Total oxidant capacity, total antioxidant capacity, ischemic modified albumin, microRNA levels, and their relationship with psoriasis area and severity index

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Abstract

Aims: To examine the differences in the levels of microRNA, ischemic modified albumin (IMA), total oxidant capacity (TOC), and total antioxidant capacity (TAC) of persons with and without psoriasis and, in the case group, the relationship between these parameters and psoriasis area and severity index (PASI).

Methods: Blood samples were collected from patients and healthy participants to examine levels of these parameters.

Results: The mean serum TOC level was higher in the case group. The mean serum TAC and IMA levels were significantly lower in the case group (P <0.001). It was observed that the mean serum miR-203 and miR-146a levels were increased in psoriasis patients. It was determined that there was only a significant positive weak correlation between miR-203 and PASI (r = 0.232, P = 0.027).

Limitations: The small sample size, not controlling serum albumin and not evaluating the effects of the treatment agents used by the patients on oxidative and inflammatory processes.

Conclusion: In the case group changes in the mean serum TOC and TAC levels provide evidence that oxidative stress may play a critical role in disease pathogenesis. The increase in the mean serum miR-203 and miR-146a levels suggest the possibility of therapies targeting these microRNAs as a new option.

Key words: Psoriasis area severity index, total antioxidant capacity, total oxidant capacity, ischemic modified albümin, microRNA

Plain Language Summary

Psoriasis is a chronic and inflammatory skin disease that has red papules and plaques. The cause of this disease is the increase in oxidative stress. Its prevalence ranges from 0.1% to 11.4%. In this study, we compared the levels of total antioxidant capacity (TAC), total oxidant capacity (TOC), ischemic modified albumin (IMA) and miRNA in individuals with and without psoriasis and investigate the relationship between these levels and psoriasis area and severity index (PASI). It was aimed to provide to a better understanding of the pathogenesis of the disease, the development of new treatment methods and these parameters use in the treatment follow-up. The mean serum TOC level was higher and the mean serum TAC and IMA levels were lower in the case group. It was observed that the mean serum miR-203 and miR-146a levels were increased in psoriasis patients. It was determined that there was positive weak correlation between miR-203 and PASI. Serum TOC levels and TAC levels changes in psoriasis patients have shown that oxidative stress could play a role in disease pathogenesis. Anti miR-203 and anti miR-146a therapies could be a new treatment option. miR-203 disease activity and severity could be used as a biomarker to evaluate the outcome of a therapeutic intervention.

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Introduction

Psoriasis is a chronic and inflammatory skin disease that has red papules and plaques covered with white or silver scales. Its prevalence ranges from 0.1 to 11.4 per cent.[1] In adolescents, on the other hand, its prevalence is about 2 per cent.[1] Psoriasis is a disease that affects both sexes equally with the age of onset being less than 46 years in 75% of patients. Based on the age of onset, this disease is classified as Type-1 (early-onset) and Type-2. Type-1 is the more severe type and has higher rates of family members also being affected.[2,3] The psoriasis area severity index is important in determining the clinical severity of the disease, treatment selection and the effectiveness of follow-up. It is a reliable and repeatable scoring method for adult plaque psoriasis.[4,5]

Although there are suggestions that psoriasis may be an autoimmune disease, autoantigens that may be responsible have not yet been identified.[2] It has been reported that in immune-mediated complex disorders, the increase in reactive oxygen species due to oxidative stress, and the deterioration of the balance between the oxidant-antioxidant system may cause the pathogenesis of these diseases.[6] Detecting total antioxidant capacity and total oxidant capacity levels in plasma or serum are simple and inexpensive methods to evaluate changes in total antioxidant and oxidant status.[7] Emre *et al.* reported that the total oxidant capacity level increased, whereas the total antioxidant capacity level decreased in psoriasis patients, compared to healthy individuals.[8] Ischemic modified albumin, a newly defined oxidative stress marker was found to be significantly higher in patients with psoriasis compared to healthy individuals.[9–11] MicroRNAs are the RNA molecules that play an important role in protein synthesis regulation, cell proliferation, DNA repair, DNA methylation, apoptosis, regulation of gene expression and the correct differentiation of immune cells. Previous studies have showed that genetic regulation mediated by abnormally expressed microRNAs contributes to psoriasis pathogenesis. The miR-146a increases in psoriatic lesions and peripheral blood mononuclear cells as a part of chronic inflammation. miR-203 is a skin-specific microRNA that is overexpressed only in psoriatic keratinocytes and plays a role in keratinocyte differentiation and angiogenesis.[12–14]

