Serum Total Protein, Albumin, Globulin, and Prealbumin in Acne Patients

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Brief communication

Keywords: Total protein, Albumin, Globulin, Prealbumin, Acne vulgaris

Posted Date: December 10th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-122981/v1>

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Abstract

Background/Objectives: This study was designed to investigate serum protein levels in acne patients.

Method: Acne patients (n=362) and healthy volunteers (n=272) were matched in terms of both age and sex. Serum levels were measured.

Results: Among the 362 acne patients and 272 age- and sex-matched healthy controls, serum albumin levels in female acne patients were lower than in the healthy controls ($P < 0.05$), serum albumin levels in male acne patients were lower than in the healthy controls ($P < 0.01$). Additionally, serum globulin and total protein levels were significantly lower in acne patients than in the healthy control group ($P < 0.01$). Serum levels of prealbumin were significantly lower in female acne patients than in the control group ($P < 0.05$). Finally, the severity of female and male acne patients was negatively correlated with serum total protein, albumin, globulin, and prealbumin levels.

Conclusions: The results of this study suggested that acne patients are potentially accompanied with protein malnutrition.

Introduction

Acne vulgaris is an inflammatory skin disease that affects more than 90% of young people[1]. The prevalence of acne peaks between ages 14 years and the start of the third decade. Adolescence is the most important period of growth and development for the human body and is accompanied by an increased demand for proteins and vitamins[2]. When proteins and vitamins cannot meet body requirements, a variety of skin diseases may ensue. Acne patients are often accompanied by dyslipidemia and hyperhomocysteinemia[3, 4, 5], which suggests that patients need vitamins such as niacin and folate for treatment. Acne patients with bacterial infections need antibiotic treatment[6]. Clinically, many acne patients are incompletely cured, and new acne lesions frequently recur after systemic treatment. This may be due to a deficiency of certain serum proteins that affect immune function. This study investigated the serum protein concentrations in acne patients.

Materials And Methods

Study subjects

Ethical approval was obtained from the ethics committees of the First Affiliated Hospital of Guangxi University of Chinese Medicine. Informed consent was obtained from all subjects. Clinical data were collected from acne patients and healthy volunteers.

The inclusion criteria for patients was that they were required to have not taken isotretinoin, doxycycline, or other acne drugs for least 1 month prior to the study. The inclusion criteria for the healthy volunteers were that they had clear and smooth skin in which no acne lesions, other inflammatory lesion were found on the skin of face and the whole body; they were also required to undergo a medical examination.

There was no history of alcoholism, drug addiction, vegetarianism, anorexia nervosa, alopecia, anemia, folliculitis, seborrheic dermatitis, hidradenitis suppurativa, eczema, or psoriasis in the healthy controls. Both acne patients and healthy controls had no chronic febrile illness, urticaria, kidney, heart, or liver dysfunction, cancer, severe anemia, congenital immune deficiency, immunosuppressive treatment, serious infectious disease, or neuroendocrine disorders. Pregnant and lactating women were excluded from the study. Participants in the patient and control groups with elevated aminotransferases, abnormal kidney and liver function, and other serious chronic diseases were excluded from the study.

Methods

The subjects maintained a general diet and were in a stable living condition at least 1 week before the study, and they avoided consuming alcohol or caffeine, participating in strenuous exercise, or becoming fatigued within 24 h of blood sampling. Subjects were required to have fasted for 12 h before venous blood samples were taken. Blood samples were collected in common biochemical (red vacuum) tubes and sent to the laboratory for testing. The tubes were gently mixed two or three times to promote agglutination, and then centrifuged at $1,000 \times g$ for 10 min at room temperature before testing. Blood samples were analyzed within 24 h. Serum protein concentrations were estimated using commercially available enzymatic colorimetric tests. Serum total protein (TP) and albumin (ALB) concentrations were detected by the biuret method and the bromocresol green-dye binding method, respectively. Prealbumin (PA) was detected by the immune turbidity method. We calculated globulin (GLO) as $GLO = TP - ALB$, where $ALB / GLO (A/G) = ALB / (TP - ALB)$. Serum protein concentrations were determined using a 7600 Biochemistry Automatic Analyzer (Hitachi, Tokyo, Japan).

