Research Article

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The role of kynurenine and kynurenine metabolites in psoriasis

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Abstract

Objectives: Psoriasis is a widespread immunological disease characterised by inflammation and primarily associated with skin and joint symptoms. The kynurenine pathway significantly influences inflammation and immune system activity. The aim of this study is to determine serum concentrations of kynurenine metabolites in patients with psoriasis and investigate their correlation with disease severity.

Methods: This study included 30 participants with psoriasis and 30 individuals without the disease as healthy controls. Serum levels of tryptophan, kynurenine, 3-OH anthranilic acid, quinolinic acid, 3-OH kynurenine, and kynurenic acid were determined by liquid chromatography-mass spectrometry (LC-MS/MS).

Results: Serum levels of kynurenic acid ($p<0.001$), tryptophan ($p<0.001$) and the tryptophan/kynurenine ratio (TKR) ($p<0.001$) were statistically significantly lower in psoriasis patients than in healthy controls, while levels of quinolinic acid ($p=0.007$) and kynurenine ($p=0.001$) were significantly higher. The psoriasis area severity index (PASI) correlated positively with 3-hydroxykynurenine and kynurenic acid.

Conclusions: Kynurenine metabolites are associated with the pathophysiology of psoriasis and could serve as valuable candidate markers for monitoring inflammation.

Keywords: psoriasis; kynurenine pathway; tryptophan to kynurenine ratio; hs-CRP; PASI

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Introduction

Psoriasis affects approximately 2–3 % of people worldwide and is associated with various comorbidities, including metabolic syndrome, systemic inflammation, and cardiovascular disease (CVD) [1, 2]. The severity of psoriasis is often assessed by measuring the psoriasis area severity index (PASI), which is a quantitative measure of the area and intensity of skin lesions [3]. High-sensitivity C-reactive protein (hs-CRP) is an acute-phase protein that indicates systemic inflammation and is known to be a risk factor for CVD and atherosclerosis [4, 5].

The disease is a persistent inflammatory skin disorder of immune-mediated origin, characterised by irregular epidermal differentiation, proliferation, and inflammation promoted by dermal infiltrates, including T cells, dendritic cells, macrophages and neutrophils [2]. T helper (Th)-17 cells, regulatory T cells, and Th22 cells as well as cytokines such as interleukin (IL)-23, IL-22 and IL-17 play a key role in the development of psoriasis [6]. In particular, the IL-23/Th17 cell axis is of fundamental importance for the development of psoriasis [7]. In addition, autoreactive T cells, the proliferation of Th1 and Th17 cells, the activation of dendritic cells and the presence of memory T cells in the epidermis and dermis are key factors contributing to the pathogenesis of the disease [8].

The kynurenine pathway is essential for the metabolism of tryptophan and leads to the formation of several biologically active metabolites. In mammals, this metabolic pathway is the main pathway for the degradation of tryptophan, ultimately producing nicotinamide adenine dinucleotide (NAD) from nothing [9]. The conversion of tryptophan to kynurenine is a crucial step in the kynurenine pathway, which is facilitated by the enzymes tryptophan 2,3-dioxygenase (TDO)/indoleamine 2,3-dioxygenase (IDO) [10]. TDO is mainly found in the liver and is mainly induced by tryptophan. The IDO enzyme has two different forms (IDO-1 and IDO-2) and is predominant in extrahepatic tissues. It is upregulated by lipopolysaccharides, amyloid peptides, some cytokines and inflammatory molecules, with interferon gamma being the strongest stimulus [11]. Kynurenine, a key metabolite in this

pathway, is further metabolized to produce a number of biologically active compounds, including quinolinic acid, 3-hydroxykynurenine (3-OH kynurenine), 3-hydroxyanthranilic acid (3-OH anthranilic acid), and kynurenic acid [9]. The kynurenine pathway and its metabolites have been associated with numerous physiological and pathophysiological processes, including immune tolerance, neurotoxicity and modulation of psychiatric disorders, indicating their potential as candidate biomarkers. In addition, the kynurenine pathway and its metabolites have been linked to various diseases, including CVD, inflammatory bowel disease, chronic disease, depression and/or neuropsychiatric disorders [12]. Disruption of kynurenine metabolism has been linked to the onset of various diseases, including inflammatory skin diseases such as psoriasis. In this disease, increased activity of kynureninase, an enzyme within the metabolic pathway, has been linked to the severity of the disease and the extent of inflammation [13, 14]. The aim of this study is to evaluate the serum concentrations of kynurenine metabolites in psoriasis patients and to investigate their association with disease severity.

