Alopecia areata (AA) is a common autoimmune dermatological disease that causes hair loss of variable severity in any hair-bearing area.\(^2\) It presents with different sizes and patterns of nonscarring hair loss mediated by targeted, organ-specific inflammatory responses of the hair follicles.\(^3,4\) There are several subtypes of alopecia, with patchy AA forming 90% of the cases. The remaining 10% include alopecia totalis (AT), alopecia ophiasis (AO), and alopecia universalis (AU), the last one being the severest and the most differentiated form of the disease.\(^2,5\) The incidence of all forms of AA in the general population varies depending on the studied ethnicity. Studies have reported a prevalence range of 0.5–6.9%.\(^6\)–\(^12\) The disease can present at any age, though it is rare in infants.\(^13\) The onset of AA has been estimated to occur in 60% of the patients before the age of 20 years, with a higher prevalence between ages 10 and 25 (70%).\(^14\) Although the disease seems to be equally distributed in both sexes, it is still debated whether AA is more predominant in males or females, depending on the studied population.\(^2,5,14,15\)

AA is a complex multifactorial disease with poorly understood etiology. The unpredictability of the phenotypic and genotypic variations associated with AA suggests the involvement of various environmental, immunological, epigenetic, and genetic factors.\(^2,16\) Immunity and genetics are likely to be the main contributors.\(^17\) It is evident from several studies that AA is triggered by autoimmune inflammatory processes, with cytokines as the vital players.\(^18\) Cytokines and interleukins (ILs) are subjected to several disease-association studies due to their critical role in the pathogenesis of various autoimmune diseases using candidate gene association studies, transcriptional profiling, and large-scale genome-wide association techniques.\(^1,14\) The genetic polymorphisms of cytokines are found to affect the transcriptional level of genes, causing

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**ABSTRACT**

*Objectives:* Alopecia areata (AA) is a multifactorial autoimmune disease with a strong genetic predisposition. A variety of genes involved in immunity and inflammatory responses, such as cytokines, are suspected to increase the risk of developing AA. In which, different interleukin (IL) genes that associated with several autoimmune diseases and AA in varied populations. The objective of this study was to investigate the possible genetic association of AA with ten variants of single nucleotide polymorphism (SNP) in \(IL12B\), \(IL13\), \(IL16\), \(IL17A\), and \(IL18\) genes among Jordanian patients. *Methods:* In this case-control study, peripheral blood samples of 152 Jordanian AA patients and 150 controls (total of 302 subjects) were collected, genomic DNA extracted and genotyped, based on which their allele and genotype frequencies were assessed. *Results:* In the rs11073001 SNP located in the exon region of the \(IL16\) gene, the A allele was distributed more frequently in AA patients \((p = 0.01)\). A difference was found between the patients and the controls for the rs17875491 SNP in the promoter region of the \(IL16\) gene \((p = 0.04)\). The mean age of onset was 27.3±12.6 with male predominance. Most patients (68.4%) were asymptomatic but some reported experiencing associated sensations before the hair loss episodes. The patchy patterns of alopecia were the most common (90.3%). Nail changes were found in 7.3% of the patients. *Conclusions:* The findings support the hypothesis of the involvement of \(IL16\) gene in the etiology of AA. Moreover, it emphasizes the variations in the genetic component of AA, as well as the clinical phenotypes among different ethnic groups.
interindividual variations and then affecting diseases outcome.\textsuperscript{14}  

Several IL genes have been selected in this study for several reasons, including \textit{IL12B}, \textit{IL13}, \textit{IL16}, \textit{IL17A}, and \textit{IL18}, are known to be associated with different autoimmune diseases and different significant clinical variables within alopecia patients, but their genetic variations that contribute to risk for AA are not well reported in the general population.\textsuperscript{18}  

In addition, these genes were selected on the basis of their known biological functions and their role in immune response.\textsuperscript{14,18}  

Moreover, in order to detect single nucleotide polymorphisms (SNPs) that could be associated with AA among the Jordanian population, several SNPs within these genes (\textit{IL12B} (rs3212227), \textit{IL13} (rs848), \textit{IL16} (rs17875486, rs17875491, rs11073001, rs1803275), \textit{IL17A} (rs2275913), and \textit{IL18} (rs187238, rs1946518, rs549908)) were selected based on previous association studies, for their position to guarantee the effects on gene expression level or based on a high degree of linkage disequilibrium (haplotype) between these SNPs. Therefore, this study aimed to determine whether these SNPs in the \textit{IL12B}, \textit{IL13}, \textit{IL16}, \textit{IL17A}, and \textit{IL18} genes involve in susceptibility to AA in the Jordanian population using the candidate gene approach and evaluate the epidemiological characteristics related to the disease.

