



A Complete Examination of The Intricate Factors Involved in Baldness

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Received: 12 Oct 2021 / Accepted: 6 Nov 2021/ Published online: 01 Jan 2022

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Abstract

Baldness is a very common problem today. Men and women can get baldness but it's more common in men. There is lots of research that has been done by Scientists on baldness. A recent study found that teens can also suffer from baldness. There are various factors that can cause baldness. Mostly, teens lose hair because of stress, genetic factors, poor nutrition, hormonal imbalance. The hair products like hair gels, hair wax, hair sprays that we use for styling in our daily routine can also cause hair loss. Using hair straightening, hair curling, and chemicals frequently can damage our hair, it can also cause permanent hair loss. Low iron level and high sodium level, it may also cause hair loss in teens and children. The medical term for baldness is Alopecia, it can develop anywhere in our body. By the age of 40, the majority of males have experienced hair loss. The review outlines are various classifications, factors, conditions associated with baldness. This study shall help the people to know about baldness, what are the factors involved in it and how to avoid these factors.

Keywords

Alopecia, Anagen effluvium, Hair loss, Telogen effluvium.

1. INTRODUCTION

Baldness is the condition where a person loses his/her hair partially or completely. It is not a very serious medical condition, but it can affect our mental health. So, we should know what the factors are involved in it. Many types of baldness are there, and they each have different causes. The most prevalent cause of hair loss in both sexes is androgenic alopecia. Anagen effluvium, Telogen effluvium, Tinea capitis (Children), Cicatricial alopecia, these are the other types of hair loss. Many different types of drugs may cause baldness like antibiotics, antifungal drugs, anticlotting drugs, birth control pills, cholesterol lowering drugs etc. Carbamazepine, Valporic acid, Lithium, fluoxetine, Lamotrigine, Haloperidol, Olanzapine, Respiridone, Oxcarbazepine – these are the drugs which may also cause hair loss. Androgenetic. Non-steroidal aromatase inhibitors like letrozole and vorozole-

these may also cause alopecia. Increase the level DHT is one of the general factors involved in baldness. Pollution also may cause hair loss. The first layer of protection against pollution is the skin and hair. Pollution-related hair loss, this is a matter of concern nowadays. Hypertension is also one of the common causes of baldness. The AR gene on the "X" chromosome is highly connected to baldness. Hair loss is a side effect of antiretroviral drugs, which are used to treat HIV infection. Women suffer from hair loss less frequently than men, but it still happens. Baldness in women gets worse as they get older. Stress is one of the biggest problems today, that is also one of the main reasons for hair loss. Mostly teens are suffered from baldness because of stress. Nowadays we are using various types of hair styling products like hair gel, hair wax etc. These are mainly made up with chemicals which can damage our hair, may also cause permanent hair loss. Junk food

consumption has increased dramatically in modern society, particularly among children and adults. It's not only bad for our body, but it's also bad for our hair. Nutritional deficiencies are one of the leading reasons of hair loss. Low level of iron in our body, it is one of the nutritional factors that may cause baldness. The most common problem impacting males is genetic hair loss, it affects maximum number of men by the age of 50. There are also some treatments presents that can help to manage the hair fall. In this review paper we will study about classifications, factors, conditions and also some treatments related to baldness.

2. Physiology of hair growth

Except the underside of the human hand and bottom of the foot, human skin possesses a vast number of hair follicles. Hair follicles can create two forms of hair after birth, depending on where on the body they are located one is vellus hair and another one is terminal hair. Aside from the palms and soles, there

are no other parts of the body that don't have vellus hair, it covers all the body, is silky, short (typically less than 2cm), and often colourless. The terminal hair is coarse and long. It has a medulla and is generally coloured or pigmented. It is found in the scalp, brows, and eyelashes during birth.[1] Individual hair shaft diameters in men can range from 15 to 120 pm. It depends on the type of hair and where the follicle is positioned on the body. Keratin is a sulfur-rich protein family, that is found in hair.[2] There are 3 stages involved in hair growth: 1. Anagen, 2. Catagen, 3. Telogen.

