# Association of Plasma Zinc Status with Severity of Lesions in Patients with Acne Vulgaris: A Cross-Sectional Study

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**KEYWORDS**
Acne Vulgaris, Zinc Deficiency, Plasma Zinc, Acne Severity, Hypozincemia.

**ABSTRACT**
Background: Zinc (Zn) is an essential trace mineral that plays a critical role in maintaining overall skin health and functionality. Zn deficiency has been linked to various dermatological conditions, including acne, eczema, and delayed wound healing, highlighting the mineral's indispensable role in promoting skin resilience and health. Some investigators have refuted these findings. Objective: was to determine plasma Zn level and Zn status in patients with Acne vulgaris (AV) belonging to Nowshera, Khyber Pakhtunkhwa (KPK) and to find any possible relationship between Zn status & severity of the acne lesions. Methods: Hundred patients of either sex with untreated AV were randomly selected in a cross-sectional study. Based on the Global Acne Grading System (GAGS) the acne lesions were categorized as mild, moderate & severe. Blood samples were taken for determination of serum Zn. The relationship of Zn status with severity of lesions was determined with Pearson Correlations coefficient (r). Results: The study included 42 males and 58 females with male to female ratio of 1:1.4. Mean age was 21.8 years. The average plasma zinc level across the cohort was 67.4 ± 12.6 µg/dL, with males showing slightly higher zinc levels (69.1 ± 11.8 µg/dL) than females (65.8 ± 13.2 µg/dL), though this difference was not statistically significant ($p = 0.092$). 22% had mild acne, 46% moderate acne and 32% had severe acne. Patients with severe acne had significantly lower plasma zinc levels (60.2 ± 10.4 µg/dL) compared to those with mild acne (73.1 ± 13.1 µg/dL) ($p < 0.01$). Pearson's correlation analysis revealed a significant inverse relationship between plasma zinc status and acne severity ($r = -0.43$, $p < 0.001$), indicating that lower zinc levels were associated with more severe acne. No significant gender differences were observed in the relationship between zinc levels and acne severity. Conclusion: Pasma Zn concentration is markedly decreased in patients with AV and the more severe is the lesion, the more Hypozincemia. Hence, Plasma Zn status is associated negatively with severity of AV lesions in the studied population.

## 1. Introduction

Zinc is a trace element which in the body is primarily found in ionic form ($Zn^{2+}$) i.e. divalent state. It has a coordination number of 4 and is highly reactive, typically binding with specific amino acids in proteins to form "zinc finger" structures. These structures with a tetrahedral disposition of ligands around the metal, help stabilize proteins and regulate gene expression, particularly those involved in cell growth, division, and repair—all crucial for healthy skin[1]. Zn is involved in various biochemical processes by acting as a cofactor for over 300 enzymes including those involved in DNA synthesis, RNA transcription, cell division, and protein synthesis, which are fundamental for skin repair and regeneration[2]. That is the reason it is essential for maintaining skin health and integrity by affecting epithelial differentiation. Zinc doesn't directly act as an antioxidant but supports enzymes like superoxide dismutase (SOD), which protect skin cells from oxidative stress caused by free radicals. Oxidative stress can lead to premature aging and damage to skin tissue[3]. Zinc plays a key role in modulating the immune system, supporting the function of macrophages and neutrophils, and regulating the production of cytokines, which helps control inflammation. It helps maintain the acid-base balance of the skin, which is essential for barrier function. It stabilizes skin's pH, ensuring it stays in the slightly acidic range, which is optimal for fighting off harmful bacteria[3, 4].AV is a common dermatological condition, being the eighth most prevalent disease in the world affecting adolescents (90–95% of the mid-teen population) and adults[5]. Four main factors contribute to its pathogenesis: excess sebum production, follicular hyperkeratinisation, inflammation & bacterial

colonization (Cutibacterium acnes formerly Propionibacterium acnes, within the follicle)[6-10]. At puberty, sebaceous glands get stimulated by the androgens to swell and secrete sebum that travels up the hair follicles and spreads to the skin surface ultimately blocking the drains and leading to acne[11, 12].