\section*{METHODS}

This study was conducted under the provisions of the Human Ethics Standard in compliance with the Institutional Review Board (IRB) guidelines. The IRB committee at Jordan University of Science and Technology approved the conducting of this study in the Jordanian community (Ref. 13/104/2017). This granted the researchers the permission to recruit participants and collect their blood samples and clinical data. Written informed consent was obtained from participants/their parents (guardians). The subjects were \(N = 152\) dermatology patients diagnosed with AA (107 male; 45 female) who were attending dermatology clinics at the Jordanian Royal Medical Services hospitals, and King Abdullah II University Hospital in Jordan. The control group comprised of 150 patients (129 male; 21 female) with no history of AA, randomly selected from among the Jordanians attending the same clinics for other dermatological issues.

The patients were in the age range 13–67 years (mean 31.1±12.4), while that of the control group was 17–64 years (mean 33.9±9.8). The age groups of the entire cohort of 302 participants (study and control) were classified into three bands of 18 years each (13–31; 32–50; 51–69). Assessment of the patients was conducted according to the standard evaluation guidelines for AA identification.\textsuperscript{19}  

This study adopted the general characteristics for controls summarized and categorized in 2017 by AL-Eitan et al.\textsuperscript{20}  

Ten SNPs within the five candidate IL genes were selected based on their known implications in AA studies or association with other autoimmune diseases. Genomic DNA was isolated using Wizard\textsuperscript{\textregistered} Genomic DNA Purification Kit (Qiagen, Germany) was provided by Al-Eitan et al,\textsuperscript{20} upon a research collaboration. DNA samples were genotyped in duplicate with a success rate of \(\geq 95\%\) using the Sequenom MassARRAY\textsuperscript{\textregistered} system (iPLEX GOLD) (Sequenom, San Diego, CA, USA), in collaboration with the Australian Genome Research Facility.

Genotyping frequencies, including examination for ascertainment bias (because there were significantly more male patients in our study) were estimated by Hardy-Weinberg equilibrium (HWE) analysis using SPSS (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and the SNPStat web tool (https://www.snpstats.net/start.htm) as well as genotypic, allelic, and haplotype association. Odds ratio (OR) with 95\% CI was used, and \(p < 0.05\) was considered statistically significant. Deviations from HWE were assessed by the chi-square test.

\section*{RESULTS}

In this study, 152 Jordanian patients (107 male; 45 female) with AA were recruited. More than half (57.3\%) of the patients were affected by AA before their thirties. There were no significant differences in terms of age or gender among the participants. The mean age of the patients when they had their first episode of AA was 27.3±12.6 (range: 13–67 years). The vast majority (90.3\%) had the patchy form of alopecia, more frequently in the scalp (60.5\%) and face (23.0\%), with 5.3\% presenting patches in both areas, and 2.3\% in other body parts. The AU and AT were present in 6.6\% and 3.3\% patients, respectively. The nail abnormalities associated with the disorder (pitting, brittleness, striations) were seen in 7.3\%
patients. Although 68.4% of the patients were asymptomatic, approximately one-third (31.6%) reported having associated sensations such as pruritus (severe itchy skin) and burning.

The studied variants are in HWE standards for minor allele frequency between AA patients and healthy individuals [Table 1]. Allelic association with AA susceptibility showed no association, except for the exon variant of \( \text{IL16} \) gene (rs11073001, \( p = 0.01 \)), where A allele occurs more frequently among alopecia patients (74% vs. 71% in controls; Table 2). Moreover, evaluation of genotype frequency revealed the absence of any possibility to be involved in the disease development [Table 2]. Genetic association analysis using the genetic models (codominant, dominant, and recessive) revealed a significant difference between the AA patients and the controls in rs17875491 only, another \( \text{IL16} \) gene variant (\( p = 0.04 \), Table 3). Data concerning the genetic models for the other genes (\( \text{IL12B, IL13, IL17A, and IL18} \)) are not shown due to the lack of significant differences. Meanwhile, haplotype frequencies estimation of \( \text{IL16} \) and \( \text{IL18} \) variants also failed to show any association with AA in our cohort (\( p > 0.05 \), Table 4).

