DOI: https://doi.org/10.54393/pjhs.v3i07.424

PAKISTAN JOURNAL OF HEALTH SCIENCES

https://thejas.com.pk/index.php/pjhs

Volume 3, Issue 7 (December 2022)

Original Article

Association of Serum Zinc Levels with Acne Vulgaris: A Case-Control Study

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ARTICLE INFO

Key Words:
Acne, Serum Zinc, Acne Vulgaris

How to Cite:
Minhaj Usmani, T. ., Mahboob Alam, S. ., Ghafoor, R. ., Quddos Latif, A. ., & Saeed, F. . (2022). Association of Serum Zinc Levels with Acne Vulgaris: A Case-Control Study: Association of Serum Zinc Levels with Acne Vulgaris. Pakistan Journal of Health Sciences, 3(07). https://doi.org/10.54393/pjhs.v3i07.424

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Received Date: 9th December, 2022
Acceptance Date: 30th December, 2022
Published Date: 31st December, 2022

ABSTRACT

Acne is an inflammatory skin disease that affects the hair follicles and sebaceous glands. The disease is multifactorial and the diagnosis is based on laboratory tests. Zinc is an element that is involved in many processes in our bodies. **Objectives:** To identify the relationship between serum zinc levels in both groups and whether zinc levels are associated with the severity of the disease and other related health outcomes in these patients. **Method:** This case-control study was carried out on 100 patients of Acne vulgaris in Dermatology ward 4, Outpatient department, Jinnah Postgraduate Medical Center, Karachi. Patients of age between 11-35 years, with untreated acne vulgaris with mild, moderate, or severe condition. Intravenous blood samples up to 3 mL were taken from both selected cases and controls in yellow top tubes. The collected blood was centrifuged at 3000 rpm for 10 minutes, and the serum was collected and stored at −40°C until further processing. **Results:** A significant correlation was observed between the case and control groups for moderate hair fall (p-value 0.045) and severe hair fall (p-value = 0.013) among participants and serum zinc levels. Whereas no significant difference was observed in the minor and unknown status of hair fall groups (p-value >0.05). **Conclusion:** The findings suggest of this study that zinc has a potent role not only in the management of acne but is also related to other factors such as hair fall, diarrhea, and vision.

INTRODUCTION

Acne is an inflammatory skin disease that affects the hair follicles and sebaceous glands. The clinical manifestations are inflammatory papules, pustules, comedones, and occasionally cystic nodules. The effects of ane are only related to physical appearance but also create trouble socially. The disease is multifactorial and the diagnosis is based on laboratory tests. During puberty, androgens stimulate the sebaceous glands, causing them to swell and secrete natural oils that rise to the top of the hair follicles and flow to the surface of the skin, and the accumulated oil, called sebaceous glands, can block the drains. The accumulation of this substance can lead to acne [1]. Zinc is an element that is involved in many processes in our bodies. It is required in a body for many physiological functions, such as DNA replication, cell division, and immune response. The role of zinc is also established in many allergic reactions and in the structural composition of many hormones. It is known to possess anti-inflammatory properties [2]. There is a well-established role of diet in the development of acne. Some studies showed a positive association while others showed a negative association, which makes it controversial [3-5]. Several studies showed the potent role of dietary intake in acne severity. Alternatively, a study of 47355 women was conducted and found a negative association between milk intake and acne. Their study showed that milk intake exacerbated acne [6]. Zinc deficiency is a common problem in Pakistan. It is known that 70-80% of the dietary requirement is obtained from grain, which is known to lack zinc. However, on the other hand, animal-sourced foods are sufficient in zinc and can help to overcome the deficiency of this metal in the body [7]. Acne Vulgaris is also known to be linked with zinc deficiency. It has been seen that people with zinc deficiency

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develop acne-like papulopustular lesions [8]. We have conducted this study to measure the zinc levels in the serum of acne patients and healthy individuals. The study aimed to identify the relationship between serum zinc levels in both groups and whether zinc levels are associated with the severity of the disease and other related health outcomes in these patients.

