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Original Research Article

Association of serum interleukin 15 level with vitiligo: a cross-sectional comparative study

Arjun Saha[1]*, Shahidullah Sikder[2], Mohammad Abul Kalam Azzad[2], A. T. M. Asaduzzaman[2], Towfiq Ahmad[3], M. Abir Hassan[4], Tanzina Begum Chowdhury[5], Wasi Deen Ahmed[1], Marufa Shahrin[1]

[1]Department of Dermatology and Venereology, Directorate General of Health Services, Dhaka, Bangladesh
[2]Department of Dermatology and Venereology, Bangladesh Medical University, Dhaka, Bangladesh
[3]Department of Dermatology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[4]Department of Dermatology, Sir Salimullah Medical College, Dhaka, Bangladesh
[5]Department of Dermatology, Sarkari Karmachari Hospital, Dhaka, Bangladesh

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***Correspondence:**
Dr. Arjun Saha,
E-mail: dr.arjun205@gmail.com

ABSTRACT

Background: Vitiligo is a chronic autoimmune skin disorder characterized by the progressive destruction of melanocytes, leading to depigmented patches. Interleukin-15 (IL-15), a pro-inflammatory cytokine, has been implicated in the persistence of vitiligo by sustaining tissue-resident memory (TRM) T cells, which contribute to disease recurrence. Objective was to investigate the association of serum IL-15 levels with vitiligo and its severity.
Methods: A total of 60 participants, including 30 vitiligo patients and 30 healthy individuals were enrolled. Serum IL-15 levels were measured using enzyme-linked immunosorbent assay (ELISA). Disease severity was assessed using the vitiligo area scoring index (VASI).
Results: Vitiligo patients exhibited significantly higher serum IL-15 levels (41.98±32.16 pg/ml) compared to healthy individuals (15.19±8.82 pg/ml, $p<0.001$). IL-15 levels were positively correlated with disease severity, as patients with VASI scores >10 had the highest IL-15 levels (61.88±31.82 pg/ml, $p=0.047$). However, no significant correlation was observed between IL-15 levels and age ($p=0.129$), duration of disease ($p=0.923$), or age of onset ($p=0.107$). Receiver operating characteristic (ROC) analysis demonstrated that IL-15 levels ≥15.9 pg/ml had 80.8% sensitivity and 65.4% specificity in distinguishing vitiligo patients from healthy individuals (AUC=0.772, $p=0.001$).
Conclusions: Serum IL-15 is found to be significantly elevated in vitiligo patients and is shown to correlate with disease severity. Future research should focus on longitudinal studies and therapeutic interventions targeting IL-15 to better understand its role in vitiligo pathogenesis and treatment.

Keywords: Interleukin-15, VASI, Vitiligo

INTRODUCTION

Multiple mechanisms have been proposed for the destruction of melanocytes in vitiligo, including genetic predisposition, autoimmune-mediated melanocyte destruction, oxidative stress, neural hypothesis and impaired melanocyte adhesion.[1] Among these, the autoimmune theory is currently the most widely accepted, given its strong association with other autoimmune diseases and the presence of autoantibodies in vitiligo patients.[2] Vitiligo is a common skin depigmentation disease characterized by milky white macules or patches, affecting individuals of all sexes, age groups and skin types.[3] The global prevalence of vitiligo is estimated to

range between 0.5% and 2%, with the highest reported incidence observed in India (8.8%) and Mexico (2.6-4%).[4,5] A significant challenge in vitiligo treatment is the high relapse rate following successful repigmentation, with an estimated 40% recurrence risk within the first year.[6] Relapses typically occur in the same areas previously affected, suggesting the formation of autoimmune memory at these sites.[7] Resident memory T (TRM) cells, a long-lived subset of T cells residing in non-lymphoid tissues after inflammation, play a key role in this process.[8] These TRM cells primarily function by recruiting circulating effector cells.[9] The presence of TRM cells in both stable and active vitiligo suggests that they may contribute to disease reactivation.[10]

