

## A role of zinc and magnesium in the pathogenesis and severity of acne vulgaris

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### Abstract

**Background:** Acne vulgaris is a chronic inflammatory condition of the pilosebaceous unit which occurs in adolescent age groups. Recently, in the dermatological fields, the serum levels and the roles of Zn and Mg have been studied, especially in acne vulgaris, but the results were controversial. **Objective:** The aim of the present study is to investigate a relationship between the severity of acne and the serum levels of zinc (Zn) and magnesium (Mg) in the pathogenesis and severity of acne vulgaris. **Methods:** This case-controlled study was conducted in the Department of Dermatology and Venereology, Integral Institute of Medical Science & Research, Kursi Road, Lucknow. 60 patients with acne vulgaris, whose ages ranged from 20-35, and 60 healthy subjects as controls, whose ages ranged from 20-35, were included in this study. Patients were subdivided into three groups according to the severity of their acne: the mild acne group (n = 20), the moderate acne group (n = 20), and the severe acne group (n = 20). Investigations included serum estimation of Zn, Cu, and Mg in both patient and control groups. **Results:** The (mean ± SD) values of serum levels of Zn and Mg did not differ significantly between the patient [all severities combined] and control groups. However, serum Zn level was significantly decreased in the severe acne group compared with controls (P = 0.0001), mild (P = 0.0001), and moderate (P = 0.000) acne groups (P<0.05). Serum Mg concentration was significantly lower in the severe acne group compared with the mild acne group (P<0.011). **Conclusion:** This study revealed a significant association between serum levels of each of Zn and Mg with the severity of acne.

**Keywords:** acne vulgaris; zinc; magnesium

### Introduction

Acne vulgaris is the most common cutaneous disorder manifested by comedones, papules, pustules, and cysts. The etiology of acne appears to be multifactorial, involving follicular hyperkeratinization, hormonal function, proliferation of *Propionibacterium acne*, increased serum production, and inflammation. Despite a significant body of scientific literature, the sequence of events leading to the production of acne lesions is not well understood [1]. Specific dietary agents and certain supplements are known to enhance the health and appearance of the skin by

improving immune function at the skin level and providing therapeutic bioactive agents that assist in the treatment of many skin conditions, such as psoriasis, eczema, and acne [2, 3]. It has become increasingly clear that nutritional factors such as vitamins and minerals are involved in the pathogenesis of acne [4].

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit occurring in the adolescent age group. [5] Approximately 85% of the population of 18–22 years of age have some degree of this disorder. [6] Acne is rarely life-threatening, but its cosmetic effects leave scars—both physical and psychological—that can be lifelong. It can cause social problems in the house, at school, and at work. [7] Acne is a multifactorial disease depending on genetic predisposition, endocrine factors, keratinization pattern of follicular epithelium, colonization of sebaceous follicle, and inflammatory response of the host. [8] Treatment of acne is far from optimal. Treatment of acne is still a perplexing problem. [9] The various pathogenetic mechanisms direct to different approaches to therapy methods of reducing sebum production, reducing pilosebaceous duct blockage, reducing bacterial colonization, and modifying inflammation in the host. [10] Topical therapy with benzoyl peroxide, antibiotics, vitamin A acid, sulfur, salicylic acid, and systemic agents like oral antibiotics [11], cis-retinoic acid, estrogen, and antiandrogens is tried with varying results. Each one has its own advantages and disadvantages. [12] The striking effect of zinc on severe pustular acne in a patient with acrodermatitis enteropathica aroused interest in zinc in acne. [13]

Zinc is anti-inflammatory. Zinc stabilizes macromolecules and biological membranes. It influences the migration rate and phagocytic activity of macrophages, interfering with the dynamics of the inflammatory process. [14] Elevated levels of zinc in vitro as well as in vivo affect various functions of cells. Functional immobilization, inactivation, and paralysis of the cell wall were proposed for such an inhibitory effect of zinc. This effect has been demonstrated so far on mast cells, platelets, macrophages, polymorphonuclear cells, and spermatozoa. Action on cell membranes has shown that mast cells are inhibited from releasing histamine and could modify the inflammatory state. [15] Zinc adversely affects neutrophil chemotaxis and complement activation. Do patients with acne have zinc deficiency or can zinc modify acne is a question that has not yet been settled.

Acne vulgaris in general was more common in males than females (74.24%) versus (61.9%) [16-17]. On a literature review, we found several studies, of which [18], conducted on female patients with acne to investigate the pathogenesis of this disease; however, few involved male acne patients. Therefore, the aim of the present study is to assess the serum concentrations of zinc and magnesium in male Iraqi patients with acne vulgaris and to clarify their correlation with the severity of acne.

## **Material and Methods**

This case-controlled study was carried out in the Department of Dermatology, Integral Institute of Medical Science & Research, Kursi Road, Lucknow. The study involved 60 male patients with acne vulgaris, aged range between 20-35 (mean  $\pm$  SD; 21.82  $\pm$  3.77 years). Patients were divided into three groups according to the severity of their acne. A mild acne group that included 20 patients, a moderate acne group of 20

patients, and a severe acne group of 20 patients. Scoring the severity of acne was according to the following rule:

### **Inclusion criteria**

- Untreated patients of acne vulgaris of either sex diagnosed on clinical grounds were included in the study.
- Patients who gave informed consent to undergo required investigations in the study.