**DISCUSSION**

Although alopecia is often claimed to have the same incidence in both sexes,\(^ {2,9,10} \) our study shows a strong male predominance of 2.4:1, which indicates that males feel less stigmatized than female patients, in agreement with some previous reports.\(^ {21–24} \) In contrast, other studies showed a higher proportion of females,\(^ {25,26} \) and thus, the possibility of the effect of sex on disease frequency remains an enigma. The mean age of onset was comparable to Singapore (25.2 years)\(^ {25} \) and China (28.98±13.43 years),\(^ {3} \) but lower than in the USA (33.6 years)\(^ {9} \) and Taiwan (32.26±14.8 years).\(^ {27} \) Studies suggest that AA onset is more frequent in younger people.\(^ {10} \) Those in the 21–40-year age group are most likely to seek medical care than the 61–80-year age group.\(^ {25} \) The vast majority (90.3%) of our patients had the patchy hair loss pattern, universally the most predominant form of AA.\(^ {1,25,28,29} \) In addition, 7.3% of our patients had nail abnormalities. These are described to be more common in patients with severe forms of alopecia, the AT and the AU.\(^ {21,32} \) Globally, nail changes have been observed in 7–20% of AA cases, with a high prevalence as 44–66% reported in some populations.\(^ {1,32,33} \) Nail pitting is the most reported change.\(^ {32} \) Such wide variations in the prevalence of nail changes might also be attributed to being overlooked during the diagnostic procedure. Hair loss is asymptomatic in most patients as in our subjects though some of them reported that they felt itching or burning sensations prior to an episode of hair loss.

\( \text{IL12B, IL13, IL16, IL17A, and IL18} \) genes were selected in this study because variations in

### Table 1: Minor allele frequencies and their calculated Hardy–Weinberg equilibrium (HWE) \( p \)-values \((N = 302)\).

| Gene | SNP       | MA | AA cases \((n = 152)\) | Control \((n = 150)\) |
|------|-----------|----|------------------------|-----------------------|
|      |           |    | MAF | \( p^* \) (HWE) | MAF | \( p^* \) (HWE) |
| **IL16** | rs17875486 | T  | 0.37 | 0.16 | 0.40 | 0.86 |
|       | rs17875491 | C  | 0.23 | 0.11 | 0.22 | 0.16 |
|       | rs11073001 | G  | 0.26 | 0.02 | 0.29 | 0.23 |
|       | rs1803275  | A  | 0.05 | 0.31 | 0.06 | 0.46 |
| **IL18** | rs187238  | G  | 0.23 | 0.37 | 0.26 | 0.19 |
|       | rs1946518  | T  | 0.41 | 0.62 | 0.43 | 1.00 |
|       | rs549908   | G  | 0.24 | 0.51 | 0.25 | 0.27 |
| **IL12B** | rs3212227 | G  | 0.33 | 0.58 | 0.31 | 1.00 |
| **IL13** | rs848      | A  | 0.24 | 0.08 | 0.28 | 0.42 |
| **IL17** | rs2275913  | A  | 0.29 | 0.44 | 0.26 | 0.13 |

AA: Alopecia areata; MA: Minor Allele; MAF: Minor Allele Frequency; SNP: single nucleotide polymorphism.