Diagram of Hair growth stage. (1)

3. Classification of hair loss

Pattern hair loss is the most prevalent reason of male and female hair loss after adolescence. Various researchers have developed several classification systems that are engaged in baldness in both males and females.[3]

a) Male pattern hair loss classifications

Beek (1950)	It was a simple and direct categorization that only covered the first 2 stages of hair loss and ignored the various evolutionary stages, but it was significant because it was the first time someone tried to categorise hair loss. Frontal baldness and Frontoverlateral baldness are the two types of baldness that he identified. [3]
Hamilton (1951)	Hamilton divides hair loss into two categories: a) non-bald scalps and b) bald scalps. The frontoparietal and frontal recessions, as well as frontal thinning, were used to classify this condition. [3][37](2)
Ogata (1953)	Based on the findings of a survey of Japanese guys, patterned hair loss has fifteen different subtypes, according to Ogata. He categorized those into 6 different groups.[3][95](3)
Setty (1970)	Setty examined 600 men, 300 of whom were white and 300 of whom were black and came up with a new categorization that simplified Hamilton's classification. He categorized them into three subtypes: Totopilosis, Indentato-pilosis, Indentato-circulo-pilosis.[96][3]
Norwood (1975)	The Norwood classification, which describes 2 major patterns of hair loss in men, as well as few less common types of hair loss, it is the most widely used classification.[97][3](4)
Bouhanna (1976)	Based on findings among European Caucasians, only three illustrations of hair loss and two variants were included in this classification.[98][3](5)
Blanchard and Blanchard (1984)	Blanchard proposed an alternative classification based on six measurements. (6)Those are: <ul style="list-style-type: none"> • Glabellar frontal • Frontal vertical • Helical vertical • Superciliary frontal • Nucho vertical distances • Interparietal[3]
Dardour and Bouhanna (1996)	They proposed a classification system that included all morphological and progressive parameters that have an effect on the hair and the scalp. This classification was more complete than the previous ones.[3]
Koo (2000)	Based on a study of Korean males, it is classified into 6 subtypes.[99](7)
BASP (2007)	There were four different types in total, with two of them being unique.[3](8)

b) Female pattern hair loss classifications

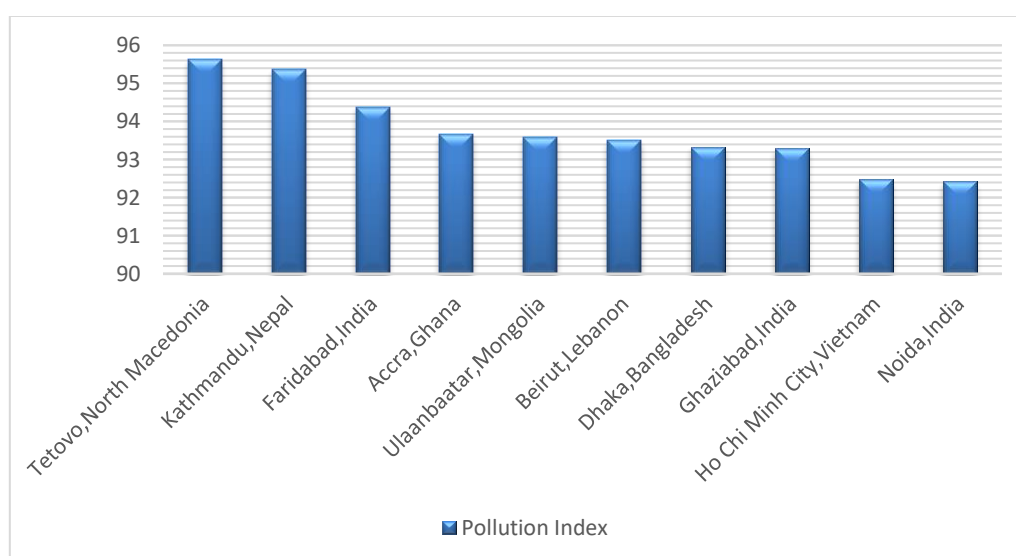
Ludwig(1977)	To figure out how much female hair loss there is, the Ludwig Scale uses three different classifications, or Types. These Types are Type I, II, and III.[100][3](9)
Ebling and Rook (1975)	A classification system that divides alopecia into five grades: The medical care is necessary for grades I–III; surgical treatment is necessary for grade IV; and there is no solution for grade V. [101][3](10)
Savin(1992)	The Savin scale depicts the progression of female scalp hair loss in gradations based on parting width. The patient's hair is evaluated by comparing eight computer-generated visualizations of central scalp hair isolated in the middle.[102] [3][100] (11)
Olsen (1994)	Olsen created a classification system that was similar to Ludwig's. It causes the central parting line to widen, which has a triangle shaped or "Christmas tree" pattern.[103][104][3](12)
Sinclair (2004)	It is a self-delineating hair loss pattern which is represented by five colour photographs of women's scalps parted in the middle.[3][105] (13)