METHODS

This case-control study was carried out during the month of November 2022, among patients of Acne vulgaris in Dermatology ward 4, Outpatient department, Jinnah Postgraduate Medical Center, Karachi. The study was approved by the Institutional Review Board (IRB) of the Basic Medical Sciences Institute (BMSI), JPMC, Karachi. The complete research work was carried out following ethical considerations, and prior to the inclusion of any participant, written consent was taken. Prior to the sampling, the sample size was estimated using an online sample size calculator of mean difference, available at www.openepi.com, after inserting the mean and SD of serum Zinc levels of Acne Vulgaris patients, and normal controls. A total of 100 samples were collected, of which 50 were from diagnosed acne patients and 50 from healthy participants without acne. The diagnosis of acne in study participants was carried out by professional dermatologists. The inclusion criteria for acne patients were set as; an age range of 11-35 years, with untreated acne vulgaris with a mild, moderate, or severe condition. The lactating and childbearing women and the patients who were taking systemic drugs, and had a problem with zinc absorption were excluded from this study. Intravenous blood samples up to 3 mL were taken from both selected cases and controls in yellow top tubes. The collected blood was centrifuged at 3000 rpm for 10 minutes, and the serum was collected and stored at −40°C until further processing. For zinc estimation, a commercially available colorimetric kit was utilized for zinc estimation. The normal range of zinc levels in the blood is 70-140 µg/dl. The data were analyzed using IBM-SPSS version 23.0. The descriptive analysis was used to count percentages, the distribution of gender, the mean age with standard deviation, and serum zinc levels in acne and non-acne samples. An independent sample t-test was used to compare the mean serum zinc levels between acne and non-acne samples in total samples, One-way ANOVA was used to check the association of gender with acne and non-acne samples. *p*-values less than 0.05 were considered statistically significant.

RESULTS

Total 100 samples was collected with no missing data (50 controls and 50 cases), in which 24% were healthy males, and 17% were cases, whereas 26% were healthy females and 33% were cases. The male-to-female ratio was 0.7. The means and standard deviations of the ages of males were 23.9 ± 5.06 and 23.1 ± 5.9 for the healthy and case groups, respectively. The respective means of age with standard deviations for females were 25.1 ± 6.95 and 23.6 ± 5.6. Table 1 shows the zinc levels in the serum of the study participants grouped into cases and controls. A significant difference (p-value 0.01) in the control and case groups was observed in the results.

Groups	N	Mean	Standard Deviation	Standard Error	p-value
Case	50	61.74	26.8	3.8	0.01
Control	50	75.086	23.6	3.3	

Table 1: Zinc levels (µg/dL) in the case and control groups

The mean zinc ion concentrations in the control group's males were 80.5 ± 23.61 (mean and SD), while the males in the case group had 66.44 ± 26.78 (Table 02). The female control group had 70.09 ± 22.82 µg/dL zinc levels in serum. In contrast, the female case group had 59.32 ± 26.96 µg/dL serum zinc levels, which was significantly different (p-value 0.044) combined in males and females of cases vs. males and females of controls.

Gender	Control			Case			p-value
	n (%)	Mean ± S.D	S.E	n (%)	Mean ± S.D	S.E	
Male	24 (58.5%)	80.5 ± 23.6	4.82	17 (41.5%)	66.4 ± 26.7	6.5	0.044
Female	26 (44.1%)	70 ± 22.8	4.48	33 (55.9%)	59.3 ± 26.9	4.69	
Total	50 (50%)	75 ± 23.5	3.33	50 (50%)	61.7 ± 26.8	3.8	

Table 2: Zinc levels (µg/dL) based on gender in the case and control groups

Similarly, the correlation of the serum zinc levels with parameters were analyzed, i.e., vision, diarrhea, fatigue, weak immunity, and ulcer. However, no significant difference (p-value > 0.05) was observed in the serum zinc levels of individuals with unhealthy vision, without diarrhea, without fatigue, without weak immunity, and without ulcers among participants in both the case and control groups. A significant correlation was observed between the case and control groups for moderate hair fall (p-value 0.045) and severe hair fall (p-value = 0.013) among participants and serum zinc levels. Whereas no significant difference was observed in the little and unknown status of hair fall groups (p-value >0.05). The data also revealed higher concentrations of zinc in control people with unhealthy vision, diarrheal status, and weak immunity, as shown in Table 3.

