Dermatology Practical & Conceptual

The Relationship Between ABO and Rh Blood Groups with Alopecia Areata

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Key words: alopecia areata, blood group, ABO, Rh

Citation: Shirazi F, Shakoei S, Nasimi M, Abedini R. The relationship between ABO and Rh blood groups with alopecia areata. *Dermatol Pract Concept*. 2023;13(1):e2023060. DOI: https://doi.org/10.5826/dpc.1301a60

Accepted: April 28, 2022; **Published:** January 2023

Funding: It is financially supported by the vice-chancellor of research affairs of the Tehran University of Medical Sciences.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication

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ABSTRACT

Introduction: Alopecia areata (AA) is a common non-scaring hair loss disease. Genetic susceptibility and environmental factors can develop the disease.

Objectives: We investigated the association between AA and ABO and Rh blood groups.

Methods: This cross-sectional study was done on 200 patients with AA and 200 healthy controls (HCs) between March 2021 and September 2021.

Results: The prevalence of blood groups O, A, B, and AB in patients with AA was 30%, 30.5%, 10.5%, and 29%, respectively. A significant difference was detected between the two groups in the frequency of the ABO and ABO*Rh blood groups (p-value < 0.05). Compared to the HCs, the prevalence of the AB and AB+ blood group was higher in AA patients. No significant relationship was detected between sex, BMI, duration of disease, age at onset, severity of alopecia tool (SALT) score, hair loss pattern, and nail involvement with ABO and Rh blood groups (p-value > 0.05).

Conclusion: In conclusion, the highest difference was related to the AB+ blood group, so compared to HCs, the AB+ blood group frequency was higher in patients with AA. However, more studies with larger sample sizes on different ethnicities should be performed to verify the results of this study.

Introduction

Alopecia areata (AA) is a common non-scaring hair loss disorder. The prevalence of the disease is 1 in 1000 cases and has a lifetime incidence of 2% [1]. The prevalence of the disorders indicated above is expected to be roughly 0.2 percent in the overall population. Moreover, genetic susceptibility and environmental factors can also induce the disease to develop [2]. However, the specific cause of the disease is unidentified. There are several lines of evidence linking AA to autoimmune diseases, like type 1 diabetes mellitus (DM), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), vitiligo, and pemphigus Vulgaris [3-6].

Human gene variation, such as HLA systems, is defined by red cell isoenzymes, blood groups, hemoglobin variations, and serum proteins [7]. The ABO blood group system includes four O, A, B, and AB common blood groups. The presence of specific carbohydrate sugars on the surface of red blood cells distinguishes these different blood groups. A is identified by N-acetylgalactosamine, and B is identified as D-galactose for the B antigen. These sugars can be built on the H antigen, and in cases of the unmodified H antigen, the blood group will be O since the A and B antigens are unable to adhere to the surface of red blood cells [7]. The Rhesus blood group system is composed of Rhesus monkey erythrocyte antigens like the D antigen that can be found on the red cells of most Rh+ humans. This system is highly complicated, and some Rh alloantigens have yet to be biochemically described [8]. Because blood types are unaffected by environmental factors, they are a useful and essential resource in the pathogenesis of diseases. In this regard, many investigations have been conducted to study the relationship between cancer types, blood types, and other disorders [9].

Objectives

Also, some case series demonstrated substantial connections between blood groups and autoimmune disorders like multiple sclerosis, psoriasis, and pemphigus [10-12]. However, the exact nature of the linkage between blood groups and AA is not identified. Thus, we investigated the association between AA and ABO, and Rh systems.

Methods

The current cross-sectional study investigated the association between AA and ABO/Rh blood groups. The study was conducted on 200 cases with AA and 200 healthy controls (HCs) that attended our dermatology clinic in Hospitals between March 2021 and September 2021. Participants with other autoimmune and systemic disorders were excluded. The patients referred to the AA clinic were enrolled in the study and our healthy control objects were selected among people who did not have known systemic and skin disorders and were often referred for cosmetic problems. We matched age and sex between the two groups.

We followed the principles of the Helsinki Declaration. The Institutional Review Board of our university approved the protocol of this study. Informed consent was attained from all participants.