IL-15 has been identified as a crucial factor for TRM cell maintenance. Studies have shown that IL-15 promotes TRM function ex vivo, while IL-15-deficient mice exhibit impaired TRM activity. Blocking IL-15 signalling with an anti-CD122 antibody reverses vitiligo in murine models. Short-term anti-CD122 treatment inhibits interferon-gamma (IFN-γ) production by TRM cells, while long-term treatment depletes TRM from skin lesions, making CD122 blockade a promising therapeutic strategy for vitiligo. IL-15 enhances the cytotoxic potential of CD49a+ TRM cells and increases IFN-γ production, a key driver of vitiligo.[11] Previous studies have demonstrated the importance of IL-15 in the development of TRM cells in skin-related conditions, such as viral infections and cutaneous lymphoma.[12] Significantly elevated IL-15 levels in the sera of vitiligo patients, which correlated with disease severity.[13] IL-15 expression was significantly upregulated in the epidermis of vitiligo patients, mainly produced by keratinocytes and strongly associated with oxidative stress levels. IL-15 and its receptor (IL-15Rα) were also found to be upregulated in keratinocytes under oxidative stress, facilitating IL-15 trans-presentation and enhancing TRM cell survival. Beyond vitiligo, IL-15 plays a pathogenic role in several autoimmune diseases, including inflammatory bowel disease, rheumatoid arthritis, systemic sclerosis, psoriasis, and alopecia areata.[14-18] While IL-15's role is well established in various autoimmune and infectious diseases, its contribution to vitiligo pathogenesis remains an area of active investigation. Recent findings indicate that IL-15 influences vitiligo development by modulating immune cells such as NK cells, dendritic cells, keratinocytes, melanocytes, TRM cells, and cytotoxic T cells, making it a potential therapeutic target in vitiligo treatment.

However, the extent of IL-15's involvement in vitiligo severity and disease recurrence remains underexplored.

This study aimed to investigate the association between serum IL-15 levels and vitiligo, with a specific focus on disease severity. By understanding IL-15's role, we may uncover new therapeutic strategies targeting TRM cells and IL-15 signalling pathways for improved vitiligo treatment.

METHODS

This was a cross-sectional comparative study. This was conducted at the department of dermatology and venereology, Bangladesh Medical University (BMU), Dhaka, Bangladesh from May 2023 to March 2025 total 60 sample 30 participants were included in each group group-A (30) + group-B (30). Consecutive type of sampling technique was applied to collect the sample from the study population during the study period. Individuals were screened based on inclusion and exclusion criteria of the study.

Group A includes patients diagnosed with vitiligo attending at the outpatient department of Dermatology and Venereology, BMU, Dhaka, Bangladesh.

Group B includes apparently healthy individuals without vitiligo (attendants of the patients, doctors, nurses, and other staff members of BMU).

Inclusion criteria

Patients diagnosed with vitiligo based on clinical features and Wood's lamp examination, which was done by investigator, and was confirmed by supervisor. Patients of all ages and sexes. Apparently healthy individuals without vitiligo.

Exclusion criteria

Patients with known cases of autoimmune or inflammatory diseases, including psoriasis, atopic dermatitis, alopecia areata, systemic sclerosis, rheumatoid arthritis, inflammatory bowel disease (IBD), multiple sclerosis, celiac disease. Patients suffering from active infections or concurrent malignancy. Patients who received topical or systemic treatment or phototherapy within last three months period. Pregnant or lactating individuals.

Data collection

A total of 30 vitiligo patients of both sexes and 30 healthy individuals of both sexes were enrolled finally in group A and group B respectively, according to the inclusion and exclusion criteria. Vitiligo diagnosis was made after taking proper history, clinical examination, and Wood's lamp examination. Each participant was provided written informed consent after receiving a detailed explanation of the study's purpose and significance. Each participant was interviewed using a structured questionnaire, and a comprehensive medical history and physical examination were conducted. Blood samples from patients and healthy individuals were collected for ELISA.

Sample collection

The venipuncture site was disinfected with 70% alcohol in an expanding circular scrub from center to periphery. Three (3) ml of blood was taken in a tube without

anticoagulant, then centrifuged at 4000 rpm for 5 minutes. Separated serum was stored at -20°C till analysis of IL-15.