AV is a disorder of the pilosebaceous glands which can present clinically as a spectrum of lesions including papules, pustules, comedones and nodules. Lesions of AV usually appear on the face and less commonly on the neck, chest, upper back and arms, areas of the body which are rich in hormonally sensitive abundant sebaceous glands[13]. Acne severity is assessed by a quantitative scoring system, GAGS. Doshi and colleagues[14] were the first to develop it in 1997. Scores of six regions i.e. forehead, cheek, chin, nose, chest and upper back are added together to get the total severity score. Each regional score is derived by multiplying the factor constant for each region (1 for chin & nose, 2 for forehead & each cheek, 3 for chest and upper back) by another factor awarded according to the presence of a highest weighted lesion in a particular region (1 for ≥ one comedone, 2 for ≥ one papule, 3 for ≥ one pustule, and 4 for ≥ one nodule)[15]. While genetic predisposition, hormonal fluctuations, and lifestyle factors are well-established contributors to acne pathogenesis, emerging evidence suggests nutritional status, particularly trace elements like Zn, have a potential role in the modulation of acne severity[1]. Zn has been shown to inhibit the activity of 5α-reductase, an enzyme that converts testosterone to dihydrotestosterone (DHT), thereby reducing sebaceous gland activity and sebum production[16]. Moreover, zinc's involvement in the antioxidant defense system, through the activity of zinc-dependent enzymes such as superoxide dismutase (SOD), helps protect skin cells from oxidative damage caused by free radicals, which can exacerbate acne lesions[17].The role of Zn in acne treatment has been supported by clinical studies showing that individuals with acne often have lower serum zinc levels compared to those without the condition, indicating a potential link between zinc deficiency and acne severity[15]. Supplementation with zinc has been associated with reduced inflammation and improvement in the clinical presentation of acne[20]. Zinc's antimicrobial properties also inhibit the proliferation of Cutibacterium acnes, the bacteria involved in acne pathogenesis, further supporting its therapeutic role in acne management. Zinc can inhibit the activation of nuclear factor-kappa B (NF-κB), a transcription factor involved in the production of pro-inflammatory cytokines, thereby reducing lesion formation and improving clinical outcomes [21].Clinical evidence has demonstrated the effectiveness of various zinc formulations, such as zinc sulfate, zinc gluconate, and topical zinc, in reducing the number of inflammatory lesions, with some studies showing comparable efficacy to antibiotics in the treatment of mild to moderate acne[22-24]. However, conflicting findings in the literature underscore the need for further investigation into this relationship, particularly in different populations and age groups.

This study aims to explore the association between plasma zinc levels and the severity of acne vulgaris in a sample of 100 patients presenting to a dermatology outpatient department. We hypothesized that lower plasma zinc levels would be associated with greater acne severity, supporting the notion that zinc status could serve as a biomarker for acne management and treatment outcomes.

## 2. Materials and Methods

The study was conducted for a period of six months, the dermatology department of a tertiary care hospital, QHAMC Nowshera in Khyber Pakhtunkhwa. This was a cross-sectional analytical study in which one hundred (100) patients of either gender in adolescent or adult age groups, presenting with different lesions of AV, taking no medication for any illness, were enrolled by convenience sampling as the study population. Patients with any disfiguring dermatological condition on the face other than AV, pregnancy, history of any malignant condition, current multivitamin or any antimetabolite treatment, cirrhosis liver, kidney failure, alcoholism or malabsorption syndrome were excluded. Written informed consent & detailed medical including the dietary history was taken from each patient before he/she had a complete physical & dermatological examination including GAGS scoring for categorization of lesions as mild, moderate & severe. Whole biodata and the history were recorded on an already designed questionnaire. Approval of the study was taken from the Ethical Committee of the institution.3mL of venous random blood sample was collected in EDTA coated vacutainer from the enrolled subject patients, and centrifuged at 3000 rpm for 10-12 min. The plasma so obtained was put into a zinc-free centrifuge test tube to which was added an equal proportion & volume of 10 % trichloroacetic acid (TCA) and thoroughly mixed. Protein precipitate was obtained after centrifuging the mixture. 1 ml of zinc reagent & 1 ml of Ammonium acetate buffer were added to 1 ml of the supernatant. A pink colored complex was formed after 15 minutes. In a UV-Visible spectrophotometer, the absorbance of the test sample was measured against the Zn standard at 560 nm. Finally, a calibration curve was created by plotting absorbance values and the concentration of the Zn standard. Based on the absorbance readings, Zn concentration was measured in μg/dL (The normal

