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REVIEW ARTICLE

Association of Serum IL-23 and IL-17 Levels with Alopecia Areata

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Abstract:

Background: Alopecia areata is a chronic, non-scarring autoimmune condition characterized by patchy hair loss.

Materials and Methods: From December 2023 to April 2024, case-control research was carried out at Al-Diwaniya Teaching Hospital. It comprised 40 formally identified alopecia areata patients as well as 40 healthy controls who were compared for gender as well as age. Comprehensive dermatology tests as well as a thorough history-taking process were performed on the participants. According to the quantity as well as the size of the alopecic patches or the degree of hair loss, alopecia areata was divided into moderate and severe variants. Levels of serum Interleukin-17 and Interleukin-23 were assessed as well as compared to illness features.

Results: Compared to healthy controls, alopecia areata patients had noticeably higher levels of interleukin-17. Nevertheless, there was not a statistically significant variance in interleukin-17 levels according to the length of the illness, family history, or recurrence. Interleukin-17A levels were slightly more elevated among participants without a family history as well as those whose condition had been present for less than a year, but those variations weren't statistically significant. Furthermore, compared to controls, alcoholics' interleukin-23 levels were noticeably greater.

Conclusion: Alopecia areata patients had significantly higher serum levels of interleukin-23 as well as interleukin-17, which may indicate a function for these molecules in the pathophysiology of the disease. The autoimmune processes that underlie alopecia areata might get exacerbated by the dysregulation of these cytokines.

Keywords: Alopecia areata, IL17., IL23., Cytokines, Autoimmune disease, Inflammation, DiseaseSeverity.

Introduction

Alopecia areata (A.A) is a chronic inflammatory illness of hair follicle cycles that is characterized by non-scarring hair loss and is caused by the breakdown of a gen-specific immunity privilege during T-lymphocyte infiltration into the hair follicle [1, 2, 3]. Although the exact origin of A.A. is yet unknown, immunological and environmental as well as genetic factors could be involved. Furthermore, one of the well-known causes as well as exacerbations of the illness is stress [4]. It produces CD4+Th17 as well as CD8+T cytotoxic cells, also called IL-17A. [5].

Pathogenesis for cancer, autoimmune diseases, allergies, and allograft transplants is linked to IL-17A. Whenever IL-17 becomes active, chemokines are released, including granulocyte-colony stimulating factor (G.C.S.F) as well as C.X.C motif ligands-1 and also motif ligands [6]. The generation of several proinflammatory cytokines, consisting of I 1. and TNF-alpha, as well as I 6. by monocyte cells, may help I 17. maintain the inflammatory network [7]. The pathogenesis of a number of inflammatory as well as autoimmune diseases is being linked to IL-17A. [8] Excessive IL-17 has been linked to a number of chronic illnesses, like multiple sclerosis, psoriasis, rheumatoid arthritis, inflammatory bowel illness, and transplant rejection, as well as systemic lupus erythematosus [9].

Macrophages and dendritic cells are two examples of activated antigen-presenting cells that generate the heterodimeric cytokine interleukin-23 (IL-23). The characteristic cytokine, I 12., shares a 40. subunit identical to the cytokine, which is composed of a distinct 19. subunit [10]. The research found that IL-23 immunohistochemistry resulted in positive cells in intra .follicular epithelium as well as peribulbar dermis of the destroyed hair.follicles of the prior-to-therapy lesion.scalp, whereas the following therapy A.A. scalp had fewer cells [11]. The progression of alopecia areata appears to be genetically predisposed [12]. Between 10 percent and 42 percent of AA cases are hereditary [13]. The approximated lifetime risk for matching twins is between 42% and 55%, while it is between 5% and 8% for first-degree relatives [14]. The majority of the genes that cause alopecia areata are found in the D.R. and D.Q.B. genes of the human hepatocellular DNA (H.L.A.) gene family [15].

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Aim of study:

Serum levels of interleukin-17A (IL-17A) as well as interleukin-23 (IL-23) in alopecia areata patients will be assessed during the present research, and their possible correlation with illness features like time frame, recurrence, and family history will be examined.

Materials and methods:

Sample size and research methods:

Forty alopecia areata patients as well as forty geographically corresponding healthy control participants were included during the current case-control research. The research project had been carried out in Al-Diwaniya Teaching Hospital in Al-Diwaniya Province from December 1, 2023, until April 1, 2024.