Materials and methods

Patients

The present study included 30 patients diagnosed with psoriasis from the Department of Dermatology of the Medical Faculty Hospital of Department of Dermatology of the Medical Faculty Hospital of Selcuk University University and 30 healthy individuals who visited our hospital for general health examinations or obtained health reports for various reasons to confirm their well-being, all of whom were free of disease. Exclusion criteria for the study included people with acute or chronic infections, people with other autoimmune or inflammatory diseases, and people who had no additional systemic diseases. Patients were disqualified if they had taken methotrexate, cyclosporine, biologic agents, systemic steroids or hormone therapy within the previous 3 months. Malignant diseases, pregnancy, breastfeeding, persons under the age of 18, obesity, smoking or alcohol consumption were also exclusion criteria for participation in the study.

Routine biochemical tests were performed on the serum samples. Aliquots of serum samples were then stored at −80 °C until analysis. The study was approved by the Ethics Committee of the Medical Faculty of Ethics Committee of the Medical Faculty of Selcuk University (approval number 2023/520).

Measurement of hs-CRP

The determination of hs-CRP was performed by the immunoturbidimetric method on the AU5800 series instrument from Beckman Coulter, Japan. The results were expressed in mg/L.

Measurement of tryptophan metabolites

Serum concentrations of metabolites of the kynurenine pathway were determined using a modified method [15]. In brief, 100 µL of the internal standard (kynurenine-d4) was pipetted into 300 µL of each sample, followed by the addition of 1,000 µL of acetonitrile (containing 1 % formic acid) for precipitation. The mixture was vortexed for 30 s and then centrifuged at 2,000 × g for 10 min. After centrifugation, 1,000 µL of the supernatant was collected in a tube and concentrated by evaporation under nitrogen gas. For analysis, 50 µL of the evaporated sample was added to an ABSciex API 3200 tandem mass spectrometer (Applied Biosystems/MDS Sciex, USA) for analysis. The separation was performed using a Phenomenex Luna C18 reverse phase column (50 × 4.6 mm with a flow rate of 0.8 mL/min. The mobile phase consisted of mobile phase A (100 % HPLC-grade water with 0.1 % formic acid) and mobile phase B (100 % acetonitrile with 0.1 % formic acid). The results (ng/mL) were then calculated using a calibration curve.

The LC-MS/MS used in this study enabled the accurate and precise measurement of metabolites of the kynurenine pathway. The method showed a linear calibration range of 48.8–25.000 ng/mL for tryptophan, 0.98–500 ng/mL for kynurenic acid, 1.2–5,000 ng/mL for kynurenine, 1.2–5,000 ng/mL for 3-hydroxyanthranilic acid, 0.98–250 ng/mL for 3-hydroxykynurenine and 0.98–500 ng/mL for quinolinic acid. The values of the limit of detection (LOD) and the lower limit of quantification (LLOQ) were as follows: LOD: 15.5 ng/mL, LLOQ: 48.8 ng/mL for tryptophan, LOD: 0.90 ng/mL, LLOQ: 1.96 ng/mL for kynurenic acid, LOD: 1.0 ng/mL, LLOQ: 2.4 ng/mL for kynurenine, LOD: 1.0 ng/mL, LLOQ: 2.4 ng/mL for 3-hydroxyanthranilic acid, LOD: 0.95 ng/mL, LLOQ: 1.96 ng/mL for 3- hydroxykynurenine and LOD: 1.0 ng/mL, LLOQ: 1.96 ng/mL quinolinic acid. The intra-assay CV% values were 4.22 % for tryptophan, 4.85 % for kynurenic acid, 5.15 % for kynurenine, 6.66 % for 3-hydroxyanthranilic acid, and 4.05 % for 3-hydroxykynurenine. The inter-assay CV% values were 5.23 % for tryptophan, 5.06 % for kynurenic acid, 5.68 % for kynurenine, 6.72 % for 3-hydroxyanthranilic acid, 4.20 % and quinolinic acid 4.28 % for 3-hydroxykynurenine, indicating high reproducibility for each metabolite. Additionally, the method offers advantages such as a short

