Kufa Medical Journal | Vol. 22, No. 1, 2026

Original article | DOI: https://doi.org/10.36330/kmj.v22i1.23824

p-ISSN: 1993-517X
e-ISSN: 2709-4464

Serum Interferon-gamma as A Potential Biomarker of Disease Activity in Vitiligo

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ABSTRACT

Background: *Vitiligo is chronic acquired depigmenting disorder with an autoimmune basis. Immunologic mediators particularly interferon-gamma (IFN-γ), have been implicated in its pathogenesis and disease activity, but their clinical utility remains incompletely defined.* ***Objective:*** *To evaluate serum IFN-γ levels in patients with vitiligo and investigate their association with disease activity and selected inflammatory parameters, as well as to assess their potential value as an adjunctive biomarker in vitiligo.* ***Methods:*** *This case-control study included 120 participants (60 patients with vitiligo and 60 healthy controls). Patients were divided into treated and untreated subgroups. Demographic and clinical data, including age, body mass index (BMI), smoking status, sun exposure, and disease activity assessed by VIDA score, were recorded. Serum IFN-γ level was measured by ELISA, and CRP, ESR, and hematological indices were also assessed.* ***Results:*** *Serum IFN-γ levels were significantly higher in vitiligo patients compared to controls ($p < 0.001$), with the highest levels observed in untreated patients. IFN-γ levels increased significantly with disease activity ($p = 0.002$). CRP was elevated ($p = 0.007$), while ESR showed no significant difference. IFN-γ demonstrated strong diagnostic performance (AUC = 0.859, sensitivity 90.0%, specificity 66.7%). Logistic regression identified IFN-γ as independent predictor of vitiligo.* ***Conclusion:*** *Serum IFN-γ levels are associated with vitiligo activity and may serve as a supportive biomarker for disease monitoring and assessment of inflammatory activity in vitiligo patients.*

Keywords: Vitiligo, Interferon-gamma, VIDA score, Autoimmune.

Article Information

Received: April 16, 2026; Revised: May 19, 2026; Online June, 2026

INTRODUCTION

Vitiligo is a common acquired depigmenting disorder characterized by the selective destruction of melanocytes, characterized by well-defined depigmented macules and patches involving the skin, hair, and mucous membranes [(1)]. The disease affects an approximate 0.5-1% of the global population and may occur at any age although onset commonly occurs before the age of 30 years, beyond its dermatological manifestations, vitiligo is associated with considerable psychological emotional and social burden, particularly in populations with darker skin phototypes, where depigmentation is more visually prominent [(2)]. The pathogenesis of Vitiligo is complex and multifactorial, involving the interaction of genetic susceptibility, autoimmune mechanisms, oxidative stress, neural factors, and environmental triggers. Current evidence strongly supports an autoimmune

mediated process as the predominant pathogenic mechanism, in which autoreactive cytotoxic CD8+T lymphocytes target and destroy melanocytes. Oxidative stress is also believed to contribute to melanocyte damage by increasing cellular susceptibility to immune-mediated injury and promoting the release of inflammatory mediators. In addition, several environmental and lifestyle related factors, including smoking, chemical exposure, emotional stress and sun exposure, have been implicated as potential contributors to disease onset or progression [3].

Although vitiligo diagnosis is mainly clinical, assessment of disease activity and progression remains challenging. Clinical indicators of activity may be subjective and inconsistent, particularly in early or slowly progressive disease. Several scoring systems have been developed to evaluate disease severity and activity, including the Vitiligo Area Score Index (VASI) and Vitiligo Disease Activity (VIDA) score. Diagnostic methods currently used primarily depend on a patient's clinical presentation to determine the cause of his/her hypopigmented skin, as there is no specific laboratory test available to provide a definitive diagnosis [4]. While some additional diagnostic techniques such as Wood's lamp and histopathological examination may aid in providing some information to help establish a diagnosis, their contribution is limited because they may also show variability and overlap with many other medical conditions [5-6-7]. It is also difficult to determine disease activity and make predictions regarding future disease progression because clinical indicators associated with the disease are subjective and inconsistent [8-9].

There is a combination of cellular and humoral mechanisms that create a disease process in vitiligo. There are numerous immune factors involved, including cytokines such as INF-γ, IL-17, TNF-α, IL-2, among other cytokines of a pro-inflammatory environment damaging to melanocytes. In particular, INF-γ has been identified as an important immunomodulatory cytokine that supports and enhances the autoimmune response by activating cytotoxic T cells and creating an inflammatory reaction, especially through the CXCL10/CXCR3 axis, which increases the influx of autoreactive T cells into the epidermis and promotes the apoptosis of melanocytes [10-11].

Despite increasing interest in cytokine profiling in vitiligo, limited local studies have evaluated the relationship between serum IFN-γ levels, disease activity, and treatment status among Iraqi patients.

MATERIALS AND METHODS

Study Design and Setting

A case-control study was conducted from July 15, 2025, to February 23, 2026, including vitiligo patients attending the Dermatology Unit at Al-Najaf Al-Ashraf Teaching Hospital, Najaf, Iraq.

Study Population and Specimen

A total of 120 participants were enrolled, including 60 vitiligo patients and 60 healthy control group. The vitiligo group was further divided into treated (no = 30) and untreated (no = 30) patients. Patients were randomly

selected from those visiting the Dermatology Unit.

