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Evaluation of serum zinc concentration in atopic dermatitis patients: A comparative study

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Abstract
Background: Atopic dermatitis (AD) is a chronic inflammatory skin condition involving complex interactions between immunologic, hereditary, and environmental influences.
Aim of the study: The aim of the study is to determine whether there is a correlation or relationship between serum zinc levels and the severity of atopic dermatitis.
Patients and Methods: This case-control study was conducted at Tikrit Teaching Hospital from August 15, 2023, to March 2024, involving 45 patients aged 2-18 years and 45 unaffected individuals as controls. Patients with acute or chronic diseases, zinc supplements, corticosteroids, antibiotics, or anti-inflammatory drugs will be excluded. The Atopic Dermatitis Score Index (SCORAD) will be used as the primary assessment tool, categorizing severity into mild, moderate, and severe. Thorough physical and dermatological evaluations will be conducted for all patients, recording comprehensive data such as age, sex, occupation, residence, disease duration, associated symptoms, and family history of atopic diseases. Serum zinc levels will be assessed using the Enzyme-Linked Immunosorbent Assay (ELISA) technique to evaluate the potential relationship between zinc deficiency and atopic dermatitis severity.
Results: The study reveals that the majority of Atopic Dermatitis disease (AD) patients are adolescents aged 14-18 years, with males accounting for 71.11% of the group. The majority of AD patients live in rural areas, with 60% in rural areas and 40% in urban ones. The study also reveals that 13.33% of AD patients are classified as mild, while 24.44% exhibit moderate AD. Serum zinc levels are significantly lower in AD patients compared to the control group, with a mean of 87.85±7.79 µg/dl. The mean serum zinc levels vary across different age groups, with younger age groups and male patients exhibiting lower levels. The study also shows a progressive decrease in mean serum zinc levels with increasing severity of AD. Patients with mild AD have the highest mean serum zinc level, followed by those with moderate AD with a mean level of 87.13±6.78 µg/dl. Conversely, patients with severe AD have the lowest mean serum zinc level. This inverse relationship between AD severity and serum zinc levels suggests a potential association between zinc deficiency and the exacerbation of AD symptoms. The findings suggest that age and gender may influence serum zinc levels in atopic dermatitis patients, with younger age groups and male patients exhibiting lower levels. These findings emphasize the importance of assessing serum zinc levels in AD patients, considering demographic factors and disease severity, to inform management strategies and improve treatment outcomes.

Keywords: Atopic dermatitis (AD), chronic inflammatory skin condition, immunologic factors

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin condition involving complex interactions between immunologic, hereditary, and environmental influences. Over the last 30 years, the prevalence of AD has risen globally, affecting 20% of children and 3% of adults worldwide [1]. In established disease, inflammation and pruritus dominate the clinical picture. Other associated features include xerosis, a propensity to develop specific skin infections, and an association with mucosal allergy [2]. As inflammation is primarily a defense mechanism and mediated by both innate and adaptive immune systems, an immunological basis for the illness is now well accepted. In children under one year of age, the face and limbs and much of the body may be affected [3]. As children get older, the areas on the insides of the knees and folds of the elbows and around the neck are most commonly affected. In adults, the hands and feet are commonly affected. Scratching the affected areas worsens the eczema and increases the risk of skin infections [4].

Proper nutrition, especially adequate intake of vitamins, minerals, and elements, plays an active role in immune health. The relationship between nutrition and AD pathogenesis has been debated for many years [1]. For humans, zinc is an essential trace nutrient, involved in structural tissues and catalytic and regulatory systems for metabolic processes. The overall amount present is regulated at around 2.6 g. The skin ranks third in zinc-containing tissue in the body at around 4.2%, with a greater proportion in the epidermis than in the dermis [5]. Serum zinc concentration is preserved by homeostatic mechanisms in healthy individuals within a narrow range, although there is a growing list of conditions where zinc homeostasis is known to be affected [6]. Zinc plays an essential role in both structure and function of a range of proteins, transcription factors, enzymes, hormone receptor sites, and surface membranes in the body. It is also involved in gene expression, signal transduction and can potentiate apoptosis. Zinc is essential to the normal functioning of immunity, particularly neutrophils, natural killer cells, and lymphocytes, as well as for the skin barrier [7, 8]. In the absence of clinical signs or reliable sensitive and specific laboratory investigations, evaluation of deficiency is challenging. Zinc may result from inadequate dietary intake, or increased losses. However, a concomitant intake of a potent inhibitor of zinc absorption are likely the most common causative factor such as unrefined cereals, nuts and legumes which contain phytic acid [5]. The role of zinc as a trace element in Atopic Dermatitis has been the subject of a limited number of studies. Three studies, one controlled and two observational, tested serum zinc level in children with varying severity of atopic dermatitis and concluded a strong correlation between zinc levels and the severity of atopic dermatitis which was statistically significant [9-11].