Acne diagnoses were determined according to physical features. Assessments of acne severity were based on the Hayashi et al. grading system[5]. According to this scale, the lesion count was used to classify acne into four groups primarily based on the number of inflammatory eruptions on half the face. Acne lesions on half of the neck, front chest, back, and buttock were also counted. Acne lesions were scored as 0–5, mild; 6–20, moderate; 21–50, severe; and >50, very severe. In this study, severe and very severe cases were included in a single group. The normal values for PA were 155–450 mg/L; TP was 65.0–85.0 g/L; ALB was 40–55 g/L; and GLO was 20–40 g/L.

Statistical analysis

Statistical analyses were performed using SPSS software (SPSS 19, SPSS Inc., Chicago, IL, USA). One-way ANOVA was used to compare variance in homogeneity. Protein detection results were expressed as mean ± SD (±s), which were evaluated using the Dunnett test in a one-way ANOVA. Differences were considered significant at *P* < 0.05 and very significant at *P* < 0.01. The severity of acne and serum TP, ALB, GLO, and PA levels were analyzed by bivariate linear analysis.

Results

This study included acne patients (n = 362) and healthy controls (n = 272) (Table 1). There was no significant difference in the average age between the acne patients and healthy controls. The maximum age of female subjects was 26 years, the youngest was 13 years of age; the maximum age of male participants was 28 years of age, the youngest was 11 years of age. There were 91 healthy volunteers in the control group who admitted that they had had mild acne or comedos that healed without a scar. There was no significant difference in BMI between the patient and normal control groups (*P* > 0.05). There were no participants with abnormal liver and kidney function.

Table 1
Acne patients and healthy controls

Acne patients	N	Age (Y)	Weight (Kg)	Height(M)
Males	190	19.69 ± 3.59	60.05 ± 6.52	1.695 ± 0.047
Females	172	19.78 ± 3.74	52.17 ± 5.21	1.608 ± 0.046
Total	362			
Controls				
Males	141	20.02 ± 3.84	60.60 ± 5.12	1.702 ± 0.044
Females	131	20.86 ± 3.51	52.43 ± 4.85	1.6155 ± 0.045
Total	272			

In the control group, there were no instances of serum ALB, GLO, or TP levels that were less than normal (Table 2). Conversely, serum ALB levels in female and male acne patients were significantly lower than the control group (*P* < 0.05). Serum GLO levels in male and female patients were also significantly lower than in the control group (*P* < 0.01). Serum GLO levels in the severe, moderate, and mild male acne patients were lower than in the control group (*P* < 0.05). Serum TP levels in mild, moderate, and severe male and female acne patients were significantly lower than in the control group (*P* < 0.01). Serum PA levels in female acne patients were significantly lower than in the control group (*P* < 0.05) (Table 2). The A/G ratio in male patients was remarkably higher than in the control group (*P* < 0.01). The severity of female and male patients was negatively correlated with serum TP, ALB, GLO, and PA levels (*P* < 0.01) (Table 3).