Inclusion Criteria

Patients aged 10–60 years diagnosed with vitiligo by a dermatologist according to standard clinical criteria.

Exclusion Criteria

Patients with other autoimmune diseases, recent surgery or local inflammation, chronic infections, cancer, immunodeficiency, or those receiving systemic corticosteroids or immunosuppressive therapy, as well as patients outside the 10–60 years age range.

Clinical and Demographic Assessment

Demographic and clinical information was collected using a structured questionnaire that included age, sex, marital status, residency, smoking status, smoking index, sun exposure, chemical exposure, regularly physical activity, treatment status and disease activity. Smoking index was calculated as pack-year using the following aquation:

Number of cigarette packs smoked x duration of smoking in years.

Body mass index (BMI) was calculated using the standard formula:

BMI= weight (kg) / height (m²)

Participants were classified according to the World Health Organization (WHO) BMI classification system.

Assessment of Disease activity

Disease activity was evaluated using the Vitiligo Disease Activity (VIDA) score, which is a six-point clinical score system based on the patient's history of disease progression.

The VIDA score was classified as follows:

VIDA Score	Vitiligo activity time
+4	Appearance of new lesions or expansion of existing lesions within the last 6 weeks
+3	Activity within the last 3 months
+2	Activity within the last 6 months
+1	Activity within the last 12 months
0	Disease stable for more than one year
-1	Improvement or regimentation within the previous year

Blood Specimen and Preparation

Approximately 3–5 mL of venous blood was collected from each participant, allowed to clot, and centrifuged at 3000 rpm for 15 minutes. The serum was aliquoted into sterile tubes and stored at -20°C until laboratory analysis, avoiding repeated freeze-thaw cycles.

Interferon Gamma Analysis by ELISA

Serum IFN-γ levels were measured using a quantitative ELISA kit (BT LAB, Shanghai,

China; Product No.: E0097 Hu; detection range 1–400 ng/mL, sensitivity 0.49 ng/mL). The assay was performed according to the manufacturer's instructions, and concentrations were determined from a standard curve at 450 nm.

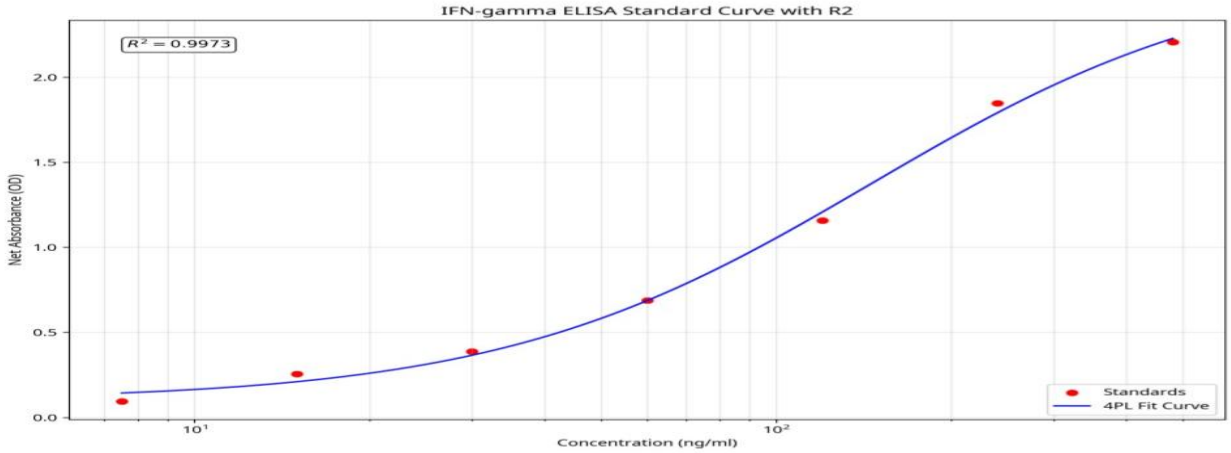

Figure (1): Human IFN-γ standard curve.

Measurement of C-Reactive Protein (CRP)

Serum CRP was measured using an immunoturbidity assay on an Indiko analyzer (Thermo Fisher Scientific Oy, Vantaa, Finland; range 5–212 mg/L, LOD 5 mg/L) following the manufacturer's instructions, with calibration and quality controls included.

Hematological Analysis

CBC parameters (hemoglobin, WBC, neutrophils, lymphocytes, platelets) were measured using an automated hematology analyzer (Diamond), and ESR was determined by the Westergren method, following standard laboratory protocols.

Statistical Analysis

Data were evaluated using the Statistical Package for the Social Sciences, version 26.0 (IBM Corp., Armonk, NY, USA), as well as applied testing (Shapiro–Wilk test) for the continuous variables. Most continuous variables showed normal distribution. Parametric data were presented as mean ± SD or SEM, while non-parametric data were expressed as median (IQR), with appropriate non-parametric tests applied for analysis. Categorical data were reported as frequencies and percentages.

The independent specimens (vitiligo patients and control subjects) were compared via the Mann-Whitney U test (continuous variables) and either chi-square ($\chi 2$) or Fisher's exact test (categorical variables), where appropriate.

