

Circulating adiponectin levels in Indian patients with psoriasis and its relation to metabolic syndrome

Shraddha Madanagobalane, Venkatswami Sandhya, Sankarasubramanian Anandan, Krishna G. Seshadri¹

Departments of Dermatology, ¹Endocrinology and Metabolism, Sri Ramachandra University, Porur, Chennai, Tamil Nadu, India

ABSTRACT

Background: Adiponectin is a cytokine mainly secreted from the adipose tissue, which has insulin-sensitizing effects, antiatherosclerotic actions, and antiinflammatory properties. There are a few studies that have demonstrated that adiponectin is reduced in patients with psoriasis suggesting that this adipocytokine may have a role in the pathogenesis of psoriasis. There have been no studies so far on adiponectin in relation to psoriasis and metabolic syndrome (MetS). **Objectives:** This study was performed to analyze serum adiponectin and insulin levels in psoriasis patients with and without MetS and in controls with and without MetS. **Materials and Methods:** We performed a case control study on 60 psoriasis patients, 29 with MetS and 31 without MetS and 40 controls, 20 with and 20 without MetS, matched for age, sex, and body mass index (BMI). Fasting serum insulin and adiponectin levels were measured in all groups. **Results:** The overall serum adiponectin levels were significantly reduced in psoriasis patients when compared with controls ($P = 0.000$). A significant reduction was also observed in psoriasis patients with MetS than those without MetS in the same group ($P = 0.000$). Similar decrease was observed between those with MetS in the psoriasis and control groups ($P = 0.001$). The lowest mean value of serum adiponectin (6387.9 ng/ml) was observed in psoriasis with MetS group and highest value (12146.3 ng/ml) in controls without MetS. **Conclusion:** Adiponectin levels are decreased in psoriasis patients irrespective of MetS thus indicating a role in its pathogenesis. This study prompts future trials on drugs increasing adiponectin levels in patients with psoriasis.

Key words: Psoriasis, metabolic syndrome, serum adiponectin

INTRODUCTION

Adiponectin is a cytokine mainly secreted from the adipose tissue. It is a known key player in the pathogenesis of metabolic syndrome (MetS) and cardiovascular disease.^[1] A greater number of patients with psoriasis have MetS.^[2,3] Serum adiponectin levels have also been demonstrated to be decreased in some but not all studies in patients with psoriasis.^[4-6] The studies so far have evaluated adiponectin levels in psoriasis patients and normal controls. Some have

studied its levels before and after therapy^[7] and some in relation to obesity.^[6,8] However, to our knowledge there are no studies examining the relation between MetS, adiponectin, and psoriasis. We therefore undertook this study to understand the role of adiponectin in relation to psoriasis and MetS. We have also studied the adiponectin pattern in Indian patients with psoriasis.

Aims and objectives

To analyze serum adiponectin, insulin levels, and insulin resistance (IR) in psoriatic patients with and without MetS and in controls with and without MetS.

Study population

The study was approved by the ethics committee of Sri Ramachandra University and was conducted in accordance with the principles of the Declaration of Helsinki. The patients were from Chennai and its suburbs. A total of 60 patients with psoriasis (plaque type) and 40 controls gave informed consent.

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Corresponding Author: Dr. Shraddha Madanagobalane, Department of Dermatology, Sri Ramachandra University, Porur, Chennai - 600 116, Tamil Nadu, India. E-mail: mshraddha22@yahoo.co.in

Inclusion criteria

Sixty patients who had psoriasis and aged more than 18 years were included from the psoriasis outpatient clinic.

They were grouped into two groups. One group had 31 patients with plaque type psoriasis without MetS or any other metabolic comorbidities like diabetes, dyslipidemia, obesity, or hypertension. The other 29 psoriatic patients who had MetS as per SAM NCEP ATP III criteria (South Asian Modified National Cholesterol Education Program Adult treatment panel III) were included in the other group.

The controls were 40 patients who attended the skin department for other noninflammatory skin ailments. Of these, 20 patients who had MetS and 20 without MetS or any other metabolic comorbidity were included.

Exclusion criteria

All psoriatic patients receiving systemic therapy or those who had received any systemic drug in the last 12 weeks were excluded from the study.

MATERIALS AND METHODS

A detailed history included duration of the disease, joint pains, smoking, alcohol consumption, diet, presence of other systemic illness, past intake of systemic agents for psoriasis, and concomitant intake of medicines for other illnesses. Clinical examination included measurement of height, weight, waist circumference, and blood pressure. The body mass index (BMI) was determined by weight and height calculations using the following equation. $BMI = \text{weight in kg/square height in meters}$. The waist circumference was measured by placing the measuring tape snugly around the abdomen at the level of the iliac crest. The blood pressure was taken in the sitting posture and the average of two measurements was recorded.

