

Review Article



A Comprehensive Relation of Psychological Disorders and Alopecia areata

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ABSTRACT

Alopecia areata is considered to be an immune-mediated disease. Nowadays many people are affected with the *Alopecia areata* associated with the psychological disorders such as anxiety. This disease generally occurs in the diffuse and patchy forms. Choice of the treatment mainly depends on the duration, severity, age and extent of the disease. Currently there is no specific treatment is available for providing complete cure from the disease but some natural home remedies and natural herbs as ayurvedic treatment is available. Natural herbs are used in different forms of the formulations such as oil, ointment, churna etc. and these provide cure from the disease with less side effects. Natural herbs provide the best treatment as comparative to the conventional drugs. But conventional drugs are also available for reducing the symptoms of the disease but these drugs have more side effects as compared to the ayurvedic treatment. In this review, we are discussing about the recent natural treatment and conventional treatment for the *Alopecia areata* developed by the psychological disorders.

Keywords: *Alopecia areata*, Anxiety, Conventional drug, Ayurvedic system, Hair-loss.

INTRODUCTION

Hair is an ornament structure along with the sebaceous gland which secretes the lubricating oil matter and helps in providing the lubrication to the skin and hair. Hairs are considered as the major part of the body which influences the appearance of the person. Hairs are generally derived from the ectoderm part of the skin. There are no nerve connections in between the hairs but they have the ability of regenerating itself²⁹. Stress is the major symptoms of psychological disorders which lead to the development of hair-fall and this type of hair-fall is known as *Alopecia areata*. *Alopecia areata* (AA) is a common dermatologic disorder characterized by inflammation and leads to high density patchy hair-loss on scalp, body and face. AA is a chronic inflammatory which generally targets the hair follicles and this disorder is generally caused by the various psychological disorders such as anxiety, depression. During stress, the white blood cells of the body attack the hair follicle then *Alopecia areata* occurs. During this attack, hair starts falling out within 1 week. AA

involves in the category of autoimmune disease which generally affect females as compared to male. Recently various psychological disorders which affects the mental ability of the patient like anxiety, depression leads to the formation of hairloss generally *Alopecia areata*. *Alopecia areata* affect different age groups involving children's and adults and all different types of hair colour¹. This condition is subsequently spread to scalp (*Alopecia totalis*) and to skin (*Alopecia universalis*) only in 1-2% cases². AA is a disorder categorised under the category of chronic dermatological disorder which produces the complete loss of hair from the scalp or even from the other parts of the body. Recently AA is considered to be caused by the auto-immune attack of the hair-follicle.

Currently there is no treatment available which is approved by the FDA (Food and Drug Administration) but some therapeutic options are available for reducing the symptoms of the disease. These therapeutic options do not provide complete cure from the disease, it just helps to prevent from severe condition of the disease and reduces the severity of the symptoms.

Table 1: Various different clinical forms of *Alopecia areata*

Name	Onset of Alopecia	Description
<i>Alopecia areata focalis</i>	-	Loss of hairs from the scalp and other parts of body (eg. Abdomen) ³
<i>Alopecia areata totalis</i>	2 years	Loss of hairs from the scalp even from eyebrows and eyelashes ⁴ .
<i>Alopecia areata universalis</i>	1.5 years	Complete loss of hairs from all parts of the body ³ .
<i>Alopecia maligna</i>	-	Long term loss of hairs and is generally resistant to treatment ⁵ .
<i>Ophiasis or alopecia areata marginata</i>	-	Loss of hairs having a snake or curly shape of hairs from the head in the temporal, frontal and occipital areas ⁵ .
<i>Ophiasis inversus</i>	-	Loss of hairs generally in the inverse pattern. Hair loss generally develops from the central to the marginal area of the head ³ .



HAIR GROWTH CYCLE

Two main parts are involved in the structure of hair mainly follicle and shaft. Follicle is that structure which remains in the skin and shaft which locates above the scalp and shaft becomes visible after growth. For the production of new hairs, follicles undergoes the growth cycle of hair. There are three different phases which are involved in the hair growth cycle and these three phases play different role for the growth of hairs. These three phases are anagen phase (growth), catagen phase (regression) and telogen phase (rest).