The Kruskal-Walli's test was performed to compare more than two independent groups, including groups such as treated patients versus untreated patients versus healthy controls or groups categorized by VIDA category for patients with varying levels of activity related to their diagnosis. For trials

involving the comparison of two independent groups (for example groups of patients receiving treatment versus no treatment) data was analyzed using a Mann-Whitney U test. When data being analyzed is categorical and involve the comparison of multiple independent groups, Chi-square test of significance (χ^2), or Fisher's Exact Test was performed.

Correlations between cytokine levels (IFN-γ) and demographic, clinical, hematological, and inflammatory parameters were assessed using Spearman's rank correlation coefficient (r).

To assess the diagnostic accuracy of IFN-γ and CRP for differentiating vitiligo patients from normal subjects, Receiver Operating Characteristic (ROC) analyses were performed. Estimates of Area Under the Curve (AUC) with 95% Confidence Intervals (CI) were calculated for both biomarkers. Optimal cut-offs were identified using the Youden index to provide maximal sensitivity and specificity.A two-tailed p-value of < 0.05 was considered statistically significant.

Binary logistic regression analysis was conducted to determine which variables could independently predict vitiligo. A univariate analysis was first completed, then multivariable analyses that included only those variables determined to be significant in the univariate analysis were developed. Results are presented as Odds Ratios (OR) with 95% Confidence Intervals (CI). The performance of the multivariable models was assessed using pseudo-R^2 values and Akaike Information Criterion (AI).

RESULTS

Baseline demographic and lifestyle characteristics of vitiligo patients and healthy controls are summarized in Table 1. Smoking was significantly more frequent among vitiligo patients than controls ($p = 0.012$), and age-group distribution also differed significantly between the groups ($p < 0.001$). No significant differences were observed in the remaining demographic or exposure-related variables.

Table (1): Demographic, Lifestyle, and Exposure Characteristics of Vitiligo Patients and Healthy Controls.

Characteristics		Vitiligo patients (NO.=60)	Healthy controls (NO.=60)	P-value	Test
Age, mean ± S.D.		31.4 ± 13.6	31.9 ± 8.3	0.410	MWU[1]
Age groups	10 - 20 (year)	16 (26.7%)	2 (3.3%)	**<0.001***	Chi[2]
	21 - 30 (year)	12 (20.0%)	27 (45.0%)		
	31 – 40 (year)	32 (53.3%)	31 (51.7%)		

Characteristics		Vitiligo patients (NO.=60)	Healthy controls (NO.=60)	P-value	Test
	41-50 (year)				
	51-60 (year)				
Sex	Male, number (%)	33 (55.0%)	30 (50.0%)	0.715	Chi²
	Female, number (%)	27 (45.0%)	30 (50.0%)		
Marital status	Single, number (%)	26 (43.3%)	24 (40.0%)	0.853	Chi²
	Married, number (%)	34 (56.7%)	36 (60.0%)		
Residency	Urban, number (%)	51 (85.0%)	52 (86.7%)	1.000	Chi²
	Rural, number (%)	9 (15.0%)	8 (13.3%)		
Smoking	Smoker, number (%)	18 (30.0%)	6 (10.0%)	**0.012***	Chi²
	Non-smoker, number (%)	42 (70.0%)	54 (90.0%)		
Smoking index, mean± S.D. (pack per year)		16.56 ± 13.85	14.25 ± 6.74	0.947	MWU[1]
Sun exposure	Exposure, number (%)	30 (50.0%)	19 (31.7%)	0.063	Chi²
	Non-Exposure, number (%)	30 (50.0%)	41 (68.3%)		
Chemical Exposure	Exposure, number (%)	19 (31.7%)	16 (26.7%)	0.688	Chi²
	Non-Exposure, number (%)	41 (68.3%)	44 (73.3%)		
Exercise regularly	YES, number (%)	35 (58.3%)	30 (50.0%)	0.464	Chi²
	NO, number (%)	25 (41.7%)	30 (50.0%)		

Data are presented as mean ± SD or n (%). Age and smoking index were compared using the Mann–Whitney U test. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Smoking index was calculated only among smokers. A p value < 0.05 was considered statistically significant.

BMI and weight-category distribution differed significantly between vitiligo patients and healthy controls. Vitiligo patients demonstrated higher BMI values and a greater frequency of obesity compared with controls, as shown in Table 2.

Table (2): Body Mass Index and Weight-category Distribution in Vitiligo Patients and Healthy Controls.

Characteristics		Vitiligo patients NO.=60	Healthy controls NO.=60	P-value
BMI, mean ±S.D. (Kg\m²)		26.79 ± 5.42	23.91 ± 4.03	0.010*
Weight categories	Mild Thinness, number (%)	2 (3.3)	3 (5.0)	0.012*
	Moderate Thinness, number (%)	0 (0.0)	5 (8.3)	
	Normal, number (%)	23 (38.3)	24 (40.0)	
	Overweight, number (%)	17 (28.3)	24 (40.0)	
	Obese Class I, number (%)	12 (20.0)	4 (6.7)	
	Obese Class II, number (%)	5 (8.3)	0 (0.0)	
	Obese Class III, number (%)	1 (1.7)	0 (0.0)	

Data are presented as mean ± SD or n (%). BMI was compared using the Mann–Whitney U test, while weight categories were analyzed using the χ^2 test or Fisher's exact test, as appropriate. A P value < 0.05 was considered statistically significant.