Each participant was thoroughly examined by two dermatologists who classified psoriasis according to the International classification of Diseases, Tenth revision. The plaque type of psoriasis is the most common type, which is most typically characterized by circular-to-oval red plaques distributed over extensor body surfaces and the scalp. Extent of involvement was assessed using Psoriasis Area and Severity Index (PASI).^[9] All patients and controls underwent the following laboratory tests at Sri Ramachandra Central Diagnostic Laboratory after overnight fasting. Serum glucose levels was measured by the hexokinase method while lipid profile, which included total cholesterol, low density lipoprotein, high density lipoprotein, and triglyceride levels was assessed by enzymatic methods.

Assay for serum adiponectin and insulin

Blood samples were collected from both patients and controls after overnight fasting in tubes without anticoagulant. These were centrifuged to obtain serum. Serum adiponectin was measured using enzyme linked immune assay (Human adiponectin; Orgenium Laboratories Business Unit, Tiihtie 3, Finland). Serum insulin levels were measured using AXSYM autoanalyzer (Abbott Laboratory, USA; CV4-6%).

Diagnostic criteria

According to the Indian Health Ministry guidelines, a BMI from 23 to 24.9 is overweight; a BMI greater than or equal to 25 is moderate obesity; a BMI greater than or equal to 30 is severe obesity.^[10] A waist circumference of more than 90 and 80 cm for men and women, respectively, was considered as abdominal obesity.^[10]

Psoriasis severity was classified into mild psoriasis (PASI < 10) and severe psoriasis (PASI > 10).^[11,12] Psoriatic arthritis was diagnosed according to standard criteria.^[13] Patients were considered to have diabetes if their fasting glucose was more than or equal to 126 mg/dl (6.9 mmol/L).^[14] Patients receiving antihypertensive medications or two or more readings more than 140/90 mmHg or blood pressure greater than 130/80 mmHg in patients with diabetes mellitus or renal disease was regarded as hypertension.^[15] Presence of dyslipidemia was diagnosed when a subject had one or more of the following criteria: (1) Low density lipoprotein (LDL) cholesterol of ≥ 100 mg/dl (2.58 mmol/L); (2) plasma triglycerides of ≥ 150 mg/dl (1.69 mmol/L); (3) High density lipoprotein (HDL) cholesterol of ≤ 40 mg/dl (1.03 mmol/L); and (4) use of one or more lipid-lowering drugs.^[16]

MetS was diagnosed using the South Asian Modified National Cholesterol Education Program Adult Treatment Panel III criteria (SAM-NCEP criteria).^[17] If three or more of the following were present: Abdominal obesity (definition of abdominal obesity was modified using Asia Pacific World Health Organization (WHO) guidelines as waist circumference $> \text{or} = 90$ cm for and $> \text{or} = 80$ cm for females, blood pressure $> 130/85$ mmHg, fasting blood glucose $> \text{or} = 100$ mg/dl, hypertriglyceridemia > 150 mg/dl, or low HDL cholesterol (< 40 mg/dl for males and < 50 mg/dl for females), the patient was diagnosed as MetS.

IR was estimated by HOMA-IR, calculated as follows; $\text{fasting serum insulin } (\mu\text{U/ml}) \times \text{fasting plasma glucose (mg/dl)} / 405$.^[18]

Statistical analysis

Analysis was carried out using SPSS (Statistical Package for social studies), South Asia Pvt. Ltd. version 17.0

software packages. Comparisons among groups were performed using unpaired *t*-test for continuous variables and Chi-square test for categorical variables. Where the standard deviation was high, nonparametric Mann-Whitney test was used. The association between BMI, abdominal girth, PASI score and duration of psoriasis, serum insulin, HOMA-IR with serum adiponectin levels was tested using the Kendall tau rank correlation analysis. Associations between adiponectin and the individual features of the MetS and serum insulin were examined using one way analysis of variance (ANOVA) test. Logistic regression analysis was used to test the hypothesis that psoriasis was independently associated with serum adiponectin levels. A *P* value of less or equal to 0.05 was considered significant. Results were expressed as means with standard deviation (SD) for continuous variables and as numbers and percentages for categorical variables.