Anagen phase: The hair shaft is produced by follicle from tip to root. This phase lasts about 3-5 years and the length of hairs goes around 18 to 30 inches. As in Asians, this growth phase is longer as comparative to others and take time of 7 years and the length of hairs goes around 1 metre.

Catagen phase: This is second phase it starts after the end of anagen phase. This phase is the short phase of the hair cycle which takes only 10 days. This phase is also known as the transitional phase.

Telogen phase: It starts after the catagen phase, which is the resting phase and where the hairs become released and falls out. The telogen phase takes time of 100 days and in this phase hairs which are in resting stage remains in the follicle. When a growth of new anagen hair develops these resting hairs become pushed out. After this, for the 3 months follicles become inactive. During the catagen phase and telogen phase of the hair growth cycle, follicles become reset and start to prepare the stem cells for the initiation of the new hair growth cycle after receiving the signal and new hair shaft develops. For the study of regulation of stem cell quiescence and activation as well as transit- amplifying cell proliferation, differentiation and apoptosis, this hair growth cycles proves to be an impressive model⁶.

ETIOPATHOGENESIS

Growth and maintenance of the hairs generally depends on the 3 main phases of the hair growth cycle involving anagen, catagen and telogen. Length and type of hair involved in the anagen phase while after the resting phase when new hair anagen develops, shedding of hairs become start in the normal healthy hair individuals. As in the case of *Alopecia areata*, shedding of hairs develop before the anagen starts leaving the empty hair follicle and leads to some defects in the hair growth cycle and generally considered to be a state of kenogen⁷.

There are various etiological factors are involved which are responsible for the initiation of *Alopecia areata*. These various factors are as following:

Genetic factors: It plays a vital role in the etiology of AA. The importances of these factors are underlines by the high frequency of a positive family history in affected individuals⁸. Generally this disorder occurs in family to family because of the genetic factor. Various studies have

been done and this study provides various correlations between the AA and histocompatibility antigens. The initiation of this disease is associated with Human leukocyte antigen (HLA). HLA is a major histocompatibility complex (MHC) gene having a region on chromosome 6 and this complex contains around 200 gene. There are three main MHC class-I gene such as HLA-A, HLA-B and HLA-C but in recent studies these are not recognised in this disorder but MHC class-II genes are associated with the AA such as HLA-DPB1, HLA-DQA1, HLA-DQB1, HLA-DRA, HLA-DRB1. The genes from the HLA gene family give some instructions for the production of various kinds of proteins known as human leukocyte antigen complex. Correlations with HLA-I class have not been established but from the reports of study but it involves the role of HLA-II class. HLA-DQB1*0301 is frequently found in infected persons with chronic Alopecia totalis, but this gene is not much found in case of patchy *Alopecia areata*⁹. Differences in the molecular pathogenesis may recognised by the genetic difference between the risks of patchy AA and Alopecia totalis¹⁰. Generally the regulation and the susceptibility of AA, different studies have been performed and in these studies focus should be on HLA class-II genes (HLA-D) located on chromosome 6.

AA also occurs in those diseases which are having link with chromosome 21 such Down's syndrome and autoimmune polyendocrinopathy¹¹. As with the APECED (autoimmune polyendocrinopathy candidiasis ectodermal dysplasia syndrome), the risk of the AA disorder become increased in 30% cases. APECED is a condition which is associated with the mutation of the gene mainly autoimmune regulator (AIRE) located on chromosome 21q22.3¹². This AA disorder is a polygenic disorder generally which involves various interactions of different genes with the different environmental factors and this disorder is similar to autoimmune diseases¹³. Recently, GWAS (genome wide association studies) are proved to be specific markers for the AA and these genetic markers may increase the risk of AA¹⁴.