value was accepted as 70–120 µg/dL).Data was analyzed using SPSS version 22. Descriptive statistics in the form of Mean±SD were calculated for zinc levels in all three severity categories of lesions. "Student-t Test" was applied to test the significance of the difference between the three different groups of severity of lesions. Pearson's correlation test was employed to assess the relationship between plasma zinc levels and acne severity. A p-value < 0.05 was considered statistically significant.

## 3. Results

A total of 100 patients were included in the study. 42 were males (42%) and 58 were females (58%). The mean age of the patients was 21.8 years with a range between 16 and 34 years. 89 (89%) subjects were single and 11 (11%) patients were married. The average plasma zinc level across the cohort was 67.4 ± 12.6 µg/dL, with males showing slightly higher zinc levels (69.1 ± 11.8 µg/dL) than females (65.8 ± 13.2 µg/dL), though this difference was not statistically significant ($p = 0.092$). Minimum Zn level was 44 µg/dL and maximum, 92 µg/dL among the studied population.The distribution of acne severity based on the GAGS scores was as follows: mild acne (22%), moderate acne (46%), and severe acne (32%). Patients with severe acne had significantly lower plasma zinc levels (60.2 ± 10.4 µg/dL) compared to those with mild acne (73.1 ± 13.1 µg/dL) ($p < 0.01$).Pearson's correlation analysis revealed a significant inverse relationship between plasma zinc levels and acne severity ($r = -0.43$, $p < 0.001$), indicating that lower zinc levels were associated with more severe acne. No significant gender differences were observed in the relationship between zinc levels and acne severity.

**Table 1: Distribution of Acne Severity by GAGS Score**

| Acne Severity | Males (n=42) | Females (n=58) | Total (n=100) |
|---|---|---|---|
| Mild Acne (%) | 9 (21.4%) | 13 (22.4%) | 22 (22%) |
| Moderate Acne (%) | 19 (45.2%) | 27 (46.6%) | 46 (46%) |
| Severe Acne (%) | 14 (33.3%) | 18 (31.0%) | 32 (32%) |

**Table 2: Plasma Zinc Levels by Acne Severity**

| Acne Severity | Plasma Zn (µg/dL) | p-value |
|---|---|---|
| Mild Acne | 73.1 ± 13.1 | < 0.01 (S) |
| Moderate Acne | 66.8 ± 12.5 | > 0.05 (NS) |
| Severe Acne | 60.2 ± 10.4 | < 0.01 (S) |
| Total (Overall) | 67.4 ± 12.6 | - |

**Table 3: Gender Differences in Statistical Measures for Plasma Zinc Levels and Acne Severity**

| Variable | Pearson's Correlation (r) | Odds Ratio (OR) | 95% CI (OR) | Mean Zinc Level (µg/dL) | | Relative Risk (RR) | p-value |
|---|---|---|---|---|---|---|---|
| | | | | Mild Acne | Severe Acne | | |
| Males (n=42) | -0.41 | 2.5 | 1.2 – 5.0 | 61.0 ± 10.2 | 72.5 ± 12.9 | 2.2 | > 0.05 |
| Females (n=58) | -0.44 | 2.9 | 1.6 – 5.3 | 59.8 ± 10.6 | 73.6 ± 13.3 | 2.4 | > 0.05 |
| Total (n=100) | -0.43 | 2.8 | 1.5 – 5.2 | 60.2 ± 10.4 | 73.1 ± 13.1 | 2.3 | < 0.001 |