c) Drugs that can cause telogen effluvium

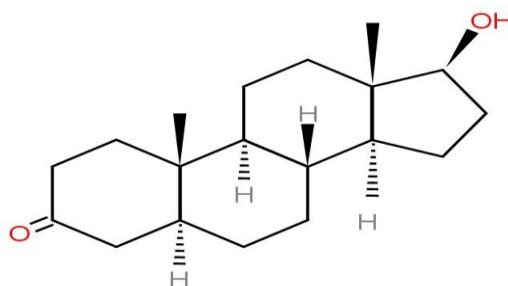
Albendazole[106]	Fluoxetine[25]	Propranolol[107]
Allopurinol[108]	Gentamicin[109]	Pyridostigmine[110]
Bromocriptine[111]	Heparin[112]	Sulfasalazine[113]
Cimetidine[114]	Ibuprofen[115]	Salicylates[114]
Valproic acid[116]	Itraconazole[117]	Terfenadine[118]
Dextran[119]	Maprotiline[120]	Thiouracils[121]
Danazol[122]	Nicotinic acid[1]	Triparanol[123]
Ethionamide[124]		

d) Cytotoxic agents that can cause alopecia

Doxorubicin[14]	Vincristine[125]
Daunorubicin[126]	Vinblastine[127]
Hydroxyurea[130]	Thiotepa[128]
Etoposide[129]	
Paclitaxel[126]	
Bleomycin[131]	
Methotrexate[132]	
Mechlorethamine[133]	



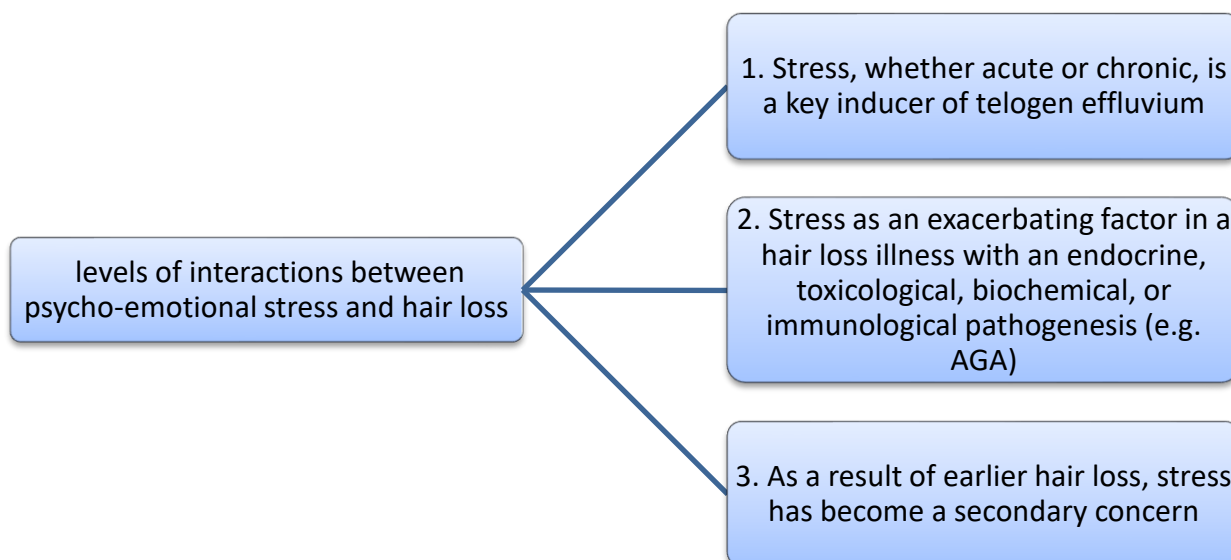
(14) Most polluted cities on Earth, Numbeo, 2021 Mid-Year Pollution Index



