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Serum Desnutrin Levels in Patients with Psoriasis and their Relationship with Metabolic Syndrome and Insulin Resistance

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Background: There is an association between psoriasis and metabolic syndrome (MetS). Desnutrin is a lipase found in the adipose tissue of mice that increases lipolysis, fatty acid oxidation within adipose tissue, and thermogenesis, resulting in higher energy expenditure and resistance to obesity.

Objective: We examined the desnutrin levels in patients with psoriasis and their association with insulin resistance and MetS.

Methods: This study enrolled 30 patients with psoriasis and 30 controls. Fasting blood glucose, serum lipids, insulin, C-reactive peptide, and desnutrin levels were measured. The extent and severity of lesions were determined using the Psoriasis Area and Severity Index (PASI) and body surface area (BSA) involvement.

Results: The mean serum desnutrin level in the patients with psoriasis (9.02 ± 1.90) was significantly ($p = 0.04$) lower than in the controls (10.66 ± 3.86). The mean serum desnutrin levels in individuals with MetS were similar to individuals without MetS.

Conclusion: Serum desnutrin levels in patients with psoriasis were lower than those of the controls. In addition, low serum desnutrin levels were not associated with MetS or insulin resistance in our study. This may be due to the low number of patients with MetS or insulin resistance or due to the actual low serum desnutrin levels.

Keywords: Psoriasis, Desnutrin, Insulin resistance, Metabolic syndrome

INTRODUCTION

The prevalence rates of metabolic syndrome (MetS), subclinical atherosclerosis, cardiovascular risk factors, diabetes, hypertension, dyslipidaemia, and obesity are higher among patients with psoriasis than they are in the general population [1,2]. The association between psoriasis and MetS is thought to be related to chronic inflammation [3]. Increased proinflammatory cytokines in chronic inflammation result in atherogenesis and peripheral insulin resistance, which in turn cause hypertension and a tendency towards type 2 diabetes [4,5]. Life expectancy is shortened in patients with psoriasis, largely due to cardiovascular disease [6].

Desnutrin, also called adipose triglyceride lipase, is a recently discovered peptide hormone. It is found primarily in adipose tissue and in lesser amounts in other tissues. Fasting and glucocorticoids stimulate the release of desnutrin [7,8].

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Desnutrin is the major triglyceride lipase in the adipose tissue of rats and decreases the storage of triacylglycerol, while it increases fatty acid oxidation and thermogenesis by increasing lipolysis when released in excess. Therefore, it results in resistance to diet-related obesity [8-10]. Whenever lipolysis in adipose tissue is altered, triacylglycerol is stored and free fatty acids are increased. This provides a basis for serious metabolic conditions such as insulin resistance, type 2 diabetes, hypertension, cardiovascular diseases, and obesity [11-13].

This study investigated the serum desnutrin levels in patients with psoriasis and their association with insulin resistance and MetS.

MATERIALS AND METHODS

Study Design

This study enrolled 30 patients with psoriasis and 30 healthy controls. The study was approved by the local ethics committee and informed consent was obtained from all participants. Exclusion criteria were as follows: age <18 years, systemic disease (diabetes, hypothyroidism, or hyperthyroidism), pregnancy, malignancy, and systemic drug or alcohol abuse. Age, gender, height, weight, and waist circumferences were recorded. Body mass index [BMI= weight (kg)/height² (m²)] was calculated and obesity was determined according to the World Health Organisation classification as follows: normal range (18.5–24.9 kg/m²), grade 1 overweight (25.0–29.9 kg/m²), grade 2 overweight (30.0–39.9 kg/m²), and grade 3 overweight (≥ 40.0 kg/m²). A BMI > 30 was deemed to represent obesity [14].

The severity of psoriasis was assessed using the Psoriasis Area and Severity Index (PASI) and percent body surface area (BSA) involvement [15]. Quality of life was evaluated using the Dermatology Life Quality Index (DLQI), which Ozturkcan et al. validated in Turkish [16].

