"ONE YEAR CROSS SECTIONAL STUDY OF ASSOCIATION BETWEEN ANDROGENETIC ALOPECIA AND BENIGN PROSTATIC HYPERPLASIA IN MALE PATIENTS VISITING KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"

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This is to certify that the dissertation entitled **"ONE YEAR CROSS SECTIONAL STUDY OF ASSOCIATION BETWEEN ANDROGENETIC ALOPECIA AND BENIGN PROSTATIC HYPERPLASIA IN MALE PATIENTS VISITING KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"** is a bonafide research work done by **Reg No. : BT0114001.**

Dr. B. S. Manjunathswamy MD,DVD
Professor & Head
Department of Dermatology,
Venereology and Leprosy
J.N. Medical College
Nehru Nagar, Belagavi- 590010

Dr. N. S. Mahantshetti MD
Principal
J.N. Medical College
Nehru Nagar,
Belagavi- 590010

Date:
Place: Belagavi

Date:
Place: Belagavi

LIST OF ABBREVATIONS USED

AGA	Androgenetic alopecia
BPH	Benign prostatic hypertrophy
5-AR	5- alpha reductase
5- AR1	5– alpha reductase isoenzyme 1
5- AR2	5– alpha reductase isoenzyme 2
5- AR3	5– alpha reductase isoenzyme 3
DHT	Dihydrotestosterone
PSA	Prostate specific antigen
DHEA	Dihydroepiandrosterone sulphate
HSD	Hydroxysteroid dehydrogenases
17-β HSD	17 beta hydroxysteroid dehydrogenases
3-β HSD	3 beta hydroxysteroid dehydrogenases
IGF-1	Insulin like growth factor 1
TGF- β1	Transforming growth factor- beta 1
IGFBP3	Insulin like growth factor binding protein 3
FT	Fronto temporal region
BASP	Basic and specific classification
BA	Basic type
SP	Specific type
HDD	Hair diameter diversity
PTG	Phototrichogram

VEGF	Vascular endothelial growth factor
ATP	Adenosine triphosphate
KGF	Keratinocyte growth factor
PRP	Platelet rich plasma
FUT	Follicular unit transplantation
FUE	Follicular unit extraction
CAD	Coronary artery disease

ABSTRACT

Background

Androgenetic Alopecia (AGA) and Benign Prostatic Hyperplasia (BPH) are both androgen dependent disorders in which the enzyme 5- alpha reductase (5-AR) plays a key role in conversion of testosterone to dihydrotestosterone (DHT). The purpose of this study is to analyze the association between AGA and BPH.

Methods

Male patients between the age group of 25-45 years attending skin OPD at KLE's Dr Prabhakar Kore Hospital and MRC, Belgaum, with AGA during the period January 2015 to December 2015 were included. Ethical clearance was obtained from the Jawaharlal Nehru Medical College Institutional Ethics Committee of Human Subjects Research. A short questionnaire recording their particulars and a detailed dermatological evaluation of the patient was done. All patients in the study were graded using Modified Hamilton Norwood Classification, underwent trans abdominal ultra sonogram and serum PSA level estimation. Data was analyzed by ANOVA and Spearmann's rank correlation.

Results

64 patients were enrolled in the study. 39.1% of patients had Grade III AGA, 32.8% had Grade IV AGA, 25% had Grade V AGA and 3.1% had Grade VI AGA. The minimum PSA level was 0.1 ng/ml and maximum was 4.8 ng/ml. The minimum prostate volume was 8.08 ml and maximum was 32.2 ml.

Conclusion

Even though an increase in the prostate volume in AGA patients was noted, this study showed no association between AGA, prostate volume and serum PSA levels.