Patients and Methods

Patients

The study will include 45 patients aged 2 to 18 years attending the Dermatology outpatient department. Additionally, 45 unaffected individuals as control group.

Methods

The primary assessment tool will be the Atopic Dermatitis Score Index (SCORAD). SCORAD comprises both objective assessments (such as erythema, edema, excoriation, lichenification, oozing/crusts, and dryness) and subjective factors (including pruritus and sleep loss). Based on SCORAD index values, severity will be categorized into mild, moderate, and severe. Mild severity will be defined as SCORAD < 25, moderate as SCORAD 25–50, and severe as SCORAD > 50. These severity categories will aid in treatment decisions.

Data Collection Methods

1. **Clinical Assessment:** Thorough physical and dermatological evaluations will be conducted for all patients to assess the severity and extent of atopic dermatitis lesions.
2. **Patient History:** Comprehensive data will be recorded, including age, sex, occupation, residence, disease duration, associated symptoms, history of asthma, allergic rhinitis, atopy, and family history of atopic diseases.
3. **Blood Samples:** Blood samples will be collected for serum zinc determination using the Enzyme-Linked Immunosorbent Assay (ELISA) technique. Serum zinc levels will be assessed to evaluate the potential relationship between zinc deficiency and atopic dermatitis severity.

Results

Demographic characteristics of atopic dermatitis patients and the control group.

The study showed that the majority of AD patients were adolescents aged 14-18 years, comprising 42.22% of the AD group. This was followed by children aged 2-6 years (31.11%) and 7-13 years (26.67%). Regarding gender, males accounted for 71.11% of AD patients, while females represented 28.89%. In terms of residence, 60% of AD patients lived in rural areas, while 40% resided in urban areas, Table 1.

Table 1: Demographic characteristics of atopic dermatitis patients and the control group

Demographic characteristics		Patients with AD				P-value
		No.	%	No.	%	
Age (Years)	2-6	14	31.11%	15	33.33%	0.57
	7-13	12	26.67%	13	28.89%	
	14-18	19	42.22%	17	37.78%	
	Total	45	100%	45	100%	
Sex	Male	32	71.11%	34	75.56%	0.52
	Female	13	28.89%	11	24.44%	
	Total	45	100%	45	100%	
Residence	Rural	27	60%	24	53.33%	0.25
	Urban	18	40%	21	46.67%	
	Total	45	100%	45	100%	

The study showed found that, 13.33% were classified as having mild AD, in contrast, 24.44% of the patients exhibited moderate AD, furthermore, 12.22% of the AD patients were classified as having severe AD, representing individuals with the most extensive and severe skin manifestations. These patients often experience intense itching, widespread inflammation, and significant impairment in their quality of life, Table 2.

Table 2: Distribution of atopic dermatitis patients regrading the severity of the disease

Severity of AD	No.	%
Mild	12	26.67%
Moderate	22	48.89%
Severe	11	24.44%

Based on SCORAD index values, severity will be categorized into mild, moderate, and severe. Mild severity will be defined as SCORAD < 25, moderate as SCORAD 25–50, and severe as SCORAD > 50

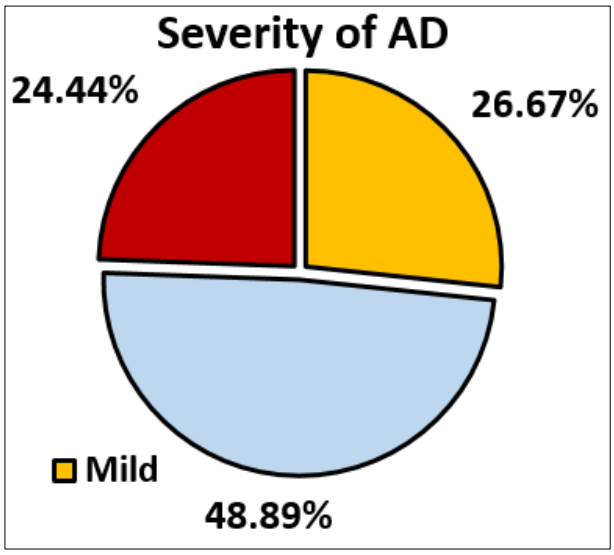

Fig 1: Distribution of atopic dermatitis patients regrading the severity of the disease

