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Metabolic derangement in patients with vitiligo: a cross-sectional study

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ABSTRACT

Vitiligo is a pigmentary disorder resulting from progressive destruction of melanocytes in the skin. There is a growing body of evidence about higher risk of metabolic syndrome and dyslipidemia in some dermatoses including vitiligo. We aimed to evaluate lipid profile, leptin and C reactive protein (CRP) status among Iranian patients with vitiligo, compared with healthy controls and perused the relationship between abnormal values of these parameters with disease duration and physical characteristics of patients. 40 patients with vitiligo and 40 age-matched and sex-matched healthy controls were enrolled in the study. Data on weight, height, lipid profile, leptin and CRP values were recorded and compared. The mean values for nearly all study parameters (except for high-density lipoprotein) were significantly higher in patients with vitiligo, compared with healthy controls, irrespective of age and sex. We could not find any correlation between vitiligo and study parameters, regarding disease severity and extension of lesions; but in patients who have been suffering from vitiligo for more than 5 years, systolic blood pressure, diastolic blood pressure and CRP values were noted to be significantly higher ($p < 0.001$, $p = 0.003$ and $p = 0.03$, respectively). In conclusion, screening of patients with vitiligo in regard to their lipid profile as well as blood pressure should be considered, especially in patients with longer disease duration or those who have other cardiovascular risk factors to prevent morbidity and mortality as a result of developing cardiovascular events.

INTRODUCTION

Vitiligo is a chronic pigmentary disorder with a relatively high prevalence in population,¹ characterized by white patches with circumscribed margins resulting from progressive destruction of melanocytes in the skin. Although the exact etiopathogenesis of vitiligo is not fully understood, current literature emphasizes the role of T cell-mediated autoimmune process in developing the disease.² It is believed that long-term release of cytokines in chronic inflammatory conditions produces metabolic derangements in terms of some disturbances in lipid/ carbohydrate metabolism resulting in dyslipidemia, insulin resistance and other components of metabolic syndrome.^{3,4}

There is also a growing body of evidence about higher risk of metabolic syndrome and

Significance of this study

What is already known about this subject?

- ▶ Long-term release of cytokines in chronic inflammatory conditions produces metabolic derangements.
- ▶ There is a higher risk of metabolic syndrome and dyslipidemia in some skin disorders such as psoriasis.
- ▶ Previous studies have shown a relationship between leptin level and insulin resistance, obesity, hypertension and dyslipidemia.

What are the new findings?

- ▶ This is the first study that investigated lipid profile and leptin level in Iranian patients who have been suffering from vitiligo.
- ▶ The mean values for nearly all study parameters (except for high-density lipoprotein) were significantly higher in patients with vitiligo, compared with healthy controls, irrespective of age and sex.
- ▶ The severity of disease and extension of lesions in terms of Vitiligo Area Severity Index score were not as important as disease duration in regard to metabolic syndrome components.

How might these results change the focus of research or clinical practice?

- ▶ Based on our results, we suggest that the screening of patients with vitiligo in regard to their lipid profile as well as blood pressure should be considered, especially in patients with longer disease duration or those who have other cardiovascular risk factors to prevent morbidity and mortality as a result of developing cardiovascular events.

dyslipidemia in some skin disorders such as psoriasis, lichen planus and vitiligo.^{5–8}

Leptin is a polypeptide hormone released by adipocytes and small intestine cells, regulating energy balance and body weight.⁹ Previous studies have shown a relationship between leptin level and insulin resistance, obesity, hypertension and dyslipidemia.^{10–14}

To the best of our knowledge, there are no data on lipid profile and leptin level in Iranian patients who have been suffering from vitiligo.



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Hence, this study was designed to evaluate lipid profile, leptin and C reactive protein (CRP) values in Iranian patients with vitiligo.

MATERIALS AND METHODS

Study design

We conducted a single-center cross-sectional study of adults (≥ 18 years of age): 40 patients diagnosed with vitiligo clinically who were seen at the dermatology clinic of Shahid Yahyanezhad Hospital, Babol University of Medical Sciences, Babol, Iran from April 2018 through March 2019 were recruited as patient group. The control group was selected from age-matched and sex-matched healthy volunteers among companions of patients attending the outpatient dermatology clinic. The following exclusion criteria were used:

For patients:

- ▶ Those who had concomitant inflammatory, infectious, autoimmune, cardiac, hepatic, endocrine or renal disorders such as diabetes, hypertension and hypercholesterolemia, as well as those who had cancer.
- ▶ Those who received any systemic treatment or phototherapy during the last 6 months.
- ▶ Pregnant or lactating women.
- ▶ Smoking habit or alcohol consumption.

For controls:

- ▶ Subjects with any known dermatologic or non-dermatologic disorders.
- ▶ Pregnant or lactating women.
- ▶ Smoking habit or alcohol consumption.

