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Assessment of Serum Desnutrin Levels in Patients with Acne Vulgaris

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ABSTRACT

Background: Acne vulgaris is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Desnutrin is the major triglyceride lipase in the adipose tissue of mice and excessive secretion from adipocytes results in decreased triacylglycerol storage and increased lipolysis, fatty acid oxidation and thermogenesis.

Objective: The aim of this study is to evaluate serum level of Desnutrin in acne vulgaris patients and correlate it with disease severity.

Patients and Methods: This study was performed on 40 patients with active acne lesions and 40 healthy subjects with no previous history of acne and no active acne lesions as controls. The control group was composed of age, gender, and Body mass index (BMI) matched individuals. All the patients were recruited from the outpatient clinic of Dermatology & Venereology Department, Ain Shams University hospitals, from March 2016 till August 2016.Serum desnutrin assessment was done by ELISA kit using Sandwich-ELISA as a method. The Micro elisa stripplate has been pre-coated with a Horse Radish Peroxidase antibody specific to desnutrin. The optical density was measured spectrophotometrically.

Results: There was a significantly lower level of serum desnutrin among cases compared to that of control group, while the fasting blood glucose level was significantly higher among cases compared to that of control group. The collective data from both study groups showed a significant negative correlation between the mean serum fasting blood glucose level and desnutrin level. There was no significant correlation between the severity of acne and serum desnutrin level.

Conclusion: The level of serum desnutrin can affect the occurrence and the progression but not the severity of acne among susceptible individuals. The level of fasting blood glucose is also of value regarding the occurrence of acne and has a negative effect on the level of desnutrin.

Keywords: Acne, Serum desnutrin, severity, fasting blood glucose, lipid profile.

INTRODUCTION

Acne vulgaris is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Acne can present as noninflammatory lesions, inflammatory lesions, or a mixture of both, affecting mostly the face but also the back and chest [(1)]. Acne vulgaris has a multifactorial pathogenesis, of which the key factor is genetics. Acne develops as a result of an interplay of the following four factors: (1) follicular epidermal hyperproliferation with subsequent plugging of the follicle, (2) excess sebum production, (3) the presence and activity of the commensal bacteria Propionibacterium acnes, and (4) inflammation [(2)].

Androgens and insulin contribute to an increase in sebum production in the pathogenesis of acne vulgaris. In addition, a correlation between insulin-like growth factor-1 (IGF-1) and facial sebum levels has been shown [(3)].

High glycemic load diets may result in increased androgen activity and IGF-1, thereby promoting the development of acne. There was significant improvement of acne severity in patients who adhered to a low glycemic load diet resulted in significant reductions in weight, body mass index, free androgen index, increased IGF-bindingprotein (IGFBP)-1 serum levels with reduced bioavailability of free IGF-1 and improved insulin sensitivity. Serum IGFBP-1 and IGFBP-3 increased from baseline in the low glycemic load group [(4)].

Desnutrin is a patatin-like domain-containing protein, desnutrin (PNPLA2), is also known as human adipose triglyceride lipase (ATGL), TTS2.2 and ipla2. Desnutrin is highly expressed in adipose tissue and produced at low levels in other tissues. Desnutrin secretion is stimulated by fasting and glucocorticoids [(5)].

Desnutrin is the major triglyceride lipase in the adipose tissue of mice and excessive secretion from adipocytes results in decreased triacylglycerol storage and increased lipolysis, fatty acid oxidation and thermogenesis. It has been reported that these

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effects result in high energy expenditure and resistance to diet-related obesity development [6].

Patients with acne vulgaris are more likely to experience an increase in serum glucose levels. This was found to probably cause suppression in serum Desnutrin levels and its function [7].

PATIENTS AND METHODS

This study was performed on 40 patients with active acne lesions and 40 healthy subjects with no previous history of acne and no active acne lesions as controls. The control group was composed of age, gender, and Body mass index (BMI) matched individuals. All the patients were recruited from the outpatient clinic of Dermatology & Venereology Department, Ain Shams University hospitals, from March 2016 till August 2016.

Demographic data were taken from all subjects and were subjected to Complete general examination, complete dermatological examination (type, number and sites of acne lesions and post acne scars), measurements of height, weight, waist circumference and calculate body mass index (Weight by Kg/ Height by Meter square), measurement of serum fasting glucose, triglycerides, LDL, VLDL, HDL, total cholesterol and serum desnutrin was carried out as well as assessment of acne severity.