Laboratory Assessment

Fasting blood glucose, total cholesterol, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), high-density lipoprotein (HDL), triglyceride, insulin, and C-peptide levels were measured. The homeostasis model assessment of insulin resistance (HOMA-IR = [insulin (mU/L) $\times$ glucose (mmol/L)] / 22.5) was used to calculate insulin resistance [17]. MetS was diagnosed using the International Diabetes Foundation criteria as obesity in the presence of two or more of the following clinical features: fasting blood glucose ≥ 100 mg/dL; hypertriglyceridemia ≥ 150 mg/dL, HDL < 40 mg/dL in males or < 50 mg/dL in females; blood pressure $\geq 130/85$ mm Hg; and waist circumference ≥ 94 cm in males or ≥ 80 cm in females [18].

Collection and storage of blood samples

As desnutrin is a peptide hormone, in order to prevent proteolysis, aprotinin (500 kallikrein units/mL) was added to

untreated collection tubes before collecting blood samples. Samples were collected at 9-10 a.m. after an overnight fast to avoid any confounding effects associated with circadian rhythms. Samples (5 mL) were collected and centrifuged at $3000 \times g$ for 5 min. The serum was transferred to microcentrifuge tubes and frozen at -80°C until analysis. Serum desnutrin levels were determined using an enzyme-linked immunosorbent assay (ELISA), according to the manufacturer's protocol (CUSABIO; cat. no: CSBE12688h, lot: N17060631) using a commercial ELISA kit (Wuhan; P.R. China). The inter- and intra-assay coefficients of variation were < 8.1% and <7.0%, respectively. The minimum detectable dose of human desnutrin is 1.56 mIU/mL, while maximum detectable dose of human desnutrin is 400 mIU/mL.

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS ver. 22.0. The data obtained in the study were expressed as means $\pm$ SD. The independent samples t-test and Mann-Whitney U-test were used to compare the groups. Differences with $p < 0.05$ were accepted as statistically significant.

RESULTS

The mean age of the psoriasis patients and controls was 30.06 ± 9.7 (range 18–55) and 28.23 ± 7.3 (range 18–45) years, respectively. There were no significant differences in mean age, BMI, or gender distribution between the groups. **Table 1** summarises the demographic and clinical characteristics of the patient and control groups.

In the psoriasis group, the mean duration of the disease was 10.23 ± 6.00 (range 1–22) years. There was nail involvement in 15 (50.0%) patients, genital mucosa involvement in six (20.0%), and scalp involvement in 24 (80.0%).

The mean serum desnutrin level was significantly ($p = 0.04$) lower in the patient group (9.02 ± 1.90 mIU/mL) than in the controls (10.66 ± 3.86 mIU/mL). **Table 2** summarises the laboratory findings of the patient and the control groups.

Increased insulin resistance was found in seven (23.3%) patients and three (10.0%) controls. There was no significant difference between the mean serum desnutrin level of the patients with insulin resistance (8.73 ± 0.60 mIU/mL) and those without insulin resistance (9.11 ± 2.15 mIU/mL).

Twelve patients (40.0%) and 10 controls (33.3%) were diagnosed with MetS. The mean serum desnutrin level in the patients with MetS and without MetS was 9.37 ± 2.84 and 8.79 ± 0.90 mIU/mL, respectively. The mean serum desnutrin level in the controls with and without MetS was 10.00 ± 2.48 and 10.99 ± 4.41 mIU/mL, respectively. The mean desnutrin levels in individuals with MetS (9.65 ± 2.64 mIU/mL) and without MetS (9.95 ± 3.41 mIU/mL) in both the patient and control groups were similar. Patients with psoriasis with or without MetS were compared with respect

to BSA involvement, PASI, and DLQI. The duration of the disease (13.91 ± 4.48 years) and BSA involvement ($24.47 \pm 16.57\%$) of the patients with MetS were significantly higher than those of the patients without MetS (7.77 ± 5.71 years

and $14.48 \pm 15.36\%$, respectively) ($p = 0.005$ and $p = 0.04$, respectively).