\(^*\) All \( p \)-values are correct to two decimal places.
| Gene | SNP          | Allele/genotype | AA patients n (%) | Control n (%) | p-value |
|------|--------------|-----------------|-------------------|---------------|---------|
|      |              |                 | AA patients n (%) | Control n (%) |         |
|      |              |                 |                   |               |         |
|      |              |                 |                   |               |         |
| IL16 | rs17875486   | C               | 192 (63.2)        | 177 (59.8)    | 0.39    |
|      |              | T               | 112 (36.8)        | 119 (40.2)    |         |
|      |              | CC              | 65 (42.8)         | 52 (35.1)     | 0.30    |
|      |              | CT              | 62 (40.8)         | 73 (49.3)     |         |
|      |              | TT              | 25 (16.4)         | 23 (15.5)     |         |
|      | rs17875491   | G               | 232 (76.8)        | 229 (77.9)    | 0.87    |
|      |              | C               | 70 (23.2)         | 65 (22.1)     |         |
|      |              | CC              | 12 (7.9)          | 4 (2.7)       | 0.06    |
|      |              | GC              | 46 (30.3)         | 57 (38.8)     |         |
|      |              | GG              | 93 (61.2)         | 86 (58.5)     |         |
|      | rs11073001   | A               | 225 (74.0)        | 206 (70.5)    | 0.01    |
|      |              | G               | 79 (26.0)         | 86 (29.5)     |         |
|      |              | AA              | 89 (58.6)         | 76 (52.1)     | 0.50    |
|      |              | AG              | 47 (30.9)         | 54 (37.0)     |         |
|      |              | GG              | 16 (10.5)         | 16 (11.0)     |         |
|      | rs1803275    | G               | 287 (95.0)        | 277 (93.6)    | 0.24    |
|      |              | A               | 15 (5.0)          | 19 (6.4)      |         |
|      |              | AA              | 1 (0.7)           | 1 (0.7)       | 0.71    |
|      |              | GA              | 13 (8.6)          | 17 (11.5)     |         |
|      |              | GG              | 137 (90.1)        | 130 (87.8)    |         |
|      | IL18         | rs187238        | C                 | 232 (76.8)    | 224 (74.0) | 0.45 |
|      |              | G               | 70 (23.2)         | 78 (26.0)     |         |
|      |              | CC              | 91 (59.9)         | 86 (57.3)     | 0.66    |
|      |              | CG              | 50 (32.9)         | 50 (33.3)     |         |
|      |              | GG              | 10 (6.6)          | 14 (9.3)      |         |
|      | rs1946518    | G               | 178 (58.6)        | 167 (56.8)    | 0.64    |
|      |              | T               | 126 (41.4)        | 127 (43.2)    |         |
|      |              | GG              | 50 (32.9)         | 47 (32.0)     | 0.84    |
|      |              | GT              | 78 (51.3)         | 73 (49.7)     |         |
|      | rs549908     | T               | 230 (76.2)        | 220 (74.8)    | 0.21    |
|      |              | G               | 72 (23.8)         | 74 (25.2)     |         |
|      |              | GG              | 10 (6.6)          | 12 (8.2)      | 0.88    |
|      |              | TG              | 52 (34.2)         | 50 (34.0)     |         |
|      |              | TT              | 89 (58.6)         | 85 (57.8)     |         |
|      | II12B        | rs3212227       | T                 | 204 (67.1)    | 205 (69.3) | 0.69 |
|      |              | G               | 100 (32.9)        | 91 (30.7)     |         |
|      |              | GG              | 18 (11.8)         | 14 (9.5)      | 0.79    |
|      |              | TG              | 64 (42.1)         | 63 (42.6)     |         |
|      |              | TT              | 70 (46.1)         | 71 (48.0)     |         |
|      | II13         | rs848           | C                 | 227 (75.7)    | 213 (72.4) | 0.07 |
|      |              | A               | 73 (24.3)         | 81 (27.6)     |         |
|      |              | AA              | 13 (8.6)          | 13 (8.8)      | 0.52    |
|      |              | AC              | 47 (30.9)         | 55 (37.4)     |         |
|      |              | CC              | 90 (59.2)         | 79 (53.7)     |         |
|      | IL17A        | rs2275913       | G                 | 215 (70.7)    | 219 (74.5) | 0.53 |
|      |              | A               | 89 (29.3)         | 75 (25.5)     |         |
|      |              | AA              | 15 (9.9)          | 13 (8.8)      |         |
|      |              | GA              | 59 (38.8)         | 49 (33.3)     |         |
|      |              | GG              | 78 (51.3)         | 85 (57.8)     |         |