Serum desnutrin assessment was done by ELISA kit using Sandwich-ELISA as a method.

Blood samples were collected at 9-10 am after overnight fasting to avoid any confounding effects associated with circadian rhythms. Samples (5 ml) were collected and centrifuged at 3000 × g for 5 min. The serum was transferred to micro centrifuge tubes and frozen at -80 ◦C prior to analysis.

The study was approved by the Ethics Board of Ain Shams University.

RESULTS

This case-control study was done on 40 Acne patients, their ages ranged from 18 to 34years with a mean ± SD of 23.73 ±4.28 years. They were 12 males (30%) and 28 females (70%), among which were 20% (8 patients) with mild acne, 65% (26 patients) with moderate acne and 15% (6 patients) with severe acne. Forty controls, their ages ranged from 18 to 33 years with a mean ± SD of 24.65 ± 3.95 years, among them thirteen were males (32.5%) and twenty-seven were females (67.5%). The cases and controls were age (P= 0.14) and sex (P= 0.809) matched.

There was no statistical significant difference between cases and controls as regard personal data. (Table 1).

Table 1: Comparison between demographic and clinical data among cases and controls

	Cases	**Controls**	**P**	**Sig**
Number	40	40		
Sex (F/M) Mean ± SD	28/12	27/13	0.809	NS
Age (years) Mean ± SD	24.65 ± 3.95	23.73 ± 4.28	0.14	NS
Height (cm) Mean ± SD	164.03 ± 9.86	163.45 ± 9.02	0.786	NS
Weight (kg) Mean ± SD	63.74 ± 9.37	64.58 ± 10.26	0.704	NS
Waist circumference (cm) Mean ± SD	84.46 ± 9.36	83.85 ± 7.84	0.752	NS
BMI (kg/m²) Mean ± SD	23.70 ± 3.23	24.01 ± 2.21	0.621	NS

- BMI: Body Mass Index.
- NS: Non-significant.

There was a high statistical significant difference between cases and controls as regard desnutrin level, a lower level was found among cases than controls. (Figure 1). Regarding fasting blood glucose level, a higher level was found among cases than controls. However, there was no significant statistical difference between cases and controls as regard the lipid profile. (Table 2).

Table 2: Comparison between desnutrin, lipid Profile and FBG among cases and controls

	Cases Mean ± SD	Controls Mean ± SD	P	Sig
Desnutrin	571.05 ± 241.53	1591.50 ± 638.79	).001	HS
FBG	88.07 ± 7.28	67.50 ± 9.89	).001	HS
Cholesterol	146.12 ± 28.20	159.53 ± 21.98	).020	NS
HDL	50.45 ± 10.89	51.60 ± 10.21	).627	NS
LDL	90.63 ± 23.48	95.97 ± 21.19	).288	NS
VLDL	16.00 ± 5.26	17.48 ± 4.09	).165	NS
Triglycerides	77.02 ± 29.13	85.55 ± 28.04	).186	NS

FBG: Fasting Blood Glucose.
HDL: High Density Lipoproteins.
LDL: Low Density Lipoproteins.
VLDL: Very Low Density Lipoproteins.
HS: Highly Significant.
NS: Non-significant.

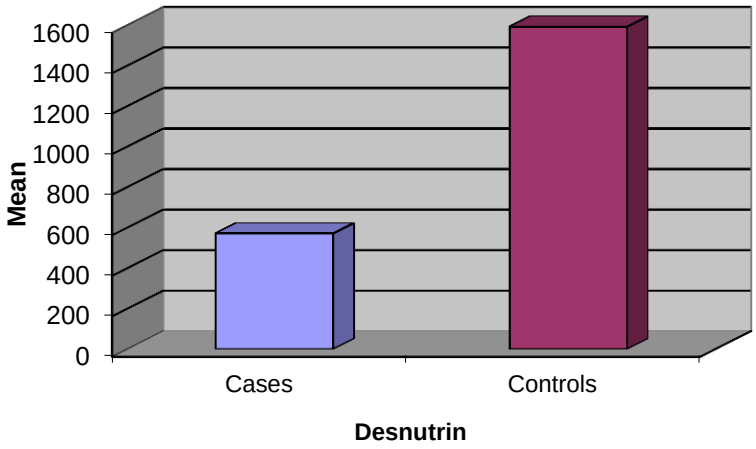

Figure 1: Comparison between cases and controls as regard desnutrin level (pg/ml).

There was no statistically significant difference between male and female cases as regards serum desnutrin level. (Table 3).

