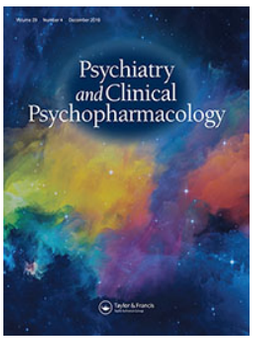

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Oxidative stress and inflammatory response in patients with psoriasis; is there any relationship with psychiatric comorbidity and cognitive functions?

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ABSTRACT

Objectives: Psoriasis is a chronic, inflammatory skin disease which has been linked to psychopathology. Oxidative stress and inflammation are associated with atherogenesis and neuronal stress thus, cognitive functions might be impaired in psoriasis patients. We aimed to compare psychiatric comorbidity, neurocognitive functions, oxidative stress and inflammatory cytokine levels in psoriasis patients with healthy controls, besides to evaluate the effect of oxidative stress and inflammation on comorbidity and cognitive functions in psoriasis patients.

Methods: A total of 37 patients (11 male and 26 female) aged between 18 and 65 years with at least 5 years of education who applied to the Dermatology Outpatient Clinic of the study hospital between study period; diagnosed with psoriasis by physical examination and histopathological evaluation were included in the study. The control group was formed from healthy individuals working for the hospital. Sociodemographic data form, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Semantic Verbal Fluency Test (K-A-S), Öktem Verbal Memory Processes Test, Auditory Consonant Trigram Test and Wisconsin Card Sorting Test were performed to all participants. In addition, blood samples of participants were analysed to assess total oxidant stress (TOS), total antioxidant status (TAS), oxidative stress index (OSI) and proinflammatory cytokines TNF-α and IL-6 levels.

Results: BDI and BAI scores, TOS, OSI, TNF-α and IL-6 levels of psoriasis patients were significantly higher than controls. Besides, the cognitive domains of learning, recall and verbal fluency in psoriasis patients were shown to be impaired. The increased levels of depression and anxiety in psoriasis did not significantly affect the serum TAS, TOS and OSI levels. Increased IL-6 and TNF-α levels were not significantly related to depression in patients with psoriasis.

Conclusion: Psoriasis patients have higher risk factors than healthy controls for cognitive impairment, independent of depression, inflammation and oxidative stress levels.

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Psoriasis; depression; anxiety; oxidative stress; inflammation

Introduction

Psoriasis is a chronic, inflammatory skin disease with a prevalence of 1–2%, whose clinical appearance varies from plaque or plaques to widespread involvement, with recurrence and recovery periods [1]. The diagnosis is made by careful morphological and histopathological evaluation. Various classifications are made according to the morphology and anatomical location of cutaneous lesions.

Plaque psoriasis

This is the most common form of psoriasis, affecting the 90% of the patients. It is characterized by red, scaly, discoid lesions varying in size from 0.5 cm in diameter to large confluent areas. There is a sharp line of demarcation between a plaque and clinically normal, uninvolved skin. It holds especially limb extensors elbows, knees, lumbosacral region, intergluteal region and scalp [2,3].

Inverse psoriasis

Inverse psoriasis is characterized mainly by its distribution: it is localized predominantly to intertriginous regions including the axillae, inframammary regions, glutaeal cleft, genitals, abdominal folds and inguinal folds. These lesions also differ in morphology from that of typical plaque psoriasis lesions in that they are well-defined shiny erythematous patches or thin plaques without significant scale. The presentation may initially be confused for bacterial or fungal intertrigo. Scrapings or cultures are sometimes needed to discriminate between these entities [4].

Guttat psoriasis

This is considered to be an eruptive form of psoriasis and is often associated with infection, especially streptococcal pharyngitis. Guttate psoriasis is more

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common in children and young adults, it can turn into chronic plaque psoriasis in 40% [4–6].

Pustular psoriasis

Pustular psoriasis cases constitute approximately 2–5% of all psoriasis cases, characterized by sterile pustules on an erythematosus base together with diffuse dermal neutrophilic infiltration and intradermal microplants in the lesions. Pustular psoriasis has localized and generalized forms. Generally, it is preceded or accompanied by systemic symptoms such as fever, weakness, anorexia and nausea. Pustular psoriasis cases usually have more severe disease processes compared to other types of psoriasis and may require hospitalization [4].

Erythrodermic psoriasis

The erythrodermic psoriasis is common erythema, holding more than 90% of the body which may be accompanied by an itch. In psoriasis patients, systemic steroids, methotrexate, cessation of drugs such as cyclosporin, phototoxic reaction, irritant topical treatments such as tar or systemic diseases and infections can be triggering factors [3–5,7].

Course

The course of the disease, particularly plaque psoriasis, is chronic with periodic remissions of variable duration occasionally lasting years (without therapy). Guttate psoriasis can become chronic and take on the features of chronic plaque psoriasis or in some cases resolve with treatment of the inciting infection, only to recur again in the future with precipitating events. The primary form of generalized and localized pustular psoriasis is also chronic, with periodic remissions. Secondary forms of pustular psoriasis, in the setting of plaque psoriasis, may be transient or may put on a new morphology after conversion. This may be seen as well in erythrodermic psoriasis (differentiated from generalized plaque psoriasis); it may be transient (weeks, months, or a few years) in duration or chronic (less often) [4].

Psychological factors affect the emergence and exacerbations of psoriasis [8]. A recent study, adjusted for aggravating or improving factors of stressful life events within one preceding year, disclosed that most psoriatic patients (76%) suffered from moderate to high levels of stress. Stressful life events may represent not only a cause but also an effect [9].

Unlike other medical diseases, skin diseases are noticeable by other people, which increases their relationship with psychological distress and psychiatric morbidity [10]. Factors involved may be cosmetic disfigurement of the exposed areas, moderate to intense pruritus, and inhibition to attend social gatherings. National Psoriasis Foundation reported that 60% of psoriasis patients may receive a psychiatric diagnosis [11].