Table 3 presents a comparison between atopic dermatitis (AD) patients and the control group concerning their serum zinc levels. Serum zinc levels, measured in micrograms per deciliter (µg/dl), were found to be significantly lower in AD patients (87.85±7.79 µg/dl) compared to the control group (98.45±13.2 µg/dl). This difference between the two groups was statistically significant (p-value: 0.001),

Table 3: Comparison between AD patients and the control group regarding serum Zinc level

Serum Zinc (µg/dl)	Patients with AD (n:45)	Control group (n:45)
Mean ± SD	87.85±7.79	98.45±13.2
Minimum value	72.81	64.78
Maximum value	107.56	124.2

P-value: 0.001

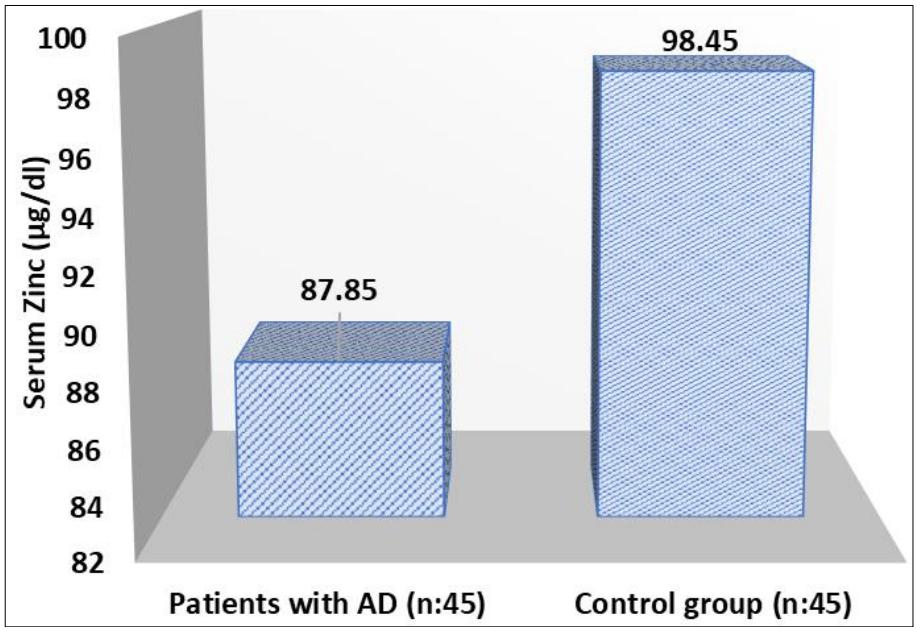

Fig 2: Comparison between AD patients and the control group regarding serum Zinc level

The study showed found that, the mean serum zinc levels varied across different age groups. Among patients aged 2-6 years, the mean serum zinc level was 83.19±7.77 µg/dl, which was significantly lower compared to patients aged 14-18 years, where the mean serum zinc level was 93.9±6.21 µg/dl (p-value = 0.003). Patients aged 7-13 years had intermediate levels of serum zinc, with a mean of 87.23±7.03 µg/dl. Male patients had a mean serum zinc level of 85.25±6.84 µg/dl, whereas female patients exhibited a higher mean level of 94.28±6.25 µg/dl. This difference was statistically significant (p-value = 0.017). No. significant difference was observed between patients residing in rural areas (mean = 87.87±6.76 µg/dl) and those in urban areas (Mean = 89.33±8.14 µg/dl) (p-value = 0.18). These findings suggest that age and gender may influence serum zinc levels in atopic dermatitis patients, with younger age groups and male patients exhibiting lower levels of serum zinc.

