# "ASSOCIATION OF ANDROGENETIC ALOPECIA WITH SMOKING: A CROSS SECTIONAL STUDY"


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**DISSERTATION SUBMITTED TO**

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# LIST OF ABBREVIATIONS USED

| | | | |
|---|---|---|---|
| 1. | AGA | : | AndrogeneticAlopecia |
| 2. | SI | : | Smoking Index |
| 3. | CAD | : | Coronary ArteryDisease |
| 4. | HN | : | Hamilton Norwood |
| 5. | MPHL | : | Male Pattern Hair Loss |
| 6. | FPHL | : | Female Pattern Hair Loss |
| 7. | PHL | : | Patterned Hair Loss |
| 8. | HF | : | Hair Follicle |
| 9. | DP | : | Dermal Papilla |
| 10. | EGF | : | Epidermal Growth Factor |
| 11. | TGF | : | Transforming Growth Factor |
| 12. | WNT | : | Wingless-type Integration Site |
| 13. | SHH | : | Sonic hedgehog |
| 14. | TFAM | : | Mitochondrial Transcription Factor A |
| 15. | MPB | : | Male Pattern Baldness |
| 16. | BMI | : | Body Mass Index |
| 17. | HTN | : | Hypertension |
| 18. | LDL-C | : | Low Density Lipoprotein- Cholesterol |
| 19. | HDL-C | : | High Density Lipoprotein- Cholesterol |
| 20. | CAD | : | Coronary Aretery Disease |
| 21. | AR | : | Androgen Receptor |
| 22. | EDA2R | : | Ectodysplasin A2Receptor |
| 23. | DHT | : | Dihydrotestosterone |

| | | | |
|---|---|---|---|
| 24. | PGD2 | : | Prostaglandin D2 |
| 25. | APM | : | Arrector Pilli Muscle |
| 26. | FT | : | Fronto Temporal Recession |
| 27. | PTG | : | Phototrichogram |
| 28. | PRP | : | Platelet Rich Plasma |

# ABSTRACT

**BACKGROUND:-**

Androgenetic alopecia (AGA) is a hereditary androgen dependent disorder, characterised by progressive thinning of the scalp hair defined by various patterns. It is the most common hair loss type affecting upto 80% of men and 50% of women in their course of life..The prerequisites for AGA are presence of androgens and genetic predisposition but clinically in the day to day practice, it is seen that blocking androgens alone is not sufficient in the treatment of AGA. Factors such as smoking, lifestyle, overweight may play a role in androgenetic pathogenesis. The mechanism by which smoking causes hair loss is multifactorial, few of them being damage to the DNA hair follicle, imbalance in follicular protease/antiprotease systems which regulates the growth cycle of hair and also causes a relative hypo-oestrogenic state.

**OBJECTIVES:-**

To document the type and extent of androgenetic alopecia.

To categorise the smoking habit of the above subjects according to smoking index.

To evaluate the frequency of smoking among the subjects with androgenetic alopecia.

**MATERIALS AND METHODS:-**

A total of 218 patients with AGA who attended the Dermatology OPD at R.L Jalappa Hospital attached to Sri Devaraj Urs Medical College between January 2019 and July 2020 were included in the study. Data was collected after obtaining written informed consent from the patient. In every case detailed history and thorough clinical examination was carried out. Information about smoking, quantity, duration and frequency of smoking and other possible

risk factors of androgenetic alopecia was collected. Cigarette smoking is calculated as per the smoking index (SI). The data was entered in Microsoft excel sheet, a master chart was prepared and it was analysed using IBM SPSS software version 22. P value < 0.05 was considered statistically significant.

**RESULTS:-**

Majority of the study population (218 patients) i.e. 44.4 % patients who presented to outpatient department were in the age group 20-30 years. Majority 42.7% had a hair loss duration between 1-5 years. 57.21% patients had a positive family history and most of them had paternal inheritance. Diabetes mellitus was seen in 10.5%, Hypertension in 9.6%, Bronchial Asthma in 1.8% and 0.9% of the subjects had CAD. History of alcohol consumption was present in 33.5 %.Majority 78% of the patients had smoking history. Among them 33% of the patients were moderate smokers, 24.3% were light smoker and 20.6% were heavy smokers. The most commonly seen grade according to HN class was type II in 27.5% of patients followed by type I. In our study most common type of AGA in light and moderate smokers was type II, in heavy smoker was type IV.

**CONCLUSION:-**

AGA is one of the most common dermatological disorders that present to dermatologists. AGA is a multifactorial disease which occurs due to interactions between various genetic and environmental factors. A positive association between smoking and Androgenetic alopecia is seen in our study.

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# INTRODUCTION

# INTRODUCTION

Androgenetic alopecia is a hereditary androgen dependent disorder, characterized by progressive miniaturization of the hair follicle, due to alteration in the hair cycle dynamics, leading to transformation of vellus to terminal hair follicle.[1] It is the most common type of hair loss.It commonly begins by 20 years of age and affects nearly 50% of men by the age of 50 years and 50% of women by the age of 60 years.[1,2] Clinical manifestations of AGA are different in both sexes. It is called male pattern hair loss (MPHL) in males and female pattern hair loss (FPHL) in females.[1]

The prerequisites for androgenetic alopecia are presence of androgens and genetic predisposition but clinically in the day to day practice, it is seen that blocking androgens alone is not sufficient in the treatment of androgenetic alopecia.[3] Factors such as smoking, lifestyle, overweight may play a role in androgenetic pathogenesis.

Studies conducted previously have shown significant association between androgenetic alopecia and smoking. Studies have shown that smoking status, current amount of cigarette smoking and smoking intensity were statistically significant factors responsible for Androgenetic alopecia.[3,4]A cross-sectional study, concluded that smokers had six times increased risk of having moderate or severe Androgenetic alopecia.[4]

The mechanism by which smoking causes hair loss is multifactorial, few of them being damage to the DNA hair follicle, imbalance in follicular protease/antiprotease systems which regulates the growth cycle of hair and also causes a relative hypo-

estrogenic state.[5]

Alopecia has a major psychological impact on affected men and women, which is why an increase in public awareness about the association between smoking and alopecia offers an opportunity in health education against smoking effectively.[5] Due to paucity of the literature in this aspect more studies are required to prove the association between smoking and androgenetic alopecia, hence this study is undertaken.

# AIMS & OBJECTIVES

# AIMS AND OBJECTIVES

The aims and objectives of the study were as follows:

- To document the type and extent of androgenetic alopecia.
- To categorize the smoking habit of the above subjects according to smoking index.
- To evaluate the frequency of smoking among the subjects with androgenetic alopecia.

# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

Alopecia refers to thinning of hair or hair loss. The word 'alopecia' was first coined from the Greek word for fox. It refers to the constant shedding of hairs seen in the lifetime of these animals.[6] Human hair plays a critical role in our physical appearance and also is of great importance in social communication. Loss of scalp hair leads to depression, anxiety and social inhibition.

"What (Time) hath scanted men in hair he hath given them in wit" by Shakespeare from "The comedy of errors".

Late in 1500 AD during the time of Shakespeare as the pathogenesis of androgenetic alopecia (AGA) was poorly understood, people had two options either to live with it or to use wig for cosmetic purposes.

One of the oldest medical specialities as stated by Greek historian Herodotus (490/480-424BC) is the Egyptian "Physician of the Head" who specialized in the affections of the scalp.[7] In 350BC, Aristotle had explained the reason for baldness in men as due to natural humidity and heat and also why eunuchs and women do not develop baldness.[8] Later in 1942, Hamilton demonstrated the involvement of male hormones in the development of classic pattern baldness in men; the term androgenetic alopecia was coined to highlight the associated genetic and hormonal factors with the development of the disease.[9]

Hair follicles (HFs) are an integral part of the mammalian skin where they produce filaments largely composed of the protein, keratin.[10]Hair can either be Lanugo hair,

short vellus hair, Intermediate hair, long terminal hair, sebaceous hair.(Figure 1)[11] Hair helps the epidermis to maintain the body‘s protective barrier against its external environment. In humans, however, the body hair has lost most of its importance as a physical protective barrier. Several hypotheses have been put forward to explain how humans evolved to have radically different patterns of hair distribution compared to most other mammals.[10] these include the process of adaptation to provide a better thermoregulatory mechanism in the hot and dry climate conditions that arose about 3 million years ago when forests gave way to hot Savanna grasslands. Another hypothesis is sexual selection based upon the dimorphism seen in the hair patterns of men and women.

Nevertheless, hair still has great social significance for human beings. Healthy hair indicates health, youth and vigor. Male pattern baldness is taken to be a sign of age and loss of vigor, which may be concealed with a toupee, hats or simply by shaving the head.[10]

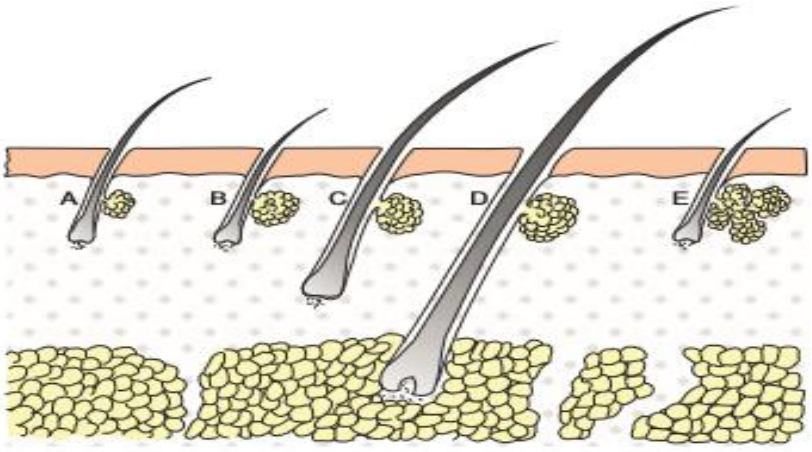



**Figure 1: Types of hair follicles[11].**

A. Lanugo hair, B. Vellus hair, C. Intermediate hair D. Terminal hair, E. Sebaceous hair

## HAIR FOLLICLE, HAIR CYCLE, STEM CELLS

### HAIR FOLLICLE

The hair follicle extends through all layers of the skin. Each strand of hair is made up of concentric regions, the medulla, cortex and cuticle. The innermost medulla is a variable space (sometimes present and sometimes not) and its function is still debated. The highly structured cortex is the primary source of the mechanical strength of the hair. The cortex contains melanin, which colours the fiber based on the number, distribution and types of melanin granules. The shape of the Hair Follicle determines the shape of the cortex, so that hairs with circular cross-section are straight, and those with oval cross-section are curly. The cuticle is the outer covering of protein coated with a single molecular layer of lipid that makes the hair repel water. The diameter of the human hair varies from 17 to 180 μm.[12]The Hair Follicle is a complex mini-organ.[13] embedded in the skin and composed of the papilla, matrix, root sheath and bulge.[14]

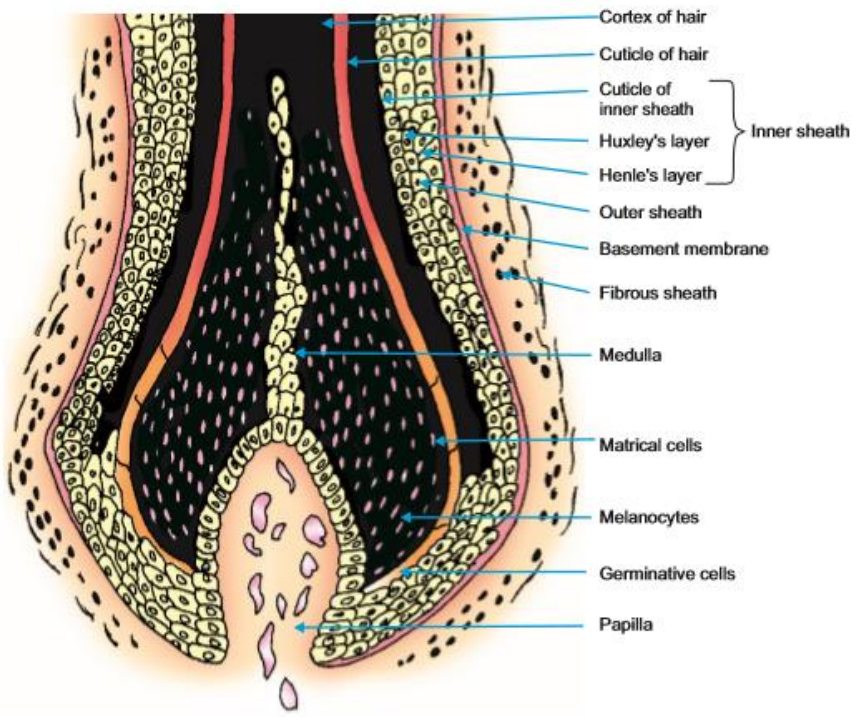



**Figure 2: Differentiation of cells of follicular matrix along seven separate lines[11]**

Structures closely associated with the Hair Follicle are sebaceous glands, apocrine glands, the arrector pili muscle and mechanoreceptors that respond to touch.[15]There are between 250,000 and 500,000 Hair Follicle on the human scalp and as many as 5,000,000 on the whole body.

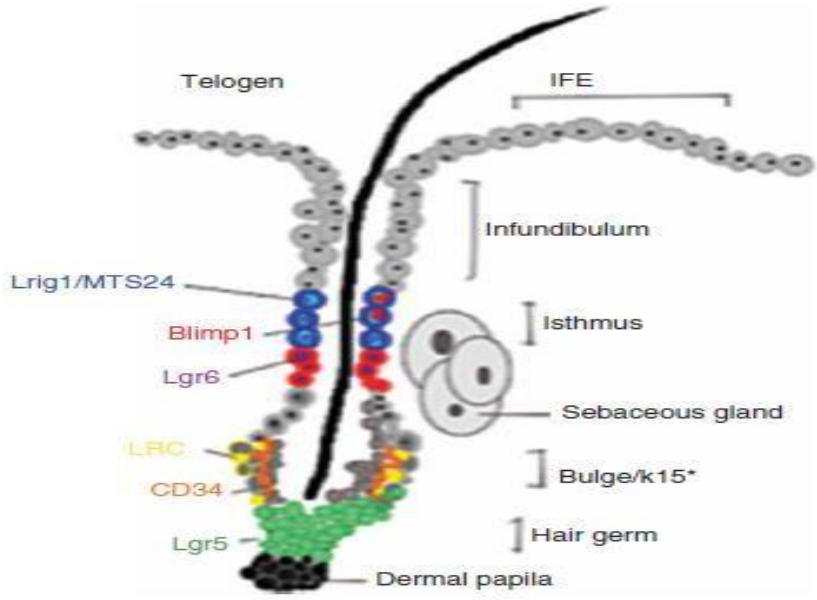



Figure 3. Schematic organization of the telogen-phase adult Hair Follicle showing location of the stem cells. The stem cell populations are represented by their well-marked gene/ protein-expression or promoter-activity: Lgr5 (hair germ and bulge), CD34 (bulge), LRC (bulge), Lgr6 (lower isthmus), Lrig1/MTS24 (isthmus), Blimp1 (sebaceous gland) and K15* (K15 promoter, bulge area). HF: Hair follicle.

The growth of hair occurs in a periodical manner and each of the follicles function as an independent unit. The stages of hair cycle are as follows:

Growth phase (Anagen)

Regression phase (Catagen)

Resting phase (Telogen)

Shedding phase (Exogen)

Lag phase (Kenogen)[11]

Anagen phase: This phase constitutes growth phase of the follicle, length of anagen varies according to the body site and it determines the final length of the hair. Itisdivided into seven stages (anagen I–VII).[16]The scalp hair has the longest anagen ranging from 2 to 8 years. It has been stated that typically 90%–93% of scalp follicles will be in anagen and remaining are in telogen.

Catagen: This is the phase of transition of the follicle between anagen and telogen. This phase lasts for 2 weeks.[11]

Telogen: The period between complete follicular regression to the onset of next anagen phase results in formation of telogen or club hair.[11]Each hair cycle has 5–10% of hair in the telogen phase with 100-150 hair being shed daily. This phase lasts for about 2-3 months.[17]

Exogen: The club hair is shed through an active process called exogen.The telogen hair shaft base has a club shaped smooth outline however the exogen shaft base is shrunken and has a more elongated shape and pitted margin.[11]

Kenogen/lag phase: It is a phase in the hair cycle where the follicle is empty after hair shedding and persists in the stage for a variable duration. It is seen more in men and women with androgenetic alopecia.[11]

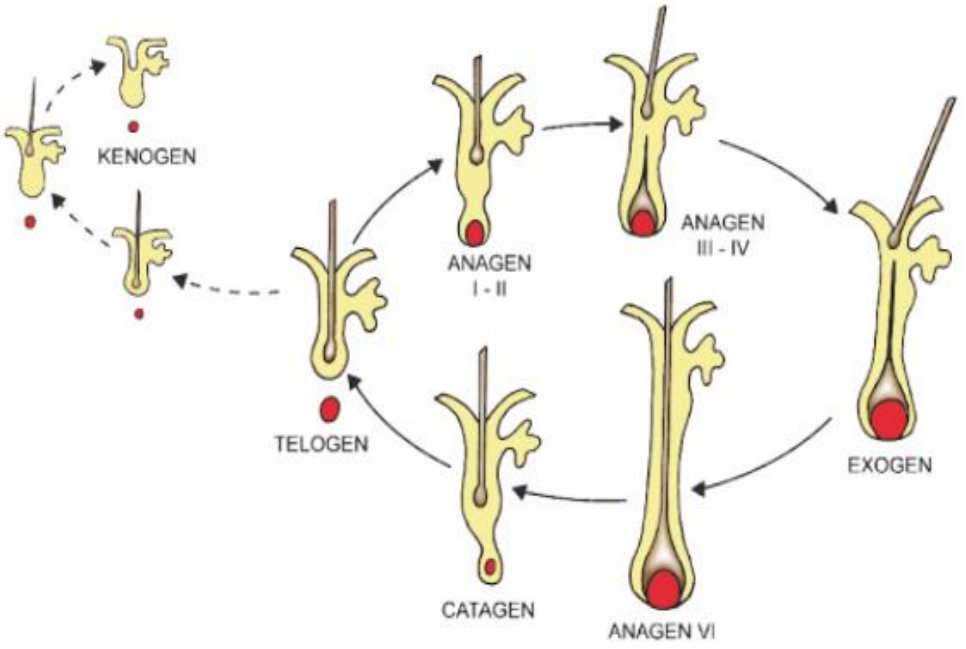



**Figure 4: Demonstrates the different phases of hair cycle[18]**

The anagen hair follicle is divided into 4 parts from deep to superficial:

1. Hair bulb
2. Suprabulbar area: This extends from the hair matrix to insertion of arrector pili muscle
3. Isthmus: This extends from insertion of arrector pili muscle to entrance of sebaceous gland duct
4. Infundibulum: This extends from sebaceous gland to the follicular orifice.[11]

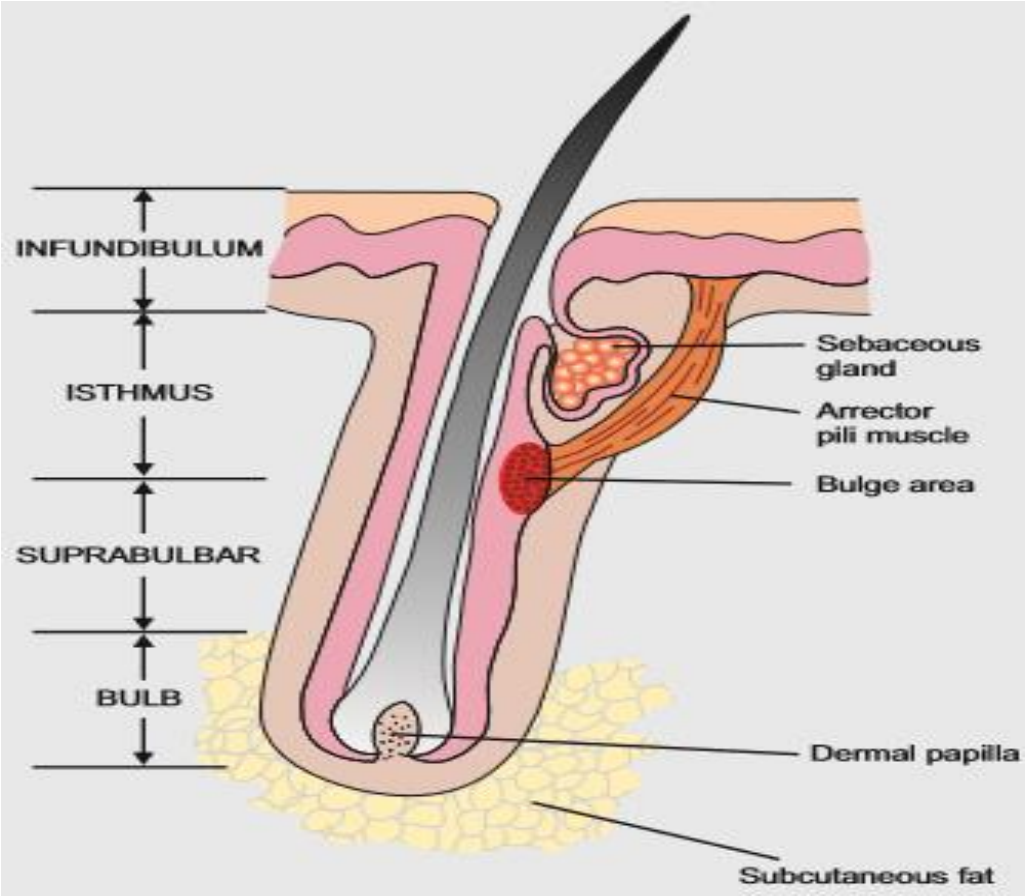



**Figure 5: Principal subdivisions of a hair follicle, based on both morphologic and biological considerations.[11]**

The signalling involved in the well-orchestrated process of hair growth and HF cycling is complex and incompletely understood.[19] The basic driving force is interaction between the mesenchymal and epithelial cell populations within the Hair Follicle unit.[20] **Figure 6**shows a schematic diagram illustrating some of the different types of stem cells and the particular differentiated structures in the skin to which they contribute. The most important mesenchymal cells in the Hair Follicle reside within the dermal papilla (DP). These cells produce signals to control sequential cycling of the follicular epithelium.[21] It is thought that epithelial stem cells, which reside in the bulge area of the Hair Follicle, can respond to the signals from the dermal papilla.[22] This activation leads to production of progenitor cells from the stem cells in the bulge

area, and then these progenitor cells become transiently amplifying cells that expand downward into the deep dermis, followed by differentiation into matrix cells that have the ability to produce the hair shaft, and its sheath. However, in both humans and especially in animals, the male or female genders have very different hair phenotypes, which are governed by the influence of sex hormones.[23]

Several growth factor families are involved in hair follicle cycling[21], namely fibroblast growth factor, EGF, hepatocyte growth factor, IGF-I, TGF-b families, among others. Signal transducer and activator of transcription 3 (stat3) is a latent cytoplasmic protein that conveys signals to the nucleus upon stimulation with cytokines/growth factors, leading to transcriptional activation of downstream genes that have the stat3 response element in their promoter region. Stat3 plays a critical role in hair follicle cycling.[24]

A series of signalling molecules is involved in each step of primary hair development and differentiation that have been elucidated in studies of embryogenesis.[25] Wingless type (Wnt) signalling is crucial for the initiation of hair follicle development.[26] Wnt-protein is a ligand that binds to a cell-surface receptor ‗Frizzled' family member, which then passes the biological signal to the intracellular protein ‗Dishevelled' (Dsh). Dsh causes the accumulation of b-catenin in the cytoplasm (by protection from degradation) and its eventual translocation into the nucleus to act as a transcriptional co-activator of transcription factors that belong to the TCF/LEF family.

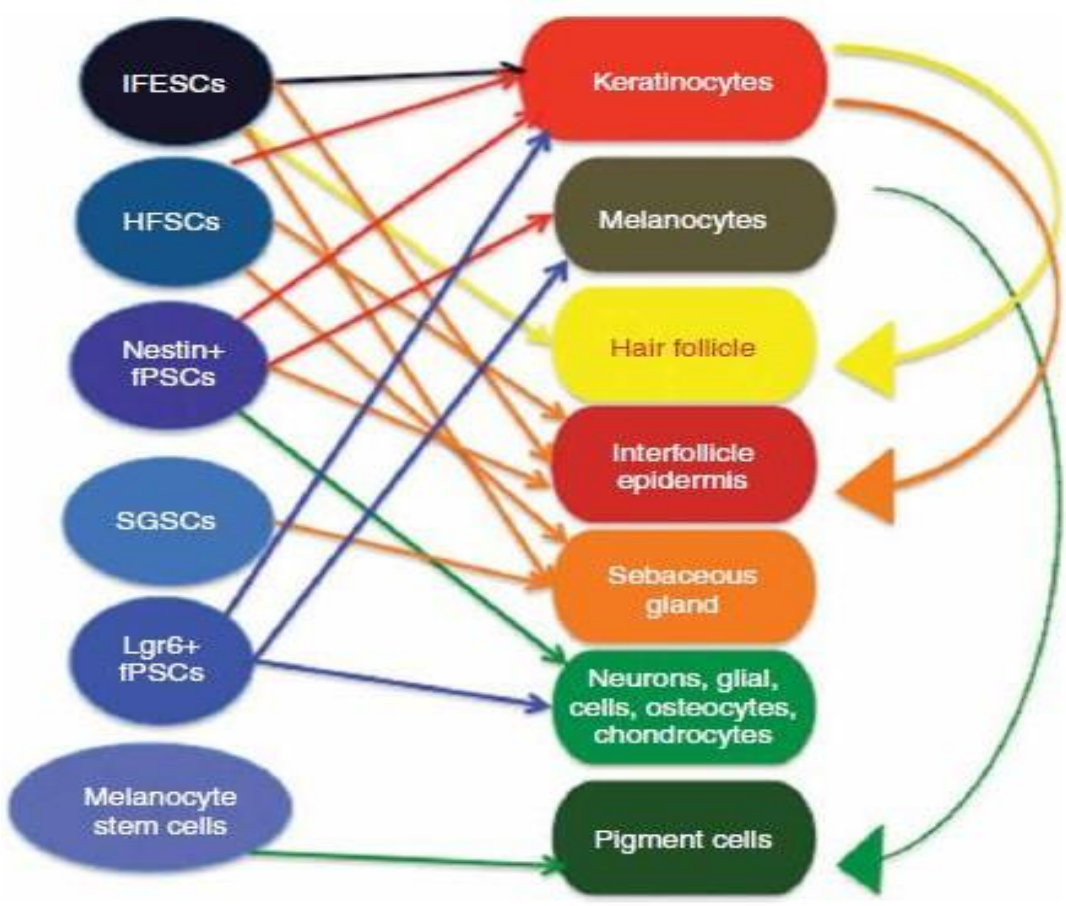



Figure 6. Interactions between stem cells, progenitor cells, and cells in and related to the skin. IFESCs: Interfollicle epidermal stem cells; hair follicle SCs: Hair follicle stem cells; SGSCs: Sebaceous gland stem cells; fPSCs: follicle nestin + pluripotent stem cells; Lgr6 + fPSCs, could be identical to fPSCs.