Presence of a bi-directional relationship between psoriasis and psychopathology yields a continuous vicious cycle and affects patient management. The risks of depression, anxiety, and suicidality are increased even among patients with mild psoriasis [12]. Increased risk of new-onset psoriasis among individuals with depression suggests that depression may predispose patients to psoriasis or that psoriasis and depression share some common etiopathogenic mechanisms, supported by both having elevated levels of pro-inflammatory cytokines [12]. Although it is not a life-threatening disease, the high level of psychiatric comorbidity of psoriasis influences the quality of life negatively as much as life-threatening diseases such as cancer and heart disease [13]. The consequences of psoriasis for patients and their families can be significant and varied chiefly by beliefs about the consequences, causes, and emotional impact of the condition. Alexithymia seems as a risk factor for the emergence and maintenance of distress, and excessive worry may bring about the resistance of disease to treatment [13]. The literature implies that for some patients there is the possibility of a link between psychologic distress and various physical manifestations of psoriasis. The possible routes connecting psychologic factors with the appearance, worsening, or resistance of psoriatic lesions to treatment, although suggestive, remain uncertain. The question how stress modulates the skin is complex and is likely to involve multiple interactions between many cardiovascular, endocrine, and immunologic parameters. Further research is required given the high levels of distress and the proposed interaction between psychologic factors and disease process, patients are likely to benefit structured psychologic interventions that are integrated into standard care [13].

Reactive oxygen species can be produced in the mitochondria by electron transport, ionizing radiation, enzymes such as NADPH oxidase, lipoxygenase, cyclooxygenase and myeloperoxidase, UV radiation, chemotherapeutic agents such as adriamycin, heavy metal exposure, environmental toxins, and ischaemia and reperfusion. Molecular oxygen (O2) superoxide anion (O2 • -), hydrogen peroxide (H2O2), hydroxyl radical (• OH), peroxynitrite (ONOOOC), and hypochloric acid (HOCl) are oxygen-free free radicals [14,15].

Antioxidant defense mechanisms prevent the damage of structural lipid and proteins in coping with oxidative stress which are prevention of radical production, removal of produced radicals, repair of cellular damage, stopping reactions leading to secondary radical production and increasing endogenous antioxidant capacity. Antioxidants are comprised of superoxide dismutase (SODs), catalase, glutathione peroxidase

(GPx), glutathione reductase (GR), thioredoxin/thioredoxin reductase system and ferritin, reductive glutathione (GSH), lipid-soluble α-tocopherol (vitamin E), ascorbic acid (vitamin C) and enzyme systems and molecules such as uric acid [16]. Cellular redox environment plays an important role in skin homeostasis and skin disease could result from an imbalance between pro-oxidant and antioxidant stimuli [17].

Total oxidant capacity and total antioxidant capacity measurement and oxidative stress index showing oxidant/antioxidant balance were used in the evaluation of oxidative stress levels in psoriasis patients [18–20]. Glutathione peroxidase, catalase, superoxide dismutase, total antioxidant capacity and enzymes of antioxidant defense system were decreased, MDA and nitric oxide (NO) which is another important inflammation marker were increased in psoriasis, and this increase was found to be associated with the progression of psoriasis [17].

Stress exerts its effects on the immune system mainly by the hypothalamic pituitary adrenal (HPA) axis and the sympathetic adrenal medullary (SAM) axis. Psychological stress factors are processed in paraventricular nucleus of hypothalamus, afterwards produce corticotropin-releasing hormone (CRH), resulting in the secretion of corticotropin (ACTH) and cortisol. At the same time, the locus coeruleus mediates the activation of the sympathetic system causing the release of norepinephrine. Corticosteroid receptors may become insensitive to the continued effects of cortisol and the effect of catecholamines on macrophages becomes predominant. Then, the secretion of TNF-α, IL-1, and IL-6 is stimulated. Psoriatic plaques also contribute to the production of these pro-inflammatory cytokines. The effect of those cytokines on the brain induces or exacerbates symptoms of depression and re-activates the HPA axes (central and peripheral) and the sympathetic system [21].

Accompanying local and systemic changes in immune function in different inflammatory diseases can lead to disease-specific immune responses to stress and might increase negative health effects. Prospective study of de Brouwer et al measured the levels of circulating cytokines (IL-1b, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IFN-g and TNF-α) before and after Trier Social Stress Test in patients with rhematoid artritis (RA), patients with psoriasis and healthy subjects. The baseline levels of all cytokines, except IL-8, were significantly higher in patients with RA. After correction for baseline levels, patients with RA showed higher stress-induced levels of IL-1b and IL-2 than patients with psoriasis and healthy controls. Stress management training not only diminished levels of subjective tension and cortisol reactivity, but also influenced the IL-8 response to acute stress in patients with RA, indicating that psychological interventions can alter immune function [22].

Multiple studies have shown that depressed individuals have increased mean levels of pro-inflammatory cytokines in blood [23]. Meta-analyses have showed that interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) are elevated in Major Depressive Disorder (MDD). The exact mechanisms underlying the link between inflammation and depression are not fully understood but inflammation activates the kynurenine pathway of tryptophan metabolism, and potentially leads to accumulation of neurotoxic metabolites such as quinolinic acid. Also, increased gastrointestinal permeability leading to translocation of gram-negative bacteria may cause low-grade systemic inflammation and subsequently generate depressive symptoms [24]. High levels of pro-inflammatory cytokines are also shared by atherosclerosis and metabolic syndrome and they lead to endothelial dysfunction, having a central role in the etiopathogenesis of cardiovascular disease and erectile dysfunction. Therefore, psoriasis comorbidities may influence each other and when we treat one of them, the others may have unintended changes [21].

Oxidative stress markers are elevated in MDD, with 8-OH 2-deoxyguanosine (8-OHdG) and F2-isoprostanes being the most prominent [25]. The brain is particularly vulnerable to oxidative damage due to high oxygen utilization and subsequent generation of free radical by-products, relatively weak antioxidant defenses, and the risk for oxidative cellular injury and necrosis. These mechanisms may be how oxidative stress is related to depressive symptoms [24].

A chronic inflammatory disease is a condition characterized by persistent inflammation. In many cases, a genetic component has been identified, but also external factors like food, smoke, or environmental pollutants can significantly contribute to worsen their symptoms. The identity, source, regulation, and biological activity of redox molecules play key-role on autoimmune disorders (rheumatoid arthritis, systemic lupus erythematosus, psoriasis and celiac disease) and neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and multiple sclerosis) [26]. Inflammation and oxidative stress may contribute to anhedonia, anxiety-like behavior, somatic symptoms, disease behavior and cognitive impairment in depression [27]. Inflammation and oxidative stress affect cognitive functions by impaired neurogenesis and synaptic plasticity, neurodegenerative processes like DNA damage, neuronal death and apoptosis especially in hippocampus and prefrontal cortex also by cardiometabolic comorbidities via microvascular damage and atherogenesis [28,29]. Although a small fraction of AD and PD cases exhibit evidence of heritability, among which many genes have been identified, the majority are sporadic without known causes. Oxidative stress is recognized as a contributing factor in aging and in the progression of

multiple neurodegenerative diseases including AD and PD, also is held responsible from the development of neuronal death and neural dysfunction [30].