Key words: Androgentic alopecia, Benign prostatic hyperplasia, prostate volume, Serum PSA level

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INTRODUCTION

Hair is an appendage of skin that is in more consideration for its cosmesis than for its medical relevance. Excess of and too little hairs are both reasons for enormous mental stress and antagonistically influence the quality of life. Hair loss is one of the commonest complaints that challenge dermatologists in light of its diverse causes that are once in a while hard to pinpoint, its poor response to accessible methods of treatment and the stress of the patient's mind. Depending on whether damage to hair follicles is permanent or not, hair loss is classified as scarring/cicatricial or non scarring/ non cicatricial.[1]

Androgenetic alopecia (AGA) is the most widely recognized cause of non scarring hair loss among males.[2] It is a progressive patterned hair loss that occurs on exposure to androgens in hereditarily predisposed individuals. [3] Even though the age of onset has been reported at 40 years, there are reports that demonstrate the onset of alopecia at 20 years. [4]

The most common benign neoplasm in men is Benign Prostatic Hyperplasia (BPH), which affects nearly 70% of men of 60 years and older, with or without any obstructive symptoms. The prostate gland weighs a couple of grams during childbirth; at the period of adolescence it experiences androgen-affected development and achieves the adult size of roughly 20 grams by around 20 years of age. The gland stays steady, both as to weight and histological attributes, for around 25 years. Starting in the fifth decade a second development spurt happens in roughly 75% of men.[5] This second development stage, not like the prior development which includes the entire organ diffusely, starts typically in the periurethral region as a localized proliferation including fibro nodular and glandular components. While this

hyperplastic procedure may stay restricted in scope and not bring about significant enlargement of the gland, in numerous people the hyperplasia advances to compress the remaining gland and eventually causes the prostate to achieve enormous size which may produce urinary tract obstruction.[6]

Both AGA and BPH are androgen-dependent diseases in which the enzyme 5-alpha reductase (5-AR) plays a key role in conversion of testosterone to dihydrotestosterone (DHT).[7] 5-AR is involved in the normal development of the human prostate and also in the pathogenesis and progression of prostatic diseases. The 5-AR family includes 5-AR1, 5-AR2 and 5-AR3. 5-AR1 is observed at very low levels in the fetal scalp and nongenital skin, while 5-AR2 is present on the external genital skin in early gestation period. In adults, 5-AR1 is present in nongenital skin, the liver and certain areas of brain, and at lower levels in the prostate, genital skin, epididymis, seminal vesicles, testis, adrenal gland and kidney. 5-AR2 is present at generally high levels in the prostate, genital skin, epididymis, seminal vesicles and liver.[8] DHT responsible for follicular miniaturization on scalp is mainly produced by the action of 5-AR2 on testosterone.[7] In the prostate, both isoenzymes 5-AR1 and 2 convert testosterone to DHT which is responsible for the growth and development of prostate gland.[7]

Prostate-specific antigen (PSA) is one of the main secretory proteins of the prostate gland. Normal healthy prostate gland secretes 0.01–0.02 mg PSA per day, while hyperplastic prostate secretes ten times larger amounts of PSA.[9]

Past studies of association between AGA and BPH were all in elderly males and analyzed the prevalence of alopecia in comparison with a control group; however, many of them did not use ultrasound to reliably rule out the presence of BPH. [5,10]

The purpose of this study is to analyze the association between AGA and BPH as determined by transabdominal ultra sonogram and serum PSA levels which may be useful in treatment and prevention of BPH.

OBJECTIVES

Primary: To establish the association between androgenetic alopecia and benign prostatic hyperplasia

Secondary: To establish the association between androgenetic alopecia and serum PSA level.

REVIEW OF LITERATURE

Androgenetic alopecia (AGA) is a progressive patterned hair loss that occurs on exposure to androgens in hereditarily predisposed individuals. It affects both genders and is characterized by hair loss in a distinctive and reproducible pattern from the scalp.[3]

PREVALANCE

Balding can occur in different frequencies in all races. Highest prevalence has been noted in Caucasian population as 30 % for men in their 30's, 40% for men in their 40's and 50% for men in their 50's.[12] In Indians, a population based study of 1005 subjects showed a prevalence of 58% among males in the age group of 30-50 years.[13] Oriental population showed a low prevalence. A Chinese study by Wang et al[12] showed a prevalence rate of 21.3% whereas a Korean study done by Paik et al[14] showed a prevalence rate of 14.1%. From above studies it is evident that there is an increase in incidence with increasing age.

