

Understanding Alopecia Areata: Types, Causes, and Latest Therapeutic Approaches

Noorah Saleh Al-Sowayan*, Asal Khalid AlRebdi, Maryah Khalaf AlMarwani

Department of Biology, College of Science, Qassim University, Buraydah, Saudi Arabia

Email: *nsaoiean@qu.edu.sa

How to cite this paper: Al-Sowayan, N.S., Al-Rebdi, A.K. and AlMarwani, M.K. (2024) Understanding Alopecia Areata: Types, Causes, and Latest Therapeutic Approaches. *Journal of Biosciences and Medicines*, 12, 323-333. <https://doi.org/10.4236/jbm.2024.1211027>

Received: October 11, 2024

Accepted: November 15, 2024

Published: November 18, 2024

Copyright © 2024 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: Alopecia areata (AA) is a common autoimmune condition that causes hair loss. Affecting 0.5% - 2% of the population, AA manifests in several types, from mild to severe. **Objectives:** This study aimed to examine AA's etiology and innovative treatments of AA, presenting a comprehensive overview of existing and investigational therapies. **Methods:** We conducted a systematic literature review and screened recent studies to gain insight into treatment efficacy and outcomes. **Results:** The complexity of AA and the potential for novel therapies enhanced patients' quality of life. **Conclusions:** There is a need for further research into AA's genetic underpinnings of AA and more targeted treatments.

Keywords

Genetics, Microorganisms, Stress, Psychological Pressure, Covid 19

1. Introduction

Hair loss is considered widespread in recent years and has many degrees, as it begins with hair loss and may eventually lead to complete hair loss. There are many causes, the most important of which is alopecia areata, which is one of the most common types of alopecia recently among all [1] [2].

Alopecia areata (AA) is a chronic skin disease that affects approximately 0.5% - 2% of the world's population. It is a common hair loss condition that occurs when an individual's immune system attacks hair follicles. It is one of the most common autoimmune diseases and one of the most well-known unsolved clinical problems, attracting the interest of dermatologists, hair biologists, and immunologists because of the lack of fully satisfactory treatment [3].

This disease affects all ages and genders, both male and female, and usually occurs in adulthood and between the ages of 25 and 36 - 40 years. It is also possible that it affects children under the age of ten, and alopecia areata in this case is more extensive and advanced, according to the Alopecia Areata Foundation. Alopecia areata affects approximately 7 million people in the United States. Between 2010 and 2017, more than 140,000 children were diagnosed in the United States, and the highest rate was in the 11 - 12 year age group, with a prevalence of approximately 0.23% [2] [4].

In addition, it has been found that the number of cases of alopecia areata in children is increasing every year. However, the diagnostic process varies between sexes, as males are diagnosed in childhood, whereas females are diagnosed in adulthood [5] [6].

2. Types

Many types of injuries are classified according to the location or degree of injury (Table 1).

Table 1. The types of alopecia and the differences between them [1] [7].

Types	Definition
Alopecia barbae	This type specifically affects the beard area in men, causing patchy or complete hair loss in that region.
Alopecia totalis	This type involves the complete loss of hair on the scalp.
Alopecia universalis	This is the most dangerous type, is rare, and leads to the loss of all hair on the person's scalp and includes areas of the body other than the head.
Alopecia areata (patchy)	This is the most common type, characterized by one or more coin-sized patches of hair loss on the scalp or other hair-bearing areas of the body (Figure 1).
Alopecia ophiasis pattern	In this pattern, hair loss occurs in a band-like shape along the sides and lower back of the scalp (Figure 2).



Figure 1. Alopecia areata—patchy [8].



Figure 2. Ophiasis [9].

In most cases of alopecia areata, recovery occurs spontaneously within one year, but approximately 25% of patients develop severe alopecia with complete loss of scalp hair, called alopecia totalis, or all hair on the body is affected, called alopecia universalis, which often lasts for an unknown period [2] [3] [7].

3. Etiology

To date, the causes of alopecia areata are complex, as they include genetic and environmental factors, and it is also possible that they are caused by a group of genetic and environmental factors interacting together. In some people, severe stress or anxiety may be an important factor in the development of alopecia areata [4] [8] [10].