Data analysis

Data were analyzed using SPSS version 26. Categorical variables were presented as frequency and percentage, while continuous variables were expressed as mean, standard deviation (SD) and range. Student's t-test was used for comparing continuous variables, while Chi-square test was applied to categorical variables. Mann-Whitney U test and Kruskal-Wallis test were used for non-normally distributed data. A p value <0.05 was considered statistically significant with a 95% confidence interval (CI).

Ethical issues

After obtaining approval of the thesis protocol and ethical clearance from the institutional review board (IRB) of BMU, this cross-sectional comparative study was conducted in the department of dermatology and venereology, BMU. No data or any information was collected without written consent of the patient. Participation in this research was fully voluntary. The respondents were entirely free to withdraw their participation at any stage or at any time of the study. Written informed consent was taken from each patient or their legal guardian. Prior to consent they were explained the aim and purpose of the research. Confidentiality was assured and maintained.

RESULTS

The Table 1 compares group A and group B based on age, sex and occupational status. Age distribution was almost similar in both groups. The majority of participants in both groups were within the 11-20 years (26.9%) and 21-30 years (26.9% in group A, 23.1% in group B) age ranges. A slightly higher proportion of group B participants are above 40 years (30.8%) compared to group A (26.9 %). The mean ages are nearly identical (29.19±15.27 years in group A and 29.54±15.3 years in group B) with no significant difference (p=0.767). In terms of sex, group A has more females (65.4%) than males (34.6%), while group B has a slightly higher proportion of males (42.3%), but this difference is not statistically significant (p=0.598).

Table 2 presents data on the duration and age of onset of disease among patients in group A. Regarding disease duration, the majority of patients (60.0 %) had the disease for less than 10 years, while 40% had it for more than 10 years. The mean disease duration was 8.38±7.66 years (range: 1-30 years), indicating a wide variation in disease duration among patients. The age of onset of the disease varies across different age groups. The highest proportion of patients (40%) developed the disease between 11-20 years, followed by 23.3% who had an onset between 0-10 years. A smaller proportion had disease onset between 21-30 years (16.7%) and 31-40 years (6.7%). A total of 13.3% of patients had disease onset after 40 years of age. The mean age of disease onset was 20.8±15.15 years, with a broad range from 2 to 56 years, reflecting a broad variation in disease onset patterns.

Table 1: Sociodemographic profile of the study subjects in group A and group B (n=60).

	Group A (n=30) (%)	Group B (n=30) (%)	P value
Age group (years)			
≤10	2 (6.7)	3 (10.0)	0.713
11-20	7 (23.3)	7 (23.3)	
21-30	10 (33.4)	9 (30.0)	
31-40	4 (13.3)	3 (10.0)	
>40	7 (23.3)	8 (26.7)	
Total	30 (100.0)	30 (100.0)	
Mean±SD	29.23±14.18	29.53±14.21	
Range (min-max)	(4-58)	(5-58)	
Sex			
Male	12 (40.0)	13 (43.3)	0.565
Female	18 (60.0)	17 (56.7)	
Total	30 (100.0)	30 (100.0)	
Occupational status			
Doctor	4 (13.3)	6 (20)	0.347
Nurse	3 (10)	4 (13.3)	
Business	4 (13.3)	3 (10.0)	
Student	9 (30.0)	11 (36.7)	
Housewife	8 (26.7)	6 (20.0)	
Others	2 (6.7)	0 (0.0)	
Total	30 (100.0)	30 (100.0)	

Table 2: Distribution of the patients in group A based on disease duration and age of onset (n=30).

Duration of disease (years)	Frequency	Percentage
<10	18	60.0
>10	12	40.0
Total	30	100.0
Mean±SD	8.27±7.66	
Range (min-max)	1 year-30 years	
Age of onset (years)		
0-10	7	23.3
11-20	12	40.0
21-30	5	16.7
31-40	2	6.7
>40	4	13.3
Total	30	100.0
Mean±SD	20.37±15.15	
Range (min-max)	2-56 years	

The distribution of patients in group A based on the type of disease (n=30) reveals that the majority, 23 individuals (76.7%), had the generalized form of the disease. This was followed by 5 individuals (16.7%) with the focal type, while mucosal and universal types were observed in 1 patient each (3.3%). Among the 30 patients in group A, the generalized type was the most prevalent.