Increased production of reactive oxygen species (ROS) associated with age- and disease-dependent loss of mitochondrial function, altered metal homeostasis, and reduced antioxidant defense directly affect synaptic activity and neurotransmission in neurons leading to cognitive dysfunction. In addition, molecular targets affected by ROS include nuclear and mitochondrial DNA, lipids, proteins, calcium homeostasis, mitochondrial dynamics and function, cellular architecture, receptor trafficking and endocytosis, and energy homeostasis. Abnormal cellular metabolism in turn could affect the production and accumulation of amyloid-β (Aβ) and hyperphosphorylated Tau protein, which independently could exacerbate mitochondrial dysfunction and ROS production, thereby contributing to a vicious cycle. While mounting evidence implicates ROS in the AD etiology, clinical trials with antioxidant therapies have not produced consistent results [31].

There is currently a dearth of data derived from psoriasis registries on mental health comorbidities and how they change with time [12]. Depression in psoriasis has traditionally been explained as a response to psychosocial factors and impaired quality of life [32]. In a recent review by Lim et al. patients with psoriasis are more likely to be alexithymic, lack body awareness and possess a Type D personality. Alcohol, but not illicit drug use disorders are also more common in patients with psoriasis. Patient groups who are found especially at risk of psychological distress include women, younger patients, patients with a younger age of disease onset, those who self-assess their psoriasis to be severe, and those with lesions on visible or sensitive areas [33].

Psoriasis is associated with poor life satisfaction, affective expression and psychological well-being, as well as anxiety or depression [36]. However, there is limited and conflicting evidence concerning oxidative stress and cognitive functions in psoriasis X. Hypothesis linking anxiety and depression, psoriasis and cognitive impairment through chronic inflammation and oxidative stress offers insights that should help to understand and treat these diseases. In this approach, new drugs can be produced, psychological interventions and lifestyle changes claimed to be useful can be suggested to patients [32].

Accompanied by all these assumptions, the aim of this study was to compare psychiatric comorbidity, neurocognitive functions, oxidative stress markers (TOS, TAS, OSI) and proinflammatory cytokine (TNF-α and IL-6) levels of psoriasis patients with healthy controls, alongside to evaluate the effect of oxidative stress and inflammation on comorbidity and cognitive functions of psoriasis patients.

Methods

This study is approved by local/Bezmialem Vakif University Clinical Research Ethics Committee on 01.10.2014 with number 71306642/050-01-04.

Patients and controls

Among 110 patients interviewed, 48 met the inclusion criteria, out of which 11 refused to give consent for the study. Hence, patient population taken up for the study was 37 in total. Twenty-six female and 11 male patients, aged between 18 and 65 years with at least 5 years of education who presented to Dermatology Outpatient Clinics of the study hospital between 01.02.2015 and 01.11.2015; diagnosed as psoriasis by physical examination and histopathological evaluation were included in the study. Control group was formed from healthy individuals working for the hospital. A total of 37 volunteers, 9 males and 28 females were included. Written informed consent was obtained from each participant; patient and control groups were matched by sociodemographic features.

Exclusion criteria

1. To be under 18 or above 65 years of age
2. To have a level of education under 5 years
3. Pregnancy or pregnancy suspicion for female subjects
4. Presence of any known metabolic, endocrine or neurological disease (diabetes mellitus, hypertension, cardiovascular diseases, thyroid and pituitary diseases, chronic liver or kidney disease and most neurological diseases including epilepsy, dementia and head trauma)
5. Mental retardation
6. Presence of psychotic disorder or history of psychosis
7. Substance or alcohol use or addiction
8. Individuals hard to communicate (blindness, deafness etc.)
9. Concomitant inflammatory diseases such as infections and autoimmune disorders
10. Any anti-psoriatic, antipsychotic, or antioxidant agents, systemic drug therapy or photo chemotherapy within 3 months

Scales and tests used in research

All the participants were interviewed by a psychiatry resident with Structured Clinical Interview for DSM-IV (SCID-IV) to evaluate psychiatric comorbidity and psychiatric exclusion criteria. Sociodemographic data is taken, Beck Depression Inventory, Beck Anxiety Inventory, Semantic Verbal Fluency Test, Öktem

Verbal Memory Processes Test, Auditory Consonant Trigram Test and Wisconsin Card Sorting Tests were administered to all participants.

1. Beck Depression Inventory (BDI)

It is a 21 item, self-report scale developed by Aaron Beck in 1961 [34]. Turkish validity and reliability study was performed by Hisli in 1988 [35]. Items in the scale are rated from 0 to 3 in increasing order of severity and total score can range from 0 to 63. The Cronbach Alpha reliability of BDI was $r = 0.90$; split half-reliability was 0.74.

2. Beck Anxiety Inventory (BAI)

This is a self-report scale, developed by Aaron Beck in 1988 [36]. It consists of 21 items, each scored from 0 to 3 in increasing order of severity. Total score can range between 0 and 63. Turkish validity and reliability study were performed by Ulusoy in 1993. Ulusoy et al. found that the Cronbach Alpha consistency of the scale score was 0.93 [37].

3. Phonemic Verbal Fluency Test (K-A-S)

It was developed by Benton in 1968 [38]. Despite the use of the words F, A, S in the original test, K, A, S were used in the standardization study in our country. A coefficient alpha (Cronbach alpha) was computed using the total number of words generated for each letter as individual items. Letter K and K, A, S total correlation (.90), A – K, A, S total (.91) ve S – K, A, S total (.89). Subjects are asked to say as many words as possible in one minute which start with each of the letters K, A and S in Turkish [39]. It is emphasized that words should not contain special names and/or should not be the words derived by adding insertions to the words already said. Total scores are sum of all words that meet required criteria for each letter.

4. Öktem Verbal Memory Processes Test

This test is an analogue of Rey Auditory Verbal Learning test [40] in Turkish language, developed by Öktem [41]. Fifteen unrelated words are read to subject at intervals of one second and then the subject is asked to tell the ones on his/her mind. The number of correct answers is Instant Memory Score of the subject. After the first attempt, same list is read up to nine more times maximum until the subject is able to recall 15 words at a time. At the end of all repetitions, number of words remembered is totalized, defined as Learning Score. Whilst calculating this score, the subject is considered to have scored 15 points in remaining repetitions if he/she has completed the test by remembering 15 words without need for all 10 repetitions. After at least 25 minutes passed through different tests, the subject is asked to count these 15 words again without repeating the list again; then, to identify and mark the correct words from a list of words in which these 15 are included. Total number of words subject spontaneously recalled and selected from list gives Total Recall Score.