Autoimmunity: AA is also associated with the autoimmune diseases. It was first proposed by the Rothman. AA is also associated with other autoimmune disease such as thyroid disease, diabetes mellitus, anaemia, vitiligo, psoriasis and these disease proves to be one of the reason for the association of AA with autoimmune diseases^{15,16}. Patients with AA having an increased level of hair follicle specific antibodies in the peripheral blood, especially to keratin 16 and trichohyalin¹⁶. Molecules of major histocompatibility complex class-I and II are not expressed in healthy hair follicles epithelium but TGF- β , IGF-1 and α -MSH are expressed more in healthy hair follicle epithelium. Perifollicular inflammation is developed when the immune privilege is collapsed in AA due to the presence of increased MHC-I and II complex and decreased immunosuppressive molecules and with high expression of adhesion molecules (ICAM-2 and ELAM-1) in the perivascular and peribulbar hair follicular epithelium¹⁴.



Activity of hair follicle is mainly affected by the peribulbar inflammation and leads to the development of the dystrophic hair. As in case of genetically susceptible individuals the autoimmune diseases are generally triggered by the environmental factors and for this reason, AA is considered as a hair follicle specific autoimmune disease¹⁷.

Atopy: This factor was placed separately in the classification of the *Alopecia areata*. After performing various studies and investigations, it has been proved that the AA is associated with the atopy but in the pathogenesis the mechanism behind the association of AA with atopy is unknown. As in the case of atopy individuals, AA occurs at an earlier onset and in severe form^{18,19}.

Stress: This is another factor which is associated with the AA. But with the result of controlled studies, the statement of stress is one of the trigger for AA is considered to be wrong. But now some studies have declared that when the white blood cells of the body attacks on the hair follicle it may lead to the development of the AA.

ALOPECIA AREATA WITH PSYCHOLOGICAL DISORDERS (ANXIETY, DEPRESSION)

Stress is the common trigger involved in these disorders. Emotional and stressful events in daily routine produces some psychological disorders such as anxiety and depression and these factors further leads to the development of the non-scarring autoimmune disease i. e. *Alopecia areata*. These psychological disorders have great prevalence in individuals infected with the AA. Recently from the different studies, it has been proved that about 93% are affected with AA due to the psychological disorders and this makes that the psychological factors have important role in the pathogenesis of AA²⁰. As with the relations of the psychological emotional stress and hairfall (AA) various levels of interaction have been distinguished. These interactions are:²¹

- Acute or chronic stress as a primary inducer of telogen effluvium
- Acute or chronic stress as an aggravating factor in a hair loss disorder
- Stress as a secondary problem in response to prior hair loss.

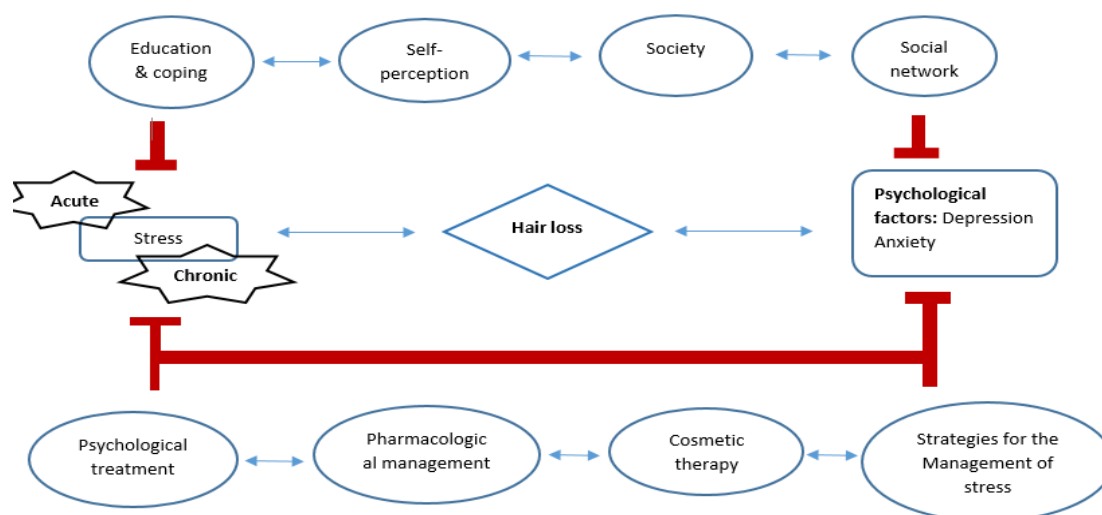


Figure 1: Factors involved in hair fall and its management of hair fall stop.