Statistical Analysis

SPSS version 20 (IBM Company, USA) was applied to analyze the variables. Continuous variables are displayed as mean (standard deviation), and categorical variables are reported as frequency (percentage). Student T-test (two-tailed) was applied for the comparison of continuous variables. The Chi-square or Fisher's exact test was employed for the comparison of the categorical variables between the two study groups. A P-value <0.05 was regarded as significant.

Results

Baseline Characteristics of Participants

Two hundred patients with AA and 200 HCs were included. The baseline characteristics of the subjects in the AA and HC groups are detailed in Table 1. The two study groups were comparable in terms of age, sex, and BMI.

Of 200 AA patients, 81 patients had patchy hair loss, 80 had Universalis hair loss, 35 had Totalis hair loss, and 3 had Ophiasis hair loss. Nail involvement was seen in 51 patients to some degree and in 19 patients as dystrophy (Table 1).

Comparison of Blood Groups Between AA Patients and HCs

Table 2 indicates the frequency of different types of blood groups in AA patients and HCs. ABO blood groups were significantly different between study groups (p=0.001). In this regard, the AA group showed a higher prevalence of the AB blood group, while the prevalence of the O, A, and B blood groups was higher in HCs (p=0.001). Nonetheless, no significant between-group differences were found based on O/non-O (p=0.391) and Rh (p=0.605) blood groups. Finally, ABO*Rh blood groups were significantly different between study groups (p=0.017). The most difference was related to the AB+ blood group, whose frequency was markedly higher in patients with AA compared to HCs (Table 2).

Association Between Blood Groups and Clinical Characteristics in Patients with AA

According to Table 3, no significant association was detected between sex, BMI, disease duration, age of onset, SALT

Table 1. Baseline characteristics of the patients in AA and HC groups.

	AA group (n=200)	HC group (n=200)	P-value
Age [years; mean (SD)]	33.26 (14.33)	33.73 (12.05)	0.726[a]
Sex [n (%)]			0.468[b]
• Male	77 (38.5%)	70 (35%)	
• Female	123 (61.5%)	130 (65%)	
BMI [kg/m^2; mean (SD)]	25.87 (17.86)	26.06 (23.11)	0.926[a]
Disease duration [years; mean (SD)]	8.56 (8.04)		
Age of onset [years; mean (SD)]	23.15 (12.94)		
Current episode [months; mean (SD)]	8.25 (7.71)		
SALT score [mean (SD)]	75.68 (29.93)		
The pattern of hair loss			
• Patchy	81 (40.6)		
• Universalis	80 (40%)		
• Totalis	35 (17.6%)		
• Ophiasis	3 (1.6%)		
Nail involvement			
• None	129 (64.6%)		
• Some	51 (25.6%)		
• Dystrophy	19 (9.6%)		

A P-value of < 0.05 was considered statistically significant.
SD: standard deviation
[a] Student T-test
[b] Chi-square test

Table 2. Comparison of different types of blood groups between AA and Healthy control group groups.

	AA group (n=200)	HC group (n=200)	P-value
ABO [n (%)]			**0.001**a
• O	60 (30%)	68 (34%)	
• A	61 (30.5%)	79 (39.5%)	
• B	21 (10.5%)	28 (14%)	
• AB	58 (29%)	25 (12.5%)	
Rh [n (%)]			0.605[a]
• Negative	17 (8.5%)	20 (10%)	
• Positive	183 (91.5%)	180 (90%)	
ABO*Rh [n (%)]			**0.017**b
• O-	9 (4.5%)	10 (5%)	
• A-	3 (1.5%)	5 (2.5%)	
• B-	3 (1.5%)	4 (3%)	
• AB-	2 (1%)	1 (0.5%)	
• O+	51 (25.5%)	58 (29%)	
• A+	58 (29%)	74 (37%)	
• B+	18 (9%)	24 (12%)	
• AB+	56 (28%)	24 (12%)	

HC: Healthy control. A P-value of < 0.05 was considered statistically significant.
a Chi-square test
b Fisher exact test

Table 3. Association between blood groups and clinical characteristics of patients with AA.