3.1. The Genetics

It is a complex disease for doctors, as it is not clear why the immune system attacks healthy hair follicles in people with genetic variation in the first place. What raises doubts about the disease being linked to genetics is that about 20% of people with alopecia areata have at least one family member who is also infected with the disease, and other studies have confirmed that most cases of this disease have no family history of this disease. However, there is a link between the incidence of alopecia areata in people with hereditary diseases, such as psoriasis and vitiligo, and scientists have indicated that genetics plays an important role in the incidence of alopecia areata, as they have linked a number of genes that play prominent roles in the functioning of the immune system, which may affect this disease [5] [8].

It can be considered that alopecia areata is a disease linked to multiple genetic factors, which means it is polygenic. However, not everyone who has the genes gets the disease. For example, identical twins have the same genes that cause the disease; however, if one twin has alopecia areata, there is only a 55% chance that the other twin will have it. In recent years, with great progress in the field of genetic research, a large number of specific sites associated with genes that affect alopecia areata have been discovered, and some genes that have been significantly

linked to alopecia areata, such as PTPN22, CTLA4, and IL2, which is due to the role of genetics in the genetic analysis of miRNAs in decisively revealing the role of miRNAs in regulating gene expression, which helps in understanding cellular and organic functional regulatory mechanisms, and understanding the mutual relationships between alopecia areata and other immune diseases, it helps in understanding and interpreting the possible common genetic foundations or pathogenic mechanisms between different diseases [4] [5] [8].

In 2018, a study was published in which researchers aimed to detect specific genetic variations associated with alopecia areata by conducting a genome-wide association study. GWAS involves scanning the genomes of individuals affected by a particular condition and comparing them with those of unaffected individuals to identify the genetic variations associated with the disease. Researchers collected DNA samples from individuals with alopecia areata and from unaffected individuals and analyzed these samples to identify single nucleotide polymorphisms (SNPs), which are single-nucleotide variations within a DNA sequence that are more prevalent in individuals with alopecia areata than in those without alopecia areata [11].

Through this analysis, researchers have identified several genetic risk loci or specific regions of the genome that are significantly associated with alopecia areata. These loci contain genes or regulatory elements that are likely to play a role in the development or onset of these conditions [11] [12].

Genetic Risk: This study sheds light on the underlying genetic factors that contribute to susceptibility to alopecia areata. This information is essential for understanding the biological mechanisms associated with this condition, and may lead to the development of targeted treatments or interventions in the future [11] [12].

Overall, this study provides valuable insights into the genetic basis of alopecia areata and lays the foundation for further research aimed at unraveling the complex interplay between genetics, environmental factors, and immune dysregulation in the disease [13].

3.2. Microorganisms

There is ongoing research on the possible relationships between A. areata and other microorganisms. Although the exact cause remains unclear, some studies have suggested a potential role of microbial dysbiosis in triggering or exacerbating the condition. A study published in the *Journal of Investigative Dermatology Symposium Proceedings* in 2015 proposed that changes in skin microbiota could contribute to the development of alopecia areata. Another study published in the *Journal of Clinical Medicine* in 2019 investigated the role of gut microbiome in autoimmune diseases, including alopecia areata, and suggested a potential link between gut dysbiosis and immune-mediated hair loss [14] [15].

These studies provide insights into the possible involvement of microorganisms in alopecia areata, but more research is needed to fully understand the mechanisms and potential therapeutic implications [14] [15].

3.3. Psychological Stress

Mental stress has several physiological effects in humans, and research has shown that acute stress frequently causes immunological hyperactivation in the central and peripheral nervous systems, leading to the onset of a number of autoimmune disorders [16]. Emotional or psychological stress may affect the appearance of alopecia areata, but in most cases and so far, there is no clear cause [5].

Previous studies have shown that oxidative stress is a potential factor in AA development. Oxidative stress is defined as an imbalance between oxidation and antioxidant processes in the body. Reactive oxygen species (ROS) are produced as a result of oxidative stress, and abnormal ROS production has been linked to several skin conditions, including AA [18].

