Comparison of serum levels of calcium, vitamin-D, phosphorous and C-reactive protein in acne patients versus healthy subjects

Azadeh Goodarzi, MD [1*]
Elham Behrangi, MD [1]
Mohammadreza Ghassemi, MD [1]
Golnaz Mehran, MD [1]
Niloofar Teymoori, MD [2]
Amir Pouyan Ghahremani, MD [2]
Maryam Biglari Abhari, MD, MPH [3]

1. Department of Dermatology, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
2. Department of General Medicine, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
3. Community Medicine Department, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

**Corresponding author:*
Azadeh Goodarzi, MD
Department of Dermatology, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
Address: Sattarkhan St., Tehran 1445613131, Iran
Email: Goodarzi.a@iums.ac.ir, A.goodarzi.dermatology@gmail.com
Tel: +98 9123882448

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Background: Acne vulgaris is among common bothersome skin problems. Recognition of contributing factors would help to prevent acne. Some dietary and inflammatory factors are among suggested etiologies. Accordingly, in this study, the serum levels of calcium, vitamin D, phosphorous and C-reactive protein (CRP) were determined and compared in acne patients and healthy subjects.

Methods: In this case-control study, 144 consecutive subjects with and without acne (moderate-very severe) referred to Rasoul Akram Hospital in 2016 were enrolled. In this regard, the serum calcium, phosphorous, CRP, vitamin D were determined in the subjects and compared between the groups.

Results: The results indicated that serum CRP, calcium, and phosphorous level were alike between the groups ($P > 0.05$) without any relation to acne severity except CRP. The serum vitamin D level was significantly different ($P = 0.0001$), but it was not associated with acne severity. Serum calcium levels of males were significantly higher in both groups.

Conclusions: Based on our results, it may be concluded that calcium, phosphorous, and CRP levels are not associated with acne incidence, but the serum vitamin D is related to acne presentation. CRP levels were positively associated with acne vulgaris severity.

Keywords: acne vulgaris, calcium, vitamin D (Vit D), C-reactive protein (CRP)

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INTRODUCTION

Acne vulgaris is considered a common skin disease in which sebaceous glands' inflammation and obstruction lead to involvement of chest, back, and face [1-3]. The genetic has been regarded as one of the main contributing factors to acne [4]. Four related mechanisms include follicular proliferation and ruptures, sebum production, inflammation, and coryne-bacterium presence [5,6]. Acne is usually observed in adolescence due to sex hormone role in the middle of the second decade of life [6-8]. Androgens level, genetic, corticosteroids, chemical agents, and psychiatric factors are among the aggravating factors for acne [9-11]. Antibiotics such as tetracycline [12-14] and retinoid [15] are the main therapeutic options. Although, these modalities are effective in the treatment of the patients, the

therapeutic outcomes are not favorable in some cases. In these cases, other etiologies such as mineral and vitamin deficiencies are proposed to be important. Some micronutrients or inflammation-related factors such as zinc, calcium, vitamin D, phosphorous, and C reactive protein (CRP) are among suggested markers. Regarding some controversies or few studies in this area [16-21], this study was conducted to determine and compare the serum levels of calcium, vitamin D, phosphorous, and CRP in acne patients and healthy subjects.

PARTICIPANTS AND METHODS

Participants and study design

In this case-control study, 144 consecutive subjects with and without acne (72 cases and 72 controls), referred to Rasoul Akram Hospital in 2016 were enrolled. Additionally, the serum calcium, phosphorous, CRP and vitamin D were determined in the subjects by the ELISA method, and compared between the groups, based on acne severity. The control group was selected from healthy personnel without acne through clinical examination. The severity was determined according to the following items:

- Mild acne: fewer than 20 comedones, or fewer than 15 inflammatory lesions, or a total lesion count more than 30;
- Moderate acne: 20-100 comedones, or 15-50 inflammatory lesions, or a total lesion count of 30-125;
- Severe acne: more than 5 cysts, or comedone count more than 100, or a total inflammatory count more than 50, or a total lesion count more than 125.

Statistical methods

Data of the 144 patients (72 subjects in each group) were analyzed using the SPSS software (version 24.0). The tests used for comparisons included Independent-Sample-T, Mann-Whitney-U, ANOVA, Kruskal-Wallis, and Pearson tests. The significance level was considered 0.05.

Ethical considerations

The written informed consent was obtained from all participants.

RESULTS

The mean age was 25.5 ± 7.9 and 26.4 ± 8.8 years in both case and control groups, respectively ($P > 0.05$); in each group, 50% were male. Table 1 shows the acne severity. Duration was less than one year, 1-5 years, 5-10 years, and more than 10 years in 34.7%, 23.6%, 16.7%, and 25%, respectively.

As Table 2 shows, diary intake (diary product usage divided based on frequency of use and considered as multiple times in a day (very much), daily (much), most days in a week (medium), 2-3 times in week in a week (few), less than 2 days in a week or even no use (very few)) was higher

Table 1. Acne grading in the case group

		Grade			Total
		Moderate	Severe	Very severe	
Group	Case	18 25.0%	24 33.3%	30 41.7%	72 100.0%
Total		18 25.0%	24 33.3%	30 41.7%	72 100.0%

Table 2. Dairy intake in the two groups

			Dairy Products Consumable Ratio					Total
			Very few	Few	Medium	Much	Very much	
Group	Case	Count % Within Group	11 15.3%	15 20.8%	26 36.1%	15 20.8%	5 6.9%	72 100.0%
	Control	Count % Within Group	21 29.2%	30 41.7%	18 25.0%	3 4.2%	0 .0%	72 100.0%
Total		Count % Within Group	32 22.2%	45 31.3%	44 30.6%	18 12.5%	5 3.5%	144 100.0%

in the case group ($P = 0.0001$). In case and control groups, sun exposure longer than three hours was 48.6% and 27.8%, respectively, with a significant difference ($P = 0.010$). Calcium, phosphorus and CRP levels were not significantly different between the two groups. The only serum marker differed between the groups was vitamin D ($P = 0.001$) (Table 3).