5. Auditory Consonant Trigram Test

It is used to evaluate short-term memory, working memory and split attention [42,43]. Turkish validity and reliability study was performed by Anıl et al. in 2003 [44]. In the first part, 3 consonants are read to subject and he/she is asked to repeat these letters as soon as the table is gently touched by hand. In the second part; after reading 3 consonants, subject is told a specific number. He/she is asked to count backward from this number, after a certain period of time subject should stop counting upon touching the table and repeat first 3 consonants. Time to wait after each question is determined in the test. Total number of letters remembered is recorded.

6. Wisconsin Card Sorting Test

It is a card matching test used for evaluation of executive functions [45–47]. Computerized version of Wisconsin Card Sorting Test (WCST) was used in our study. WCST entails matching stimulus cards with one of four category cards, in which stimuli are multidimensional according to colour (C), shape (S) and number (N), each defining a sorting rule. Participant answers via pressing 1, 2, 3 or 4 buttons on keyboard. Participant has to settle a preordained sorting rule given just feedback ("Right" or "Wrong") on screen after each sort. After 10 consecutive correct sorts, the rule changes without warning. Testing continues until all 128 cards are sorted.

Scores of WCST are automatically calculated and recorded by computer programme. 11 principal measures are grouped into four main types: (A) General Performance measures: total correct responses, total response errors and the number of categories completed; (B) Perseveration: Perseverative responses (Although the criterion for matching has been changed, it is sum of repetitive responses according to principle of matching for the previous category or according to principle of perseveration developed by the individual regardless of whether it is correct or incorrect), perseverative errors (perseverative responses that are also errors) and non-perseverative errors; (C) Conceptual Ability: The number of trials needed to complete first category and percentage of conceptual level responses (refers to what percentage the correct responses, consisting of at least three consecutive correct answers found in total number of responses); and (D) Response Consistency: Failure to maintain set measure, computed as the number of reaction blocks where subject gives 5–9 correct responses consecutively

but does not reach successive 10 correct response criteria; and learning to learn, a measure of decrement in the number of responses needed to achieve each successive category (calculation of this score requires at least three categories to be completed) [48].

Biochemical examination

Blood samples from all participants were centrifuged at 3000 rpm for 5 minutes and stored in a −80°C freezer for measurement of parameters to be studied.

1. Measurement of serum TNF-α and IL-6 Levels

IL-6 and TNF-α (Eastbiopharm, Ref. No: 20151124155 and Ref. No. 20151124160) in eluted serum samples by using commercial ELISA (Enzyme-Linked Immunosorbent Assay) kits measured in ELISA microplate reader (Thermo Scientific™ Varioskan™ Flash Multimode Reader).

2. Total Antioxidant Status (TAS) and Total Oxidative Stress (TOS) Measurement

Antioxidants work in cooperation with each other in plasma. Therefore, instead of measuring individual antioxidants TAS measurement is used [49,50]. Similarly; effects of different oxidative metabolites when together are augmented when compared to their total isolated effects. Measurement of individual oxidative molecule amounts takes excess amount of time and requires very complicated techniques so, to determine oxidative status of blood, TOS measurement is performed [51].

The collected sera were run on commercial ELISA (Total Antioxidant Capacity – Eastbiopharm, Ref. No: E20141108019, Total Oxidative Stress – Ref .No: E20141108089) kits; measured in ELISA Microplate Reader (Thermo Scientific™ Varioskan™ Flash Multimode Reader). TAS and TOS measurements are fully automated methods developed by Erel [49,51]. Oxidative Stress Index (OSI) is calculated by dividing TOS/TAS [52].

Statistical analysis

IBM SPSS Statistics v.22.0 (armonkNY: ibmcorp.) was used for statistical analysis. The distribution of data was evaluated with Kolmogorov–Smirnov test. Descriptive statistics were used for sociodemographic features. To evaluate differences between the groups; "Mann-Whitney *U*" test was used for variables without normal distribution, "Levene test" and "Independent Sample (Student's) *t*-test" were used for variables with normal distribution. Pearson correlation test was used for normally distributed variables. "Spearman" correlation test was used for two variables not normally distributed, or for -one normally distributed, one not-two variables; $p < 0.05$ was used as the statistical significance level.

Table 1. Kolmogorov–Smirnov normal distribution analysis of variables.

Variables	Statistic	df	*p*
Age	0.133	23	0.200*
Education	0.264	23	0.000
Smoking	0.415	23	0.000
Beck Depression Score	0.149	23	0.200*
Beck Anxiety Score	0,160	23	0.131*
Öktem Instant memory	0.162	23	0.120*
Öktem Learning	0.147	23	0.200*
Recall	0.216	23	0.007
Kas – K	0.099	23	0.200*
Kas – A	0.125	23	0.200*
Kas – S	0.132	23	0.200*
Auditory Consonant Trigram Test	0.109	23	0.200*
Wcs2	0.121	23	0.200*
Wcs3	0121	23	0.200*
Wcs4	0.141	23	0.200*
Wcs5	0.241	23	0.001
Wcs6	0.151	23	0.191*
Wcs7	0.177	23	0.061*
Wcs8	0.151	23	0.190*
Wcs9	0.283	23	0.000
Wcs10	0.127	23	0.200*
Wcs11	0.240	23	0.001
Wcs12	0.180	23	0.053*
Psoriasis Area and Severity İndex	0.171	23	0.081*
Interleukin-6	0.088	23	0.200*
Tumour Necrosis Factor Alfa	0.167	23	0.098*
Total Antioxidant Status	0.110	23	0.200*
Total Oxidative Stress	0.150	23	0.198*
Oxidative Stress Index	0.204	23	0.014
Duration of disease	0.144	23	0.200*

*$p < 0.05$, Normal distribution.

Results

The distribution of variables was assessed by means of the Kolmogorov–Smirnov test shown in Table 1. As the distribution of variables tested did not meet the normality criterion, nonparametric tests were applied for the statistical analysis.

Demographic characteristics of the participants

Table 2 shows the sociodemographic and clinical features of participants. 29.7% of psoriasis patients were male, 70.3% was female and 24.3% of the control

Table 2. Sociodemographic and clinical variables.

Patient (*n* = 37)			Control (*n* = 37)
Age (Mean ± SD)		42 ± 22	38 ± 14
Sex	Male	29.7(11)	24.3(9)
	Female	70.3(26)	75.7(28)
Education (Mean ± SD)		10 ± 5 years	9 ± 4 years
Smoking	+	27.0(10)	29.7(11)
	–	73.0(27)	70.3(26)
PASI (Psoriasis Area Severity Index)	0–1	13.5(5)	
	1–2	24.3(9)	
	2–3	21.6(8)	
	3–4	18.9(7)	
	4–5	13.5(5)	
	More than 5	8.1(3)	
Disease Duration	0–4 years	5.4(2)	
	5–9 years	21.6(8)	
	10–14 years	21.6(8)	
	More than 15 years	51.4(19)	

Table 3. Beck depression and beck anxiety scores of patient and control groups.

