy controls (290.0 ± 220.0 ng/mL vs. 92.6 ± 67.6 ng/mL, p<0.001).[5]

Similarly, Sabry et al. demonstrated markedly higher serum NGAL levels in patients with acne vulgaris and suggested that Lipocalin-2 may play an important role in the inflammatory pathophysiology of the disease.[6] The close similarity between our findings and those of previous studies strengthens the evidence that Lipocalin-2 is consistently elevated in acne vulgaris and may represent a reliable biomarker of disease activity. The observed relationship between Lipocalin-2 and acne severity is particularly noteworthy. In our study, serum Lipocalin-2 levels

increased from 156.8 ± 72.4 ng/mL in mild acne to 521.4 ± 134.2 ng/mL in very severe acne. These findings are consistent with Sabry et al., who reported significant differences in NGAL levels across acne severity groups.[6] Likewise, Wolk et al. demonstrated a strong positive correlation between circulating Lipocalin-2 concentrations and disease severity in hidradenitis suppurativa (r_s=0.65, $p<0.001$), a chronic inflammatory follicular disorder sharing several pathogenic mechanisms with acne vulgaris.[7] Similarly, Nguyen and Nguyen reported positive associations between plasma Lipocalin-2 levels and disease severity indices in psoriasis.[8] Collectively, these studies suggest that Lipocalin-2 reflects the intensity of cutaneous inflammation and may serve as an objective indicator of disease severity.

The biological mechanisms underlying elevated Lipocalin-2 levels in acne are increasingly being elucidated. Lumsden et al. demonstrated increased expression of NGAL within acne lesions and showed that Cutibacterium acnes directly stimulates NGAL production through Toll-like receptor-2-mediated signaling pathways. The same authors reported that inflammatory cytokines, particularly IL-1β, significantly enhance NGAL expression in sebocytes. These observations support the hypothesis that elevated serum Lipocalin-2 in acne results from activation of innate immune pathways triggered by microbial colonization and inflammatory cytokine release within the pilosebaceous unit.[9]

Further mechanistic support is provided by Ren and Xia, who described Lipocalin-2 as an active inflammatory mediator rather than a passive biomarker. They demonstrated that Lipocalin-2 promotes neutrophil recruitment, amplifies cytokine production, and participates in IL-17-driven inflammatory pathways.

Since neutrophilic infiltration and cytokine activation are characteristic features of inflammatory acne lesions, elevated Lipocalin-2 levels may contribute directly to lesion development and progression.[10] Similarly, Wolk et al. identified activated granulocytes and keratinocytes as major sources of Lipocalin-2 and proposed a self-amplifying inflammatory loop involving TNF-α, neutrophils, and Lipocalin-2.[7] This mechanism may explain the strong association observed between Lipocalin-2 levels and acne severity in the present study.

Beyond its inflammatory role, Lipocalin-2 appears to function as an important component of innate immunity. Sabry et al., Lumsden et al., and Al Jaberi et al. highlighted the antimicrobial properties of Lipocalin-2, particularly its ability to sequester iron-containing bacterial siderophores and limit microbial growth. Given the central role of Cutibacterium acnes in acne pathogenesis, increased Lipocalin-2 production may represent a protective host response aimed at controlling bacterial proliferation. However, persistent activation of this pathway may also contribute to chronic inflammation and tissue damage.[6], [9], [11]

Recent evidence also suggests a link between Lipocalin-2 and metabolic dysfunction. Al Jaberi et al. described Lipocalin-2 as a multifunctional adipocytokine involved in insulin sensitivity, glucose homeostasis, lipid metabolism, and inflammatory signaling.[11] Likewise, Romejko et al. reported associations between elevated NGAL levels and obesity, insulin resistance, metabolic syndrome, and chronic inflammatory states.[12] These observations are relevant because acne vulgaris has increasingly been linked to metabolic disturbances and low-grade systemic inflammation. Therefore, elevated Lipocalin-2 levels may reflect the complex interaction between inflammatory and metabolic pathways involved in acne pathogenesis.

Another important aspect of Lipocalin-2 biology is its interaction with matrix metalloproteinase-9 (MMP-9). According to Romejko et al. and Al Jaberi et al., Lipocalin-2 stabilizes MMP-9 and enhances extracellular matrix remodeling. Since MMP-9 contributes to tissue destruction and scar formation, elevated Lipocalin-2 levels may partially explain the increased risk of scarring observed in severe inflammatory acne.[11], [12]

The findings of the present study suggest that serum Lipocalin-2 is not merely a marker of inflammation but may actively participate in the pathogenesis of acne vulgaris through modulation of innate immunity, cytokine signaling, neutrophil recruitment, and tissue remodeling.

The strong positive correlation with disease severity further supports its potential clinical utility as a biomarker for assessing disease activity and monitoring therapeutic response. Nevertheless, larger multicenter studies and longitudinal investigations are required to clarify the causal role of Lipocalin-2 and to evaluate its potential as a therapeutic target in acne management.

Conclusion

Serum Lipocalin-2 levels were significantly elevated in patients with acne vulgaris and increased progressively with disease severity. The significant positive correlation between Lipocalin-2 levels and GAGS scores suggests that Lipocalin-2 may serve as a valuable biomarker of inflammatory activity and disease severity in acne vulgaris. Further large-scale prospective studies are warranted to validate its clinical utility.

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