Table 4 presents the comparison of serum IL-15 levels between group A and group B. The mean IL-15 level in group A (41.98±32.16 pg/ml) was significantly higher than in group B (15.19±8.82 pg/ml). The difference was statistically significant (p<0.001). Additionally, the median IL-15 level was higher in group A (26.7 pg/ml) compared to group B (14.6 pg/ml). The interquartile range (IQR) for IL-15 levels was 16.4-74.4 pg/ml in group A and 8.0-23.8 pg/ml in group B, indicating greater variability in IL-15 levels among vitiligo patients.

Table 3: Distribution of the patients in group A by type of disease (n=30).

Type of disease	Frequency	Percentage	Serum IL-15 mean (pg/ml)
Focal	5	16.7	21.53
Generalized	23	76.7	44.46
Mucosal	1	3.3	29.50
Universal	1	3.3	99.50
Total	30	100.0	41.98

Table 4: Comparison of IL-15 between group A and group B (n=60).

Serum IL-15 level (pg/ml)	Group A (n=30)	Group B (n=30)	P value
Mean±SD	41.98±32.16	15.19±8.82	<0.001
Median	26.7	14.6	
IQR (interquartile range)	16.4-74.4	8.0-23.8	

Table 5: Comparison of serum IL-15 level of group A patients among different age groups (n=30).

Age group (years)	N	Mean±SD (pg/ml)	Median	Range (min-max)	P value
≤10	2	13.35±5.44	13.35	9.50-17.20	0.124
11-20	7	28.75±31.74	16.80	9.03-99.50	
21-30	10	35.16±23.33	29.60	13.50-89.20	
31-40	4	45.45±17.46	41.70	29.50-68.90	
>40	7	71.13±28.25	75.00	10.90-93.80	

Table 6: Distribution of the patients in group A by VASI score (n=30).

VASI score	Frequency	Percentage
<5	8	26.7
5-10	9	30.0
>10	13	43.3
Total	30	100.0
Mean±SD (pg/ml)	17.31±22.68	
Range (min-max)	0.06-86.31	

Serum IL-15 levels in group A varied across age groups, with the lowest mean in the ≤10 years group (13.35±5.44 pg/ml) and the highest in the >40 years group (71.13±28.25 pg/ml). Median IL-15 levels increased with age, ranging from 13.35 pg/ml in the youngest to 75.00 pg/ml in the oldest group. Though serum IL-15 levels showed an increasing trend with age, the Kruskal-Wallis test yielded a p value of 0.124, indicating no significant difference among age groups.

Table 6 presents the distribution of patients in Group A based on their Vitiligo Area Scoring Index (VASI) scores. Among the 30 patients, 8 (26.7%) had a VASI score of less than 5, 9 (30.0%) had scores between 5 and 10, and 13 (43.3%) had scores greater than 10. The mean VASI score was 17.31 ± 22.68, with a range from 0.06 to 86.31, reflecting wide variability in disease severity within the group.

Table 7: Comparison of serum IL-15 levels among VASI category (n=30).

VASI category	N	Mean±SD (pg/ml)	Median	Range (pg/ml) (min-max)	P value
<5	8	25.41±13.59	22.3	9.03-51.60	0.047
5-10	9	27.94±20.74	22.1	10.9-75.0	
>10	13	61.88±31.82	68.9	9.50-99.50	

Table 8: Correlation of serum IL-15 levels with age, duration of disease, age of onset and VASI score in group A (n=30).

		Spearman's Correlation test	
		Rho value	**P value**
Serum IL-15 with	Age (years)	0.297	0.129
	Duration of disease (years)	0.020	0.923
	Age of onset (years)	0.311	0.107
	VASI score	0.564	0.003

Table 9: ROC analysis of serum IL-15 levels for differentiating vitiligo patients from healthy individuals (n=60).