In this study, we aimed to compare the levels of total antioxidant capacity, total oxidant capacity, ischemic modified albumin and microRNA in individuals with and without psoriasis and investigate the relationship between these levels and psoriasis area severity index in the case group. A significant relationship between psoriasis area severity index and these parameters would help in follow-up after treatment and thus, the treatment results would be assessed more accurately. In addition, significant differences between the case group and control group would lead to a better understanding of the pathogenesis of the disease and the possible development of new treatment modalities.

Materials and Methods

This study was conducted as a case-control study. The research population consisted of psoriasis vulgaris patients over 18 years of age who applied to the Necmettin Erbakan University in Turkey, faculty of medicine, department of dermatology outpatient clinic, as the case group, and healthy individuals over 18 years of age who did not have any systemic disease and were medication-free, as the control group.

Research sample

The incidence of psoriasis in Turkey was estimated to be between 0.5 and 4.7%, in previous studies.[15,16] The number of participants required for the study was determined as 84 based on the formula given below:

$$n = t^2.p.q/d^2$$

where

n = number of subjects in the study,
t = study duration,
p = number of individuals in the universe,
q = prevalence of psoriasis in our country, and
d = standard deviation.

However, considering the possibilities of incomplete filling of the questionnaire and refusal to participate in the study, it was decided to add 10% so that 92 participants could be recruited. The control and case groups were determined to be similar in terms of gender and employment status. The study was finally completed with a total of 182 participants including 91 in the control group and 91 in the case group.

Exclusion criteria

Diseases such as cerebrovascular-peripheral vascular disease, acute infections, malignancies, diabetes mellitus, chronic obstructive pulmonary disease, thyroid disorders, polycystic ovary syndrome and prostatic hyperplasia affects the serum ischemic modified albumin level. Therefore, individuals with these diseases were excluded from the study.

Sociodemographic attributes

All participants were informed about the purpose of the study prior to the questionnaire and a consent form was obtained from all participants. A sociodemographic questionnaire containing questions related to age, gender, marital status, educational status, profession, smoking and alcohol habits was administered to individuals who agreed to participate in the study. In addition, another questionnaire was prepared by the researcher based on literature review and had questions about age of disease onset, the duration of the disease, the type of treatment (topical, phototherapy and systemic) taken for the last month, the psoriasis medications used, the presence of nail involvement and psoriatic arthritis, family history (1–2–3. relatives). This was administered to the case group. The anthropometric measurements and arterial blood pressure

measurements were performed by the same researcher to reduce the error rate. The body mass index was calculated using the formula of weight (kg)/height squared (m²).

Determination of psoriasis area and severity index

The severity of erythema (E), infiltration (I), desquamation (D) in the lesion was graded from 0 to 4 (0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = severe symptoms, 4 = very severe symptoms) and evaluated in psoriasis patients. Percentages of the occupied area were taken into consideration to evaluate the area (0 = %0, 1 = <%10, 2 = %10–29, 3 = %30–49, 4 = %50–69, 5 = % 70–89, 6 = %90–100). The psoriasis area and severity index score was calculated using the following formula:

Psoriasis area and severity index score:

- Head: 0.1 [E(0–4)+İ(0–4)+D(0–4)] x A(1–6) +
- Upper limb: 0.2 [E(0–4)+İ(0–4)+D(0–4)] x A(1–6) +
- Truncus: 0.3 [E(0–4)+İ(0–4)+D(0–4)] x A(1–6) +
- Lower limb: 0.4 [E(0–4)+İ(0–4)+D(0–4)] x A(1–6)