Hematological indices of vitiligo patients and healthy controls are presented in Table 3. Significant differences were observed in neutrophil percentage, lymphocyte percentage, platelet count, and NLR between the two groups, whereas hemoglobin level and total WBC count showed no significant differences.

Table (3): Comparison of Hematological Indices between Vitiligo Patients and Healthy Controls.

Characteristics	Vitiligo patients NO.=60	Healthy controls NO.=60	P-value
Hemoglobin level, mean ±S.D. (g/dl)	13.26 ± 1.63	13.30 ± 1.97	0.977
WBC count, mean ±S.D. (x 10^9/liter)	6.92 ± 1.66	6.53 ± 1.04	0.211
Neutrophile (%)	53.83 ± 9.06	60.13 ± 4.40	<0.001*
Lymphocyte (%)	36.92 ± 8.37	32.25 ± 4.94	0.001*
Platelet count, mean ±S.D. (x10^9/liter)	244.98 ± 47.31	268.55 ± 52.17	0.012*
NLR	1.60 ± 0.67	1.92 ± 0.40	<0.001*

Data are presented as mean ± SD. Comparisons were performed using the Mann–Whitney U test. WBC = white blood cell count; NLR = neutrophil-to-lymphocyte ratio. A p value < 0.05 was considered statistically significant.

Traditional inflammatory markers in vitiligo patients and healthy controls are presented in Table 4. CRP levels were significantly higher in vitiligo patients than in healthy controls, whereas ESR levels showed no significant difference between the two groups.

Table (4): Traditional Nonspecific Inflammatory Markers in Vitiligo Patients and Healthy Controls.

Characteristics	Vitiligo patients NO.=60	Healthy controls NO.=60	P-value
ESR level, mean ±Std. Error Mean (mm/h)	10.40 ± 0.81	11.00 ± 0.81	0.505
CRP level, mean ±Std. Error Mean (ml/dl)	4.00 ± 0.52	2.03 ± 0.20	0.007*

Data are presented as mean ± standard error of the mean (SEM). Comparisons were performed using the Mann–Whitney U test. ESR = erythrocyte sedimentation rate; CRP = C-reactive protein. A p value < 0.05 was considered statistically significant.

The serum IFN-γ levels were compared between vitiligo patients and healthy controls. IFN-γ was significantly elevated in vitiligo patients compared with healthy controls ($p < 0.001$), consistent with a heightened inflammatory state in patients, as shown in Figure 2

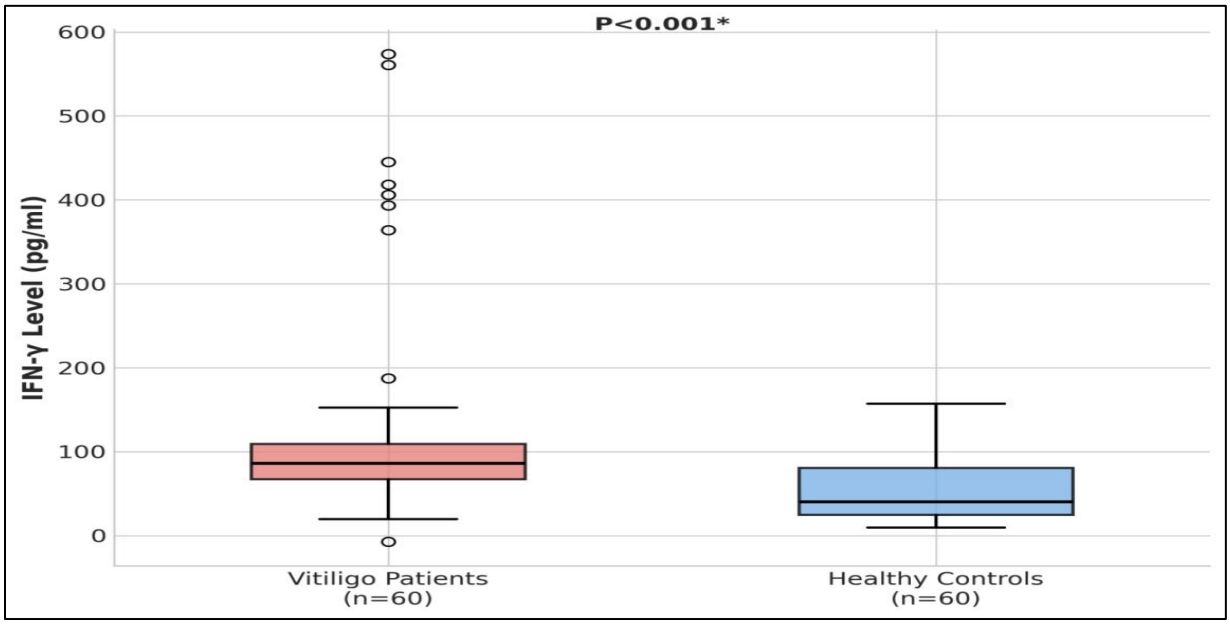

Figure (2): Box plot Comparing IFN-γ Levels between the Vitiligo Patients and Healthy Controls.