Table 1. Demographics and clinical characteristics of the patient and control groups

	Psoriasis vulgaris	Control
n	30	30
Gender (M/F)	15/15	15/15
Age* (year)	30.06±9.7	28.23±7.3
BMI* (kg/m²)	23.64±2.51	22.45±2.40
Waist Circumference* (cm)	84.00±10.84 (F) 85.40±11.28 (M)	75.73±6.81 (F)[‡] 87.20±10.05 (M)[‡]
PASI*	6.70±4.86	
Body Surface Area*	18.47±16.35	

*(Mean±SD), f=Female, M=Male, [‡]($p=0.001$)

Table 2. The laboratory findings of the patient and the control groups

Parameter	Psoriasis vulgaris	Control	p
Glucose* (mg/dL)	86.26±12.07	81.33±10.79	p>0.05
Triglycerides* (mg/dL)	115.20±71.33	101.63±54.57	p>0.05
LDL-cholesterol* (mg/dL)	112.05±35.42	97.18±34.69	p>0.05
HDL-cholesterol* (mg/dL)	45.23±9.47	48.36±17.07	p>0.05
VLDL-cholesterol* (mg/dL)	22.20±10.62	21.76±16.92	p>0.05
Total cholesterol* (mg/dL)	117.40±41.06	168.83±29.31	p>0.05
Insulin* (μIU/mL)	8.07±7.10	7.11±3.79	p>0.05
C-peptid* (ng/mL)	1.84±0.76	1.75±0.61	p>0.05
HOMA-IR values*	1.70±1.49	1.43±0.83	p>0.05
Desnutrin* (mIU/mL)	9.02±1.90	10.66±3.86	p=0.04

*(Mean±SD)

The mean serum desnutrin level was higher in men (10.40 ± 4.03 mIU/mL) than in women (8.54 ± 0.39 mIU/mL); however, the difference was not significant. There was also no significant association between the BMI, BSA, PASI score and mean desnutrin level.

DISCUSSION

Desnutrin increases lipolysis by decreasing the secretion of insulin during a prolonged fast [19]. Insulin is also a powerful antilipolytic hormone and inhibits lipolysis in the postprandial state [20]. Desnutrin increases the sensitivity to insulin by increasing fatty acid oxidation and energy use in adipocytes [9]. The inhibition of the activity of desnutrin by insulin contributes to the development of obesity, insulin resistance, and hyperlipidaemia [13]. In one study, patients with MetS were fed diets containing different proportions of fat for 12 weeks. At the end of the diet intervention, desnutrin gene synthesis was increased in both the fasting and postprandial periods in the adipose tissue of individuals who were on a high-fat diet. Increased desnutrin synthesis combined with increased glucose, insulin resistance, and HOMA-IR levels in patients with MetS has been explained by corruption of the suppressive function of insulin on desnutrin by saturated fatty acids [21]. Another study reported that the lipolytic activity of desnutrin in adipocytes after fatty meals decreased at the end of the postprandial period due to the inhibitory effect of insulin on intracellular lipase [22]. These studies involved diet interventions. However, it was also reported that desnutrin gene synthesis in the adipose tissue in patients with MetS continued without being affected by changes in the fat composition of the diet, and the gene synthesis was reported to increase after consuming low-fat, high-carbohydrate diets [23].

In obese individuals, desnutrin increases due to inflammation in adipose tissue and decreases after weight loss [24]. Similarly, in a study of 28 patients, the patients lost weight while on a low-energy diet for 2 months and they were followed for 10 months with the goal of preserving their post-diet weights. The desnutrin level in adipose tissue during the weight-loss period was positively correlated with weight loss; however, the desnutrin level increased during the 10-month follow-up period [25]. Camargo et al. found a positive correlation between desnutrin mRNA levels in the fasting state after a dietary intervention period and BMI [21].