Patients and Sample Collection

Five milliliters of venous blood were carefully extracted from every participant utilizing single-use syringes. Three milliliters of the blood specimens were placed in gel tubes, allowed to coagulate at the ambient temperature, and subsequently centrifuged for ten minutes at 2,500 rpm in order to separate the two sections. The serum was then placed in Eppendorf tubes and stored at -20°C until the cytokines IL-17 and IL-23 were tested by ELISA. The remaining 2 mL of blood was extracted into EDTA tubes within a day, and its CD-25 levels were assessed using flow cytometry.

Inclusion Criteria:

- Patients clinically and trichoscopically diagnosed with alopecia areata.
- Presence of patchy hair loss and positive hair pull test.
- Supportive trichoscopic and nail signs.
- Family history of autoimmune diseases considered.
- Age- as well as sex-matched healthy controls.

Exclusion Criteria:

- Refusal to participate.
- Diagnoses other than alopecia areata.
- Unclear or uncertain diagnosis.
- Patients treated locally or systemically for alopecia areata.

Ethical Approval

The University of Al-Qadisiyah's College of Medicine Ethics Committee gave its approval to the study plan. Prior to enrollment, all individuals provided written informed consent. Participants' data was kept private and confidential at all times. Every method complied with the Declaration of Helsinki's ethical guidelines for studies involving human participants.

Statistical Analysis:

The information was examined using the S.P.S.S. edition. The continuous parameters have been defined as mean±standard deviation (S.D.) as well as using the independent-samples t-test or, if appropriate, the Mann-Whitney U-test. Categorical variables were assessed using the chi-square (χ^2) test. The Kruskal-Wallis test was used when comparing more than two groups. Statistical significance was defined as P-values below 0.05.

Results:

Demographic characteristics of patients with alopecia areata as well as healthy control subjects

The current research compressed forty patients diagnosed with having alopecia areata as well as forty age- and sex-matched healthy control subjects. The demographic details of both groups are presented in Table (1). The mean age for patients was 27.80±12.64 years, while the control group was 25.80±5.69 years. The mean age for two groups didn't vary significantly, according to statistical analysis (P=0.364). Furthermore, there wasn't a discernible difference between patients and controls in the age-group distribution of participants (P=0.118). In terms of gender, the control group had 18 men (45.0%) as well as 22 females (55.0%), while the patient group had 24 males (60.0%) as well as 16 females (40.0%). This difference in gender distribution was also not statistically significant (P=0.179). In order to reduce potential bias in case-control research, suitable matches must be confirmed by the lack of substantial variations in the distribution of age and gender among the two groups.

Table(1): Demographic Characteristics of Patients having Alopecia Areata as well as Matched Healthy Controls.

Characteristic	Patients $n = 40$	Healthy control $n = 40$	P
Age (years)			
Mean ±SD	27.80 ± 12.64	25.80 ± 5.69	0.364 † NS
Range	5 –65 years	18– 40 years	
< 20, *n* (%)	10 (25.0%)	7 (17.5%)	0.118 ¥ NS
20-29, *n* (%)	11 (27.5%)	20 (50.0%)	
≥ 30, *n* (%)	19 (47.5%)	13 (32.5%)	
Gender			
Male, *n* (%)	24 (60.0%)	18 (45.0 %)	0.179 ¥ NS
Female, *n* (%)	16 (40.0%)	22 (55.0%)	

n:Number cases; S.D:Standard Deviation; †: Independent Samples t-test; ¥: Chi-square test; N.S:none-Significant at P>0.05.

Frequency Distribution of Alopecia. Areata Patients

Based on Family History:

Among the 40 patients diagnosed with alopecia areata, 6 individuals (15.0%) reported a positive family history of the condition, while the remaining 34 patients (85.0%) had no family history of alopecia areata.

Interleukin-17A (IL-17A) level in patients having alopecia areata as well as healthy. control.

The findings of research comparing the levels of IL-17A in patients with alopecia areata as well as healthy control participants are shown in table (2). The mean IL-17 levels within patients having alopecia areata were 15.84±3.22 and 4.95±1.71, correspondingly; these levels were significantly higher in patients with alopecia areata than in healthy controls (P < 0.001).