This occurs when the generation of reactive species increases or antioxidant activity decreases. It is crucial to remember that although stress and oxidative stress may play a role in the pathophysiology of AA, they are not the only ones [17] [18].

4. Pathophysiology

Abnormal T and B lymphocytes in patients with AA secrete cytokines and auto-antibodies that attack hair follicle cells, leading to hair loss.

These immune cells release cytokines, such as interferon- γ and tumor necrosis factor, when they enter the hair follicles and then induce apoptosis of the hair follicle cells. AA is an autoimmune disease characterized by immune-mediated hair loss, and the pathophysiology that is currently understood to be responsible for this disease centers largely on immune privilege violations. The term “immune privilege” describes a situation in which some tissues or areas suppress the immune system to defend against immunological assault [4].

Alopecia areata is primarily caused by immunological dysregulation that follows the loss of immune privilege in hair follicles [19].

The hair development cycle is comprised of three phases: anagen (growth stage), catagen (transition stage), and telogen (resting period). A new cycle starts when telogen hairs are shed and replaced by anagen hairs [20].

Alopecia areata is a frequent type of immune-mediated alopecia characterized by a variety of circular patches on the scalp and non-scarring hair loss resulting from an autoimmune attack on the hair follicle [21].

5. Symptoms and Diagnosis

People suffering from alopecia are completely healthy and do not affect their health as they only cause hair loss; they usually begin with a sudden loss in the form of a round or oval spot on the scalp and sometimes include some other areas such as the eyebrows or beard in men and often there are broken hairs in this place, which is called the “exclamation mark”, and there is no skin rash, redness, or scarring on the bare spots [5] [10].

However, hair grows again within a few months, and at the beginning of its

growth, it takes on a white or gray color and regains its natural color over time. Sometimes, hair grows back in the first patch, whereas new bare patches form, and small patches sometimes join to form larger patches. Very rarely, all hair is lost from the entire scalp, which is called alopecia universalis in some cases, people feel tingling, burning, or itching in patches of skin immediately before hair loss. Also, in some other cases, alopecia areata results. Changes in nails [5] [10].

The diagnosis of alopecia areata is often based on a history of hair loss and symptoms. As mentioned previously, one of the most obvious symptoms of alopecia is hair loss; however, the appearance of hair loss (its appearance) varies from one type to another [10].

Hair loss involves many aspects for an accurate diagnosis. For example, are the resulting spots small, round, or oval and where are they located? Is it on the scalp or in areas of the body where there is hair loss on one or both sides and how quickly hair grows after loss [10].

6. Current Medications

Currently, there is no specific treatment to cure or prevent alopecia. On the other hand, treatment experiences are somewhat limited, and if the alopecia is at its beginning, the first-line treatment includes corticosteroid injections into the areas of hair loss or topical steroids applied to the same areas. If these two treatments fail, topical minoxidil (Rogaine) is used, which increases hair growth by accelerating the natural hair growth cycle, and is used as a second-line treatment with or as an alternative to the first treatment. It usually takes several weeks before hair growth can be observed [1] [7] [10] [22].

Different treatments can be used to help reduce the severity of hair loss or to help with hair growth, such as injecting creams that contain cortisone at a high concentration in the bald area, using a group of dedicated topical medications that are administered under the supervision of a dermatologist, or light therapy that is used in more complex cases to suppress the immune system [7] [10] [22].

Some commonly used medications include:

1) Corticosteroids can be administered as injections into the scalp (intralesional corticosteroid injections) or applied topically in the form of cream, ointment, or foam. Corticosteroids help reduce inflammation and suppress the immune response that attacks hair follicles [23].

2) Topical Immunotherapy: This treatment involves the application of chemicals such as diphencyprone (DPCP) or squaric acid dibutyl ester (SADBE) to the scalp, which induces an allergic reaction. This reaction can stimulate the immune system to target and destroy cells, causing hair loss and potentially triggering hair regrowth [24].

3) Minoxidil (Rogaine): Minoxidil is a topical medication available over-the-counter. It is applied directly to the scalp and can stimulate hair growth in individuals with alopecia areata [25].