AA: Alopecia areata. SNP: single nucleotide polymorphism.
the immune system and inflammation mechanism genes are considered to increase AA susceptibility but are not fully elucidated. IL12B/rs3212227 and IL13/rs484 showed to lack genetic association with AA in Jordanians. IL12B is known to be associated with asthma and psoriasis, lack association with Crohn’s disease, rheumatoid arthritis, and AA in patients of Central European origin, and Turkey, consistent with this study. Contrarily, a recent study proved the association of IL12B (rs3212227) polymorphism with the probability to develop AA in Iranian patients. Another gene variant, IL13/rs484, was a susceptibility locus associated with atopic dermatitis in Europeans, Japanese, and Chinese populations. Association of this polymorphism needs further investigation using other robust genetic approaches, where to the best of our knowledge, there is a dearth of reports that investigate its association with AA. Meanwhile, other regions of IL13 were identified by genome-wide association in asthma, and alopecia.

Both rs17875486 and rs1803275 SNPs of the IL16 gene showed no linkage with AA susceptibility in this study, consistent with the findings in the Korean population. On the other hand, the A allele of rs11073001 and the homozygous CC genotype of rs17875491 may increase the risk for AA in Jordanian patients. Nevertheless, rs17875491 was significantly different between AA patients and controls, while rs11073001 differ between patients with and without a family history of AA. Overall, these findings suggest that IL16 gene may play a key role in AA pathogenesis. IL17A variant rs2275913, fail genetic association in the current report as well as in other IL17A variants. Despite our negative findings regarding rs187238, rs1946518, and rs549908 SNPs of IL18 gene, the latter two variants were associated with AA in the Turkish population. Therefore, IL18 variants are considered major contributors to the etiopathogenesis of AA in some populations.

A limitation in this study is its small sample size. Another is the significantly low proportion of

| Table 3: Genetic haplotype frequencies estimation of IL16 and IL18 genes. |
|-------------------------|-----------------|------------------------|-------------------------|-----------------|-----------------|--------------------------|
| Gene       | SNP            | Model       | Genotype | AA cases n (%) | Controls n (%) | OR (95% CI) | p-value |
|------------|----------------|-------------|----------|---------------|---------------|-------------|---------|
| IL16       | rs17875491     | Codominant  | G/G      | 93 (61.6)     | 86 (58.5)     | 1.00        | 0.06    |
|            |                |             | G/C      | 46 (30.5)     | 57 (38.8)     | 0.75 (0.46–1.21) |        |
|            |                |             | C/C      | 12 (8.0)      | 4 (2.7)       | 2.77 (0.86–8.93) |        |
|            |                | Dominant    | G/G      | 93 (61.6)     | 86 (58.5)     | 1.00        | 0.59    |
|            |                |             | G/C–C/C  | 58 (38.4)     | 61 (41.5)     | 0.88 (0.55–1.40) |        |
|            |                | Recessive   | G/G–G/C  | 139 (92)      | 143 (97.3)    | 1.00        | 0.04    |
|            |                |             | C/C      | 12 (8.0)      | 4 (2.7)       | 3.09 (0.97–9.80) |        |

SNP: single nucleotide polymorphism; AA: Alopecia areata; OR: odds ratio.

| Table 4: Genetic model associated with AA susceptibility (Data for IL16 gene only). |
|-------------------------|-----------------|------------------------|-------------------------|-----------------|-----------------|--------------------------|
| Gene       | Haplotype | AA cases n (%) | Control n (%) | Total n (%) | OR (95% CI) | p-value |
|------------|----------|----------------|--------------|-------------|-------------|---------|
| IL16       | TGAG     | 0.338          | 0.344        | 0.341       | 1.00        | –       |
|            | CCAG     | 0.220          | 0.210        | 0.215       | 1.07 (0.68–1.66) | 0.78    |
|            | CGGG     | 0.186          | 0.210        | 0.198       | 0.93 (0.59–1.46) | 0.74    |
|            | CGAG     | 0.177          | 0.140        | 0.159       | 1.26 (0.78–2.05) | 0.35    |
|            | CGGA     | 0.039          | 0.036        | 0.037       | 1.15 (0.47–2.82) | 0.77    |
|            | TGGA     | 0.012          | 0.027        | 0.020       | 0.48 (0.13–1.77) | 0.27    |
|            | TGGG     | 0.013          | 0.019        | 0.016       | 0.76 (0.17–3.42) | 0.72    |
| IL18       | CGT      | 0.575          | 0.569        | 0.572       | 1.00        | –       |
|            | GTG      | 0.226          | 0.253        | 0.239       | 0.90 (0.62–1.33) | 0.61    |
|            | CTT      | 0.181          | 0.173        | 0.177       | 1.04 (0.67–1.62) | 0.86    |

