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Do Serum Bilirubin and Uric Acid Reflect Oxidative Stress in Vitiligo? A Cross-Sectional Analysis

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Abstract

BACKGROUND/AIMS: Oxidative stress is central to vitiligo, driven by excess reactive oxygen species and weakened antioxidant defenses. Although bilirubin and uric acid (UA) are important endogenous antioxidants routinely measured, current evidence regarding their systemic relevance to vitiligo is limited.

MATERIALS AND METHODS: To compare serum bilirubin and UA levels between vitiligo patients and healthy controls and to determine whether these biomarkers correlate with clinical characteristics or reflect disease burden. This cross-sectional study included 44 patients with non-segmental vitiligo and 45 healthy controls. Serum total bilirubin (Tbil), direct bilirubin (Dbil), and UA levels were measured. Disease severity was evaluated using the vitiligo extent score (VES) and vitiligo area scoring index (VASI). Disease stability was defined as the absence of new or enlarging lesions for ≥12 months. Correlation and subgroup analyses were performed to assess associations between biomarkers and clinical parameters. Receiver operating characteristic (ROC) analysis was used to evaluate diagnostic performance.

RESULTS: No significant differences were found between vitiligo patients and controls in Tbil (p=0.070), Dbil (p=0.978), or UA (p=0.311). Subgroup analyses showed no associations of bilirubin or UA with disease activity, severity (VES, VASI), duration, or anti-thyroid peroxidase status (all p>0.05). Correlation analyses revealed no significant relationships between these markers and clinical features. ROC analyses demonstrated low diagnostic accuracy.

CONCLUSION: Serum bilirubin and UA levels appear unaltered in vitiligo and show no correlation with clinical features. These findings suggest that oxidative stress may be predominantly localized, highlighting the need for research on skin-specific oxidative pathways and alternative biomarkers.

Keywords: Vitiligo, oxidative stress, bilirubin, uric acid, antioxidants

INTRODUCTION

Vitiligo is a chronic autoimmune depigmenting disorder characterized by the progressive loss of melanocytes, leading to well-defined depigmented macules on the skin. The prevalence of vitiligo ranges from 0.5% to 2% worldwide, and its unpredictable course and visible skin changes often result in a significant psychosocial burden for affected individuals.[1,2] While the precise etiology of vitiligo remains unclear, growing evidence suggests that oxidative stress plays a pivotal role in its pathogenesis. Several genetic, autoimmune, and environmental factors have been implicated in melanocyte destruction; however, oxidative stress is increasingly recognized as a key trigger for disease onset and progression.[3,4]

Oxidative stress occurs when there is an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms,

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leading to lipid peroxidation, DNA damage, mitochondrial dysfunction, and apoptosis of melanocytes. Several studies have demonstrated that melanocytes in vitiligo patients are particularly vulnerable to oxidative damage, primarily due to their high metabolic activity and ROS accumulation during melanogenesis. Previous research has reported elevated serum malondialdehyde (MDA) levels, a marker of lipid peroxidation, and reduced antioxidant enzyme activity, including catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx) in vitiligo patients compared to healthy controls.[5,6] Additionally, hydrogen peroxide accumulation has been observed in vitiligo lesions, further supporting the role of oxidative stress in melanocyte degeneration.[7,8] A systematic review by Speeckaert et al.[9] confirmed that oxidative stress pathways are significantly dysregulated in vitiligo patients, highlighting increased lipid peroxidation, disrupted antioxidant enzyme activity, and an overall imbalance in the oxidative stress response.

Recent studies have further demonstrated that oxidative stress correlates with the severity and activity of vitiligo. Mathachan et al.[10] have found that oxidative stress markers were more significantly altered in patients with generalized and active vitiligo, suggesting that oxidative imbalance worsens as the disease progresses. Given this association, assessing oxidative stress in relation to disease severity is crucial for understanding its impact on vitiligo pathogenesis.