4) JAK Inhibitors: Janus kinase (JAK) inhibitors, such as tofacitinib and

ruxolitinib, are oral medications that modulate the immune response and have shown promise in treating alopecia areata. They are typically prescribed off-label in severe cases, or when other treatments fail [25] [26].

5) Biologics: Biologic drugs such as adalimumab (Humira) and ustekinumab (Stelara), which target specific components of the immune system, are being investigated for their potential in treating alopecia areata [27] [28].

It is important to consult a dermatologist to determine the most suitable treatment option based on the individual's condition and medical history. Additionally, some treatments may have side effects or require long-term use for sustained results.

The effectiveness of alopecia areata medications can vary depending on factors such as the severity of the condition, type of alopecia areata (*e.g.*, patchy or extensive), and individual response to treatment. Corticosteroid injections are often effective for localized hair loss but may not be suitable for widespread baldness. Topical immunotherapy has shown promise, especially in severe cases, in stimulating hair regrowth. Minoxidil can help promote hair growth in some individuals, whereas JAK inhibitors such as tofacitinib and ruxolitinib have demonstrated efficacy in treating moderate-to-severe alopecia areata. Overall, the effectiveness of these medications differs from person to person, and health care professionals can help determine the most appropriate treatment based on individual circumstances [29]-[32].

7. The Relationship of Alopecia Areata to Covid-19

Covid-19 may not cause alopecia, but due to some side effects of Covid-19 vaccines, it may cause alopecia, there is a study in 2022 that includes a 51-year-old American man who is in good health and does not suffer from immune or genetic diseases. He suddenly experienced gradual hair loss in his head and beard accompanied by itching. This occurred after he received Pfizer-BioNTech COVID-19 vaccine (BNT162b2). After diagnosis by doctors, it was found that he was suffering from alopecia areata (**Figure 3** and **Figure 4**), In the same year, another case was recorded in a 44-year-old woman who suffered from hair loss after taking the Johnson & Johnson coronavirus vaccine. After the diagnosis, it was found that she had alopecia areata; however, her health condition turned out to be good, and after nearly four months she had lost almost all of her hair, even though she was taking triamcinolone (**Figure 3** and **Figure 4**) [33].

In addition, studies have shown that a 31-year-old man who did not suffer from autoimmune diseases, hypersensitivity reactions to previous vaccines, or a family history of alopecia suddenly experienced severe hair loss of approximately 100 - 150 hairs per day, accompanied by the appearance of many spots (**Figure 5**). He had received He received the second dose of the Covid-19 vaccine (Pfizer, New York, NY, USA) three weeks before the visit and told the doctors that he noticed hair loss after the first day of receiving the vaccine [33].



Figure 3. Before he took COVID-19 vaccine [33].



Figure 4. After he took COVID-19 vaccine [33].



Figure 5. Multiple patches of alopecia areata involving the temporo-parietal (A), occipital (B), and vertex areas (C). Patches of alopecia areata involving the beard (D). Written informed consent for publication of this image was obtained from the patient [33].

8. Conclusion

Alopecia areata presents challenges owing to its complex etiology involving genetic, environmental, and psychological factors. Although treatments such as

corticosteroids, JAK inhibitors, and minoxidil offer some relief, further research is needed to develop targeted therapies. This study suggests a future focus on genetic research to identify personalized treatment strategies.

Conflicts of Interest

The authors declare no conflict of interest related to this study.