analysis time (5 min), simple sample preparation steps, and high extraction efficiency. Matrix effects were below 6.7 % and were minimal for all metabolites [16].

Statistical analysis

All statistical analyses were performed with R version 4.2.1 (www.r-project.org) statistical software. The Shapiro-Wilk normality test and the Levene test were used to check the normality and homogeneity of variance. Numerical variables were presented as mean ± standard deviation or median with quartiles [25th percentile – 75th percentile]; and categorical variables were described as number (n) and percentage (%). A Student's t-test, Welch's t-test, Mann-Whitney U-test and chi-square test with Yates continuity correction were applied to compare the control and psoriasis groups in terms of demographic and clinical characteristics and laboratory parameters. Spearman's rho correlation coefficients were also calculated to assess the relationship between hs-CRP and PASI with patient age and laboratory parameters. Receiver operating characteristic (ROC) curve analysis was performed to investigate the diagnostic performance of laboratory parameters in distinguishing psoriasis patients from healthy controls. The area under the curve (AUC) values were determined with 95 % confidence intervals (CIs) and the optimal cut-off values were determined using the Youden index criteria. Specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) with 95 % CIs were calculated for the determined optimal cut-off values. A two-tailed p-value of less than 0.05 was defined as statistically significant.

Results

The study groups had a similar average age and gender distribution (p=0.145 and p=0.196 respectively). Psoriasis patients had significantly lower levels of kynurenic acid (ng/mL), tryptophan (ng/mL), and tryptophan to kynurenine ratio (TKR), while levels of quinolinic acid (ng/mL) and kynurenine (ng/mL) were significantly higher. On the other side, we did not observe a statistically significant differences in 3-OH anthranilic acid and 3-OH kynurenine between study groups (Figure 1, Table 1).

The hs-CRP values showed a positive correlation with the age of the patients (Spearman's rho=0.398, p=0.029) and a negative correlation with the kynurenine values (Spearman's rho=−0.405, p=0.026). In addition, Spearman's rho correlation analysis showed a statistically significant positive relationship between PASI and 3-OH kynurenine (Spearman's rho=0.388, p=0.034), as well as kynurenic acid (Spearman's rho=0.373, p=0.042) in patients with psoriasis (Figure 2). No significant correlation was observed between hs-CRP and PASI with other parameters (Table 2). Additionally, significant positive correlation was observed between kynurenic acid and tryptophan (Spearman's rho=0.585, p<0.05), while significant negative correlation was observed between kynurenine and TKR (Spearman's rho=−0.79, p<0.05) (Figure 2).