### **Exclusion Criteria**

- Treated cases of acne vulgaris in whom the acne is inactive.
- Pregnant, lactating, and women on oral contraceptives.
- Patients taking the following systemic drugs.

**Mild acne:** In which the count of papules is less than 10 and the count of pustules is less than 20.

**Moderate acne:** In which the count of papules ranges from 10 to 30 and the count of pustules ranges from 20 to 40.

**Severe acne:** In which the count of papules is more than 30 and the count of pustules is more than 40 [19].

### **Blood sample collection and analysis**

Five milliliters of peripheral venous blood were collected from each patient and control male in plain test tubes, left to clot, then centrifuged at 2500 rpm for 10 minutes. The separated serum was stored at -20 °C until the time of the mineral assay. Serum zinc and magnesium were determined using a flame atomic absorption spectrophotometer (AA-646 Shimadzu, Japan). Samples were diluted 1:10 with n-butanol solution as diluent [20]. Levels of serum Zn and Mg were calculated after application of absorbance on a suitable calibration curve for each element made from standard solutions.

### **Statistical Analysis**

The experimental data were expressed as mean  $\pm$  standard deviation. The significance of the differences between treatments and respective controls was analyzed using the Student's t-test and SPSS-2024.

### **Observation and result**

The control group consisted of 60 healthy males without acne and were matched for age 20-35 years (mean  $\pm$  SD; 27.87 $\pm$ 4.8 years) and body mass index (mean  $\pm$  SD; 22.7 $\pm$ 1.7 kg/m<sup>2</sup>).

**Table 1: Clinical and biochemical data for healthy male controls and patients with acne vulgaris.**

Characteristic	Control	Acne patients(	p-value
	Group (n=60)	Group (n=60)	
	mean ± SD	mean ± SD	
Age (years)	27.87±4.8	26.43±4.42	0.09
BMI(Kg/m <sup>2</sup> )	22.7±1.7	22.16±1.58	0.074
Zn(mg/dl)	100.9±5.2	98.1±7.2	0.016
Mg(mg/dl)	1.07±0.16	0.99±0.19	0.014

Table 1 shows the clinical [age and BMI values as mean ( $\pm$ SD)] and biochemical data for healthy male subjects and male patients with acne. The results showed that the mean  $\pm$  SD value of serum Zn levels of acne patients (98.1 $\pm$ 7.2 mg/dl) was lower than that of controls (100.9 $\pm$ 5.2 mg/dl), but the difference did not reach the significant level. Similarly, the mean ( $\pm$  SD) values of serum Cu and Mg levels did not differ significantly between acne male patients and controls.

**Table 2: Mean ( $\pm$  SD) values of serum zinc and magnesium concentrations in healthy controls and patients with mild-, moderate-, and severe acne vulgaris.**

Parameters	Controls (n=45)	Mild acne(n=15)	Moderate acne(n=15)	Severe acne(n=15)
Zn(mg/dl)	100.9±5.2	114.9±7.41	92.45±7.28	81.1±6.6
Mg(mg/dl)	1.07±0.16	1.2±0.11	1.09±0.14	0.99±0.13

The mean ( $\pm$ SD) values of serum Zn and Mg concentrations in patients with mild, moderate, and severe acne types and the male control group are shown in Table 2 and Figures 1 and 2. These results revealed that the mean value of serum Zn levels of severe acne (81.1 $\pm$ 6.6 mg/dl) was significantly lower than that of healthy males (100.9 $\pm$ 5.2 mg/dl, P = 0.0001), mild acne (114.9 $\pm$ 7.41 mg/dl), and moderate acne-types (92.45 $\pm$ 7.28 mg/dl). Moreover, patients with a moderate type of acne had significantly lower levels of serum Zn mean ( $\pm$  SD) value than those with a mild acne type (P = 0.0001).

The mean ( $\pm$ SD) value of serum Cu levels did not differ significantly between the acne group types and controls as well as between the acne patient groups themselves. With regard to serum Mg level, the mean ( $\pm$ SD) value of serum Mg levels was significantly decreased in severe type of acne patients (0.99 $\pm$ 0.13 mg/dl) when compared with that of mild acne type (1.2 $\pm$ 0.11 mg/dl). However, the mean values of serum Zn and Mg concentrations of acne patients did not differ significantly with respect to their BMI values. Furthermore, the results of the present study revealed no

significant correlation between the serum levels of the studied elements (Zn and Mg) and the values of BMI and age of patients and control groups ( $p > 0.05$ ).

