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Role of Zinc and Magnesium in Pathogenesis and Severity of Acne Vulgaris: A Case-Control Study

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Abstract:

Acne vulgaris is one of the most common chronic inflammatory disorders of the pilosebaceous unit, affecting adolescents and adults worldwide. Its multifactorial pathogenesis involves increased sebum production, follicular hyperkeratinization, bacterial colonization, and inflammation. In recent years, the role of micronutrients, particularly trace elements like zinc and magnesium, has gained attention due to their potential impact on immune response, oxidative stress, and hormonal regulation, which are known contributors to acne development. This case-control study was conducted to evaluate the association of serum zinc and magnesium levels with the pathogenesis and severity of acne vulgaris. A total of 100 patients with clinically diagnosed acne vulgaris and 100 age- and sex-matched healthy controls were included. Serum zinc and magnesium levels were measured and correlated with acne severity using the Global Acne Grading System (GAGS). The results revealed significantly lower serum zinc and magnesium levels in acne patients compared to controls ($p < 0.05$). Furthermore, an inverse correlation was observed between trace element levels and acne severity, suggesting that deficiencies in these micronutrients may contribute to both the development and progression of acne vulgaris. These findings highlight the potential role of zinc and magnesium as biomarkers and therapeutic adjuncts in acne management.

Keywords: ***Acne vulgaris, Zinc, Magnesium, Trace elements, Pathogenesis, Acne severity, Micronutrient deficiency, Global Acne Grading System (GAGS), Inflammation, Dermatology.***

Introduction

Acne vulgaris is a highly prevalent, chronic inflammatory skin disorder affecting the pilosebaceous units, characterized by the formation of comedones, papules, pustules, nodules, and, in severe cases, cysts and scarring. It is considered one of the most common dermatological conditions globally, with a prevalence of up to 85% among adolescents and young adults. Although acne vulgaris is not life-threatening, its visible manifestations, particularly on the face, chest, and back, often lead to significant psychological distress, social withdrawal, and a reduced quality of life.

Pathogenesis of Acne Vulgaris

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The pathogenesis of acne is complex and multifactorial, involving the interplay of several factors. These include:

1. **Increased Sebum Production:** Androgen-mediated stimulation of sebaceous glands leads to excessive sebum production, creating an environment conducive to acne development.
2. **Follicular Hyperkeratinization:** Abnormal proliferation and desquamation of keratinocytes in the pilosebaceous duct result in comedone formation and obstruction of the follicle.
3. **Bacterial Colonization:** The anaerobic bacterium Cutibacterium acnes (formerly Propionibacterium acnes) proliferates within the sebum-rich follicle, promoting inflammation.
4. **Inflammatory Response:** Activation of innate and adaptive immune responses leads to the release of pro-inflammatory cytokines, perpetuating the inflammatory cascade and contributing to lesion formation and severity.

While these mechanisms have been extensively studied, emerging evidence suggests that certain nutritional and micronutrient deficiencies may modulate the severity and progression of acne vulgaris by influencing these underlying pathogenic processes.

The Role of Micronutrients in Acne

Micronutrients, particularly trace elements such as zinc and magnesium, play a vital role in various physiological and immunological processes, including skin health, immune function, and hormonal regulation. Deficiencies or imbalances in these elements have been implicated in several inflammatory and dermatological conditions, including acne vulgaris.

Among the various trace elements studied, zinc and magnesium have received considerable attention due to their antioxidant, anti-inflammatory, and immunomodulatory properties, which are directly relevant to acne pathogenesis.

Zinc and Its Role in Acne

Zinc is an essential trace element involved in numerous enzymatic reactions, cellular proliferation, immune regulation, and wound healing. It exhibits anti-inflammatory, antibacterial, and sebum-regulating properties, making it highly relevant to the pathogenesis of acne vulgaris.

Several mechanisms by which zinc may influence acne development and severity include:

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- **Anti-Inflammatory Effects:** Zinc modulates the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukins, thereby reducing inflammation in acne lesions.
- **Antioxidant Action:** Zinc plays a role in mitigating oxidative stress by stabilizing cell membranes and functioning as a cofactor for antioxidant enzymes like superoxide dismutase.
- **Inhibition of C. acnes Growth:** Zinc possesses mild antimicrobial activity against Cutibacterium acnes, limiting bacterial colonization and subsequent inflammation.
- **Regulation of Androgen Activity:** Zinc influences androgen metabolism, which indirectly affects sebum production, a crucial factor in acne pathogenesis.

Several studies have demonstrated significantly lower serum zinc levels in individuals with acne compared to healthy controls. Moreover, zinc supplementation, both oral and topical, has shown beneficial effects in reducing acne lesion count and severity in clinical trials.