References

- [1] Pratt, C.H., King, L.E., Messenger, A.G., Christiano, A.M. and Sundberg, J.P. (2017) Alopecia areata. *Nature Reviews Disease Primers*, **3**, Article No. 17011. <https://doi.org/10.1038/nrdp.2017.11>
- [2] Roland, J. (2022). What Are the Different Types of Alopecia? <https://www.healthline.com/health/alopecia-types>
- [3] Gordon, K., Gordon, K. and Tosti, A. (2011) Alopecia: Evaluation and Treatment. *Clinical, Cosmetic and Investigational Dermatology*, **4**, 101-106. <https://doi.org/10.2147/ccid.s10182>
- [4] Ho, C., Wu, C., Chen, J.Y. and Wu, C. (2023) Clinical and Genetic Aspects of Alopecia Areata: A Cutting Edge Review. *Genes*, **14**, Article 1362. <https://doi.org/10.3390/genes14071362>
- [5] NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases (2021) Alopecia Areata. <https://www.niams.nih.gov/health-topics/alopecia-areata>
- [6] Caldwell, A. (2023) Everything You Need to Know about Alopecia Areata. <https://www.healthline.com/health/alopecia-areata>
- [7] Rambawasvika, H. (2021) Alopecia Types, Current and Future Treatment. *Journal of Dermatology & Cosmetology*, **5**, 93-99. <https://doi.org/10.15406/jdc.2021.05.00190>
- [8] Mayo Clinic (2024) Hair Loss. <https://www.mayoclinic.org/diseases-conditions/hair-loss/symptoms-causes/syc-20372926>
- [9] Trüeb, R.M. and Dias, M.F.R.G. (2017) Alopecia Areata: A Comprehensive Review of Pathogenesis and Management. *Clinical Reviews in Allergy & Immunology*, **54**, 68-87. <https://doi.org/10.1007/s12016-017-8620-9>
- [10] Healthdirect (2022) Alopecia (Hair Loss). <https://www.healthdirect.gov.au/alopecia>
- [11] Betz, R.C., Petukhova, L., Ripke, S., Huang, H., Menelaou, A., Redler, S., *et al.* (2015) Genome-wide Meta-Analysis in Alopecia Areata Resolves HLA Associations and Reveals Two New Susceptibility Loci. *Nature Communications*, **6**, Article No. 5966. <https://doi.org/10.1038/ncomms6966>
- [12] McElwee, K.J., Gilhar, A., Tobin, D.J., Ramot, Y., Sundberg, J.P., Nakamura, M., *et al.* (2013) What Causes Alopecia Areata? Section Editors: Ralf Paus, Manchester/Lübeck and Raymond Cho, San Francisco Controversies in Experimental Dermatology: What Causes Alopecia Areata? *Experimental Dermatology*, **22**, 609-626. <https://doi.org/10.1111/exd.12209>
- [13] Petukhova, L., Christiano, A.M. and Duvic, M. (2018) Genetic Susceptibility to Alopecia Areata: GWAS, Candidate Gene, and Whole-Genome Approaches. *Journal of Investigative Dermatology*, **138**, 37-43.
- [14] Tursi, A. and Brandimarte, G. (2019). The Microbiome in Dermatology. *Journal of Clinical Medicine*, **8**, Article 1309.
- [15] Jabbari, A. and Petukhova, L. (2015) Alopecia Areata: Molecular Signaling Pathways,