RESULTS

Characteristics of the study population

The demographic data of both psoriasis patients and controls are summarized in Table 1. Both groups were matched for age, sex, BMI, and abdominal girth. Mean PASI score was 5.10. Majority of patients (86.6%) had mild psoriasis. Mean duration of the disease was 5.1 years. Nearly 28% had psoriatic arthritis. Serum adiponectin was significantly lower in psoriasis patients (mean = 7630 ng/ml) when compared with controls (mean = 10058 ng/ml) (*P* = 0.000). There was a significant inverse relationship between serum insulin, HOMA-IR index and serum adiponectin (*P* = 0.04, correlation coefficient (*r*) = -0.394; *P* = 0.001, correlation coefficient (*r*) = -0.423) in both groups. Although there were no differences in the adiponectin levels between normal weight and overweight groups, there was a significant decrease in adiponectin levels in obese patients when compared with normal weight patients in both groups (*P* = 0.01) [Table 5]. There was also no difference in serum adiponectin levels between males and females in both groups. Patients with MetS in both groups had significantly higher BMI when compared with those without MetS. There was no significant difference in the HOMA-IR values between the psoriasis and control groups.

Serum adiponectin and severity of metabolic syndrome

Five patients with psoriasis had all the five criteria, 13 had four criteria, and 11 patients had the required three criteria for the diagnosis of MetS. Among controls, 6 patients had four criteria, 14 had three criteria, and none had all the five. There was a significant inverse correlation between serum adiponectin and the number of criteria in patients

Table 1: Characteristics of patients with psoriasis and controls

	Psoriatics (n=60)	Controls (n=40)	P value
Age in years (mean±S.D)	45.18±12	41.90±10.7	0.16
Males- no (%)	29 (48.3)	16 (40)	0.53
Current smokers-no (%)	10 (16.7)	2 (5)	0.07
Alcohol consumption- no (%)	11 (18.3)	2 (5)	0.052
Obesity (BMI>25)	39 (65)	25 (62.5)	0.62
BMI	27.25±4.4	26.94±4	-
Abdominal girth	89.6±12	88.20±7.4	0.47
PASI	5.10±4.4	-	-
Duration of psoriasis in years (mean)	5.19	-	-
Psoriatic arthritis-no (%)	17 (28.3)	-	-
Diabetes-no (%)	15 (25)	5 (12.5)	0.09
Hypertension-no (%)	13 (21.7)	3 (7.5)	0.05
Fasting blood sugar-(mean±S.D)	103.40±24.7	102.95±21	0.92
Hypercholesterolemia no (%)	10 (16.6)	9 (22.5)	0.07
Increased LDL no (%)	34 (56.6)	23 (57.5)	0.13
Decreased HDL no (%)	25 (41.6)	19 (47.5)	0.35
Triglyceridemia no (%)	17 (28.3)	11 (27.5)	0.76
Serum insulin-(mean±S.D)	37.95±31	36.10±38.6	0.79
Serum adiponectin- ng/ml (mean±S.D)	7630±2018.8	10058.7±2947	0.00
HOMA-IR (mean±S.D)	10.11±9.3	9.6±11	0.82

SD: Standard deviation, BMI: Body mass index, PESI: Psoriasis area and severity index, HOMA-IR: Homeostatic model assessment of insulin resistance

with psoriasis and controls. (*r* = -0.371, *P* = 0.000 and *r* = -0.583, *P* = 0.000).

Characteristics of psoriasis patients with and without metabolic syndrome

Characteristics of psoriasis patients with and without MetS are given in Table 2. Patients with MetS were older. Serum insulin levels and HOMA-IR index were significantly higher in the MetS group as expected (*P* = 0.00 and 0.04). Serum adiponectin levels was significantly lower in psoriasis patients with MetS when compared with those without MetS (*P* = 0.00), which remained significant after adjustment for age and insulin resistance (HOMA-IR).

Characteristics of psoriasis patients with metabolic syndrome and controls with metabolic syndrome

Psoriasis patients had a significantly lower levels of serum adiponectin when compared with controls with MetS (*P* = 0.001) as seen in [Table 3]. The serum adiponectin levels were lowest in psoriasis patients with MetS and highest in controls without MetS as shown in Figure 1. Associations between adiponectin and the individual components of MetS revealed that adiponectin was significantly and negatively correlated with waist circumference (*P* = 0.001), triglycerides (*P* = 0.02), fasting blood glucose (*P* = 0.01) in both the groups. Nearly 18.3% had arthritis in the MetS group.