_Sonic hedgehog‘(Shh) signaling plays an important role in both embryonic and adult hair follicle development. Shh binds to and inhibits the extracellular domain _Patched,‘ allowing the intracellular domain _Smoothened‘ to accumulate and inhibit the proteolytic cleavage of the Gli family of zinc-finger transcription factors.[27] Shh signaling (and in particular activation of Gli2[28] is obligatory for development of the epithelial hair germ, comprising epidermal placodes and associated dermal condensates.[29] Noggin[30], bone morphogenetic protein (BMP)[31] and ectodysplasin[32]

signalling also play important roles at early stages of hair follicle placode development. Dlx homeobox transcription factors regulate epidermal, neural and osteogenic cellular differentiation.[33] It was found DLX3 played a central role as a transcriptional regulator of hair formation and regeneration. DLX3 co-localized with phosphorylated Smad1/5/8 complex, and regulated BMP signalling during hair morphogenesis in animal models.[34]

An interesting study by Hamanaka et al.[35] showed that mitochondrial-generated reactive oxygen species (ROS) were critical mediators of cellular differentiation and hair follicle morphogenesis. They generated mice with a keratinocyte-specific deficiency in mitochondrial transcription factor A (TFAM), which is required for the transcription of mitochondrial genes encoding electron transport chain subunits. Ablation of TFAM in keratinocytes impaired epidermal differentiation and hair follicle growth and resulted in death 2 weeks after birth. TFAM deficient keratinocytes failed to generate mitochondria-derived ROS, a deficiency that prevented the transmission of Notchand -catenin signals essential for epidermal differentiation and hair follicle development.[36] In vitro keratinocyte differentiation was inhibited in the presence of antioxidants, and the decreased differentiation marker abundance in TFAM deficient keratinocytes was partly rescued by application of exogenous H2O2.

The Dermal Papilla remains associated with the overlying epithelial matrix cells, which differentiate to give rise to the different hair follicle lineages such as the cells that make the medulla, cortex and cuticle of the hair shaft and the inner root sheath (IRS).[37] The matrix is derived from epithelial stem cells located in the bulge region of

the hair follicle.[38] Several important pathways and transcription factors that initiate and promote differentiation of the matrix cells have been determined, including Gata3 and Cutl (which regulate IRS differentiation and BMP signaling[39], and transcription factors such as Gdsma3[40] , Msx2[41] , Foxn1[42] and Hoxc13[43] that are required for complete hair follicle development and optimal hair shaft structure.

Cells with stem cell properties have recently been described in many integumental appendages including feathers[44] and teeth[45] but the hair follicle stands out as one of the best model systems for studying adult stem cells.[46] The identification, characterization and transplantation of adult stem cells is currently one of the most intensively investigated areas of biological and biomedical research. It is thought that stem cells and TA cells are not interchangeable, and once the TA cell has left the niche, its progress toward differentiation is irreversible. The role of tissue maintenance throughout the lifespan of an organism requires stem cells to preserve their genomic integrity. They do this by dividing infrequently, so as to reduce DNA replication errors, and are also commonly protected from environmental and chemical assault by the niches they inhabit.

**1.7 FUNCTIONS OF HAIR**

Hair serve to retain heat in cold climate and loose the heat in a hot environment, thus helping in thermoregulation which helps the species to survive under extreme climatic variations. It protects the body against trauma and also against ultraviolet damage. Hair coloration helps to camouflage against predators and in some instances serves as a sexual attractant. It has rich nerve supply which helps in tactile and communicative functions. The arrector pili muscle connects the lower portion of each hair shaft with

the underside of the skin. Upon emotional stimuli, these small muscles contract, causing the hair to stand. In human beings, specialized hair such as eye lashes and hair in the nostrils and external ears afford some protection from the environment. Eyebrows prevent sweat from getting into the eyes. Scalp hair assists in maintaining the temperature of the brain. Hair can also excrete toxic substances like arsenic, and are thus of use in forensic medicine. The loss of hair and excessive growth of hair cause significant psychological distress and anxiety in an individual.[47]

## 5. ALOPECIA

**Definition**: Alopecia refers to thinning of hair or hair loss.

The disorders that cause alopecia can be classified as diffuse, patterned, focal hair loss as well as into cicatricial (scarring) and non-cicatricial (nonscarring) forms.

Scarring alopecia is characterized by permanent destruction of hair follicular stem cell structure resulting in loss of hair producing capabilities. In contrast, in nonscarring alopecia the hair follicle is destroyed and subsequent hair regrowth follows periods of hair shedding.[47]

Non scarring alopecia's include:

Alopecia areata (AA)

Alopecia areata incognita (AAI)

Androgenetic alopecia (AGA)

Female pattern hair loss (FPHL)

Telogen effluvium (TE)

Anagen Effluvium

Tinea capitis (TC)

Trichotillomania (TTM)

Traction alopecia

Temporal triangular alopecia (TTA)

Syphilitic alopecia.

Loose anagen syndrome.

Short anagen syndrome.[6]

## Androgenetic alopecia (AGA)

**Synonyms:** Male pattern hair loss (MPHL), Female pattern hair loss (FPHL), Patterned or premature baldness, Hereditary balding or thinning.[50]

**Definition**: It is an androgen-dependent, hereditary disorder resulting from the conversion of scalp terminal hair into miniaturized vellus hair in a characteristic pattern.

AGA is characterized by varying degrees of hair loss/thinning primarily in the frontal areas (temples) and at the vertex of the scalp. In men with AGA, the residual hairs tend to be of various diameters and lengths as each follicle is in a different phase of the hair cycle, so the presence of dissimilar hair length and texture is a classic feature of this condition.[1]

## EPIDEMIOLOGY

### Incidence, prevalence and ethnicity

### Men

AGA affects all races but prevalence rate of AGA varies according to the race. Its prevalence is considered to be highest in Caucasians. In a study done on the Caucasian population the prevalence rate of AGA was linked with age and was found to be 30%, 40% and 50% in 30s, 40s, 50s years of age respectively.[51,52] In India, the prevalence of AGA according to a population based study of 1005 subjects estimated it to be around 58% in males aged 30-50 years.[53]

The commonest type/grade based on the Hamilton Norwood (HN) classification showed difference results in different studies. In studies conducted on the Indian population had grade II as the commonest pattern of AGA.[54,55]

In addition to the Hamilton Norwood classification even a female pattern hair loss was observed in men by few authors.[56,57]

### Women

There are fewer studies on the epidemiological studies of AGA in women. Norwood T. in his study showed a prevalence of around 19% in the Caucasian population.[56] It was also seen that the prevalence was only 6.0% in the Chinese population and relatively similar lower prevalence of 5.6% in the Korean population, indicating that the prevalence was as similar to that seen in men, lower in oriental races when compared to Caucasians.[58,59] The incidence of AGA in women ameliorated with age.[56] Female AGA is not exactly similar to AGA in males. It is better referred to as

"female pattern alopecia" or "female pattern hair loss" (FPHL). There is a clear difference between the clinical pattern of male and female pattern hair loss suggesting that these are two separate entities. This is also based on studies which have shown no clear relation between excess testosterone levels and female pattern hairloss.[56]

**Children and Adolescents**

AGA was reported in children and adolescents with a genetic predisposition, the first signs of AGA was noticed with rising androgens at puberty[60] and was observed as early as 6 years of age.[61]

**Age**

The age of onset of AGA differs, but usually in both sexes it starts after puberty, when enough testosterone is available to be transformed into dihydrotestosterone. Therefore the onset of AGA is not expected to be seen in prepubertal patients without abnormal androgen levels.[62] There is no definite age for development of baldness but according to a study if early balding is defined as HN grade II hair loss, then 40% begin to develop balding between the ages of 18 and 29 years, a further 24% first develop balding in their thirties, 3% in their forties, 5% in their fifties, 9% in their sixties, 2%in their seventies and 1% at or beyond the age of 80years.[53,63]

It was seen that early onset MPB develop more rapidly when compared to those with lateonseti.e. those who develop balding in their twenties tend to advance one to two grades per decade, whereas late onset AGA takes two decades to progress a single grade.[51]

## AGA and associated diseases

### Trichodynia

Trichodynia seen in AGA is associated with the increased hair shedding and settles with treatment.[64]

### Body Mass Index (BMI)

The body fat is negatively correlated with levels of androgens in men. It was seen that dihydrotestosterone decreases with increasing BMI,[65] waist size and body fat.[66]

### Hypertension (HTN)

Studies suggest an association between hypertension and AGA. Hence, AGA could be considered as a clinical marker for hypertension. The proposed explanations for the association of HTN and AGA are as follows:

The high level of circulating androgens which bind to mineralocorticoid receptors might be responsible for the observed difference in blood pressure.

Hyperaldosteronism; itself may directly participate in the development of alopecia.[67]

### Dyslipidemia

Dyslipidemia has been observed in patients with MPB.[68] Studies showed increased LDL cholesterol and HDL cholesterol ratio as well as total cholesterol and HDL-cholesterol ratio in MPB, which is considered as a predictor of coronary artery disease (CAD) in men.[69]

**Coronary artery disease**

Several authors have observed an association between MPB and CAD.[69]It was observed that vertex baldness was associated with an increased risk of CAD. Sharma et al. in his study on young Indian population observed early vertex baldness may be a non- modifiable risk factor for CAD.[69] Studies suggested that early onset AGA may serve as a useful clinical marker to identify men with increased risk for CAD.[69]

**Metabolic syndrome**

A significant association between metabolic syndrome and AGA has been observed.[70] Among the components of metabolic syndrome, increased HDL-C is an important factor associated with AGA. Patients with moderate or severe AGA may be at higher risk for developing metabolic syndrome. Matilainen V et al. reported a strikingly increased risk of hyperinsulinaemia and insulin resistance associated disorders such as obesity, hypertension, and dyslipidemia in men with early onset of androgenetic alopecia.[70]

**Prostrate carcinoma**

Vertex balding was seen in those with prostate cancer but there is no clear association with MPB.[71]

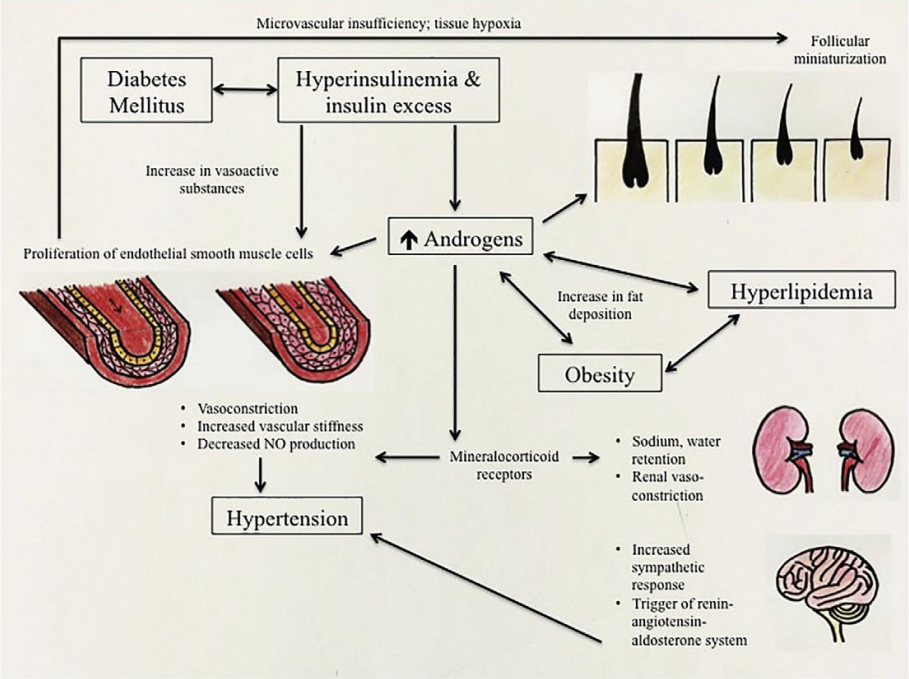



**Figure7: Schematic representation of the androgen and hormonal crosstalk between androgenetic alopecia and metabolic disorders. (NO-nitric oxide)[72]**

## ETIOLOGY:

The etiology of patterned baldness in males and females has been widely researched and although it is still not fully understood. The important factors associated with the patterned baldness are considered to be made up of genetic predisposition and hormone dependency.[9]

### Genetics

The genetic association in AGA was poorly understood earlier but multiple genomic studies have proved that it is a genetically determined condition inherited from either parent.[73,74] Although clearly familial, the exact mode of inheritance has not yet been clarified. The concept of a single autosomal dominant gene, with reduced penetrance in women, now appears more like a polygenic type of inheritance.

## Androgen receptor (AR) gene

The gene that is strongly linked with MPB is the androgen receptor (AR) gene located on chromosome Xq12. This region also contains another gene ectodysplasin A2 receptor (EDA2R), but it is still not fully understood whether one or both genes play a role in the progression of AGA.[75] The AR/EDA2R region forms the major risk factor for development of MPB because it enhances the effect of androgens by increasing the number of androgen receptors in affected scalp tissue.[76]The androgen receptor gene *Stu1* restriction fragment length polymorphism (RFLP) was found in almost all (98.1%) young bald men, and most older bald men (92.3%), but only in 77% of non-bald men.

### 20p11.22 loci

A second locus identified associated with male AGA at *20p11.22* by two genomic wide associated studies.[79] Cobb et al. found the second strongest association with MPB from the 20p11 region between PAX1 encoding paired box protein 1 and FOXA2 encoding forkhead box protein A2.[80]Richards et al. observed that 14% of men had risk alleles at both the *AR* and *20p11* loci and this was associated with a seven fold increase in the risk of balding.[77]

## Other associated loci

Ten additional loci have been reported to be associated with MPB [79,80]

**Table 1: Loci associated with MPB**

| | |
|---|---|
| HDAC9 (chr 7) | SETBP1 (chr18) |
| region 17q21.31 | WNT10A (chr2q35) |
| TARDBP (chr1) | SUCNR1(chr3q25) |
| HDAC4 (chr2) | EBF1 (chr5q33.3) |
| AUTS2 (chr7) | SSPN (chr12p12.1) |

Subsequent studies found none of the loci except WNT10A to be associated with MPB.[79,80]

**WNT10A gene**

WNT10A (Wnt family member 10A) gene is involved in regulating WNT signalling showed a positive correlation in AGA. The decreased expression of WNT10A was observed in AGA risk allele carriers for SNP (rs7349332) which leads to a delay in telogen–anagen transition and a shortening of anagen duration, this results in changes in the hair cycle as seen in AGA.[80]

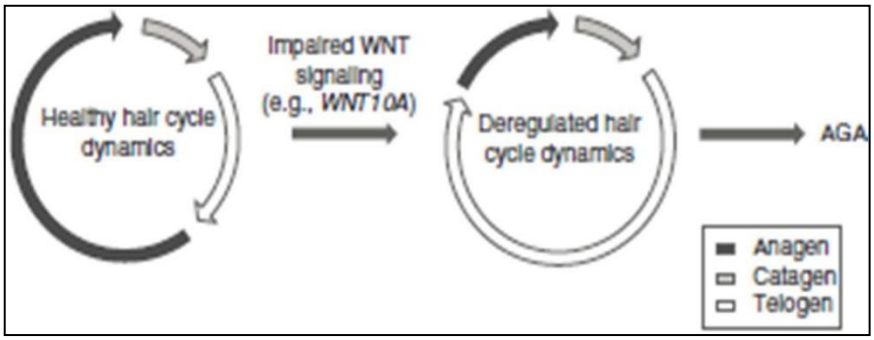



**Figure 8:WNT10A signalling in hair cycle[80]**

5α-reductase enzyme

The role of 5α-reductase enzyme has been postulated in MPB. Two known iso-enzymes of 5α-reductase exists i.e. Type I (localized to the skin and scalp) & Type II (on scalp). Genetic association studies of the 5α-reductase enzyme genes (SRD5A1 on chromosome 5 and SRD5A2 on chromosome 2) conducted using dimorphic intragenic restriction fragment length polymorphisms were not associated with MPB.[81] Genes like aromatase, estrogen receptor and IGF-2 genes have not been proved to be associated with MPB.[82]

**Hormonal factors**

**Androgens**

Testosterone is an important factor in the development of MPB. The hormone testosterone is converted to dihydrotestosterone (DHT) in the presence of the enzyme 5α-reductase. DHT is a more potent androgenic metabolite in charge of driving follicular regression.[82] The concentration of DHT, 5α reductase and ARs were found to be increased in the balding scalp.[82] Other enzymes such as 3 β hydroxysteroid dehydrogenase (3β HSD) and 17 β hydroxysteroid dehydrogenase (17β HSD), which are involved in conversion of weak androgens to potent androgens were elevated in the bald scalp.[83] Androgens do not act equally on all hairs. In men, body and facial hair growth is stimulated at puberty but the scalp hair is lost.[84] Sensitivity of the hormones on the scalp varies hair loss first occurs over the temples and subsequently hairs miniaturize in a well-organized fashion to produce patterned baldness. The circulating androgens, local factors determine individual susceptibility and severity of baldness.[85]

**Prostaglandin D2**

In recent studies on MPHL, prostaglandin D2 (PGD2), a known inhibitor of hair growth, was found to be elevated. PGD2 synthase has also been shown to be elevated at mRNA and protein levels in the bald scalp. The PGD2 acts via the G protein (heterotrimeric guanine nucleotide) coupled receptor 44 (GPR44) for inhibition of hairgrowth.[86]

**Environmental factors**

**Demodex infestation**

Demodex infestation was seen in association with MPB by many authors.[87,88] An indirect role of demodex by inducing inflammation in the scalp was suggested in the pathogenesis. Demodex mite is an obligatory ectoparasite and resides in the pilosebaceous units. Two species of demodex folicularum and brevis are known to be present in humans.[87] Demodex mite contain an immunoreactive lipase that might be responsible for the induction of inflammation or demodex induces immune reaction and hair follicle depletion by prolonged invasion of hair follicle which ultimately cause shift of the hair cycle from anagen phase totelogen.[88]

**Smoking**

Smoking plays arole in the pathogenesis of AGA. The association between smoking and AGA has been addressed in multiple studies.A Taiwan study states that smoking status, current amount of cigarette smoking, and smoking intensity were statistically significant factors responsible for Androgenetic alopecia.[3]

A cross -sectional study done in Rome, Italy concluded that smokers had six times increased risk of having moderate or severe Androgenetic alopecia[4]

A study on the degree of hair loss among monozygotic twins aged over 50 have shown that intrapair differences were negligible in 92%,slight in 8% and striking in none. A sailent feature differing the two brothers in their personal histories was that the balding brother admitted to heavy cigarette smoking, while the other was a non-smoker.[89]

Several mechanisms have been discussed by which smoking causes AGA which are asfollows:

- Smoking may be detrimental to the microvasculature of the dermal hair papilla, cutaneous collagen and elastic tissue.
- Hair growth has a negative impact on it due to blood flow restriction. Due to lack of blood flow, hair follicles will have reduced supply of oxygen, growth factors and nutrients that are needed to sustain a better hair growth cycle.
- Smoke genotoxicants may cause damage to DNA of the hair follicle.
- Smoking may lead to an imbalance in the follicular protease or antiprotease system.The pro-oxidant effect of smoking causes oxidative stress that may lead to the release of proinflammatory cytokines that, ultimately results in the follicular microinflammation and fibrosis.
- Cigarette smoking might yield a relative hypoestrogenic state by inducing increased hydroxylation of oestradiol and inhibition of aromatase; which converts androgens toestrogens.[3]
- Smoking can increase the levels of DHT in the blood. DHT causes follicles to shrink. Thus affecting the hair growth.
- Follicles that still function tend to grow brittle hair and more prone to breakage, which leads to thinning of hair.
- Hair follicles along with the skin will age prematurely due to smoking. This

may lead to premature gray hair.

- Smoking decreases vitamin C, collagen and Vitamin A supplies in the body, which facilitates proper hair growth and strength.[90]

**Alcohol consumption**

Earlier it was considered that alcohol consumption would be associated with a decreased risk of AGA because of its association with increased serum oestradiol.[91] Severi G at al. observed that drinking alcoholic beverages more than once a month on an average was associated with a increased risk for frontal and vertex AGA.[92]

## PATHOPHYSIOLOGY

MPHL occurs in a characteristic pattern affecting the front-vertical scalp, which has been described earlier.[52] Hairs in the affected area are shed and replaced by small vellus hairs in androgenetic alopecia. Three areas of the scalp are affected usually: temples, vertex and mid frontal scalp. The hair loss at each of these areas start in a particular pattern: in bitemporal region it starts at the anterior hairline and moves posteriorly over the scalp; in vertex scalp it starts centrally and spreads outwards circumferentially; in mid frontal scalp, hair follicle miniaturization leads to a pattern of hair loss resembling a Christmas tree.[11] As the three zones are not affected equally leads to clinical variations in the PHL.

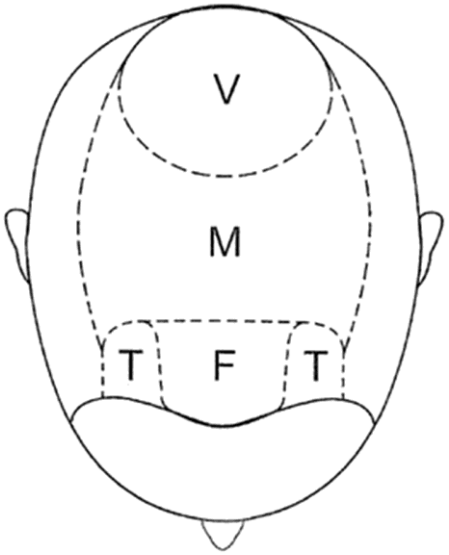



**Figure 9: Areas of hair loss in AGA. V, Vertex; M, Mid scalp; T, Temporal; F, Frontal[11]**

The three important key features of **AGA are:**

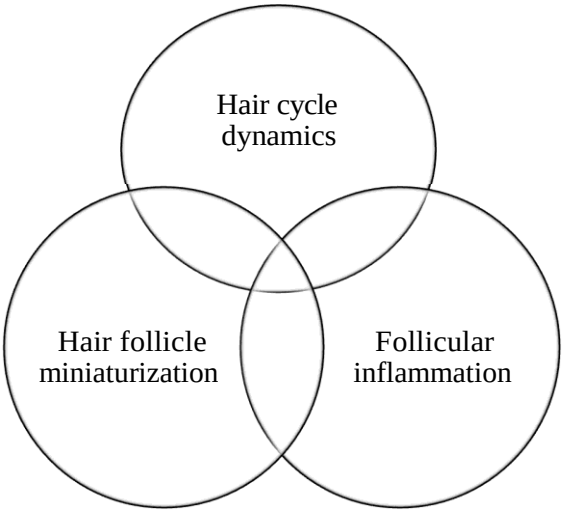



**Figure 10: Pathophysiology of AGA Hair cycle dynamics:**

Normally the hair cycle is not synchronized among the adjacent units and assumes a mosaic pattern in the scalp. It is commonly divided into three phases.[11]

**Table 2: Phases of the hair cycle**

| Phases of hair cycle | Duration | % of hair at a time in normal scalp |
|---|---|---|
| Anagen (growth phase) | 2 - 8 years | 80-90% |
| Catagen (regression) | 2 - 3 weeks | 1-2% |
| Telogen (resting phase) | 3 months | 10-20% |

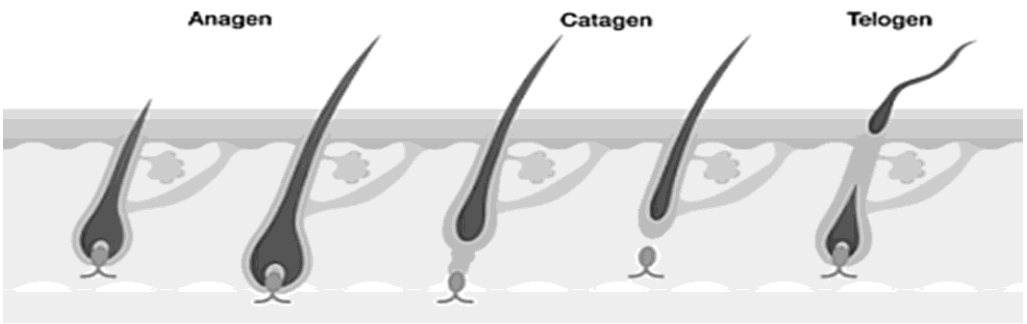



**Figure 11: Phases of hair cycle[93]**

At the end of the telogen phase, the hair falls out (exogenous phase) and is replaced by a new hair at early growth stage.