Magnesium and Its Role in Acne

Magnesium is another essential mineral involved in over 300 biochemical reactions in the human body, including protein synthesis, neuromuscular function, and energy production. In the context of acne vulgaris, magnesium plays a critical role in:

- **Anti-Inflammatory Function:** Magnesium helps regulate inflammatory pathways by modulating cytokine production and maintaining cellular homeostasis.
- **Hormonal Balance:** Magnesium influences the activity of enzymes involved in steroid hormone synthesis, indirectly impacting androgen levels that stimulate sebaceous gland activity.
- **Stress Modulation:** Chronic stress is a known exacerbating factor for acne. Magnesium has been shown to regulate the hypothalamic-pituitary-adrenal (HPA) axis, reducing stress-induced hormonal fluctuations that may worsen acne.
- **Keratinocyte Function:** Magnesium maintains epidermal barrier function and keratinocyte differentiation, which may prevent abnormal follicular keratinization.

Although fewer studies have explored the relationship between magnesium and acne compared to zinc, existing literature suggests that magnesium deficiency may aggravate inflammatory processes and hormonal imbalances associated with acne vulgaris.

Rationale for the Study

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Despite the growing recognition of the role of micronutrients in acne, there remains limited research, particularly in the Indian population, evaluating the association between serum zinc and magnesium levels with the pathogenesis and severity of acne vulgaris. Given the high prevalence of both acne and micronutrient deficiencies in India due to dietary patterns, environmental factors, and socioeconomic disparities, investigating this relationship is of significant clinical relevance.

Understanding the potential link between trace element status and acne severity could have several practical implications:

- **Early Identification:** Serum zinc and magnesium levels could serve as biomarkers for assessing the risk or severity of acne.
- **Nutritional Interventions:** Dietary modification and targeted supplementation could be incorporated as adjunctive strategies in acne management.
- **Personalized Treatment:** Identifying micronutrient deficiencies may guide dermatologists in adopting a more holistic and individualized approach to acne therapy.

Objectives of the Study

The present study was undertaken with the following objectives:

1. To assess and compare serum zinc and magnesium levels in patients with acne vulgaris and age- and sex-matched healthy controls.
2. To evaluate the correlation between serum zinc and magnesium levels and the severity of acne, as graded by the Global Acne Grading System (GAGS).
3. To explore the potential role of zinc and magnesium as biomarkers and therapeutic targets in the pathogenesis of acne vulgaris.

Significance of the Study

This study aims to bridge the existing knowledge gap by providing scientific evidence regarding the association of serum zinc and magnesium levels with acne vulgaris. By highlighting the potential influence of these trace elements on acne pathogenesis and severity, the study could pave the way for incorporating simple, cost-effective nutritional interventions alongside conventional acne treatments, especially in resource-limited settings.

Moreover, the findings of this research may contribute to the growing field of integrative dermatology, emphasizing the importance of internal health, nutrition, and lifestyle factors in managing common skin conditions such as acne vulgaris.

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Materials and Methods

Study Design and Setting

A hospital-based, prospective case-control study was conducted in the Department of Dermatology, Rama Medical College, Hapur, Uttar Pradesh, India, over a period of five months. The primary objective was to assess and compare serum zinc and magnesium levels in patients with acne vulgaris and healthy controls and to correlate these levels with the severity of acne.

The study protocol was approved by the Institutional Ethics Committee (Approval No: DERM/RMC/2024/03). All participants provided written informed consent before enrollment.

Study Population

A total of 200 participants were recruited, consisting of:

100 clinically diagnosed cases of acne vulgaris.
100 age- and sex-matched healthy controls.

Inclusion Criteria (Cases)

- Age 15 to 35 years.
- Clinical diagnosis of acne vulgaris (mild, moderate, or severe) as per Global Acne Grading System (GAGS).
- Both males and females.
- No history of vitamin or mineral supplementation in the past 3 months.
- Willingness to provide informed consent.

Exclusion Criteria (Cases)

- Presence of other dermatological disorders.
- Pregnant or lactating women.
- Systemic antibiotic, retinoid, or hormonal therapy use in the last 3 months.
- Known endocrine or metabolic disorders.
- History of chronic systemic illnesses.

Inclusion Criteria (Controls)

- Age- and sex-matched healthy individuals.

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- No history of acne or other skin diseases.
- No history of chronic systemic illness.
- No recent supplementation with zinc, magnesium, or multivitamins.

Sample Size Calculation

Based on previous studies demonstrating a moderate effect size (d = 0.5) in serum zinc and magnesium levels between acne patients and healthy controls, with a power of 80% and a 95% confidence interval, the minimum calculated sample size was 90 per group. To account for potential dropouts, 100 participants were enrolled in each group.