IFN-γ concentration was elevated in both treatment groups compared to healthy controls to assess the effect of treatment on IFN-γ levels. At baseline (see Fig. 2), both treatment groups were elevated relative to controls. The untreated patients had elevated IFN- γ levels compared to healthy controls and were significantly elevated compared to the treated group (Fig. 3). In addition, treatment resulted in lower concentrations of IFN- γ compared to untreated patients, but IFN-γ levels remained elevated compared to healthy-controls.

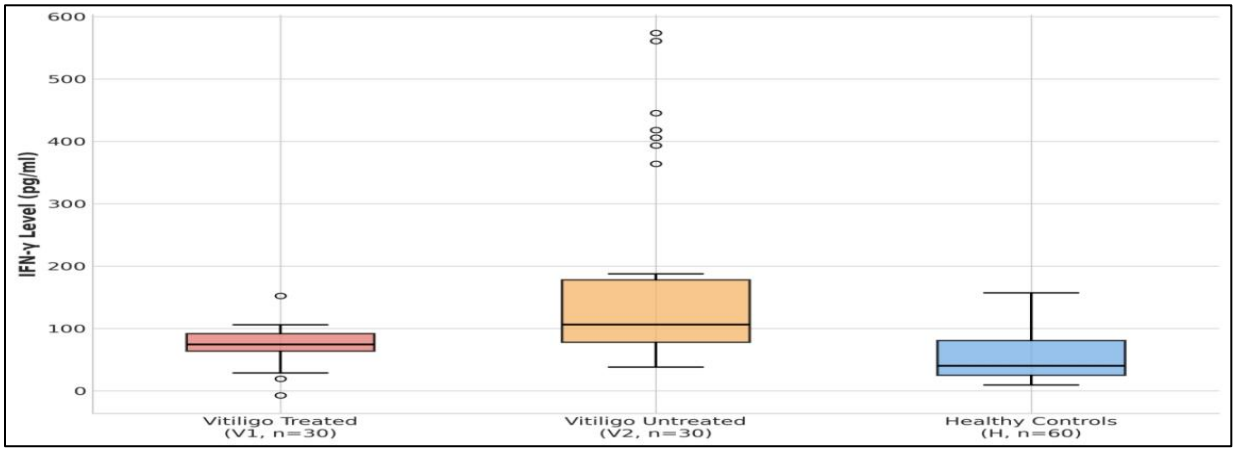

Figure (3): Box plot Comparing IFN-γ Levels between the Vitiligo Patients Groups (Treated and Untreated) and Healthy Controls.

The association between disease activity and cytokine levels was assessed to determine whether cytokine expression tracked with clinical activity. IFN-γ levels differed significantly across VIDA groups (p = 0.002), as shown in Figure 3.

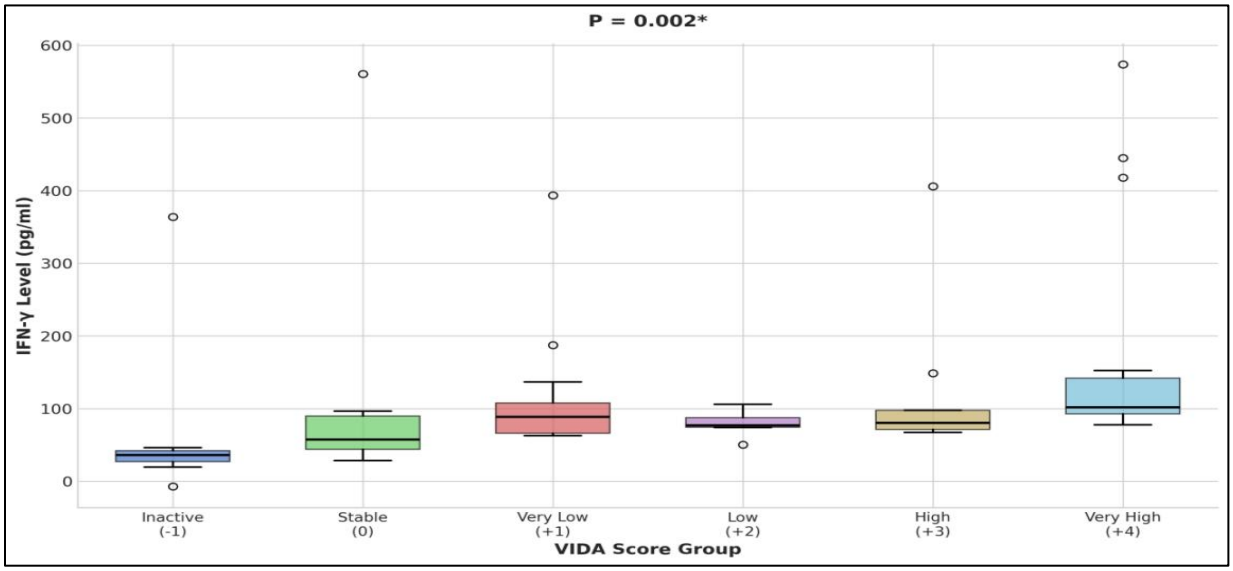

Figure (4): **Box plot Comparing IFN-γ Level of the Vitiligo Patients among Different VIDA Disease Activity Groups.**

ROC analysis was used to assess the ability of several biomarkers to differentiate between patients diagnosed with vitiligo compared with those who were healthy. Of the three biomarkers evaluated, the performance of IFN-γ was impressive, as evidenced by having a greater area under the curve (AUC) than the other two biomarkers (0.859), and having greater sensitivity (90.0%) but less specificity (66.7%) than CRP (0.645, 26.7%, and 95%, respectively).