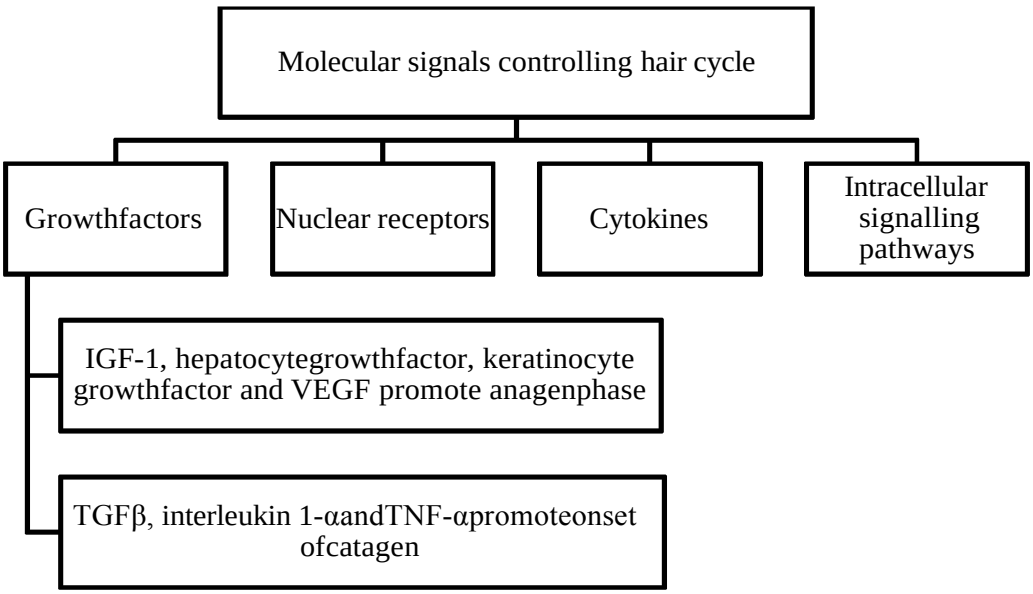



**Figure 12: Molecular signals controlling hair growth[93]**

In AGA, anagen phase duration decreases with each cycle but length of telogen remains constant or is prolonged; this causes a reduction in the anagen to telogen ratio.[11] As the hair growth rate remains relatively constant throughout, the anagen phase duration determines hair length. Thus, with each successive hair cycle, the length of each hair shaft is reduced. Ultimately, duration of anagen phase becomes so short that the hair which grows subsequently fails to achieve sufficient length to reach the surface of the skin, thus leaving an empty follicular pore. Prolongation of the kenogen phase (lag phase or the delayed replacement of telogen hair) is seen which contributes to a higher percentage of empty hair follicles contributing tobalding.[11,93]

**Hair follicle miniaturisation:**

Hair follicle miniaturization is the characteristic histological feature of androgenetic alopecia.[11] During development, hair follicles are made of both mesenchymal and ectodermal components. Ectodermal component consists of the invagination of epidermis into the dermis and subcutaneous fat. The hair matrix composes the hair

bulb, which produces the hair shaft. The hair bulb surrounds the dermal papilla (DP), which is the mesenchymal component.

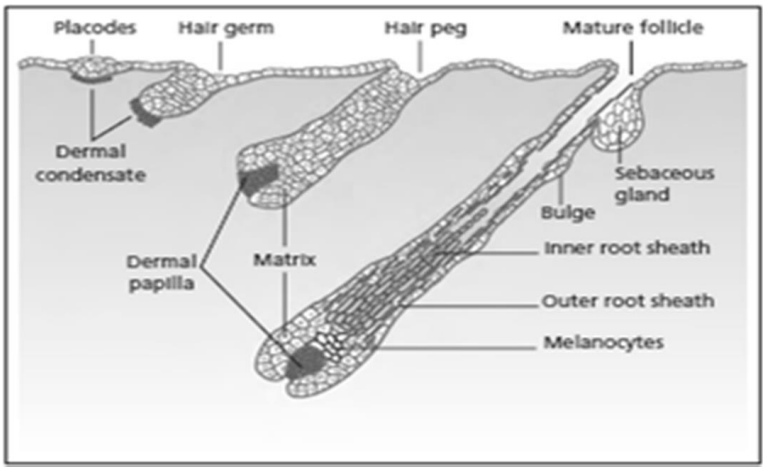



**Figure 13: Development of hair follicle[1]**

**Dermal papilla (DP)**

The DP regulates the epithelial follicle and determines the type of hair produced. As the dermal papilla maintains and controls the hair growth, it is presumably the target of androgen-mediated events that can lead to miniaturization and hair cycle changes. The volume of the dermal papilla is directly related to the size of the hair shaft produced.[11] There is reduction extracellular matrix and the total number of cells present in the dermal papillae which leads to the process of follicular miniaturization. In the hair cycle, during the catagen phase, cells travel out of the dermal papilla and into the dermal sheath, and re-enters the dermal papilla from the dermal sheath during the anagen phase. This reduction in the number of cells re-entering the dermal papilla will result inminiaturization.[11]

The mechanism by which this reduction in the number of cell occurs is unexplained, and may be the result of either apoptosis, decreased keratinocytes proliferation,[94] displacement of cell into dermis with loss of cellular adhesion leads to decline in the

dermal papilla fibroblasts, or DP cells migration into the dermal sheath associated with the outer root sheath of the hair follicle.[95.] In vitro studies have demonstrated that balding DP cells secrete inhibitory factors that affect the growth of both human and rodent DP cells and by causing the formation of smaller dermal papillae and smaller hairs in AGA.[96]

The process of follicular miniaturization is thought to occur in a stepwise fashion although but authors have suggested that it can occur rapidly, possibly in the space of a single hair cycle.[94] Follicular miniaturization leaves behind stelae also known as fibrous tracts or streamers, as dermal remnants of the full-sized follicle that extends from the subcutaneous tissue along the old follicular tract to the miniaturized hair and marks the formal position of the original terminal follicle.[97] Within the follicular stelae, Arao–Perkins bodies may be seen with elastic stains. An Arao– Perkins body starts as a small cluster of elastic fibers in the neck of the dermal papilla. They remain situated at the lowest point of origin of the follicular stelae and clump during catagen.[98]

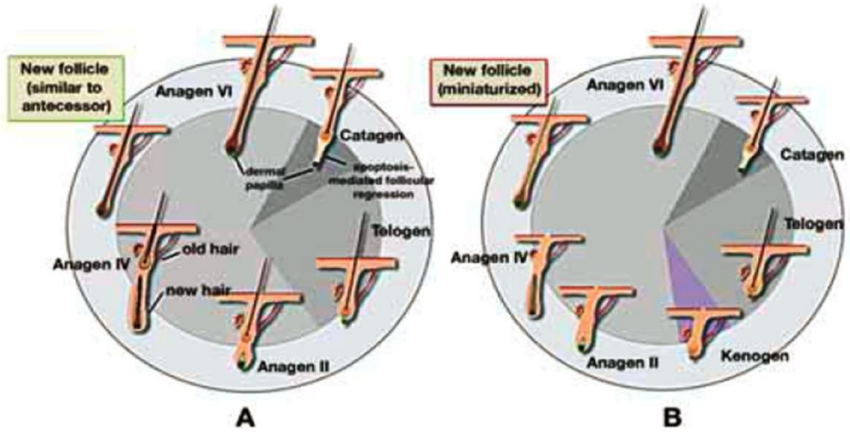



Figure 14: Representative schemes of the hair cycle. A – Normal cycle of the follicle. B – Alterations occurring in baldness: shortening of the anagen phase, increase in the latency period (kenogen phase) and hair follicle miniaturization.[6]

**Arrector pili muscle (APM)**

Hair exists as follicular units in the scalp consisting of 3-5 terminal hairs per follicular unit whereas in the beard and body they exist as single hair per follicle. The follicular units are nourished by a single arborizing arrector pili muscle that attaches circumferentially around the primary follicle with variable attachment to other follicles that forms the secondary follicles.[99] A recent concept for the pathogenesis and mechanism of AGA suggested that in the early stages of AGA, the APM remains attached to the primary follicle, yet loses attachment to a number of the regressing secondary follicles in some follicular units.[99] A study by Yazdabadi et al. demonstrated that in AGA and FPHL, where follicle miniaturization is irreversible or only partially reversible, there was a regular loss of attachment of the APM to vellus hair follicles.[100] Another study suggested that the persisting contact between APM and follicular unit predicts reversibility of miniaturization.[101]As further miniaturization occurs, patients first notices a change in their hair density and complain of thinning of hair. Once the APM has detached from all secondary follicles and primary follicles, then the hair loss is likely irreversible.[100] This suggested mechanism establishes the importance of early treatment to halt scalp balding prior to the loss of primary hair follicles.

**Inflammation:**

Scalp biopsies have demonstrated activated T-cells infiltrating about the lower portions of follicular infundibula.[102] Histopathological examination showed moderate perifollicular, lymphohistiocytic infiltrate, possibly with concentric layers of collagen deposition in the perifollicular region, was present in about 40% of cases of AGA, but only 10% of normal controls showed these change.[97] Occasional eosinophils and mast

cells may be seen. The cellular inflammatory changes were also seen around lower follicles in some cases and occasionally in the follicular stelae.[102]

## CLINICAL FEATURES

The clinical appearance of AGA is universally and instantly recognizable in most cases. The progression of the hair loss occurs in a systematic manner and has been documented by Hamilton and Norwood.[51,52] Both the authors used a modified grading scale for MPHL. The affected hairs are miniaturized and there is reduced hair density. Progressive replacement of terminal hairs by vellus hairs lead to an overall reduction in the hair density in the affected zones preceding to total baldness.

There are some useful classifications for AGA. Hamilton, in the year 1951 studied the developing patterns of scalp hair in men from the prenatal period through the 10th decade and divided balding patterns into 8 types with 3 subdivisions.[51] Approximately after 25 years, Norwood revised Hamilton's classification by eliminating type III and divided the patterns into 7 with 4 subdivisions (I, II, III, IIIv, IIIa, IV, IVa, V, Va, VI and VII) in which the letter ‘a’ was applied for advanced recession of the frontal hairline, and the term ‘vertex’ was applied for an isolated balding patch on the crown.

**Table 3: Modified Norwood-Hamilton (HN) classification [51,52]**

| Type | Clinical definition |
|---|---|
| **I** | Minimal recession of the hairline along the anterior border in the frontotemporal (FT) region. |
| **II** | The anterior border of the hair in the FT region has triangular areas of recession that tend to be symmetrical. These areas extend no further posterior than approximately 2 cm anterior to a line drawn in a coronal plane between the external auditory meatus on both sides. Hair is either lost or sparse along the mid-frontal border of the scalp. |
| **III** | Characterized by deep FT hair recession, usually symmetrical and either bald or sparsely covered with hair. These areas of hair recession extend further posterior than a point that lies approximately 2 cm anterior to a line drawn in a coronal plane between the external auditory meatus on either side. |
| **IIIv** | Hair is mainly lost in the vertex. There may be some frontal recession but it does not exceed than that seen in type III. |
| **IV** | The frontal and FT recession is more severe than type III. There is also sparseness or absence of hair in the vertex area. These bald areas are extensive, but separated from each other by a band of moderately dense hair that joins the fully haired fringe on each side of the head. |
| **V** | The hair loss over the vertex and FT areas is larger than in type IV and the band of hair between them is narrower and sparser. |
| **VI** | The hair loss over the FT and vertex regions is confluent and the bridge of hair that crosses the crown is absent. |

| | |
|---|---|
| **VII** | There is only a narrow horseshoe-shaped band of hair that begins laterally just anterior to the ear and extends posteriorly on the sides and fairly low on the occipital area. |
| | Constitutes 3% of all cases of AGA: (i) the entire anterior border of the hairline progresses posteriorly without the normal island of hair in the midfrontal region and<br>(ii) there is no simultaneous development of a bald area on the vertex. Instead, the anterior recession just advances posterior to the vertex. |
| **II a** | The entire anterior border of the hairline lies high on the forehead. The usual mid- frontal island of hair is represented by only a few sparse hairs. The area of denudation extends no farther than 2 cm from the frontal line. |
| **III a** | The area of denudation reaches the mid-coronal line. |
| **IV a** | The area of denudation extends beyond the mid-coronal line and there may be considerable thinning of hair posterior to the actual hair line. |
| **Va** | Most advanced degree of alopecia; however, the bald area does not reach vertex |

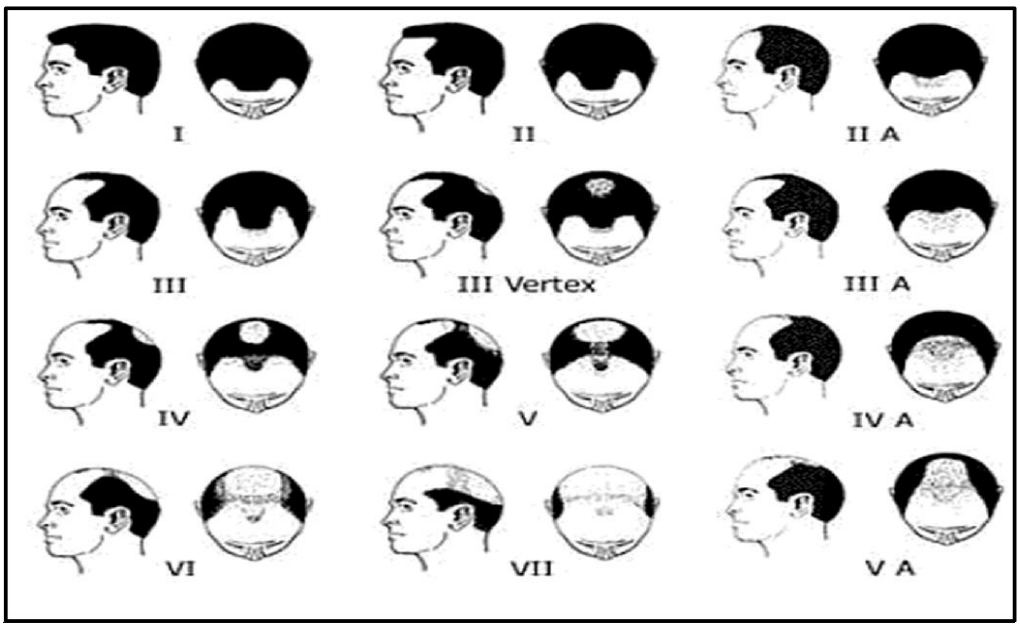



**Figure 15: Hamilton- Norwood Classification[51,52]**

**Ludwig classification:**

'Female pattern' refers to a hair loss pattern that could not be categorized using the HN classification. These findings showed that the frontal hairline was preserved with only diffuse hair loss on the mid-frontal and parietal scalp as in Ludwig's classification. FPHL in men, with diffuse thinning of hair on the crown and preservation of the frontal fringe hairline, is attributed to a hormone ratio similar to that seen in females with baldness.[57]

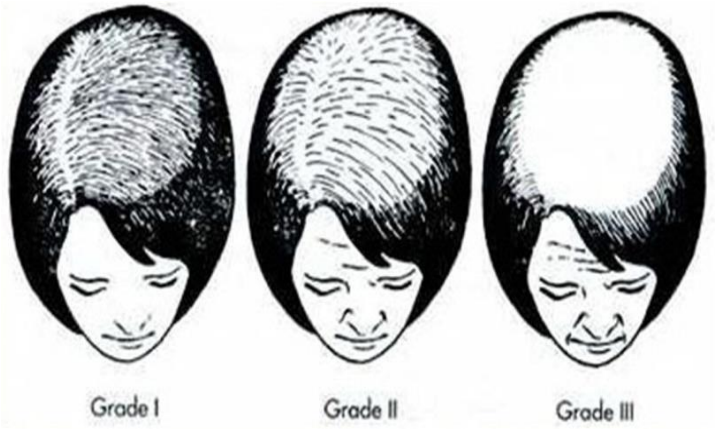



Figure 16: Ludwig classification[57]

**History:**

The typical history is of chronic hair loss with thinning mainly over the frontal, parietal or vertex areas. The patient might also complain of itching and trichodynia. Present history of systemic diseases. Family history is usually positive for AGA. Diet is another important aspect of history, to rule out nutrition related hair loss. Lifestyle related enquiries should cover effect of traction, smoking and ultraviolet exposure on AGA, all of which have been implicated as aggravating factors.[3]

**General scalp and hair examination:**

Usually the scalp is normal in AGA but examine scalp for factors which can aggravate AGA like seborrheic dermatitis and photo-damage. [102]The main aim of clinical examination is to identify whether or not if the hair loss is PHL.

**Hair pull test:**

It is a simple method to assess the severity of hair loss.[11] About 60 hairs are grasped between the thumb and the index and middle fingers. The hairs are then gently but firmly pulled. Test is positive if more than six hairs or 10% obtained which indicates active hair shedding and test is negative if six or less hairs/less than 10% obtained which indicates normal shedding. Shampooing should be withheld 24 hours prior to test. In MPHL, the test is usually negative except in the active phase and that too only in the affected sites. Positive test diffusely over the scalp suggests the probability of other diagnosis like telogen effluvium.

**Trichogram**: Trichogram can be used to differentiate between different types of hair loss. The patient is asked to abstain from washing hair for five days, following which

60-80 hairs are plucked using a rubber tipped forceps. The hair roots are examined immediately. The unit-area trichogram-density of hair follicle, proportion of anagen fibers, and hair shaft diameter are estimated after plucking hairs in a defined area-usually about $30/mm^2$. This procedure requires good technical expertise and experience for valid and reliable results.[11]

**Phototrichogram (PTG)**

– PTG is a non-invasive method. In this method, serial and close-up photographs of the specific areas to assess hair growth rate, hair follicle density and hair shaft thickness are taken. Variants of this technique include the contrast enhanced PTG and the automated PTG (Trichoscan). One of the essential components of this procedure is to trim the hairs over the selected.[11]

**Hair wash test**:

It is also known as the AGA/Telogen effluvium wash test to distinguish between AGA and telogen effluvium. In this test, patient is asked to abstain from washing and shampooing hair for 5 days. Then the number of vellus and terminal telogen hairs are counted from the rinsed out hair. The results are given in terms of total telogen hairs and the percentage of telogen vellus hairs. However, this method has certain disadvantages; hair breakage leads to double counting. It is not useful in patients with curly hair and is highly time consuming.[11]

**Dermoscopic features:**

The trichoscopic findings seen in alopecia areas (vertex, frontal and temporal hair line) in MPHL and crown area in FPHL patients include hair shaft thickness

heterogenesity, brown peripilar sign, white peripilar sign, yellow dots, pinpoint white dots, focal atrichia, scalp honeycomb pigmentation, epidermal scaling and arborizing red lines.Hair shaft thickness heterogeneity, also named “hair diameter diversity” or “anisotrichosis” is seen in the affected region of the scalp due to miniaturisation. Brown peripilar sign is characterized by a brown halo around the emergent hair shaft with a diameter of approximately 1 mm. It is due to superficial perifollicular infiltrates mainly composed of lymphocytes. The peripilar sign is white in colour due to fibrosis. Hence, in the absence of terminal hair, intact sebaceous glands can produce excessive sebum to form yellow dots. Scalp honeycomb pigmentation is due to sun exposure formed by hypomelanotic areas (less in overlying dermal papillae) surrounded by hyperchromic lines (melanin of rete ridges)seen in balding areas of scalp.[103]

**Scalp biopsy:**

Scalp biopsy is not a routine procedure in AGA because it is an invasive technique. Biopsy is taken from the centre of the most affected areas. Biopsies from the bitemporal areas are avoided as this area tends to have miniaturized hairs even in the absence of AGA.[11] Using a 4 mm punch, two biopsies are taken ideally – one for transverse sectioning and the other for horizontal sectioning. In the horizontal section, it gives us an idea about the number, density and morphology of the follicles. Total number of follicles is about 35 per 4 mm punch biopsy (Caucasian) at the superficial dermis. The ratio of terminal to vellus hairs in normal adult scalp is greater than 7:1, while in AGA it is typically less than 3:1.[104] Other important findings that can be seen in AGA include presence of fibrous “streamers” below miniaturized hairs, increased follicular stelae, increased telogen to anagen ratio, slightly increased telogen count

(15%-20% typical), a minimal perifollicular lymphohistiocytic infiltrate with or without mild fibrosis around the upper part of the follicle, or no significant inflammation[104] and solar elastosis in well-established cases.

**Global photography:**

A global photograph of a patient with hair loss is a useful tool especially for the follow-up and assessment of the treatment responses. Multiple images should be taken covering all areas of the scalp. The four specific views recommended are: vertex, mid-pattern, frontal, and temporal views. The key to good global photography is standardization of image with respect to magnification, position and lighting.[105]

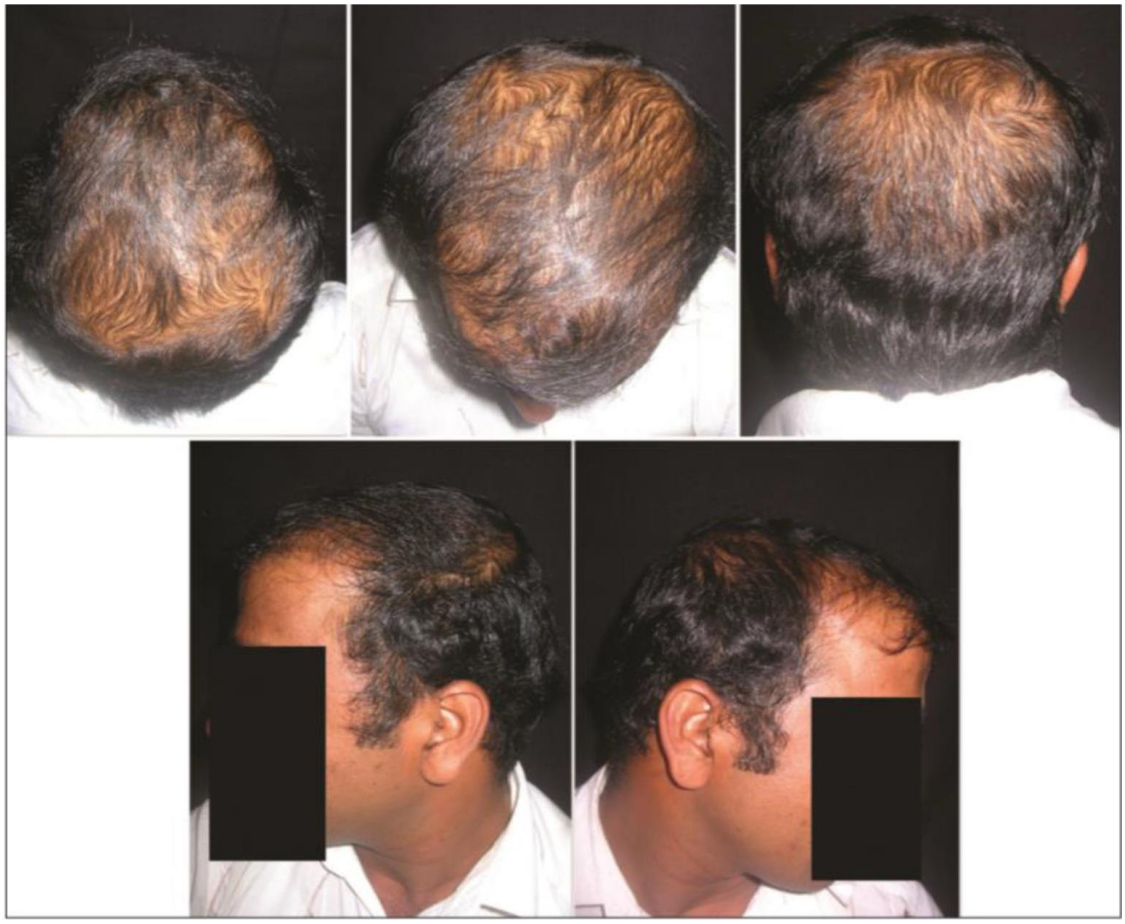


**Figure 17: Global photography[105]**

## TREATMENT

Specific therapy aims to promote hair regrowth and slow further thinning. All medical therapies may need to be used indefinitely to maintain their effects. The therapeutic response is slow and a minimum 6-12 months trial should be anticipated. Some of the commonly used therapeutic strategies include:

**Minoxidil**: Minoxidil is converted to minoxidil sulphate, the active form of the drug which opens ATP-sensitive potassium channels in cell membranes, leading to a vasodilatory effect. It has its greatest effect in less severe early presentations of AGA primarily involving the crown and parietal regions with a maximum diameter of the bald area of less than 10 cm and in whom the pretreatment hair density was in excess of 20 hairs/$cm^2$.[11] Minoxidil is available as lotions and foam formula.

**5 alpha reductase inhibitors**: The enzyme 5-alpha-reductase converts testosterone to its active form dihydrotestosterone (DHT) and inherited sensitivity of the hair follicles to DHT is one of the etiological factors in AGA. Two drugs inhibiting the 5-alpha-reductase used in AGA are finasteride which is a type II 5-alpha-reductase-inhibitor, and dutasteride, which inhibits both type I and type II 5-alpha-reductase. Oral finasteride 1 mg a day is recommended to improve or to prevent progression of AGA. Oral dutasteride 0.5 mg a day is another option.[11]

**Hormonal treatment:** Studies have shown no significant efficacy or role for hormonal therapy – like anti-androgens in male AGA. Cyproterone acetate (25-50 mg per day, days 1-10) is usually prescribed together with an oral contraceptive like estradiol with studies have shown conflicting results regarding its use in AGA.[106]

Alfatradiol is a topical estrogen which results in deceleration or stabilization of hair loss.[107]

**Surgery:**Hair restoration surgery for AGA essentially includes various forms of hair transplantation. Hair transplant is a good option in both males and females with sufficient donor hair. It is recommended to combine hair transplant with oral finasteride for best results. Hair is harvested from the donor site using either strip method, follicular unit extraction or a combination of the two. The grafting of follicular units is generally considered the optimum method nowadays, with meticulous stereoscopic microscopic dissection being the "gold standard".[106]

**Camouflage:** Hair extensions, prostheses and wigs are commonly used to improve cosmesis in AGA. A topical combination of caffeine, niacinamide, dimethicone, panthenol and an acrylate polymer (CNDPA) has been shown to improve hair fiber diameter thus helping in enhancing the cosmetic appearance of patients with thinning hair.[108]

**Miscellaneous treatments:**A number of other treatment modalities have been tried in AGA.[105] Promotion of hair regrowth by activation of the dermal papillae leading to induction of anagen hair re-growth (Iron supplements, millet seeds, Ginkgo Biloba, Aloe vera, Hibiscus, retinoids, cyclosporine), improving the perifollicular vascularization (prostaglandin analogues like latanoprost, aminexil, mesotherapy, benzyl nicotinate, beta-sitosterol), hormonal effects like inhibition of 5-alpha-reductase (polysorbate, green tea, ketoconazole, saw palmetto extract), anti-inflammatory activity (zinc pyrithione, corticosteroids) and improvement of hair

follicle nutrition (vitamin supplements, trace elements).[106]

Other topical applications which have been used in AGA, but are not supported bysufficient evidence include – carpronium chloride, t-flavanone, adenosine, cytopurine /pentadecane and cepharanthine.[109]

**Botulinum toxin:**A pilot study on 50 male patients suggested an improvement in AGA with the use of 150 units of botulinum toxin injection into the muscles around the scalp (the dose divided over 30 injection sites). Botulinum toxin relaxes the scalp muscles thus reducing pressure on the perforating vasculature and improving blood flow and oxygen concentration.[110]

**Lasers and lights:** Paradoxical hair growth after using lasers and lights for hair removal has triggered interest in using these devices as a treatment modality for various types of alopecia, including AGA. Light of 650-900 nm wavelengths at 5mW has been suggested as an effective option forAGA.[111]

**Platelet rich plasma therapy (PRP):** Platelet-rich plasma (PRP) is an autologous preparation of platelets in the concentrated plasma. PRP has attracted attention in several medical fields because of its ability to promote wound healing. Few authors observed a significant improvement in hair density and stimulation of growth when follicular units were pretreated with platelet plasma growth factors before their implantation in hair transplantation surgeries. Based on this finding PRP has been used in the treatment of MPHL.[112]

Stem cell therapy is already being used in many centers. Bio-engineered hair follicles

derived from stem cells has been found to be effective in animal studies and in future this could be a definite option for AGA.[113] Research is also focusing on possible newer medical interventions like copper peptides.

