

Evaluation of serum IL-6, IL-17, and TNF- α as Potential Immunological Biomarkers in Patients with Vitiligo.

Abstract:

Background: Vitiligo is a chronic immune-mediated depigmenting disorder accompanied by both hyperactive inflammatory and autoimmunity pathways.

Objective: To evaluate the serum levels of interleukin-6 (IL-6), interleukin-17 (IL-17), and tumor necrosis factor- α (TNF- α) in vitiligo patients, determine the correlation of these cytokines with vitiligo severity, and estimate their diagnostic performance.

Methods: A hospital-based cross-sectional case-control study was performed at Al-Diwaniya Teaching Hospital-Iraq. A total of 180 subjects, including 88 clinically diagnosed vitiligo patients and 92 apparently healthy controls, were enrolled. With respect to the extent of disease involvement, patients were classified in mild (n=42), moderate (n=33) and severe (n=13) disease involvement groups. Enzyme-linked immunosorbent assay (ELISA) was used to measure serum levels of IL-6, IL-17 and TNF- α .

Results: Serum IL-6, IL-17, and TNF- α were elevated in vitiligo patients compared to controls ($P < 0.05$). IL-6 levels rose from mild to severe vitiligo significantly and significantly differed between severity groups ($P = 0.030$); there were no significant differences in the levels of IL-17 or TNF- α according to disease severity ($P = 0.163$ and $P = 0.247$, respectively). Receiver operating characteristic curve analysis revealed IL-6 (AUC=0.810), IL-17 (AUC=0.790) and TNF- α (AUC=0.740) performed significantly in the diagnosis.

Conclusions: Enhanced serum levels of IL-6, IL-17 and TNF- α in vitiligo patients suggest the participation of these cytokines in the inflammatory activity of vitiligo. Among the studied biomarkers, IL-6 had the most robust association to disease severity and the best diagnostic performance. These results indicate

that IL-6, IL-17, and TNF- α might be used as immunological biomarkers in vitiligo.

Keywords: Vitiligo, IL-6; IL-17; TNF- α , Inflammation

Introduction

Vitiligo is a chronic acquired depigmenting disorder due to the progressive loss or dysfunction of epidermal melanocytes causing well demarcated areas of depigmented skin (AL-smadiet al., 2023). Most patients with vitiligo are not physically disabled per se, but the visible effects can lead to significant psychosocial complications such as decreased quality of life, social stigma and psychological distress (Salama et al., 2023). Recent global epidemiological modelling suggests that vitiligo is associated with a substantial burden globally and calls for more comprehensive understanding of its pathogenesis, diagnosis, and disease monitoring (Akl et al. 2024).

The pathogenesis of vitiligo is multifactorial involving complicated interaction between genetic susceptibility, oxidative stress, melanocyte intrinsic dysfunctions/environment environmental triggers and dysregulated innate and adaptive immune responses (Marchioro et al., 2022). Current evidence particularly favors an autoimmune mechanism whereby melanocyte-specific immune responses contribute to gradual destruction of melanocytes. Central to the pathology are autoreactive CD8⁺ T cells and inflammatory mediators, while cytokine networks involving interferon- γ , interleukins, tumor necrosis factor- α (TNF- α), and chemokines amplify local inflammation and drive sustained melanocyte injury (Ju & Bae, 2024; Speeckaert et al., 2024). Newer reviews also indicate that activation of the innate arm of the immune system can precede or bolster adaptive immunity, arguing that vitiligo be viewed as a consequence arising from networks among inflammatory pathways, and not simply as a process narrowly limited to melanocyte-specific cytotoxicity (Wang et al., 2025).

Interleukin-6 (IL-6) as an essential pleiotropic cytokine is an inflammatory mediator that plays a crucial role in both the innate and adaptive immune response, also being closely related to Vitiligo disease (Al-Fahham et al., 2024). IL-6 can both enhance inflammatory responses and alter T-cell differentiation and has a role in establishing a cytokine milieu permissive for facilitating pathogenic immune activation in high risk patients (Hirano, 2021). Serum concentrations of IL-6 are higher in patients with vitiligo than healthy controls, but the extent of this elevation and its relationship to clinical parameters have differed between studies. For instance, Yang et al. (2021) combined serum IL-6 with IL-2 and TNF- α in stable and progressive vitiligo to show the relevance of inflammatory cytokines to differences of disease status. Most recently, ongoing case-control research has also evaluated increased levels of circulating inflammatory cytokines as potential biomarkers and disease severity and activity indicators specifically prompting additional clinical validation studies for IL-6 (George et al., 2023).