Studies on the commonest grade/type of AGA, as per Norwood classification have shown that type II and III are commonest in Indian population.[15] Another Indian population based study showed the same results.[16] Chinese study by Wang et al[12] showed type IV as the commonest whereas Korean study by Paik et al[14] showed type III as the commonest in their respective population.

ETIOLOGY

Four different but interrelated factors determine whether an individual will develop baldness namely susceptibility to AGA, age of onset, rate of progression and pattern of hair loss.

Universally boys of prepubertal age group have a straight frontal hairline. By the age of 20 over 90% of men exhibit some amount of fronto-parietal recession of the hairline.[17]As observed by Hamilton, three males castrated at the age of 15 and 16 years failed to develop minimal recession of the frontal hairline, which shows that this hair loss occurs by androgen-mediated miniaturization of terminal hair follicles.[18]

Age of onset of AGA is highly variable. If early AGA is defined by a type II hair pattern, then 40% of men first develop AGA between the age of 18 and 29 years, a further 24% first develop AGA in their 30's, 3% in their 40's, 5% in their 50's, 9% in their 60's, 2% in their 70's and 1% at or beyond the age of 80 years.[19]

In the rate of progression of hair loss in AGA, a wide range of individual variation has been noted. A small percentage of men may develop type V or VI hair loss in their twenties, which indicates a very rapid rate of progression. In contrast, approximately 25% of men with AGA show no visible hair loss on standardized clinical photographs over a 5-year period.[20] A rapid rate of progression is seen in early-onset AGA. Men who develop AGA in their twenties tend to progress one to two stages per decade, whereas men with late-onset AGA may take two decades to progress a single stage.[19] Not all men with AGA may go bald. Even though 40% of men start losing their hair in their twenties, only 30% ever progress to reach stage VI or VII. Hence, even for those with early onset AGA complete baldness is not inevitable.

Genetic influence over susceptibility, age of onset, pattern and rate of progression was indicated by twin studies in male population.[21,22] The significant influence of genes on susceptibility, age of onset and pattern of hair loss was also

confirmed by the Korean study by Paik et al[14] which showed low age related prevalence of AGA and higher proportion of men with Ludwig pattern hair loss.

A polygenic inheritance explains the high prevalence rate of AGA in the general population, different racial frequencies in age related incidence of balding, the finding of increased risk of baldness with the number of affected family members and increased frequency of baldness in fathers of affected men.[23]

PATHOGENESIS

Hair Cycle Dynamics

There are 3 phases in the normal growth cycle of hair. First is the anagen phase which lasts on an average for about 2-6 years which is the growing phase. In this phase hair growth starts by division of epithelial cells at its base, the bulb. The dermal papilla is an extension of the epidermis which is surrounded by the hair bulb. Androgen receptors and androgen receptor transcriptional co regulators are highly concentrated in the dermal papilla, where there is active synthesis and metabolism of androgen and also production of growth factors and cytokines which initiate the activity of the hair bulb. Cessation of cell division marks the end of anagen phase and start of catagen phase which is the phase of regression or transitional phase which lasts approximately for 2-3 weeks. Due to regression of lower part of hair there is thinning, miniaturization and shortening in the length of hair. Regression affects dermal papilla also with decrease and inactivation of its cells. Telogen is the last phase of hair cycle with variable duration ranging from 1-3 months. Towards the end of telogen, dermal papilla is reactivated, cell division begins and a new long phase of anagen starts forming a new hair.[24-26]