Psychiatric test scores	Patient Mean ± SD ($n = 37$)	Control Mean ± SD ($n = 37$)	t	p
Beck depression score	17.73 ± 10.02	9.49 ± 6.41	4.213	<0.001*
Beck anxiety score	17.81 ± 13.85	10.27 ± 9.85	2.698	<0.001*

Independent samples t-test. *$p < 0.05$.
Abbreviations: n, Number; SD, Standard deviation.

Table 4. Depression and anxiety severity distribution in patients and controls according to beck depression and beck anxiety scores.

Control			Patient		
Beck Depression	n	(%)	Beck Depression	n	(%)
Normal	21	56.8	Normal	9	24.3
Mild Depression	14	37.8	Mild Depression	11	29.7
Moderate Depression	2	5.4	Moderate Depression	12	32.4
Severe Depression	–	–	Severe Depression	5	13.5
Total	37	100.0	Total	37	100.0
Beck Anxiety	n	(%)	Beck Anxiety	n	(%)
Normal	18	48.6	Normal	9	24.3
Mild	8	21.6	Mild	12	32.4
Moderate	8	21.6	Moderate	5	13.5
Severe	3	8.1	Severe	11	29.7
Total	37	100.0	Total	37	100.0

group was male, 75.7% was female. The mean age was 42 years for patients and 38 years for controls.

Table 3 shows mean BDI and BAI scores and Table 4 shows the severity of depression and anxiety in patient and control groups ($p < 0.05$).

The control group's Öktem Learning, KAS-K, KAS-A, KAS-S scores and completed category number were higher than the patient group as shown in Table 5.

Nonperseverative error, number of trials until completion of first category and failure in maintaining set scores did not show a statistically significant difference between controls and patients. Total recall scores of the control group were higher than patients ($U = 503.00$, $p < 0.05$) according to Mann–Whitney U test (Table 6).

Table 6. Mann–Whitney U test of cognitive test scores in patient-control groups.

Cognitive test scores	Group	n	Mean rank	U	p
Öktem Total Recall	Patient	37	32,59	503,00	0.048*
	Control	37	42.41		
Nonperseverative Error	Patient	37	40.22	584.00	0.277
	Control	37	34.78		
Number of trials needed to complete first category	Patient	37	36.63	412.00	0.126
	Control	37	29.48		
Failure to maintain set	Patient	37	40.31	547.00	0.173
	Control	37	33.78		

Patient group IL-6, TNF-α and TOS levels were higher and TAS level was lower than controls ($p < 0.05$) as demonstrated in Table 7.

There was no significant relationship between TNF-α and cognitive test scores of patient group in Pearson and Spearman's correlation analysis (Tables 8 and 9).

A low positive correlation between IL-6 and Öktem instant memory ($0.20 < r < 0.40$) ($r = 0.328$) and between IL-6 and number of completed categories ($0.20 < r < 0.40$) ($r = 0.356$) was found in Pearson correlation analysis (Tables 10 and 11).

There was no significant relationship between TAS, TOS, OSI, BDI, BAI scores and cognitive test scores of patients in results of Pearson and Spearman's correlation analysis (Tables 12–15).

Pearson correlation analysis gave no significant relationship between patient BDI, BAI score and IL-6, TNF-α, TAS, TOS ($p > 0.05$) as shown in Table 16. There was no significant correlation between depression, anxiety and OSI in Spearman's correlation analysis ($p > 0.05$) (Table 17).

Pearson correlation analysis yielded no significant relationship between depression and disease duration ($p > 0.05$); there was a significant negative correlation between the number of categories completed and duration of disease ($p = 0.030$), ($20 < r < 0.40$ $r = -0.357$). In Spearman's correlation analysis, there was a significant, positive relationship between duration of disease and number of trials until first category was completed ($p = 0.020$), ($0.40 < r < 0.60$, $r = 0.408$).

Table 5. Cognitive test scores of patient and control groups.

	Cognitive Test Scores	Patient Mean ± SD ($n = 37$)	Control Mean ± SD ($n = 37$)	t	p
Öktem Verbal Memory Processes Test	Öktem Instant Memory	5.38 ± 1.48	6.11 ± 2.46	1.547	0.127
	Öktem Learning	106.68 ± 18.49	122.32 ± 17.33	3.756	0.000*
Phonemic Verbal Fluency Test (K-A-S)	KAS-K	10.35 ± 3.74	14.57 ± 6.03	3.615	0.001*
	KAS-A	7.27 ± 3.39	10.73 ± 5.20	3.391	0.001*
	KAS-S	7.08 ± 3.24	11.30 ± 4.78	4.441	0.000*
Auditory Consonant Trigram Test	Short-term working memory, split attention	45.57 ± 5.28	47.73 ± 7.27	1.464	0.147
Wisconsin Card Sorting Test	Total correct	74.14 ± 19.68	80.30 ± 19.48	1.354	0.180
	Total error	53.86 ± 19.68	46.92 ± 19.12	1.540	0.128
	Perseverative reaction	35.57 ± 19.52	31.89 ± 21.93	0.762	0.449
	Perseverative error	30.68 ± 14.67	27.35 ± 16.60	0.913	0.364
	Completed category number	3.24 ± 2.57	4.51 ± 2.68	2.082	0.041*
	Perseverative error percentage	23.98 ± 11.47	21.50 ± 13.02	0.869	0.388
	Conceptual level response percentage	44.09 ± 21.84	52.23 ± 21.12	1.631	0.107
	Learning to learn score	−1.16 ± 6.37	−1.31 ± 7.33	0.082	0.935

Independent samples t-test, *$p < 0.05$.

Table 7. Results of inflammatory markers for patients and controls.

Blood values	Patient Mean ± SD ($n = 37$)	CV	Control Mean ± SD ($n = 37$)	CV	t	p
IL-6	224.57 ± 38.42	17.10	81.33 ± 12.40	15.24	21.584	0.127
TNF-α	453.33 ± 98.12	21.64	227.07 ± 43.59	19.19	12.818	0.000*
TAS	1.18 ± 0.11	9.32	1.37 ± 0.15	10.94	6.139	0.001*
TOS	13.96 ± 1.33	9.52	11.41 ± 0.58	5.08	10.699	0.001*

Independent samples t-test, *$p < 0.05$.
Abbreviations: n, Number; SD, Standard deviation; CV, Coefficient of variation; IL-6, Interleukin-6; TNF-α, Tumour necrosis factor-α; TAS, Total antioxidant status; TOS, Total oxidative stress.