Interleukin-17 (IL-17) is an additional crucial mediator of the inflammatory network in vitiligo, mainly produced by Th17 cells. It can combine with other cytokines and cellular pathways involved in melanocyte dysfunction and tissue inflammation (Hadi et al., 2024). In this context, experimental data suggest that IL-17 may modulate melanocyte survival and also melanin production, whilst enhanced Th17 activity and IL-17 production by CD4⁺⁺T-cells have been described in vitiligo patients. In a systematic review and meta-analysis including 11 case-control studies, IL-17 was significantly higher in vitiligo patients than healthy controls from both active disease and stable disease (>1,100 participants total) (Acharya & Mathur, 2020).

Another pro-inflammatory cytokine known to be involved in vitiligo is TNF- α . It plays a role in inflammatory signaling, immune-cell activation and subsequent tissue responses, and may cooperate with other cytokines to maintain the inflammatory microenvironment of melanocytes. An increased level of TNF- α

has been reported in the serum studies of vitiligo patients over the pre-study levels showing that TNF- α levels also correlates with the clinical disease activity (Dwivedi et al., 2018; Karagün&Baysak, 2020). Finally, genetic data indicates that TNF- α -related variant was associated with vitiligo in some populations, providing biological significance for the inflammatory pathway (Dutta et al., 2024).

Accordingly, their assessment in parallel may offer a more complete view of systemic immune activation than the measurement of a single cytokine. Although considerable advances have been made in our knowledge of vitiligo immunopathogenesis, robust circulating biomarkers to aid in the assessment of disease activity and inflammatory state in vitiligo are lagging. Previous systematic investigations have highlighted the fact that reproducible and clinically useful biomarkers must be identified (Speeckaert et al., 2017).

Therefore, the current study aims to evaluate the serum levels of interleukin-6 (IL-6), interleukin-17 (IL-17), and tumor necrosis factor- α (TNF- α) in vitiligo patients, determine the correlation of these cytokines with vitiligo severity, and estimate their diagnostic performance

Methods

Study Design and Setting

This study aimed to investigate serum IL-6, IL-17, and TNF- α concentrations among patients with vitiligo as potential immunological biomarkers in a case–control design compared to healthy individuals. A cross-sectional study was carried out at Al-Diwaniya Teaching Hospital, Al-Diwaniya Governorate, Iraq, from January/2026 to May/2026.

Study Population

A total of 180 participants, including 88 patients with clinically diagnosed vitiligo and 92 healthy controls, were included in this study. The study was conducted at Al-Diwaniya Teaching Hospital, and patients were recruited

during this period. Diagnosis of vitiligo was made by the treating dermatologists based on history, the presenting clinical picture and a cutaneous examination. The control group was comprised of apparently healthy individuals who had no personal history of any skin disorder including vitiligo, nor a personal history of relevant autoimmune or inflammatory disorders at the time of enrollment. A standardized data collection forms was used to collect information on demographic and clinical characteristics from all participants. Additional clinical information was collected in vitiligo patients, including age of disease onset, disease duration, family history of vitiligo, disease distribution and clinical severity. Then, venous blood specimens were taken from patients and control cases for the measurements of serum interleukin-6 (IL-6), interleukin-17 (IL-17), and tumor necrosis factor-alpha (TNF- α) concentrations.

Determination of Vitiligo Severity

Dermatological assessment of vitiligo severity was performed according to the extent of involved depigmented skin. Percent affected body surface area was estimated using validated clinical evaluation. The Vitiligo Area Scoring Index (VASI) can be used for a more standardized quantitative assessment of disease extent where appropriate. The VASI quantifies the degree of body surface area affected by depigmentation, and here we use it to test whether circulating cytokine concentrations relate to the degree of vitiligo involvement. Patients were classified into mild, moderate, and severe vitiligo according to the extent of skin involvement.