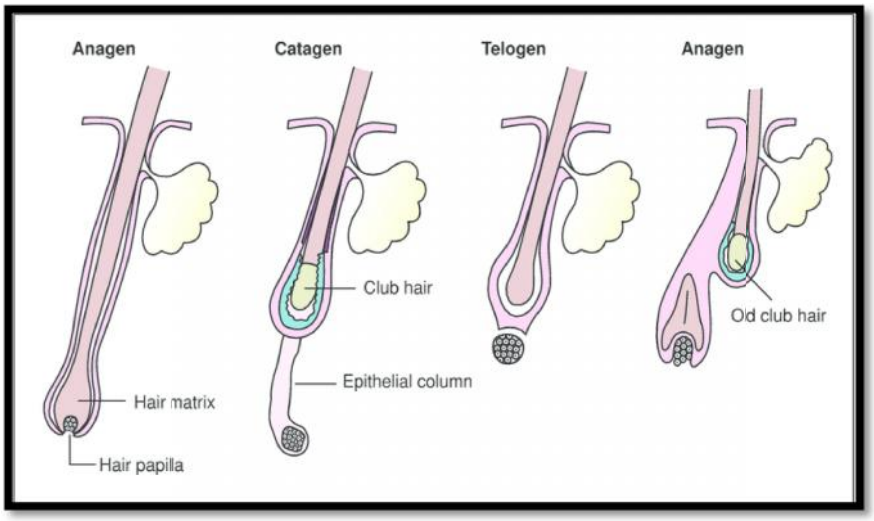


Figure 1: Normal Hair cycle

In AGA, with each consecutive cycle, duration of anagen phase reduces whereas duration of telogen is prolonged or is constant. Latent phase of telogen (also called kenogen) is prolonged in particular followed by shedding of club hair (also called exogen). This results in decrease in anagen : telogen ration which coincides with episodes of heavy hair shedding, most commonly noticed while washing or combing the hair. An increase in proportion of empty hair follicles occurs due to increase in duration of kenogen which further adds to the process of balding.[24,27]

Multiple environmental factors also have an impact on course on maintenance of normal and pathological hair cycle. Along with androgen, main inducers of hair growth, development and of hair loss in scalp, cytokines, growth factors, hormones, neural activity, seasonal variations, ageing and nutrition regulate the androgen action and its effects on hair.[28,29]

Hormonal Influences

American anatomist James Hamilton observed that men castrated before puberty did not develop balding unless treated with testosterone thus establishing the role of androgens in the pathogenesis of AGA.[30] Estimation of serum androgens, testosterone, dihydroepiandrosterone sulphate (DHEA), and free testosterone levels showed a lack of significant difference between cases and controls.[31] Increased levels of cortisol and androstenedione were observed in patients with AGA in a study which assessed different levels of hormones in AGA patients and age matched controls which suggested that a wide range of hormones influence AGA.[32] In women, hyperandrogenism is characterized by loss of scalp hair and hirsutism but many investigations did not reveal raised androgen levels in women.[33] This suggested that in genetically predisposed individuals normal levels of androgen are sufficient to produce hair loss.

An increase in the number of androgen receptors, functional polymorphism of the androgen receptors, increase in the local production of DHT, decrease in the local metabolism of DHT may be the cause for over activity of the intrafollicular androgen.[34]

Skin and its appendages, which includes hair follicles, sebaceous glands, and eccrine/apocrine glands, have all the important enzymes required for androgen synthesis and metabolism similar to the gonads and adrenal gland. Main role is played by 5-AR which mediates conversion of testosterone to DHT intrafollicularly.[35] DHT binds to the androgen receptor with 5 times the affinity of testosterone and is more intense in its capacity to bring about downstream initiation.[36] Three types of 5-AR

isoenzymes 5-AR1, 5-AR2 and 5-AR3 are expressed in different patterns in human body.[37]

5-AR1 and 5-AR2 are both expressed throughout human life.[38,39] Low levels of 5-AR1 can be present in the fetal scalp and nongenital skin, while 5-AR2 is present in the external genital skin in early gestation period.[40-42] In adults, 5-AR1 is found in nongenital skin, the liver and certain brain regions, and also at lower levels in the prostate, genital skin, epididymis, seminal vesicles, testis, adrenal gland and kidney. 5-AR2 is expressed at high levels in the prostate, genital skin, epididymis, seminal vesicles and liver.[39-41,43,44] Godoy et al[45] observed the presence of 5-AR3 in various benign and malignant tissues and reported the over expression of 5-AR3 in lung adenocarcinoma, testicular seminoma and yolk sac tumors, androgen sensitive prostate cancer and castration recurrent prostate cancer relative to their benign counterparts. In skin activity of 5-AR1 is more in sebaceous glands especially of the face and scalp and also strongly expressed in dermal papilla of occipital hair.[46] 5-AR2 has been located in the dermal papilla, the inner layer of the outer root sheath, the sebaceous ducts and proximal inner root sheath of scalp hair follicles.[47]