# MATERIALS AND METHODS

# MATERIALS AND METHODS

**Source of data:**

The present study was an Cross-sectional analytical study carried out in the Department of Dermatology at RL Jalappa Hospital and Research Centre attached to Sri DevarajUrs Medical College, Tamaka, Kolar from January 2019 to July 2020. Two hundredand eighteen patients who were diagnosed with Androgenetic alopecia were included in the study.

**Inclusion criteria:**

All men aged between 20 years to 60 years diagnosed with Androgenetic alopecia according to Norwood Hamilton and Ludwig classification.

**Exclusion criteria:**

Those having psychiatric disorder or personality disorder, systemic diseases like thyroid disorders, iron deficiency anemia, metabolic disturbances (liver disorders, renal diseases), malignancy, chemotherapeutic drugs, anticoagulants, anticonvulsants, antihypertensives, lithium, lamotrigine, retinoids.

**Methods of data collection:**

Data was collected after obtaining written informed consent from the patient. In every case detailed history and thorough clinical examination was carried out. Information about smoking,quantity,duration and frequency of smoking and other possible risk factors of androgenetic alopecia was collected. Cigarette smoking is calculated as per the smoking index(SI). The formula used for smoking index is the product of number

of cigarettes smoked per day and duration in years.

Based upon SI, patients will be categorized into the following groups:

I. Never-smokers

IIa. Light smokers [SI=1-100]

IIb. Moderate smokers [SI=101-300]

III. Heavy smokers [SI≥301][114]

Diagnosis of AGA was done based on the clinical features and classified according to HN classification.

Relevant laboratory investigations was done wherever necessary. The data thus collected were entered in to a specially designed Case Record Form and subjected to statistical analysis.

**STATISTICAL METHODS USED FOR DATA ANALYSIS:**

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.

**Graphical representation of data:** MS Excel and MS word was used to obtain various types of graphs such as bar diagram and pie diagram.

**P value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

**Statistical software:** MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze the data.

**Sample size calculation:**

Sample size was estimated based on the prevalance of androgenetic alopecia among smokers on an average in above 40 years of age is found to be 5.4% in a Taiwan study by Su LH.[3]

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies $P$ values are considered significant below 0.05 hence 1.96 is used in formula.

p = Expected proportion in population based on previous studies or pilot studies.

d = Absolute error or precision – Has to be decided by researcher.

**Sample size for a frequency in a population**

P= 5.4% or

q= 4.4% or

d= 3% or 0.3

Using the above values at 95% confidence level the estimated sample size was 218 subjects. A total of 218 subjects with Androgenetic alopecia were included in this study.

# RESULTS

# RESULTS

**Table 4:- Distribution of subjects according to age group.**

| Age | Number of patients | Percentage |
|---|---|---|
| 20-30yrs | 97 | 44.5 |
| 31-40yrs | 69 | 31.7 |
| 41-50yrs | 46 | 21.1 |
| 51-60yrs | 6 | 2.8 |
| Total | 218 | 100.0 |

Majority 44.5% of the subjects were between 20-30yrs age group followed by 31.7% of the subjects were between 31-40yrs age group, 21.1% of the subjects were in 41-50yrs age group and only 2.8% of the subjects were in 51-60yrs age group.

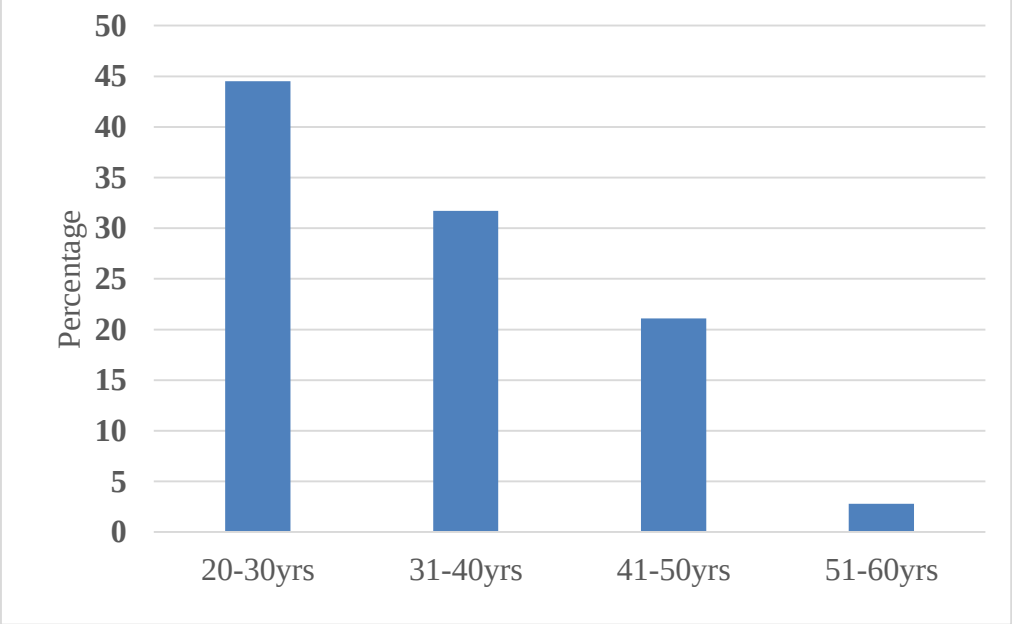



**Figure 18:-Graph showing Distribution of subjects according to age group.**

**Table 5:- Distribution of subjects according to occupation.**

| Occupation | Number of patients | Percentage |
|---|---|---|
| White collared work | 46 | 21.1 |
| Skilled work | 61 | 28.0 |
| Semiskilled work | 33 | 15.1 |
| Manual laborer | 21 | 9.6 |
| Agriculturist | 23 | 10.6 |
| Student | 34 | 15.6 |
| Total | 218 | 100.0 |

Majority 28.0% of the subjects were skilled workers followed by 21.1% of the subjects were White collared workers, 15.6% of the subjects were students, 15.1% of the subjects were Semiskilled workers, 10.6% of the subjects were Agriculturists and 9.6% of the subjects were Manual laborers.

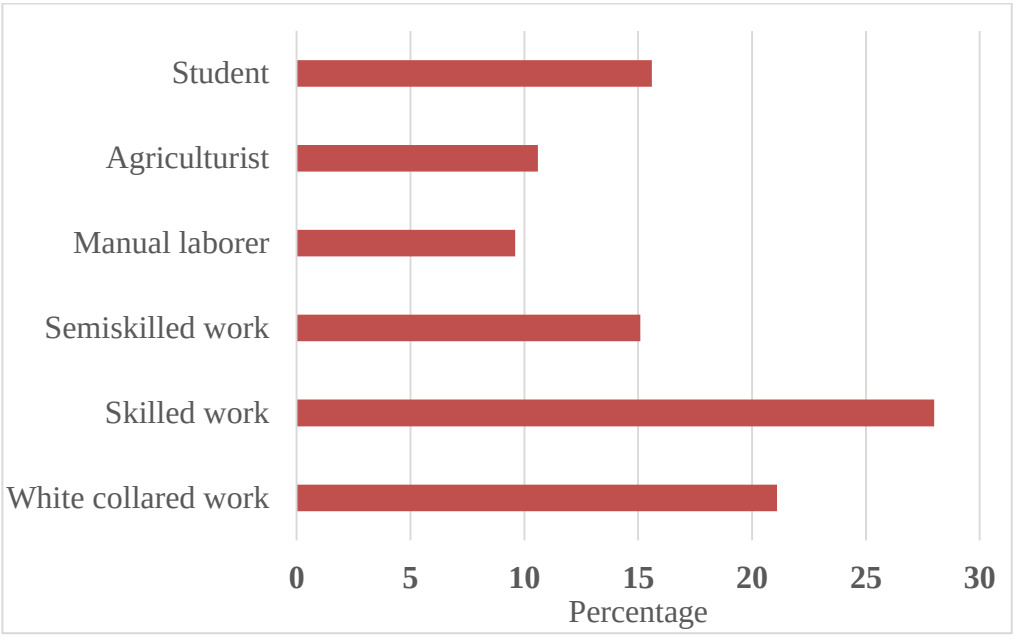



**Figure 19:- Graph Showing Distribution of subjects according to occupation.**

**Table 6:- Distribution of subjects according to Socioeconomic status**

| Socioeconomic status | Number of patients | Percentage |
|---|---|---|
| Upper | 21 | 9.6 |
| Upper middle | 85 | 39.0 |
| Lower middle | 40 | 18.3 |
| Upper lower | 48 | 22.0 |
| Lower | 24 | 11.0 |
| Total | 218 | 100.0 |

Majority 39% of the subjects were in upper middle class followed by 22% of the subjects were in upper lower class, 18.3% of the subjects were lower middle class, 11% of the subjects were in lower class and 9.6% of the subjects were in upper class.

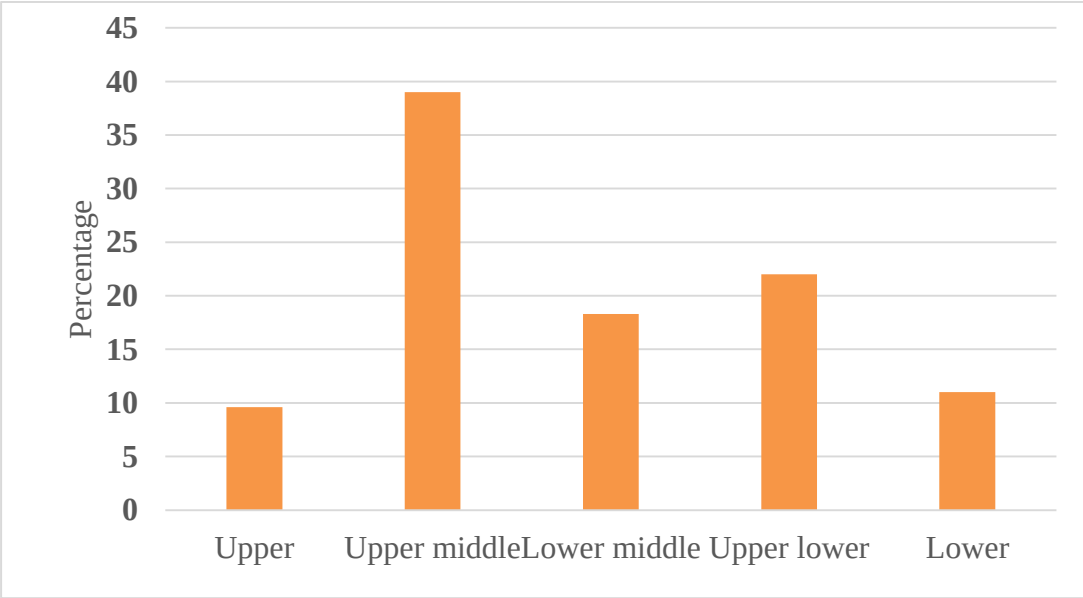



**Figure 20:- Graph showing distribution of subjects according to Socio Economic Status.**

**Table 7:- Distribution of subjects according to onset.**

| Onset | Number of patients | Percentage |
|---|---|---|
| Insidious | 210 | 96.3 |
| Sudden | 8 | 3.7 |
| Total | 218 | 100.0 |

Majority 96.3% of the subjects had insidious onset and only 3.7% of the subjects had sudden onset.

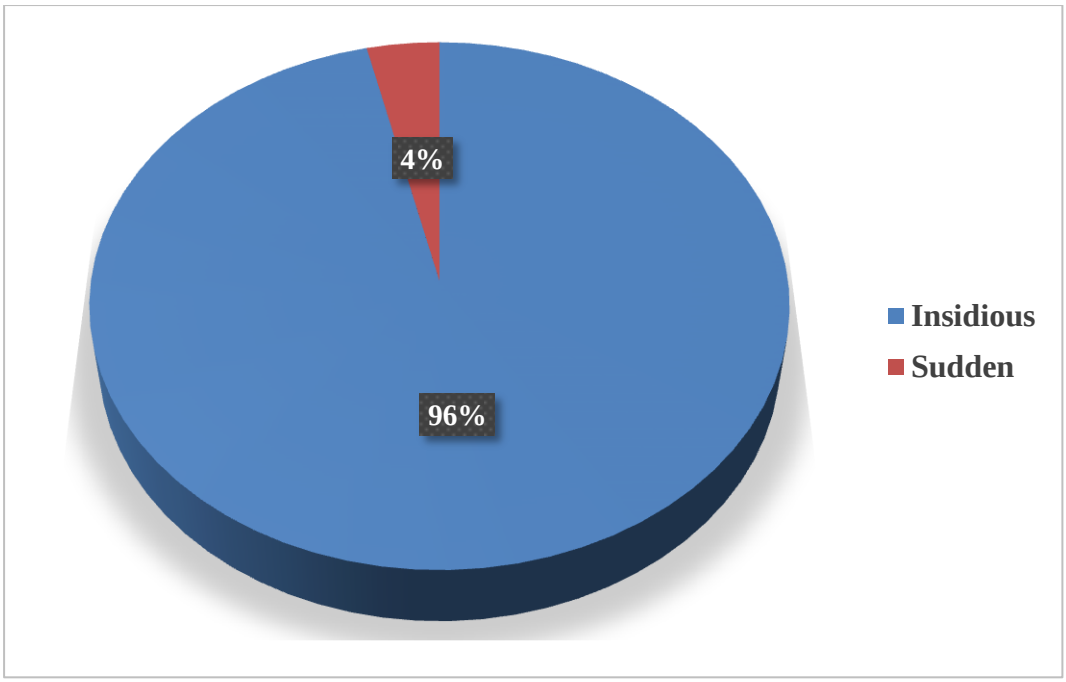



**Figure 21:-Graph showing Distribution of subjects according to onset.**

**Table 8:- Distribution of subjects according to duration of AGA**

| Duration of hair loss | Number of patients | Percentage |
|---|---|---|
| 0-6month | 29 | 13.3 |
| 7- 12months | 26 | 11.9 |
| 1-5yrs | 93 | 42.7 |
| 5-10yrs | 64 | 29.4 |
| >10yrs | 6 | 2.8 |
| Total | 218 | 100.0 |

Majority 42.7% of the subjects had duration hair loss between 1-5years followed by 29.4% of the subjects had duration hair loss between 5-10 years, 13.3% of the subjects had duration hair loss between 0-6month,11.9% of the subjects had duration hair loss between 7- 12months. And only 2.8% of the subjects had duration hair loss more than 10years.

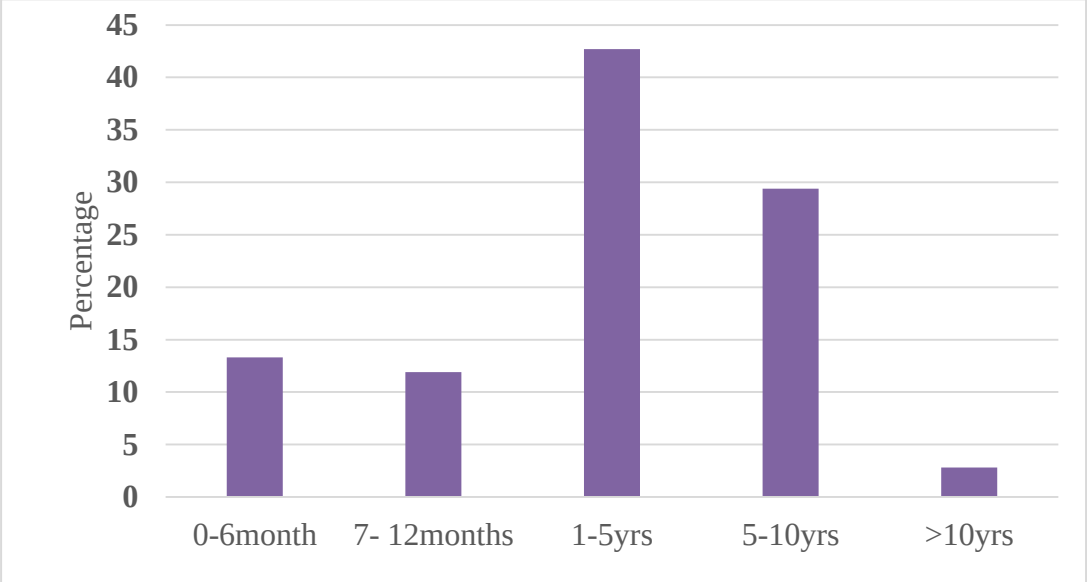



**Figure 22:- Graph Showing Distribution of subjects according to duration of AGA**

**Table 9:- Distribution of subjects according to age of onset.**

| Age of onset | Number of patients | Percentage |
|---|---|---|
| <20yrs | 2 | .9 |
| 21-25yrs | 55 | 25.2 |
| 26-30yrs | 65 | 29.8 |
| 31-35yrs | 47 | 21.6 |
| 36-40yrs | 33 | 15.1 |
| 41-45yrs | 16 | 7.3 |
| Total | 218 | 100.0 |

Age of onset in 29.8% of the subjects were between 26-30years age group followed by 25.2% of the subjects were between 21-25years age group, 21.6% of the subjects were in 31-35years age group and only 0.9% of the subjects had age of onset less than 20years.

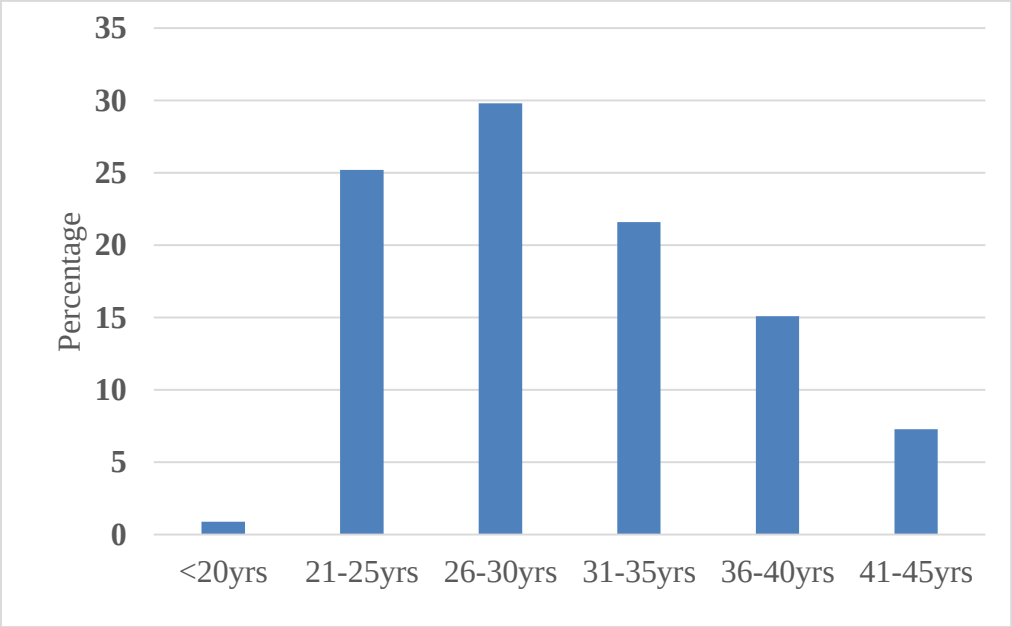



**Figure 23:- Graph Showing Distribution of subjects according to age of onset.**

**Table 10:- Distribution of subjects according to progression**

| Progression | Number of patients | Percentage |
|---|---|---|
| Gradual | 213 | 97.7 |
| Rapid | 5 | 2.3 |
| Total | 218 | 100.0 |

Majority 97.7% of the subjects had gradual progression and only 2.3% of the subjects had rapid progression.

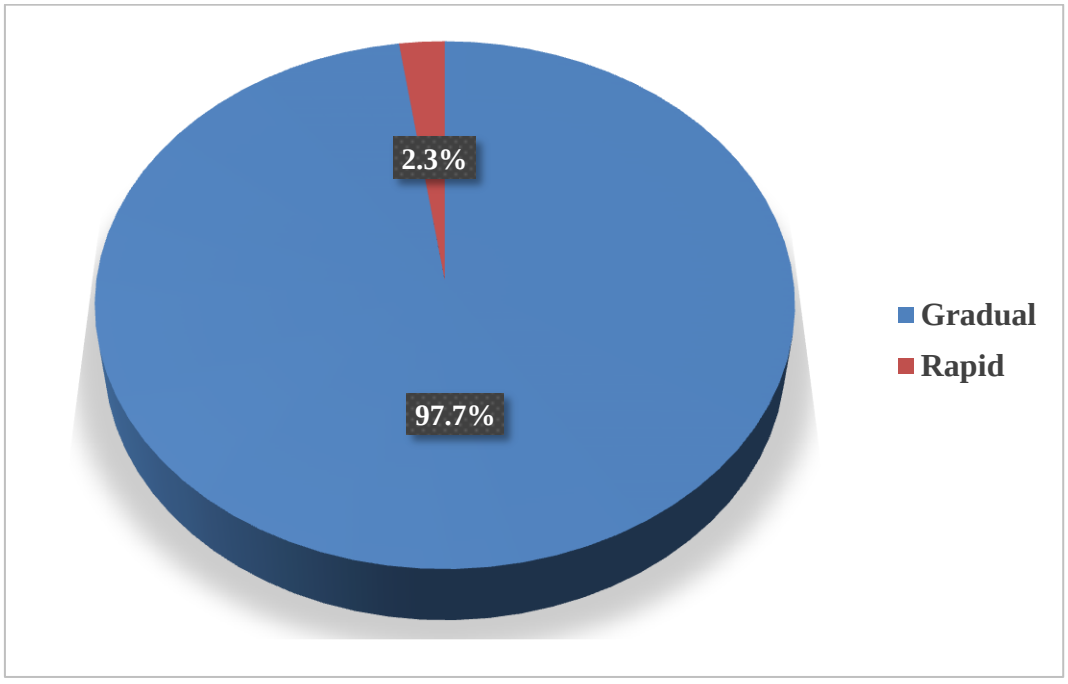



**Figure 24:- Graph Showing Distribution of subjects according to progression.**

**Table11:- Distribution of subjects according to family history.**

| Family history | Number of patients | Percentage |
|---|---|---|
| Paternal | 46 | 21.1 |
| Maternal | 16 | 7.3 |
| Sibling | 29 | 13.3 |
| Paternal & Sibling | 28 | 12.8 |
| Maternal & Sibling | 6 | 2.8 |
| No family history | 93 | 42.7 |
| Total | 218 | 100.0 |

Majority 42.79% of the subjects did not have family history. 21.1% of the subjects had paternal family history, 13.3% of the subjects had sibling family history, 12.8% of the subjects had both sibling and paternal family history, 7.3% of the subjects had maternal family history, 2.8% of the subjects had both sibling and maternal family history.

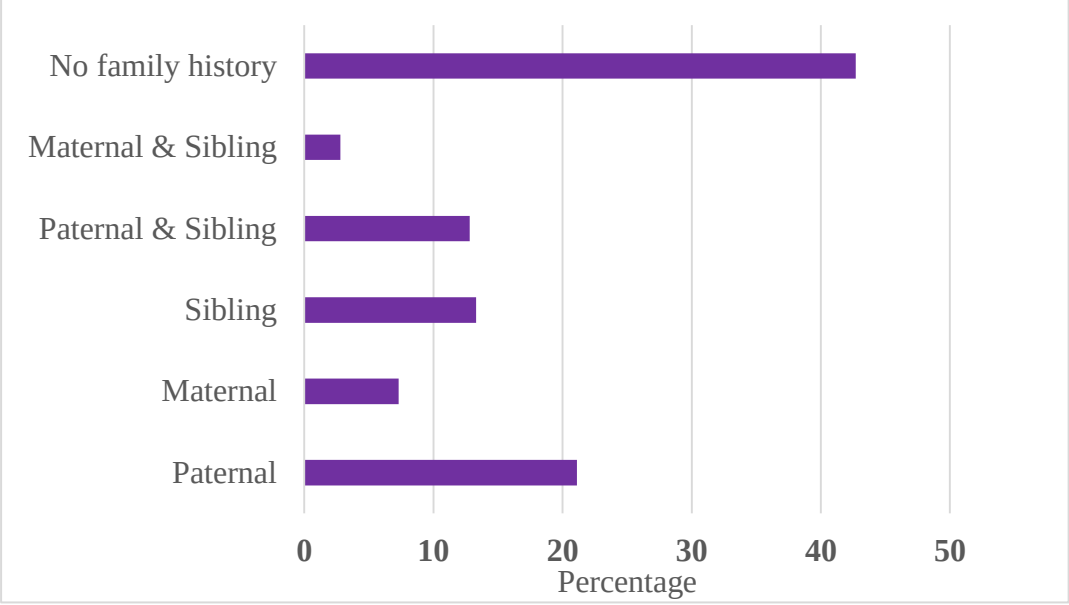



**Figure 25:- Graph Showing Distribution of subjects according to family history.**

**Table 12:- Distribution of subjects according to smoking history**

| Smoking history | Number of patients | Percentage |
|---|---|---|
| Yes | 170 | 78.0 |
| No | 48 | 22.0 |
| Total | 218 | 100.0 |

Majority 78% of the subjects had smoking history and 22% of the subjects did not had smoking history.