To counteract oxidative damage, the body relies on enzymatic and non-enzymatic antioxidants. Enzymatic antioxidants, such as SOD, CAT, GPx, and glutathione reductase, directly neutralize ROS, whereas non-enzymatic antioxidants, including vitamins C and E, glutathione, albumin, ceruloplasmin, bilirubin, and uric acid (UA), act as circulating free radical scavengers. Studies in vitiligo have consistently reported reduced enzymatic antioxidant activity and altered levels of non-enzymatic antioxidants, indicating a defective oxidative defense system.[11]

Among non-enzymatic antioxidants, bilirubin and UA play crucial roles in neutralizing oxidative damage. Bilirubin, a product of heme degradation, is generated through the heme oxygenase-1 (HO-1) pathway, which breaks down heme into biliverdin, carbon monoxide, and free iron. Biliverdin is subsequently reduced to bilirubin by biliverdin reductase, forming a biliverdin-bilirubin redox cycle that provides continuous antioxidant protection.[12] Earlier studies demonstrated that bilirubin has a greater antioxidant capacity than vitamin C and α-tocopherol, particularly in preventing lipid peroxidation in cellular membranes.[13,14]

UA is another endogenous antioxidant that acts as a free radical scavenger, neutralizing hydroxyl radicals, singlet oxygen, and peroxynitrite. Additionally, UA has metal-chelating properties, reducing iron-catalyzed oxidative damage and preventing further ROS generation.[15] Studies have shown that UA contributes significantly to total plasma antioxidant capacity, offering protection against oxidative stress-related conditions, including cardiovascular diseases, neurodegenerative disorders, and autoimmune diseases.[16]

Several studies have investigated the role of bilirubin and UA in inflammatory and autoimmune diseases, such as pemphigus vulgaris (PV), Crohn's disease, and polymyositis/dermatomyositis, in which these markers have generally been found to be lower, suggesting potential antioxidant depletion during oxidative stress.[17-19] However, findings are not entirely consistent across diseases; for example, studies in psoriasis have shown differing trends. Despite the recognized role of oxidative stress in vitiligo, research on bilirubin and UA in this condition is scarce, and their potential involvement remains unclear. Further investigation is needed to determine whether these antioxidants play a role in oxidative imbalance and disease progression in vitiligo.

Based on their well-established antioxidant properties, bilirubin and UA are hypothesized to be potential biomarkers of oxidative imbalance in vitiligo, offering a cost-effective and widely accessible option for clinical monitoring. Therefore, this study aimed to compare serum bilirubin and UA levels between vitiligo patients and healthy controls and to evaluate their association with disease progression.

MATERIALS AND METHODS

This cross-sectional study was conducted between June 2024 and December 2024 and included patients aged 18 to 65 years diagnosed with non-segmental vitiligo and healthy control subjects. Ethical approval for the study was obtained from the Uşak University Non-Interventional Clinical Research Ethics Committee (approval no: 349-349-07, date: 04.04.2024). Written informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

The required sample size was calculated using G*Power (version 3.1.9.7). Using an Independent Samples t-test and assuming a moderate effect size (Cohen's d=0.5, based on prior studies of antioxidant markers in autoimmune skin diseases), a power of 80%, and an alpha of 0.05, the minimum required sample size was 42 per group.

Patients were included if they had a dermatologist-confirmed clinical diagnosis of non-segmental vitiligo. Healthy controls had no history of vitiligo, autoimmune diseases, or chronic inflammatory diseases. Participants were excluded if they had systemic diseases (e.g., diabetes mellitus, cardiovascular disorders, hepatic disorders, or renal disorders), hyperbilirubinemia (e.g., Gilbert's syndrome), hyperuricemia, metabolic disorders that influence oxidative stress, or recent infections or malignancies. Additional exclusions were antioxidant supplementation (e.g., vitamins C/E, N-acetylcysteine), immunosuppressive or UA-lowering drugs (e.g., allopurinol), corticosteroid use, pregnancy/lactation, active smoking (≥10 cigarettes/day), regular alcohol consumption, significant dietary restrictions (e.g., vegan, ketogenic diets), or high-intensity physical activity (>5 hours/week) and chronic stress, due to their potential impacts on oxidative biomarkers.