Biochemical parameter analysis

After 15 minutes of rest in the outpatient clinic, 12 hour fasting blood samples were drawn from the antecubital vein by using the vacutainer system, a total of 12 mL, with anticoagulant tubes for plasma, and vacuum smooth tubes without anticoagulant for serum from the psoriasis patients and the control group. The drawn blood was mixed by gently inverting 5–10 times and centrifuged at 2000 rpm for 10 minutes. The upper part of the plasma was pipetted into Eppendorf tubes. This sample was centrifuged again at 2000 rpm for 10 minutes. Then, 250 µl of the upper part of the plasma was pipetted into sterile Eppendorf tubes for microRNA. All samples were stored at –80°C until the experiment. The samples were kept at room temperature before the study started. All analyzes were performed on the same day in the Necmettin Erbakan University, Faculty of Medicine, Department of Medical Biochemistry.

Rel Assay Diagnostics commercial kit was used to measure serum total antioxidant capacity and total oxidant capacity levels. Total antioxidant capacity results were calculated in mmol Trolox Equiv/L. Total oxidant capacity results were also calculated in µmol H202 Equiv/L.

Human ischemia modified albumin enzyme-linked immunosorbent assay kit based on biotin double antibody sandwich technology was used to measure serum ischemic modified albumin levels. Measurements were performed based on the kit recommendations and the results were calculated in ng/mL.

A total microRNA isolation kit was used for serum microRNA measurement. Real-time polymerase chain reaction was processed by using the Light Cycler96 system. Two different microRNAs (mir-146a and mir-203) were analysed using two internal controls according to the kit recommendations.

Statistical evaluation of data

The data obtained in the study were analysed using the SPSS version 20.0 program. As descriptive statistics, mean and standard deviation were used for continuous variables, and frequency and percentage were used for the categorical variables. The independent samples *t*-test was used to compare the normally distributed quantitative data. A chi-square test was used to compare categorical data. Univariate and multiple linear regression analyses were performed to determine independent risk factors for psoriasis. Results were evaluated at a 95% confidence interval, a significance level of $P < 0.05$. Relationships between the parameters were determined using the Pearson correlation analysis. The value range of 0.00–0.24, 0.25–0.49, 0.50–0.74 and 0.75–1.00 were considered as weak, moderate, strong and very strong relationships, respectively.

Results

The study was conducted with 182 participants (91 patients with psoriasis and 91 healthy individuals). The case group were 43 females (44.8%), while 48 (55.8%) were male. The control group were 53 females (55.2%), and 38 (44.2%) were male. It was determined that education level of psoriasis patients was significantly lower compared to the control group ($P < 0.001$). Seventy-one (56.7%) individuals of the case group and 54 (43.2%) individuals of the control group were obese ($P = 0.007$). Sociodemographic characteristics of the participants are presented in Table 1.

The mean age at first diagnosis of psoriasis patients was 31.3 ± 14.5 years, and the mean duration of disease was 11.9 ± 9.3 years. In 24 (26.4%) patients, there was a family history in their 1st and 2nd-degree relatives. The mean psoriasis area severity index values of the case group were obtained to be 3.2 ± 4.0. In the last month, 50 (54.9%), 17 (18.7%), 15 (16.5%), 2 (2.2%) and 2 (2.2%) of the patients were receiving topical and systemic treatment, systemic therapy, topical treatment, topical treatment and phototherapy, phototherapy and systemic treatment, respectively. On the other hand, 5 (5.5%) of the patients had not received treatment. Nail involvement, and joint involvement were detected in 32.9% and 54.9% of the case group, respectively.

In the case group, weight ($P = 0.003$), body mass index ($P = 0.001$), neck circumference ($P < 0.001$), waist circumference ($P < 0.001$) and systolic blood pressure ($P < 0.001$) were significantly higher compared to the control group. Significant relationship was found in terms of TAC, IMA and miR-203 in the case group ($P < 0.001$) [Table 2]. The comparison of anthropometric and biochemical parameters in the case and control groups is given in Table 2.