Discussion

In this study, we found that psoriasis patients' depression and anxiety severity, oxidative stress, TNF-α and IL-6 levels were significantly higher than healthy controls. Öktem learning, recall and semantic verbal fluency scores and number of categories completed in WCST of psoriasis patients were significantly lower than the control group. However, increased depression and anxiety scores were not associated with increased oxidative stress and inflammatory markers in patients. Also, deteriorations in cognitive fields of learning, recall, verbal fluency were not related to oxidative stress, inflammation, depression or anxiety. In concordant with the literature, psoriasis patients had higher mean BDI and BAI scores than controls [5,8,9,12,13,21,32].

In psoriasis patients glutathione peroxidase, catalase, superoxide dismutase, total antioxidant capacity and enzymes of antioxidant defense system were decreased, MDA and nitric oxide (NO) which is another important inflammation marker were increased and this increase was found to be associated with the progression of psoriasis [17]. Oxidative stress levels of psoriasis patients were reported to be increased independently of age, duration of disease, body mass index etc. [18,19,53].

While there are many studies about oxidative stress in pathogenesis of psoriasis and psychiatric disorders separately [44], the effect of depression on oxidative system in 39 psoriasis patients and 25 healthy controls was evaluated by Karababa et al. Psoriasis patients' HADS scores, TOS and OSI levels were significantly higher; just TAS levels were significantly lower than controls. Presence of depression did not have a significant effect on TAS, TOS and OSI levels of psoriasis patients but significantly affected TAS and OSI levels in healthy controls [54]. Consistently, in our study, depression and anxiety levels of patients had no significant relationship with TAS, TOS and OSI levels. Explanation might be that the psoriasis patients have already significantly higher levels of oxidative stress compared to controls and any more effects of depression and anxiety on oxidative system could be masked. Regrettably, variety of subtypes and severity of psoriasis and depression were not taken into consideration. Therefore, clinically significant depression may not be reflected and relationship of each depression severity subtype with oxidative stress and relationship of psoriasis severity and subtype with oxidative stress could not be studied. In addition, when evaluting the association of depression with oxidative stress, there are many confounders like age, sex, socio-economic status or education, ethnicity, smoking, alcohol use, BMI, physical activity, presence of somatic disease and antidepressant or mood stabilizer used. So, not adjusting for these confounders, may have led to a false result that there is no significant relationship between depression and oxidative stress markers.

The natural and acquired immune system provide intercellular communication by molecules which are

Table 8. Pearson correlation analysis results between TNF-α and cognitive test scores in patient group.

Cognitive test scores		Tumour necrosis factor α
Öktem Instant Memory	r	−0.001
	p	0.994
Öktem Learning	r	−0.007
	p	0.967
Kas-K	r	−0.265
	p	0.112
Kas-A	r	−0.259
	p	0.122
Kas-S	r	−0.044
	p	0.795
Auditory Consonant Trigram Test	r	−0.131
	p	0.441
Wcs Total correct	r	0.073
	p	0.666
Total error	r	−0.073
	p	0.666
Perseverative reaction	r	−0.026
	p	0.880
Perseverative error	r	−0.020
	p	0.907
Number of completed categories	r	−0.024
	p	0.887
Perseverative error percentage	r	−0.020
	p	0.906
Percentage of conceptual level responses	r	0.070
	p	0.679
Learning to learn score	r	−0.015
	p	0.945

Table 9. Spearman's correlation analysis results between cognitive test scores and tumour necrosis factor α in patient group.

Cognitive test scores		Tumour necrosis factor α
Öktem Total Recall	r	0.007
	p	0.966
Nonperseverative Error	r	−0.086
	p	0.612
Number of trials needed to complete first category	r	−0.032
	p	0.862
Failure to maintain set	r	0.240
	p	0.159

Table 10. Pearson correlation analysis results between IL-6 and cognitive test scores in patient group.

Cognitive test scores		Interleukin-6
Öktem Instant Memory	*r*	0.328
	p	0.048*
Öktem Learning	*r*	0.150
	p	0.375
Kas-K	*r*	0.200
	p	0.235
Kas-A	*r*	0.034
	p	0.842
Kas-S	*r*	0.163
	p	0.336
Auditory Consonant Trigram Test	*r*	−0.102
	p	0.547
Wcs Total correct	*r*	0.288
	p	0.084
Total error	*r*	−0.288
	p	0.084
Perseverative reaction	*r*	−0.180
	p	0.286
Perseverative error	*r*	−0.197
	p	0.242
Number of completed categories	*r*	0.356
	p	0.031*
Perseverative error percentage	*r*	−0.197
	p	0.242
Percentage of conceptual level responses	*r*	0.290
	p	0.082
Learning to learn score	*r*	−0.330
	p	0.124

Table 12. Pearson correlation analysis results between TAS, TOS, OSI and cognitive test scores in patient group.

Cognıtıve test scores		TAS	TOS	OSI
Öktem Instant Memory	*r*	−0.123	0.182	0.259
	p	0.467	0.281	0.122
Öktem Learning	*r*	−0.228	0.051	0.206
	p	0.175	0.764	0.222
Kas-K	*r*	0.219	−0.042	0.229
	p	0.192	0.803	0.172
Kas-A	*r*	0.053	0.031	−0.030
	p	0.756	0.854	0.859
Kas-S	*r*	−0.154	0.112	0.025
	p	0.364	0.508	0.884
Auditory Consonant Trigram Test	*r*	0.073	0.186	0.233
	p	0.667	0.271	0.165
Wcs Total correct	*r*	−0.073	−0.186	0.174
	p	0.667	0.271	0.303
Total error	*r*	0.066	−0.150	0.115
	p	0.697	0.374	0.497
Perseverative reaction	*r*	0.020	−0.163	−0.115
	p	0.908	0.335	0.497
Perseverative error	*r*	0.032	0.217	−0.121
	p	0.853	0.198	0.475
Number of completed categories	*r*	0.018	−0.164	0.049
	p	0.914	0.332	0.775
Perseverative error percentage	*r*	0.053	0.176	−0.091
	p	0.758	0.298	0.590
Percentage of conceptual level responses	*r*	−0.041	0.025	0.201
	p	0.854	0.910	0.233
Learning to learn score	*r*	−0.123	0.182	−0.094
	p	0.467	0.281	0.582

called cytokines and chemokines. By activation of dermal and plasmacytoid dendritic cells, the secretion of cytokines such as IL-12 and IL-23 differentiates T cells in the direction of TH 1 and TH 17 [55]. In psoriasis lesions, cytokines such as IL-1, 6, 8, 12, TNF-α, IFN- γ and also IL-23, IL-1 levels, which are defined as Type 1 cytokines secreted by activated T lymphocytes are high [56]. Most of the psoriatic T cells discretely produce interferon-γ, IL-17 and IL-22. Keratinocytes are the main cutaneous cell type expressing IL-17 receptors and hence the immune circuit is amplified by keratinocytes upregulating mRNAs for a range of inflammatory products [57].