Inclusion Criteria

Participants were recruited if they met the following criteria:

1. Adults aged 18–65 years.
2. Patients with clinically diagnosed vitiligo.

3. Individuals with no history of vitiligo, recruited as controls.
4. Absence of acute bacterial, viral, or fungal infection in the 4 weeks prior.
5. Not have taken systemic corticosteroid, immunosuppressive or biological therapy in the three prior months.

Exclusion Criteria

Participants were excluded if they had the following:

1. Other chronic inflammatory or autoimmune diseases
2. Previously diagnosed malignancy or history of malignancy.
3. Chronic rubbing appendage incurable disease or chronic lint disease.
4. Diabetes mellitus or uncontrolled hypertension.
5. Pregnancy or lactation.
6. Active smoking or alcohol consumption.
7. Acute infectious diseases or sepsis.
8. Recent major surgery or trauma.
9. Histological criteria or other conditions that may have a significant impact on circulating inflammatory cytokines.

Blood Sample Collection

Venous blood was collected aseptically in 5ml sterile disposable syringes from all the participants. Blood was put in plain gel tubes and left for ~30 minutes to clot at room temperature. After which, these samples were centrifuged at 3000rpm for 10 minutes to separate serum. The serum was centrifuged and collected into sterile Eppendorf tubes and stored at -80°C until laboratory examination. To avoid repeated freeze-thaw cycles, serum aliquots were prepared, where appropriate, since this might result in instability of some cytokines.

Measurement of Serum Biomarkers

Serum levels of IL-6, IL-17 and TNF- α were determined with commercial ELIAS kits (Usen Life Science Inc, Wuhan, China) based on the manufacturer's instructions. Samples of serum were then thawed to room temperature prior to analysis. Without any further treatment, standards, controls, and serum samples were added to the wells of the microplate pre-coated with antibodies specific to each target cytokine. All steps were carried out as per the standard protocols as follows: incubation, washing, addition of enzyme-conjugated detection antibodies, followed by chromogenic substrate. Optical density was measured at 450 nm on a BioTek ELx800 microplate reader (BioTek Instruments, USA). The values of IL-6, IL-17, and TNF- α were determined from their respective standard calibration curves and expressed in pg/mL.

Ethical Considerations

Ethical approval prior to data collection was obtained from the relevant Research Ethics Committee and from the administration of Al-Diwaniya Teaching Hospital. Written informed consent was obtained from all participants following a detailed explanation of study aims, procedures and potential risks. The study ensured the confidentiality and anonymity of participants information. All procedures were carried out in accordance with the ethical standards of the Declaration of Helsinki.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as means ($\pm$ SD) and categorical variables as frequencies and percentages. We applied the Shapiro–Wilk test in order to study the normality of continuous variables. An independent-samples t-test was used for normally distributed continuous variables for comparisons between patients with vitiligo and healthy controls. For continuous variables that failed the assumptions of parametric analysis the Mann–Whitney U test was used. Where appropriate categorical variables between the two groups were compared using the chi-square test. ROC curve

analysis was used to assess the diagnostic utility of serum IL-6, IL-17, and TNF- α for differentiating patients with vitiligo from healthy controls. The measurement area under the curve (AUC) sensitivity, specificity and optimal cutoff value as necessary. Statistical significance was prior defined as a two-tailed P-value of <0.05 .

The Results

As Table 1 illustrates, there were no statistically significant differences for age, gender, or residence between vitiligo patients and controls ($p > 0.05$). The majority of subjects were ≥ 50 years old, while the female genitalia ratio was slightly higher in vestibular vitiligo. Both types of groups were predominantly urban residents. These findings suggest that both groups were matched in the demographics variables that we evaluated for our analyses.