AA: Alopecia areata; OR: odds ratio.
women who were willing to participate, perhaps due to the social stigma attached to this condition.

**CONCLUSION**

Our findings indicate that there is a considerable association of IL16 gene in Jordanians affected by various forms of AA. In addition, the varied genetic components among ethnicities suggest the variation in genetic association and outcomes of the disease. When comparing the Jordanians with other populations, a variation in the type of correlation, if any, can be seen between AA and different polymorphisms. In view of the dearth of studies in Jordan on genetic associations of alopecia, more studies with larger sample sizes and more equitable representation of both sexes are suggested.

**Disclosure**

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**REFERENCES**

1. Pratt CH, King LF Jr. Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. Nat Rev Dis Primers 2017 Mar;3(1):7011.
2. Juárez-Rendón KJ, Rivera Sánchez G, Reyes-López MÁ, García-Ortiz JE, Bocanegra-García V, Guardiola-Avila I, et al. Alopecia Areata: Current situation and perspectives. Arch Argent Pediatr 2017 Dec;115(6):e404-e411.
3. Celik SD, Aras O. Genetic analysis of interleukin 18 genetic polymorphisms in alopecia areata. J Clin Lab Anal 2018 Jun;32(5):e22386.
4. Trüeb RM, Dias MF. Alopecia areata: a comprehensive review of pathogenesis and management. Clin Rev Allergy Immunol 2018 Feb;54(1):68-87.
5. Lee HH, Gwillim E, Patel KR, Hua T, Rastogi S, Ibler E, et al. Epidemiology of alopecia areata, ophiasis, totaills, and universalis: A systematic review and meta-analysis. J Am Acad Dermatol 2020 Mar;82(3):675-682.
6. Safavi KH, Muller SA, Suman VJ, Mossholl AN, Melton LJ III. Incidence of alopecia areata in Olmsted County, Minnesota, 1975 through 1989. InMayo Clinic Proceedings 1995 Jul 1 (Vol. 70, No. 7, pp. 628-633). Elsevier.
7. Safavi K. Prevalence of alopecia areata in the first national health and nutrition examination survey. Arch Dermatol 1992 May;128(5):702.
8. Yang S, Yang J, Liu JB, Wang HY, Yang Q, Gao M, et al. The genetic epidemiology of alopecia areata in China. Br J Dermatol 2004 Jul;151(1):16-23.
9. Mirzoyev SA, Schrum AG, Davis MD, Torgerson RR. Lifetime incidence risk of alopecia areata estimated at 2.1% by Rochester Epidemiology Project. 1990-2009. J Invest Dermatol 2014 Apr;134(4):1141-1142.
10. Villasante Frick AC, Mitteva M. Epidemiology and burden of alopecia areata: a systematic review. Clin Cosmet Investig Dermatol 2015 Jul;8:397-403.
11. Wolff H, Fischer TW, Blume-Peytavi U. Diagnostik und Therapie von Haar-und Kopfhauterkrankungen. Dtsch Arztebl 2016;113:377-386.
12. Alzolibani AA. Epidemiologic and genetic characteristics of alopecia areata (part 1). Acta Dermatovenereol Alp Pannonica Adriat 2011;20(4):191-198.
13. Jabbari A, Petukhova L, Cabral RM, Clynes R, Christiano AM. Genetic basis of alopecia areata: a roadmap for translational research. Dermatol Clin 2013 Jan;31(1):109-117.
14. Alzolibani AA, Zari S, Ahmed AA. Epidemiologic and genetic characteristics of alopecia areata (part 2). Acta Dermatovenereol Alp Pannonica Adriat 2012;22(1):15-19.
15. Qi J, Garza LA. An overview of alopecias. Cold Spring Harb Perspect Med 2014;4(3):a013615.