For each participant, demographic data including age, sex, and body mass index (BMI) were recorded. Vitiligo severity was evaluated using two validated scoring systems: the vitiligo area scoring index (VASI) and the vitiligo extent score (VES). The VASI score was calculated by estimating the body surface area (BSA) involvement in hand units (1 hand ≈1% of total BSA) across body regions, each multiplied by the degree of depigmentation (graded from 0 to 1.0). The VES classification was used to categorize patients based on the extent of BSA affected by vitiligo, grouping them into five severity categories: no vitiligo (0%), mild (1-10%), moderate (11-30%), severe (31-50%), and extensive (>50%). This classification system allows for a structured comparison of disease severity across different patient groups. In addition to severity, disease activity was assessed to determine whether patients had active or stable vitiligo. Disease activity was classified as active if new depigmented lesions had appeared or existing lesions had expanded within the past 12 months, whereas vitiligo was considered stable if no new lesions had developed, and existing depigmented areas remained unchanged for at

least one year.[20] The presence of thyroid autoimmunity was evaluated by measuring anti-thyroid peroxidase (anti-TPO) antibody levels.

Fasting (8-12 hours) venous blood samples were collected from all participants. Serum total bilirubin (Tbil), direct bilirubin (Dbil) and UA levels were measured using an automated enzymatic colorimetric method on a fully automated biochemical analyzer. Blood samples were processed by centrifugation at 3,500 rpm for 10 minutes, and serum was separated and stored at -80 °C until analysis.

Statistical Analysis

Statistical analyses were conducted using PASW 18.0 for Windows. The normality of continuous variables was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For comparisons between vitiligo patients and the control group, Independent Samples t-tests were used for normally distributed variables, while Mann-Whitney U tests were applied for non-normally distributed data. For comparisons involving multiple groups, one-way ANOVA was used for normally distributed data, while the Kruskal-Wallis test was applied for non-normally distributed data. Correlation analyses between bilirubin, UA, disease severity (VASI), disease duration, and anti-TPO positivity were conducted using Pearson's correlation coefficient for normally distributed variables and Spearman's rank correlation coefficient for non-normally distributed data. As an exploratory analysis, receiver operating characteristic (ROC) curve analysis was conducted to evaluate the potential diagnostic performance of bilirubin and UA in distinguishing vitiligo patients from healthy controls, and area under the curve (AUC) values were calculated. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 89 participants were included in this study, comprising 44 patients with non-segmental vitiligo and 45 healthy controls. No significant differences were found between vitiligo patients and healthy controls regarding age (30.25±8.7 vs. 29.87 ±7.9 years, p=0.838), gender distribution (male: 50% vs. 51.1%, p=0.912), BMI (24.85±4.5 kg/m^2 vs. 24.34±4.2 kg/m^2, p=0.597), weight (68±14 kg vs. 66±13 kg, p=0.483), or height (168.3±9.5 cm vs. 168.4±9.7 cm, p=0.996) (Table 1). The mean VASI score among vitiligo patients was 5.4±2.2 (Table 1). The median VES score among vitiligo patients was 2.5% (range: 0.4-95%). According to the VES classification, most patients were categorized as mild (n=31), followed by moderate (n=7), severe (n=3), and extensive (n=3).

The comparison of serum Tbil, Dbil and UA levels between vitiligo patients and controls revealed that Tbil levels were 0.39±0.20 mg/dL in vitiligo patients and 0.33±0.20 mg/dL in controls, with no significant difference (p=0.070). Similarly, Dbil levels were comparable between vitiligo patients (0.33±0.20 mg/dL) and controls (0.33±0.10 mg/dL, p=0.978), and serum UA levels were also similar between vitiligo patients (4.83±1.23 mg/dL) and controls (5.14±1.22 mg/dL, p=0.311), indicating that bilirubin and UA metabolism do not significantly differ between vitiligo patients and healthy individuals (Table 2).

Further subgroup analyses did not reveal statistically significant differences in serum Tbil, Dbil, or UA levels when patients were stratified by gender, anti-TPO positivity, disease activity (active vs. stable), or vitiligo severity assessed by VES (p>0.05 for all comparisons) (Table 3).

Correlation analysis was performed to determine associations of bilirubin and UA with vitiligo severity (as assessed by the VASI), disease duration, and anti-TPO positivity. Tbil, Dbil, and UA levels did not correlate with VASI (p=0.579, 0.457, 0.693, respectively) or disease duration (p=0.798, 0.552, 0.245, respectively). Similarly, anti-TPO positivity was not associated with bilirubin or UA levels (p=0.692, 0.620, 0.364, respectively) (Table 4).