Table 1. Assessment of age, gender and residence in both vitiligo Patients and control

Items		Vitiligo Patients (N= 88)		Control (N= 92)		Chi Square	(P value)
		Freq.	%	Freq.	%		
Age	20-29	5	5.7	5	5.4	3.261	0.352 NS
	30-39	5	5.7	12	13		
	40-49	6	6.8	8	8.7		
	≥ 50	72	81.8	67	72.8		
Gender	Male	42	47.7	47	51.1	0.203	0.653 NS
	Female	46	52.3	45	48.9		
Residence	Rural	17	19.3	19	20.7	0.049	0.823 NS
	Urban	71	80.7	73	79.3		

The distribution of patients according to disease severity demonstrates that moderate vitiligo was the predominant clinical presentation, accounting for 48% of the studied cases, whereas mild disease activity represented 38%, and severe disease constituted only 14% (figure 1)

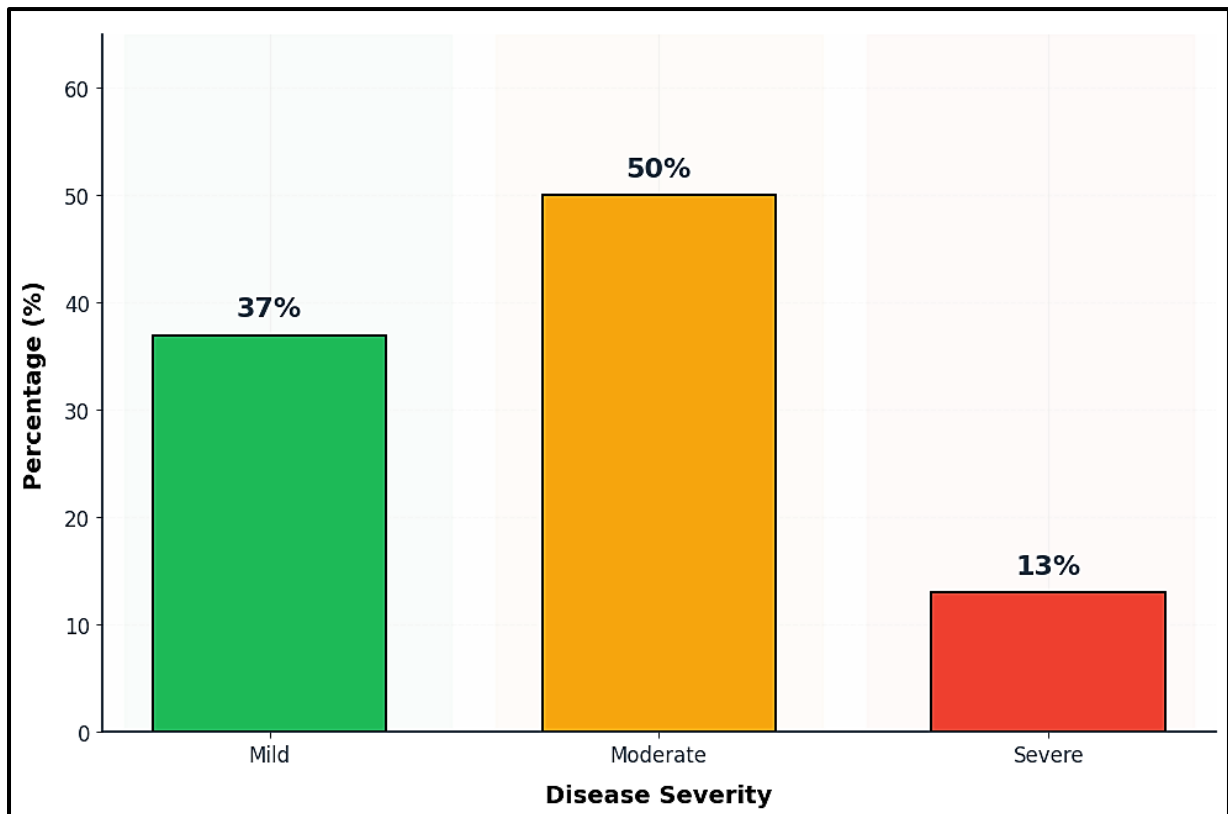


Figure 1. Distribution of vitiligo Patients according to the severity of the disease

The results indicated that serum levels of all three of the inflammatory biomarkers were significantly increased in patients with vitiligo versus healthy controls. Compared with controls (7.40 ± 3.20 pg/mL), IL-6 levels were elevated in patients with vitiligo (12.80 ± 5.10 pg/mL), $t = 8.47$, $P < 0.001$. Likewise, IL-17 was also significantly elevated in vitiligo patients compared with the controls (vitiligo: 18.60 ± 6.70 pg/mL vs controls: 10.90 ± 4.50 pg/mL; $t = 9.01$, $P < 0.001$). In addition, a significantly higher plasma TNF- α level (12.40 ± 4.80 ng/mL) was also found in subjects with vitiligo compared with normal controls (8.90 ± 3.10 ng/mL; $t = 5.78$, $P < 0.001$).