After obtaining informed written consent from participants, all of them were subjected to a detailed review of their demographics and clinical characteristics. Then, their weight and height were measured to calculate the body mass index (BMI) using the following formula: $\text{weight (kg)}/[\text{height (m)}]^2$.

Systolic and diastolic blood pressures (SBP and DBP, respectively) were also measured after a 15-minute rest.

Moreover, patients were physically examined and Vitiligo Area Severity Index (VASI) score was calculated as follows: the extension of vitiligo lesions was calculated in terms of hand units which is considered as 1% of total body surface area. On the other hand, the amount of depigmentation was determined according to previous studies.¹⁵ Then, VASI score was calculated by the following formula: $\text{VASI} = \sum S$ all body sites (hand units) \times (residual depigmented). Severity of

disease was determined based on VASI score as follows: mild (VASI: 0%–25%), moderate (VASI: 25%–50%), severe (VASI: 50%–75%) and serious involvement (VASI: 75%–100%).¹⁵

Blood sample analysis

Blood samples were taken from participants after 12 hours of fasting. Analysis of all samples was performed at the laboratory of Shahid Yahyanezhad Hospital. Leptin level was measured using ELISA (ME E-0300, Leptin, Germany).

We measured serum levels of CRP, total cholesterol (Chol), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) using a photometric autoanalyzer and triglyceride (TG) with calorimetric enzymatic method (GPO-PAP).

Statistical analysis

Statistical analysis was performed using SPSS V.25. Means and SDs were calculated for continuous variables and frequency and percentages for categorical ones. The relationship between variables was tested using independent t-test, Mann-Whitney, X^2 and Fisher's exact tests depending on the type of variables and distribution of their values. A p value of <0.05 was considered statistically significant and all of the statistical analyses were done with a 95% CI.

RESULTS

Subject characteristics

A total of 80 participants were enrolled in this study, 40 subjects in each group of case and control. A summary of demographics and physical characteristics of subjects is provided in table 1.

The mean age in patient and control groups was 37.95 ± 7.25 years and 37.5 ± 7.16 years, respectively, with 38 male subjects (17 patients and 21 controls) and 42 female subjects (23 patients and 19 controls).

Regarding age group, 44 (23 patients and 21 controls) and 36 subjects (17 patients and 19 controls) were <40 and ≥ 40 years old, respectively.

There was no statistically significant difference between two groups in terms of age, sex and BMI ($p=0.78$, $p=0.37$, $p=0.77$, respectively). In contrast, SBP and DBP in patients were significantly higher than controls ($p<0.001$ and $p=0.003$, respectively).

All of our patients had non-segmental subtype of vitiligo. The mean duration of disease was 116.3 ± 59 months and

Table 1 A summary of baseline characteristics of participants in each group

	Patient	Control	P value
Mean age (y)	37.95 ± 7.25	37.50 ± 7.16	0.78
Sex, n (%)			
Male	17 (42.5)	21 (52.5)	0.37
Female	23 (57.5)	19 (47.5)	
Mean BMI (kg/m^2)	24.61 ± 3.04	24.42 ± 2.71	0.77
Mean SBP (mm Hg)	137.2 ± 16.1	121.7 ± 8.7	<0.001
Mean DBP (mm Hg)	80.5 ± 10.3	73.0 ± 11.1	0.003
Disease severity, n (%)			
Mild	24 (60)		
Moderate	16 (40)		
Severe or serious involvement	0 (0)		

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2 Biochemical parameter comparison of study participants

	Patient	Control	P value
Mean CRP (mg/dL)	5.98±2.35	4.83±2.38	0.03
Mean TG (mg/dL)	150.75±18.64	137.60±21.58	0.005
Mean Chol (mg/dL)	163.02±18.69	149.19±26.48	0.009
Mean HDL (mg/dL)	33.47±4.8	35.24±3.03	0.03
Mean LDL (mg/dL)	101.96±10.16	97.69±11.12	0.03
Mean leptin (ng/dL)	24.42±2.71	21.64±4.32	0.077

Chol, total cholesterol; CRP, C reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride.

mean VASI score was 7.08 ± 4.42 with a range of 0.1–39.9. The majority of patients had mild disease (24 patients, 60%) and the rest of them were considered to have moderate disease according to VASI score.

Biochemical assays

The leptin, CRP, Chol, TG, LDL and HDL values for patients and controls are reported in [table 2](#).

As seen from the table, all these parameters were significantly higher in patients with vitiligo, compared with healthy controls (except for HDL) ([table 2](#)).

Several subgroup analyses were performed to evaluate the association between participants' characteristics with

parameters of this study. The results of these analyses were summarized in [table 3](#).

Age-wise analyses revealed that there was a significant intergroup difference in regard to SBP, DBP, leptin, Chol, LDL and HDL values in participants less than 40 years old. On the other hand, some parameters including SBP, leptin and TG values showed significant differences in older participants.

Regarding gender of participants, our results showed that SBP, DBP, CRP and HDL values had significant intergroup differences in women. On the other hand, SBP, leptin and Chol values were meaningfully higher in male patients, compared with male controls.