Table 3: Comparison between serum desnutrin level among male and female cases

	Sex				P	Sig
	Male		Female			
	Mean	±SD	Mean	±SD		
Desnutrin	557.50	182.128	576.86	265.764	0.820	NS

There was no statistically significant correlation between age and serum desnutrin level among cases. (Table 4).

Table 4: Correlation between age and serum desnutrin among cases

		Desnutrin
Age	**r**	.108
	P	.509
	Sig	NS

There was no statistical significant difference between males and females (within the control group) regarding serum desnutrin level. (Table 5).

Table 5: Comparison between serum desnutrin level among male and female controls

	Sex				**P**	**Sig**
	Male		**Female**			
	Mean	**±SD**	**Mean**	**±SD**		
Desnutrin	1537.31	702.100	1617.59	618.381	.715	NS

There was no statistical significant correlation between age and serum desnutrin level among cases. (Table 6).

Table 6: Correlation between age and serum desnutrin among controls

		Desnutrin
Age	**r**	-.139
	P	.392
	Sig	NS

There was no statistical significant difference in serum desnutrin level between cases of acne with different grades of severity. (Table 7 and figure 2).

Table 7: Comparison between serum desnutrin levels between cases according to the severity degree.

	Severity						**P**	**Sig**
	Mild		**Moderate**		**Severe**			
	Mean	**±SD**	**Mean**	**±SD**	**Mean**	**±SD**		
Desnutrin	607.50	276.93	566.92	227.03	540.33	294.25	0.872	NS

- NS: Non-significant.

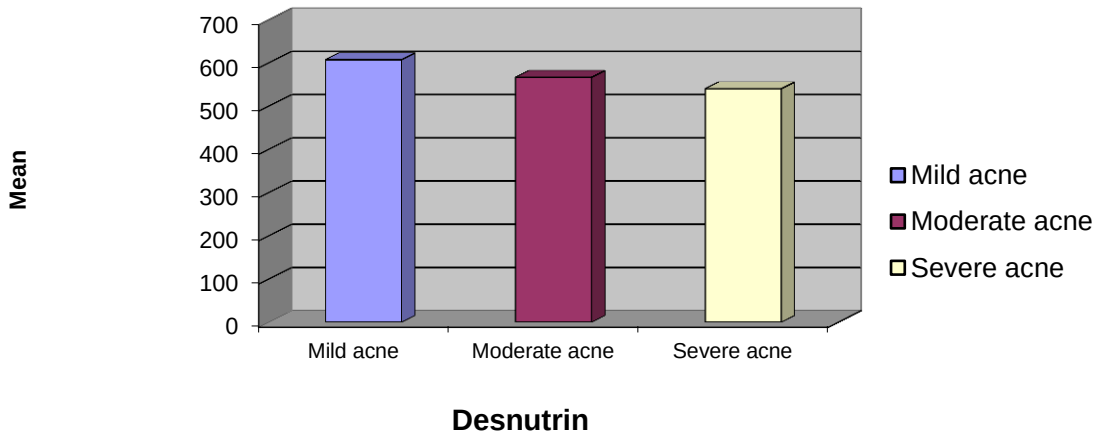

Figure 2: Comparison of serum desnutrin between cases according to severity

There was no statistically significant correlation between each of the mean serum fasting blood glucose level, lipid profile and serum desnutrin level among acne patients (table 8).

Table 8: Correlations between each of FBG, lipid profile and serum desnutrin among cases

		Desnutrin
FBG	r	-.017
	P	.919
	Sig	NS
Cholesterol	r	-.044
	P	.789
	Sig	NS
HDL	r	-.276
	P	.084
	Sig	NS
LDL	r	-.040
	P	.808
	Sig	NS
VLDL	r	-.029
	P	.858
	Sig	NS
Triglycerides	r	.025
	P	.879
	Sig	NS

NS: Non-significant.

There was no statistical significant correlation between each of the mean serum fasting blood glucose level, lipid profile and desnutrin level among controls (table 9).

Table 9: Correlations between each of FBG, lipid profile and desnutrin among controls

		Desnutrin
FBG	R	-.010
	P	.952
	Sig	NS
Cholesterol	R	-.084
	P	.608
	Sig	NS
HDL	R	-.054
	P	.741
	Sig	NS
LDL	R	.171
	P	.292
	Sig	NS
VLDL	R	-.071
	P	.664
	Sig	NS
Triglycerides	R	.086
	P	.598
	Sig	NS

NS: Non-significant.