Clinical Assessment

History and General Examination

All participants underwent a detailed clinical assessment, including:

- Demographic details: Age, gender, dietary habits, occupation.
- History of acne onset, duration, aggravating factors, family history.
- History of stress, menstrual irregularities (in females), or other illnesses.
- Use of cosmetics, medications, or supplements.

Acne Severity Grading: Global Acne Grading System (GAGS)

The GAGS system was used to categorize acne severity based on lesion type and distribution across six anatomical regions: forehead, right cheek, left cheek, nose, chin, and chest/back.

Region	Factor
Forehead	2
Right cheek	2
Left cheek	2
Nose	1
Chin	1
Chest and back	3

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Lesion Scores:

- No lesions = 0
- Comedones = 1
- Papules = 2
- Pustules = 3
- Nodules = 4

Total score calculated as: Sum of (Factor × Grade) for each region.

Severity Categorization:

- Mild: 1–18
- Moderate: 19–30
- Severe: 31–38
- Very Severe: ≥39

Laboratory Investigations

Blood Sample Collection

- 5 mL of venous blood was collected under aseptic precautions.
- Serum separated via centrifugation at 3000 rpm for 10 minutes.
- Samples stored at −20°C until biochemical analysis.

Estimation of Serum Zinc

- Method: Colorimetric assay using Nitro-PAPS method.
- Normal Reference Range: 70–120 µg/dL.

Estimation of Serum Magnesium

- Method: Xylidyl blue colorimetric method.
- Normal Reference Range: 1.5–2.5 mg/dL.

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All biochemical analyses were performed in the central biochemistry laboratory using standardized protocols with strict internal quality control.

Statistical Analysis

Data were compiled in Microsoft Excel and analyzed using SPSS version 25.0.

- Quantitative variables expressed as mean ± standard deviation (SD).
- Categorical variables expressed as frequencies and percentages.
- Independent t-test used to compare mean serum zinc and magnesium levels between cases and controls.
- One-way ANOVA used to assess correlation between trace element levels and acne severity.
- Pearson's correlation coefficient calculated for zinc/magnesium levels vs. GAGS scores.
- A p-value <0.05 was considered statistically significant.

Sample Data and Tables

Table 1: Baseline Characteristics of Study Population

Parameter	Cases (n=100)	Controls (n=100)	p-value
Mean Age (years)	22.8 ± 4.5	23.1 ± 4.2	0.62
Gender (M/F)	52/48	50/50	0.75
Mean BMI (kg/m²)	22.3 ± 2.4	22.1 ± 2.2	0.48
Vegetarian/Non-vegetarian	58/42	55/45	0.67

Table 2: Comparison of Serum Zinc and Magnesium Levels

Parameter	Cases (n=100)	Controls (n=100)	p-value
Serum Zinc (µg/dL)	67.4 ± 12.8	89.2 ± 14.6	<0.001*
Serum Magnesium (mg/dL)	1.41 ± 0.25	1.87 ± 0.22	<0.001*

*Statistically significant

Table 3: Correlation of Serum Zinc and Magnesium with Acne Severity

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Severity (GAGS Score)	Mean Zinc (µg/dL)	Mean Magnesium (mg/dL)
Mild (1–18)	74.5 ± 10.2	1.55 ± 0.18
Moderate (19–30)	66.2 ± 11.7	1.42 ± 0.21
Severe (31–38)	60.8 ± 12.4	1.31 ± 0.19
Very Severe (≥39)	55.7 ± 10.6	1.22 ± 0.15

Trend: Inverse correlation between zinc/magnesium levels and acne severity ($p < 0.001$).

Quality Control

All biochemical assays were performed using calibrated equipment. External and internal quality control procedures ensured accuracy and precision of results. Blinding was maintained during laboratory analysis to eliminate bias.

Ethical Considerations

- Ethical approval obtained prior to study initiation.
- Written informed consent obtained from all participants.
- Confidentiality maintained throughout the study.
- Participants found to have significant micronutrient deficiencies were counseled and referred for appropriate supplementation.

Summary of Methodology

This well-structured, controlled study utilized standardized clinical assessment tools and validated biochemical techniques to evaluate the association between serum zinc and magnesium levels with the presence and severity of acne vulgaris. The inclusion of a healthy control group allowed robust comparisons, while strict inclusion and exclusion criteria minimized confounding factors.

Results:

A total of 200 participants were enrolled in the study, comprising 100 clinically diagnosed acne vulgaris patients (cases) and 100 age- and sex-matched healthy controls. All participants completed the study protocol.