Table 2. Comparison of biomarkers between vitiligo patients and healthy control

Biomarkers	Vitiligo Patients (N= 88)		Control (N= 92)		T Test	(P value)
	Mean	SD	Mean	SD		
IL-6(pg/mL)	12.8	5.1	7.4	3.2	8.47	<0.001*
IL-17 (pg/mL)	18.6	6.7	10.9	4.5	9.01	<0.001*
TNF- α (ng/mL)	12.4	4.8	8.9	3.1	5.78	<0.001*

* High Significant at P value <0.01

The serum IL-6 gradually elevated among the non-segmental vitiligo patients with mild to severe disease, and the difference was significant (P=0.030). In a similar vein, IL-17 and TNF- α were elevated, though not significantly (P=0.163 and P=0.247, respectively) with increasing disease severity.

Table 3. Comparison of biomarkers among vitiligo patients classified according to disease severity

Biomarkers	Mild (N= 42)	Moderate (N= 33)	Severe (N= 13)	(P value)
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	
IL-6(pg/mL)	10 $\pm$ 6	15 $\pm$ 6	10 $\pm$ 6	15.0 $\pm$ 6.0
IL-17 (pg/mL)	15 $\pm$ 7	19 $\pm$ 7	15 $\pm$ 7	19.0 $\pm$ 7.0
TNF- α (ng/mL)	10 $\pm$ 6	13 $\pm$ 6	10 $\pm$ 6	13.0 $\pm$ 6.0

* Significant at P value <0.05

As shown in table 4, IL-6 demonstrated the highest diagnostic performance, with an AUC of 0.810, followed by IL-17 (AUC=0.790) and TNF- α (AUC=0.740). All three biomarkers showed statistically significant diagnostic discrimination (P $\leq$ 0.001).

Table 4. Diagnostic power of the studied biomarkers in the diagnosis of vitiligo

Biomarker	(AUC)	Sig. p-value	Cut-off Point	Sensitivity (%)	Specificity (%)
IL-6(pg/mL)	0.81	<0.001	9.5	78.4	75

IL-17 (pg/mL)	0.79	<0.001	13.5	75	72.8
TNF- α (ng/mL)	0.74	0.001	10.5	70.5	68.5

AUC: Area Under the curve

Discussion

This study aimed to compare serum interleukin-6 (IL-6), interleukin-17(IL-17) and tumor necrosis factor- alpha (TNF- α) between patients with vitiligo and controls and to assess their association with disease severity and their diagnostic performance. The results showed that all three inflammatory biomarkers were significantly higher in the serum of patients with vitiligo compared with healthy controls. Moreover, IL-6 demonstrated a statistically significant, progressive increase with mild, moderate and severe disease, while numerical increases in IL-17 and TNF- α were not statistically significant. Cox regression was also used to improve understanding of disease prognosis, even though all 3 biomarkers were able to discriminate well, as seen from the ROC analysis, the highest AUC was seen produced by IL-6 (Wei et al., 2015).

This high IL-6 level, confirmed in vitiligo patients, clearly supports the fact that systemic (but also local) inflammatory pathways are involved in the pathogenesis of the disease. IL-6 is a pleiotropic cytokine, having both pro-inflammatory and anti-inflammatory properties, which plays a central role in innate and adaptive immune responses, capable of modulating differentiation and activation of several immune-cell populations (Yukcu et al., 2025). And in vitiligo, inflammatory signaling may both perpetuate an environment that is conducive to melanocyte stress and immune-mediated destruction. The results are in accordance of the study of Sushama et al. (2019) who reported data indicates that the serum IL-6 is significantly elevated in both localized (those cases = 5% of body surface area affected) vitiligo. In a similar manner, Karagün and Baysak (2021), found IL-6 levels to be significantly higher in patients with active vitiligo than healthy controls. These findings indicate the potential

importance of IL-6 as it is likely not simply a marker of secondary inflammation but also part of the broader cytokine network involved in the pathogenesis of vitiligo.