There was a highly statistical significant negative correlation between the mean serum fasting blood glucose level and desnutrin level among both study groups (table 10 and figure 3), but no statistical significant correlation between the mean serum lipid profile and desnutrin level was found among both study groups (table 11).

Table 10: Correlations between FBG and desnutrin among both study groups

		Desnutrin
FBG	R	-.566(**)
	P	.001
	Sig	HS

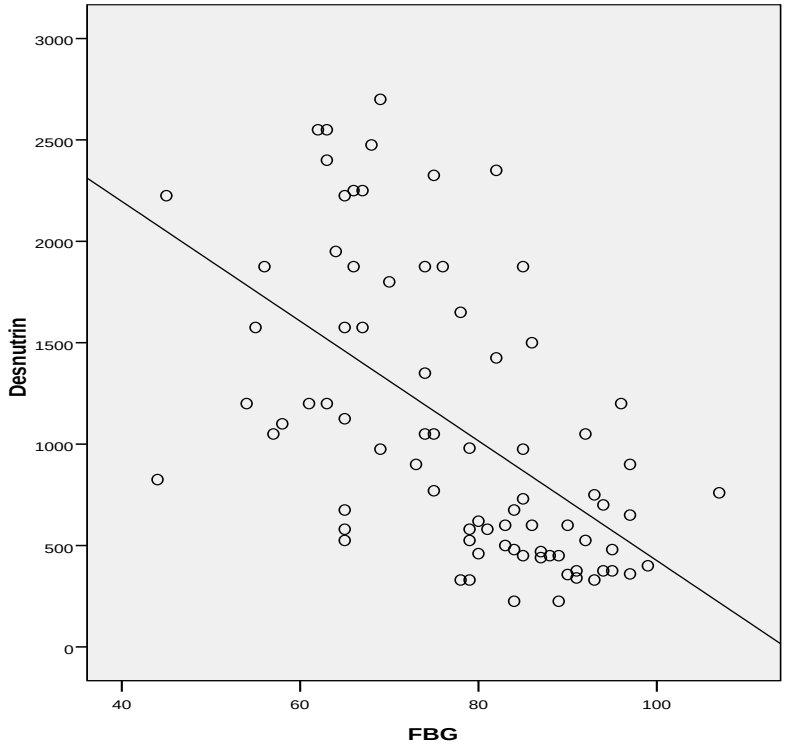

Figure 4: Correlations between FBG and desnutrin among both study groups

Table 12: Correlations between lipid profile and desnutrin among both study groups

		Desnutrin
Cholesterol	R	-.044
	P	.789
	Sig	NS
HDL	R	-.276
	P	.084
	Sig	NS
LDL	R	-.040
	P	.808
	Sig	NS
VLDL	R	-.029
	P	.858
	Sig	NS
Triglycerides	R	.025
	P	.879
	Sig	NS

NS: Non-significant.

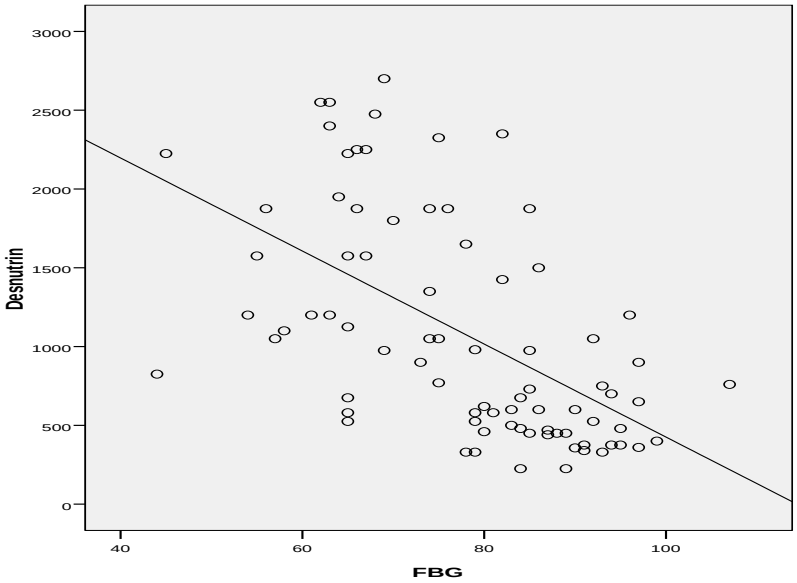

Figure 4: Correlations between FBG and desnutrin among both study groups

Table 12: Correlations between lipid profile and desnutrin among both study groups

		Desnutrin
Cholesterol	R	-.044
	P	.789
	Sig	NS
HDL	R	-.276
	P	.084
	Sig	NS
LDL	R	-.040
	P	.808
	Sig	NS
VLDL	R	-.029
	P	.858
	Sig	NS
Triglycerides	R	.025
	P	.879
	Sig	NS

NS: Non-significant.