Table 2
Serum protein levels and BMI in female and male patients

Female	Normal Control Group (131)	Severe Acne Patients (22)	P Value	Moderate Acne Patients (61)	P Value	Mild Acne Patients (89)	P Value	Acne Patients (172)	P value
ALB* (g/L)	47.81 ± 2.303	46.536 ± 2.971	0.299	46.515 ± 3.173 [▽]	0.031	46.935 ± 2.979	0.170	46.737 ± 3.034 [▽]	0.011
GLO(g/L)	26.286 ± 2.456	24.404 ± 3.237 [▽]	0.039	25.226 ± 3.193	0.127	25.433 ± 2.888	0.201	25.228 ± 3.044 [▽]	0.015
TP(g/L)	74.096 ± 3.192	70.941 ± 4.634 [▽]	0.005	71.748 ± 4.044 [▽]	0.001	72.363 ± 4.268 [▽]	0.014	71.965 ± 4.223 ^{▽▽}	0.000
A/G	1.8364 ± 0.1933	1.9367 ± 0.26691	0.420	1.8798 ± 0.3184	0.802	1.868 ± 0.237	0.890	1.881 ± 0.2713	0.546
PA(mg/L)	239.809 ± 32.063	221.227 ± 39.793	0.199	226.131 ± 37.384	0.129	230.416 ± 40.480	0.359	227.721 ± 39.22 [▽]	0.044
BMI	20.067 ± 1.344	19.763 ± 2.257	0.948	20.4386 ± 1.934	0.666	20.102 ± 1.844	1.000	20.178 ± 1.933	0.984
Male	Normal Control Group(N = 70)	Severe Acne Patients(N = 30)	P Value	Moderate Acne Patients (N = 53)	P Value	Mild Acne Patients(N = 107)	P Value	Acne Patients (N = 190)	P Value
ALB(g/L)	48.4518 ± 2.428	47.247 ± 2.877	0.176	47.613 ± 2.500	0.306	47.7364 ± 2.927	0.238	47.625 ± 2.797 [▽]	0.048 < 0.05
GLO(g/L)	25.499 ± 2.058	23.5267 ± 3.358	0.016	23.893 ± 3.819 [▽]	0.014	24.055 ± 3.292 ^{▽▽}	0.003	23.926 ± 3.443 [▽]	0.000 < 0.01
TP(g/L)	73.954 ± 2.862	70.773 ± 4.389 ^{▽▽}	0.001 < 0.01	71.506 ± 4.582 ^{▽▽}	0.005 < 0.01	71.792 ± 4.339 ^{▽▽}	0.000 < 0.01	71.551 ± 4.4095 ^{▽▽}	0.000 < 0.01
A/G	1.9139 ± 0.196	2.0491 ± 0.325	0.143	2.041 ± 0.337	0.053	2.022 ± 0.3099 [△]	0.032	2.031 ± 0.3186 ^{△△}	0.003 < 0.01
PA(mg/L)	275.326 ± 51.03	251.200 ± 44.88	0.158	258.170 ± 53.302	0.262	272.421 ± 55.638	0.993	265.095 ± 53.865	0.411
BMI	20.907 ± 1.573	20.837 ± 2.162	1.000	20.7184 ± 2.162	0.970	20.963 ± 1.804	0.999	20.875 ± 1.9597	1.000
*ALB = albumin; GLO = globulin; TP = total protein; A/G = albumin/globulin ratio;									
PA = prealbumin. BMI = Body Mass Index.									
△, Significantly higher than the control group, $P < 0.05$;									
△△, remarkably significantly higher than the control group, $P < 0.01$;									
▽, Significantly lower than the control group, $P < 0.05$;									
▽▽, remarkably significantly lower than the control group, $P < 0.01$.									

Table 3
Correlations between serum protein and BMI with the severity of acne

The correlation between serum protein and the severity of acne					
male			female		
	r value	P value		r value	P value
TP	-0.308**	P = 0.000 < 0.01	TP	-0.272**	P = 0.000 < 0.01
ALB	-0.127*	P = 0.021 < 0.05	ALB	-0.172**	P = 0.003 < 0.01
GLO	-0.257**	P = 0.000 < 0.01	GLO	-0.171**	P = 0.003 < 0.01
PA	-0.144**	P = 0.009 < 0.01	PA	-0.204**	P = 0.000 < 0.01
The correlation between serum protein and the BMI of acne patients					
male			Female		
TP	0.250##	P = 0.000 < 0.01	TP	0.190##	P = 0.001 < 0.01
ALB	0.136##	P = 0.002 < 0.01	ALB	0.163##	P = 0.004 < 0.01
GLO	0.197##	P = 0.000 < 0.01	GLO	0.90	P = 0.118 > 0.05
PA	0.038	P = 0.390 > 0.05	PA	0.013	P = 0.821 > 0.05
*There was a significant correlation between the indicated protein and the severity of acne.					
**There was a very significant correlation between the indicated protein and the severity of acne.					
#There was a significant correlation between the indicated protein and BMI in acne patients.					
##There was a very significant correlation between the indicated protein and BMI in acne patients.					

Serum ALB was lower than the normal range (40 g/L) in one male patient and three female patients. There were 26 male and 10 female patients who showed serum GLO levels lower than the normal range (20 g/L). Serum TP levels were lower than normal (65 g/L) in seven male patients; however, no patients had a serum TP levels below 60 g/L. All patients had serum PA levels within the normal range. The maximum serum ALB, GLO, TP, and PA values in each group were all within the normal range.