Table 4: Mean of serum zinc levels among atopic dermatitis patients based on age, gender, and residence

General properties		No.	Serum Zinc (µg/dl)	P-value
Age (Years)	2-6	14	83.19±7.77	0.003
	7-13	12	87.23±7.03	
	14-18	19	93.9±6.21	
Gender	Male	32	85.25±6.84	0.017
	Female	13	94.28±6.25	
Residence	Rural	27	87.87±6.76	0.18
	Urban	18	89.33±8.14	

The study showed a progressive decrease in mean serum zinc levels with increasing severity of AD. Specifically, patients classified with mild AD exhibited the highest mean serum zinc level of 94.55±6.45 µg/dl, followed by those with moderate AD with a mean level of 87.13±6.78 µg/dl. Conversely, patients with severe AD demonstrated the lowest mean serum zinc level of 82.1±5.69 µg/dl (P-value: 0001). This inverse relationship between AD severity and serum zinc levels suggests a potential association between zinc deficiency and the exacerbation of AD symptom, Table 5 and Figure 3.

Table 5: Distribution of atopic dermatitis patients regrading the severity of the disease and serum zinc

Severity of AD	Serum Zinc (µg/dl)
Mild	94.55±6.45
Moderate	87.13±6.78
Severe	82.1±5.69

P-value: 0001

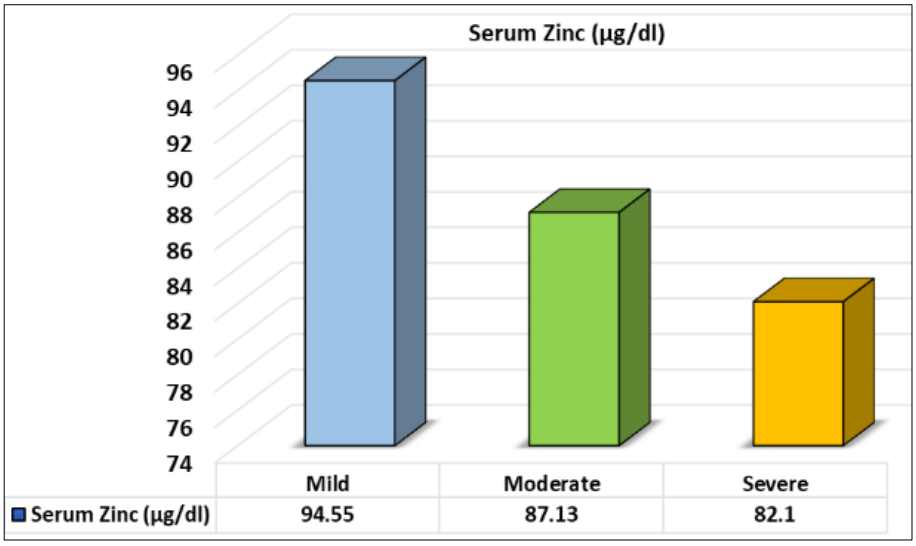

Fig 3: Distribution of atopic dermatitis patients regrading the severity of the disease and serum zinc

Discussion

The majority of AD patients were adolescents aged 14-18 years, comprising 42.22% of the AD group. This was followed by children aged 2-6 years (31.11%) and 7-13 years (26.67%). Regarding gender, males accounted for 71.11% of AD patients, while females represented 28.89%. In terms of residence, 60% of AD patients lived in rural areas, while 40% resided in urban areas. This observation aligns with several studies suggesting that AD often manifests or persists into adolescence, possibly due to hormonal changes and increased exposure to environmental triggers during this developmental stage [12-14]. In terms of gender distribution, our study reported a higher prevalence of AD among males, compared to females. This finding is consistent with previous literature suggesting a male predominance in childhood AD, although the underlying reasons for this gender disparity remain to be fully elucidated [15, 16]. It has been postulated that hormonal, genetic, and immunological factors may contribute to the observed differences in AD prevalence between males and

females, warranting further investigation into these potential mechanisms [17].

Regarding residential distribution, our findings indicate that a higher proportion of AD patients reside in rural areas compared to urban areas. This contrasts with some previous studies reporting a higher prevalence of AD in urban settings, possibly due to differences in environmental exposures, lifestyle factors, and access to healthcare services in addition to increased exposure to indoor allergens and air pollution [18] it is consistent with other research demonstrating variable AD prevalence across different geographical regions and socioeconomic backgrounds [19]. The discrepancy in AD prevalence between rural and urban areas may reflect differences in lifestyle factors, environmental exposures, and access to healthcare services, underscoring the complex interplay of socio-environmental determinants in AD pathogenesis [16].

The study demonstrated a significantly lower mean serum zinc level among AD patients (87.85±7.79 µg/dl) compared to the control group (98.45±13.2 µg/dl), with a statistically significant difference observed (p-value: 0.001).