ROC curve analysis was performed to assess the diagnostic value of bilirubin and UA in distinguishing vitiligo patients from healthy controls. The results showed that Tbil had an AUC of 0.53, indicating poor discriminatory ability, whereas Dbil had an AUC of 0.50, indicating limited diagnostic value. UA had an AUC of 0.54, indicating that it does not effectively differentiate vitiligo patients from controls. The optimal cut-off values for Tbil (0.37 mg/dL), Dbil (0.095 mg/dL), and UA (4.65 mg/dL) exhibited low sensitivity and specificity, making them unsuitable as diagnostic biomarkers for vitiligo (Table 5). The results of ROC analysis are also illustrated in Figure 1.

DISCUSSION

In this study, we evaluated bilirubin and UA-two endogenous antioxidants-to determine their potential role as oxidative stress biomarkers in vitiligo. Although we hypothesized that these markers might be altered due to their ROS-scavenging properties, no significant differences in Tbil, Dbil, or UA levels were observed between vitiligo patients and healthy controls.

Subgroup analyses further showed that these markers did not differ according to disease activity, severity (VES), or anti-TPO status, suggesting that bilirubin and UA are not influenced by disease burden or thyroid autoimmunity. These findings indicate that systemic antioxidant levels do not adequately reflect the oxidative processes underlying vitiligo.

Table 1. Baseline characteristics of vitiligo patienrs and healthy controls

Characteristic	Vitiligo patients (mean ± SD or n%)	Controls (mean ± SD or n%)	p-value
Age (years)	30.25±8.7	29.87±7.9	0.838[a]
Gender (male/female)	22 (50%)/22 (50%)	23 (51.1%)/22 (48.9%)	0.912[b]
BMI (kg/m^2)	24.85±4.5	24.34±4.2	0.597[a]
Weight (kg)	68±14	66±13	0.483[a]
Height (cm)	168.3±9.5	168.4±9.7	0.996[a]
VASI (mean ± SD)	5.4±2.2	N/A	N/A

[a]Independent t-test, [b]Chi-square test.
BMI: Body mass index, VASI: Vitiligo area severity index, SD: Standard deviation.

A plausible explanation is that oxidative stress in vitiligo predominantly operates at a localized, skin-specific level, rather than being systemic. A lternative antioxidant defense mechanisms, such as enhanced local enzymatic activity (CAT, SOD, or GPx), may restrict oxidative stress to affected skin sites, thereby preventing measurable alterations in circulating bilirubin and UA levels.

No correlations were found between bilirubin/UA levels and VASI score, disease duration, or anti-TPO positivity. ROC analyses also demonstrated low diagnostic accuracy (AUC <0.7), reinforcing that these systemic antioxidants are neither sensitive nor specific markers for diagnosing vitiligo or assessing its characteristics.

To date, only one previous study has assessed serum bilirubin and UA levels in vitiligo, reporting significantly lower bilirubin levels in patients while UA remained unchanged.[21] Our study, in contrast, found slightly higher though not statistically significant, Tbil levels, suggesting an alternative oxidative-stress response rather than systemic depletion. This discrepancy may reflect differences in patient selection, disease duration at enrollment, the proportion of active versus stable cases, and methodological variation in bilirubin assay techniques or pre-analytical variables such as fasting status and sample storage. From a biological standpoint, the slightly higher bilirubin levels in our cohort may reflect an early adaptive response mediated by HO-1, a cytoprotective enzyme induced under oxidative stress, which generates bilirubin as a byproduct of heme catabolism. In low-grade or early oxidative states, as may occur in stable vitiligo, HO-1 upregulation could transiently elevate circulating bilirubin before sustained oxidative damage potentially depletes these reserves. Unlike Türkmen and Altunışık,[21] our study further examined Tbil, Dbil, and UA in relation to disease severity (VES and VASI), activity, duration, and anti-TPO positivity-none of which showed significant associations-which reinforces the conclusion that systemic antioxidant status is not a reliable indicator of disease burden in vitiligo. Of note, a recent Mendelian randomization study reported a causal association between genetically elevated bilirubin levels and reduced vitiligo risk, with no significant reverse causality.[22] While this supports the biological relevance of bilirubin in the pathogenesis of vitiligo, the mechanistic relationship between genetically determined bilirubin levels and changes in circulating antioxidants observed in established disease warrants further investigation.