## **Discussion**

Zinc is an essential trace element that is necessary for growth and development at all stages of life [21]. Zinc has been recognized as a distinct element since 1509 but was not identified as an essential mineral until the 1900s. In 1961, a link was established between zinc deficiency, endemic hypogonadism, and dwarfism in rural Iran [22]. Zinc plays a key role in physical growth and development, functioning of the immune system, reproductive health, sensory function, and neurobehavioral development. Zinc might play an important role in the development of alterations in keratinocytes with aging [23]. It has been estimated that around 33% of the world's human population has diets deficient in zinc, but this ranges between 4 and 73% in different countries [24]. Mild zinc deficiency is associated with depressed immunity, impaired taste and smell, onset of night blindness, and decreased spermatogenesis. Severe zinc deficiency is characterized by severely depressed immune function, frequent infections, bullous pustular dermatitis, diarrhea, and alopecia [25]. Zinc and vitamin A are essential for normal epithelial development. A decreased serum zinc level could also lead to increased androgenic production, which influences the activity of sebaceous glands.

The present study showed that serum Zn level was lower in acne patients than in healthy male controls, but the difference was not significant. This finding is consistent with that observed by Nasiri et al. in 2009 [26], who found an insignificant decrease of serum Zn in their Indian people compared with healthy controls. However, the present study has shown that serum Zn levels of the severe type of acne were significantly lower than those of healthy controls, mild, and moderate types of acne. These data are in agreement with that reported by Michaelsson et al. and Amer et al. [27], who showed that serum Zn level was significantly reduced in severe acne male patients compared with controls. These authors suggested that low levels of zinc in the serum of patients with severe acne may provide a rationale for the beneficial effect of oral zinc treatment seen in clinical practice [27].

The mineral zinc is emerging as a vital nutrient for skin health and appearance. Zinc nutritional status is necessary for oil gland function, local skin hormone activation, wound healing, skin inflammation control, and regeneration of skin cells. Zinc supplementation has been used with success in the treatment of many acne cases [28]. Studies indicated that most individuals consume only 8–9 mg/day of zinc from dietary sources, whereas the recommended daily acquisition (RDA) for zinc is set at 15 mg/day for adults [29]. A review reported by Dr. Preston indicated that lack of zinc is a recipe for acne [30]. Nasiri et al. in 2009 concluded from their study that zinc as an anti-inflammatory element may play a role in the pathogenesis of acne, and there is a need for further studies [26].

The present study also found that serum magnesium level was significantly decreased in severe acne patients compared with mild acne patients. This element (Mg) is vital for the production of proteins and enzymes in every tissue of the body. This includes the proteins and enzymes of skin cells, also absolutely essential for the proper use of the vitamin Pyridoxine [30]. where new cells are constantly being produced. It is also

absolutely essential for the proper use of the vitamin Pyridoxine [30]. The author of the latter review suggested taking supplements of about 500 mg of this mineral each day is essential.

Elements are also important to the mammalian target of the rapamycin (mTOR) protein. This serine and threonine protein kinase regulates protein translation through a rapamycin-sensitive pathway. mTOR protein integrates signals from mitogens and the nutrients glucose and amino acids to regulate cellular growth and proliferation. The study of Lynch et al. [31] indicated that Zn<sup>2+</sup> regulates, but is not absolutely required for, mTOR protein kinase activity. Zinc also stimulated a recombinant human form of mTOR. The stimulatory effects of Zn<sup>2+</sup> were maximal at >100 μM. Concentrations of other divalent cations, Ca<sup>2+</sup>, Fe<sup>2+</sup>, and Mn<sup>2+</sup>, had no effect on the protein kinase activity of mTOR in the presence of excess Mg<sup>2+</sup>. μM but decreased and became inhibitory at higher physiologically irrelevant concentrations. Micromolar concentrations of other divalent cations, Ca<sup>2+</sup>, Fe<sup>2+</sup>, and Mn<sup>2+</sup>, had no effect on the protein kinase activity of mTOR in the presence of excess Mg<sup>2+</sup>. These authors also suggested that zinc acts at multiple steps in amino acid- and insulin cell-signaling pathways, including mTOR, and that the additive effects of Zn<sup>2+</sup> on these steps may thereby promote insulin and nutritional signaling. A study conducted by Saleh concluded that Iraqi acne patients, particularly those suffering from the severe type, have a significant elevation of serum levels of growth hormone-like growth factor-1 (IGF-1), which can stimulate androgen hormone synthesis and secretion, leading to the proliferation of sebocytes and keratinocytes resulting in aggravation of acne [32]. The results of the study conducted by Vastano et al. [33] underlined that spleen enlargement, a parameter expressing low-grade chronic inflammatory status, was a major determinant of low IGF-I/IGFBP-3 ratio than mass% fat mass (FM%) *per se*. The investigators also found a significant negative correlation between all the components of the IGF-I axis investigated and fat mass % (FM%), insulin resistance, or hepatic steatosis severity. However, FM% was a better determinant of IGF-I and IGFBP-1 than HS *per se* in the same population. In

## **Conclusion**

The present study revealed a significant association between each of the Zn and Mg levels with the severity of acne. Further studies that deal with serum concentrations of zinc, magnesium, and mTOR in severe acne patients are required.

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