Types of hair-loss due to psychological factors: generally there are three types of hair loss due to the stress. These are following:

- **Telogen Effluvium:** When the body reactions to stress the telogen effluvium develops. This type generally belongs to the telogen phase of hair growth cycle in which around 5-7% of hairs of can grow. With telogen effluvium, stress develops the termination of hair growth by transferring the number of hair follicles in the resting phase. Thinning of hair generally occurs in this condition.
- **Alopecia areata:** In this the hair follicles are turned on by the immune system and falling out of hairs

becomes start even in patchy forms on the scalp. There are so many factors like genetic factors, autoimmunity, atopy but stress is the major factor which triggers the AA.

- **Trichotillomania:** In this condition the subsequently pulling their own hairs from their head, eyebrows or other parts of the body and so for this reason this type is totally different from the other two types.

PATHOGENESIS OF HAIR FALL

In case of female pattern hair fall, some interruption have been occurred such as shortening of the growth phase i. e. anagen phase and elongation of the telogen phase which leads to the development of some alterations in

the normal hair growth cycle. Due to these alterations, the hair ratio of anagen to telogen become decreased about 12: 1 to < 8: 1. The length of the anagen phase become decreased with every hair growth cycle but the length of the telogen phase remains constant for each cycle and this generally affects the hair fibre length and leads to the development of the shortening of the terminal hair. In other way, due to the miniaturization of the entire follicles, diameter of the hairs becomes reduced²². In humans, follicle unit generally consist of larger, central primary follicles which are surrounded by the smaller secondary follicles and within these follicle

units, scalp hair follicles are exist. A single arrector pili muscle is predominantly attached to the primary follicle with variable attachment to secondary follicles²². When the follicular unit gets miniaturised, the complete baldness arises.

PHARMACOLOGICAL MANAGEMENT OF ALOPECIA AREATA

The Pharmacological management of AA have been done by various drugs²⁵. These are used and have effective against *Alopecia areata*. However, serious side effects of this treatment depends on percentage of hair loss.

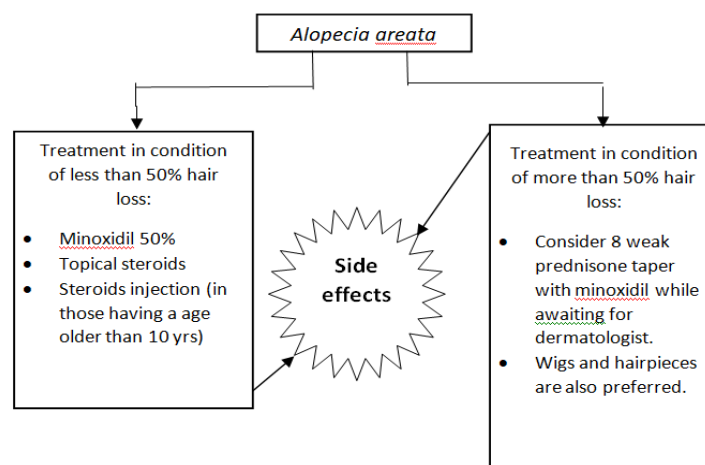


Figure 2: Management of alopecia areata by Pharmacological system

Immunosuppressive treatment: These drugs are commonly used for the treatment of *Alopecia areata*.

- **Glucocorticoids:** These are used as anti-inflammatory drugs and these can be used topically, systemically and intra-lesionally. Corticosteroids are generally used because these are known to having inhibitory activity against the activation of the T-lymphocytes²⁶. Systemic corticosteroids are used in AA, because they helps in allowing entry of hair follicles into the new hair growth cycle by affecting the peribulbar lymphocytes. Number of non-controlled studies have been proves the effective role of systemic corticosteroids in the treatment of AA²⁶. Intra-lesional corticosteroids are used as a first line therapy for the treatment of AA.
- **Triamcinolone acetonide:** It is used as an intra-lesional injection of corticosteroids as crystal suspension. This injection helps in promoting the hair growth at the site of injection. This injection is generally injected in deep dermal or upper s. c. plane by using a 20 gauge needle with half inch long needle. At the interval of every 4-6 weeks 0. 1ml of dose is injected at 0. 5-1cm. various different concentrations are used but for the scalp and face only preferred concentrations have to be used. In case of younger patients before the injection, topical