16. Petukhova L. An Imperative Need for Further Genetic Studies of Alopecia Areata. InJournal of Investigative Dermatology Symposium Proceedings 2020 Nov 1 (Vol. 20, No. 1, pp. S22-S27). Elsevier.
17. Simakou T, Butler JP, Reid S, Henriquez FL. Alopecia areata: A multifactorial autoimmune condition. J Autoimmun 2019 Mar;98:74-85.
18. Ito T, Tokura Y. The role of cytokines and chemokines in the T-cell-mediated autoimmune process in alopecia areata. Exp Dermatol 2014 Nov;23(11):787-791.
19. Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, et al; National Alopecia Areata Foundation. Alopecia areata investigational assessment guidelines—Part II. J Am Acad Dermatol 2004 Sep;51(3):S40-S47.
20. Al-Eitan LN, Al Momani RO, Al Momani KK, Al Warawrah AM, Aljamaa HA, Alghamdi MA, et al. Candidate gene analysis of alopecia areata in Jordanian population of Arab Descent: a case-control study. Appl Clin Genet 2019 Nov;12:221-228.
21. Sharma VK, Dawn G, Kumar B. Profile of alopecia areata in Northern India. Int J Dermatol 1996 Jan;35(1):22-27.
22. Golnicki H, Orfano CE. Alopecia areata: pathogenesis and clinical picture. In: Orfano CE, Happel R, editors. Hair and hair diseases. Springer, Berlin, Heidelberg; 1990. p. 529-569.
23. De Waard-van der Spek FB, Oranje AP, De Raeymaecker DM, Peereboom-Wynia JD. Juvenile versus maturity-onset alopecia areata—a comparative retrospective clinical study. Clin Exp Dermatol 1989 Nov;14(6):423-433.
24. Kavak A, Yeşildal N, Parlak AH, Gökdemir G, Aysögan I, Anul H, et al. Alopecia areata in Turkey: demographic and clinical features. J Eur Acad Dermatol Venereol 2002 Nov;16(5):e223-e229.
25. Jabbari A, Petukhova L, Cabral RM, Clynes R, Christiano AM. Epidemiologic and genetic characteristics of alopecia areata (part 1). Acta Dermatovenereol Alp Pannonica Adriat 2011;20(4):191-198.
26. Alzolibani AA. Epidemiologic and genetic characteristics of alopecia areata (part 2). Acta Dermatovenereol Alp Pannonica Adriat 2012;22(1):15-19.
27. Qi J, Garza LA. An overview of alopecias. Cold Spring Harb Perspect Med 2014;4(3):a013615.
28. Petukhova L. An Imperative Need for Further Genetic Studies of Alopecia Areata. InJournal of Investigative Dermatology Symposium Proceedings 2020 Nov 1 (Vol. 20, No. 1, pp. S22-S27). Elsevier.
29. Simakou T, Butler JP, Reid S, Henriquez FL. Alopecia areata: A multifactorial autoimmune condition. J Autoimmun 2019 Mar;98:74-85.
30. Ito T, Tokura Y. The role of cytokines and chemokines in the T-cell-mediated autoimmune process in alopecia areata. Exp Dermatol 2014 Nov;23(11):787-791.
31. Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, et al; National Alopecia Areata Foundation. Alopecia areata investigational assessment guidelines—Part II. J Am Acad Dermatol 2004 Sep;51(3):S40-S47.
32. Al-Eitan LN, Al Momani RO, Al Momani KK, Al Warawrah AM, Aljamaa HA, Alghamdi MA, et al. Candidate gene analysis of alopecia areata in Jordanian population of Arab Descent: a case-control study. Appl Clin Genet 2019 Nov;12:221-228.
29. Qi S, Xu F, Sheng Y, Yang Q. Assessing quality of life in Alopecia areata patients in China. Psychol Health Med 2015;20(1):97-102.

30. Sehgal VN, Jain S. Alopecia areata: clinical perspective and an insight into pathogenesis. J Dermatol 2003 Apr;30(4):271-289.