DISCUSSION

In this study, we aimed at finding a relation between serum desnutrin level and acne of different grades of severity, together with correlating these results with the levels of fasting blood glucose and lipid profile in serum of acne patients versus normal controls.

The level of serum desnutrin was significantly lower in cases than in controls. This result is aligned with that of the study done by ***Demir et al.*** [9], on 25 patients presenting with acne vulgaris and 25 control subjects.

In the study done by ***Demir et al.*** [9], patients with acne vulgaris also had a mean serum desnutrin level significantly lower compared to that of control group. There also was a significantly higher level of fasting blood glucose among cases than controls which was also in harmony with those found by ***Demir et al.*** [9]. There was also a negative correlation between fasting blood glucose level and serum desnutrin level which also is aligned with the study done by ***Demir et al.*** [9].

In addition, ***Demir et al.*** [9], found that patients also had insulin levels and HOMA-IR values significantly higher than the control group. A positive correlation was found between insulin and desnutrin levels. This may explain the results of our study in relation to fasting blood glucose levels and its relation to serum desnutrin levels in patients and controls. It could be due to the negative feedback on serum desnutrin levels by insulin resistance in patients rather than controls. These results were explained by those found by ***Kershaw et al.*** [10], on mice. That study measured the level of adipose tissue desnutrin, blood glucose twice daily and insulin level among two groups of mice, a fasting group for 6, 12, 18 and 24 hours and a group fed on ad libitum. The results showed that the high blood glucose among mice results in consequent stimulation of insulin release which in turn inhibits desnutrin; concluding that in patients with acne vulgaris, as a result of increased

levels of serum glucose and insulin, the function of desnutrin was suppressed, perhaps contributing to insulin resistance.

Blood glucose levels have been reported to be elevated in patients with acne vulgaris in comparison with healthy controls. This was linked to the relatively high glycemic load diet in relation to flaring of acne lesions compared to significant decrease in the activity of acne when lowering the glycemic load in the diet and the subsequent drop in the fasting blood glucose of acne patients [(4)].

This occurs primarily because an increase in blood glucose levels stimulates the secretion of insulin, which decreases the binding protein for IGF-1, facilitating the effects of IGF-1 on cell proliferation. High insulin concentrations in the fasting and/or post-prandial states may exacerbate acne by increasing the proliferation of basal keratinocytes. Insulin also stimulates the synthesis of androgens, leading to high sebum production, a recognized correlate of acne severity [(8)].

We found that there was no significant difference in the level of triglycerides, total cholesterol, LDL, HDL and VLDL between cases and controls. This result is consistent to that done by ***Demir et al.*** [(9)], which can be explained by the outcome of a study done by ***Villena et al.*** [(5)], stating that desnutrin is strictly an adipose tissue triglyceride hydrolase, which doesn't affect cholesterol or phospholipids transforming them into free fatty acids intracellularly within the adipose tissue fat cells, which in turn are transferred rapidly to the medium as free fatty acids not triglycerides, and this explains the drop in triglycerides stores in adipose tissue cells without a reciprocal increase in serum triglycerides level.

Also, a study carried by ***Ahmadian et al.*** [(11)], found that there was no significant increase in the level of circulating non -esterified fatty acids (NEFAs) in relation to desnutrin overexpression. This was linked to the increased energy expenditure corresponding to increased fatty acid release and the increased insulin sensitivity. Combining the data from both cases and controls showed a significant negative statistical correlation between fasting blood glucose level and serum desnutrin level, which consequently aligns with the previous results of this study as well as those obtained by ***Demir et al.*** [(9)].

In this study, there was no significant correlation between acne severity and the level of serum desnutrin. We also found no significant difference between serum desnutrin level in males and in females in both cases and controls. Also, there was no correlation between age and serum desnutrin level either in cases nor in controls. Up to our knowledge this study is the first to correlate between severity of acne and the level of desnutrin in patients. Previous reports only assessed serum desnutrin in relation to presence or absence of acne. This means that the single most important factor affecting desnutrin is the glycemic load.

Conflict of interest

There is no conflict of interest.

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