anaesthetic cream should be applied for minimizing the pain. By using the small concentrations of drug or by minimizing the number of injections per site, major side effects including atrophy and telangiectasia can be prevented²⁷. For the topical form, corticosteroids are used in the form of ointment, lotion and creams are used for the treatment of AA. But from various studies the use of topical corticosteroids have been failed because of the improper penetration of the drug.

- **Minoxidil:** It is first used as an anti-hypertensive agent. In 1980s, the effective role of minoxidil in promoting hair growth was seen. Various studies have been performed but donot provide the exact mechanism of the minoxidil but some studies have been proved monixidil with different mechanisms such as immunosuppressive, angiogenesis, potassium channel opening, vasodilation and enhancing cell proliferation²⁸. Minoxidil produces the hypertrichosis as a side effect due to the anti-hypertensive activity²⁶. It is not preferred in case of severe AA. Combination therapy of the minoxidil 5% lotion with anthralin shows effective result².
- **Anthralin:** It is also a drug is used in the form of cream. For short contact therapy, anthralin 1% cream is used and applied daily for 15-20 mins and

then washed. Daily the contact time should be increased by 5 mins weekly and then fixed the contact time and continue for 3 months. Some different side effects are produced by the anthralin including severe irritation, folliculitis and staining of

skin. The patient should always be recommended to avoid eye contact with this drug and the area which is to be treated, that area should be protected from the sun²⁷.

Table 2: List of plants used in the treatment of *Alopecia areata*

Common name	Biological name	Family	Part used	Chemical constituents	Benefits
Aloevera	<i>Aloe barbadensis</i>	Liliaceae	Leaves	Aloe-emodin; Aloesone; Aloecutin A and B.	It provides nutritional support. ²³
China rose	<i>Hibiscus rosa-sinensis</i>	Malvaceae	Leaves and flowers	Flavonoids; Anthocyanins; Quercetin 3,7-diglucoside; Quercetin 3-diglucoside.	Maintains the hair growth ²⁴ .
Dodder	<i>Cuscuta reflexa</i>	Convolvulaceae	Stems	Cuscutin; Cuscutalin; Luteolin; Bergenin; Kaempferol.	It prevents hairloss. ²⁴
Chines-e wild ginger	<i>Asiasari radix</i>	Aristolochiaceae	Roots and rhizome.	Safrrole; Methyl eugenol; methoxy toluenes and 3-benzodioxole derivatives.	Promotes hair growth. ²⁴
Maidenhair tree	<i>Ginkgo bilibo</i>	Ginkgoaceae	Leaves	Quercitin; Kaempferol; Ginkgolides A, B and C	It prevents hairloss. ²⁴
Tridax daisy	<i>Tridax procumbens</i>	Compositae	Leaves	Luteolin; Glucoluteolin; Quercetin; Iso-Quercetin; Fumaric acid; Tannins; Alkaloids.	It promotes the hair growth. ²⁴
Bitter apple	<i>Citrullus colocynthis</i>	Cucurbitaceae	Fruits	Cucurbitacins; Cucurbitacin E and I; Citrullol; Pectin; Resinous glycosides	Works as hair growth promoter. ²⁴
Bhringraj	<i>Eclipta alba</i>	Asteraceae	Whole plant	Wedelolactone; Triterpene; Glycosides; Saponins.	It prevents hairloss. ²⁴
Bathua	<i>Amaranthus spinosus</i>	Amaranthaceae	Seeds and leaves	Minerals	It provides nutritional support. ²³
Lettuce	<i>Lactuca sativa</i>	Asteraceae	Leaves	Folic acid and vit. A	It provides nutritional support. ²³
Amla	<i>Phyllanthus emblica</i>	Euphorbiaceae	Fruit	Gallic acid; Quercitin; vitamin C	Provides nutritional support. ²³
Badam	<i>Prunus amygdalus</i>	Rosaceae	Seed oil	Minerals; fats; vitamin E, B1, B2 and B3.	It provides nutritional support for hair growth. ²³
Cedar wood	<i>Cedrus atlantica</i>	Pinaceae	Wood chips and saw dust	Terpenoids	Work as armotherapy. ²³
Jabarondi	<i>Pilocarpus jabarondi</i>	Rutaceae	Leaves	Terpenoids	Work as armotherapy ²³
Ginseng	<i>Panax ginseng</i>	Araliaceae	Roots	Minerals and phytoestrogens	inhibiting the 5- α reductase inhibitor. ²³