Recent studies by Hoffmann et al showed that there are other enzymes involved in the pathogenesis of AGA such as 17β and 3β-hydroxysteroid dehydrogenases (HSD), with 5-AR2 within the dermal papilla, playing a major role in the intrafollicular conversion of testosterone to DHT.[48] The important role of small levels of certain isoenzymes in normal state in pathogenesis of disease state was suggested by Fritsch et al.[49] Major steroidogenic enzymes involved in formation of potent androgens are steroid sulfatase, 3β -HSD1, 17 β-HSD3, and 5-AR1 whereas

17β -HSD2, 3α-HSD, and aromatase are responsible for inactivation of excess androgen locally in order to regulate the androgen levels in hair follicles.[49,50]

During puberty an androgen dependant growth is seen in genetically susceptible human hair follicles at specific sites of the body. Androgens have a diverse effect on human hair follicles depending upon the body site. In genetically predisposed individuals androgen stimulated growth occurs in beard, axilla and pubic area whereas growth of frontal scalp hair is suppressed. Itami et al suggested that the response of androgen sensitive follicles to androgens by either miniaturization or enhancement is determined by second messenger system.[51] Stimulation of cultured dermal papilla cells from beard area with androgen resulted in increase in transcription of insulin-like growth factor 1 (IGF-1) and increase in growth of co-cultured keratinocytes whereas stimulation of dermal papilla cells from balding scalp resulted in inhibition of growth of the co- cultured keratinocytes. Transforming growth factor-beta1 (TGF- β1) derived from dermal papilla cells of men with AGA indicated that it is an important mediator for suppression of growth of the keratinocytes.[52] In response to testosterone, dermal papilla cell in the beard are known to produce autocrine growth factors which result in an increase in the size of dermal papilla, enlargement of hair follicle and cortex. The major component of secreted cytokines has been recognized as IGF-1.[53]

Factors within each hair follicle function progressively in an orderly and reproducible pattern resulting in hair loss on scalp. Response to androgens is self-regulated by the hair follicles by controlling the expression of 5-AR and androgen receptors.[54-56] The noticeable difference in number of androgen receptors and 5-AR activity between balding and non balding areas of scalp has been postulated to be

produced by this self regulating activity.[54,55,57,58] Maintenance of resistance to AGA by occipital hair when transplanted to vertex and scalp hair from vertex when transplanted to the forearm which miniaturize at the same speed as neighboring hair of the donor site demonstrate this intrinsic regulation activity.[59]

Miniaturization of hair follicle

The significant histological sign of AGA is hair follicle miniaturization.[60] A progressive, methodical hair follicle miniaturization occurs simultaneously with the changes in hair cycle dynamics. Various aspects of epithelial follicle and the hair type produced are determined by the dermal papilla which is located at the follicle base in the middle of the hair bulb.[61,62] The main target of androgen mediated events resulting in miniaturization and changes in hair cycle is the dermal papilla, as it plays a key role in maintenance and control of hair growth.[63-65] A decrease in hair follicle size is likely to occur when there is a tenfold decrease in the number of cells.[66] Mechanism by which this decrease occurs is unknown, but may be as a result of apoptotic cell death, reduced proliferation of keratinocytes,[67] displacement of cells with loss of adhesion resulting in fibroblasts of dermal papilla falling into the dermis, or movement of dermal papilla cells into the dermal sheath which is associated with the outer root sheath of hair follicle.[68,69] In vitro studies have shown that certain inhibitory factors are secreted by dermal papilla cells of balding scalp in humans which affect their growth in both human and rodents and also delay anagen onset in mice in vivo. Formation of smaller dermal papillae and smaller hair in AGA in most likely due to these inhibitory factors.[70] In transgenic mice studies, an inhibitory effect on keratinocyte proliferation by Insulin-like growth factor binding protein 3 (IGFBP3) has been demonstrated.[71]