Table (8): Diagnostic Performance of IFN-γ and CRP for Distinguishing Vitiligo Patients from Healthy Controls.

Parameter	IFN-γ	CRP
AUC	0.859	0.645
95% CI	0.787–0.931	0.546–0.744
p-value	<0.001	0.004
Cutoff (pg/mL)	63.86	5.0
Sensitivity (%)	90.0	26.7
Specificity (%)	66.7	95.0

AUC = area under the curve; CI = confidence interval; ROC = receiver operating characteristic. Cutoff point values are expressed in pg/mL. A p value < 0.05 was considered statistically significant.

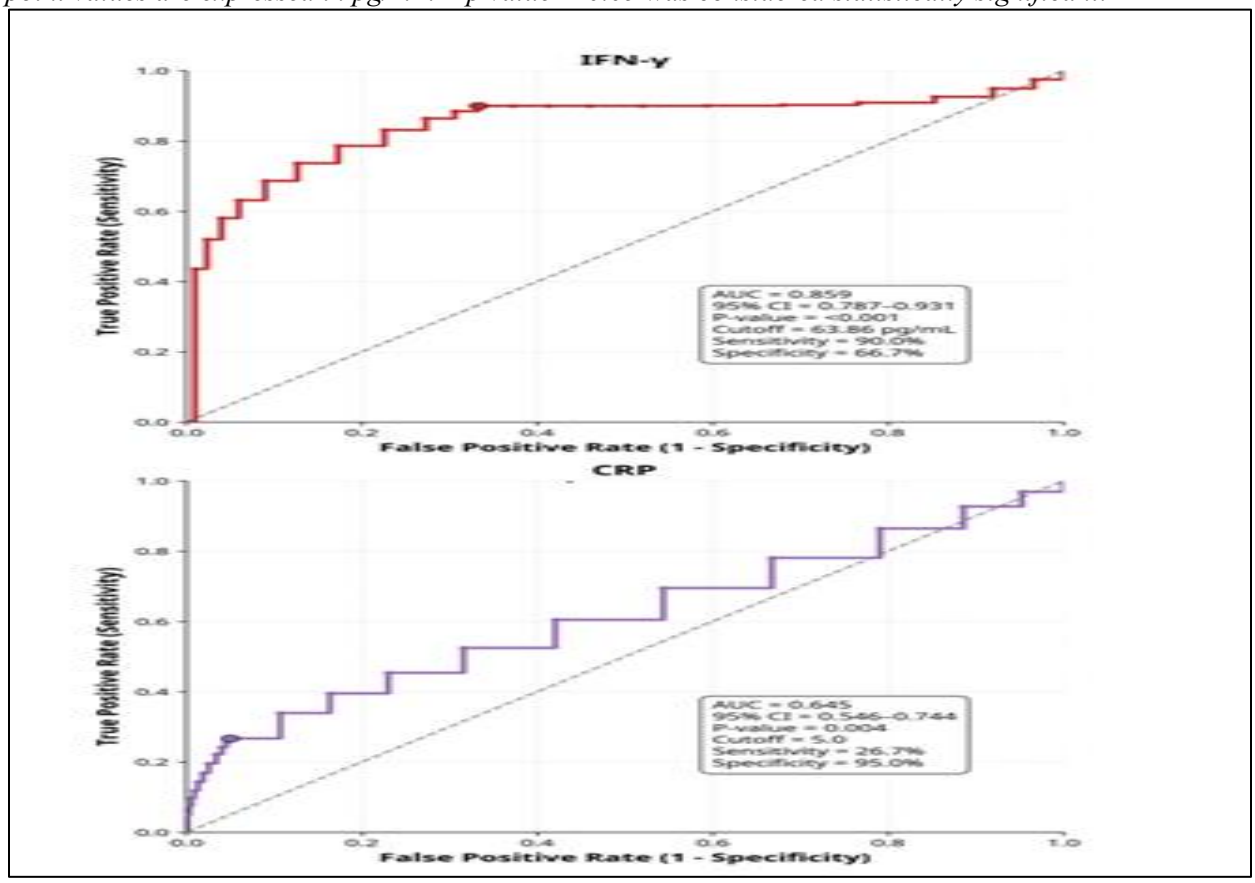

Figure (5): ROC Curves for IFN-γ and CRP in Discriminating Vitiligo Patients from Healthy Controls.

Spearman correlation analysis was performed to evaluate the relationship between serum IFN-γ levels and hematological indices in vitiligo patients. No significant correlations were observed between IFN-γ levels and hemoglobin concentration, total WBC count, neutrophil percentage, lymphocyte percentage, platelet count, or NLR, as shown in Table 9.

Table (9): Spearman Correlations of Serum IFN-γ, with Hematological Indices in Vitiligo Patients.