His very high level of IL-17 in our patient is also substantiated by considerable previous evidence. Although IL-17 is most well-studied in the context of Th17-mediated immune responses, it has garnered a substantial amount of interest in the context of vitiligo due to its potential role in the destruction of melanocytes and progression of the disease. Gomes et al. (2018) reported that IL-17 was identified by as the inflammatory cytokine most consistently linked to vitiligo and provided a detailed look at how its activity interacts with other inflammatory mediators (such as IL-6). More importantly, a meta-analysis of 11 case-control studies with a total of 626 patients with vitiligo and 475 healthy controls found significantly elevated serum IL-17 levels. Congruence of these findings with those presented here further supports the notion that elevated IL-17 is part of the inflammatory milieu of vitiligo (Acharya & Mathur, 2020).

These concentrations of TNF- α in the present study were also found to be significantly higher among patients with vitiligo. TNF- α is a presiding pro-inflammatory cytokine which is involved in the recruitment of immune cells, amplification of inflammatory responses and tissue injury (Laddha et al., 2012). This finding is comparable with that reported by Sushama et al. (2019) who reported increased TNF- α in localized as well generalized vitiligo. In line with this, Karagün and Baysak (2021) observed considerably elevated TNF- α levels in subjects with active vitiligo. On the other similar results were reported by Yang et al. (2023), who were not able to find statistically significant differences in serum TNF- α between the vitiligo and control group. Differences may also be due to differences in disease activity, severity, treatment status, sample size, assay methodology, or characteristics of the study populations. So, TNF- α needs to be viewed as part of an intricate inflammatory network and not just as an isolated vitiligo marker.

The most significant finding from the current study was the association between the concentrations of biomarkers and the severity of the clinical presentation. The serum IL-6 levels were increased from mild to moderate and severe disease ($P=0.030$). The gradually increased level of IL-6 seems to better relate to the severity of clinical disease than the other cytokines studied. This finding is consistent with previous observations that circulating inflammatory mediators may differ by vitiligo activity and extent. As part of a multicenter study, Speeckaert et al. (2017) showed that IL-6 and IL-17 were increased in vitiligo and that levels of serum inflammatory markers might vary depending on disease activity. Sushama et al. (2019) mentioned that cytokine levels have been related to clinical characteristics (including disease extent).

While IL-17 tended to increase with increasing severity in the current study, the difference among the three severity groups was not statistically significant ($P=0.163$). This does not necessarily oppose the classical role of IL-17 in vitiligo. While Acharya and Mathur (2020) consistently reported higher levels of IL-17 in vitiligo than controls, pooled comparisons of specific clinical subgroups may be affected by sample size and heterogeneity. In comparison, while TNF- α levels also trended higher in severe disease over mild disease, there was no statistical significance ($P = 0.247$). Previous evidence supports that TNF- α might relate to disease activity more than an ordinal categorical measure of severity. Therefore, while the severity analysis in the current study was not statistically significant, the current data is not evidence against a role of IL-17 or TNF- α in vitiligo.

The ROC analysis further documented the possible clinical relevance of these biomarkers. IL-6 had the best diagnostic indicator, (AUC: 0.810), followed by IL-17 (AUC=0.790) and TNF- α (AUC=0.740). All three biomarkers clearly show significant discrimination of patients from controls. The moderately high AUC obtained for IL-6 is particularly consistent with previous findings which highlighted IL-6 as a candidate circulating marker. IL-6 was shown as the most

sensitive serum marker to differentiate between active and stable vitiligo in a study performed in 5 centers (Speeckaert et al., 2017). However, the diagnostic performance presented here should be taken with caution as ROC-derived cut-off values are population-/assay-dependent and need to be validated in independent cohorts.

Conclusion

Both serum IL-6, IL-17, and TNF- α levels were extremely elevated in vitiligo patients when compared with healthy donors. While IL-6 increased significantly with disease severity, IL-17 and TNF- α were not significantly associated with severity. ROC analysis revealed promising potential diagnostic performance for all three biomarkers. Our data indicate that IL-6, IL-17 and TNF- α could be useful immunological biomarkers of vitiligo.