## 4. Discussion

Some of the researchers have reported an association between acne vulgaris & low plasma zinc status while others didn't find the same. The findings of our study demonstrate a significant inverse correlation between plasma zinc levels and acne severity, suggesting that zinc deficiency may exacerbate the condition. This aligns with prior studies, such as those by Yeşim Kaymak et al [25], Goodarzi et al [26], Gaber et al [27], Kazeminejad et al [28]& Alhassan et al [29], which reported similar findings in diverse populations.

Our study didn't demonstrate any correlation between age of patients & Zn level. This result is in agreement with that demonstrated by Rostami et al [15]. They observed no correlation between Zn level and age in patients with acne vulgaris.

Our results were consistent with a study conducted by Yee et al [30]. This was a meta-analysis and the mean serum zinc levels reported in the twelve studies mentioned in this study were slightly higher 96.308 ± 4.053 µg/dL in patients with AV compared to our study in which Zn level (mean ± STD) was 67.4 ± 12.6 µg/dL. The large sample size in that meta-analysis as compared to ours may be the reason for this difference in both studies. Importantly, the twelve studies included in that meta-analysis were from different countries, including USA, UK, Italy, Iran, Iraq, France, Sweden and India. These depended on the supply of zinc and determination of Zn levels for a certain period of time.

In a study by Amer et al.[31] serum zinc levels were found to be significantly lower in patients with acne vulgaris in advanced grades compared to the control group. In another study by Ozuguz [32] et al, serum zinc levels were determined in patients with acne and healthy controls who were sex- and age-matched. Acne severity was assessed in all patients and grouped as mild, moderate, severe, and very severe. A negative correlation was found between acne severity and zinc levels.

Michaelsson [33] et al conducted a study by comparing the levels of retinol binding protein (RBP) and zinc in patients with acne and controls. RBP is formed and secreted by the liver for which Zn is essential. The plasma RBP level reflects the available amount of vitamin A to the tissues. This was low in patients with severe acne. They suggested that treatment with oral zinc may have a good effect in patients with severe acne. These findings are consistent with results of our study in which there was a significant correlation between serum zinc levels with severity and type of acne lesions.

In a study by Arora PN [34] et al, plasma zinc levels were determined in patients of various skin diseases and healthy controls. The Zn levels were found to be significantly lower in AV & certain other disorders as compared to healthy controls while in some of other skin disorders like aphthous ulcers & vitiligo, no significant correlation was found.

El-Dibany [35] et al in their study observed no statistically significant correlation between severity of acne lesions & serum zinc level which observation is in disagreement with our study.

However, this study is not without limitations. The cross-sectional design precludes the establishment of causality between zinc deficiency and acne severity. Moreover, factors such as dietary intake and absorption rates of zinc were not assessed, which could influence plasma zinc levels. Longitudinal studies with larger sample sizes and controlled zinc supplementation protocols are needed to further elucidate the role of zinc in acne management.

## 5. Conclusion

This study provides evidence of a significant inverse association between plasma zinc levels and acne severity, highlighting the potential importance of zinc status in the pathophysiology of acne vulgaris. These findings suggest that zinc supplementation could serve as a valuable adjunct therapy in managing patients with moderate to severe acne. Future research should aim to explore the therapeutic efficacy of zinc in randomized controlled trials.

Limitations:

This study's limitations include a relatively small sample size, restricting the generalizability of findings to a broader population. Additionally, the cross-sectional design limits the ability to establish causation between zinc deficiency and acne severity. Dietary intake and lifestyle factors affecting zinc levels were not considered, which may influence plasma zinc levels independently of acne.

Future Findings:

Future research should include larger, multi-center studies to confirm the association between plasma zinc levels and acne severity. Longitudinal studies assessing zinc supplementation's impact on acne progression and severity could provide insight into potential therapeutic benefits. Investigating other minerals and nutritional factors may also enhance understanding of acne's complex etiology.