31. Gilhar A, Erzioni A, Paus R. Alopecia areata. N Engl J Med 2012 Apr;366(16):1515-1525.

32. Chelidze K, Lipner SR. Nail changes in alopecia areata: an update and review. Int J Dermatol 2018 Jul;57(7):776-783.

33. Strazzulla LC, Wang EH, Avila L, Lo Sicco K, Brinster N, Christiano AM, et al. Alopecia areata: Disease characteristics, clinical evaluation, and new perspectives on pathogenesis. J Am Acad Dermatol 2018 Jan;78(1):1-12.

34. Rajabi F, Drake LA, Senna MM, Rezaei N. Alopecia areata: a review of disease pathogenesis. Br J Dermatol 2018 Nov;179(5):1033-1048.

35. Padrón-Morales J, Sanz C, Dávila I, Muñoz-Bellido F, Lorente F, Isidoro-García M. Polymorphisms of the IL12B, IL1B, and TNFA genes and susceptibility to asthma. J Investig Allergol Clin Immunol 2013 Jan;123(7):487-494.

36. Randolph AG, Lange C, Silverman EK, Lazarus R, Silverman ES, Raby B, et al. The IL12B gene is associated with asthma. Am J Hum Genet 2004 Oct;75(4):709-715.

37. Nair RP, Ruether A, Stuart PE, Jenisch S, Tecjovi T, Hremagalore R, et al. Polymorphisms of the IL12B and IL23R genes are associated with psoriasis. J Invest Dermatol 2008 Jul;128(7):1653-1661.

38. Zwiers A, Seegers D, Heijmans R, Koch A, Hampe J, Nikolaus S, et al. Definition of polymorphisms and haplotypes in the interleukin-12B gene: association with IL-12 production but not with Crohn's disease. Genes Immun 2004 Dec;5(8):675-677.

39. Orozco G, González-Gay MA, Paco L, López-Nevo MA, Guzmán M, Pascual-Sáucedo D, et al. Interleukin 12 (IL12B) and interleukin 12 receptor (IL12RB1) gene polymorphisms in rheumatoid arthritis. Hum Immunol 2005 Jun;66(6):710-715.

40. Aytekin N, Akcali C, Pehlivan S, Kirtak N, Inaloz S. Investigation of interleukin-12, interleukin-17 and interleukin-23 receptor gene polymorphisms in alopecia areata. J Int Med Res 2015 Aug;43(4):526-534.

41. Tabatabaei-Panah PS, Moravvej H, Delpassand S, Jafari M, Sepehri S, Abgoon R, et al. IL12B and IL23R polymorphisms are associated with alopecia areata. Genes Immun 2020 May;21(3):203-210.

42. Ellinghaus D, Baurecht H, Espanza-Gordillo J, Rodríguez E, Matanovic A, Marenholz I, et al. High-density genotyping study identifies four new susceptibility loci for atopic dermatitis. Nat Genet 2013 Jul;45(7):808-812.

43. Xi L, Howard TD, Zheng SL, Haselkorn T, Peters SP, Meyers DA, et al. Genome-wide association study of asthma identifies RAD50-IL13 and HLA-DR/DQ regions. J Allergy Clin Immunol 2010 Feb;125(2):328-335.e11.

44. Jagielska D, Redler S, Brockschmidt FF, Herold C, Pasternack SM, Garcia Bartels N, et al. Follow-up study of the first genome-wide association scan in alopecia areata: IL13 and KIAA0350 as susceptibility loci supported with genome-wide significance. J Invest Dermatol 2012 Sep;132(9):2192-2197.

45. Lew BL, Chung JH, Sim HY. Association between IL16 gene polymorphisms and susceptibility to alopecia areata in the Korean population. Int J Dermatol 2014 Mar;53(3):319-322.

46. Lew BL, Cho HR, Hah S, Kim HJ, Chung JH, Sim HY. Association between IL17A/IL17RA gene polymorphisms and susceptibility to alopecia areata in the Korean population. Ann Dermatol 2012 Feb;24(1):61-65.

47. Kim SK, Park HJ, Chung JH, Kim JW, Seok H, Lew BL, et al. Association between interleukin 18 polymorphisms and alopecia areata in Koreans. J Interferon Cytokine Res 2014 May;34(5):349-353.