A few studies have analysed serum desnutrin levels. Demir et al. found a positive correlation between the levels of serum fasting insulin and desnutrin in patients with acne vulgaris [26]. In a study comparing 66 patients with diabetes and 48 obese, overweight, or normal weight individuals with normal glucose tolerance, Yang et al. reported that serum fasting desnutrin levels were lower in obese or overweight individuals compared to the normal weight individuals, including those with type 2 diabetes, and that desnutrin

levels were negatively correlated with HOMA-IR, triglycerides, and BMI [27]. In our study, no significant associations were found among psoriasis patients between decreased serum desnutrin levels and MetS, insulin resistance, HOMA-IR, or BMI. Serum desnutrin levels may have been affected by inflammatory processes, in addition to metabolic factors.

In psoriasis, proinflammatory cytokines, such as IL-6 and TNF- α , increase locally and systemically [28]. Inflammation and, in particular, TNF- α have been reported to increase lipolysis [29]. Camargo et al. observed that desnutrin gene synthesis affected lipid metabolism and inflammatory markers and they also reported a positive correlation between desnutrin mRNA levels in adipose tissue and fasting and postprandial plasma TNF- α concentrations after completion of the diet intervention [21].

Desnutrin is a newly discovered molecule and its functions are affected by many factors, such as inflammatory processes, fasting-satiety, a fatty diet, and insulin. Analyses of the desnutrin levels in adipose tissue have demonstrated that desnutrin is an adipokine and its rate of synthesis in adipose tissue is not fully reflected in the serum. In this study, we also encountered difficulty measuring the serum desnutrin with an ELISA method, since its serum levels are very low.

In conclusion, the level of desnutrin, which has an important role in carbohydrate and fat metabolism, was significantly lower in psoriasis patients in this study. It was not directly related to MetS or insulin resistance, possibly due to the low number of patients with MetS or insulin resistance or due to the low serum desnutrin levels observed in the study. Desnutrin level helped to distinguish patients with psoriasis from control subjects. Therefore, we believe that desnutrin may serve as a circulating bio-marker reflecting the inflammatory condition in psoriasis. Larger controlled studies should evaluate the relationship between desnutrin and psoriasis as well as other inflammatory diseases.

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REFERENCES

1. Karoli R, Fatima J, Shukla V, et al. (2013) A study of cardio-metabolic risk profile in patients with psoriasis. *J Assoc Physicians India* 61: 798-803.
2. Neimann AL, Shin DB, Wang X, et al. (2006) Prevalence of cardiovascular risk factors in patients with psoriasis. *J Am Acad Dermatol* 55: 829-835.
3. Padhi T (2013) Metabolic syndrome and skin: psoriasis and beyond. *Indian J Dermatol* 58: 299-305.