Abbreviations of this study

1. Zn - Zinc
2. AV - Acne Vulgaris
3. KPK - Khyber Pakhtunkhwa
4. GAGS - Global Acne Grading System
5. SD - Standard Deviation
6. r - Pearson Correlation Coefficient
7. p - p-value

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## References

[1] King JC, Cousins RJ. Zinc. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR (Eds.), Modern Nutrition in Health and Disease. 11th ed. Philadelphia: Lippincott Williams & Wilkins, 2014. 189-202

[2] Vasudevan DM, Sreekumari S, Vaidyanathan K. Textbook of Biochemistry. 7th ed. Philadelphia: Jaypee Brothers Medical Publishers; 2013. Chapter 39. Mineral Metabolism and Abnormalities (Zinc); 522

[3] Nitzan YB, Cohen AD. Zinc in skin pathology and care. Journal of Dermatological Treatment. 2006; 17 (4): 205–210

[4] Bangash HK, Sethi A. Zinc and skin health: an overview. In: Handbook of Diet, Nutrition and the Skin. Human Health Handbooks no. 1 (Vol 2). Wageningen Academic; 2012. 178–195. https://doi.org/10.3920/978-90-8686-729-5_11.

[5] Bhate K, Williams HC. Epidemiology of acne vulgaris. Br J Dermatol. 2013; 168: 474-485

[6] Bellew S, Thiboutot D, Del Rosso JQ. Pathogenesis of acne vulgaris: what's new, what's interesting and what may be clinically relevant. J Drugs Dermatol. 2011;10 (6): 582-585

[7] Healy E, Simpson N. Acne vulgaris. BMJ. 1994;308 (6932): 831-3.

[8] Dawson AL, Dellavalle RP. Acne vulgaris. BMJ. 2013; 346: f 2634

[9] Aydemir EH. Acne vulgaris. Turkish Archives of Pediatrics. 2014; 49 (1): 13-16.

[10] Zouboulis CC, Eady A, Philpott M, Goldsmith LA, Orfanos C, Cunliffe WC, Rosenfield R. What is the pathogenesis of acne? Exp Dermatol. 2005: 14: 143–152.

[11] Walton S, Wyatt E, Cunliffe WJ. Genetic control of sebum excretion and acne. A twin study. Br J Dermatol 1988; 18: 393–396.

[12] Makrantonaki E, Ganceviciene R, Zouboulis C. An update on the role of the sebaceous gland in the pathogenesis of acne. Dermatoendocrinol. 2011 Jan;3(1):41-9. doi: 10.4161/derm.3.1.13900

[13] Mohiuddin AK. A Comprehensive Review of Acne Vulgaris. Clin Res Dermatol. 2019; 6 (2): 1-34. DOI: http://dx.doi.org/10.15226/2378-1726/6/2/00186

[14] Doshi A, Zaheer A, Stiller MJ. A comparison of current acne grading systems and proposal of a novel system. International Journal of Dermatology 2006; 36 (6): 416–418

[15] Mogaddam MR, Ardabili NS, Soflaee M. Correlation between the Severity and Type of Acne Lesions with Serum Zinc Levels in Patients with Acne Vulgaris. Biomed Res Int. 2014; 474108:1-8.

[16] Stamatiadis D, Bulteau-Portois MC, Mowszowicz I. Inhibition of 5 alpha-reductase activity in human skin by zinc and azelaic acid. The British Journal of Dermatology. 1988; 119 (5): 627-632. DOI: 10.1111/j.1365-21331988.tb03474x. PMID: 3207614.

[17] Altobelli GG, Susan VN, Balato A, Cimini V. Copper/Zinc Superoxide Dismutase in Human Skin: Current Knowledge. Frontiers in Medicine. 2020; 7:

[18] Altobelli GG, Van Noorden S, Balato A and Cimini V Copper/Zinc Superoxide Dismutase in Human Skin: Current Knowledge. Front. Med. 2020; 7: 183.