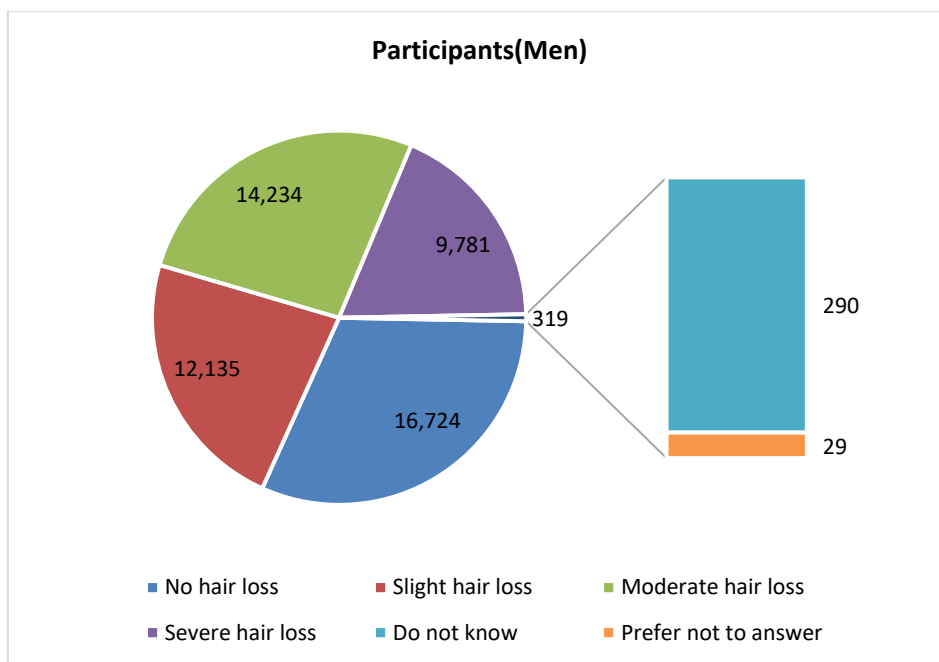
(15) Structure of DHT



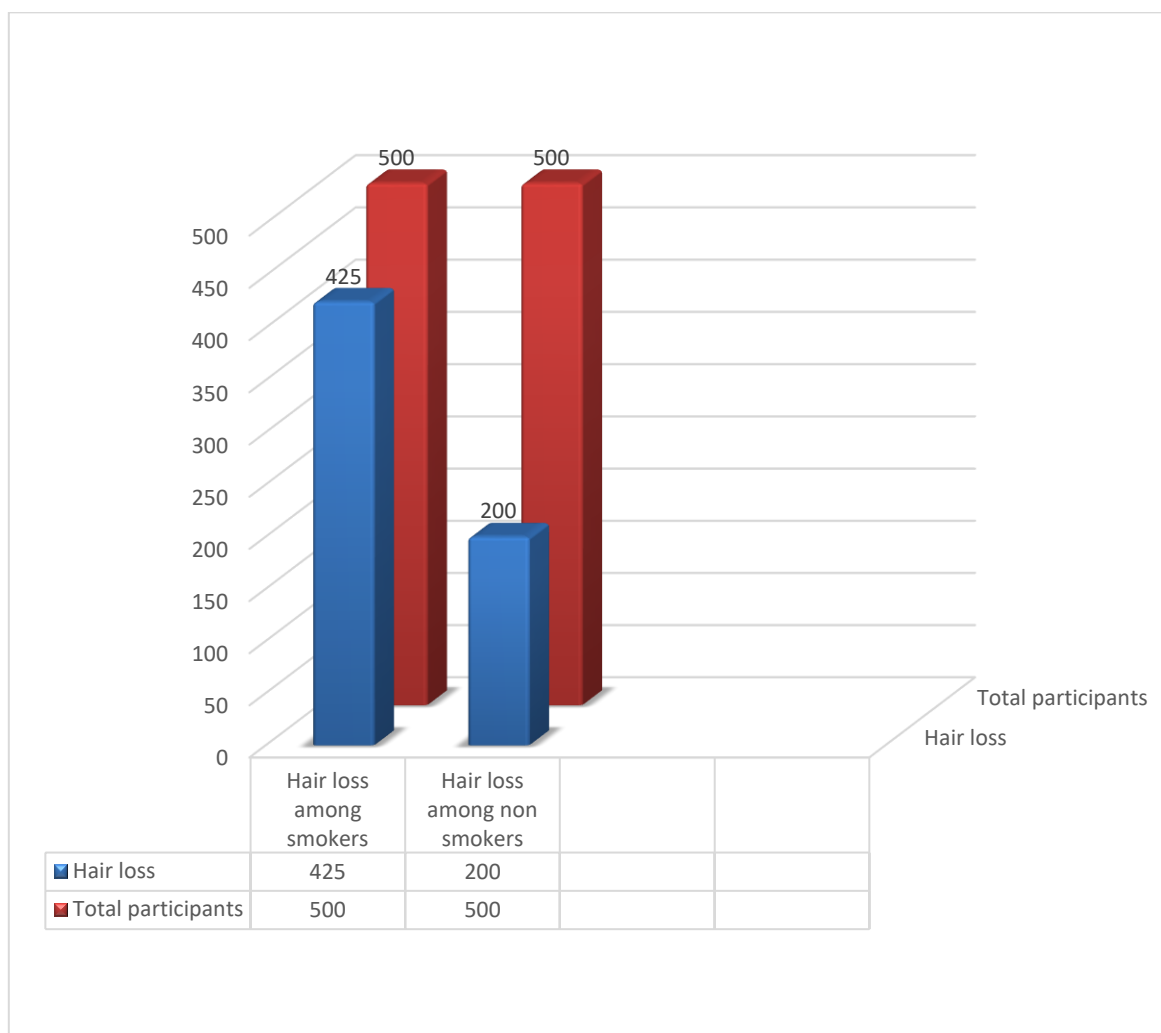
(16) Relation between stress, hair loss and depression anxiety