Variables		Control	Case	p-value
Hair fall	Little	63.6 ± 12.41	75.13 ± 21.4	0.054
	Moderate	66.17 ± 13.78	54.38 ± 12.1	0.045
	Severe	26.2 ± 0	32.39 ± 9.55	0.013
	Don't Know	92 ± 23.7	113.38 ± 24.33	0.084
Vision	Healthy	73.02 ± 22.44`	61.5 ± 26.42	0.035
	Unhealthy	84.51 ± 27.54	63.23 ± 31.51	0.172
Diarrhea	Present	67.22 ± 19.61	62.16 ± 24.87	0.592
	Absent	77.57 ± 24.37	61.62 ± 27.68	0.009
Fatigue	Present	71.71 ± 24.28	63.61 ± 27.2	0.259
	Absent	79.05 ± 22.56	59.54 ± 26.84	0.011
Weak immunity	Present	82.81 ± 29.94	58.47 ± 35.61	0.19
	Absent	73.61 ± 22.28	62.19 ± 25.92	0.031
Ulcer	Present	77.67 ± 26.42	59.72 ± 39.71	0.351
	Absent	74.73 ± 23.46	62.18 ± 23.79	0.061

Table 3: The correlation of the analyzed parameters with the serum zinc levels (µg/dL)