Taking into account the literature, the cases were classified as 40 years and below (early-onset) ($n = 69$), and over 40 years

Table 1: Sociodemographic characteristics

	With psoriasis		Without psoriasis		Total		χ^2	*P*
	n	%	*n*	%	*n*	%		
Gender								
Female	43	44.8	53	55.2	96	100.00	2.204	0.138
Male	48	55.8	38	44.2	86	100.00		
Marital status								
Married	76	58.0	55	42.0	131	100.00	12.013	0.001
Unmarried	15	29.4	36	70.6	51	100.00		
Employment status								
Employed	50	47.2	56	52.8	106	100.00	0.813	0.367
Unemployed	41	53.9	35	46.1	76	100.00		
Smoking status								
Smoker	55	48.7	58	51.3	113	100.00	0.210	0.647
Non-smoker	36	52.2	33	47.8	69	100.00		
Level of education								
≤Secondary school	58	69.0	26	31.0	84	100.00	22.639	<0.001
≥High school	33	33.7	65	66.3	98	100.00		
Body mass index								
Thin and normal weight	20	35.1	37	64.9	57	100.00	7.382	0.007
Overweight and obese	71	56.7	54	43.2	125	100.00		

Table 2: Anthropometric and biochemical parameters

	With psoriasis M ± SD	Without psoriasis M ± SD	*t*	*P*
Age (year)	43.2 ± 13.2	31.7 ± 8.7	6.904	**<0.001**
Weight (kg)	81.4 ± 14.4	74.8 ± 15.3	2.979	**0.003**
Height (cm)	167.5 ± 9.0	166.7 ± 19.7	0.351	0.726
Neck circumference (cm)	40.5 ± 3.4	38.1 ± 2.7	5.261	**<0.001**
Waist circumference (cm)	97.4 ± 13.9	90.1 ± 13.7	3.561	**<0.001**
Hip circumference (cm)	109.5 ± 13.3	106.0 ± 10.7	1.946	0.053
Systolic blood pressure (mm Hg)	132.5 ± 21.7	123.0 ± 14.1	3.556	**<0.001**
Diastolic blood pressure (mm Hg)	82.2 ± 14.5	77.2 ± 12.6	2.569	0.011
TOC (µmol H202 Equiv/L)	27.6 ± 12.5	25.3 ± 11.7	1.268	0.206
TAC (mmol Trolox Equiv/L)	0.06 ± 0.06	1.07 ± 0.37	−25.776	**<0.001**
IMA (ng/mL)	24.3 ± 16.8	40.8 ± 25.8	−5.114	**<0.001**
miR-146a	0.046 ± 0.222	0.000 ± 0.001	1.974	0.050
miR-203	69.6 ± 118.8	14.3 ± 18.5	4.390	**<0.001**
BMI (kg/m^2)	28.5 ± 4.9	25.9 ± 5.4	3.403	**0.001**

M ± SD: Mean value ± standard deviation, IMA: Ischemic modified albumin, TOC: total oxidant capacity, TAC: total antioxidant capacity, BMI: body mass index

old (late-onset) (n = 22) in terms of age at initial diagnosis. Serum total antioxidant capacity level was observed to be significantly lower in early-onset cases (P = 0.010). No significant relationship was found in terms of total oxidant capacity, ischemic modified albumin, miR-146a, miR-203, psoriasis area and severity index, joint involvement, nail involvement, family history and treatment type [Table 3].

No significant relationship was observed between disease duration, age at first diagnosis, psoriasis area and severity index, serum total oxidant capacity, total antioxidant capacity, ischemic modified albumin, miR-146a and miR-203 levels in patients with and without a family history, joint involvement. Psoriasis area and severity index values were found to be significantly higher in patients with only nail involvement (P = 0.020). The mean disease duration and the age at the first diagnosis in psoriasis patients who were smokers, were observed as longer (P = 0.017) and earlier (P = 0.047), respectively. Serum total oxidant capacity and miR-146a levels were found to be significantly higher in thin and normal-weight psoriasis patients. The comparison of body mass index with disease duration, age at first diagnosis, psoriasis area and severity index, total antioxidant capacity, total oxidant capacity, ischemic modified albumin and microRNA levels in psoriasis patients are presented in Table 4.