Fine hair result from small follicles. A reduction of hair shaft caliber from 0.08mm to less than 0.06mm occurs. The gap between full sized and miniaturized terminal hair is represented by transitional indeterminate hair on the balding scalp.[3] Transition from terminal to vellus hair occurs as an abrupt, large step process.[72] Throughout fully developed anagen cross sectional area of individual hair shaft remains constant which show that the hair follicle and its dermal papilla maintain the same size.[3] This indicates that follicular miniaturization occurs between the anagen cycles and not during the anagen phase. The delay between commencement of therapy and clinical response can be explained by this short period of androgen effect.[3]

Dermal remnants of full sized follicles are a mark of follicular miniaturization. These marks are also known as fibrous tracts or streamers.[73,74] Within the follicular marks Arao-Perkins bodies may be seen with elastic stains. An Arao-Perkins body starts in the neck of dermal papilla as a small group of elastic fibers. During catagen they form a clump and remain at the lowest point of origin of the follicular mark. Multiple elastic clumps may be found in these fibrous tracts, resembling ladder rungs with the progressive shortening of anagen hair in AGA.[72]

A decrease in anagen duration results in decrease in hair length, and increase in telogen duration delays regeneration resulting in thin hair fibers in AGA. Thus the resulting hair are short and fine and fail to achieve adequate length to reach the scalp.[3]