We did not find any relationship between IL-6 and TNF-α levels and depression among psoriasis patients. Particularly vegetative symptoms of depression such as sleep and appetite disruptions and fatigue are associated with cytokines [58]. In a cardiology study, TNF-α was found to be specific for depressive symptoms like guilt, shame and hopelessness [59]. Therefore, lacking the investigation of relationship between neurovegetative, mood subgroups of depressive symptoms or severity levels of depression, anxiety with IL-6 and TNF-α is one of our limitations. Besides, not adjusting for the confounders described above for oxidative markers is still valid for inflammatory mediators and may have led us to a false result that there is no significant relationship between depression and inflammatory markers. Increased depression and anxiety levels of psoriasis patients might be related to other mechanisms than inflammation and oxidative stress, such as Hypothalamo Pituitary Adrenal (HPA) axis impairments, increased neuropeptide levels and/or psychosocial burden of disease, the way disease is perceived, inadequate coping skills and certain personality traits [43,44].

In our study, learning, recall, verbal fluency scores and number of completed categories in WCST of psoriasis patients were significantly lower than the control group. Prolonged exposure to increased proinflammatory cytokines and increased oxidative neuronal stress may adversely affect neurogenesis and cause cognitive impairment [60–64]. It is possible that psoriasis and cognitive impairment may have a common genetic background associated with ApoE gene polymorphism [65,66]. Another explanation is activation of HPA axis

Table 11. Spearman's correlation analysis results between cognitive test scores and IL-6 in patient group.

Cognitive test scores		Interleukin-6
Öktem Total Recall	*r*	0.065
	p	0.700
Nonperseverative Error	*r*	−0.177
	p	0.295
Number of trials needed to complete first category	*r*	−0.301
	p	0.094
Failure to maintain set	*r*	−0.072
	p	0.677

Table 13. Spearman's correlation analysis results between TAS, TOS, OSI and cognitive test scores in patient group.

Cognitive test scores		TAS	TOS	OSI
Öktem Total Recall	*r*	−0.137	0.201	0.229
	p	0.418	0.232	0.172
Nonperseverative Error	*r*	−0.173	−0.057	0.049
	p	0.304	0.738	0.775
Number of trials needed to complete first category	*r*	0.007	−0.004	0.015
	p	0.969	0.983	0.937
Failure to maintain set	*r*	0.067	−0.020	−0.046
	p	0.696	0.907	0.788

Table 14. Pearson correlation analysis results of beck depression and anxiety scores and cognitive test scores in patient group.

Cognitive test scores		Beck depression	Beck anxiety
Öktem Instant Memory	*r*	0.065	0.182
	p	0.704	0.281
Öktem Learning	*r*	0.060	0.051
	p	0.723	0.764
Kas-K	*r*	0.264	−0.042
	p	0.114	0.803
Kas-A	*r*	0.264	0.031
	p	0.115	0.854
Kas-S	*r*	0.054	0.112
	p	0.750	0.508
Auditory Consonant Trigram Test	*r*	0.172	0.186
	p	0.310	0.271
Total correct	*r*	−0.002	−0.186
	p	0.992	0.271
Total error	*r*	0.002	−0.150
	p	0.992	0.374
Perseverative reaction	*r*	0.019	−0.163
	p	0.913	0.335
Perseverative error	*r*	−0.001	0.217
	p	0.993	0.198
Number of completed categories	*r*	−0.052	−0.164
	p	0.761	0.332
Perseverative error percentage	*r*	−0.002	0.176
	p	0.991	0.298
Percentage of conceptual level responses	*r*	−0.045	0.025
	p	0.790	0.910
Learning to learn score	*r*	−0.011	0.182
	p	0.961	0.281

in psoriasis and enhancement of stress-related neuropeptides causing neuronal changes and cognitive impairment [67,68].

Brain-derived neurotrophic factor (BDNF) takes part in neuroplasticity and synaptic strengthening, simply decreases due to stress which provokes cognitive impairment in psoriasis patients [69,70]. Still, association of psoriasis with psychological, inflammatory, metabolic or other systemic diseases may pose these patients at risk for cognitive impairment [71]. Gisondi et al. applied neuropsychological tests to 41 patients with chronic plaque psoriasis between 55 and 65 years of age who were not receiving systemic treatment and to 37 healthy controls. Mild cognitive impairment was detected in 18 of 41 psoriasis patients and in 4 of 37 healthy controls. In 12 out of 41 patients, delayed recall of Rey 15-word test was deteriorated, 18 had deterioration in trail making test, 12 in Weigl's card pairing test while there was no significant

Table 15. Spearman's correlation analysis results between cognitive test scores and beck depression and anxiety scores in patient group.

Cognitive test scores		Beck depression	Beck anxiety
Öktem Total Recall	*r*	−0.182	0.024
	p	0.281	0.889
Nonperseverative Error	*r*	0.070	0.086
	p	0.683	0.614
Number of trials needed to complete first category	*r*	0.077	0.113
	p	0.676	0.539
Failure to maintain set	*r*	0.176	0.084
	p	0.305	0.626

Table 16. Pearson correlation analysis results between beck depression and anxiety scores and IL-6, TNF-α, TAS, TOS in patient group.

		Beck depression	Beck anxiety
IL-6	*r*	0.119	0.005
	p	0.484	0.977
TNF-α	*r*	−0.256	−0.297
	p	0.127	0.075
TAS	*r*	0.127	0.128
	p	0.454	0.449
TOS	*r*	−0.061	0.138
	p	0.718	0.417

difference in verbal fluency and praxis between psoriasis patients and controls. Psoriasis was the only significant predictor of mild cognitive impairment independent of age, gender, education level, smoking, hypertension, diabetes and hypercholesterolemia. Serum CRP and homocysteine levels were significantly higher in psoriasis patients; and on MRI scan there was a decrease in cortical thickness especially in brain areas responsible from cognitive functions [72]. In the mentioned study, age range of the sample was 55–65 years. This difference from our study may have led to a more significant deterioration in cognitive functions due to both long course of the disease and drugs used.