Pearson correlation analysis was performed between psoriasis area severity index, total antioxidant capacity, total

Table 3: Comparison of PASI and TAC, TOC, IMA and microRNA levels between early-onset and late-onset cases in psoriasis patients

	Early-onset cases M ± SD	Late-onset cases M ± SD	*t*	*P*
PASI	3.4 ± 4.3	3.0 ± 3.0	0.360	0.719
TOC (µmol H202 Equiv/L)	27.4 ± 12.4	28.3 ± 13.1	−0.289	0.773
TAC (mmol Trolox Equiv/L)	0.05 ± 0.02	0.09 ± 0.11	−2.644	**0.010**
IMA (ng/mL)	28.1 ± 4.5	2.7 ± 2.7	−1.364	0.176
miR-146a	0.06 ± 0.25	0.01 ± 0.03	0.778	0.438
miR-203	76.6 ± 132.9	47.7 ± 51.8	0.991	0.324

IMA: Ischemic modified albumin, TOC: total oxidant capacity, TAC: total antioxidant capacity, PASI: psoriasis area and severity index, M ± SD: Mean value ± standard deviation, miR-146a: MicroRNA-146a, miR-203: MicroRNA-203

Table 4: Comparison of BMI with disease duration, age at first diagnosis, PASI, TAC, TOC, IMA and microRNA levels in psoriasis patients

	Thin/normal weight M ± SD	Overweight/obese M ± SD	*t*	*P*
Disease duration (year)	9.5 ± 7.8	12.5 ± 9.7	−1.278	0.204
Age at first diagnosis (year)	26.6 ± 15.8	32.7 ± 14.0	−1.684	0.096
PASI	3.2 ± 3.2	3.3 ± 4.2	−0.066	0.942
TOC (µmol H202 Equiv/L)	33.7 ± 16.7	25.9 ± 10.6	2.564	0.012
TAC (mmol Trolox Equiv/L)	0.04 ± 0.00	0.06 ± 0.07	−1.316	0.191
IMA (ng/mL)	26.3 ± 25.7	24.0 ± 13.4	0.582	0.562
miR-146a	0.14 ± 0.47	0.02 ± 0.03	2.285	0.025
miR-203	71.2 ± 81.5	69.1 ± 127.9	0.069	0.945

IMA: Ischemic modified albumin, TOC: total oxidant capacity, TAC: total antioxidant capacity, PASI: psoriasis area and severity index, SD: standard deviation, BMI: body mass index

oxidant capacity, ischemic modified albumin, miR-146a, miR-203, disease duration and age at first diagnosis. Whereas there was a positive weak correlation between miR-203 and psoriasis area and severity index ($r = 0.232$, $P = 0.027$), there was a negative weak correlation between ischemic modified albumin and total oxidant capacity ($r = -0.235$, $P = 0.025$). A moderate and statistically significant positive correlation was determined between total oxidant capacity and miR-146a ($r = 0.257$, $P = 0.014$) [Table 5].

Univariate linear regression analysis and multiple linear regression analysis were conducted to determine the independent risk factors of psoriasis. The univariate model results showed that the relationship of the total antioxidant capacity in psoriasis was negative and statistically significant ($\beta = -0.887$, $P < 0.001$). Thus, a one-unit increase in this value results in an 88.7% reduction in psoriasis risk. This explains 78.7% of the variance in the risk of psoriasis ($R^2 = 0.787$). The relationship of ischemic modified albumin on psoriasis was also negative and statistically significant ($\beta = -0.356$, $P < 0.001$). Based on this result, it can be said that a one-unit increase in this value results in a 35.6% reduction in the risk of psoriasis. This explains 12.7% of the variance in the risk of psoriasis ($R^2 = 0.127$). The relationship of miR-203 on psoriasis was positive and statistically significant ($\beta = 0.311$, $P < 0.001$). Therefore, a one-unit increase in it leads to a 31.1% increase in the risk of psoriasis. It explains 9.7% of the variance in the risk of psoriasis ($R^2 = 0.097$). The relationship of total oxidant capacity and miR-146a on psoriasis were found to be positive. However, it was not statistically significant. The relationship of total antioxidant capacity on psoriasis was to be only negative and statistically significant according to the results of multiple linear regression analysis ($\beta = -0.887$, $P < 0.001$) [Table 6].