Parameters	Value
Area under the curve (AUC)	0.772
95% confidence interval (AUC)	0.647-0.898
P value	0.001
Optimal cut-off value of IL-15	15.9
Sensitivity (%)	80.8
Specificity (%)	65.4
Positive predictive value (%)	70.0
Negative predictive value (%)	77.3
Accuracy (%)	73.1

Table 10: Comparison of cut of value of IL-15 between group A and group B (n=60).

Serum IL-15 level	Group A (n=30) (%)	Group B (n=30) (%)	OR 95%CI	P value
≥15.9	25 (83.33)	11 (36.7)	7.85 (2.24-28.2)	0.001
<15.9	5 (16.67)	19 (63.3)		
Total	30 (100)	30 (100)		

Table 7 compares serum IL-15 levels among different VASI score categories in group A (n=30). Patients with VASI scores >10 had the highest mean IL-15 level (61.88±31.82 pg/ml) and a median of 68.9 pg/ml. In contrast, those with VASI scores between 5-10 had a mean of 27.94±20.74 pg/ml, and those with scores <5 had 25.41±13.59 pg/ml. The Kruskal-Wallis test revealed a statistically significant difference in IL-15 levels among the groups (p=0.047), indicating a potential association between higher IL-15 levels and greater disease severity.

Table 8 presents the correlation of serum IL-15 levels with various factors in the group A (vitiligo patients). The Spearman's correlation test results show that serum IL-15 levels do not significantly correlate with age (Rho =0.297, p=0.129), duration of disease (Rho=0.020, p=0.923) or age of onset (Rho=0.311, p=0.107) as indicated by the p-values greater than 0.05. However, a significant positive correlation was found between serum IL-15 and VASI score (Rho=0.564, p=0.003), indicating that higher IL-15 levels are associated with higher VASI scores.

The ROC analysis of serum IL-15 levels for differentiating vitiligo patients from healthy individuals showed a significant result (p=0.001) with an area under the curve (AUC) of 0.772, indicating good diagnostic performance. The optimal cut-off value for serum IL-15 was 15.9 pg/ml. At this threshold, the test had a sensitivity of 80.8%, specificity of 65.4%, a positive predictive value of 70.0%, and a negative predictive value of 77.3%. The overall accuracy of the test was 73.1%.

Table 10 shows the association between serum IL-15 cut-off level (≥15.9 pg/ml) and the presence of vitiligo in group A compared to healthy controls in group B (n=60). A significantly higher proportion of group A patients (83.33%) had IL-15 levels ≥15.9, compared to 36.7% in group B (p=0.001). The calculated odds ratio (OR) was 7.85 with a 95% confidence interval (CI) of 2.24-28.2, indicating that individuals with elevated IL-15 levels were nearly eight times more likely to have vitiligo.

DISCUSSION

The study included 30 vitiligo patients (group A) from the outpatient department and 30 healthy individuals (group B). Participants were selected using a consecutive sampling technique. The primary objective of this study was to evaluate the association between serum IL-15 levels and vitiligo and to assess its relationship with disease severity.

The mean age in Group A was 29.23±14.18 years, while in Group B, it was 29.53±14.21 years, indicating that vitiligo affects individuals across a broad age spectrum without a clear age-related pattern. This finding aligns with prior research, including the study by Atwa et al, which reported a mean age of 39.37±13.13 years for vitiligo patients and 36.23±12.72 years for controls, with no statistically significant difference.[13] Similarly, Hamza et al found comparable mean ages between vitiligo patients (27.70±18.54 years) and healthy controls (25.27±1.91 years).[19] Group A included 40.0% males and 60.0% females, while group B comprised 43.3% males and 56.7% females. These findings suggest that vitiligo affects both genders without a strong gender bias. This is consistent with previous studies, such as Atwa et al, who reported a patient distribution of 46.8% males and 53.2% females, and Eladl et al, where the case group included 33.3% males and 66.7% females, compared to 70.0% females and 30.0% males in the control group.[13,20] The majority of participants were students (30.0%), followed by housewives (26.7%) and service workers (23.3%). This pattern suggests that occupational factors may not play a significant role in the development or prevalence of vitiligo.