[19] Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016; 74: 945e973.e33.

[20] Gupta M, Mahajan VK, Mehta KS, Chauhan PS. Zinc Therapy in Dermatology: A Review. Dermatology Research and Practice. 2014; Article ID 709152, 11 pages http://dx.doi.org/10.1155/2014/709152

[21] Jarosz, M., Olbert, M., Wyszogrodzka, G. et al. Antioxidant and anti-inflammatory effects of zinc. Zinc-dependent NF-κB signaling. Inflammopharmacol 2017; 25: 11–24 https://doi.org/10.1007/s10787-017-0309-4

[22] Bae YS, Hill ND, Bibi Y, Dreiher J, Cohen AD. Innovative uses for zinc in dermatology. Dermatologic Clinics. 2010; 28 (3): 587–597

[23] Orris L, Shalita AR, Sibulkin D, London SJ, Gans EH. Oral zinc therapy of acne. Absorption and clinical effect. Archives of Dermatology. 1978; 114 (7): 1018–1020.

[24] Weimar VM, Puhl SC, Smith WH, TenBroeke JE. Zinc sulfate in acne vulgaris. Archives of Dermatology. 1978; 114 (12): 1776–1778s

[25] Kaymak Y, Adisen E, Erhan M, Celik B, Gurer MA. Zinc levels in patients with acne vulgaris. J Turk Acad Dermatol. 2007; 1(3): 71302a

[26] Goodarzi A, Roohaninasab M, Atefi NS, Bazargan AS, Ghassemi M, et al. Determination of serum levels of zinc in acne vulgaris patients: a case control study. Iranian Journal of Dermatology. 2020; 23(1): 28-31

[27] Gaber HA, Abozied AA, Abd-Elkareem IM, El-Shazly YN. Serum Zinc Levels in Patients with Acne Vulgaris and its Relation to the Severity of Disease. The Egyptian Journal of Hospital Medicine. 2019; 75(5): 2845-8.

[28] Kazeminejad A, Hajheydari Z, Taghian SS, Gholizadeh N. Serum zinc, selenium, and vitamin D levels in patients with acne vulgaris: A case−control study. J Cosmet Dermatol. 2024; 00:1-6. doi:10.1111/jocd.16494

[29] Alhassan TMMO, Abdalla AM, Alhassan EMMO, Ahmed SA. Evaluation of serum zinc level; Sudanese females patients with acne vulgaris in Khartoum State. Professional Med J 2018; 25(2): 307-312.

[30] Yee BE, Richards P, Sui JY, Marsch AF. Serum zinc levels and efficacy of zinc treatment in acne vulgaris: A systematic review and meta-analysis. Dermatologic Therapy. 2020; 33 (6): e14252. doi: 10.1111/dth.14252

[31] Amer M, Bahgat MR, Tosson Z, Mowla MY, Amer K. Serum zinc in acne vulgaris. International journal of dermatology. 1982; 21(8): 481-4. doi: 10.1111/j.1365-4362. 1982.tb03188.x

[32] Ozuguz P, Dogruk Kacar S, Ekiz O, Takci Z, Balta I, Kalkan G. Evaluation of serum vitamins A and E and zinc levels according to the severity of acne vulgaris. Cutan Ocul Toxicol. 2014; 33(2): 99-102

[33] Michaëlsson G, Vahlquist A, Juhlin L. Serum zinc and retinol-binding protein in acne. British Journal of Dermatology. 1977; 96(3): 283-6. doi: 10.1111/j. 1365-2133. 1977.tb06138.x

[34] Arora PN, Dhillon KS, Rajan SR, Sayal SK, Das AL. Serum Zinc Levels in Cutaneous Disorders. Med J Armed Forces India. 2002; 58(4): 304-306.

[35] El-Dibany SA, Elhassi R. Evalution Serum Zinc Level in Acne and Correlation with Severity Acne Vulgaris Benghazi - Libya. Int J Clin Dermatol Res. 2019; 7(1): 197-200.