Table 2: Characteristics of patients with psoriasis with and without MetS

	Psoriatics with MetS (n=29)	Psoriatics without MetS (n=31)	P value
Age	46.52±14.6	43.94±8.95	0.004
Males	11 (18.3)	18 (30)	-
BMI	29.86±4.3	24.82±3.06	0.06
PASI	5.20±5.19	5±3.6	0.82
Duration of psoriasis in years (mean)	5.05	5.41	0.78
Psoriatic arthritis no (%)	11 (18.3)	6 (10)	0.09
PASI>10 no (%)	5 (17.2)	3 (9.6)	-
Diabetes no (%)	15 (25)	0	-
Hypertension no (%)	13 (21.7)	0	-
Fasting blood sugar (mean±S.D)	118±28.2	89.6±7.1	0.00
Hypercholesterolemia no (%)	10	0	0.00
Increased LDL no (%)	21 (72.4)	13 (42)	0.06
Decreased HDL no (%)	21 (72.4)	4 (13)	0.002
Triglyceridemia no (%)	17 (58.6)	0	0.002
Serum insulin	54.48±32.2	22±13.4	0.00
Serum adiponectin	6387.93±1580.8	8793.23±1671.3	0.00
HOMA-IR	15.74±10.5	6.12±6	0.04

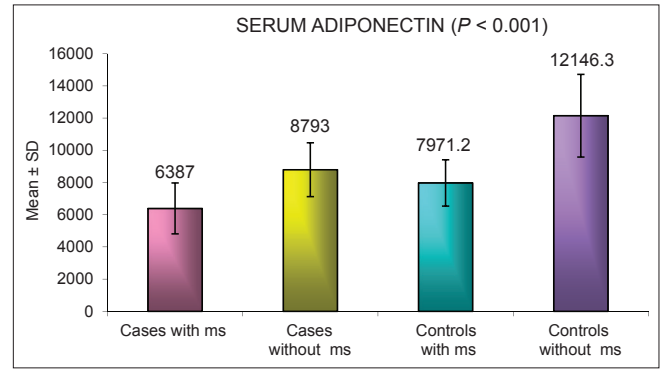
SD: Standard deviation, BMI: Body mass index, PASI: Psoriasis area and severity index, HOMA-IR: Homeostatic model assessment of insulin resistance

Table 3: Characteristics of patients with psoriasis with MetS and controls with MetS

	Psoriatics with MetS (n=29)	Controls with MetS (n=20)	P value
Age	46.52±14.6	42.95±10.6	0.33
Males	11 (18.3)	6 (30)	-
BMI	29.86±4.3	28.59±4.4	0.31
PASI	5.20±5.19	-	-
Duration of psoriasis in years (mean)	5.05	-	-
Psoriatic arthritis no (%)	11 (18.3)	-	-
Diabetes no (%)	15 (25)	5 (12.5)	0.01
Hypertension no (%)	13 (21.7)	3 (7.5)	0.07
Fasting blood sugar (mean±S.D)	118±28.2	112.50±27.7	0.49
Hypercholesterolemia n (%)	10 (34.4)	8 (40)	0.58
Increased LDL no (%)	21 (72.4)	9 (45)	0.31
Decreased HDL no (%)	17 (58.6)	14 (70)	0.57
Triglyceridemia no (%)	17 (58.6)	11 (55)	0.50
Serum insulin (mean±S.D)	54.48±32.2	46.05±35.8	0.41
Serum adiponectin (mean±S.D)	6387.93±1580.8	7971.25±1436.8	0.001
HOMA-IR (mean±S.D)	15.74±10.5	13.30±11.8	0.45

SD: Standard deviation, BMI: Body mass index, PASI: Psoriasis area and severity index, HOMA-IR: Homeostatic model assessment of insulin resistance

In both groups without MetS, adiponectin was significantly reduced in psoriasis group [Table 4].


Figure 1: Mean serum adiponectin values in all groups

Serum adiponectin and arthritis, duration, and severity of psoriasis

There was no significant association between PASI score and serum adiponectin levels (correlation coefficient (T) = -0.014, $P = 0.873$). Likewise there was no association between arthritis and the duration of psoriasis with adiponectin levels. There was also no relationship between IR and arthritis or duration of psoriasis.