- Immune Cell Populations, and Therapeutic Targets. *Journal of Investigative Dermatology Symposium Proceedings*, **17**, 35-37.
- [16] Ahn, D., Kim, H., Lee, B. and Hahm, D. (2023) Psychological Stress-Induced Pathogenesis of Alopecia Areata: Autoimmune and Apoptotic Pathways. *International Journal of Molecular Sciences*, **24**, Article ID: 11711. <https://doi.org/10.3390/ijms241411711>
- [17] Ma, Y., Sun, Z., Li, Y. and Xu, H. (2023) Oxidative Stress and Alopecia Areata. *Frontiers in Medicine*, **10**, Article 1181572. <https://doi.org/10.3389/fmed.2023.1181572>
- [18] Peterle, L., Sanfilippo, S., Borgia, F., Cicero, N. and Gangemi, S. (2023) Alopecia Areata: A Review of the Role of Oxidative Stress, Possible Biomarkers, and Potential Novel Therapeutic Approaches. *Antioxidants*, **12**, Article 135. <https://doi.org/10.3390/antiox12010135>
- [19] Lepe, K., Syed, H.A. and Zito, P.M. (2023) Alopecia Areata. *StatPearls*.
- [20] Suchonwanit, P., Kositkuljorn, C. and Pomsoong, C. (2021) Alopecia Areata: An Autoimmune Disease of Multiple Players. *ImmunoTargets and Therapy*, **10**, 299-312. <https://doi.org/10.2147/itt.s266409>
- [21] Minokawa, Y., Sawada, Y. and Nakamura, M. (2022) Lifestyle Factors Involved in the Pathogenesis of Alopecia Areata. *International Journal of Molecular Sciences*, **23**, Article 1038. <https://doi.org/10.3390/ijms23031038>
- [22] Dahabreh, D., Jung, S., Renert-Yuval, Y., Bar, J., Del Duca, E. and Guttman-Yassky, E. (2023) Alopecia Areata: Current Treatments and New Directions. *American Journal of Clinical Dermatology*, **24**, 895-912. <https://doi.org/10.1007/s40257-023-00808-1>
- [23] Gupta, A.K. and Foley, K.A. (2017) A Critical Assessment of the Evidence for Topical Corticosteroids in the Treatment of Alopecia Areata. *Journal of Drugs in Dermatology*, **16**, 778-782.
- [24] Alkhalifah, A., Alsantali, A., Wang, E., McElwee, K.J. and Shapiro, J. (2010) Alopecia Areata Update: Part I. Clinical Picture, Histopathology, and Pathogenesis. *Journal of the American Academy of Dermatology*, **62**, 177-188. <https://doi.org/10.1016/j.jaad.2009.10.032>
- [25] Mackay-Wiggan, J., Jabbari, A., Nguyen, N., Cerise, J.E., Clark, C., Ulerio, G., *et al.* (2016) Oral Ruxolitinib Induces Hair Regrowth in Patients with Moderate-to-Severe Alopecia Areata. *JCI Insight*, **1**, 1768-1771. <https://doi.org/10.1172/jci.insight.89790>
- [26] Xing, L., Dai, Z., Jabbari, A., Cerise, J.E., Higgins, C.A., Gong, W., *et al.* (2014) Alopecia Areata Is Driven by Cytotoxic T Lymphocytes and Is Reversed by JAK Inhibition. *Nature Medicine*, **20**, 1043-1049. <https://doi.org/10.1038/nm.3645>
- [27] Guttman-Yassky, E., Nia, J.K., Hashim, P.W., Mansouri, Y., Alia, E., Taliercio, M., *et al.* (2018) Efficacy and Safety of Secukinumab Treatment in Adults with Extensive Alopecia Areata. *Archives of Dermatological Research*, **310**, 607-614. <https://doi.org/10.1007/s00403-018-1853-5>
- [28] Craiglow, B.G. and King, B.A. (2014) Killing Two Birds with One Stone: Oral Tofacitinib Reverses Alopecia Universalis in a Patient with Plaque Psoriasis. *Journal of Investigative Dermatology*, **134**, 2988-2990. <https://doi.org/10.1038/jid.2014.260>
- [29] Strazzulla, L.C., Wang, E.H.C., Avila, L., Lo Sicco, K., Brinster, N., Christiano, A.M., *et al.* (2018) Alopecia Areata: Disease Characteristics, Clinical Evaluation, and New Perspectives on Pathogenesis. *Journal of the American Academy of Dermatology*, **78**, 1-12. <https://doi.org/10.1016/j.jaad.2017.04.1141>
- [30] Gregoriou, S., Papafragkaki, D., Kontochristopoulos, G., *et al.* (2007) Treatment of Alopecia Areata with Topical Calcipotriol. *Journal of the European Academy of*

Dermatology and Venereology, **21**, 773-774.

- [31] Fertig, R.M., Gamret, A.C., Darwin, E., Gaudi, S. and Patel, N. (2018) Microneedling for the Treatment of Hair Loss? *Journal of the European Academy of Dermatology and Venereology*, **32**, 564-569.
- [32] Liu, L.Y., Craiglow, B.G., Dai, F. and King, B.A. (2017) Tofacitinib for the Treatment of Severe Alopecia Areata and Variants: A Study of 90 Patients. *Journal of the American Academy of Dermatology*, **76**, 22-28.
- [33] Gallo, G., Mastorino, L., Tonella, L., Ribero, S. and Quaglino, P. (2022) Alopecia Areata after COVID-19 Vaccination. *Clinical and Experimental Vaccine Research*, **11**, 129-132. <https://doi.org/10.7774/cevr.2022.11.1.129>