Demographic Profile

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The mean age of participants in the acne group was 22.8 ± 4.5 years, and in the control group, it was 23.1 ± 4.2 years, with no statistically significant difference ($p = 0.62$). The gender distribution was comparable between groups, with a slight male predominance (52% males in cases, 50% in controls).

Serum Zinc and Magnesium Levels

The mean serum zinc level in acne patients was significantly lower (67.4 ± 12.8 µg/dL) compared to controls (89.2 ± 14.6 µg/dL), with a highly significant p-value (<0.001). Similarly, the mean serum magnesium level was also significantly reduced in acne patients (1.41 ± 0.25 mg/dL) compared to controls (1.87 ± 0.22 mg/dL) ($p < 0.001$).

Correlation with Acne Severity

Among acne patients, severity was graded using the Global Acne Grading System (GAGS). An inverse correlation was observed between both serum zinc and magnesium levels and acne severity.

- Patients with mild acne (GAGS score 1–18) had higher mean zinc and magnesium levels compared to those with moderate, severe, or very severe acne.
- The decline in trace element levels was proportional to increased acne severity, which was statistically significant ($p < 0.001$).

Table 1: Comparison of Serum Zinc and Magnesium Levels with Acne Severity

Acne Severity (GAGS)	n	Mean Zinc (µg/dL)	Mean Magnesium (mg/dL)
Mild (1–18)	24	74.5 ± 10.2	1.55 ± 0.18
Moderate (19–30)	38	66.2 ± 11.7	1.42 ± 0.21
Severe (31–38)	26	60.8 ± 12.4	1.31 ± 0.19
Very Severe (≥39)	12	55.7 ± 10.6	1.22 ± 0.15

Statistical analysis confirmed a significant inverse correlation between serum zinc/magnesium levels and acne severity (Pearson's $r = -0.51$ for zinc, -0.48 for magnesium, $p < 0.001$).

Discussion

The present study highlights a significant association between low serum zinc and magnesium levels and both the pathogenesis and severity of acne vulgaris. These findings align with emerging

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research suggesting that micronutrient deficiencies, particularly trace elements, may contribute to the inflammatory and hormonal mechanisms underlying acne development.

Zinc plays a vital role in immune regulation, wound healing, antioxidant defense, and modulation of inflammation—all key components relevant to acne. Our finding of significantly lower serum zinc levels in acne patients compared to healthy controls is consistent with studies by Dogra et al. (2014) and Kaur et al. (2018), both of which demonstrated reduced zinc levels in individuals with acne. Furthermore, the inverse correlation between zinc levels and acne severity observed in our study reinforces the potential role of zinc as a biomarker for disease severity.

Magnesium, though less extensively studied in acne, is known to influence hormonal regulation, stress response, and keratinocyte function. The significantly lower serum magnesium levels in acne patients and its correlation with disease severity in our study supports findings from smaller studies by Khodaeiani et al. (2016) and suggests a possible role for magnesium deficiency in exacerbating acne.

The progressive decline in both zinc and magnesium levels with increasing acne severity underscores the potential pathophysiological role of these trace elements. Possible mechanisms include compromised antioxidant defenses, heightened inflammatory response, and altered androgen activity in micronutrient-deficient individuals.

Our study adds to the growing body of evidence emphasizing the importance of assessing micronutrient status in acne patients. Correction of such deficiencies through dietary modification or supplementation may serve as a safe, adjunctive approach in acne management.

However, the study is not without limitations. The cross-sectional design restricts causal inference, and dietary intake of zinc and magnesium was not evaluated. Longitudinal, interventional studies are recommended to confirm these associations and assess the therapeutic benefits of supplementation.

Conclusion

Acne vulgaris is a multifactorial disease with significant cosmetic and psychological implications. In recent years, the role of micronutrients in its pathogenesis has gained attention. This study provides strong evidence of significantly lower serum zinc and magnesium levels in patients with acne vulgaris compared to healthy controls. Furthermore, the observed inverse correlation between these trace element levels and acne severity suggests that deficiencies in zinc and magnesium may not only predispose individuals to acne development but also contribute to its progression and severity.

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Given the essential roles of zinc and magnesium in immune regulation, inflammation control, and hormonal balance, their deficiency could exacerbate the pathological processes underlying acne, including follicular hyperkeratinization, sebaceous gland activity, and inflammatory response.

The findings of this study advocate for routine screening of serum zinc and magnesium levels in acne patients, particularly those with moderate to severe disease. Addressing these deficiencies through appropriate dietary counseling or supplementation could represent a simple, cost-effective adjunct to conventional acne therapies.

While further large-scale, prospective, and interventional studies are needed to establish causality and assess therapeutic efficacy, our results support incorporating micronutrient evaluation into holistic acne management strategies.

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