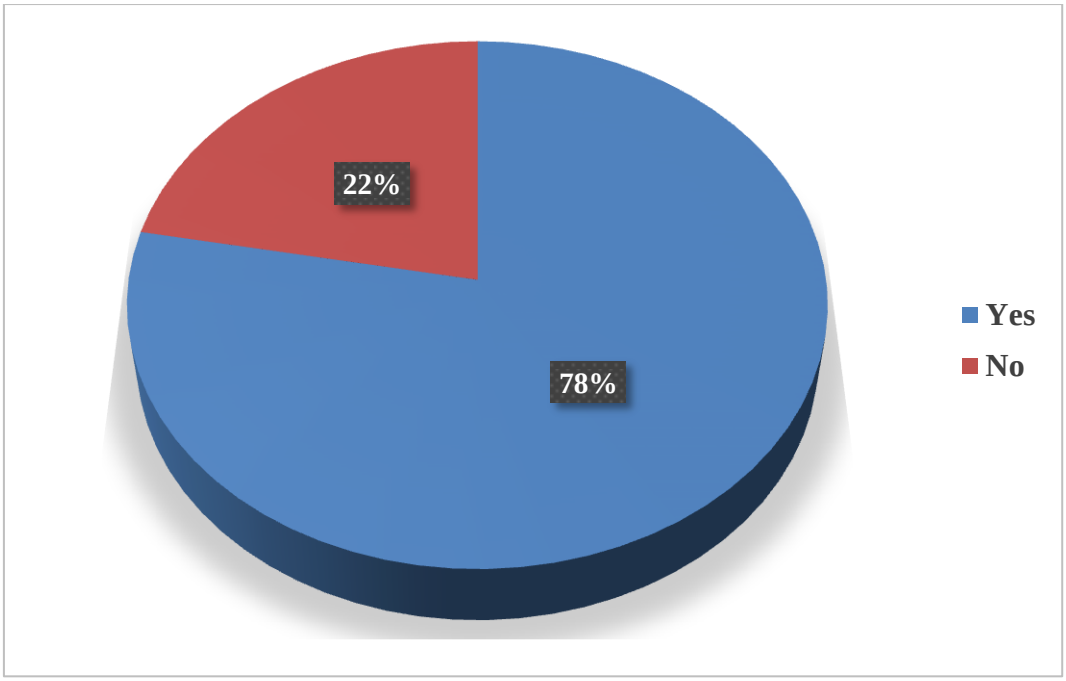



**Figure 26:- Graph Showing Distribution of subjects according to smoking history**

**Table 13:- Distribution of subjects according to alcohol history**

| Alcohol history | Number of patients | Percentage |
|---|---|---|
| Yes | 73 | 33.5 |
| No | 145 | 66.5 |
| Total | 218 | 100.0 |

Majority 66.5% of the subjects did not have alcohol history and 33.5% of the subjects had alcohol history.

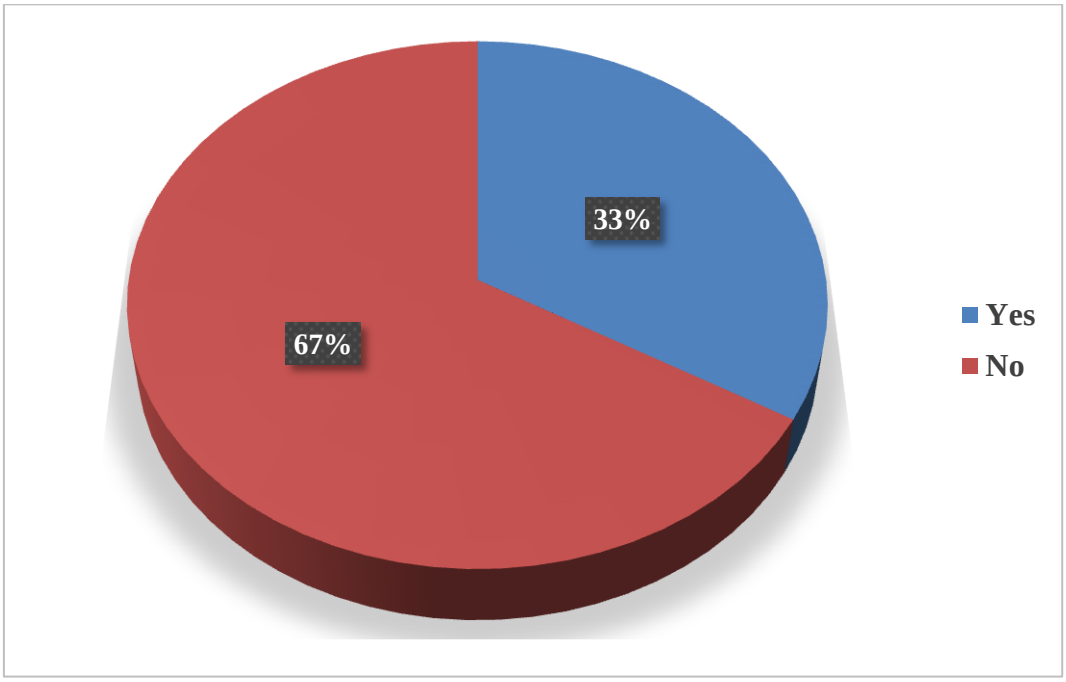



**Figure 27:- Graph Showing Distribution of subjects according to alcohol history**

**Table 14:- Distribution of subjects according to smoking index**

| Smoking Index | Number of patients | Percentage |
|---|---|---|
| Never | 48 | 22.0 |
| Light smoker | 53 | 24.3 |
| Moderate smoker | 72 | 33.0 |
| Heavy smoker | 45 | 20.6 |
| Total | 218 | 100.0 |

33% of the subjects were moderate smokers, 24.3% of the subjects were light smokers and 20.6% of the subjects were heavy smokers.

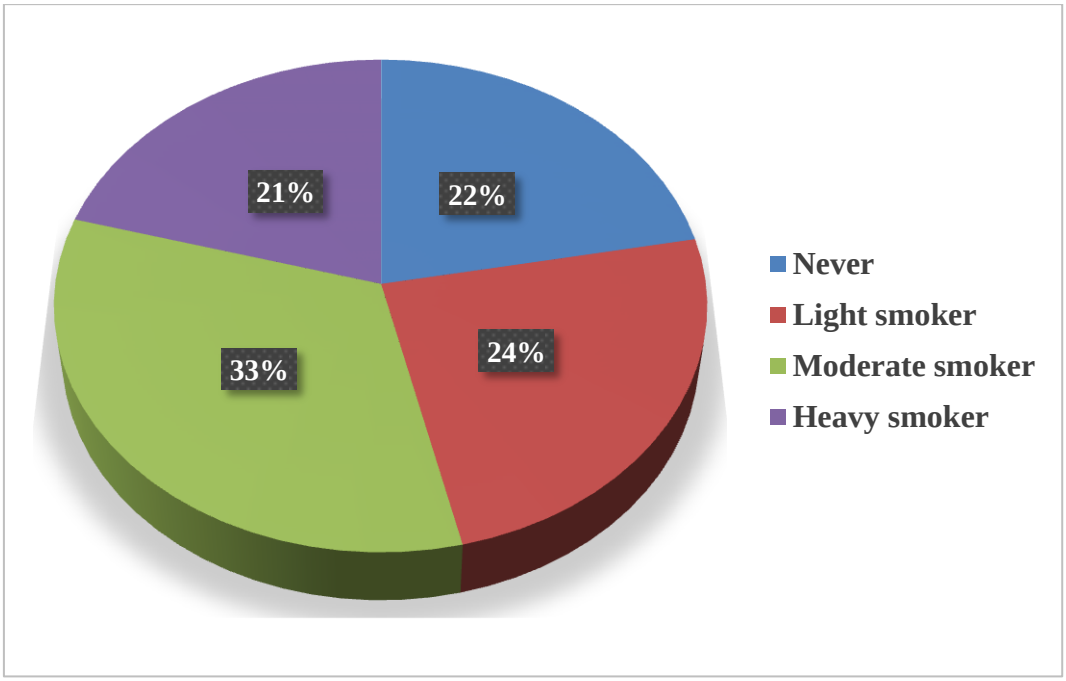



**Figure 28:- Graph Showing Distribution of subjects according to smoking index**

**Table 15:-Distribution of subjects according to comorbidities**

| Comorbidties | Number of patients | Percentage |
|---|---|---|
| NONE | 175 | 80.3 |
| DM | 23 | 10.5 |
| Hypertension | 21 | 9.6 |
| BA | 4 | 1.8 |
| CAD | 2 | .9 |

10.5% of the subjects had DM, 9.6% of the subjects had Hypertension,1.8% of the subjects had BA and 0.9% of the subjects had CAD.

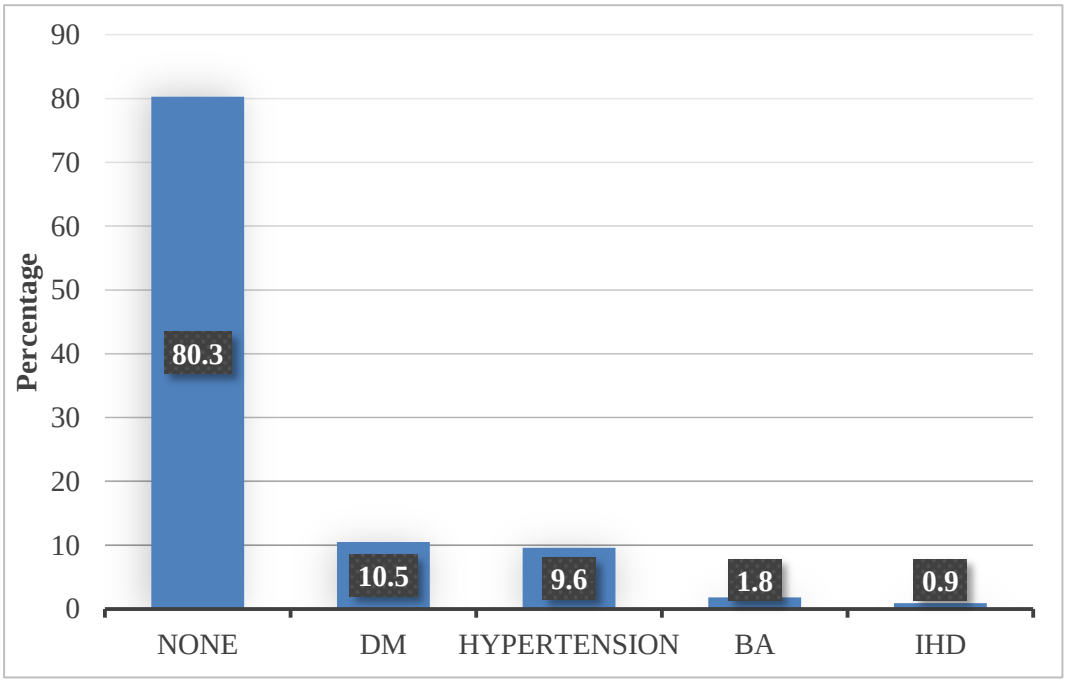



**Figure 29:- Graph Showing Distribution of subjects according to comorbidities**

**Table 16:- Distribution of subjects according to Norwood Hamilton classification**

| Norwood Hamilton | Number of patients | Percentage |
|---|---|---|
| I | 40 | 18.3 |
| II | 60 | 27.5 |
| IIa | 21 | 9.6 |
| III | 38 | 17.4 |
| IIIv | 14 | 6.4 |
| IIIa | 17 | 7.8 |
| IV | 11 | 5.0 |
| Iva | 10 | 4.6 |
| V | 5 | 2.3 |
| VI | 2 | 0.9 |
| Total | 218 | 100 |

Majority 27.5% of the patients had II, 18.3% of the patients had I, 17.4% of the patients had III,9.6% of the patients had IIa,7.8% of the patients had IIIa, 6.4% of the patients had IIIv,5% of the patients had IV,4.6% of the patients had IVa,2.3% of the patients had V and 0.9% of the patients had VI.

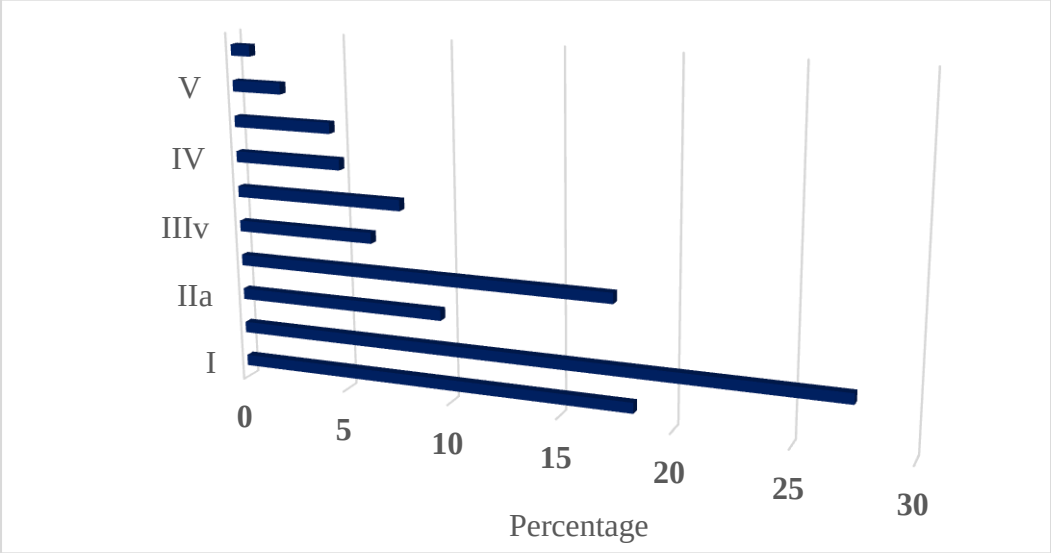



**Figure 30:- Graph Showing Distribution of subjects according to Norwood Hamilton classification**

**Table 17:- Distribution of subjects according to Norwood Hamilton classification and smoking index**

| Norwood Hamilton | Non smoker | Light smoker | Moderate smoker | Heavy smoker |
|---|---|---|---|---|
| I | 9 | 21 | 1 | 9 |
| | 18.8% | 39.6% | 1.3% | 20% |
| II | 14 | 21 | 24 | 1 |
| | 29.2% | 39.6% | 33.3% | 2.2% |
| IIa | 8 | 2 | 11 | 0 |
| | 16.7% | 3.8% | 15.3% | 0% |
| III | 8 | 6 | 20 | 4 |
| | 16.7% | 11.3% | 27.8% | 8.9% |
| IIIv | 4 | 1 | 4 | 5 |
| | 8.3% | 1.9% | 5.6% | 11.1% |
| IIIa | 2 | 0 | 12 | 3 |
| | 4.2% | 0% | 16.7% | 6.7% |
| IV | 0 | 0 | 0 | 11 |
| | 0% | 0% | 0% | 24.4% |
| IVa | 3 | 0 | 0 | 7 |
| | 6.3% | 0% | 0% | 15.6% |
| V | 0 | 0 | 0 | 5 |
| | 0% | 0% | 0% | 11.1% |
| VI | 0 | 2 | 0 | 0 |
| | 0% | 3.8% | 0% | 0% |
| Total | 48 | 53 | 72 | 45 |
| | 100.0% | 100.0% | 100.0% | 100.0% |

Most common in non-smokers was II 29.2% followed by I in 18.8%, 16.7% had IIa and III each.

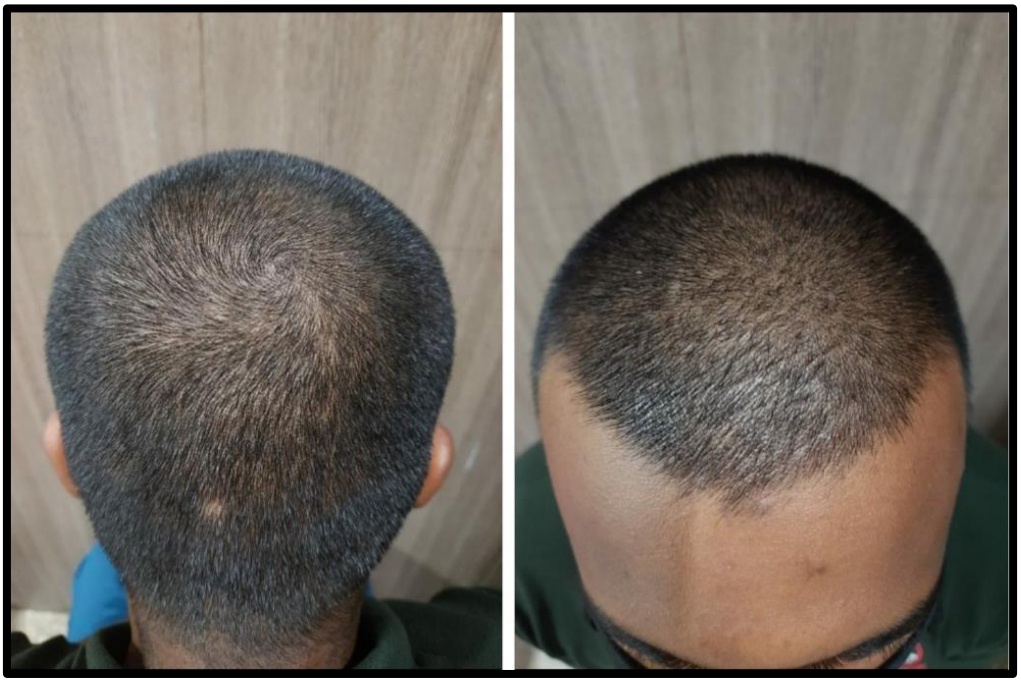
Most common in light smokers was I and II,39.6% of light smokers had I and II each.

Most common in moderate smokers was II 33.3% of them had, followed by III were present in 27.8% among moderate smokers.

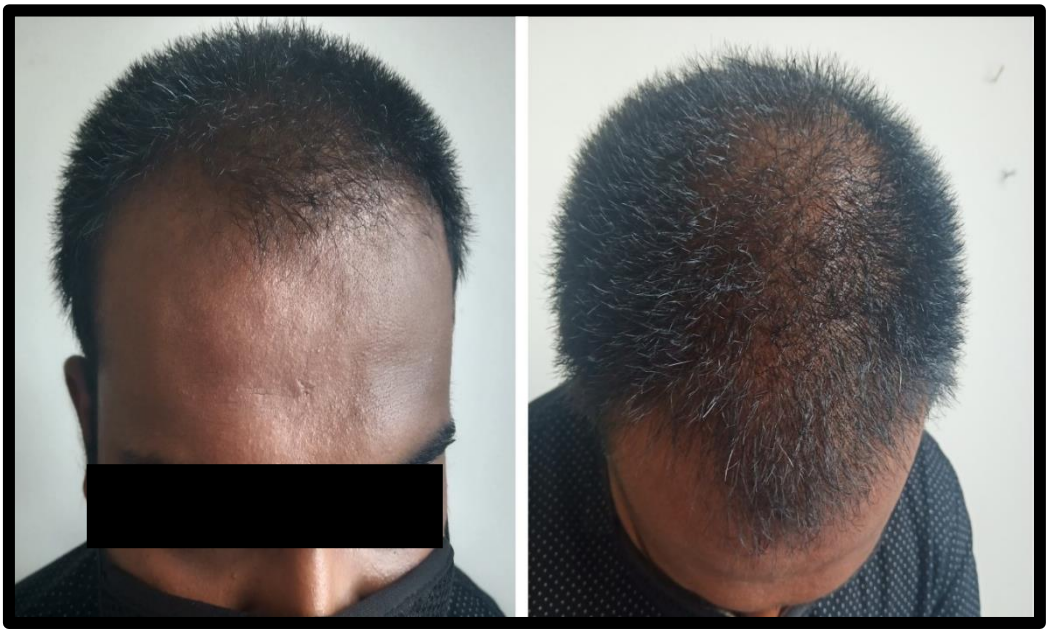
Most common in heavy smokers was IV 24.4%.

Statistical analysis showed that p value was highly significant with a p value < 0.001.

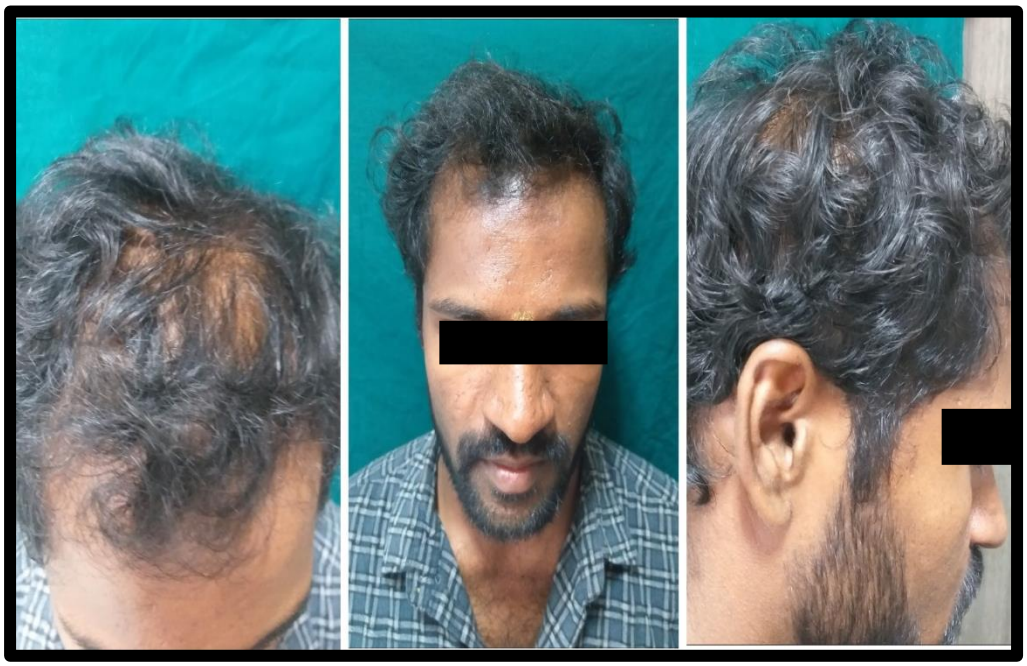
# PHOTOGRAPHS



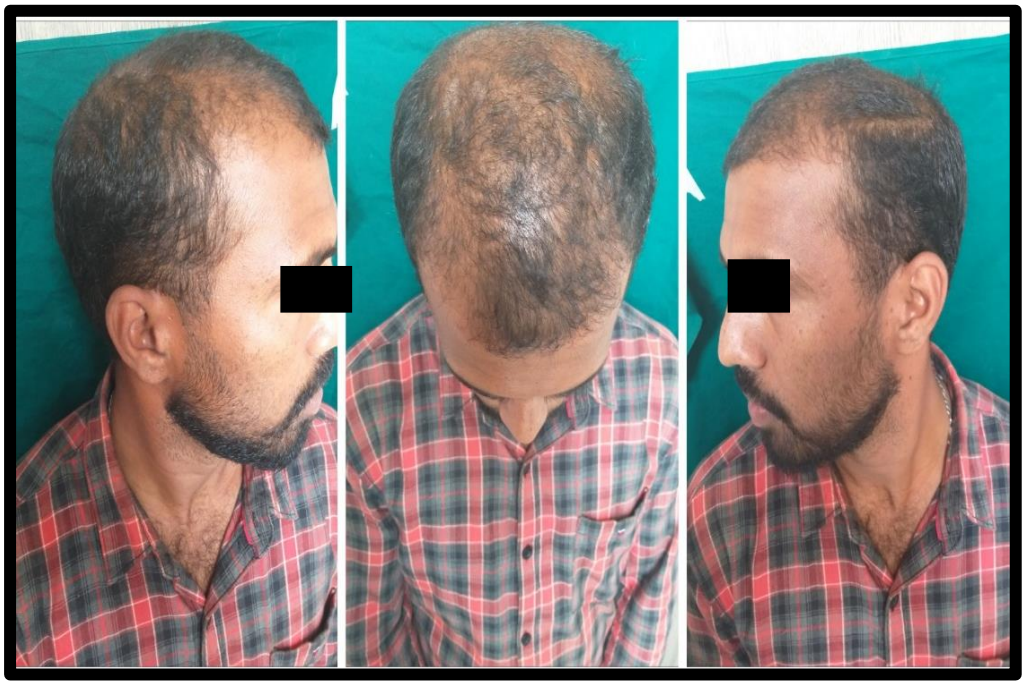
**Photograph 31: Hamilton Norwood Grade II**



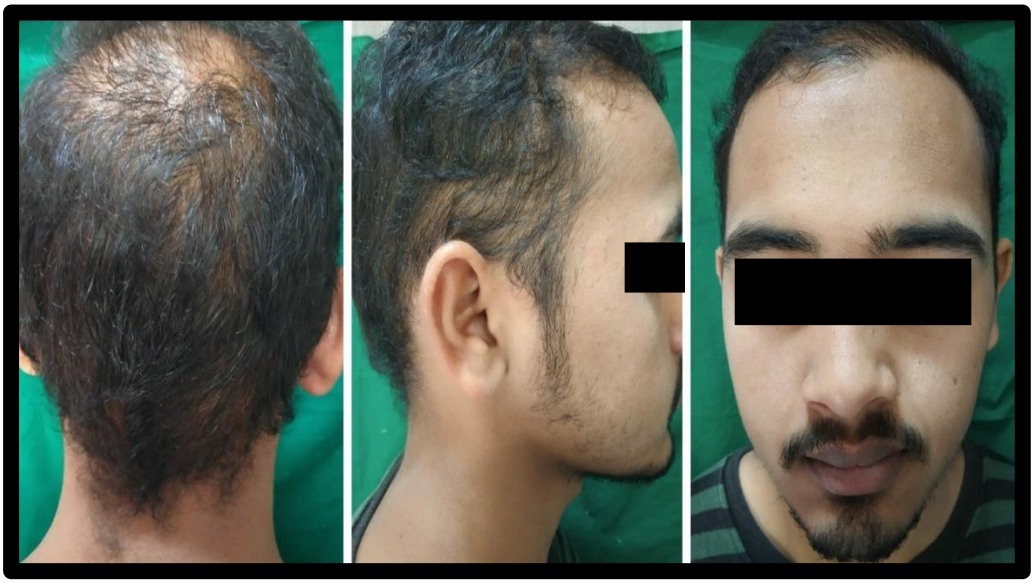
**Photograph 32: Hamilton Norwood Grade II a**