ROC analysis was performed to evaluate the candidate laboratory biomarkers for differentiating of psoriasis patients from healthy controls. This showed that the AUCs of kynurenic acid, quinolinic acid, kynurenine, tryptophan, and TKR for the diagnosis of psoriasis were 0.768 (95 % CI, 0.641–0.867; p<0.001), 0.706 (95 % CI, 0.574–0.816; p=0.003), 0.741 (95 % CI, 0.612–0.846; p<0.001), 0.803 (95 % CI, 0.680–0.894; p<0.001) and 0.873 (95 % CI, 0.762–0.945; p<0.001), respectively (Table 3 and Figure 3). Kynurenic acid value of 3.5 ng/mL was found to be the optimal cut-off value with a sensitivity of 100 % (95 % CI, 88.4–100), a specificity of 56.67 % (95 % CI, 37.4–74.5), a PPV of 69.8 % (95 % CI, 60.5–77.7), and an NPV of 100 % (95 % CI, 100–100). The optimal cut-off value of quinolinic acid was 14.2 ng/mL with a sensitivity of 70 % (95 % CI, 50.6–85.3), specificity of 70 % (95 % CI, 50.6–85.3), PPV of 70 % (95 % CI, 56.3–80.9), and an NPV of 70 % (95 % CI, 56.3–80.9). We found the optimal cut-off value for kynurenine to be 313.6 ng/mL with a sensitivity of 73.33 % (95 % CI, 54.1–87.7), a specificity of 70 % (95 % CI, 50.6–85.3), a PPV of 71 % (95 % CI, 57.6–81.5), and an NPV of 72.4 % (95 % CI, 58.1–83.2). The optimal cut-off value for tryptophan was 8,150 ng/mL with a sensitivity of 83.33 % (95 % CI, 65.3–94.4), a specificity of 70 % (95 % CI, 50.6–85.3), a PPV of 73.5 % (95 % CI, 61.6–83.1), and an NPV of 80.8 % (95 % CI, 64.6–90.6). An optimal TKR cut-off value of 24.89 with a sensitivity of 80 % (95 % CI, 61.4–92.3), a specificity of 83.33 % (95 % CI, 65.3–94.4), a PPV of 82.8 % (95 % CI, 67.9–91.6), and an NPV of 80.6 % (95 % CI, 66.7–89.7) for the prediction of psoriatic disease was determined. An optimal hs-CRP cut-off value of 2.53 with a sensitivity of 46.67 % (95 % CI, 28.3–65.7), specificity of 93.33 % (95 % CI, 77.9–99.2), PPV of 87.5 % (95 % CI, 63.5–96.6), and NPV of 63.6 % (95 % CI, 55.3–71.3) was determined to predicting Psoriasis disease. The AUC was calculated as 0.677 (0.544–0.792) for hs-CRP.

Discussion

Kynureninase and IDO are key enzymes in the kynurenine pathway, with kynureninase being highly expressed in psoriatic plaques compared to healthy skin, suggesting that