	O	A	B	AB	P-value	Rh -	Rh +	P-value
Sex [n (%)]					0.201[a]			0.201[a]
• Male	22 (36.7%)	30 (49.2%)	7 (33.3%)	18 (31%)		9 (52.9%)	115 (62.8%)	
• Female	38 (63.3%)	31 (50.8%)	14 (66.7%)	40 (69%)		8 (47%)	68 (37.2%)	
BMI [kg/m2; mean (SD)]	24.37 (4.00)	24.39 (4.62)	30.16 (35..47)	28.61 (35.31)	0.687[a]	25.87 (17.86)	26.06 (23.11)	0.926[a]
Disease duration [years; mean (SD)]	8.90 (8.68)	7.81 (7.55)	7.48 (8.02)	9.71 (7.93)	0.290[a]	8.83 (8.17)	6.75 (6.44)	0.310[a]
Age of onset [years; mean (SD)]	23.81 (11.61)	20.67 (11.30)	19.76 (9.43)	26.31 (16.06)	0.175[a]	23.03 (13.11)	24.41 (11.14)	0.667[a]
SALT score [mean (SD)]	71.80 (31.40)	77.44 (29.64)	82.66 (25.92)	75.31 (30.15)	0.508[a]	75.51 (30.71)	77.41 (28.06)	0.804[a]
Hair loss [n (%)]					0.544[a]			0.060[a]
• Patchy	28 (46.7%)	20 (33.3%)	8 (38.1%)	25 (43.1%)		7 (41.2%)	74 (40.7%)	
• Universalis	22 (36.7%)	29 (48.3%)	10 (47.6%)	19 (32.8%)		9 (52.9%)	71 (39%)	
• Totalis	9 (15%)	9 (15%)	3 (14.3%)	14 (24.1%)		0 (0%)	35 (19.2%)	
• Ophiasis	1 (1.7%)	2 (3.3%)	0 (0%)	0 (0%)		1 (5.9%)	2 (1.1%)	
Nail involvement [n (%)]					0.090[a]			0.457[a]
• None	39 (66.1%)	43 (70.5%)	16 (76.2%)	31 (53.4%)		13 (76.5%)	116 (63.7%)	
• Some	15 (25.4%)	15 (24.6%)	5 (23.8%)	16 (27.6%)		4 (23.5%)	47 (25.8%)	
• Dystrophy	5 (8.5%)	3 (4.9%)	0 (0%)	11 (19%)		0 (0%)	19 (10.4%)	

P-value of < 0.05 was considered statistically significant.
an Independent t-test

score, patterns of hair loss, nail involvement, and ABO/Rh blood groups in patients with AA ($p>0.05$).

Discussion

We assessed the relationship between AA and ABO and Rh blood groups. The prevalence of blood groups O, A, B, and AB in patients with AA was 30%, 30.5%, 10.5%, and 29%, respectively. A significant difference was detected between the two study groups regarding the frequency of the ABO blood group. The highest difference was related to the AB blood group, so compared to HCs, patients with AA showed a higher frequency of the AB blood group. The highest difference was related to the AB+ blood group, so compared to HCs, patients with AA showed a higher frequency of the AB+ blood group.

AA is a recurrent inflammatory disorder that affects people of all ages and genders. Despite the disease's importance, the specific etiology has yet to be fully understood. The ABO blood group family antigens have long been identified. Blood group alloantigens can be found on the membrane of epithelial cells and red blood cells. There is a link between blood types and various dermatologic conditions [9, 13, 14], leading to the elucidation of disease pathogenesis. For instance, malignant melanoma was found to have a statistically significant higher risk in patients with the O blood group [9]. Several previous reports have linked certain infections to specific ABO blood groups [15]. Tuberculoid leprosy is linked to the O blood group, while lepromatous leprosy is linked to the A and B blood groups, gonorrhea to the B blood group, smallpox to the A and B blood groups, and Escherichia coli O 157 infection to the O blood type [16]. Many studies have investigated the association between blood groups and autoimmune disorders like pemphigus Vulgaris, DM, RA, spondyloarthropathy, vasculitis, Behcet's disease, SLE, systemic sclerosis, and Sjogren's syndrome [10,17, 18]. Among these, no link was found between the ABO blood types and pemphigus Vulgaris, which is a well-known autoimmune skin disorder [18, 19]. In the etiopathogenesis of AA, autoimmunity is more prominent. Different researchers have established the relevance of T cells in the disease [20]. However, genetic variables play a role in illness susceptibility and severity as well. In single-twin investigations, the frequency of concurrent disease was found to be 55 percent, indicating that genetic and environmental variables play a role in the disease's development [20, 21]. The genes that code for blood group antigens are found on chromosome 9q34.2 (for the ABO blood group) and chromosome 1p36.11 (for the Rh blood group) [22].