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DISCUSSION

This study was conducted to correlate serum zinc levels with acne vulgaris. It is reported that zinc reduces inflammation in acne pathogenesis by inhibiting chemotaxis, followed by the release of lysosomal enzymes, and transforming lymphocytes [9]. Several variables were analyzed in this study to check the impact of serum zinc levels on vision, diarrhea, fatigue, immunity, and ulcers. In this study, a significant difference was observed between the serum zinc level and acne case samples. The control group had significantly higher serum zinc levels compared to the cases. These results were consistent with a meta-analysis study by Yee et al. [9]. However, the average serum zinc levels in the 12 studies mentioned in this meta-analysis were slightly higher (96.308 ± 4.053 µg/dL in acne and 102.442 ± 3.744 µg/dL in controls) compared to our study, which was 75.1± 23.6 µg/dL in healthy subjects and 61.7 ± 26.8 µg/dL (mean ± STD). This difference in both studies can be attributed to the number of subjects, as Yee et al., (2020) did a meta-analysis of the 12 studies. Notably, these 12 studies were from several countries, including Italy, France, Sweden, the United Kingdom, Iran, Iraq, the United States of America, and India were dependent on the zinc supply and assessment of serum zinc levels for a certain duration. Furthermore, no significant difference was observed in the comparative analysis for serum zinc levels between the healthy male vs. case male and healthy female vs. case female groups. However, the levels of zinc in males and females were found to be significant (p-value= 0.044) in our study. These results were consistent with the findings of another study in which they found higher serum zinc levels in males compared to females [10]. It is also worth mentioning that the age of the participants in both studies was not too different, which could have influenced the zinc levels. A possible reason for this contradiction could be the sampling time as the zinc status is subject to change with diurnal variation from morning to evening [11]. Moreover, the correlation between the serum zinc levels and other variables like healthy or unhealthy vision showed a significant difference in the healthy vision of cases and control groups (p-value 0.035), with and/or without diarrhea showed a significant difference in participants without diarrhea of both cases and control groups (p-value 0.009), with or/and without fatigue showed a significant difference in case and control group participants without fatigue (p-value 0.011), with or/and without weak immunity showed a significant difference in the case and control group participants without weak immunity (p-value 0.031), and with or/and without ulcer were also analyzed. No significant differences were observed in the other groups in the ANOVA, i.e., participants with unhealthy vision, participants with diarrhea, participants with fatigue, participants with weak immunity, participants with ulcers, and participants with little or unknown hair fall status in both the case and control groups with serum zinc levels (p-value > 0.05). However, a significant difference was observed between the moderate and severe hair fall groups. These findings are consistent with those of Kil., et al [12]. Overall, these findings suggest that serum zinc levels are inversely correlated with acne vulgaris and with hair fall, as in individuals, the moderate and severe hair fall groups of both healthy and case samples had lower serum zinc levels compared to normal serum zinc levels. Recently, it has become clear how important zinc is for maintaining human health, particularly the health and integrity of the skin [13]. According to Amer et al the serum zinc levels of 50 patients with acne vulgaris and 38 control subjects were examined [14]. The results showed that the zinc levels in the acne patients were statistically significantly lower than those in the control group. Additionally, Michalsson et al study's measured the serum zinc levels and retinol binding protein (RBP) in 173 acne sufferers and compared them to those from a control group [15]. They noted that male patients with severe acne had considerably lower mean serum zinc levels than the healthy group. In addition, 40 healthy control volunteers and 47 patients with acne vulgaris were included in the study by Kaymak et al [16]. Regarding the serum zinc level, there was a statistically significant difference between the control group and acne sufferers. Additionally, the study found no connection between zinc levels and the severity of acne or the persistence of the disease. Moreover, Ozuguz et al. assessed serum levels of zinc, vitamins A and E, and 94 acne sufferers who were matched for age and sex and 56 healthy volunteers as the control group [17]. According to GAGS, all patients were categorised into four groups: mild, moderate, severe, and very severe. The amounts of zinc and vitamin E were negatively correlated with the severity of acne. Similar to this, El-Dibany and Elhassi's findings showed that there was a significantly significant difference in the median serum zinc levels between acne patients and their controls (P value = 0.0001) [18]. The results of the study were statistically insignificant (P value = 0.522), and they did not demonstrate a relationship between the level of serum zinc and the severity of acne. The effectiveness of topical zinc treatment, however, was assessed by Cochran et al. in 30 individuals with mild to moderate acne vulgaris [19]. Regarding the quantity or kind of acne lesions over a 12-week period, participants who received zinc were not different from those who received a placebo. Before, during, or after therapy, serum zinc levels were not substantially different between the two regimens. They claimed that treating acne vulgaris with topical zinc therapy is ineffective. Similar to this, Mogaddam et al. found no discernible difference between acne patients and healthy persons in terms of serum zinc levels [20]. Although there was a strong association between serum zinc levels and the kind and severity of acne lesions. Furthermore, Erpolat et al. conducted a study with 37 healthy control volunteers and 43 patients with acne vulgaris [21]. The Global Acne Grading System was used to categorize acne severity. In comparison to healthy people, acne patients had serum zinc levels of 81.48µg/dl and 83.69µg/dl. They recommended additional research because there was no connection between serum zinc levels and acne. The difference between our findings and

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those of other researchers may be due to variations in the number of cases in different studies, the relationship of other epidemiological factors affecting zinc, and variations in the threshold value for zinc deficiency.

CONCLUSIONS

Our study has revealed lower levels of zinc serum in acne-bearing patients. On the other hand, the data also showed that hair fall is also strongly associated with elevated levels of zinc. These findings suggest that zinc has a potent role not only in the management of acne but is also related to other factors such as hair fall, diarrhea, and vision. The role of zinc needs more insight to better understand the effects of levels of zinc in different aspects of the body. Acne-prone skin can be treated with zinc-containing products to identify the effect of zinc on the skin, while also maintaining the diet under the supervision of a physician.

Conflicts of Interest

The authors declare no conflict of interest

Source of Funding

The author(s) received no financial support for the research, authorship and/or publication of this article

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