4. Henseler T, Christophers E (1995) Disease concomitance in psoriasis. *J Am Acad Dermatol* 32: 982-986.
5. Sommer DM, Jenisch S, Suchan M, et al. (2006) Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. *Arch Dermatol Res* 298: 321-328.
6. Abuabara K, Azfar RS, Shin DB, et al. (2010) Cause-specific mortality in patients with severe psoriasis: a population-based cohort study in the U.K. *Br J Dermatol* 163: 586-592.
7. Zimmermann R, Strauss JG, Haemmerle G, et al. (2004) Fat mobilization in adipose tissue is promoted by adipose triglyceride lipase. *Science* 306: 1383-1386.
8. Villena JA, Roy S, Sarkadi-Nagy E, et al. (2004) Desnutrin, an adipocyte gene encoding a novel patatin domain-containing protein, is induced by fasting and glucocorticoids: ectopic expression of desnutrin increases triglyceride hydrolysis. *J Biol Chem* 279: 47066-47075.
9. Ahmadian M, Duncan RE, Varady KA, et al. (2009) Adipose Overexpression of Desnutrin Promotes Fatty Acid Utilization and Attenuates Diet-induced Obesity. *Diabetes* 58: 855-866.
10. Lake AC, Sun Y, Li JL, et al. (2005) Expression, regulation, and triglyceride hydrolase activity of Adiponutrin family members. *J Lipid Res* 46: 2477-2487.
11. Ahmadian M, Duncan RE, Jaworski K, Sarkadi-Nagy E, Sul HS (2007) Triacylglycerol metabolism in adipose tissue. *Future Lipidol* 2: 229-37.
12. Unger RH (2002) Lipotoxic diseases. *Annu Rev Med* 53: 319-336.
13. Kralisch S, Klein J, Lossner U, et al. (2005) Isoproterenol, TNF alpha, and insulin downregulate adipose triglyceride lipase in 3T3-L1 adipocytes. *Mol Cell Endocrinol* 240: 43-49.
14. WHO (1995) Physical status: the use and interpretation of anthropometry: report of a WHO expert committee. *WHO Tech Rep Ser* 854: 1-452.
15. Henseler T, Schmitt-Rau K (2008) A comparison between BSA, PASI, PLASI, and SAPASI as measures of disease severity and improvement by therapy in patients with psoriasis. *Int J Dermatol* 47: 1019-1023.
16. Ozturkcan S, Ermertcan AT, Eser E, Sahin MT (2006) Cross validation of the Turkish version of dermatology life quality index. *Int J Dermatol* 45: 1300-1307.
17. Matthews DR, Hosker JP, Rudenski AS, et al. (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28: 412-419.
18. Prodromas IS, Stylianos S, Dimitros T (2008) Metabolic syndrome in rheumatic diseases: epidemiology, pathophysiology, and clinical implications. *Arthritis Research and Therapy* 2008; 10: 207.
19. Boden G, Shulman GI (2002) Free fatty acids in obesity and type 2 diabetes: defining their role in the development of insulin resistance and betacell dysfunction. *Eur J Clin Invest* 32: 14-23.
20. Kershaw EE, Hamm JK, Verhagen LA, et al. (2006) Adipose triglyceride lipase: function, regulation by insulin, and comparison with adiponutrin. *Diabetes* 55: 148-157.
21. Camargo A, Meneses ME, Pérez-Martínez P, et al. (2014) Dietary fat modifies lipid metabolism in the adipose tissue of metabolic syndrome patients. *Genes Nutr* 9: 409.
22. Fielding B (2011) Tracing the fate of dietary fatty acids: metabolic studies of postprandial lipaemia in human subjects. *Proc Nutr Soc* 70: 342-350.
23. van Hees AM, Jocken JW, Essers Y, et al. (2012) Adipose triglyceride lipase and hormone-sensitive lipase protein expression in subcutaneous adipose tissue is decreased after an isoenergetic low-fat high-complex carbohydrate diet in the metabolic syndrome. *Metabolism* 61: 1404-1412.
24. Jocken JW, Langin D, Smit E, et al. (2007) Adipose triglyceride lipase and hormone-sensitive lipase protein expression is decreased in the obese insulin-resistant state. *J Clin Endocrinol Metab* 92: 2292-2299.
25. Verhoeve SP, Camps SG, Bouwman FG, et al. (2013) Physiological response of adipocytes to weight loss and maintenance. *PLoS One* 8: e58011.
26. Demir B, Ucak H, Cicek D, et al. (2014) Changes in serum desnutrin levels in patients with acne vulgaris. *Eur J Dermatol*.
27. Yang L, Chen SJ, Yuan GY, et al. (2014) Association of serum adipose triglyceride lipase levels with obesity and diabetes. *Genet Mol Res* 13: 6746-6751.
28. Schon MP, Boehncke WHO (2005) Psoriasis. *N Engl J Med* 352: 1899-1912.

29. Langin D, Arner P (2006) Importance of TNF alpha and neutral lipases in human adipose tissue lipolysis. Trends Endocrinol Metab 17: 314-320.