Çölgeçen et al evaluated cognitive functions of 77 psoriasis patients aged 18–70 and 83 healthy controls using Montreal Cognitive Assessment Test (MoCA). MoCA scores showing visuospatial and executive functions were significantly lower in psoriasis patients, regardless of their education level and disease characteristics [28]. Józefowicz et al. assessed the dorsolateral prefrontal cortex functions of patients with psoriasis. The Trail Making Test and the Stroop test were applied to 97 patients with psoriasis and 91 healthy controls. Compared to healthy subjects, psoriatics scored lower in neuropsychological tests assessing memory and executive functions [73]. These studies showed differences in design, but psoriasis was an independent risk factor for cognitive impairment. The Rotterdam study which has a high number of non-psoriatic participants (318 psoriatic and 9678 non-psoriatic, mean age: 66.1 years, 58% women) included magnetic resonance imaging (MRI)-markers in addition to cognitive test scores. Cognitive test scores and volumetric, microstructural, focal measures on brain MRI did not differ between psoriasis (28% systemic/UV treatment) and non-psoriasis participants and psoriasis was not associated with mild cognitive impairment (MCI) [74]. This study included patients taking systemic/UV treatment alongside it was a population-based

Table 17. Spearman's correlation analysis results of beck depression and anxiety scores and OSI in patient group.

		Beck depression	Beck anxiety
OSI – oxidative stress index	*r*	−0.147	0.045
	p	0.386	0.789

study and findings should be replicated in clinical population too.

Although basal levels of IL-6 are implied to take part in healthy cognitive processes, prolonged IL-6 exposure during normal aging process or neurodegenerative diseases may disrupt adult neurogenesis [75]. In our study, IL-6 levels of psoriasis patients correlated positively with Öktem instant memory and number of completed categories in WCST. Given it has both neuroprotective and neurodegenerative effects in Central Nervous System (CNS), the role of IL-6 in cognitive functions may vary depending on specific conditions in which it increased, the duration and level of increase [76]. IL-6 protects neurons from NMDA-mediated neurotoxicity, particularly by reducing release of glutamate in cerebral cortex [77] and functions in long-term potentiation and synaptic plasticity. Prolonged IL-6 overexpression may affect hippocampus-induced learning processes negatively; on the other side, impaired learning after anterior brain ischaemia showed improvement with endogenous IL-6 [78–80]. Therefore, in our study, positive correlation of IL-6 with instant memory and number of completed categories might be explained by neuroprotective effect of IL-6 in prefrontal brain regions depending on magnitude of increase and duration of exposure.

IL-6 and TNF-α levels in CNS, CSF or blood have been increased in Alzheimer's disease and other cognitive problems [81–85], however in our study which includes psoriasis patients, serum TNF-α and IL-6 were not related to current deterioration in cognitive functions. Since psoriasis is characterized by peripheral inflammation, unlike neurodegenerative diseases, proinflammatory cytokine overexpression in CNS is not likely and apart from that blood levels of cytokines may not adequately reflect their levels in CNS [86].

In patients with depression, as a result of inability to transfer short-term memory into long-term; a deterioration in verbal learning processes may be observed [87]. Decreased hippocampal neurogenesis in both major depression and cognitive impairment is the common pathway [29,88]. In our study, current cognitive impairment was demonstrated, independent of the presence of depression. This may be related to lack of enough duration or number of depressive episodes to cause neurodegenerative changes. Rodrigo Grassi-Oliveira et al. observed that verbal memory performance decrement in recurrent depression was correlated with the severity of depression [89]. Therefore, parameters such as duration, number of episodes and severity should be taken into consideration while evaluating depression and cognitive impairment relationship.

In our study, duration of psoriasis was not related to psychiatric comorbidity. Other studies showed clearance of psoriasis may improve stress, patients' wellbeing, anxiety or depression symptoms, on the other side, some patients with severe psoriasis may have progressively adapted to the impact of the disease [9]. From parameters of WCST, when the duration of disease prolonged, number of categories completed decreased and number of trials until first category completed increased. The longer the duration of disease, the more likely is the deterioration due to progression of disease and rise in metabolic and atherogenetic comorbidities. In addition, chronic course of the disease with relapses may cause a shift from topical psoriasis treatments to systemic agents, long-term and multiple drug use.

Agents used in systemic treatment of psoriasis mostly inhibit cytokines such as TNF-α. Patients with psoriasis would benefit from psychodermatologic assessment in order to define whether or not an underlying mental disorder exists, the kind of psychopathology and the underlying etiological factors. For instance, TNF antagonists may lead to manic or hypomanic episodes. So, potential side effects should be thoroughly analysed when the patient has a personal or family history of bipolar disorder [21]. In chronic inflammatory diseases, TNF-α inhibitors are shown to improve depressive symptoms [90] but in another study, TNF-α inhibitor infliximab was not found to be effective in depression [91]. The study by Jin et al showed that depression symptoms at baseline independently predicted a worse clinical response to etanercept treatment in psoriasis patients [92]. In our study, we excluded patients taking anti-psoriatic, antipsychotic, or antioxidant agents, systemic drug therapy or photo chemotherapy within 3 months. Due to lack of past records of BDI, BAI scores; systemic treatments, doses and durations could not be compared retrospectively so we could not assess effect of drugs on depressive symptoms. The relatively small sample size limits generalizing results to entire population, certainly, larger-scale studies are needed to extend the evidence on oxidative stress in depression in patients with psoriasis. Patients were not differentiated by subtypes of psoriasis and severity of depression can be noted as limitations of our study.

Conclusion

We found depression, anxiety, blood oxidative stress, TNF-α and IL-6 levels to be significantly higher in psoriasis patients compared to healthy controls. Besides, the cognitive domains of learning, recall and verbal fluency were impaired in psoriasis patients. Taking into account the younger sample compared to previously reported psoriasis-cognitive impairment studies our study suggests deteriorations of cognitive fields of learning, recall, verbal fluency in psoriasis patients were not related to oxidative stress, inflammation, depression or anxiety. However, variety of depression subtypes, sociodemographic variables, metabolic parameters and severity of psoriasis were not specified.

Detection of early psychopathology and cognitive impairment in psoriasis patients may improve

preventive perspective. Further studies with larger sample sizes, adjusted for confounders described in our limitations, assessing HPA axis, BDNF, other associated neuropeptides, other oxidative and inflammatory markers are needed to elucidate pathogenesis underlying neurocognitive impairment in psoriasis patients.

Disclosure statement

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