The duration of vitiligo was found to vary among patients in this study. Approximately 60% of patients had the condition for less than 10 years, while 40% had it for more than 10 years. The mean duration of the disease was 8.27±7.66 years, ranging from 1 to 30 years, highlighting substantial variability in disease duration. In this present study, the mean age of onset of vitiligo was 20.37±15.15 years, with the majority of patients developing the disease between 11-20 years (40.0%) and 0-10 years (23.3%). These findings indicate that vitiligo commonly manifests in childhood or early adulthood, which is consistent with previous research suggesting early-onset vitiligo is more frequently observed and may have a stronger autoimmune component. This closely aligns with findings from Ahmed et al, who reported a mean age of onset of 21.7±10.2 years with a wide range of onset ages, emphasizing the variable nature of vitiligo onset.[21] Vitiligo was classified into distinct subtypes in this study, with generalized vitiligo being the most common presentation (76.7%), followed by focal vitiligo (16.7%), mucosal vitiligo (3.3%), and universal vitiligo (3.3%). These findings align with previous research highlighting generalized vitiligo as the predominant subtype. Atwa et al reported that generalized vitiligo affected 60% of their study population, while acrofacial vitiligo accounted for 20%, and localized vitiligo made up the remaining 20%, demonstrating a similar pattern to the present study.[13] Additionally, Eladl et al found that 48.3% of patients had generalized vitiligo, followed by 36.7% with acrofacial vitiligo, 11.7% with focal vitiligo, and 3.3% with mucosal vitiligo.[20]

Serum IL-15 levels were significantly associated with VASI categories, with patients having a VASI score >10 exhibiting the highest IL-15 levels (mean 61.88±31.82 pg/ml, median 68.9 pg/ml, range 9.50-99.50 pg/ml), followed by those with VASI 5-10 (mean 27.94±20.74 pg/ml, median 22.1 pg/ml), and the lowest IL-15 levels in the <5 VASI category (mean 25.41±13.59 pg/ml, median 22.3 pg/ml). The statistically significant p value of 0.047, confirming an association between IL-15 levels and disease severity. Similar findings were reported by Atwa et al, who found that IL-15 levels were significantly higher in vitiligo patients (mean 45.67±22.80 pg/ml) compared to controls (26.40±13.69 pg/ml, p=0.001), and by Ahmed et al, who noted a median IL-15 of 94 pg/ml in vitiligo patients versus 25.4 pg/ml in controls (p<0.001).[13,21] It was demonstrated by receiver operating characteristic (ROC) analysis that serum IL-15 has good diagnostic accuracy for differentiating vitiligo patients from healthy individuals, with an AUC of 0.772 (p=0.001). At the optimal cut-off value of 15.9 pg/ml, IL-15 had a sensitivity of 80.8%, specificity of 65.4%, positive predictive value (PPV) of 70.0%, and negative predictive value (NPV) of 77.3%, yielding an overall diagnostic accuracy of 73.1%. These results are consistent with previous studies; Eladl et al reported an AUC of 0.937, with a cut-off of 18.5 pg/ml, sensitivity of 98.3%, and specificity of 83.3%, while Ahmed et al found an AUC of 0.917.[20,21] A significant association between IL-15 levels and vitiligo diagnosis was shown by further analysis of the IL-15 cut-off value (≥15.9 pg/ml). A significantly higher proportion of vitiligo patients (83.33%) had IL-15 ≥15.9 pg/ml compared to only 36.7% of controls (p=0.001). The odds ratio (OR) was 7.85 (95% CI: 2.24-28.2), indicating that individuals with IL-15 levels above 15.9 pg/ml were nearly eight times more likely to have vitiligo. This finding is in agreement with Ahmed et al, who found IL-15 to be an independent predictor of vitiligo with an OR of 1.06 per pg/ml increase (p<0.001).[21] Our results reinforce the strong association between elevated IL-15 levels and vitiligo.

CONCLUSION

IL-15 was elevated in the sera of patients of vitiligo compared to healthy individuals. Serum IL-15 levels were positively correlated with disease severity, but there was no significant association between serum IL-15 levels and age, disease duration, and disease onset. So, a conclusion can be made that IL-15 may have a major impact on vitiligo autoimmune pathogenesis.

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