Table 2. Comparison of serum bilirubin and uric acid levels in vitiligo and control groups

Parameter	Vitiligo patients mean ± SD)	Controls (mean ± SD)	p-value*
Total bilirubin (mg/dL)	0.39±0.20	0.33±0.20	0.070
Direct bilirubin (mg/dL)	0.33±0.20	0.33±0.10	0.978
Uric acid (mg/dL)	4.83±1.23	5.14±1.22	0.311

*Independent t-test.
SD: Standard deviation.

Table 3. Subgroup analysis of serum bilirubin and uric acid levels

Variable	Category	n	Tbil (mg/dL) Median (min-max)	Statistical analysis (Tbil)	Dbil (mg/dL) Median (min-max)	Statistical analysis (Dbil)	UA (mg/dL) median (min-max)	Statistical analysis (UA)
Anti-TPO	Negative	23	0.6 (0.36-2.23)	p=0.638*	0.29 (0.08-1.46)	p=0.629*	5.6 (2.6-7.6)	p=0.546*
	Positive	21	0.69 (0.37-1.4)		0.31 (0.17-0.6)		4.8 (3.0-7.9)	
Disease activity	Active	34	0.62 (0.36-2.23)	p=0.922*	0.3 (0.08-1.46)	p=0.575*	5.2 (2.6-7.9)	p=0.713*
	Stable	10	0.625 (0.36-1.19)		0.29 (0.18-0.41)		5.1 (3.1-6.9)	
Gender	Female	22	0.57 (0.36-1.71)	p=0.192*	0.29 (0.08-0.65)	p=0.626*	5.1 (3.0-7.4)	p=0.469*
	Male	22	0.69 (0.37-2.23])		0.3 (0.17-1.46)		5.2 (2.6-7.9)	
	Mild	35	0.6 (0.36-2.23)		0.3 (0.08-1.46)		5.25 (2.6-7.9)	
VES	Moderate	3	0.65 (0.37-0.85)	p=0.843**	0.34 (0.18-0.37)	p=0.882**	4.25 (3.5-5.0)	p=0.617**
	Severe	1	N/A		N/A		N/A	
	Extensive	5	0.75 (0.38-1.12)		0.29 (0.19-0.41)		6.3 (3.9-6.9)	

*Mann-Whitney U test, **Kruskal-Wallis test.
Anti-TPO: Anti-thyroid peroxidase, VES: Vitiligo extent score, Tbil: Total bilirubin, Dbil: Direct bilirubin, UA: Uric acid.

Table 4. Correlation analysis of bilirubin, uric acid, and clinical parameters

Biomarker	Correlation with	Spearman r	p-value
Tbil	VASI	-0.101	0.579
Dbil	VASI	-0.136	0.457
UA	VASI	-0.06	0.693
Tbil	Disease duration	-0.042	0.798
Dbil	Disease duration	-0.108	0.552
UA	Disease duration	-0.198	0.245
Tbil	Anti-TPO	0.06	0.692
Dbil	Anti-TPO	0.08	0.620
UA	Anti-TPO	-0.14	0.364

Tbil: Total bilirubin, Dbil: Direct bilirubin, UA: Uric acid, VASI: Vitiligo area severity index, Anti-TPO: Anti-thyroid peroxidase.

Unlike our findings, previous studies in other autoimmune and inflammatory diseases have reported significant alterations in bilirubin and UA levels. Chen et al.[19] found that patients with polymyositis and dermatomyositis (PM/DM) had significantly lower serum bilirubin and UA levels, with oxidative stress identified as a major factor in these diseases. Similarly, Li et al.[17] reported that PV patients exhibited lower total, direct, and indirect bilirubin, along with lower UA levels, with disease severity negatively correlated with bilirubin. In Crohn's disease, Su et al.[18] demonstrated that bilirubin and UA levels were significantly lower in patients, correlating with disease progression and oxidative stress severity. These studies support the idea that oxidative stress leads to systemic depletion of antioxidants in inflammatory diseases, contrasting with our vitiligo findings where bilirubin and UA remained unchanged.