Discussion

In previous studies on psoriasis, a statistically significant difference was not observed between early-onset and late-onset cases in terms of psoriasis area severity index value, nail and joint involvement, and the need for systemic treatment.[17,18] On the other hand, family and history was observed to be significantly more frequent in early-onset cases.[17,18] In this study, it was found that the age of three quarters of the cases at the first diagnosis was 40 years and below. A significant relationship between early-onset and late-onset cases was not found in terms of total oxidant capacity, ischemic modified albumin, miR-146a, miR-203, psoriasis area severity index, joint involvement, nail involvement, family history and treatment method. Serum total antioxidant capacity level was determined to be significantly lower in early-onset cases.

Obesity and psoriasis have similar aetiological and genetic mechanisms.[19] Bremmer *et al.* reported that obesity prevalence was high in patients with psoriasis.[19] In this study, mean body mass index was found to be significantly higher

Table 5: Correlation of disease duration, age at first diagnosis, PASI, TAC, TOC, IMA and microRNA levels in psoriasis patients

		PASI	TOC	TAC	IMA	miR-146a	miR-203	Disease duration	Age at first diagnosis
PASI	*R*	1							
	P								
TOC	*R*	0.111	1						
	P	0.295							
TAC	*R*	−0.410	0.199	1					
	P	0.699	0.058						
IMA	*R*	−0.034	−0.235*	−0.044	1				
	P	0.748	0.025	0.676					
miR-146a	*R*	−0.053	0.257*	0.032	−0.092	1			
	P	0.615	0.014	0.761	0.383				
miR-203	*R*	0.232*	0.137	0.060	−0.013	0.143	1		
	P	0.027	0.196	0.570	0.906	0.176			
Disease duration	*R*	−0.049	−0.087	−0.147	0.083	0.024	−0.140	1	
	P	0.646	0.413	0.165	0.433	0.819	0.186		
Age at first diagnosis	*R*	−0.053	0.026	0.152	−0.162	−0.147	−0.116	−0.458*	1
	P	0.620	0.807	0.150	0.124	0.163	0.275	0.000	

*Correlation is significant ($P < 0.05$). IMA: Ischemic modified albumin, TOC: total oxidant capacity, TAC: total antioxidant capacity, PASI: psoriasis area and severity index

Table 6: Univariate and multiple linear regression analysis of independent risk factors affecting psoriasis

	Univariate model				Multiple model (stepwise)			
	R2	β	t	*p*	R2	β	t	*p*
TOC	0.009	0.094	1.268	0.206				
TAC	0.787	−0.887	−25.776	<0.001*	0.787	−0.887	−25.776	<0.001*
IMA	0.127	−0.356	−5.114	<0.001*				
miR-203	0.097	0.311	4.390	<0.001*				
miR-146a	0.021	0.146	1.974	0.050				

β: Standardised regression coefficient. IMA: Ischemic modified albumin, TOC: total oxidant capacity, TAC: total antioxidant capacity, PASI: psoriasis area and severity index

in psoriasis patients, which was consistent with the literature. Vincent and Taylor emphasised that obesity was a trigger factor for oxidative stress and inflammation. In addition, they highlighted that oxidative stress parameters were found to be significantly higher in obese patients.[20] Roos *et al.* reported that miR-146a was elevated in adipocytes under inflammatory conditions.[21] In the present study, mean serum total oxidant capacity and miR-146a levels were determined to be significantly higher in the subgroup of cases with thin and normal weight (body mass index < 25). These results were inconsistent with previous reports. In the control group, both total oxidant capacity and miR-146a levels were observed to be higher in overweight and obese patients. However, the difference was not significant. Total oxidant capacity and miR-146a could be detected at lower levels in overweight and obese patients because the agents used for treating psoriasis patients could affect the oxidative and inflammatory processes.