Table(2): IL:17A level within patients having Alopecia.areata as well as healthy.control.

	Cases –control comparison		
	Patients $n = 40$	Healthy control $n = 40$	*P*
Interleukin-17A (IL-17A) levels			
Mean± SD	15.48 ± 3.28	4.95 ± 1.71	< 0.001 † HS
Range	10.49 – 23.00	0.21-12.29	

n:Number.Cases; SD:Standard.Deviation; †: Independent. Samples t.test; H.S: Highly.Significant at P≤0,001.

Frequency distribution of IL-17A levels according to some characteristics.

A comparison of IL-17A concentrations based on several attributes was conducted, and the outcomes are shown in table (3). According to the current findings, patients with less than a year's length had non-significantly elevated IL-17A concentrations compared to those in other groups (16.3±3.05 vs. 14.37±3.31 as well as 15.32±3.09, correspondingly; P=0.119). Additionally, individuals with a negative family history had non-significantly elevated mean levels of IL-17A compared to patients with a positive family history (15.57±3.25 vs. 14.96±3.73), correspondingly (P=0.678). Additionally, the current findings indicate that there is no significant variation in IL .17A concentrations based on illness recurrence (P=0.552).

Table (3) Frequency distributing of IL-17A levels based on some characteristics.

Characteristics		Mean ± SD	Range	*P*
Duration of disease	< 1 years n=18	16.63 ± 3.05	12.04–23.0	0.119 K NS
	1-3 years n=18	14.37 ± 3.31	10.49 –22.38	
	≥ 4 years n=4	15.32 ± 3.09	11.40-18.80	
Family history	Positive *n* = 6	14.96 ± 3.73	10.49 – 19.52	0.678 † NS
	Negative *n* = 34	15.57 ± 3.25	11.38- 23.00	
Recurrence of disease	Positive *n* =11	15.99 ± 3.06	11.44 – 20.64	0.552 † NS
	Negative *n* = 29	15.29 ± 3.39	10.49- 23.00	

n:Number.Cases; S.D: Standard.Deviation; †:Mann. Whitney test; K:Kruskal.Wallis test; N.S: none.Significant at P>0.05.

Interleukin.23 (IL.23) level within patients having Alopecia. areata as well as healthy.control.

The results of the research that compared the IL.23 levels in alopecia areata patients as well as healthy control subjects are displayed within figure (2) as well as table (4). Alopecia areata patients had significantly higher mean levels of IL.23 (P=0.001) than healthy controls, with mean levels of 774.51±80.21 as well as 1116.84±170.24 in the former.group, respectively.

Table (4): IL-23 level within patients having Alopecia.areata as well as healthy.control.

	Cases –control comparison		
	Patients $n = 40$	Healthy control $n = 40$	*P*
Interleukin-23 (IL-23) levels			
Mean± SD	1116.84 ± 170.24	774.51 ± 80.21	0.001 † S
Range	906.78 – 1530.81	608.32-892.54	

n:Number.Cases; S.D:Standard.Deviation;†: Independent. Samples t.test; S:Significant at P<0.05.

A comparison of IL-23 levels based on several attributes was conducted, and the outcomes are shown in table (5). According to the current findings, patients with less than a year's length had non-significantly higher I 23. levels than those in other groups (1151.08±174.4 vs. 1094.38±170.2 and 1063.85±161.3) (P=0.501). But the mean levels of IL-23 were non-significantly lower within patients with a positive family history compared to patients with a negative family history (1040.16±174.1 vs. 1130.38±168.6), respectively (P=0.236).Also, the present results show no significant difference of I 23. levels according to recurrence of disease (P=0.642). I

Table (5): Frequency distribution of IL-23 levels according to some characteristics

Characteristics		Mean ± SD	Range	P
Duration of disease	< 1 years n=18	1151.08 ± 174.4	926.14–1450.62	0.501 K NS
	1-3 years n=18	1094.38 ± 170.2	906.78 –1530.81	
	≥ 4 years n=4	1063.85 ± 161.3	950.38-1300.0	
Family history	Positive *n* = 6	1040.16 ± 174.1	922.59 –1390.88	0.236 † NS
	Negative *n* = 34	1130.38 ± 168.6	906.78 – 1530.81	
Recurrence of disease	Positive *n* =11	1137.5 ± 170.6	906.78 – 1530.81	0.642 † NS
	Negative *n* = 29	1109.0 ± 155.9	922.59 –1450.62	

n: number of cases; SD: standard deviation; †: Mann Whitney test; K: Kruskal–Wallis test; NS: not significant at P>0.05.