Discussion

This study showed that most acne patients had serum ALB, GLO, and TP concentrations that were within the normal range. However, serum levels of ALB, GLO, and TP in male and female acne patients were lower than in the control group. We suggest that the requirements for protein of acne patients are higher than those of health people and that acne patients are deficient in protein, even when serum ALB, GLO, and TP levels are above the normal range.

Oxidative damage plays an important role in acne pathogenesis[7]. ALB is the most abundant circulating protein in plasma and has important antioxidant activities[8]. Serum ALB levels have been considered to be one of the best indicators of nutritional status; furthermore, hypoalbuminemia has been thought to indicate protein deficiency[9]. Abnormal liver function can also lead to decreased ALB synthesis, but transaminase levels in patients of this study were within the normal range. Some recent reports have shown that serum ALB is more significantly influenced by factors other than nutritional intake. Inflammation may reduce serum ALB concentrations independently of malnutrition[10]. Macrophages and neutrophils secrete proinflammatory cytokines such as TNF- α , IL-1 β , and IL-8, which might affect serum protein production[11]. The molecular weight of albumin is small, and it is easy to leak out from urine. Excessive exercise or micro-pathological changes of the glomerulus and renal tubules may lead to microalbuminuria. Serum ALB levels in acne patients were lower than in the control group ($P < 0.05$), suggesting that the serum ALB in acne patients was not enough to prevent and inhibited the oxidative damage from acne lesions.

The GLO fraction includes hundreds of serum proteins, including carrier proteins, enzymes, the complement system, and immunoglobulins[12]. Immune GLO contains a broad range of immune antibodies that oppose pathogens and foreign antigens. These antibodies are critical for replacement therapy in patients with humoral immune deficiencies. GLO plays an important role in immunity and hormones[12]. Acne patients with reduced immunoglobulin cannot effectively protect

themselves against bacterial infections. The serum GLO levels in male patients with moderate, severe, and mild acne were significantly lower than those in the control group ($P < 0.05$). The serum GLO levels in all female acne patients were significantly lower than in the control group ($P < 0.05$).

Serum TP comprises ALB and GLO. The serum ALB concentrations in both male and female mild, moderate, and severe acne groups were not significantly different from the normal control group ($P > 0.05$). Serum GLO levels of female patients with mild, moderate, and severe acne were not significantly lower than those in the control group ($P > 0.05$). Conversely, serum TP levels in mild, moderate, and severe male and female acne patients were significantly lower than in the control group ($P < 0.01$). The severity of female and male patients was negatively correlated with serum ALB, GLO, TP, and PA levels ($P < 0.01$).

The ALB/GLO ratio ($AGR = ALB / (TP - ALB)$) is the ratio of serum ALB to non-ALB proteins[13]. The AGR of female patients was not significantly higher than that of the normal control group, which is probably due to the lower serum ALB level in female patients, who showed no significant decrease in GLO. The AGR in male acne patients was significantly higher than in the control group ($P < 0.01$). Serum ALB and GLO levels in acne patients were lower than in healthy people, but GLO was remarkably decreased. Increased AGR indicated decreased immunity of acne patients.

PA, also known as transthyretin, has a half-life in serum of 2–3 days, which is much shorter than that of ALB. PA is therefore more sensitive to changes in protein-energy status than ALB, and its concentration closely reflects recent dietary intake rather than overall nutritional status[14]. However, low serum PA levels may signal not only malnutrition, as it is affected by other factors. Inflammatory stress, metabolic stress, and zinc deficiency downregulate PA, which is synthesized in the liver. Our results showed that serum PA levels in female acne patients were significantly lower than in the control group. Although there was not a significant decrease in serum PA concentration in male patients, serum PA concentrations in male and female patients were inversely correlated to the severity of acne. These results suggested that serum PA levels may affect acne inflammation.

Most of the patients in this study were from low income groups, such as young students, graduate students, and ordinary workers. Some patients were pursuing a weight loss by excessive dieting. Many young acne patients were studying and working hard for entrance examinations, employment, and jobs, and neglecting their nutrition: their diets were deficient in protein. The average age of the acne patients in this study was less than 20, and most were teenagers.