A key explanation for these differences lies in the nature of the oxidative process: systemic diseases such as PV, Crohn's disease, and PM/DM involve widespread chronic inflammation that depletes circulating antioxidant reserves, while vitiligo's oxidative stress appears predominantly confined to melanocyte-rich skin areas. However, systemic depletion of bilirubin and UA has been observed in some localized inflammatory skin diseases. A previous study in 2020 has shown that rosacea patients exhibited significantly reduced bilirubin and UA levels, suggesting that oxidative stress can lead to systemic depletion even in disorders with primarily localized pathology.[23] On the other hand, Rahimi et al.[24] have shown that bilirubin levels were significantly higher in melasma patients and positively correlated with disease extent. Since melasma involves functional but oxidatively stressed melanocytes, elevated bilirubin may reflect an HO-1-mediated adaptive antioxidant response in structurally intact cells. In vitiligo, by contrast, melanocytes are progressively destroyed, potentially rendering a compensatory bilirubin response insufficient or transient. Our finding of no correlation of bilirubin or UA levels with disease duration further suggests that systemic antioxidant levels do not track disease progression. Future studies should directly assess oxidative stress markers within lesional skin to better characterize the spatial and temporal dynamics of the oxidative imbalance in vitiligo.

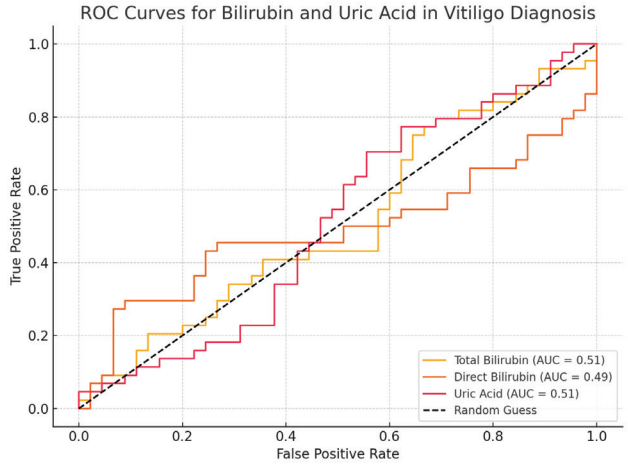

Figure 1. ROC curves assessing the diagnostic performance of serum bilirubin and uric acid in vitiligo.

ROC: Receiver operating characteristic, AUC: Area under the curve.

Table 5. ROC curve analysis for diagnostic performance of bilirubin and uric acid

Biomarker	AUC	95% CI	p-value
TBil	0.53	0.44-0.62	0.307
Dbil	0.50	0.41-0.59	0.857
UA	0.54	0.45-0.63	0.285

AUC: Area under the curve, CI: Confidence interval, Tbil: Total bilirubin, Dbil: Direct bilirubin, UA: Uric acid, ROC: Receiver operating characteristic.

Studies in other inflammatory skin diseases have yielded variable results regarding systemic antioxidant profiles.[25] In psoriasis, Solak et al.[26] reported elevated UA levels suggesting a compensatory antioxidant response, while Nemati et al.[27] found no significant difference in bilirubin or UA despite elevated MDA and SOD. Severin et al.[28] similarly observed elevated bilirubin and UA in psoriasis patients, yet total antioxidant capacity remained unchanged. While a psoriatic arthritis study reported significantly lower indirect bilirubin, inversely correlating with CRP.[29] In lichen planus, Barikbin et al.[30] found slightly lower bilirubin and UA levels that did not reach statistical significance, though vitamin C levels were markedly reduced, indicating selective antioxidant depletion. As summarized in Table 6, these heterogeneous findings suggest that bilirubin and UA are inconsistent indicators of oxidative stress, and that our vitiligo results align most closely with conditions characterized by localized oxidative stress and preserved systemic antioxidant status.