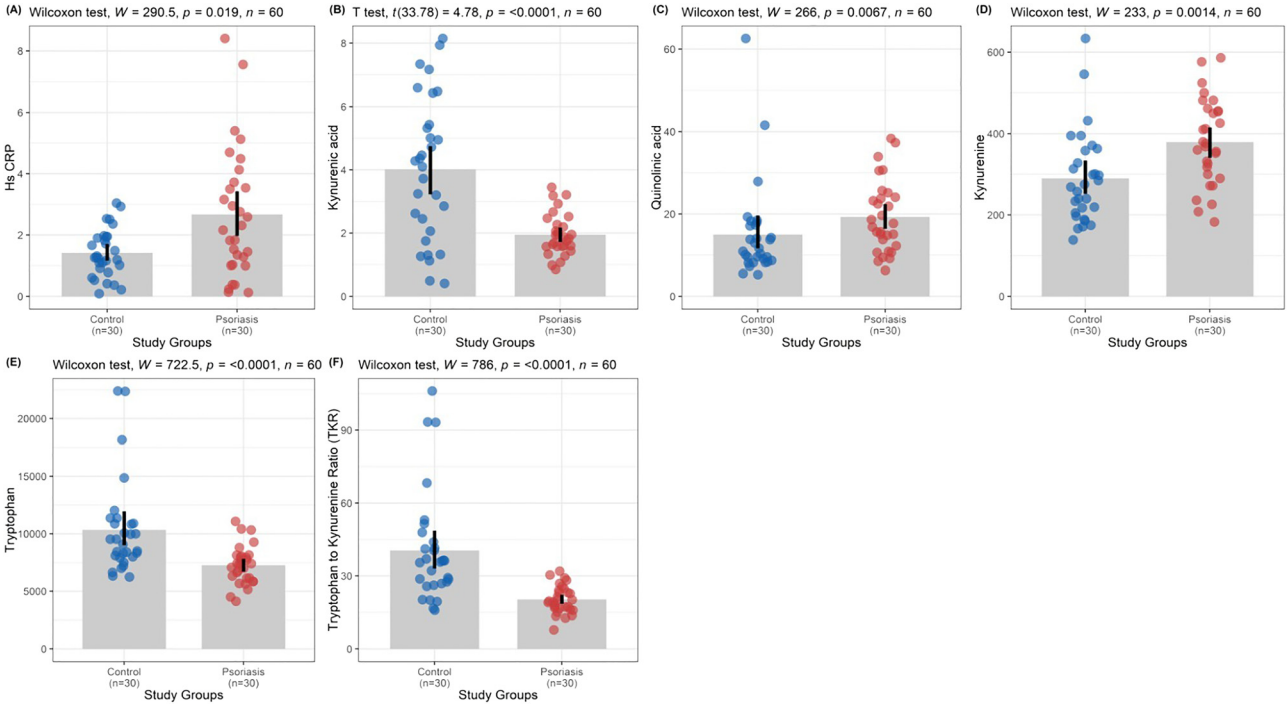

Figure 1: The serum level of (A) hs-CRP (mg/L), (B) kynurenic acid (ng/mL), (C) quinolinic acid (ng/mL), (D) kynurenine (ng/mL), (E) tryptophan (ng/mL), and (F) tryptophan to kynurenine ratio (TKR) in Psoriasis patients and healthy controls. The black line represented as mean and 95 % confidence intervals, and blue and red dots represented as individual values. Wilcoxon test: Un-paired Mann–Whitney U test. T-test: Welch's t-test.

Table 1: Demographic and clinical characteristics, and laboratory parameters of the study groups.

	Control (n=30)	Psoriasis (n=30)	p-Value
Demographical characteristics			
Age, years	40.13 ± 11.61	44.90 ± 13.35	0.145[a]
Gender, male/female	13 (43.3)/17 (56.7)	19 (63.3)/11 (36.7)	0.196[b]
Clinical characteristics			
Hs-CRP, mg/L	1.26 [0.95–1.93]	2.24 [1.09–3.67]	0.019[c]
PASI		8.28 ± 4.17	
Laboratory parameters			
3-OH anthranilic acid, ng/mL	3.88 [1.84–5.78]	3.04 [1.88–4.53]	0.730[c]
3-OH kynurenine, ng/mL	1.40 [0.72–1.92]	1.50 [0.99–1.86]	0.559[c]
Kynurenic acid, ng/mL	4.02 ± 2.28	1.95 ± 0.66	<0.001[d]
Quinolinic acid, ng/mL	11.30 [8.80–17.25]	17.26 [12.62–23.97]	0.007[c]
Kynurenine, ng/mL	272 [208–350.8]	372 [304.5–455.5]	0.001[c]
Tryptophan, ng/mL	9,300 [8,025–10,891.67]	7,375 [6,131.25–8,031.25]	<0.001[c]
TKR	35.97 [27.02–43.34]	19.44 [16.67–23.80]	<0.001[c]

[a]Student's t-test; [b]Chi-square test with Yates continuity correction; [c]Mann-Whitney U test; [d]Welch's t-test. Data were expressed as mean ± standard deviation or median with quartiles [25th percentile – 75th percentile]; and count (n) and percentage (%). PASI, psoriasis area severity index; TKR, tryptophan to kynurenine ratio.

it is a potential therapeutic target for psoriasis [17, 18]. Previous studies have shown that the expression of IDO and kynureninase is increased in psoriatic lesions and is positively associated with pro-inflammatory molecules involved in the pathophysiology of psoriasis [19]. In our study, significantly lower tryptophan serum levels and TKR and significantly higher kynurenine levels were detected in psoriasis patients compared to control subjects. These results indicate an increased activity of the IDO enzyme in psoriasis, which is reflected in a reduced TKR due to tryptophan deficiency, which is associated with increased inflammation and immune activation. The optimal TKR cut-off value of 24.89 showed good diagnostic performance for psoriasis.