This finding is consistent with existing literature suggesting a potential association between zinc deficiency and the development or exacerbation of AD [10, 11]. Toyran *et al.* [19] also found low serum zinc level in patients with AD as compared with control group. Several other studies found hypozincemia was observed in children with AD [20-21]. Moreover, Gray *et al.* [22] in a systematic and meta-analysis on and atopic dermatitis conclude that low zinc is associated with AD. Farhood Gray *et al.* [9] in recent study found that serum zinc was lower in patients than in controls Serum zinc was significantly lower in female controls than in male controls (P=0.009). While, Al-Ghurabi *et al.* [23] found no statistical difference in serum zinc level between patients with AD and control groups. The discrepancy in findings regarding serum zinc levels between different studies, can be attributed to several factors, including serum zinc quantification include diet, co-medications, co-morbidities, risk of external contamination during specimen collection or analysis, Improper specimen processing, hemolysis can also falsely increase zinc concentration & can contribute to falsely elevated concentrations [4, 25].

The observed lower serum zinc levels in AD patients highlight the importance of assessing zinc status in individuals with AD and considering zinc supplementation as a potential adjunctive therapy in their management. However, further research is needed to elucidate the precise mechanisms underlying the relationship between zinc deficiency and AD and to determine the efficacy of zinc supplementation as a therapeutic intervention in AD management [26, 27].

The study found significant variations in serum zinc levels among different age groups of atopic dermatitis (AD) patients. Children aged 2-6 years had lower levels, while adolescents aged 14-18 years had higher levels. Male patients also had lower levels. No significant difference was found between rural and urban areas. The study also found a progressive decrease in serum zinc levels with increasing severity of AD, suggesting a potential association between zinc deficiency and exacerbation of symptoms. For instance, a study by Toyran *et al.* [28] observed similar trends, reporting lower serum zinc levels in younger age groups compared to older ones. They attributed this difference to the higher nutritional requirements of growing children, potentially leading to lower zinc levels. Similarly, Al-Ghurabi *et al.* [29] found significant variations in serum zinc levels among different age groups of AD patients, supporting our study's observations. While, Farhood Gray *et al.* [29] in recent study found that serum zinc was significantly lower in female controls than in male controls. Several other studies also found that serum zinc level was highly significantly low in patients with severe AD followed by moderate AD and mild AD. Serum zinc level was highly significantly low in patients with moderate AD than in those with mild AD, low zinc level could affect the severity of AD as it causes membrane barriers' problem, which could increase trans epidermal water loss, which lead to xerotic skin, and easier allergens penetration [27]. Our finding were agreed with previous studies [30]. Karabacak *et al.* [28] demonstrated in a similar controlled study on AD patients that serum zinc level, had a significant negative correlation with SCORAD index. Kim *et al.* [16] demonstrated a correlation between lower serum zinc levels and more severe AD symptoms, indicating a potential role for zinc supplementation in managing AD.

Several mechanisms contribute to the association between zinc deficiency and the severity of AD symptoms; Zinc plays a crucial role in modulating immune responses, including the function of T lymphocytes, natural killer cells, and cytokine production [28]. Zinc deficiency can impair immune function, leading to dysregulated inflammatory responses characteristic of AD.: Zinc is involved in the synthesis of proteins essential for maintaining the integrity of the skin barrier, such as keratinocytes and filaggrin. A compromised skin barrier is a hallmark feature of AD, allowing for increased allergen penetration and triggering inflammatory responses [29]. Zinc acts as a cofactor for antioxidant enzymes that protect cells from oxidative damage. Oxidative stress is implicated in the pathogenesis of AD and can exacerbate inflammation and skin damage in affected individuals. Zinc possesses anti-inflammatory properties and can inhibit the activation of inflammatory pathways, such as nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) signaling [30]. Inadequate zinc levels may fail to adequately regulate these pathways, leading to sustained inflammation in AD. Zinc deficiency can alter the composition of the skin microbiota, leading to dysbiosis. Changes in the skin microbiome composition have been associated with AD exacerbations and may contribute to disease severity [9, 10].

Conclusion

1. Males, Adolescents and who lived in rural area aged were more prevalent among AD patients.
2. AD patients exhibited significantly lower serum zinc levels compared to the control group.
3. Serum zinc levels were significantly lower in younger age groups, particularly among children aged 2-6 years and male AD patients had lower mean serum zinc levels compared to females.
4. A progressive decrease in mean serum zinc levels was observed with increasing severity of AD, suggesting a potential link between zinc deficiency and the exacerbation of AD symptoms.

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