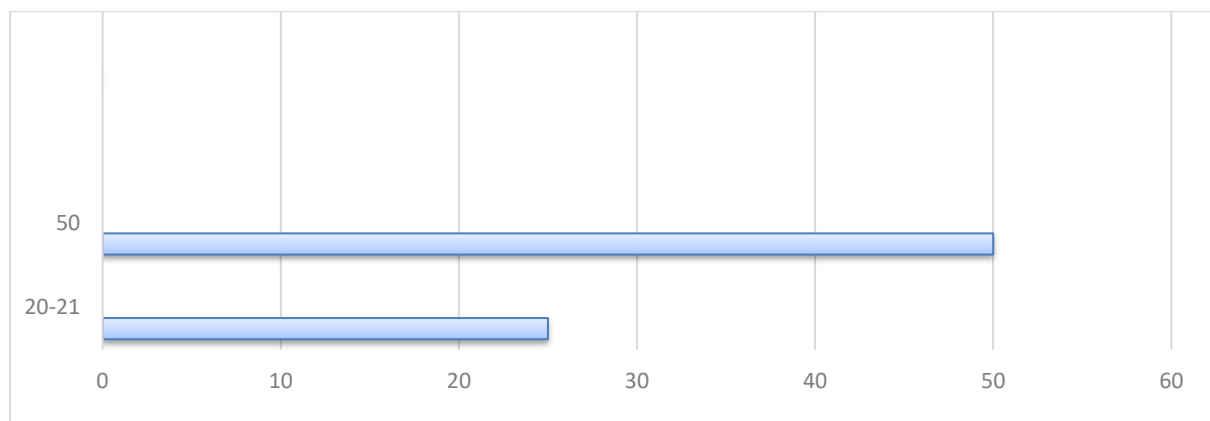
(17)levels of interactions between psycho-emotional stress and hair loss (According to a 2014 study)



(18) Genome wide study of baldness (UK biobank,2017)



(19)Hair loss among smokers vs Hair loss among non-smokers (Age between 20-35)



(20)Percentage of men losing hair (MPB) vs Age (NHS report)

4. Factors

There are various factors which may cause baldness. It can be caused by hormonal changes, medical conditions, or simply ageing. Hair loss can manifest itself in a number of ways, depending on the condition. People lose 50 to 100 hairs per day on average. It is normal because simultaneously, new hair is growing. When your hair begins to fall out, and new hair does not grow in its place, it is known as baldness. Hair loss is referred to as alopecia in medical terms. Now let's talk about the factors which are involved in baldness.

4.1 Is your medication causing you to lose your hair?

Drugs may also cause hair loss. There are mainly 3 types of hair loss which may induced by drugs. They are (i) Anagen effluvium, (ii) Telogen effluvium and (iii) Cicatricial alopecia.[4] Anticoagulants, Antineoplastic agents; these may also cause alopecia. Other medications like Antiretroviral drugs, Oral contraceptives- these are also the reason for baldness.[4] Hair loss caused by medications is usually reversible once the medication is stopped. The drug used, and also a person's genetic predisposition, determine the prevalence and severity of alopecia. Some drugs cause baldness in the majority of patients who are given the correct dosages, while others cause hair abnormalities only on rare occasions.[1]