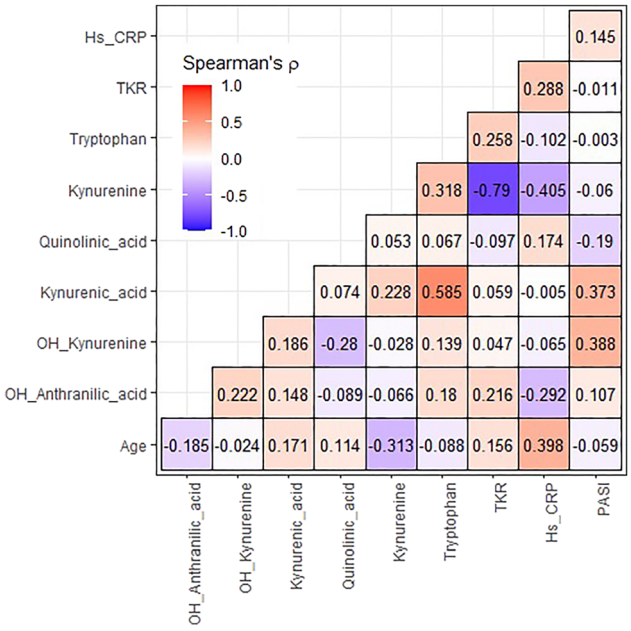

Figure 2: The heatmap diagram showing the relationship between hs-CRP and PASI, and age and biomarkers in Psoriasis patients. Correlation coefficients were represented by colored gradation, red color represents positive correlation level, purple color represents negative correlation level.

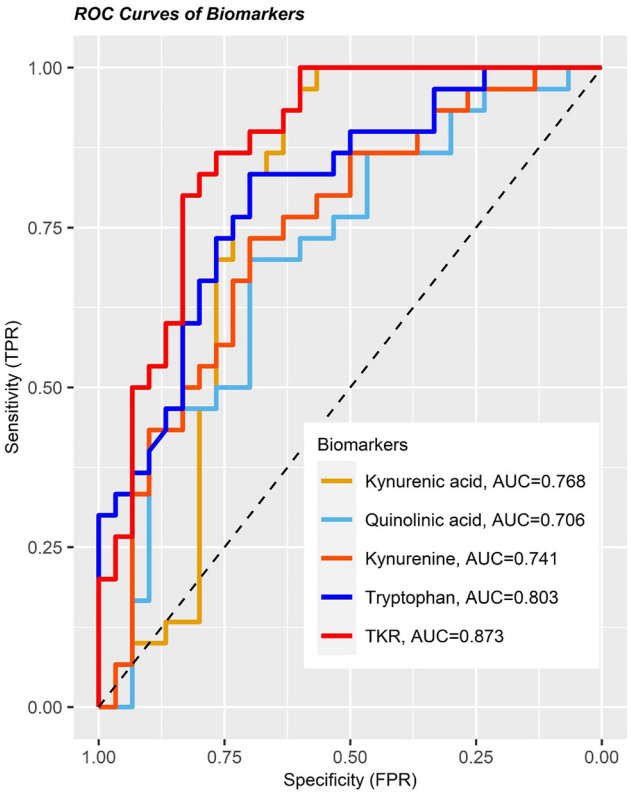

Figure 3: ROC curves of the laboratory parameters for prediction of Psoriasis.

The catabolism of tryptophan leads to the formation of numerous metabolically active metabolites in this pathway, and these metabolites, also known as metabolites of the kynurenine pathway, have regulatory effects on T cells. In psoriasis, a persistent inflammatory skin disease, Th17, Th22 and regulatory T cells as well as cytokines such as IL-23, IL-22 and IL-17 are involved in the pathogenesis [6, 20]. The metabolites of the kynurenine pathway, such as kynurenine and 3-OH-kynurenine, act as ligands for the aryl hydrocarbon receptor (AHR). This receptor plays a role in various processes in the skin, including regulating the immune response, maintaining the skin barrier and responding to potential environmental threats such as ultraviolet radiation. Activation of the AHR can lead to increased synthesis of proinflammatory cytokines (IL-17, etc.), resulting in accelerated skin progression and increased psoriatic plaque formation. The increased production of metabolites such as kynurenine has the potential to activate this receptor and thus contribute to disease progression [21].