It was thought that the increase in reactive oxygen species due to oxidative stress and the deterioration of the balance between the oxidant-antioxidant systems was responsible for the pathogenesis of this disease.[22] Whereas some studies[8,23] found that total antioxidant capacity and total oxidant capacity levels decreased in patients with psoriasis compared to healthy individuals, others[4,24] found that it increased. In the present study, an increase in total oxidant capacity level was found in psoriasis patients. These results were consistent with the literature. However, the difference was not statistically significant. Total antioxidant capacity was also significantly lower.

In previous studies, the mean ischemic modified albumin values were found to be significantly higher in patients with psoriasis compared to healthy individuals.[9,11] In this study, the mean serum ischemic modified albumin value in patients with psoriasis and healthy individuals were found as 24.3 ±

16.8 ng/mL, and 40.8 ± 25.8 ng/mL, respectively. Thus it was observed that these values significantly lower in psoriasis patients which was inconsistent with the previous reports. It has been suggested that these concentrations are unreliable and not clinically informative in individuals with very low or very high serum albumin levels.[25,26] Since serum albumin levels had not been examined in this study, the significance of lowered ischemic modified albumin in psoriasis cannot be commented upon.

It was thought that serum miR-146a could be effective in the pathogenesis of the disease by affecting the TNF-α signalling pathway regulators.[12] It was suggested that miR-203 could cause the development of psoriatic plaques via STAT3.[12–14,27] Koga *et al.* also emphasised that serum miR-125b, miR-146a, miR-203 and miR-205 levels significantly decreased in patients with psoriasis and miR-146a and miR-203 could be used in the diagnosis of psoriasis vulgaris.[28] In the present study, serum miR-203 and miR-146a levels were found to be high in patients with psoriasis. These results were inconsistent with the study of Koga *et al.* Raaby *et al.* investigated microRNA changes in psoriatic skin during adalimumab treatment which is one of the TNF-α inhibitors. Their study revealed that the miR-146a level increased after 14 days of treatment and the miR-203 level did not change.[29] On the other hand, Pivarcsi *et al.* examined 38 microRNA serum levels before and after 12 weeks of treatment with etanercept and methotrexate. They reported significant alteration in patients on etanercept while methotrexate affects only 4 microRNA levels.[30] In our study, it was determined that 18 of the psoriasis patients had been using TNF-α inhibitor and 22 of the psoriasis patients had been using methotrexate for the last month which could have caused higher levels of serum miR-203 and miR-146a in psoriasis patients.

Whereas some studies[11,23] found that there was a significant relationship between serum total antioxidant capacity, total oxidant capacity, ischemic modified albumin levels, and psoriasis area severity index, other studies[8,9,31] did not find any significant relationship. Ichihara *et al.* found a weak inverse correlation between miR-1266 and psoriasis area severity index, while Yang *et al.* found a significant positive correlation with miR-146a and a significant negative correlation with miR-99a.[32,33] Lovendorf *et al.* found a significant correlation between miR-143, miR-223, and psoriasis area severity index score.[34] The present study was the first study examining the relationship between miR-203 and psoriasis area severity index. A weak positive correlation was determined between miR-203 and psoriasis area severity index. It was also found that alterations in total antioxidant capacity, total oxidant capacity, ischemic modified albumin and miR-146a were not associated with psoriasis area severity index. This could be because the mean psoriasis area severity index values were low due to the fact that the majority of psoriasis patients in the study were receiving regular treatment.

Oxidative stress plays an important role in the development and progression of chronic diabetic complications.[35] It was determined that miR-146a expression decreased in endothelial cells in patients with diabetic retinopathy.[35] The serum total oxidant capacity and ischemic modified albumin levels were found significantly higher compared to healthy individuals.[36] In the present study, ischemic modified albumin and total oxidant capacity showed a weak inverse correlation, while total oxidant capacity was moderately related to miR-146a. The reason for this could be the effect of the treatment agents that psoriasis patients had been taking for the last month on the oxidative and inflammatory process and the effect of serum albumin levels on ischemic modified albumin. The systemic treatment agents such as methotrexate, cyclosporine and the biological agents such as adalimumab and etanercept may have caused a lower reactive oxygen species level. In addition, serum ischemic modified albumin could have been lower due to reactive oxygen species.