4.2 Do chemotherapeutic medicines induce anagen effluvium?

Anagen effluvium is mainly caused by chemotherapy drugs but gold, colchicine, or arsenic poisoning, as well as bismuth, thallium, or boric acid poisoning, can also cause it.[5] Hair loss caused by chemotherapeutic agents has a major effect on patients' quality of life. According to a study, chemotherapy is most painful when it comes to hair loss (47% of female patients), among them 8% of patients refused chemotherapy because they were afraid of losing their hair.[6][7][8] Hair loss that arises

throughout the anagen phase of growth is called anagen effluvium, when the cells in the hair bulb divide fast and are susceptible to cytotoxic agents.[9] In constantly developing hair follicles, hemotherapeutic drugs disrupt mitotic and metabolic activities, causing the shaft to thin and become fragile, vulnerable to fracture with minor trauma.[10] Hairs on the scalp that are in the telogen phase are completely unchanged; after chemotherapy, an estimated 85% of the total amount of anagen hairs are casting off.[11] Chemotherapy-induced hair loss has been linked to premature apoptosis-driven hair follicle regression, with p53, Fas, and c-kit being involved factors.[12][13] Chemotherapy administered at high doses for a long period of time and with multiple exposures can affect beard, eyebrow, and eyelash hairs, as well as the axillary and pubic regions.[14] Although anagen effluvium caused by chemotherapy is usually reversible, but certain chemotherapy regimens have been known to cause permanent alopecia.[15]

4.3 Hair loss due to pollution

PAHs can cause hair loss. Exhaust from automobiles, highways made of asphalt, blazing wood, smoke and waste from industry all release PAHs. PAHs can last a long time in the atmosphere, soil, and groundwater. PAHs have the ability to boost xenobiotic metabolism; quinones are formed by converting PAHs to quinones. Quinones are redox-cycling chemicals that are important in PM toxic effects and generate reactive oxygen radicals. Skin infiltration can occur when people are revealed to high levels of PM on a daily basis, either transepidermally or through the hair follicles.[16] In his research projects, Philpott found that high levels of pollution increase oxidative pressure in hair follicle cells, as a result, hair thinning is increased, a mechanism related to people with androgenic alopecia (AA).[17] Pollution is increasing all over the world but especially in Indian cities.[14][16] The first line of

defence against pollution is the skin and hair. The scalp and hair are irritated and damaged by large, suspended particles, small particles in the air, smoke, and pollutant gas. In 1994, the Industrial Toxicology Research Center in Lucknow published a study on the effects of pollutions on human hair.[18][16] The quantity of vehicles on the road, urbanization, Burning of garbage in cities, Combustion of agricultural residues, a faulty transportation system, insufficient environmental law, and many other factors are all contributing to increased air pollution on a daily basis.[19][20] Air quality has an influence on human and animal health, as well as forestry, climate change, and other variables.[21] Scalp discomfort, hair breakage, hair root pain, and even hair loss are all indications of air pollution sensitivity, according to a 2015 research.[22] [16]

4.4 What types of psychotropic medicines cause hair loss?

Psychotropic Medications may also cause alopecia. Imipramine [23], Desipramine [24](Nonselective cyclic antidepressants); Fluoxetine[25], Fluvoxamine[26], Paroxetine[27], Sertraline[28] (Selective serotonin-reuptake inhibitors); Venlafaxine[29](Selective serotonin-norepinephrine reuptake inhibitors); Bupropion[30] (Second generation antidepressants)-These are the psychotropic medicines which can cause hair loss. Hair loss is a adverse effect of lithium therapy, which is a psychotropic medication. Hair thinning was reported in 17% of 99 lithium users.[31] Hypothyroidism is a side effect of lithium, and it's possible that's why you're losing your hair. Beta-blocker have also been linked to hair loss. These are also coming under psychotropic medicines. Beta-blockers lower cAMP levels, which have been linked to epidermal cell mitosis suppression. Beta-blockers also prevent catecholamine-induced glycolysis and lipolysis, as well as catecholamine's vasodilating effect on peripheral blood vessels.[32] Carbamazepine comes under anticonvulsant medication, can also cause alopecia. In an 8-year-old girl, carbamazepine was found to cause hair loss.[33] Hair loss began within a week of starting the drug. It lasted about a month before the drug was stopped.[32]

4.5 DHT and Baldness

5-alpha reductase is an enzyme that transforms testosterone to DHT (15) (dihydrotestosterone).[34] In males, dihydrotestosterone is the most common cause of hair loss, it is a male steroid hormone that connects to scalp receptors and causes hair loss in males who are genetically predisposed.[34] DHT is received to be the androgen responsible for follicular miniaturisation by binding to androgen receptors.