MANAGEMENT OFALOPECIA AREATA BY AYURVEDIC SYSTEM

Natural drugs belongs to different families, genus, species and are always free from side effects and these drugs provide beneficial advantage in the management of diseases and good patient compliance. Natural drugs also have various different modes of actions in the management of *Alopecia areata* by using different parts of the drugs. The herbs which are used in the treatment of AA provide nutritional support and promoters the hair

growth by inhibiting the 5- α reductase. Also these natural herbs are improved the blood circulation of the scalp and also works as an armotherapy.

Armotherapy: This armotherapy can be used as a supplement for the treatment of AA²³. These natural products are generally used in the form of formulations i. e. herbal formulations and these formulations are made by the use of different parts of the plant such as root, leaves, stem, rhizomes or even the whole plant. These formulations are used as the hair growth promoter, hair



tonic, hair conditioner, hair cleansing agents, anti-dandruff agents etc²⁴. The main use of these herbal formulations is in the treatment of AA and lice infection.

Numbers of Natural home remedies are used for the treatment of *Alopecia areata* such as:

- **Onion juice:** It helps in the initiation of hair regrowth in the patchy areas and also increases the hair growth in case of AA. It can fight with free radical damage because it contains the high amount of the sulphur. It helps by preventing the hairs from any kind of hair infection and improves the blood circulation of the scalp.
- **Garlic juice:** this juice contains the high amount of sulphur as like onion juice and provides the natural treatment for the AA. It helps in promoting the hair growth and prevents the hairloss by increasing the production of collagen.
- **Lavender oil:** this oil is categorised under the calming essential oil and is generally used to calm the peoples who are suffering with the anxiety, depression and stress means it helps in reducing the psychological disorders. This oil also proved to be beneficial for the treatment of the AA. The major advantage is that this essential oil contains lavender which helps in strengthening the hair follicle and improves the hair growth.
- **Fenugreek seeds:** These seeds help in improving the hair growth by blocking the synthesis of the dihydrotestosterone, which is the major cause of hair loss. This natural product is very beneficial in the treatment of the AA.
- **Honey:** Generally honey prevents the hairs from various hair infections and prevents hair loss. It can be used by combining with other home remedies and proves to be a natural and best treatment for the AA.
- **Liquorice root:** It is mainly used as a calming substance and it prevents from the hair infections which causes hair loss. It helps in making the healthy hairs and maintains the growth of hairs in case of AA. Recently from the studies, it has been proved that the liquorice root also helps in promoting the hair growth especially in case of females.
- **Green tea:** It works as an anti-oxidant and it contains polyphenols. It is the best and home remedy for the treatment of the *Alopecia areata*. It helps in regenerating the healthy cells on the scalp and provides strength to hair follicles and prevent from other hair infections.
- **Mustard oil:** It is the most easily available home remedy. It helps in boosting up the hair growth and increase the volume of hairs in case of AA. It also helps in reducing the hair loss.

Curry leaves: It stimulates the growth of hair follicles and helps in avoiding the premature greying of hairs.

CONCLUSION

Alopecia areata is an autoimmune disease which is triggered by the stress. Various psychological disorders are involved which leads to the development of hairfall. The treatment of *Alopecia areata* are available like ayurvedic treatment is considered to be beneficial because this is a natural kind of treatment with less side effects. But some conventional drugs are also available for the treatment of *Alopecia areata*. However, These drugs help in promoting the hair growth and preventing the hair loss. Hairs can regrow when proper treatment should be provided.

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