Parameters	IFN-γ ®	IFN-γ (p)
Hemoglobin level	0.049	0.709
WBC count	-0.012	0.924
Neutrophil (%)	0.097	0.462
Lymphocyte (%)	-0.056	0.673
Platelet count	0.198	0.129
NLR	0.082	0.534

Correlation coefficients are presented as Spearman's r with corresponding p values. WBC = white blood cell count; NLR = neutrophil-to-lymphocyte ratio. A p value < 0.05 was considered statistically significant.

Correlation analysis between serum IFN-γ and traditional inflammatory markers is presented in Table 10. No significant correlations were observed between IFN-γ levels and either CRP or ESR. However, ESR showed a weak but statistically significant positive correlation with CRP (r = 0.263, p = 0.042).

Table (10): Correlation Matrix of Serum IFN-γ and Traditional Nonspecific Inflammatory Markers in Vitiligo Patients.

Parameters		Vitiligo patients NO.=60	
		IFN-γ	CRP
IFN-γ (pg/ml)	r	—	
	p	—	
CRP titer (mg/dl)	r	-0.123	—
	p	0.348	—
ESR (mm/h)	r	-0.016	0.263
	p	0.906	0.042*

*Values are Spearman correlation coefficients (r) with corresponding p values. ESR = erythrocyte sedimentation rate; CRP = C-reactive protein. * p < 0.05, ** p < 0.01, *** p < 0.001.*

Binary logistic regression analysis was performed to identify factors independently associated with vitiligo. In univariate analysis, IFN-γ, CRP, NLR, and BMI showed significant associations with vitiligo. In the biomarker-only multivariable model, IFN-γ lost statistical significance, whereas CRP remained independently associated with vitiligo. In the full multivariable model, IFN-γ, CRP, NLR, and BMI all demonstrated significant independent associations with vitiligo. The full model showed better overall performance than the biomarker-only model, as indicated by higher pseudo-R^2 and lower AIC values (Table 11).

Table (11): Binary Logistic Regression Models for Factors Associated with Vitiligo Diagnosis.

Predictor	Univariate OR (95% CI)	p-value	Biomarker-only multivariable OR (95% CI)	p-value	Full multivariable OR (95% CI)	p-value
IFN-γ	1.025 (1.012–1.037)	<0.001	1.015 (0.999–1.032)	0.068	1.025 (1.005–1.046)	0.016
CRP	1.326 (1.097–1.604)	0.004	1.485 (1.066–2.069)	0.019	1.511 (1.016–2.246)	0.041
NLR	0.328 (0.156–0.691)	0.003	—	—	0.145 (0.042–0.506)	0.002
BMI	1.138 (1.047–1.237)	0.002	—	—	1.224 (1.060–1.415)	0.006
Model performance						
Biomarker-only model	—	—	Pseudo R^2 = 0.407	AIC = 108.6	Log-likelihood = -49.3	—
Full multivariable model	—	—	Pseudo R^2 = 0.532	AIC = 91.8	Log-likelihood = -38.9	—

OR = odds ratio; CI = confidence interval; CRP = C-reactive protein; NLR = neutrophil-to-lymphocyte ratio; BMI = body mass index. The biomarker-only multivariable model included IFN-γ, and CRP. The full multivariable model included, IFN-γ, CRP, NLR, and BMI. A p value < 0.05 was considered statistically significant.

DISCUSSION

In the present study, serum IFN-γ levels were significantly higher in vitiligo patients than in healthy controls, supporting the role of Th1-mediated immune responses in vitiligo pathogenesis. Increased IFN-γ may reflect activation of autoreactive CD8+ T lymphocytes and stimulation of the CXCL9/CXCL10 pathway, which contribute to melanocyte destruction and disease progression [12], These findings are consistent with previous reports of elevated

IFN-γ levels in vitiligo patients [13-14], who also reported elevated IFN-γ levels in vitiligo patients. In contrast, Author [15], observed lower IFN-γ levels, which may be related to differences in specimen size, disease activity, clinical subtype, or assay methods. Collectively, these findings support the role of IFN-γ as an important pro-inflammatory cytokine involved in vitiligo immunopathogenesis.

The present study demonstrated significantly higher IFN-γ levels in both treated and untreated vitiligo patients compared with healthy controls, with the highest levels observed in untreated patients. This finding may reflect persistent activation of Th1-mediated immune responses and ongoing melanocyte destruction in untreated disease. Although treatment was associated with reduced IFN-γ levels, cytokine concentrations remained elevated compared with controls, suggesting partial persistence of inflammatory activity despite therapy. These findings are consistent with previous findings reported in study [16], who reported decreased IFN-γ levels following systemic glucocorticoid therapy, as well as [17], who observed elevated IFN-γ levels in vitiligo patients. Similarly, study [18], found higher IFN-γ levels in unstable vitiligo, supporting its association with disease activity. Unlike several previous studies, the present study separately evaluated treated and untreated patients, providing additional insight into treatment-related immunological changes in vitiligo.