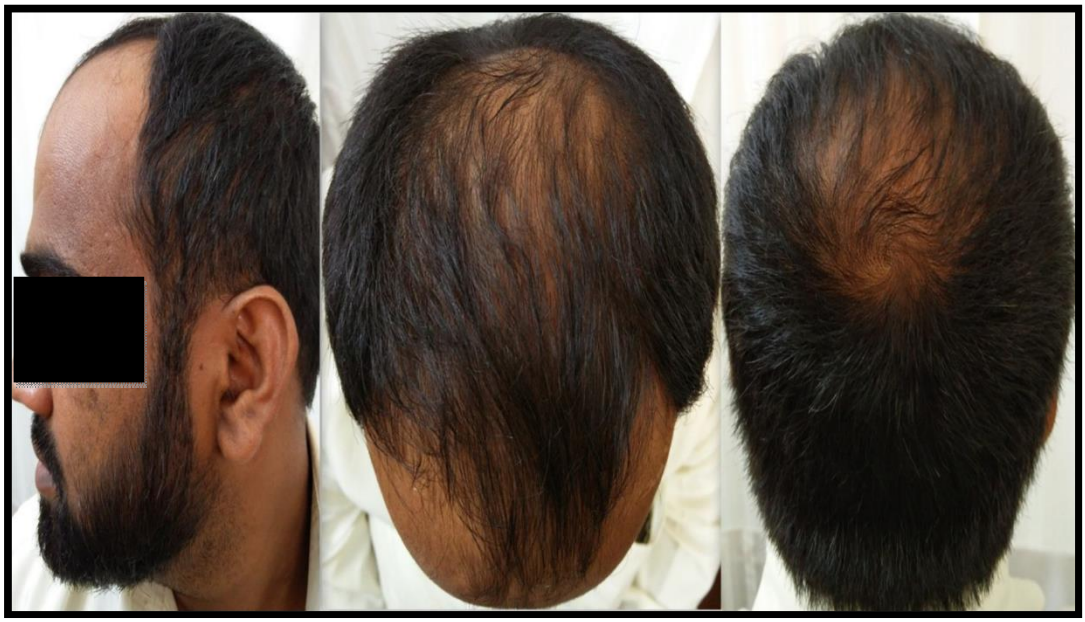
**Photograph 33: Hamilton Norwood Grade III**



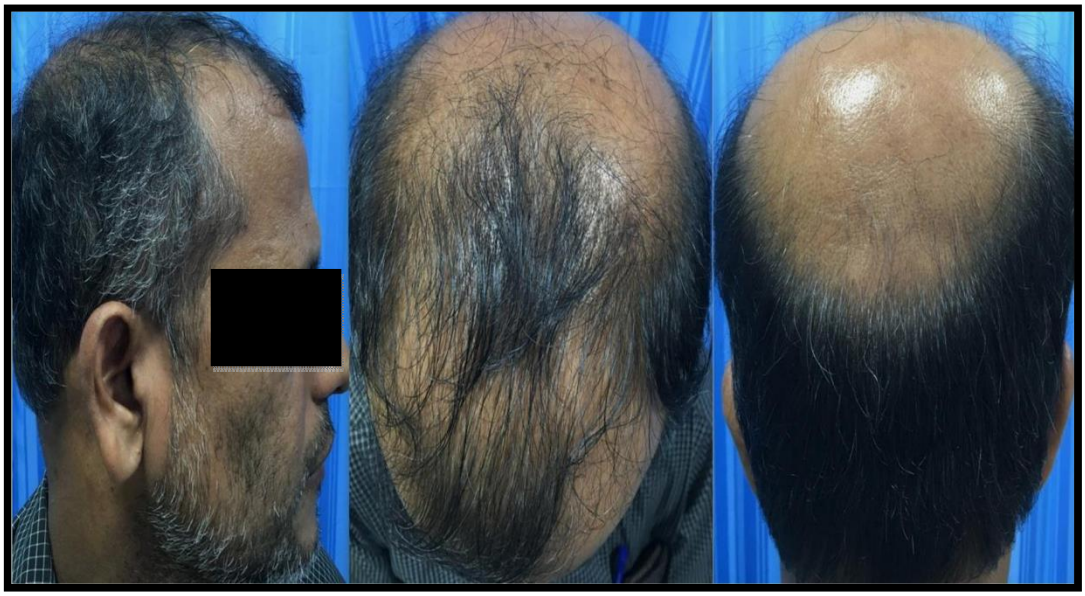
**Photograph 34: Hamilton Norwood Grade III vertex**



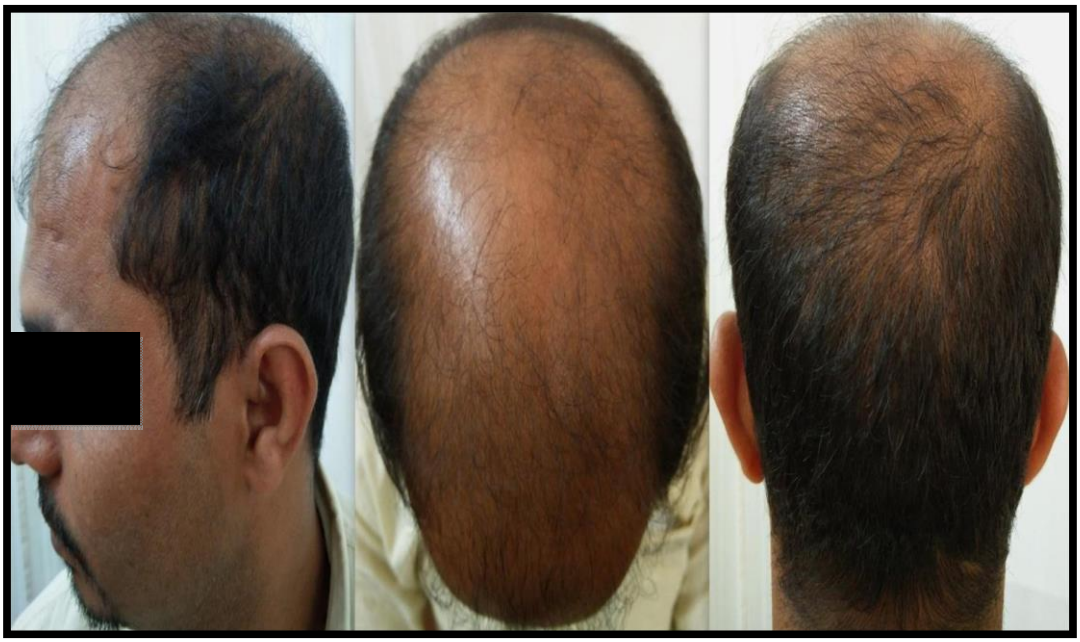
**Photograph 35: Hamilton Norwood Grade IV**



**Photograph 36: Hamilton Norwood Grade IV**



**Photograph 37: Hamilton Norwood Grade V**



**Photograph 38: Hamilton Norwood Grade VI**

# DISCUSSION

# DISCUSSION

The term AGA is used to define hair loss under the influence of androgens against a background of genetically determined susceptibility with respect to the hair follicle.[1] AGA in men produces patterned hair loss, which starts with bitemporal recession of the frontal hair line, followed by the thinning of hair over the vertex.[51] Gradually this leads to complete hair loss centrally on the vertex, producing an area of complete baldness.

**Age distribution:**

Many studies reported a gradual rise in AGA with age. A study on Caucasian population shown prevalence of about 30 percent of men in their 30s, 40 percent in their 40s and 50 percent in their 50s as estimated by Wang TL et al.[115] In a population based study of 1005 Indian patients by Shankar DK et al. showed 58% prevalence of AGA in males aged 30-50 years.[53] According to our study a prevalence of 44.4 %AGA was seen in between 20-30 years aged men , 31.7 % in between 31-40 years aged men, 21.1% in between 41-50 years aged men and 2.8 % in between50-60 years aged men. This is in agreement with Qi Ding et al study and Gupta et al study, where the maximum prevalence of AGA was seen in the age group 21- 30years.[116, 117]Some environmental and genetic factors which leads to early AGA and the lack of interest in aged men to get treated for AGA, might be the reasons for such distribution in our study.

**Age of onset:**

Previous studies shown onset of AGA with puberty.[8] In a study by Jang WS et al. in the Korean population, he observed that the age of onset of AGA in his patients were

mostly in their 20's.[59] Another study on Indian population by Sehgal VN et al. shown that, in 50% of patients onset was in 20 to24 age groups.[55]In Our study most of the patients belonged to the age group 26-30years . Onset of AGA in such younger age groups might be because of stress factors like the need to be competitive in the present society and lifestyle modifications.

**Duration of AGA:**

Duration plays an important role in deciding the management of hair loss. Most of the patients had a duration of 1-4 years of gradual onset of hair loss as noted by Sehgal VN et al.[55]In our study 42.5% patients presented within 1-5years duration ofhair loss. This was comparable with studies by Gupta et al and Elsaie et al.[117, 118]This is because the younger age groups are more concerned about hair loss than the older ones. Bitemporal recession of the hairline is the commonest and the earliest sign of AGA in men, a feature observed in many studies including our study.

**Occupation:**

AGA was predominantly seen among the skilled workers (61, 28%) in our study. This could be due to more stress levels associated with the occupation. But a study by Sawant et al concluded that there is no relation for AGA with the occupation associated stress levels.[119]

**Relation with Socioeconomic status:**

In our study, we noted most patients of AGA in the upper middleclass status (85, 39%). But there were no proper evidence which conclude that AGA is related to socioeconomic status.

**Onset and progression of AGA**

Majority of the patients (210, 96.3%) had insidious onset of AGA and very few had sudden onset (8, 3.7%). 213 (97.7%) patients had gradual progression. A study by Salman K et al also states that AGA has insidious onset after puberty and is gradually progressive.[120]

**Risk factors and their effect of AGA:**

**Family history:**

Though AGA is deemed to be a genetical predisposed condition, the inheritance mode was not described well. In a study by Nagris T et al and Salman K et al reported a positive family history of AGA in 68% and 71.02% of patients.[120,121] Male patients tend to be more likely to have a father or male sibling with a similar problem, whereas female patients tend to be more likely to have a mother or female sibling with AGA.[74]In another study by Su LH et al. found that family history of AGA in the first or second degree relatives is statistically significantly associated with the risk of early onset AGA and higher chances of developing moderate to severe AGA.[3] We also observed that 125 (57.21%) patients with a positive family history had onset of AGA, paternal in 46 (21.1%), maternal in 16 (13.3%), sibling in 29 (13.3%), both paternal and sibling in 28 (12.8%) and both maternal and sibling in 6 (2.8%).

This suggests that those patients with a family history of AGA in 1$^{st}$ or 2$^{nd}$ degree relatives have more chances of getting early AGA. Patients with early AGA requires early advice to avoid further progression of the condition. This implies that expression of AGA can be influenced by familial prevalence. The prevalence of maternal AGA has less effect than prevalence of paternal AGA on AGA expression.

**Alcohol history:**

Alcohol consumption twice or more than twice a month on an average was associated with increased chances of about 50-60% of AGA according to a study by Severi G et al.[92]In our study, only 33.5% patients gave history of alcohol consumption.

**Smoking history:**

Many studies have been done on the effects of smoking and AGA with varying results. In a study by Su LH et al. a positive relation was observed between AGA and smoking, though he didn't quantify the number of cigarettes smoked.[3]In our study, 170 (78%) patients gave a history of smoking which was in accordance with an Italian study and Egyptian study which also showed a positive association.[4,122]

**Associated Systemic diseases**:

AGA is commonly associated with diabetes, hypertension and hyperlipidemia as reported by Yeo IK et al .[123] In our study, 23 (10.5%) were diabetic, 21 (9.6%) were hypertensive, 4 (1.8%)had bronchial asthma and 2 (0.9%) had history of coronary artery disease.

Several studies have shown association between hypertension (HTN) and AGA. In a study by El Esawy FM et al., higher blood pressure values were observed in patients with AGA than in those without AGA and reported AGA to be an early marker for hypertension.[124]In our study we noted 21 AGA patients (9.6%) with hypertension. This was compatible with a Gupta et al study which reported that 7% were hypertensive.[117]

**Hamilton Norwood (HN) classification:**

Hamilton in his study noticed type II was most common, but in the Norwood study in which type I was the most common.[51,52] Vora RV in his study noticed type III was most common.[125]Sehgal VN et al. on his study on the Indian population, observed the most common as type II according to Hamilton- Norwood grading.[55]

In our study most number of Androgenetic alopecia patients belongs to Norwood Hamilton type II 60(27.5%). This was in accordance with previous studies.

This might be because patients in the younger age group are more concerned about their appearance and mostly report for the treatment. However this younger age group gradually can develop severe AGA.

In our study, 72 (33%) of the patients were moderate smokers, 53 (24.3%) were light smoker and 45 (20.6%) were heavy smokers. In our study most common type of AGA in light and moderate smokers was type II, in heavy smokers was type IV.

# CONCLUSION

## CONCLUSION

- Androgenetic alopecia is a multifactorial disease which occurs due to interactions between various genetic and environmental factors.
- Factors such as smoking, overweight and lifestyle may play a role in androgenetic pathogenesis.
- A positive association between smoking and Androgenetic alopecia is seen in our study.
- In addition to gathering data this study also educates public about the association between smoking and hair loss and provides a good opportunity to prevent smoking and there by hair loss.

# SUMMARY

# SUMMARY


- AGA cases attending the Department of Dermatology at R.L Jalappa Hospital attached to Sri Devaraj Urs Medical College, Tamaka, Kolar from January 2019 to July 2020 were identified and a total of 218 cases satisfying the inclusion criteria were included in the study.
- A detailed history was taken, thorough examination was done and all the findings were documented as per proforma.
- Majority of the patients belonged to the age group of 20-30 years.
- Of the 218 patients, majority 42.7% had a hair loss duration between 1-5 years of onset.
- 57.21% patients had a positive family history and most of them had paternal inheritance.
- Diabetes mellitus was seen in 10.5%, Hypertension in 9.6%, Bronchial Asthma in 1.8% and 0.9% of the subjects had CAD.
- History of alcohol consumption was present in 33.5 %.
- Majority 78% of the patients had smoking history. Among them 33% of the patients were moderate smokers, 24.3% were light smoker and 20.6% were heavy smokers.
- The most commonly seen grade according to HN class was type II in 27.5% of patients followed by type I in 18.3% and type III in 17.4%.
- Most common type of AGA in light and moderate smoker was II.
- Most common type of AGA in heavy smoker was IV.

# BIBLIOGRAPHY

# BIBLIOGRAPHY


1. Sinclair RD. Disorders of Hair. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Textbook of Dermatology. 9th edition. West Sussex: Blackwell Publishing Ltd;2016:66.16-31.
2. RhodesT,GirmanCJ,SavinRC,KaufmanKD,GuoS,LillyFRetal.Prevalence of male pattern hair loss in 18-49 year old men. Dermatol Surg 1998;24:1330-2.
3. SuLH, Chen TH. Association of androgenetic alopecia with smoking and its prevalence among Asian men: A community-based survey. Arch Dermatol 2007;143:1401-6.
4. Fortes C, Mastroeni S, Mannooranparampil TJ, Ribuffo M. The combination of overweight and smoking increases the severity of androgenetic alopecia. Int J Dermatol 2017;56:862-7.
5. Trueb RM. Association between smoking and hair loss: another opportunity for health education against smoking? Dermatology 2003;206:189-91.
6. Ramos PM, Miot HA. Female pattern hair loss: a clinical and pathophysiological review. Anais Brasileirosde Dermatologia2015;90:529-43.
7. Klingman AM, Freeman B. History of baldness: from magic to medicine. Clin Dermatol1988;6:83-8.
8. Olsen EA. Androgenetic alopecia. In: Oslen EA, editor. Disorders ofHair Growth: Diagnosis and Treatment, New York,McGraw-Hill;1994:257-83.
9. Hamilton JB. Male hormone stimulation is prerequisite and an incident in common baldness. Am J Anat1942;71:451-80.
10. Santos Z, Avci P, Hamblin MR. Drug discovery for alopecia: gone today, hair tomorrow. Expert Opin Drug Discov 2015;10(3):269–92.

11. Dhurat R, Sukesh MS. Hair and scalp disorders. In: Sacchidanand S, Oberoi C, Inamadar AC, editors. IADVL textbook of Dermatology. 4th ed.Mumbai: Bhalani Publishing House; 2015. p. 1468-57.
12. Draelos ZK. Hair cosmetics. Dermatol Clin 1991;9(1):19–27. 34.
13. Schneider MR, Schmidt-Ullrich R, Paus R. The hair follicle as a dynamic miniorgan. Curr Biol 2009;19(3):R132–R42. 35.
14. Mokos ZB, Mosler EL. Advances in a rapidly emerging field of hair follicle stem cell research. Coll Antropol 2014;38(1):373–78. 36.
15. Paus R, Cotsarelis G. The biology of hair follicles. N Engl J Med 1999;341(7):491– 97. Hamilton JB. Patterned loss of hair in man: types and incidence. Ann NY Acad Sci1951;53:708-28.
16. Callen JP, Horn TD, Mancini AJ, Salasche JS, et al. Development of skin appendages. In: Bolognia JL, Jorizzo LJ, Schaffer JV, editors. Dermatology. 4th ed. USA: Elsevier Ltd;2018. p.1078-79.
17. Malkud S. Telogen Effluvium: A Review. J Clin Diagn Res 2015;9:1-3.
18. Vogt A, McElvee KJ, Peyatavi UB. Biology of the hair follicle. In: Peyatavi UB, Tosti A, Whting D, Trueb R, editors. Textbook on hair - From basic science to clinical application. Berlin: Springer Verlag; 2008. p. 1-22.
19. Oro AE, Scott MP. Splitting hairs: dissecting roles of signaling systems in epidermal development. Cell 1998;95(5):575–78.
20. Jahoda CA, Reynolds AJ. Dermal-epidermal interactions. Adult follicle-derived cell populations and hair growth. Dermatol Clin 1996;14(4):573-83.
21. Peus D, Pittelkow MR. Growth factors in hair organ development and the hair growth cycle. Dermatol Clin 1996;14(4):559-72.
22. Cotsarelis G, Sun TT, Lavker RM. Label-retaining cells reside in the bulge area

of pilosebaceous unit: Implications for follicular stem cells, hair cycle, and skin carcinogenesis. Cell 1990;61(7):1329–37.

23. Mayer JA, Chuong CM, Widelitz R. Rooster feathering, androgenic alopecia, and hormone-dependent tumor growth: what is in common? Differentiation 2004;72(9- 10):474-88.
24. Sano S, Kira M, Takagi S, Yoshikawa K, Takeda J, Itami S. Two distinct signaling pathways in hair cycle induction: Stat3-dependent and -independent pathways. Proc Natl Acad Sci U S A 2000;97(25):13824-9.
25. Rishikaysh P, Dev K, Diaz D, Qureshi WM, Filip S, Mokry J. Signaling involved in hair follicle morphogenesis and development. Int J Mol Sci 2014;15(1):1647-70.
26. Andl T, Reddy ST, Gaddapara T, et al. WNT signals are required for the initiation of hair follicle development. Dev Cell 2002;2(5):643–53.
27. Harris PJ, Takebe N, Ivy SP. Molecular conversations and the development of the hair follicle and basal cell carcinoma. Cancer Prev Res (Phila) 2010;3(10):1217-21.
28. Mill P, Mo R, Fu H, Grachtchouk M, Kim PC, Dlugosz AA, et al. Sonic hedgehogdependent activation of Gli2 is essential for embryonic hair follicle development. Genes Dev 2003; 17(2):282-94.
29. Chiang C, Swan RZ, Grachtchouk M, Bolinger M, Litingtung Y, Robertson EK, et al. Essential role for Sonic hedgehog during hair follicle morphogenesis. Dev Biol 1999; 205(1):1-9.
30. Botchkarev VA, Botchkareva NV, Roth W, Nakamura M, Chen LH, Herzog W, et al. Noggin is a mesenchymally derived stimulator of hair-follicle induction. Nat Cell Biol 1999; 1(3):158-64.

31. Mou C, Jackson B, Schneider P, Overbeek PA, Headon DJ. Generation of the primary hair follicle pattern. Proc Natl Acad Sci U S A 2006;103(24):9075-80.
32. Pummila M, Fliniaux I, Jaatinen R, James MJ, Laurikkala J, Schneider P, et al. Ectodysplasin has a dual role in ectodermal organogenesis: inhibition of Bmp activity and induction of Shh expression. Development 2007;134(1):117-25.
33. Takechi M, Adachi N, Hirai T, Kuratani S, Kuraku S. The Dlx genes as clues to vertebrate genomics and craniofacial evolution. Semin Cell Dev Biol 2013;24(2):110-18.
34. Hwang J, Mehrani T, Millar SE, Morasso MI. Dlx3 is a crucial regulator of hair follicle differentiation and cycling. Development 2008;135(18):3149-59.
35. Hamanaka RB, Glasauer A, Hoover P, Yang S, Blatt H, Mullen AR, et al. Mitochondrial reactive oxygen species promote epidermal differentiation and hair follicle development. Sci Signal 2013;6(261):ra8.
36. Aubin-Houzelstein G. Notch signaling and the developing hair follicle. Adv Exp Med Biol 2012;727:142-60.
37. Millar SE. Molecular mechanisms regulating hair follicle development. J Invest Dermatol 2002;118(2):216-25.
38. Taylor G, Lehrer MS, Jensen PJ, Sun TT, Lavker RM. Involvement of follicular stem cells in forming not only the follicle but also the epidermis. Cell 2000;102(4):451-61.
39. Ellis T, Gambardella L, Horcher M, Tschanz S, Capol J, Bertram P, et al. The transcriptional repressor CDP (Cutl1) is essential for epithelial cell differentiation of the lung and the hair follicle. Genes Dev 2001;15(17):2307-19.
40. Li J, Zhou Y, Yang T, Wang N, Lian X, Yang L. Gsdma3 is required for hair

follicle differentiation in mice. BiochemBiophys Res Commun 2010;403(1):18-23.

41. Kim BK, Yoon SK. Hairless down-regulates expression of Msx2 and its related target genes in hair follicles. J Dermatol Sci 2013;71(3):203-9.
42. Potter CS, Pruett ND, Kern MJ, Baybo MA, Godwin AR, Potter KA, et al. The nude mutant gene Foxn1 is a HOXC13 regulatory target during hair follicle and nail differentiation. J Invest Dermatol 2011;131(4):828-37.
43. Jave-Suárez LF, Schweizer J. The HOXC13-controlled expression of early hair keratin genes in the human hair follicle does not involve TALE proteins MEIS and PREP as cofactors. Arch Dermatol Res 2006;297(8):372-6.
44. Lin SJ, Wideliz RB, Yue Z, Li A, Wu X, Jiang TX, et al. Feather regeneration as a model for organogenesis. Dev Growth Differ 2013;55(1):139-48.
45. Ponnaiyan D. Do dental stem cells depict distinct characteristics? - Establishing their "phenotypic fingerprint". Dent Res J (Isfahan) 2014;11(2):163-72.
46. Mokos ZB, Mosler EL. Advances in a rapidly emerging field of hair follicle stem cell research. Coll Antropol 2014;38(1):373–78. Norwood OT, Male pattern baldness. Classification and incidence. South Med J 1975;68:1359-65.
47. Yesudian P. Human hair - An evolutionary relic?Int J Trichol 2011;3:69.
48. Otberg N, Shapiro J.Hair growth disorders.In:Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, LeffellDJ,Wolff K, editors. Fitzpatrick's Dermatology in General Medicine. 8th ed. USA: The McGraw-Hill Companies Inc.;2012. p. 979-82.
49. Elghblawi E. Frontier in hair loss and trichoscopy:a review. J Surg Dermatol 2016;1:80–96.

50. Kabir Y, Goh C. Androgenetic alopecia: update on epidemiology, pathophysiology, and treatment. J Egypt Women Dermatol Soc 2013;10:107–16.

51. Hamilton JB. Patterned loss of hair in man: types and incidence. Ann NY Acad Sci1951;53:708-28.

52. Norwood OT, Male pattern baldness. Classification and incidence. South Med J 1975;68:1359-65.

53. Shankar DK, Chakravarthi M, Shilpakar R. Male androgenetic alopecia: Population-based study in 1,005 subjects. Int J Trichol2009;1:131-3.

54. Grover S. A study of patterns of androgenetic alopecia in men: An Indian perspective. Br J Dermatol2005;152:572-4.

55. Sehgal VN, Kak R, Aggarwal A, Srivastava G, Rajput P. Male pattern androgenetic alopecia in an Indian context: a perspective study. J Eur Acad Dermatol Venereol2007;21:473-9.

56. Norwood OT. Incidence of female androgeneticalopecia(femalepattern alopecia). Dermatol Surg2001;27:53-4.

57. Lee WS, Lee HJ. Characteristics of androgenetic alopecia in asian. Ann Dermatol 2012;24:243-52.

58. Paik JH, Yoon JB, Sim WY, Kim BS, Kim NI. The prevalence and types of androgenetic alopecia in Korean men and women. Br J Dermatol2001;145:95-9.

59. Jang WS, Son IP, Yeo IK, Park KY, Li K, Kim BJ et al. The annual changes of clinical manifestation of androgenetic alopecia clinic in orean males and females: a outpatient-based study. Ann Dermatol2013;25:181-8.