DISCUSSION

The overall mean serum adiponectin was significantly lower in psoriasis patients when compared with controls. This is similar to earlier studies, which have demonstrated lower adiponectin levels in psoriasis patients.^[19] Tumor necrosis factor alpha (TNF- α) and interleukin-6 (IL-6) are cytokines, which are found to be elevated in psoriasis patients.^[20] TNF- α inhibits adiponectin production, which explains the lower adiponectin levels in psoriasis.^[21]

In this study we have shown that serum adiponectin was significantly lower in psoriasis patients with MetS when compared with controls with MetS, thus suggesting a role in psoriasis irrespective of the presence of MetS. An *in vitro* study on the effects of adiponectin on the production of cytokines and chemokines in monocytic human acute monocytic leukemia cell line (THP-1) cells and keratinocytes has shown that adiponectin significantly suppressed lipopolysaccharide (LPS)-induced production of TNF- α and IL-6 by THP-1 cells and normal human keratinocytes.^[22] Adiponectin has been shown to inhibit the proliferation of myelomonocytic cell lineages and to inhibit the production of TNF- α by stimulated macrophages,^[23] thus probably exerting an antiinflammatory action in psoriasis and other inflammatory diseases mediated by TNF- α . Adiponectin receptor R1 has been found to be reduced in psoriatic epidermis when compared with uninvolved or normal skin.^[23] In the same study suppressive effects by adiponectin on keratinocytes accompanied by

Table 4: Characteristics of patients with psoriasis without MetS and controls without MetS

	Psoriatics without MetS (n=31)	Controls without MetS (n=20)	P value
Age	43.94±8.95	40.85±10.8	0.27
Males	18 (30)	10 (25)	-
BMI mean±SD)	24.82±3.06	25.2±2.8	0.58
PASI (mean±SD)	5±3.6	-	-
Duration of psoriasis in years	4.32	-	-
Psoriatic arthritis	6 (19)	-	-
Diabetes	0	0	-
Hypertension	0	0	-
Fasting blood sugar in mg/dl (mean±SD)	89.6±7.1	112.50±27.7	0.04
Hypercholesterolemia no (%)	0	1 (5)	0.16
Increased LDL no (%)	13 (42)	14 (70)	0.22
Decreased HDL no (%)	4 (13)	5 (25)	0.40
Triglyceridemia no (%)	0	0	0.55
Serum insulin (mean±SD)	22±13.4	46.05±35.8	0.59
Serum adiponectin (mean±SD)	8793.23±1671.3	12146.3±1436.8	0.00

SD: Standard deviation, BMI: Body mass index, PESI: Psoriasis area and severity index, HOMA-IR: Homeostatic model assessment of insulin resistance

Table 5: Relationship between BMI and serum adiponectin levels

BMI of patients with psoriasis (n=60)	Serum adiponectin in ng/ml	Significance
<23	8657.14±957.66	-
23-25	7534.29±2296.10	-
25-30	8016.67±2060.08	0.08
>30	6624.00±1743.04	0.019

BMI: Body mass index

differentiation of keratinocytes was observed.^[23] Another study reported that adiponectin suppressed cell proliferation using a human keratinocyte cell line, all pointing to an antiinflammatory role at the level of the epidermis.^[24]

As expected there was a significant relationship between IR, lower values of adiponectin, and MetS in both psoriasis patients and controls. Adiponectin is an adipocyte-secreted polypeptide hormone with molecular weight 30 kDa (244 amino acids), which modulates a number of metabolic processes, and regulates insulin sensitivity and energy homeostasis, as well as glucose and lipid metabolism.^[25] This hormone plays a principal role in the suppression of the metabolic derangements that may result in insulin resistance, type 2 diabetes, MetS, and cardiovascular disease.^[26,27] Studies have demonstrated that adiponectin modulates insulin sensitivity by stimulating glucose utilization and fatty acid oxidation via phosphorylation and activation of AMP-activated protein kinase (AMPK) in muscle and liver.^[25] Earlier studies have shown that IR is common in

patients with psoriasis.^[6] The interrelationships involving psoriasis, IR, and adiponectin are yet to be explored.

We did not find any relationship between psoriatic arthritis and serum adiponectin, which is probably due to the small number of patients having psoriatic arthritis.

The mean serum adiponectin levels in patients with psoriasis was 7360 ng/ml, which is similar to a recent study in which the mean adiponectin value in patients with psoriasis was 7400 ng/ml.^[28] The serum insulin levels and mean HOMA-IR in our study is much higher in patients with psoriasis when compared with the general Indian adult population. This is probably because patients with psoriasis are prone to insulin resistance.^[6]

There are approximately 25 studies on serum adiponectin and psoriasis. However, this is the first study that has attempted to study adiponectin levels in psoriasis patients with regard to MetS and has shown that its levels are decreased irrespective of MetS. The limitations of this study are the small sample size. However, this is a preliminary study and future large scale studies are warranted.

This study has future implications regarding the treatment of psoriasis. Considering the antiinflammatory role of adiponectin in psoriasis especially in the setting of MetS, future trials on the drugs that increase the adiponectin levels such as PPAR (peroxisome proliferator-activated receptor) agonists, angiotensin receptor blockers, and exogenous adiponectin administration apart from life style modifications are required.

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