Smoking is more common in patients with psoriasis, especially in relation to psychological problems.[37] In recent study in Germany, it was determined that the smoking ratio of patients was 60.7% for men, 45.6% for women, 45.4% on average and 21% for the control group.[37] In Turkey, the frequency of smoking in psoriasis patients varies between 28.2% and 54.5%.[16,38–40] In this study, the smoker:non-smoker ratio of psoriasis patients was found to be 58.3% in males, 18.6% in females and 39.6% on average. The average was 36.3% in the control group. The results were generally consistent with the literature. Although the average smoking frequency was found to be higher in psoriasis patients compared to the control group, this difference was not statistically significant. Regional, socioeconomic and cultural reasons could have affected the smoker:non-smoker ratio in the study. Smoking was found to be significantly higher in patients with longer disease duration and younger age at the first diagnosis. This situation was thought to be related to an increase in psychological problems and comorbidities as the disease duration increases.

Aykol *et al.* and Emre *et al.* found that the mean psoriasis area severity index value in psoriasis patients who were smokers was higher than in those who were non-smokers.[9,39] In some studies, no significant relationship was found between smoking and psoriasis area severity index.[17,40] In the present study, no statistically significant relationship was found between smoking and psoriasis area severity index, total antioxidant capacity, total oxidant capacity, ischemic modified albumin, miR-203, miR-146a, nail involvement, joint involvement and treatment method. The participants were only asked whether they smoked or not, but pack/year information was not obtained. In patients who are short-term smokers, the process of oxidative stress may not have caused molecular damage. More comprehensive studies are needed on this subject.

Limitations

One of the limitations of this study was that it was conducted in a tertiary healthcare institution with a small sample size. Another limitation was that the majority of psoriasis patients receiving regular treatment and were on follow up. Therefore, the mean psoriasis area severity index values were low. This could also be the reason why there was no significant relationship between serum total antioxidant capacity, total oxidant capacity, ischemic modified albumin, miR-146a and psoriasis area severity index. Another limitation was that serum albumin levels were not checked. Serum albumin levels may affect serum ischemic modified albumin values. A third limitation was the effect of the treatment agents taken by psoriasis patients for the last month on oxidative and inflammatory processes. Serum miR-203 and miR-146a levels may have increased due to systemic agents such as methotrexate, cyclosporine, adalimumab and etanercept, affecting oxidative and inflammatory processes.

Conclusion

This study aimed to determine the relationship between serum total antioxidant capacity, total oxidant capacity, ischemic modified albumin, miR-203 and miR-146a and psoriasis area severity index in psoriasis patients. To the best of our knowledge, this is the first study evaluating these parameters together. The increase in serum total oxidant capacity levels and decrease in total antioxidant capacity levels in psoriasis patients provides evidence that oxidative stress could play a critical role in disease pathogenesis. Determination of total antioxidant capacity and total oxidant capacity values can be applied as an easy, inexpensive, and applicable method to evaluate changes in total antioxidant and oxidant levels. Specific microRNA expression changes in psoriasis can be used as a potential biomarker in disease diagnosis, treatment follow-up, and reflection of disease severity. Moreover, based on the activity state of microRNAs, new therapies can be developed for the future. In this study, since serum miR-203 and miR-146a levels were found to be increased, therapies targeting these microRNAs could be a new treatment option. Since a weak correlation between miR-203 and psoriasis area severity index was detected, these could be used as biomarkers to evaluate the outcome of a therapeutic intervention. Because an increase in serum miR-203 and miR-146a values are implicated in the pathogenesis of psoriasis, future studies including animal experiments could see whether anti-miR-203 and anti-miR-146a agents are effective in the treatment of psoriasis.

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Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflict of interest

There are no conflicts of interest.

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