However, because DHT (dihydrotestosterone) is a stronger form of testosterone, and androgens are supposed to transform vellus to terminal hair follicles, not vice versa, this assumption creates a contradiction.[35] The hair root and follicle are miniaturized by dihydrotestosterone, resulting in finer new hair growth. Dihydrotestosterone miniaturizes the hair follicle again when fresh fine hair is lost, and so on till baldness develops.[36] Androgens connect to nuclear receptors and are steroid hormones. They regulate genetic transcription. Follicular miniaturisation occurs in men with MPHL due to an inborn sensitivity of scalp hair follicles to usual levels of circulating androgens. In a series of seminal articles, Hamilton thoroughly documented the disease's genetic and androgenic origins.[37][38] Hamilton's research showed that Testosterone, & one of the metabolites, was found to play a role in the formation of MPHL, and its expression was genetically determined.[39] Patients with female-pattern baldness produce more testosterone but less DHT.[40]

4.6 Can stress cause alopecia?

Alopecia areata has been linked to psychosocial stress, which has been linked to the onset and/or exacerbation of the condition.[41](16) Increased stress can cause several common "stress-responsive" skin diseases, leading an actual or perceived worsening of the illness.[42][43] This is especially true for Telogen effluvium. The association between a stressor and any subsequent shift in the hair development cycle is known as the brain hair follicle axis.[43] Along this brain hair follicle axis, the ejection of particular neuropeptides may induce the transition of anagen hairs into the telogen phase, resulting in notable changes in the hair development cycle.[44] It may cause hair disorder.[45][43] During this Covid 19 pandemic, people are facing various types of problems in their life. These problems may affect them mentally. People are experiencing massive hair fall because of this mental stress.[46] According to a 2014 study, There are several levels of interactions between psycho-emotional stress and hair loss.[17][47] In a study by Muller et al, In 12 percent of 736 cases of alopecic patients, acute emotional stress such as a relative death or serious terror was identified to be a triggering or exacerbating cause.[48][49] Stress is unlikely to be the sole cause of AA, but stress can exacerbate its symptoms. Excessive amounts of stress and anxiety are both likely to cause and worsen the development of AA.[49]

4.7 Relation between gene and baldness

The AR gene, present on the "X" chromosome, has been related to baldness.[50] One of the autosomal

hits revealed in the research was in a gene linked to Parkinson's disease. A recent review report identified fifteen loci from six researches that were shown to be related with baldness at a genome-wide level (P5x10⁻⁸); there were two of them on the X chromosome.[51] But AR gene isn't the only gene that controls whether you'll go bald. Only six of the 63 genes present on the "X" chromosome may play a role in male pattern baldness, according to a 2017 analysis.[52] According to UK biobank 2017 genome wide study of baldness, out of 52,874 men (Average age: 57.2), 16,724 (31.6%) said they had no hair loss, 12,135 (23.0%) said they had minor hair loss, 14,234 (26.9%) said they had moderate hair loss, and 9,781 (18.5%) said they had severe hair loss. (18)[50] So, this research established a link between biological genes and hair loss. Alopecia has been linked to the expression of two genes. CYP17 is a steroid metabolism gene that helps to release more estradiol by coding for the P450 aromatase enzyme. This gene was discovered in women with PCOS and their brothers who were balding at an early age.[53][54] A new gene on chromosome locus 3q26 has been discovered which is also related to baldness.[55]

4.8 Lifestyle, Nutritional factors and hair loss

Recent study found that, working styles, poor nutrition, smoking and sleeping habits may all have a role in the intensity of AGA. After adjusting the age group, National Nature Science Foundation of China noticed that age group between thirty and forty, married marital status, bad sleep habit, junk food consumption[56][57] and heavy physical labour are all factors that raise the threat of androgenic alopecia.[58][57][59] Lack of sleep can lead to higher levels of stress, which has been linked to hair loss.[60][61] The connection between anxiety and the hair follicle was studied in the American Journal of Pathology.[62] The cycle of hair growth would be disrupted, according to their findings, because the adult stem cells responsible for hair growth rely on the internal circadian clock to activate. If this is the case, then your hair doesn't know what to do because you aren't getting enough sleep.[63] Hair loss has been associated with excessive amounts of certain nutrients like selenium, Vitamin A, and Vitamin E.[64][65][66] Iron deficiency (ID) is the most prevalent dietary deficit in the world, and it is a well-known reason of baldness.[67] In a survey of 312 patients with AA, it was discovered that male pattern hair loss, female pattern hair loss or telogen effluvium, all groups had significantly lesser zinc levels versus 30 healthy controls.[68] Hair thinning and hair loss can arise as a result of protein malnutrition, such as in kwashiorkor and

marasmus.[69] Niacin deficiency is also one of the reason of alopecia.[70] The mechanism by which smoking causes hair loss is complex and likely involve effects of cigarette smoke on the microvasculature of the dermal hair papilla.[71][72][62] In a study published in 2020, researchers compared the prevalence of early onset androgenetic alopecia in male smokers and nonsmokers aged 20 to 35.[73] Male-pattern baldness and female-pattern baldness are both terms for androgenetic alopecia.[40] The researchers have found that smokers are more likely to have hair loss than non-smokers. (19)[74]