References

1. Acharya, P., & Mathur, M. (2020). Interleukin-17 level in patients with vitiligo: A systematic review and meta-analysis. *Australasian Journal of Dermatology*, 61(2), e208–e212. <https://doi.org/10.1111/ajd.13233>
2. Acharya, P., & Mathur, M. (2020). Interleukin-17 level in patients with vitiligo: A systematic review and meta-analysis. *Australasian Journal of Dermatology*, 61(2), e208–e212. <https://doi.org/10.1111/ajd.13233>
3. Akl, J., Lee, S., Ju, H. J., Parisi, R., Kim, J. Y., Jeon, J. J., Heo, Y. W., Eleftheriadou, V., Hamzavi, I., Griffiths, C. E. M., Ashcroft, D. M., Mysore, V., Gupta, S., Parsad, D., Lim, H. W., Bae, J. M., & Ezzedine, K. (2024). Estimating the burden of vitiligo: A systematic review and modelling study. *The Lancet Public Health*, 9(6), e386–e396. [https://doi.org/10.1016/S2468-2667\(24\)00026-4](https://doi.org/10.1016/S2468-2667(24)00026-4)
4. Al-Fahham, A. A., Zwamel, A. H., Mousa, H. M., & Abdul Azeez, B. A. M. (2024). Inflammatory response and pathophysiology of IL-6 overproduction: A review article. *International Journal of Health & Medical Research*, 3(8), 568–572. <https://doi.org/10.58806/ijhmr.2024.v3i08n05>

5. AL-smadi, K., Imran, M., Leite-Silva, V. R., & Mohammed, Y. (2023). Vitiligo: A Review of Aetiology, Pathogenesis, Treatment, and Psychosocial Impact. *Cosmetics*, 10(3), 84. <https://doi.org/10.3390/cosmetics10030084>
6. Desai, K., Kumar, H. K., Naveen, S., & Somanna, P. (2023). Vitiligo: Correlation with cytokine profiles and its role in novel therapeutic strategies: A case-control study. *Indian Dermatology Online Journal*, 14(3), 361–365. https://doi.org/10.4103/idoj.idoj_6_23
7. Dutta, T., Sengupta, S., Adhya, S., Saha, A., Sengupta, D., Mondal, R., Naskar, S., Bhattacharjee, S., & Sengupta, M. (2024). Identification of TNF- α as major susceptible risk locus for vitiligo: A systematic review and meta-analysis study in the Asian population. *Dermatology*, 240(3), 376–386. <https://doi.org/10.1159/000536480>
8. Gomes, I. A., de Carvalho, F. O., de Menezes, A. F., Almeida, F. M., Shanmugam, S., de Souza Siqueira Quintans, J., Quintans-Júnior, L. J., de Moura, T. R., Oliveira, P. D., & de Souza Araújo, A. A. (2018). The role of interleukins in vitiligo: A systematic review. *Journal of the European Academy of Dermatology and Venereology*, 32(12), 2097–2111. <https://doi.org/10.1111/jdv.15016>
9. Gomes, I. A., de Carvalho, F. O., de Menezes, A. F., Almeida, F. M., Shanmugam, S., de Souza Siqueira Quintans, J., Quintans-Júnior, L. J., de Moura, T. R., Oliveira, P. D., & de Souza Araújo, A. A. (2018). The role of interleukins in vitiligo: A systematic review. *Journal of the European Academy of Dermatology and Venereology*, 32(12), 2097–2111. <https://doi.org/10.1111/jdv.15016>
10. Hadi, H. S., Shubar, S. N. A., Jaffar, A. M., & Alfahham, A. A. (2024). Structure and physiological significance of IL-17: A review article. *International Journal of Health & Medical Research*, 3(9), 666–669. <https://doi.org/10.58806/ijhmr.2024.v3i09n03>
11. Hirano T. (2021). IL-6 in inflammation, autoimmunity and cancer. *International immunology*, 33(3), 127–148. <https://doi.org/10.1093/intimm/dxaa078>
12. Ju, H. J., & Bae, J. M. (2024). Bridging molecular mechanism and clinical practice in vitiligo treatment: An updated review. *Dermatology*, 240(3), 474–486. <https://doi.org/10.1159/000537810>
13. Karagün, E., & Baysak, S. (2020). Levels of TNF- α , IL-6, IL-17, IL-37 cytokines in patients with active vitiligo. *Aging Male*, 23(5), 1487–1492. <https://doi.org/10.1080/13685538.2020.1806814>
14. Karagün, E., & Baysak, S. (2021). Levels of TNF- α , IL-6, IL-17, IL-37 cytokines in patients with active vitiligo. *The Aging Male*, 24(1), 1–6. <https://doi.org/10.1080/13685538.2020.1806814>
15. Laddha, N. C., Dwivedi, M., & Begum, R. (2012). Increased Tumor Necrosis Factor (TNF)- α and its promoter polymorphisms correlate with