Up to now, only two investigations have examined the relationship between blood type and AA. In 2018, İslamoğlu et al. [23] conducted a clinical study in Turkey to investigate the association between alopecia areata and ABO and Rh blood groups. They indicated a similar distribution of the ABO blood group in the patient and healthy groups. However, the Rh+ blood group was markedly higher in the healthy group than the patient group. Also, Rather et al. [24] conducted a case-control study in Kashmir to examine the relationship between ABO blood groups and different skin diseases (psoriasis, vitiligo, AA, pemphigus Vulgaris). Also, 37.1% of patients with psoriasis showed O blood group, followed by type B (30%) and A (25.7%), with no significant differences between study groups. In cases with vitiligo, 47.4% showed the B blood group, followed by blood groups O (36.8%) and A (10.5%). The frequency of A and B blood groups was significantly different between vitiligo patients and controls. In AA patients, blood group B was detected in 45.2% of patients, and groups O (28.6%) and A (19%) ranked second and third, with no significant differences between study groups. In patients with pemphigus Vulgaris, 40% of patients showed O and B blood groups, followed by blood group A (20%), with no significant differences between the groups. Contrary to the results of these studies, a significant difference was found between the two groups in our study. The highest difference was related to the AB+ blood group, so compared to the control group, patients with AA belonged to the AB blood group with higher frequency. We also examined the relationship between the characteristics of AA and the frequency of ABO and Rh blood groups; no significant association was detected between ABO or Rh blood groups and sex, BMI, disease duration, age of onset, SALT score, hair loss pattern, and nail involvement in patients with AA.

Conclusion

A significant difference was found between the two groups regarding the frequency of the ABO*Rh blood group. The frequency of the AB+ blood group was higher in patients with AA. Further studies could verify the results of this study.

References

1. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: a systematic review. *Clinical, cosmetic and investigational dermatology*. 2015;8:397-403. doi:10.2147/ccid.S53985
2. Sterkens A, Lambert J, Bervoets A. Alopecia areata: a review on diagnosis, immunological etiopathogenesis and treatment options. *Clinical and experimental medicine*. May 2021;21(2):215-230. doi:10.1007/s10238-020-00673-w
3. Chang Y-J, Lee Y-H, Leong P-Y, Wang Y-H, Wei JC-C. Impact of Rheumatoid Arthritis on Alopecia: A Nationwide Population-Based Cohort Study in Taiwan. Original Research. 2020-April-28 2020;7(150)doi:10.3389/fmed.2020.00150