hs-CRP, an indicator of systemic inflammation, is significantly elevated in psoriasis patients, indicating a strong correlation with disease severity [1]. Our results also showed that hs-CRP levels were statistically higher in psoriasis patients compared to the control group, further supporting the link between psoriasis and systemic inflammation. Elevated hs-CRP levels suggest that psoriasis may cause both local and systemic inflammation, which increases the risk of metabolic syndrome and CVD. The aryl hydrocarbon receptor (AHR) signaling pathway, which is influenced by kynurenine metabolites, may contribute to vascular inflammation and CVD [12, 22]. An imbalance of kynurenine metabolites can lead to endothelial dysfunction, oxidative stress, and vascular inflammation, all of which have been linked to CVD [23]. Chronic inflammation in psoriasis in conjunction with these metabolic changes may synergistically increase the risk of cardiovascular events.

Our studies revealed a significant increase in kynurenine levels in the serum of psoriasis patients, indicating increased IDO/TDO enzyme activity, which correlates with increased inflammation and activation of the immune system. Elevated kynurenine levels, with an optimal cut-off value of 313.6 ng/mL, showed a sensitivity of 73.33 % and a specificity of 70 % for the diagnosis of psoriasis, indicating its potential as a diagnostic candidate biomarker.

Kynurenine plays an important role in the modulation of immune responses. Activation of the AHR signalling pathway by kynurenine can induce immunosuppressive effects by inhibiting the proliferation of effector T cells and natural killer cells while promoting the activation of regulatory T cells. Elevated kynurenine levels not only alter cellular metabolism, but also have anti-inflammatory

Table 2: Spearman's *rho* correlation coefficients among age and laboratory parameters in Psoriasis patients, by hs-CRP and PASI.

	hs-CRP		PASI	
	Spearman's rho	p-Value	Spearman's rho	p-Value
Demographical characteristics				
Age, years	0.398	**0.029**	−0.059	0.755
Laboratory parameters				
3-OH anthranilic acid, ng/mL	−0.292	0.117	0.107	0.573
3-OH kynurenine, ng/mL	−0.065	0.735	0.388	**0.034**
Kynurenic acid, ng/mL	−0.005	0.978	0.373	**0.042**
Quinolinic acid, ng/mL	0.174	0.359	−0.190	0.313
Kynurenine, ng/mL	−0.405	**0.026**	−0.060	0.753
Tryptophan, ng/mL	−0.102	0.592	−0.003	0.987
TKR	0.288	0.123	−0.011	0.955

Significant relationships denoted as bold.

effects. In addition, increased kynurenine concentrations can trigger cell death through the formation of reactive oxygen species [24]. Kynurenine is associated with many diseases, especially inflammatory diseases [14]. In our study, we observed a statistically significant increase in kynurenine levels in the patient cohort. Elevated kynurenine levels usually signify increased activity of IDO/TDO enzymes and may correlate with increased inflammation and activation of the immune system. The optimal kynurenine cut-off value of 313.6 ng/mL showed significant diagnostic sensitivity and specificity for psoriasis. There was also a negative correlation between kynurenine (ng/mL) and hs-CRP (mg/L). We believe that the negative correlation in this increase indicates a limitation of the increase in kynurenine due to the activation of anti-inflammatory mechanisms.

Quinolinic acid, a neurotoxic metabolite and precursor of NAD synthesis [25], was also found in significantly higher concentrations in psoriasis patients. This increase is probably due to IDO activity triggered by inflammatory processes [26]. Elevated quinolinic acid levels, with an optimal cut-off value of 14.2 ng/mL, showed a sensitivity and specificity of 70 % for the prediction of psoriasis. The role of quinolinic acid as an N-methyl-D-aspartate receptor agonist suggests that it is involved in psoriasis via neurotoxicity and immunomodulation [27].