60. Bedocs LA, Bruckner AL. Adolescenthair loss. CurrOpinPediatr2008;20:431-5.

61. TostiA, IorizzoM, Piraccini BM. Androgenetic alopecia in children: report of 20 cases. Br J Dermatol2005;152:556-9.

62. Price VH. Androgenetic alopecia in adolescents. Cutis2003;71:115-21.

63. Gonzalez ME, Cantatore-Francis J, Orslow SJ. Androgenetic alopecia in the paediatric population: a retrospective review of 57 patients. Br J Dermatol 2010;163:378-85.

64. Kivanç-Altunay I, Savaş C, Gökdemir G, Köşlü A, Ayaydin EB. The presence of trichodynia in patients with telogen effluvium and androgenetic alopecia. Int J Dermatol2003;42:691-3.

65. Giagulli VA, Kaufman JM, Vermeulen A. Pathogenesis of the decreased androgen levels in obese men. J Clin Endocrinol Metab1994;79:997-1000.

66. Couillard C, Gagnon J, Bergeron J, Leon AS, Rao DC, Skinner JS etal. Contribution of body fatness and adipose tissue to the age variation in plasma steroid hormone concentrations in men: the HERITAGE Family Study. J Clin Endocrinol Metab2000;85:1026-31.

67. Ahouansou S, Le Toumelin P, Crickx B, Descamps V.Association of androgenetic alopecia and hypertension. Eur J Dermatol2007;17:220-2.

68. Arias-Santiago S, Gutiérrez-Salmerón MT, Buendía-Eisman A, Girón-Prieto MS, Naranjo-Sintes R. A comparative study of dyslipidaemia in men and woman with androgenic alopecia. Acta DermVenereol2010;90:485-7.

69. Sharma KH, Jindal A. Association between androgenetic alopecia and coronary artery disease in young male patients. Int J Trichology2014;6:5-7.

70. MatilainenV, Koskela P, Keinänen-Kiukaanniemi S. Early androgenetic alopecia as a marker of insulin resistance. Lancet2000;356:1165-6.

71. Amoretti A, LaydnerH, Bergfeld W. Androgenetic alopecia and risk of prostate

cancer: a systematic review and meta-analysis. J Am Acad Dermatol 2013;68:937-43.

72. Cheryl Lie, Choon Fong Liew, Hazel H. Oon. Alopecia and the metabolic syndrome. Clinics in Dermatology (2018) 36, 54–61.
73. Nyholt DR, Gillespie NA, Heath AC, Martin NG. Genetic basis of male pattern baldness. J Invest Dermatol2003;121:1561-4.
74. Goh CL. A retrospective study on the characteristics of androgenetic alopecia among Asian races in the National Skin Centre, a tertiary dermatological referral centre in Singapore. Ann Acad Med Singapore2002;31:751-5.
75. Ellis JA, Stebbing M, Harrap SB. Polymorphism of the androgen receptor gene is associated with male pattern baldness. J InvestDermatol 2001;116:452-5.
76. Prodi DA, PirastuN, Maninchedda G, Sassu A, Picciau A, Palmas MA etal. EDA2R is associated with androgenetic alopecia. J Invest Dermatol 2008;128:2268-70.
77. Richards JB, Yuan X, Geller F, Waterworth D, BatailleV, Glass D, et al. Male pattern baldness susceptibility locus at 20p11. Nat Genet2008;40:1282-4.
78. Cobb JE, Zaloumis SG, Scurrah KJ, Harrap SB, Ellis JA. Evidence for two independent functional variant for androgenetic alopecia around the androgen receptor gene. Exp Dermatol2010;19:1026-8.
79. Heilmann S, Kiefer AK, Fricker N, Drichel D, Hillmer AM, Herold C, etal. Androgenetic alopecia: Identification of four genetic risk loci and evidence for the contribution of WNT signaling to its etiology. J Invest Dermatol 2013;133:1489- 96.
80. Millar SE, Willert K, Salinas PC, RoelinkH, Nusse R, Sussman DJ, et al. WNT signaling in the control of hairgrowth and structure. Dev Biol 1999;207:133-49.

81. Ellis JA, Harrap SB. The genetics of androgenetic alopecia. Clin Dermatol 2001;19:149-54.

82. Pitts RL. Serum elevation of dehydroepiandrosterone sulfate associated with male pattern baldness in young men. J Am Acad Dermatol1987;16:571-3.

83. Sawaya ME, Honig LS, Garland LD, Hsia SL. Delta 5-3 beta-hydroxysteroid dehydrogenase activity in sebaceous glands of scalp in male-pattern baldness. J Invest Dermatol 1988;91:101-5.

84. Ellis JA, Sinclair R, Harrap SB. Androgenetic alopecia: pathogenesis and potential for therapy. Expert reviews in molecular medicine2002;4:1-11.

85. Orentreich N. Autografts in alopecias and other selected dermatological conditions. Ann N Y Acad Sci1959;83:463-79.

86. Garza LA, Liu Y, Yang Z, Alagesan B, Lawson JA, Norberg SM. Prostaglandin $D_2$Inhibits Hair Growth and Is Elevated in Bald Scalp of Men with Androgenetic Alopecia. Sci Transl Med2012;4:126.

87. Millikan LE. Androgenetic alopecia: The role of inflammation andDemodex. Int JDermatol 2001;40:475-6.

88. Jimenez-Acosta F, Planas L, PenneysN. Demodex mites contain immuno reactive lipase. Arch Dermatol1989;125:1436-7.

89. Hayakawa k, Shimizu T,ObhaY,etal:Intra-pair differences of physical aging and longevity in identical twins.Acta Genet Med Gemellol 1992;41:177-185

90. Mosley JG, Gibbs AC. Premature grey hair and hair loss among smokers: a new opportunity for health education? BMJ1996;313:1616.

91. Hsieh CC, SignorelloLB, Lipworth L, Lagiou P, Mantzoros CS, Trichopoulos D. Predictors of sex hormone levels among the elderly: a study in Greece. J Clin Epidemiol1998;51:837–41.

92. Severi G, Sinclair R, Hopper JL, English DR, McCredie MR, Boyle P etal.Androgenetic alopecia in men aged 40-69 years: prevalence and risk factors. Br J Dermatol 2003;149:1207-13.

93. Courtois M, Loussouarn G, Hourseau C, Grollier JF. Hair cycle and alopecia. Skin pharmacology: the official journal of the SkinPharmacology Society 1994;7:84-9.

94. Weger N, Schlake T. Igfbp3 modulates cell proliferation in the hair follicle. J Invest Dermatol 2005;125:847-9.

95. Prieto VG, Sadick NS, Shea CR. Androgenetic alopecia: analysis of proliferation and apoptosis. Arch Dermatol2002;138:1101-2.

96. Hamada K, Randall VA. Inhibitory autocrine factors produced bythe mesenchyme-derived hair follicle dermal papilla may be a key to male pattern baldness. Br J Dermatol2006;154:609-18.

97. Whiting DA. Possible mechanisms of miniaturization during androgenetic alopecia or pattern hair loss. J Am Acad Dermatol2001;45:S81-6.

98. PinkusH. Differential patterns of elastic fibers in scarring and non-scarring alopecias. J CutanPathol1978;5:93-104.

99. Sinclair R, Torkamani N, Jones L. Androgenetic alopecia: new insights into the pathogenesis and mechanism of hair loss. F1000Res2015;4:585.

100. Yazdabadi A, Whiting D, RufautN, Sinclair R. Miniaturized Hairs Maintain Contact with the Arrector Pili Muscle in Alopecia Areata but not in Androgenetic Alopecia: A Model for Reversible Miniaturization and Potential for Hair Regrowth. Int J Trichology2012;4:154-7.

101. Jaworsky C, Kligman AM, Murphy GF. Characterization ofinflammatory infiltrates in male pattern alopecia: implications for pathogenesis. Br J Dermatol

1992;127:239-46.

102. SuekiH, Stoudemayer T, Kligman AM, Murphy GF. Quantitative and ultrastructural analysis of inflammatory infiltrates in male pattern alopecia. Acta dermato-venereologica1999;79:347-50.
103. Hu R et al. Trichoscopic findings of androgenetic alopecia and their association with disease severity. J Dermatol 2015;42:1–6.
104. Whiting DA. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in male pattern androgenetic alopecia. J Am Acad Dermatol 1993;28:755-63.
105. Kaliyadan F, Nambiar A, Vijayaraghavan S. Androgenetic alopecia: Anupdate.Indian J Dermatol VenereolLeprol2013;79:613-25.
106. BlumeyerA,TostiA,MessengerA,ReygagneP,DelMarmolV,SpulsPI,etal.Evidence based (S3) guideline for the treatment of androgenetic alopecia in women and in men. J Dtsch Dermatol Ges2011;9:S1-57.
107. Blume-PeytaviU, Kunte C, KrispA, Garcia Bartels N, EllwangerU, Hoffmann R.Comparisonof the efficacy and safety of topical minoxidil and topical alfatradiol in the treatment of f androgenetic alopecia in women. J Dtsch Dermatol Ges2007;5:391-5.
108. DavisMG,ThomasJH,vandeVeldeS,BoissyY,DawsonTLJr,IvesonRetal.A novel cosmetic approach to treat thinning hair. Br J Dermatol 2011;165:24-30.
109. Tsuboi R, Itami S, Inui S, Ueki R, KatsuokaK, Kurata S et al. Guidelines for the management of androgenetic alopecia (2010). J Dermatol2012;39:113-20.
110. Freund BJ, Schwartz M. Treatment of male pattern baldness with botulinum toxin: A pilot study. PlastReconstr Surg2010;126:246-8.
111. Rangwala S, Rashid RM. Alopecia: A review of laser and

lighttherapies.Dermatol Online J 2012;18:3.

112. Dhurat R, Sukesh MS. Principles and methods of preparation of platelet-rich plasma: A review and author's perspective. JCutanAesthet Surg 2014;7:189-97.
113. Toyoshima KE, Asakawa K, Ishibashi N, Toki H, Ogawa M, Hasegawa T etal.Fully functional hair follicle regeneration through the rearrangement of stem cellsand their niches.NatCommun 2012;3:784.
114. Gupta M, Mysore V. Classifications of patterned hair loss: a review. J CutanAesthetSurg 2016;9:3-12.
115. Wang TL, Zhou C, Shen YW, Wang XY, Ding XL, Tian S, et al. Prevalence of Androgenetic alopecia in China: A community-based study in six cities. Br J Dermatol2010;162:843-7.
116. Ding Q, Xu YX, Sun WL, Liu JJ, Deng YY, Wu QF, Cao CY, Zhou LB, Lu Y, Fan WX. Early-onset androgenetic alopecia in China: a descriptive study of a large outpatient cohort. J Int Med Res. 2020 Mar;48(3):300060519897190.
117. Gupta S, Goyal I, Mahendra A. Quality of Life Assessment in Patients with Androgenetic Alopecia. Int J Trichology. 2019 Jul-Aug;11(4):147-152.
118. Elsaie LT, Elshahid AR, Hasan HM, Soultan FAZM, Jafferany M, ElsaieML. Cross Sectional Quality of Life Assessment in Patients with Androgenetic Alopecia. Dermatol Ther. 2020 Jun 10:e13799.
119. Sawant N, Chikhalkar S, Mehta V, Ravi M, Madke B, Khopkar U. Androgenetic Alopecia: Quality-of-life and Associated Lifestyle Patterns. Int J Trichology. 2010 Jul;2(2):81-5.
120. Salman KE, Altunay IK, Kucukunal NA, Cerman AA. Frequency, severity and related factors of androgenetic alopecia in dermatology outpatient clinic: hospital-based cross-sectional study in Turkey. An Bras Dermatol

2017;92(1):35–40

121. Nargis T, Bejai V, Pinto M, Shenoy MM. Early onset androgenetic alopecia in men and associated risk factors: a hospital based study. Int J Res Dermatol. 2017; 6:22-27

122. Salem A, Ibrahim H, Abdelaziz H, and Mohamed L.Implications of Cigarette Smoking on Early Onset Androgenetic Alopecia: A Cross Sectional Study. J. Cosmet. Dermatol . 2020 Sepdoi: 10.1111/JOCD.13727

123. Yeo IK, Jang WS, Min PK, Cho HR, Cho SW, Hong NS et al. An epidemiological study of androgenic alopecia in 3114 Korean patients. Clin Exp Dermatol 2014;39:25-9.

124. El-Esawy FM, SherineH, El-Rahman A. Androgenetic alopecia asan early marker for hypertension. Egypt J Dermatol Venereol2013;33:63-6.

125. Vora RV, Kota RKSK, Singhal RR, Anjaneyan G. Clinical Profile of Androgenetic Alopecia and its Association with Cardiovascular Risk Factors. Indian J Dermatol. 2019 Jan-Feb; 64(1): 19-22.

# ANNEXURES

# ANNEXURES

## PROFORMA

Name: Date of examination:

Age: IP/OPD No:

Sex:

Address:

Educational Status:

Occupation:

**A) HISTORY**

Complains:

1. Age of onset:

2. Duration of hair loss:

3. Itching:

4. Stress/anxiety:

5. weight loss/systemic illness:

6. Habitual pulling of hair:

8. Smoking history: number of cigarettes per day, duration of smoking

9. Alcohol intake

13. History of any medical illness or surgery:

14. Family history:

15. Treatment history:

16. Cosmetic procedures done? If yes, then specify:

**ON EXAMINATION:**

B) General physical examination:

C) Systemic examination:

RS:

CVS:

P/A:

CNS:

D) Dermatological examination:

Hamilton Norwood grade

Ludwig grade

Diagnosis:

# PATIENT INFORMATION SHEET

**Study title:** ASSOCIATION OF ANDROGENETIC ALOPECIA WITH SMOKING: A CROSS SECTIONAL STUDY

**Study site**: R.L Jalappa Hospital, Tamaka, Kolar.

**Aim**:

- To document the type and extent of androgenetic alopecia.
- To categorize the smoking habit of the above subjects according to smoking index.
- To evaluate the frequency of smoking among the subjects with androgenetic alopecia.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study we will collect information (as per proforma) from you. Relevant blood investigations will be carried out if required. This information collected will be used for dissertation and publication only.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. The expenses required for the above investigations will be funded by the study investigator. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

**For any further clarification you can contact the study investigator:**

Dr. GVL. Naveena

Mobile no: 8686900404

E-mail id: naveenaganesam@gmail.com

# CONSENT FORM

**Study title:**

**ASSOCIATION OF ANDROGENETIC ALOPECIA WITH SMOKING: A CROSS SECTIONAL STUDY**

**Chief researcher/ PG guide's name:** DR.GVL.NAVEENA

**Under the guidance of:** DR. RAJASHEKAR T.S

**Name of the subject:**

**Age :**

**Address :**

a. I have been informed in my own vernacular language the purpose of the study, the necessity of relevant investigations to be carried out and photographs to be taken.
b. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
c. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
d. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
e. I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that I may experience, in my

own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant's signature

Signature of the witness: Date:

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date:

# KEY TO MASTER CHART

1) **Age:**

20-30 years- 1

31-40 years- 2

41-50 years- 3

51-60 years- 4

2) **Occupation**:

White collared work- 1

Skilled work-2

Semiskilled work-3

Manual laborer-4

Agriculturist- 5

Student-6

3) **Socio-economic status:**

Upper-1

Upper middle-2

Lower middle-3

Upper lower-4

Lower-5

4) **onset:**

Insidious-1

Sudden-2

5) **Duration of hair loss :**

0-6 months-1

7 months- 1 year-2

1-5years- 3

5-10 years-4

> 10 years-5

6) **Age of onset:**

< 20 years- 1

21-25 years-2

26-30 years-3

31-35 years-4

36-40 years- 5

41-45 years-6

>45 years-7

7) **Progression:**

gradual- 1

rapid- 2

8) **Family history:**

Paternal-1

Maternal-2

Sibling-3

Both sibling and paternal-4

Both sibling and maternal-5

No family history- 6

**9) Smoking history:**

Yes-1

No-2

10**) Duration of smoking in years:**

11) **Quantity/day:**

12) **Smoking Index:**

Never-0

Light smokers-1

Moderate smokers-2

Heavy smokers-3

13) **Alcohol history:**

Yes-1

No-2

14) **Comorbidities:**

Nil-1

DM-2

HTN-3

BA-4

CAD-5

15)**Norwood Hamilton classification:**

I - 1

II- 2

IIa- 3

III- 4

IIIv- 5

IIIa- 6

IV- 7

IVa- 8

V- 9

Va- 10

VI- 11

VII- 12

**16) Ludwig:**

| SL. No. | OP/IP no. | Age | Occupation | Socio-economic status | Onset | Duration of hair loss | Age of onset | Progression | Family History | Smoking history | Duration of smoking (in years) | Quantity/day | Smoking index | Alcohol history | Comorbidities | Norwood hamilton | Ludwig |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 667618 | 1 | 1 | 2 | 1 | 2 | 3 | 1 | 1 | 1 | 5 | 10 | 1 | 2 | 1 | 1 | 0 |
| 2 | 508782 | 1 | 1 | 2 | 1 | 3 | 2 | 1 | 3 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 3 | 667712 | 1 | 2 | 1 | 1 | 1 | 3 | 1 | 1 | 1 | 5 | 8 | 1 | 2 | 1 | 1 | 0 |
| 4 | 493512 | 1 | 1 | 1 | 1 | 2 | 3 | 1 | 6 | 1 | 10 | 20 | 2 | 2 | 1 | 2 | 0 |
| 5 | 622216 | 2 | 2 | 2 | 1 | 3 | 3 | 1 | 4 | 1 | 12 | 25 | 2 | 2 | 1 | 3 | 0 |
| 6 | 664416 | 2 | 2 | 3 | 1 | 4 | 3 | 1 | 6 | 1 | 12 | 20 | 2 | 2 | 1 | 4 | 0 |
| 7 | 669915 | 2 | 1 | 1 | 1 | 3 | 4 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 3 | 0 |
| 8 | 670131 | 3 | 5 | 4 | 1 | 4 | 5 | 1 | 1 | 2 | 0 | 0 | 0 | 1 | 2 | 4 | 0 |
| 9 | 666551 | 1 | 3 | 3 | 1 | 3 | 3 | 1 | 1 | 1 | 10 | 20 | 2 | 2 | 1 | 3 | 0 |
| 10 | 670490 | 1 | 6 | 2 | 1 | 2 | 3 | 1 | 6 | 1 | 7 | 15 | 2 | 2 | 1 | 2 | 0 |
| 11 | 662134 | 2 | 3 | 4 | 1 | 3 | 3 | 1 | 2 | 1 | 8 | 10 | 1 | 2 | 1 | 1 | 0 |
| 12 | 664275 | 1 | 6 | 2 | 1 | 1 | 1 | 1 | 4 | 1 | 1 | 10 | 1 | 2 | 1 | 1 | 0 |
| 13 | 616120 | 1 | 2 | 2 | 2 | 1 | 2 | 2 | 3 | 1 | 2 | 6 | 1 | 2 | 1 | 1 | 0 |
| 14 | 602474 | 2 | 4 | 5 | 1 | 2 | 4 | 1 | 6 | 1 | 12 | 30 | 3 | 1 | 1 | 1 | 0 |
| 15 | 677866 | 2 | 2 | 2 | 1 | 2 | 4 | 1 | 6 | 1 | 12 | 10 | 2 | 2 | 1 | 2 | 0 |
| 16 | 658151 | 1 | 1 | 2 | 1 | 3 | 2 | 1 | 2 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 17 | 566511 | 1 | 6 | 1 | 1 | 2 | 2 | 1 | 4 | 1 | 2 | 20 | 1 | 2 | 1 | 1 | 0 |
| 18 | 565851 | 2 | 1 | 1 | 1 | 3 | 4 | 1 | 1 | 1 | 20 | 10 | 2 | 2 | 3 | 4 | 0 |
| 19 | 313134 | 2 | 5 | 4 | 1 | 3 | 3 | 1 | 6 | 1 | 13 | 15 | 2 | 2 | 1 | 2 | 0 |
| 20 | 475123 | 1 | 2 | 2 | 1 | 3 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 21 | 677152 | 1 | 6 | 2 | 1 | 1 | 2 | 1 | 3 | 1 | 3 | 9 | 1 | 2 | 1 | 1 | 0 |
| 22 | 677182 | 2 | 4 | 5 | 1 | 3 | 3 | 1 | 1 | 1 | 6 | 16 | 1 | 2 | 1 | 2 | 0 |
| 23 | 574809 | 2 | 1 | 1 | 1 | 3 | 3 | 1 | 2 | 1 | 10 | 15 | 2 | 2 | 1 | 2 | 0 |
| 24 | 662803 | 1 | 5 | 4 | 1 | 3 | 2 | 1 | 1 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 25 | 67 8041 | 2 | 2 | 2 | 2 | 1 | 4 | 2 | 6 | 1 | 14 | 25 | 3 | 1 | 1 | 1 | 0 |
| 26 | 679110 | 1 | 5 | 5 | 1 | 3 | 3 | 1 | 4 | 1 | 10 | 20 | 2 | 2 | 1 | 2 | 0 |
| 27 | 679769 | 1 | 2 | 2 | 1 | 3 | 2 | 1 | 6 | 1 | 4 | 20 | 1 | 2 | 1 | 1 | 0 |
| 28 | 680236 | 1 | 3 | 4 | 1 | 2 | 3 | 1 | 6 | 1 | 8 | 15 | 2 | 2 | 1 | 2 | 0 |
| 29 | 680880 | 2 | 5 | 4 | 1 | 4 | 4 | 1 | 6 | 1 | 18 | 10 | 2 | 2 | 1 | 4 | 0 |
| 30 | 491978 | 2 | 3 | 3 | 2 | 1 | 4 | 1 | 1 | 1 | 10 | 35 | 3 | 1 | 1 | 1 | 0 |
| 31 | 675227 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 3 | 1 | 8 | 15 | 2 | 2 | 1 | 5 | 0 |
| 32 | 682879 | 2 | 4 | 5 | 1 | 4 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 33 | 683252 | 2 | 2 | 3 | 1 | 3 | 4 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 2 | 3 | 0 |
| 34 | 352761 | 3 | 1 | 2 | 1 | 4 | 5 | 1 | 6 | 1 | 20 | 10 | 2 | 1 | 2,3 | 4 | 0 |
| 35 | 684153 | 1 | 1 | 1 | 1 | 1 | 3 | 1 | 6 | 1 | 8 | 10 | 1 | 2 | 1 | 1 | 0 |
| 36 | 683935 | 3 | 5 | 4 | 1 | 4 | 4 | 1 | 6 | 1 | 20 | 10 | 2 | 1 | 1 | 4 | 0 |
| 37 | 685112 | 2 | 5 | 3 | 1 | 4 | 4 | 1 | 1 | 1 | 15 | 10 | 2 | 2 | 3 | 2 | 0 |
| 38 | 685555 | 1 | 2 | 2 | 1 | 3 | 2 | 1 | 3 | 1 | 8 | 20 | 2 | 2 | 1 | 3 | 0 |
| 39 | 682482 | 2 | 3 | 4 | 1 | 4 | 4 | 1 | 6 | 1 | 15 | 25 | 3 | 1 | 1 | 2 | 0 |
| 40 | 739692 | 1 | 2 | 2 | 2 | 1 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 3 | 0 |
| 41 | 614020 | 1 | 6 | 4 | 1 | 3 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 42 | 739471 | 1 | 2 | 3 | 1 | 2 | 2 | 1 | 4 | 1 | 4 | 15 | 1 | 2 | 1 | 1 | 0 |
| 43 | 705137 | 2 | 2 | 3 | 1 | 2 | 4 | 1 | 1 | 1 | 15 | 25 | 3 | 1 | 1 | 1 | 0 |
| 44 | 739897 | 3 | 1 | 2 | 1 | 3 | 6 | 1 | 3 | 1 | 21 | 10 | 2 | 1 | 3 | 4 | 0 |
| 45 | 740304 | 2 | 3 | 5 | 2 | 1 | 5 | 2 | 6 | 1 | 22 | 15 | 3 | 1 | 1 | 1 | 0 |
| 46 | 740396 | 1 | 6 | 4 | 1 | 2 | 2 | 1 | 6 | 1 | 4 | 20 | 1 | 2 | 1 | 1 | 0 |
| 47 | 740334 | 2 | 1 | 1 | 1 | 4 | 4 | 1 | 1 | 1 | 20 | 10 | 2 | 2 | 1 | 3 | 0 |
| 48 | 732144 | 1 | 2 | 3 | 1 | 3 | 2 | 1 | 3 | 2 | 0 | 0 | 0 | 2 | 1 | 3 | 0 |
| 49 | 740843 | 4 | 1 | 2 | 1 | 4 | 6 | 1 | 1 | 1 | 25 | 10 | 2 | 1 | 2,3 | 4 | 0 |
| 50 | 733703 | 2 | 1 | 2 | 1 | 4 | 3 | 1 | 1 | 1 | 10 | 10 | 1 | 2 | 1 | 2 | 0 |
| 51 | 736523 | 3 | 2 | 1 | 1 | 4 | 6 | 1 | 6 | 1 | 28 | 15 | 3 | 1 | 2,3 | 9 | 0 |
| 52 | 741352 | 3 | 1 | 2 | 1 | 4 | 6 | 1 | 1 | 1 | 26 | 20 | 3 | 1 | 4 | 7 | 0 |
| 53 | 741433 | 2 | 2 | 2 | 1 | 1 | 4 | 1 | 2 | 1 | 14 | 25 | 3 | 1 | 1 | 1 | 0 |
| 54 | 627338 | 2 | 4 | 5 | 1 | 3 | 5 | 1 | 6 | 1 | 15 | 10 | 2 | 2 | 1 | 5 | 0 |
| 55 | 690771 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 6 | 1 | 4 | 22 | 1 | 2 | 1 | 2 | 0 |
| 56 | 464104 | 1 | 2 | 3 | 1 | 3 | 2 | 1 | 3 | 1 | 7 | 20 | 2 | 2 | 1 | 2 | 0 |
| 57 | 657108 | 3 | 1 | 2 | 1 | 3 | 5 | 1 | 1 | 2 | 0 | 0 | 0 | 1 | 1 | 5 | 0 |
| 58 | 743210 | 3 | 2 | 1 | 1 | 3 | 6 | 1 | 6 | 1 | 20 | 10 | 2 | 1 | 1 | 6 | 0 |
| 59 | 741101 | 1 | 1 | 2 | 1 | 3 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 60 | 743889 | 2 | 3 | 4 | 1 | 4 | 4 | 1 | 6 | 1 | 18 | 10 | 2 | 2 | 1 | 6 | 0 |
| 61 | 742912 | 3 | 2 | 3 | 1 | 4 | 5 | 1 | 6 | 1 | 12 | 10 | 2 | 1 | 2 | 5 | 0 |
| 62 | 686240 | 1 | 6 | 3 | 1 | 1 | 2 | 1 | 6 | 1 | 2 | 15 | 1 | 2 | 1 | 1 | 0 |
| 63 | 686721 | 1 | 3 | 5 | 1 | 3 | 2 | 1 | 4 | 1 | 8 | 20 | 2 | 2 | 1 | 4 | 0 |
| 64 | 686810 | 3 | 5 | 2 | 1 | 3 | 5 | 1 | 1 | 1 | 22 | 15 | 3 | 1 | 1 | 1 | 0 |
| 65 | 684196 | 2 | 2 | 1 | 1 | 3 | 4 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 66 | 689254 | 1 | 3 | 4 | 2 | 1 | 3 | 1 | 4 | 1 | 11 | 30 | 3 | 1 | 1 | 1 | 0 |
| 67 | 689724 | 1 | 2 | 2 | 1 | 3 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 4 | 0 |
| 68 | 690202 | 3 | 1 | 2 | 1 | 4 | 5 | 1 | 1 | 1 | 25 | 15 | 3 | 1 | 3 | 9 | 0 |
| 69 | 627972 | 1 | 3 | 4 | 1 | 3 | 2 | 1 | 4 | 1 | 7 | 10 | 1 | 2 | 1 | 2 | 0 |
| 70 | 691925 | 1 | 4 | 5 | 1 | 3 | 2 | 1 | 4 | 1 | 6 | 20 | 2 | 2 | 1 | 2 | 0 |
| 71 | 692479 | 1 | 6 | 5 | 1 | 1 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 72 | 692576 | 4 | 4 | 5 | 1 | 4 | 6 | 1 | 6 | 1 | 25 | 15 | 3 | 1 | 3,4 | 8 | 0 |
| 73 | 693070 | 3 | 2 | 2 | 1 | 4 | 6 | 1 | 6 | 1 | 20 | 10 | 2 | 1 | 1 | 6 | 0 |
| 74 | 693596 | 3 | 1 | 2 | 1 | 4 | 6 | 1 | 1 | 2 | 0 | 0 | 0 | 2 | 1 | 5 | 0 |
| 75 | 690771 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 6 | 1 | 8 | 15 | 2 | 2 | 1 | 2 | 0 |
| 76 | 694043 | 1 | 6 | 3 | 1 | 2 | 2 | 1 | 3 | 1 | 1 | 12 | 1 | 2 | 1 | 1 | 0 |
| 77 | 695156 | 2 | 3 | 2 | 1 | 4 | 3 | 1 | 1 | 1 | 10 | 20 | 2 | 2 | 1 | 2 | 0 |
| 78 | 339762 | 2 | 3 | 2 | 2 | 1 | 4 | 1 | 6 | 1 | 10 | 15 | 2 | 2 | 1 | 2 | 0 |
| 79 | 696623 | 1 | 6 | 3 | 1 | 2 | 2 | 1 | 3 | 1 | 3 | 15 | 1 | 2 | 1 | 1 | 0 |
| 80 | 653966 | 3 | 2 | 3 | 1 | 4 | 5 | 1 | 1 | 1 | 20 | 10 | 2 | 1 | 2 | 5 | 0 |
| 81 | 698079 | 1 | 1 | 2 | 1 | 3 | 2 | 1 | 1 | 1 | 9 | 15 | 2 | 2 | 1 | 2 | 0 |
| 82 | 698829 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 1 | 1 | 9 | 15 | 2 | 2 | 1 | 2 | 0 |
| 83 | 468797 | 2 | 4 | 4 | 1 | 4 | 4 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 6 | 0 |
| 84 | 628953 | 1 | 2 | 3 | 1 | 4 | 2 | 1 | 3 | 1 | 8 | 10 | 1 | 2 | 1 | 2 | 0 |
| 85 | 678424 | 3 | 1 | 1 | 1 | 3 | 5 | 1 | 2 | 2 | 0 | 0 | 0 | 1 | 2 | 6 | 0 |
| 86 | 673080 | 1 | 2 | 2 | 1 | 3 | 2 | 1 | 6 | 1 | 5 | 15 | 1 | 2 | 1 | 2 | 0 |
| 87 | 664928 | 3 | 2 | 1 | 1 | 4 | 5 | 1 | 2 | 1 | 20 | 10 | 2 | 1 | 3 | 4 | 0 |
| 88 | 764678 | 1 | 2 | 3 | 2 | 1 | 3 | 1 | 3 | 1 | 8 | 40 | 3 | 1 | 1 | 1 | 0 |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 89 | 802176 | 1 | 1 | 2 | 1 | 3 | 3 | 1 | 1 | 1 | 9 | 20 | 2 | 2 | 1 | 2 | 0 |
| 90 | 802209 | 3 | 5 | 3 | 1 | 4 | 5 | 1 | 3 | 1 | 20 | 10 | 2 | 2 | 3 | 4 | 0 |
| 91 | 802107 | 2 | 4 | 5 | 1 | 4 | 4 | 1 | 6 | 1 | 20 | 10 | 2 | 1 | 1 | 2 | 0 |
| 92 | 619348 | 2 | 2 | 3 | 1 | 3 | 3 | 1 | 3 | 1 | 9 | 10 | 1 | 1 | 1 | 2 | 0 |
| 93 | 796601 | 1 | 6 | 4 | 1 | 3 | 3 | 1 | 4 | 1 | 10 | 40 | 3 | 1 | 1 | 1 | 0 |
| 94 | 787970 | 1 | 3 | 3 | 1 | 3 | 2 | 1 | 3 | 2 | 0 | 0 | 0 | 2 | 1 | 3 | 0 |
| 95 | 781111 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 6 | 1 | 10 | 20 | 2 | 1 | 1 | 2 | 0 |
| 96 | 802913 | 2 | 2 | 2 | 1 | 4 | 3 | 1 | 6 | 1 | 10 | 15 | 2 | 2 | 1 | 3 | 0 |
| 97 | 800947 | 2 | 1 | 1 | 1 | 3 | 4 | 1 | 2 | 1 | 9 | 6 | 1 | 2 | 1 | 2 | 0 |
| 98 | 748488 | 1 | 6 | 3 | 1 | 3 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 99 | 804712 | 2 | 3 | 4 | 1 | 3 | 4 | 1 | 6 | 1 | 6 | 10 | 1 | 2 | 1 | 2 | 0 |
| 100 | 804614 | 3 | 1 | 2 | 1 | 4 | 5 | 1 | 1 | 1 | 20 | 10 | 2 | 2 | 2 | 4 | 0 |
| 101 | 805478 | 1 | 6 | 3 | 1 | 1 | 2 | 1 | 3 | 1 | 3 | 16 | 1 | 2 | 1 | 1 | 0 |
| 102 | 752971 | 1 | 1 | 1 | 1 | 3 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 103 | 573274 | 1 | 1 | 2 | 1 | 2 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 3 | 0 |
| 104 | 661151 | 1 | 6 | 3 | 1 | 1 | 2 | 1 | 3 | 1 | 4 | 14 | 1 | 2 | 1 | 1 | 0 |
| 105 | 806275 | 1 | 6 | 2 | 1 | 2 | 2 | 1 | 6 | 1 | 5 | 25 | 2 | 1 | 1 | 4 | 0 |
| 106 | 763185 | 2 | 4 | 5 | 1 | 3 | 4 | 1 | 4 | 1 | 8 | 10 | 1 | 2 | 1 | 2 | 0 |
| 107 | 714999 | 3 | 3 | 4 | 1 | 4 | 6 | 1 | 6 | 1 | 23 | 20 | 3 | 1 | 1 | 5 | 0 |
| 108 | 807081 | 2 | 2 | 3 | 1 | 4 | 3 | 1 | 3 | 1 | 15 | 10 | 2 | 1 | 1 | 2 | 0 |
| 109 | 806795 | 1 | 6 | 2 | 1 | 1 | 1 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 110 | 806803 | 1 | 2 | 2 | 1 | 3 | 2 | 1 | 1 | 1 | 5 | 25 | 2 | 2 | 1 | 3 | 0 |
| 111 | 806721 | 1 | 1 | 1 | 1 | 1 | 3 | 1 | 2 | 1 | 7 | 10 | 1 | 2 | 1 | 3 | 0 |
| 112 | 807844 | 2 | 5 | 4 | 1 | 4 | 3 | 1 | 6 | 1 | 8 | 10 | 1 | 2 | 1 | 2 | 0 |
| 113 | 808024 | 3 | 5 | 5 | 1 | 5 | 4 | 1 | 4 | 2 | 0 | 0 | 0 | 2 | 1 | 5 | 0 |
| 114 | 808291 | 1 | 3 | 3 | 1 | 3 | 2 | 1 | 6 | 1 | 5 | 15 | 1 | 2 | 1 | 1 | 0 |
| 115 | 808384 | 3 | 2 | 2 | 1 | 4 | 5 | 1 | 6 | 1 | 26 | 20 | 3 | 1 | 3 | 6 | 0 |
| 116 | 808721 | 1 | 1 | 2 | 1 | 3 | 2 | 1 | 1 | 1 | 6 | 20 | 2 | 1 | 1 | 3 | 0 |
| 117 | 808671 | 3 | 5 | 4 | 1 | 4 | 6 | 1 | 4 | 1 | 26 | 20 | 2 | 2 | 2 | 6 | 0 |
| 118 | 802021 | 2 | 3 | 4 | 1 | 3 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 119 | 809739 | 1 | 4 | 5 | 1 | 3 | 3 | 1 | 4 | 1 | 8 | 10 | 1 | 1 | 1 | 1 | 0 |
| 120 | 809701 | 3 | 2 | 2 | 1 | 4 | 4 | 1 | 6 | 1 | 10 | 15 | 2 | 2 | 3 | 6 | 0 |
| 121 | 737014 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 6 | 1 | 7 | 20 | 2 | 2 | 1 | 3 | 0 |
| 122 | 665857 | 2 | 4 | 5 | 1 | 3 | 4 | 1 | 4 | 1 | 8 | 10 | 1 | 2 | 1 | 2 | 0 |
| 123 | 812962 | 2 | 5 | 3 | 1 | 3 | 3 | 1 | 3 | 1 | 7 | 9 | 1 | 2 | 1 | 3 | 0 |
| 124 | 808443 | 2 | 1 | 2 | 1 | 4 | 4 | 1 | 1 | 1 | 20 | 10 | 2 | 2 | 3 | 4 | 0 |
| 125 | 814138 | 3 | 2 | 2 | 1 | 4 | 5 | 1 | 1 | 1 | 25 | 20 | 3 | 1 | 5 | 6 | 0 |
| 126 | 814224 | 1 | 6 | 2 | 1 | 1 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 1 | 0 |
| 127 | 807826 | 3 | 3 | 4 | 1 | 3 | 6 | 1 | 6 | 1 | 18 | 10 | 2 | 2 | 2 | 7 | 0 |
| 128 | 808914 | 1 | 6 | 2 | 1 | 3 | 2 | 1 | 6 | 1 | 5 | 25 | 2 | 2 | 1 | 3 | 0 |
| 129 | 757990 | 4 | 5 | 3 | 1 | 5 | 5 | 1 | 3 | 1 | 15 | 5 | 1 | 2 | 2 | 11 | 0 |
| 130 | 732150 | 1 | 6 | 4 | 1 | 3 | 2 | 1 | 4 | 1 | 6 | 10 | 1 | 2 | 1 | 2 | 0 |
| 131 | 815360 | 2 | 4 | 5 | 1 | 3 | 3 | 1 | 4 | 2 | 0 | 0 | 0 | 2 | 1 | 3 | 0 |
| 132 | 806612 | 2 | 2 | 2 | 1 | 4 | 4 | 1 | 1 | 1 | 20 | 10 | 2 | 2 | 3 | 6 | 0 |
| 133 | 816026 | 1 | 3 | 4 | 1 | 3 | 3 | 1 | 4 | 1 | 9 | 10 | 1 | 2 | 1 | 2 | 0 |
| 134 | 815566 | 2 | 2 | 2 | 1 | 3 | 4 | 1 | 6 | 1 | 5 | 10 | 1 | 2 | 1 | 4 | 0 |
| 135 | 818558 | 1 | 1 | 2 | 1 | 3 | 2 | 1 | 6 | 1 | 8 | 20 | 2 | 1 | 1 | 4 | 0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 136 | 743603 | 1 | 5 | 4 | 1 | 3 | 2 | 1 | 4 | 1 | 8 | 20 | 2 | 2 | 1 | 2 | 0 |
| 137 | 702924 | 2 | 3 | 4 | 1 | 4 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 138 | 703008 | 1 | 6 | 3 | 1 | 2 | 2 | 1 | 3 | 1 | 5 | 15 | 1 | 1 | 1 | 1 | 0 |
| 139 | 703707 | 3 | 2 | 2 | 1 | 4 | 5 | 2 | 1 | 1 | 20 | 10 | 2 | 2 | 5 | 6 | 0 |
| 140 | 662099 | 2 | 3 | 4 | 1 | 4 | 4 | 1 | 6 | 1 | 10 | 10 | 1 | 2 | 1 | 4 | 0 |
| 141 | 704147 | 3 | 4 | 5 | 1 | 5 | 5 | 1 | 4 | 1 | 18 | 10 | 2 | 1 | 2 | 6 | 0 |
| 142 | 705587 | 1 | 2 | 2 | 1 | 3 | 3 | 2 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 143 | 706048 | 1 | 1 | 2 | 1 | 2 | 3 | 1 | 1 | 1 | 5 | 25 | 2 | 2 | 1 | 2 | 0 |
| 144 | 706024 | 3 | 5 | 3 | 1 | 5 | 5 | 1 | 3 | 1 | 25 | 20 | 3 | 1 | 2 | 7 | 0 |
| 145 | 692847 | 1 | 2 | 2 | 1 | 3 | 2 | 1 | 1 | 1 | 3 | 10 | 1 | 2 | 1 | 2 | 0 |
| 146 | 723421 | 2 | 1 | 2 | 1 | 3 | 4 | 1 | 6 | 1 | 20 | 10 | 2 | 1 | 1 | 6 | 0 |
| 147 | 706209 | 1 | 2 | 2 | 1 | 2 | 3 | 1 | 2 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 148 | 706288 | 1 | 3 | 4 | 1 | 3 | 3 | 1 | 2 | 1 | 7 | 5 | 1 | 2 | 1 | 2 | 0 |
| 149 | 706473 | 1 | 6 | 3 | 1 | 1 | 2 | 1 | 6 | 1 | 3 | 10 | 1 | 2 | 1 | 1 | 0 |
| 150 | 817202 | 1 | 6 | 3 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 10 | 1 | 2 | 1 | 1 | 0 |
| 151 | 708008 | 1 | 6 | 2 | 1 | 2 | 2 | 1 | 2 | 1 | 2 | 15 | 1 | 2 | 1 | 4 | 0 |
| 152 | 742311 | 3 | 5 | 4 | 1 | 4 | 5 | 1 | 6 | 1 | 22 | 10 | 2 | 2 | 3 | 6 | 0 |
| 153 | 733164 | 1 | 3 | 4 | 1 | 3 | 3 | 1 | 6 | 1 | 8 | 5 | 1 | 2 | 1 | 2 | 0 |
| 154 | 700730 | 1 | 3 | 4 | 1 | 2 | 2 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 4 | 0 |
| 155 | 742224 | 2 | 2 | 2 | 1 | 3 | 3 | 1 | 3 | 1 | 9 | 15 | 2 | 2 | 1 | 2 | 0 |
| 156 | 615097 | 2 | 1 | 2 | 1 | 4 | 4 | 1 | 6 | 1 | 10 | 20 | 2 | 1 | 1 | 2 | 0 |
| 157 | 711412 | 4 | 5 | 3 | 1 | 5 | 5 | 1 | 2 | 1 | 6 | 15 | 1 | 2 | 2,3 | 11 | 0 |
| 158 | 484063 | 1 | 6 | 4 | 1 | 1 | 2 | 1 | 4 | 1 | 5 | 25 | 2 | 1 | 1 | 4 | 0 |
| 159 | 648105 | 2 | 4 | 5 | 1 | 3 | 4 | 1 | 5 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 160 | 701472 | 3 | 3 | 4 | 1 | 3 | 6 | 1 | 6 | 1 | 25 | 10 | 2 | 2 | 2 | 6 | 0 |
| 161 | 713468 | 2 | 2 | 2 | 1 | 3 | 3 | 1 | 6 | 1 | 12 | 10 | 2 | 2 | 1 | 2 | 0 |
| 162 | 542906 | 1 | 6 | 3 | 1 | 1 | 2 | 1 | 6 | 1 | 5 | 25 | 2 | 1 | 1 | 4 | 0 |
| 163 | 684261 | 1 | 2 | 4 | 1 | 3 | 3 | 1 | 4 | 1 | 6 | 10 | 1 | 2 | 1 | 2 | 0 |
| 164 | 713524 | 2 | 3 | 4 | 1 | 3 | 4 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 4 | 0 |
| 165 | 671393 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 4 | 1 | 8 | 5 | 1 | 2 | 1 | 2 | 0 |
| 166 | 713503 | 1 | 1 | 2 | 1 | 3 | 2 | 1 | 5 | 1 | 3 | 15 | 1 | 2 | 1 | 4 | 0 |
| 167 | 716595 | 3 | 2 | 2 | 1 | 4 | 5 | 1 | 1 | 1 | 28 | 20 | 3 | 1 | 2 | 7 | 0 |
| 168 | 716741 | 1 | 1 | 1 | 1 | 3 | 3 | 1 | 4 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 169 | 717610 | 1 | 2 | 3 | 1 | 2 | 2 | 1 | 2 | 1 | 20 | 20 | 3 | 1 | 1 | 4 | 0 |
| 170 | 717718 | 3 | 2 | 2 | 1 | 4 | 5 | 1 | 6 | 1 | 24 | 20 | 3 | 1 | 2 | 7 | 0 |
| 171 | 717695 | 3 | 1 | 1 | 1 | 3 | 6 | 1 | 6 | 1 | 25 | 20 | 3 | 1 | 3 | 5 | 0 |
| 172 | 717832 | 2 | 4 | 5 | 1 | 3 | 3 | 1 | 6 | 1 | 10 | 15 | 2 | 2 | 1 | 4 | 0 |
| 173 | 718243 | 1 | 6 | 3 | 1 | 1 | 2 | 1 | 3 | 2 | 0 | 0 | 0 | 2 | 1 | 4 | 0 |
| 174 | 715396 | 3 | 4 | 5 | 1 | 4 | 5 | 1 | 3 | 1 | 25 | 20 | 3 | 1 | 4 | 7 | 0 |
| 175 | 718732 | 2 | 4 | 5 | 1 | 4 | 4 | 1 | 1 | 1 | 12 | 6 | 1 | 2 | 1 | 5 | 0 |
| 176 | 721020 | 2 | 2 | 3 | 1 | 4 | 4 | 1 | 4 | 1 | 7 | 10 | 1 | 2 | 1 | 4 | 0 |
| 177 | 692847 | 1 | 6 | 2 | 1 | 3 | 2 | 1 | 6 | 1 | 5 | 25 | 2 | 1 | 1 | 4 | 0 |
| 178 | 599392 | 2 | 2 | 2 | 1 | 4 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 4 | 0 |
| 179 | 722039 | 3 | 4 | 3 | 1 | 3 | 6 | 1 | 1 | 1 | 23 | 20 | 3 | 1 | 2 | 5 | 0 |
| 180 | 724615 | 2 | 2 | 2 | 1 | 4 | 4 | 1 | 4 | 1 | 20 | 20 | 3 | 1 | 1 | 7 | 0 |
| 181 | 727657 | 3 | 2 | 2 | 1 | 4 | 5 | 1 | 5 | 1 | 22 | 20 | 3 | 1 | 3 | 7 | 0 |
| 182 | 727737 | 1 | 1 | 2 | 1 | 3 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 183 | 728045 | 1 | 6 | 4 | 1 | 1 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 184 | 728418 | 2 | 5 | 3 | 1 | 3 | 4 | 1 | 6 | 1 | 8 | 20 | 2 | 2 | 1 | 4 | 0 |
| 185 | 723209 | 2 | 4 | 5 | 1 | 4 | 4 | 1 | 5 | 1 | 14 | 5 | 1 | 1 | 1 | 2 | 0 |
| 186 | 670937 | 2 | 3 | 4 | 1 | 3 | 4 | 1 | 1 | 2 | 0 | 0 | 0 | 2 | 1 | 4 | 0 |
| 187 | 728454 | 3 | 2 | 2 | 1 | 4 | 4 | 1 | 2 | 1 | 23 | 20 | 3 | 1 | 1 | 5 | 0 |
| 188 | 473975 | 2 | 1 | 1 | 1 | 3 | 3 | 1 | 5 | 1 | 10 | 15 | 2 | 2 | 1 | 4 | 0 |
| 189 | 727601 | 3 | 1 | 2 | 1 | 4 | 5 | 1 | 6 | 1 | 7 | 10 | 1 | 2 | 1 | 4 | 0 |
| 190 | 730891 | 3 | 2 | 2 | 1 | 4 | 5 | 1 | 6 | 1 | 25 | 20 | 3 | 1 | 3 | 7 | 0 |
| 191 | 731091 | 2 | 4 | 5 | 1 | 3 | 3 | 1 | 1 | 2 | 0 | 0 | 0 | 2 | 1 | 4 | 0 |
| 192 | 732832 | 3 | 3 | 4 | 1 | 4 | 5 | 1 | 4 | 1 | 20 | 20 | 3 | 1 | 1 | 7 | 0 |
| 193 | 732858 | 1 | 6 | 2 | 1 | 2 | 3 | 1 | 2 | 1 | 9 | 40 | 3 | 1 | 1 | 4 | 0 |
| 194 | 731645 | 4 | 5 | 4 | 1 | 5 | 6 | 1 | 2 | 1 | 30 | 15 | 3 | 1 | 2,4 | 9 | 0 |
| 195 | 728487 | 1 | 3 | 4 | 1 | 2 | 3 | 1 | 6 | 1 | 10 | 40 | 3 | 1 | 1 | 4 | 0 |
| 196 | 696836 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 5 | 2 | 0 | 0 | 0 | 2 | 1 | 5 | 0 |
| 197 | 733262 | 2 | 1 | 2 | 1 | 4 | 4 | 1 | 1 | 1 | 25 | 20 | 3 | 1 | 1 | 9 | 0 |
| 198 | 713474 | 1 | 6 | 4 | 1 | 2 | 3 | 1 | 1 | 1 | 11 | 30 | 3 | 1 | 1 | 4 | 0 |
| 199 | 728156 | 2 | 1 | 2 | 1 | 3 | 4 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 8 | 0 |
| 200 | 734037 | 1 | 6 | 4 | 1 | 2 | 3 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 201 | 734057 | 4 | 5 | 4 | 1 | 4 | 6 | 1 | 6 | 1 | 25 | 15 | 3 | 1 | 2,3 | 9 | 0 |
| 202 | 734305 | 2 | 1 | 1 | 1 | 3 | 4 | 1 | 6 | 1 | 16 | 20 | 3 | 1 | 1 | 8 | 0 |
| 203 | 730092 | 2 | 6 | 3 | 1 | 1 | 4 | 1 | 1 | 1 | 10 | 40 | 2 | 2 | 1 | 3 | 0 |
| 204 | 609158 | 2 | 4 | 5 | 1 | 4 | 3 | 1 | 3 | 2 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| 205 | 650615 | 3 | 3 | 4 | 1 | 3 | 5 | 1 | 4 | 1 | 20 | 25 | 3 | 1 | 1 | 8 | 0 |
| 206 | 655883 | 1 | 2 | 2 | 1 | 3 | 3 | 1 | 3 | 1 | 12 | 30 | 3 | 1 | 1 | 8 | 0 |
| 207 | 651214 | 3 | 1 | 2 | 1 | 4 | 4 | 1 | 1 | 1 | 22 | 20 | 3 | 1 | 1 | 8 | 0 |
| 208 | 567468 | 2 | 1 | 2 | 1 | 3 | 4 | 1 | 1 | 1 | 16 | 20 | 3 | 1 | 1 | 6 | 0 |
| 209 | 670958 | 3 | 1 | 1 | 1 | 4 | 5 | 1 | 3 | 1 | 25 | 20 | 3 | 1 | 3 | 8 | 0 |
| 210 | 735338 | 3 | 3 | 4 | 1 | 4 | 5 | 1 | 1 | 1 | 25 | 20 | 3 | 1 | 2 | 7 | 0 |
| 211 | 735564 | 3 | 3 | 4 | 1 | 4 | 5 | 1 | 6 | 2 | 0 | 0 | 0 | 2 | 1 | 8 | 0 |
| 212 | 736095 | 2 | 2 | 3 | 1 | 4 | 3 | 1 | 6 | 1 | 15 | 25 | 3 | 1 | 1 | 5 | 0 |
| 213 | 726957 | 2 | 5 | 4 | 1 | 3 | 4 | 1 | 6 | 1 | 10 | 15 | 2 | 2 | 1 | 6 | 0 |
| 214 | 615317 | 3 | 5 | 3 | 1 | 4 | 5 | 1 | 3 | 1 | 25 | 15 | 3 | 1 | 2 | 8 | 0 |
| 215 | 737014 | 1 | 6 | 2 | 1 | 3 | 2 | 1 | 1 | 2 | 0 | 0 | 0 | 2 | 1 | 8 | 0 |
| 216 | 725138 | 1 | 6 | 4 | 1 | 2 | 2 | 1 | 6 | 1 | 2 | 15 | 1 | 2 | 1 | 2 | 0 |
| 217 | 709615 | 1 | 3 | 4 | 1 | 1 | 3 | 1 | 6 | 1 | 6 | 20 | 2 | 2 | 1 | 3 | 0 |
| 218 | 737492 | 1 | 1 | 2 | 1 | 2 | 3 | 1 | 1 | 2 | 0 | 0 | 0 | 2 | 1 | 3 | 0 |