Adolescence is a nutritionally critical period of life. The dramatic increase in physical growth and development puts greater pressure on nutritional requirements, as it is during this period that adolescents experience a weight gain equivalent to 65% of their weight at the beginning of the period (or 40% of their final weight) and a height increase equivalent to 15% of their adult height. The nutritional requirements of adolescents are higher than in any other age group[15]. The severity of female and male acne patients was negatively correlated with serum TP, ALB, GLO, and PA levels ($P < 0.01$). These results suggested that protein deficiency is an important factor in the pathogenesis of acne. If acne patients have protein malnutrition, it will not only lead to acne relapse and delayed healing, but will also impair the patient's quality of life and hinder their normal growth and development. However, the correlation coefficient is low ($r < 0.75$), indicating that the correlation between protein malnutrition and the severity of acne is not conspicuousness or insidious. Acne is a multifactorial disease. There are many pathogenic factors that cause acne, such as vitamin deficiency, insomnia, fatigue, infection and other factors. Protein malnutrition is a hidden and latent pathogenic factor of acne, which is easy to ignore, or misdiagnosed by doctors.

According to the mean and standard deviation of males and females in the normal control group (Table 2), the lower 95% confidence interval reference value of ALB, GLO, TP, and PA in males and females in the control group were evaluated by the formula: $(\bar{X} - 1.96 s)$. The results for male participants were: $ALB \geq 43.69$ g/L, $GLO \geq 21.465$ g/L, $TP \geq 68.34$ g/L, and $PA \geq 175.307$ g/L; for female participants the results were: $ALB \geq 43.296$ g/L, $GLO \geq 21.47$ g/L, $TP \geq 67.84$ g/L, and $PA \geq 176.97$ g/L. When serum protein ALB, GLO, TP, and PA are lower than these values, it indicates that the patient has increased demand for protein. If the patient continues to diet without adequate protein supplementation, acne lesions will be recurrent and difficult to cure even with systemic drug treatment.

There were limitations to this study. First, some patients may not have protein malnutrition but still show abnormal serum lipid profiles and hyperhomocysteinemia. Due to the limitations of conditions, this study did not make a comprehensive assessment of the nutritional status of patients. Second, the number of patients in this study was small. Third, there is no further research or analysis on the causes of protein malnutrition in these acne patients.

The results of this study showed that the serum protein concentrations of acne patients were significantly lower than healthy controls. We assume that acne patients are in malnutrition and/or that their requirements for protein are higher despite the serum protein concentrations range. A low serum protein concentration can be primarily regarded as a signal to identify

severe acne patient who require careful assessment and monitoring and for whom nutritional support may be needed as part of the treatment plan. Nutritional assessment and monitoring protocols should be developed for acne patients, and these protocols should include assessments of adequate nutritional intake and possibly serial measurements of serum proteins. A suitable high protein diet and vitamin supplementation (High dose niacin[16], folic acid, and vitamin B12) may benefit all acne patients, even if they are not definitely in malnutrition.

Conclusion

Acne patients are potentially accompanied with protein malnutrition. It is necessary to make a clear diagnosis according to the clinical manifestations and laboratory test of patients.

Abbreviations

ALB
albumin
ANOVA
analysis of variance
AGR
ALB/GLO ratio, $AGR = ALB / (TP - ALB) = ALB / GLO$
GLO
globulin
PA
prealbumin
SPSS
Statistic Package for Social Science
TP
Total Protein

Declarations

Ethics approval and consent to participate

The ethics committee of the First Affiliated Hospital of Guangxi University of Traditional Chinese Medicine reviewed and approved this study. The authors have no ethical conflicts of interest to disclose.

Consent for publication

The manuscript was agreed to be published

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest: None declared

Funding Sources: National Natural Science Foundation of China (CN). No. 81560760. Jianqi Lu. Prof. & MD

Authors' contributions: All authors contribute equally to the first author

Prof. Lu Jiangqi is the leader and moderator of the research work. Dr. Jiang Hao designed the study and wrote the paper. Other staff completed the physical examination of the participants, data collection, statistical analysis and other works.

Disclosure Statement

The authors of the article have no conflict of interest to declare.

Acknowledgement

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