We could not find any significant difference in SBP, DBP, leptin, Chol, LDL and HDL values in participants regarding disease severity as well as the extension of lesions (data were not shown), but disease duration seems to matter in this way. In patients who have been suffering from vitiligo for more than 5 years, SBP, DBP and CRP values were noted to be significantly higher ($p < 0.001$, $p = 0.003$ and $p = 0.03$, respectively).

DISCUSSION

In the current study, we have shown that patients who have suffered from vitiligo had a significant metabolic derangement in terms of an increase in Chol, TG, LDL and leptin levels as well as a decrease in HDL value in comparison with healthy controls. The evidence has been growing rapidly in the literature in regard to the relationship of some inflammatory

Table 3 Biochemical parameter comparison of study participants regarding age, sex and disease duration

		Age		Sex		Disease duration	
		≤40 years	>40 years	Male	Female	≤5 years	>5 years
TG (mg/dL)	Case	153.29	146.93	147.52	153.13	148.14	156.15
	Control	143.04	130.94	134.80	140.68		
	P value	0.1	0.01	0.06	0.06	0.2	
Chol (mg/dL)	Case	167.74	155.94	163.97	162.31	162.82	163.43
	Control	150.72	147.51	145.47	153.31		
	P value	0.02	0.26	0.009	0.25	0.92	
HDL (mg/dL)	Case	33.52	33.40	34.76	32.52	33.24	33.96
	Control	35.55	34.85	35.51	34.93		
	P value	0.03	0.33	0.53	0.03	0.61	
LDL (mg/dL)	Case	103.09	102.76	101.60	103.96	100.86	107.30
	Control	96.33	99.36	98.19	97.14		
	P value	0.03	0.37	0.31	0.06	0.06	
Leptin (mg/dL)	Case	23.35	20.57	22.23	21.21	20.85	23.27
	Control	18.14	15.96	15.89	18.57		
	P value	0.01	0.01	0.002	0.1	0.09	
CRP (mg/dL)	Case	5.83	6.19	5.29	6.48	5.96	6
	Control	4.73	4.94	5.10	4.53		
	P value	0.1	0.17	0.75	0.01	0.03	
SBP (mm Hg)	Case	138.3	135.6	141.1	134.3	133.8	138.8
	Control	123.1	120.0	122.8	120.5		
	P value	0.003	0.001	<0.001	0.005	<0.001	
DBP (mm Hg)	Case	81.6	78.7	80.5	80.4	74.6	83.3
	Control	70.0	76.6	75.7	70.0		
	P value	0.002	0.48	0.13	0.008	0.003	
BMI (kg/m ²)	Case	24.37	24.97	25.20	24.17	24.39	25.06
	Control	24.42	24.42	24.34	24.51		
	P value	0.95	0.6	0.34	0.71	0.52	

BMI, body mass index; Chol, total cholesterol; CRP, C reactive protein; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; TG, triglyceride.

dermatoses such as psoriasis, lichen planus and vitiligo with metabolic syndrome and its related factors including dyslipidemia. Our findings are in a good agreement with previous studies in this regard.^{3-6 16 17}

In a study by Dragoni *et al*, same to ours, vitiligo was revealed not to have any relationship with BMI.¹⁸ In contrast, Singh *et al* reported higher BMI in patients with vitiligo, compared with controls.¹⁷ This discrepancy between results might be explained by different mean values of BMI in these studies.

Based on the fact that prolonged dyslipidemia due to chronic inflammatory process leads to atherosclerotic plaque formation and an elevated risk of cardiovascular accidents, some studies suggested measuring of inflammatory markers such as CRP to assess cardiovascular risk.^{19 20} The inclined CRP level in patients, compared with healthy controls in our study, was noted indicating the presence of inflammatory process which explains the significant dyslipidemia observed in this study.

A notable finding of this study was the correlation of vitiligo and different components of metabolic syndrome irrespective of age or sex of participants.

Another interesting finding was the association between study parameters and disease duration, unlike disease severity and extension of lesions. To the best of our knowledge, this is the first study reporting such an interesting finding.

Along with the success of this study, we had some limitations. Owing to the cross-sectional design of this study, it is not possible to detect any causal effect from its results. The small number of participants due to some financial constraints as well as rigid recruitment criteria was another limitation. Further prospective studies with a larger number of patients are needed to confirm our results.

CONCLUSION

In this study, we found significant higher mean values of lipid parameters (except for HDL), leptin and CRP in patients with vitiligo, compared with healthy controls. Moreover, we reported that severity of disease and extension of lesions in terms of VASI score are not as important as disease duration in regard to metabolic syndrome components. Therefore, screening of patients with vitiligo in regard to their lipid profile as well as blood pressure should be considered, especially in patients with longer disease duration or those who have other cardiovascular risk factors to prevent morbidity and mortality as a result of developing cardiovascular events.

However, this should be further investigated in future studies.

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