Kynurenic acid is produced by kynurenine aminotransferases and plays a decisive role in the modulation of inflammatory reactions. It acts as an endogenous agonist at the AHR and has antioxidant and neuroprotective effects [28]. The serum level of kynurenic acid decreases in various inflammatory and neurological diseases and it suppresses the production of IL-17 and IL-23 *in vitro* [28–30]. Our study showed that kynurenic acid has a good sensitivity for the prediction of psoriasis with an optimal cut-off value of 3.5 ng/mL, suggesting its potential as a candidate biomarker for disease severity. In addition, the kynurenic acid level correlated with the PASI score, indicating its usefulness in assessing disease severity.

3-OH kynurenine levels (ng/mL), although not significantly different between groups, were associated with disease severity, indicating their usefulness in assessing psoriasis progression. Our findings are consistent with previous research [17, 29] inking elevated levels of 3-OH-kynurenine to inflammatory conditions and its regulatory role in immune responses. According to these results, 3-OH-kynurenine could be a valuable candidate parameter for the assessment of disease severity.

The role of kynurenine metabolism has been investigated in Behçet's disease, a chronic and inflammatory disease similar to psoriasis. Serum levels of the metabolites are

Table 3: ROC curve analysis and statistical diagnostic measures of parameters in predicting Psoriasis.

	Kynurenic acid	Quinolinic acid	Kynurenine	Tryptophan	TKR	hs-CRP
ROC curve analysis						
AUC (95 % CI)	0.768 (0.641–0.867)	0.706 (0.574–0.816)	0.741 (0.612–0.846)	0.803 (0.680–0.894)	0.873 (0.762–0.945)	0.677 (0.544–0.792)
p-Value	<0.001	0.003	<0.001	<0.001	<0.001	<0.001
Cut-off, ng/mL	≤3.5	>14.2	>313.6	≤8,150	≤24.89	>2.53
Statistical diagnostic measures						
Sensitivity (95 % CI)	100 (88.4–100)	70 (50.6–85.3)	73.33 (54.1–87.7)	83.33 (65.3–94.4)	80 (61.4–92.3)	46.67 (28.3–65.7)
Specificity (95 % CI)	56.67 (37.4–74.5)	70 (50.6–85.3)	70 (50.6–85.3)	70 (50.6–85.3)	83.33 (65.3–94.4)	93.33 (77.9–99.2)
PPV (95 % CI)	69.8 (60.5–77.7)	70 (56.3–80.9)	71 (57.6–81.5)	73.5 (61.1–83.1)	82.8 (67.9–91.6)	87.5 (63.5–96.6)
NPV (95 % CI)	100 (100–100)	70 (56.3–80.9)	72.4 (58.1–83.2)	80.8 (64.6–90.6)	80.6 (66.7–89.7)	63.6 (55.3–71.3)

elevated, suggesting that they may be valuable markers for diagnosis, prognosis and monitoring of clinical symptoms in Behçet's disease patients [30].

This study is one of the first to comprehensively investigate kynurenine metabolites in psoriasis patients and their correlation with disease severity. It adds to the literature by identifying potential candidate biomarkers of disease activity and severity and suggests new therapeutic targets for the treatment of psoriasis Understanding the pathophysiology of psoriasis is crucial as it significantly affects patients' daily lives and causes psychological, physical and economic difficulties. Therefore, research into new treatment strategies and potential candidate biomarkers for diagnosis and disease activity is essential.

Limitations

The study has several limitations. The lack of measurement of anthranilic acid levels limits insights into the role of the kynurenine pathway in psoriasis. Future research should incorporate these measurements to gain a more comprehensive understanding. In addition, the small sample size and variability of metabolites limit the generalizability of the results. Larger studies with a broader range of kynurenine metabolites, cytokine analyses, and cardiovascular assessments (e.g., electrocardiography, carotid intima-media thickness, echocardiography, arterial stiffness) are needed to validate and extend the results.

Research ethics: The study received approval from the Selçuk University Faculty of Medicine Ethics Committee (approval number 2023/520).
Informed consent: Not applicable.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Use of Large Language Models, AI and Machine Learning Tools: None declared.
Conflict of interests: The authors state no conflict of interest.
Research funding: None declared.
Data availability: The raw data can be obtained on request from the corresponding author.

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