4.9 Is it true that high blood pressure causes hair loss?

Hypertension is also one of the reasons for baldness and it may cause coronary heart disease also.[75][76] According to a recent study, hypertension and the use of antihypertensive medicines are more general among Finnish males with androgenetic alopecia.[77] Although hypertension, or high blood pressure, is clearly linked to or correlated with hair loss, but it is unclear whether hypertension causes hair loss. Hypertension was highly linked to male pattern baldness in one such study published in 2007. 250 men between the ages of 35 and 65 were interviewed for this study. Researchers observed that males with blood pressure readings of more than 120 (systolic) and 80 (diastolic) had significantly higher risk of hair loss as those with blood pressure readings of less than 120 (systolic) and 80 (diastolic).[78] Not only high blood pressure, but also the medications used to effectively control high blood pressure, may increase the risk of hair loss.

4.10 Hormonal imbalance may cause baldness

Thyroid [79] and glucocorticoid hormones [80], as well as pregnancy [81] have an impact on human hair growth.[82] Male pattern baldness is caused by lack of testosterone in body.[82] Male hormones don't start working until a man reaches sexual maturity, so there is minimal chance of hair loss before puberty.[36]

4.11 Does dandruff cause hair loss?

Dandruff is usually caused by a fungus named *malassezia*. The majority of people with dandruff are men between the ages of 20 and 40. The majority of people who suffer from dandruff experience hair loss and it may also cause alopecia or permanent hair loss.[83]

4.12 Hair loss due to cosmeceuticals

1. **Shampoo:** Shampoo which contains sulfur can cause hair loss. In today's scenario, most of the people mainly use synthetic shampoo which is not good for our scalp. It may also cause serious hair loss problem.[84] There are a variety of herbal shampoos on the market, we should use

those products instead of using cosmetic products.[83]

2. **Conditioner:** Hair conditioners include sodium chloride can cause hair loss. It might result dry, itchy scalp and promote hair loss. Products containing TEA, DEA, SLS are also harmful for our hair.
3. **Hair wax:** Isopropyl alcohol is present in hair wax. It dehydrates our scalp, makes our hair dry and causes hair loss.[85]

4.13 Diabetes cause hair loss

Diabetes impairs blood circulation, which may interfere the regular functioning of hair follicles. We use various types of medicine for diabetes, which has the capacity to disrupt the natural cycle of hair growth. Diabetes cause stress and we all know that one of the most prevalent causes of alopecia is stress.[86]

4.14 What are some of the other causes of baldness?

Other reasons of hair loss are: Aging (20) , Radiation, weather [87], Injury and impairment, Covid 19, Toxic substances, Infections.[36] Nowadays we are using various types of hair styling products, improper use of these products may also cause permanent hair loss.[88]

5. TREATMENTS

Drug therapies are the most promising approaches to the treatment of baldness in men. Minoxidil and finasteride are most common medicines used to treat baldness.[89] Nowadays, low level laser therapy is used to treat alopecia. It is safe and effective.[90] It's a good idea to quit smoking as soon as possible if you want to avoid hair loss.[71] Herbal remedies of hair loss are onion juice[91], bhringraj[92] and green tea[36]. There is some evidence that taking biotin supplements by mouth can help prevent hair loss, but the majority of the research has been conducted on women.[93] Janus Kinase inhibitors are also used to treat baldness. Hair transplantation treatment is also used to treat alopecia.[94]

6. CONCLUSION

Hair loss is one of the today's major issues. Hormonal imbalance, poor diet, genetic problem, aging, hypertension, side effects of medicines- these are the most common causes of baldness. But we can control our hair loss by some medications and therapies. Hair loss isn't just a matter of appearance, but also a psychological and sociological one. So, we should think about this seriously- how to avoid baldness. Currently only few medicines are available for the treatment of baldness in the market, and

most of the medicines are under research and I hope these medicines will be available in the market for future use with better effectiveness and fewer side effects. Researchers are also trying to find out the other factors which are involved in baldness. If we can find out the factors, then it will be easy for us to control the hair loss.

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