Study Limitations

Several limitations of this study should be considered. First, its cross-sectional design limits the ability to assess temporal changes in, or causal relationships between, oxidative biomarkers and disease dynamics. Second, although we implemented strict exclusion criteria, unmeasured variables such as subclinical stress, unreported supplement use, or genetic predispositions may still have influenced systemic antioxidant levels. Third, subgroup comparisons by VES category (Table 3) are exploratory, as certain severity tiers-particularly the severe (n=1) and extensive (n=5) subgroups-have very small sample sizes; therefore, interpretations of null findings for these subgroups should be made with caution. Furthermore, only systemic markers were assessed; the lack of lesional oxidative stress markers and additional antioxidants (e.g., MDA, SOD) limits mechanistic interpretation. Future studies should incorporate longitudinal designs, larger sample sizes, and tissue-level sampling to better understand the role of bilirubin and UA in vitiligo.

CONCLUSION

This study showed that serum bilirubin and UA levels did not differ between vitiligo patients and controls, nor did they correlate with disease activity, severity, duration, or thyroid autoimmunity. These findings suggest that systemic antioxidant levels remain stable and do not reflect disease burden in this cohort. The slightly higher bilirubin levels observed in patients may represent a limited compensatory response rather than a meaningful oxidative stress marker. Overall, oxidative stress in vitiligo may be predominantly localized to the skin, highlighting the need for future studies focusing on lesional oxidative markers rather than serum antioxidants.

Table 6. Comparative overview of serum bilirubin and uric acid levels in vitiligo and other autoimmune or inflammatory diseases

Disease	Study (author, year)	Bilirubin findings	Uric acid findings	Summary conclusion
Vitiligo	Türkmen and Altunışık,[21]	↓ Bilirubin	No change	Possible systemic depletion.
Pemphigus vulgaris	Li et al.,[17]	↓ Total, direct, indirect	↓ Uric acid	Reduced antioxidants with severity.
PM/DM	Chen et al.,[19]	↓ Bilirubin	↓ Uric acid	Systemic oxidative imbalance.
Crohn's disease	Su et al.,[18]	↓ Bilirubin	↓ Uric acid	Depletion linked to disease activity.
Rosacea	Turkmen[23]	↓ Bilirubin	↓ Uric acid	Systemic effect despite local disease.
Melasma	Rahimi et al.,[24]	↑ Bilirubin	Not assessed	Compensatory antioxidant response.
Psoriasis	Solak et al.,[26]	Not assessed	↑ Uric acid	Possible compensation.
Psoriasis	Nemati et al.,[27]	No change	No change	Stable systemic antioxidants.
Psoriasis	Severin et al.,[28]	↑ Bilirubin	↑ Uric acid	Elevated antioxidants; total capacity normal.
Psoriatic arthritis	Wang et al.,[29]	↓ Indirect Bilirubin	Not assessed	IBIL inversely correlated with CRP.
Lichen planus	Barikbin et al.,[30]	No change	No change	Slightly lower levels; not statistically significant.
Vitiligo (current study)	Yüksek and Ünal Işık	No change	No change	Suggests localized oxidative stress.

↓: Decreased, ↑: Increased, PM/DM: Polymyositis/dermatomyositis, IBIL: Indirect bilirubin, CRP: C-reactive protein.

MAIN POINTS

- Although oxidative stress is considered central in vitiligo pathogenesis, systemic antioxidant markers such as bilirubin and uric acid may remain unchanged.
- These biomarkers were also not associated with disease severity, activity, duration, or thyroid autoimmunity.
- The findings suggest that oxidative stress in vitiligo may predominantly occur at the cutaneous rather than the systemic level.
- Future research should focus on lesional oxidative stress pathways and skin-specific biomarkers rather than circulating antioxidants.

ETHICS

Ethics Committee Approval: Ethical approval for the study was obtained from the Uşak University Non-Interventional Clinical Research Ethics Committee (approval no: 349-349-07, date: 04.04.2024).

Informed Consent: Written consent was obtained from the patient participating in this study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: T.Y., S.Ü.I., Concept: T.Y., S.Ü.I., Design: T.Y., Data Collection and/or Processing: T.Y., S.Ü.I., Analysis and/or Interpretation: T.Y., S.Ü.I., Literature Search: T.Y., Writing: T.Y.

DISCLOSURES

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