- disease progression and higher susceptibility towards vitiligo. *PloS one*, 7(12), e52298. <https://doi.org/10.1371/journal.pone.0052298>
16. Marchioro, H. Z., Silva de Castro, C. C., Fava, V. M., Sakiyama, P. H., Dellatorre, G., & Miot, H. A. (2022). Update on the pathogenesis of vitiligo. *Anais brasileiros de dermatologia*, 97(4), 478–490. <https://doi.org/10.1016/j.abd.2021.09.008>
17. Ranjkesh, M. R., Rahimi Partovi, M., & Pashazadeh, M. (2021). The study of serum level of interleukin-2, interleukin-6, and tumor necrosis factor-alpha in stable and progressive vitiligo patients from Sina Hospital in Tabriz, Iran. *Indian Journal of Dermatology*, 66(4), 366–370. https://doi.org/10.4103/ijd.IJD_300_20
18. Salama, A. H., Alnemr, L., Khan, A. R., Alfakeer, H., Aleem, Z., & Ali-Alkhateeb, M. (2023). Unveiling the Unseen Struggles: A Comprehensive Review of Vitiligo's Psychological, Social, and Quality of Life Impacts. *Cureus*, 15(9), e45030. <https://doi.org/10.7759/cureus.45030>
19. Speeckaert, R., Speeckaert, M., De Schepper, S., & van Geel, N. (2017). Biomarkers of disease activity in vitiligo: A systematic review. *Autoimmunity Reviews*, 16(9), 937–945. <https://doi.org/10.1016/j.autrev.2017.07.005>
20. Speeckaert, R., Speeckaert, M., De Schepper, S., & van Geel, N. (2017). Biomarkers of disease activity in vitiligo: A systematic review. *Autoimmunity Reviews*, 16(9), 937–945. <https://doi.org/10.1016/j.autrev.2017.07.005>
21. Speeckaert, R., Van Caelenberg, E., Belpaire, A., Speeckaert, M. M., & van Geel, N. (2024). Vitiligo: From pathogenesis to treatment. *Journal of Clinical Medicine*, 13(17), 5225. <https://doi.org/10.3390/jcm13175225>
22. Sushama, S., Dixit, N., Gautam, R. K., Arora, P., Khurana, A., & Anubhuti, A. (2019). Cytokine profile (IL-2, IL-6, IL-17, IL-22, and TNF- α) in vitiligo—New insight into pathogenesis of disease. *Journal of Cosmetic Dermatology*, 18(1), 337–341. <https://doi.org/10.1111/jocd.12517>
23. Wang Y, Cao J, Liu X, Xiong C, Xu D, Bian F. Innate immune activation in vitiligo: mechanisms and pathophysiological implications. *Front Immunol*. 2025 Oct 15;16:1631074. doi: 10.3389/fimmu.2025.1631074. PMID: 41169396; PMCID: PMC12568694.
24. Wei, S. T., Sun, Y. H., Zong, S. H., & Xiang, Y. B. (2015). Serum Levels of IL-6 and TNF- α May Correlate with Activity and Severity of Rheumatoid Arthritis. *Medical science monitor : international medical journal of experimental and clinical research*, 21, 4030–4038. <https://doi.org/10.12659/msm.895116>
25. Yukcu, F., Akcilar, R., & Namdar, N. D. (2025). Investigation of Interleukin-6 -572G/C Gene Polymorphism in Vitiligo Patients. *Journal*

456 *of clinical practice and research*, 47(1), 53–59.
457 <https://doi.org/10.14744/cpr.2025.82711>

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