The present study demonstrated a significant increase in IFN-γ levels with increasing vitiligo activity, with the highest levels observed in patients with highly active disease. This finding suggests that IFN-γ expression reflects ongoing immune activation and clinical instability in vitiligo. Persistent elevation of IFN-γ may enhance recruitment of autoreactive T lymphocytes and promote continued melanocyte destruction through activation of inflammatory chemokine pathways [19]. These findings are consistent with study [17-20], who reported significant positive associations between IFN-γ levels and both VIDA and VASI scores. Collectively, these observations support the potential role of IFN-γ as an adjunctive biomarker for assessing disease activity and monitoring disease progression in vitiligo.

ROC analysis demonstrated good discriminatory performance of IFN-γ in differentiating vitiligo patients from healthy controls, with high sensitivity but moderate specificity. These findings suggest that elevated IFN-γ levels may reflect the inflammatory immune activity associated with vitiligo rather than disease-specific pathology alone [21]. The relatively lower specificity may be explained by the involvement of IFN-γ in other inflammatory and autoimmune conditions. These findings are consistent with study [22], who reported excellent discriminative performance of IFN-γ and observed decreased cytokine levels following treatment. Similarly, study [23], demonstrated that elevated IFN-γ levels were associated with recurrent vitiligo, supporting its potential prognostic significance. Collectively, these findings suggest that IFN-γ may serve as an adjunctive

inflammatory biomarker for evaluating disease activity and monitoring treatment response in vitiligo.

Binary logistic regression analysis demonstrated significant associations between IFN-γ, CRP, BMI, and NLR and vitiligo in univariate analysis. However, in the biomarker-only multivariable model, IFN-γ lost statistical significance after adjustment, suggesting possible overlap between inflammatory markers and shared immune-related pathways. In contrast, the full multivariable model showed improved predictive performance, indicating that vitiligo is influenced by multiple interacting inflammatory and metabolic factors rather than a single biomarker alone.

The positive association of CRP and BMI may reflect the contribution of systemic inflammation and metabolic dysregulation to vitiligo pathogenesis, whereas the inverse association with NLR could indicate alterations in immune-cell balance in affected patients. Collectively, these findings suggest that combining inflammatory and hematological parameters may improve assessment of vitiligo-related immune activity.

No significant correlations were observed between serum IFN-γ levels and routine hematological parameters, including hemoglobin concentration, total WBC count, neutrophil percentage, lymphocyte percentage, platelet count, and NLR. This finding suggests that although IFN-γ plays a central role in vitiligo immunopathogenesis through activation of cytotoxic T lymphocytes and promotion of melanocyte destruction, its systemic expression may not be directly reflected by routine hematological indices [24]. A possible explanation is that IFN-γ-mediated immune responses in vitiligo are predominantly localized within the skin microenvironment rather than associated with marked systemic hematological alterations.

Although CRP is an established systemic inflammatory marker, it showed no significant correlation with IFN-γ levels ($r = -0.123$, $P = 0.348$), indicating limited association with cytokine-mediated immune activity in vitiligo.

There is no significant relationship between ESR (erythrocyte sedimentation rate) and IFN-γ (interferon gamma), $r= 0.016$, $P=0.9016$, indicates that ESR is either a poor general indicator of immunopathology as well as IFN-γ, emphasizing the potential need for assessment of cytokine profiles and not solely depending on other general systemic markers.

Limitations

Some important features of this research are that it only looked at serological levels (IFN-γ) of people with vitiligo in Iraq, comparing people who were treated to those who were not treated and also included healthy controls; also examined relationships between IFN-γ and disease activity to show that IFN-γ has both some value as a diagnostic test (ROC curve) and some prognostic value (multivariate logistic regressions).

There are a few limitations of this study that need to be taken into consideration. Due to the single (case control) center design, the amount of causality that can be inferred as well as the ability to generalize the results

are limited. Specimen sizes were small, particularly once sub grouped. In addition, only one serum IFN-γ measurement was taken at one time point, thereby making it impossible to apply a longitudinal assessment to this study. Along with that, there was no stratification of treated cases based on treatment and time period and there was no additional analysis of the broader immune system other than serum IFN-γ and some routine inflammatory indicators.

CONCLUSION

In patients with vitiligo, serum IFN-γ levels were significantly elevated, particularly in clinically active or treatment-resistant cases. This elevation supports the involvement of IFN-γ in the immunopathogenesis of vitiligo and its potential association with disease activity. IFN-γ also demonstrated good diagnostic performance and remained an independent predictor of vitiligo in multivariate analysis. Based on these findings, serum IFN-γ may represent a promising biomarker for the diagnosis and assessment of disease activity in vitiligo; however, further large-scale, multicenter longitudinal studies are required to confirm its clinical utility.

RECOMMENDATIONS

Further multicenter longitudinal studies with larger specimen sizes are recommended to better evaluate the role of IFN-γ and other cytokines in vitiligo pathogenesis, disease activity assessment, and treatment response monitoring.

DECLARATIONS

Ethical Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and received ethical approval from the Committee on Publication Ethics at the College of Medicine, University of Kufa (Reference No: MEC-42). Written informed consent was obtained from all individual participants included in the study.

Acknowledgments

The authors extend their sincere thanks to the dermatology consultants at Najaf Al-Ashraf Teaching Hospital in Najaf Al-Ashraf for their assistance in collecting the specimens. We also express our deep gratitude to all the patients and volunteers who participated in this study.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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