The age was not related to vitamin D, CRP, calcium and phosphorous ($P > 0.05$). The gender was not associated with determined serum markers except calcium that was higher in males in both case and control groups. ($P = 0.0001$ and $P = 0.003$, respectively). Although, the CRP level was not different between the case and control groups, it was positively associated with acne severity or its grade ($P = 0.034$). Other serum factors were not related to acne severity ($P > 0.05$). The only factor relevant to sun exposure in both groups was the serum vitamin D level ($P = 0.0001$). Furthermore, calcium ($P = 0.0001$) and phosphorous ($P = 0.042$) were associated with the diary intake in the two groups. Duration of acne was not associated with serum markers levels ($P > 0.05$).

The determined serum levels were not relevant to acne severity, except CRP ($P = 0.034$) (Tables 4 and 5).

Table 3. Serum levels of vitamin and minerals in the two groups

Group	Mean	Std. Deviation
Ca (mg/dl)		
Case	9.59	.64
Control	9.40	.61
Phosphorous (mg/dl)		
Case	3.19	.96
Control	3.31	.53
VitD (ng/ml)		
Case	29.30	16.21
Control	20.39	14.89
CRP (mg/l)		
Case	6.95	3.11
Control	6.36	2.23

DISCUSSION

Acne is a common dematological disease worldwide, particularly in adolescents. Determination of the related factors can help to plan a better program to reduce the burden of acne. According to our findings, between calcium, phosphorous, CRP, and vitamin D indices, only the serum vitamin D level was related to acne. Interestingly, the patients with acne had higher serum levels of vitamin D. In other words, vitamin D can reduce the acne rate, being inconsistent

Table 4. Association of gender with serum parameters

Group	Gender	Ca (mg/dl)	Phosphorous (mg/dl)	VitD (ng/ml)	CRP (mg/l)
Case	Female				
	Mean	9.31	3.39	31.51	6.69
	Std. Deviation	.41	1.18	17.57	3.13
	Male				
	Mean	9.88	3.00	27.08	7.21
	Std. Deviation	.71	.63	14.64	3.11
Control	Female				
	Mean	9.20	3.33	23.46	6.50
	Std. Deviation	.52	.57	16.08	3.00
	Male				
	Mean	9.61	3.29	17.32	6.22
	Std. Deviation	.62	.49	13.11	1.05

Table 5. Association of acne severity with serum parameters

Group	Grade	Ca (mg/dl)	Phosphorous (mg/dl)	VitD (ng/ml)	CRP (mg/l)
Case	Moderate/Severe				
	Mean	9.58	3.18	26.67	6.30
	Std. Deviation	0.60	0.51	15.83	1.82
	Very Severe				
	Mean	9.62	3.21	32.97	7.87
	Std. Deviation	0.70	1.37	16.27	4.19

with some other studies. Our study showed that patients with acne had higher exposure to the sun or higher intake of dairy products that may explain the higher levels of vitamin D in the case group; future studies with participant matching need to be conducted in these regard. Namazi *et al.* reported that CRP levels (as an indicator of systemic effect of acne) were not significantly different between acne patients and controls even in very severe clinical forms [21]. We also found that CRP levels were not different between the acne patients and controls; however, we found a positive correlation between the acne severity and CRP levels.

Toosi *et al.* showed that the mean vitamin D level was 8.4 ng/ml and 10.4 ng/ml in both case and control groups, respectively, which was not statistically different [22]. There was no significant relation between severity of disease, BMI, age at onset of disease, duration of disease, and serum 25(OH) D levels. Contrary to the study conducted by Toosi *et al.* [22], our results indicated that the control group had significantly lower vitamin D levels. Moreover, we did not found any correlation between vitamin D and demographic characteristics of the patients, as well as between vitamin D and acne. Two related studies in Turkey and Korea demonstrated that patients with acne had lower levels of vitamin D; the latter study reported an inverse correlation between the acne severity and serum levels of vitamin D, being inconsistent with our results; this result is justified by the above-mentioned probable confounders [23,24].

In conclusion, to the best of our knowledge, calcium, phosphorous, and CRP levels are not associated with acne, but the serum vitamin D is relevant to acne. Furthermore, among these determined factors, CRP is the only factor related to acne severity.

Calcium level is higher in males with higher exposure to the sun, based on cultural or occupational condition in our country that may differ in other countries with different nutritional habits and different sun exposure. Owing to the high prevalence of acne, it is recommended that the probable related factors be focused to better manage or prevent acne vulgaris, since there are many related articles in this regard [25].

However, more comprehensive matched studies with a larger sample size are required to obtain more definite results particularly with consideration of confounding factors.

Considering the high prevalence and great burden of acne vulgaris there are many articles emphasizing on acne associations [25], treatments [26-29] and management of its complications especially scars [30-32]. In this study, one of the controversial associations of acne vulgaris is studied and discussed.

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Conflict of Interest: None declared.

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