Discussion

The current investigation found that patients with alopecia areata (AA) had significantly higher serum evels of interleuki 17-A (I 17-A) and also interleuki 23- (I 23-) than did healthy controls. This finding supports the theory that Th17-related cytokines play a role in the immunopathogenesis of AA. The IL-17A levels in A.A. patients were found to be significantly higher (15.84±3.22) than in controls (4.95±1.71) (P<0.001). Several current research studies support these findings. According to Kaur et al. (2022), for instance, A.A. patients' serum as well as lesional skin had noticeably greater levels of IL17-A, which may be related to follicular inflammation as well as autoimmunity. [16]. Similarly, Wang et al. (2021) demonstrated increased expression of IL-17A in scalp biopsies of AA patients and correlated it with disease activity [17]. In contrast, a study by Yamazaki et al. (2020) found no statistically significant difference in IL-17 levels between mild and severe AA patients, although levels were elevated in both compared to controls, consistent with our finding that IL-17A levels did not significantly differ based on disease duration, recurrence, or family history (P > 0.05). [18]. IL-23 levels were also significantly elevated in AA patients (1116.84 ± 170.24) versus controls (774.51 ± 80.21) (P = 0.001). This result is in agreement with a study by Hou et al. (2023), which demonstrated increased IL-23 expression in peribulbar infiltrates and circulating levels in AA patients, highlighting its role in sustaining the Th17 inflammatory response [19]. Similarly, González-Moro et al. (2022) found significantly increased IL-23 serum levels in active AA and suggested its potential as a therapeutic target [20]. However, our results did not demonstrate significant correlations between IL-23 levels and disease characteristics such as duration, recurrence, or family history, which is in line with the findings of Barahimi et al. (2021), who also reported no association between cytokine levels and clinical features of AA [21]. In this study, 85% of patients had no family history of AA, and both IL-17A and IL-23 levels did not significantly differ based on familial status. This observation is comparable to findings by Petukhova et al. (2020), who reported that although genetic predisposition plays a key role, cytokine expression may be more reflective of current disease activity than hereditary background [22]. Taken together, our findings support the central role of the IL-23/IL-17 axis in AA pathogenesis. Elevated levels of these cytokines are indicative of an activated Th17-mediated immune response, which may contribute to hair follicle destruction. The lack of association with disease duration or family history suggests these cytokines are involved in both early and chronic stages, independent of genetic predisposition. Therapeutically, these insights are crucial. Biologic agents targeting IL-17 or IL-23 (such as secukinumab or ustekinumab) may offer promising treatment avenues for resistant or extensive AA, as suggested by early-phase clinical trials [23]. The research is subject to numerous limitations. First, because of the small specimen size, the results might not be as widely relevant as they could be. Second, the cross-sectional design precludes drawing conclusions about causality. Third, this study did not assess cytokine levels over time or in response to medication. Finally, no assessment of other immunological markers that might interact with I 17-A as well as I 23- was conducted.

Conclusion

This study found that patients with alopecia areata (A.A.) have significantly higher serum levels of IL-17A and IL-23 compared to healthy controls, highlighting the importance of the IL-23/IL-17 axis in the autoimmune attack on hair follicles. The elevated cytokine levels were not linked to disease duration, recurrence, or family history, suggesting they represent a core and early feature of disease activity rather than clinical severity. These findings support the potential of IL-17 and IL-23 as therapeutic targets, especially for chronic or resistant cases, and call for larger studies to evaluate the role of biologic therapies in A.A. management.

Recommendations:

Further large-scale, longitudinal studies are recommended to confirm the role of IL-17A and IL-23 in the pathogenesis of alopecia areata. Exploring the effect of targeted anti-IL-17/IL-23 therapies may provide new therapeutic strategies. Additionally, future research should investigate correlations between cytokine levels and treatment response or disease prognosis.

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