4. Forouzan P, Cohen PR. Systemic Lupus Erythematosus Presenting as Alopecia Areata. *Cureus*. 2020;12(6):e8724-e8724. doi:10.7759/cureus.8724
5. Inamadar AC. Association of alopecia areata, vitiligo and pemphigus vulgaris. *Indian journal of dermatology, venereology and leprology*. May-Jun 1995;61(3):157-8.
6. Makino S, Uchihashi T, Kataoka Y, Fujiwara M. Recovery from alopecia areata in a patient with autoimmune polyglandular syndrome type 3. *Endocrinology, Diabetes & Metabolism Case Reports*. 01 Feb. 2015 2015;2015:14-0084. doi:10.1530/EDM-14-0084
7. Storry JR, Olsson ML. The ABO blood group system revisited: a review and update. *Immunohematology*. 2009;25(2):48-59.
8. Westhoff CM. The Rh blood group system in review: a new face for the next decade. *Transfusion*. Nov 2004;44(11):1663-73. doi:10.1111/j.0041-1132.2004.04237.x
9. de Giorgi V, Grazzini M, Gori A, et al. ABO blood group and risk of cutaneous malignant melanoma. *European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP)*. Mar 2011;20(2):121-2. doi:10.1097/cej.0b013e3283429e1d
10. Bakhtiari S, Toosi P, Azimi S, Esmaili N, Montazami A, Rafieian N. Is There a Relation between ABO Blood Groups and Clinical Outcome in Patients with Pemphigoid? A Case-Control Study. *Dermatol Res Pract*. 2016;2016:3916750-3916750. doi:10.1155/2016/3916750
11. Lopetegi I, Muñoz-Lopetegi A, Arruti M, et al. ABO blood group distributions in multiple sclerosis patients from Basque Country; O(-) as a protective factor. *Mult Scler J Exp Transl Clin*. 2019;5(4):2055217319888957-2055217319888957. doi:10.1177/2055217319888957
12. Tirant M, Scala J, Jafferany M, Goldust M, Sadoughifar R, Lotti T. Therapeutic and etiologic considerations related to blood group and triggers in psoriasis-A retrospective study. *Dermatologic therapy*. May 2020;33(3):e13401. doi:10.1111/dth.13401
13. Valikhani M KS, Toosi S, Kavand G, Ghiasi M. . ABO blood groups, rhesus factor and pemphigus. *Indian J Dermatol*. 2007;52:176-8
14. Eiermann TH, Vejbaesya S, Prestel H, Roepke A, Müller-Myhsok B, Schmitt-Egenolf M. Association and Linkage of Human Leukocyte Antigens with Psoriasis – Revisited. *Transfusion Medicine and Hemotherapy*. 2002;29(6):326-330. doi:10.1159/000068267
15. Garratty G. Blood groups and disease: a historical perspective. *Transfusion medicine reviews*. Oct 2000;14(4):291-301. doi:10.1053/tmrv.2000.16228
16. G. G. Relationship of blood groups to disease: do blood group antigens have a biological role? *Rev Med Inst Mex Seguro Soc*. 2005;(43(Suppl: 1):113-121.)
17. Çildağ S, Kara Y, Şentürk T. ABO blood groups and rheumatic diseases. *European journal of rheumatology*. Dec 2017;4(4):250-253. doi:10.5152/eurjrheum.2017.17044
18. Tirado-Sánchez A, Ponce-Olivera RM. ABO and Rhesus blood groups and their non-existent relationship with pemphigus vulgaris. *Acta dermatovenerologica Alpina, Pannonica, et Adriatica*. Oct 2010;19(3):47-8.
19. Shahkar H, Fallahzadeh MK, Namazi MR. ABO blood groups and pemphigus vulgaris: no relationship. *Acta dermatovenerologica Alpina, Pannonica, et Adriatica*. 2010;19(1):49-51.
20. Norris D. Alopecia areata: current state of knowledge. *Journal of the American Academy of Dermatology*. Jul 2004;51(1 Suppl):S16-7. doi:10.1016/j.jaad.2004.01.013
21. Martinez-Mir A, Zlotogorski A, Ott J, Gordon D, Christiano AM. Genetic linkage studies in alopecia areata. *The journal of investigative dermatology Symposium proceedings*. Oct 2003;8(2):199-203. doi:10.1046/j.1087-0024.2003.00809.x
22. Mouhari-Toure A, Saka B, Kombaté K, et al. Is There an Association between Keloids and Blood Groups? *ISRN Dermatology*. 2012/12/06 2012;2012:750908. doi:10.5402/2012/750908
23. İslamoğlu ZGK, Unal M. Is there an association of ABO blood groups and Rhesus factor with alopecia areata? 2018;17(6):1271-1274. doi:https://doi.org/10.1111/jocd.12491
24. Rather PA, Hassan I, Naaz S, Rasool F, Reshi R. Evaluation of ABO blood types in various dermatoses in Kashmiri population: A casecontrol study. *Journal of Pakistan Association of Dermatologists*. 01/01 2014;24:224-230.