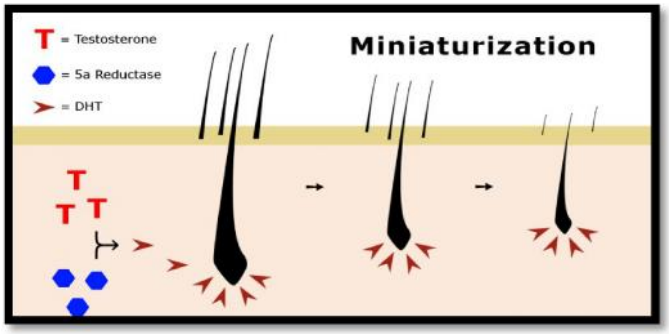


Figure 2: Progressive miniaturization of hair follicle

CLINICAL FEATURES AND GRADING

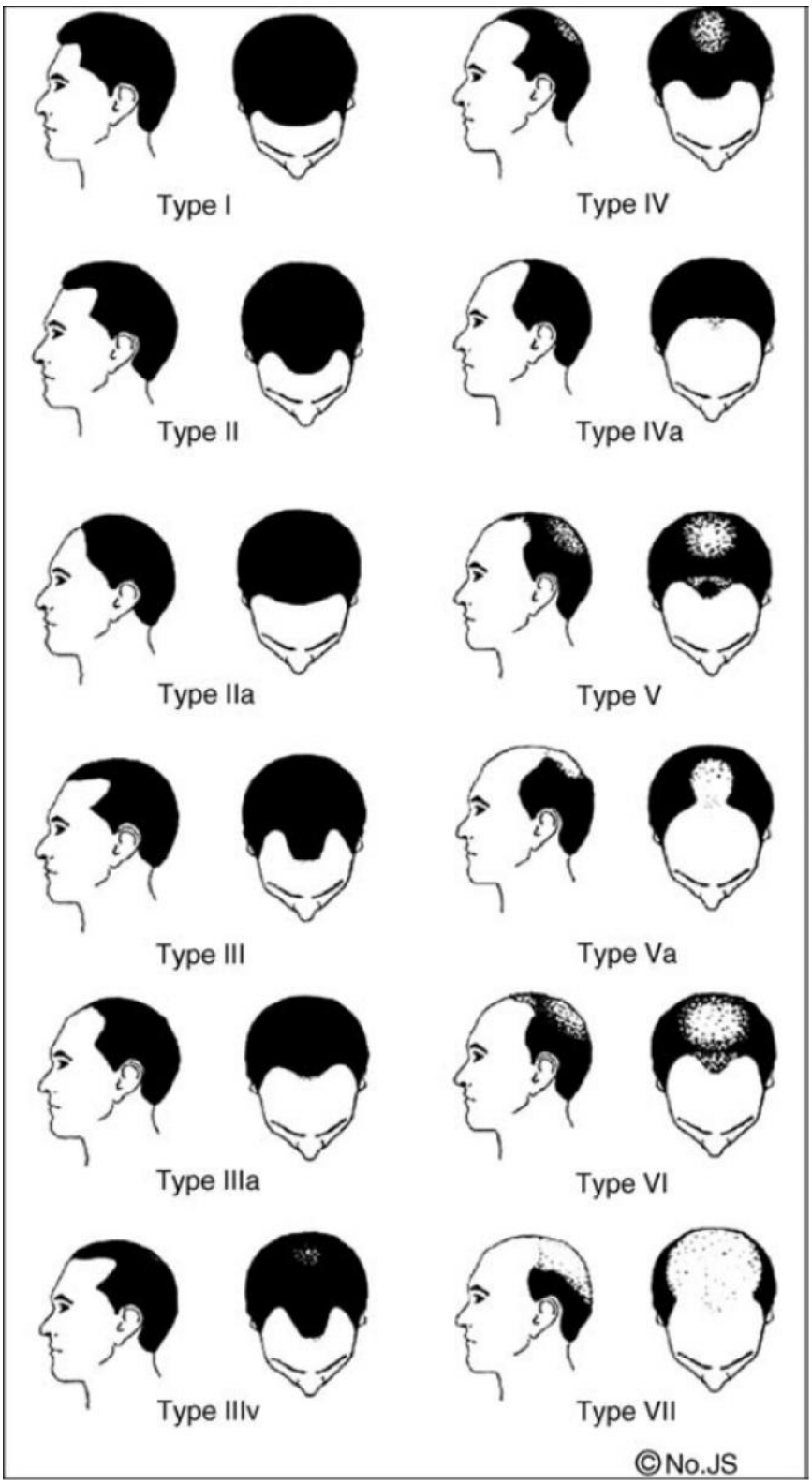
Various grading systems are available for AGA and the most widely accepted system is the modified Norwood-Hamilton classification (Table 1) (Figure 3), consisting of seven broad groups and four specific variant types.[16,17,19]

Table 1: Modified Hamilton-Norwood classification of AGA

Type	Clinical Definition
I	Minimal recession of hairline along the anterior border in the Fronto-temporal (FT) region
II	The anterior border of the scalp in the FT region has triangular areas of recession that tend to be symmetrical. The areas extend no more posterior than a point that lies approximately 2 cms anterior to a line drawn in a coronal plane between the external auditory meatus on both sides. Hair is either sparse or lost along the mid-frontal border.
III	Characterized by deep FT hair recession, usually symmetrical and either bald or sparsely covered with hair. These areas of recession extend further posterior than a point that lies approximately 2 cms anterior to a line drawn in a coronal plane between the external auditory meatus on both sides.
IIIv	Hair is mainly lost in the vertex. There may be some frontal recession but it does not exceed that seen in type III.
IV	The frontal and FT recession is more than type III. There is also sparseness or loss of hair in the vertex. These bald areas are extensive, but separated from each other by a band of moderately dense hair that joins the fully haired fringe on either side of scalp.
V	The hair loss in vertex and FT region is more than type IV and band of hair between them is narrower and sparser.
VI	The hair loss over 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 that begins laterally, anterior to the ear and extends posteriorly on the sides and fairly low on the occipital area.
Variants (type variants a)	Constitutes 3% of all cases of AGA: 1)The anterior border progresses posteriorly without the normal island of hair in the mid-frontal region. 2) There is no simultaneous development of the bald area over the vertex. Instead the anterior recession advances posterior to the vertex.
IIa	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
IIIa	The area of denudation reaches the mid-coronal line
IVa	The area of denudation extends beyond the mid-coronal line and there may be considerable thinning of hairposterior to the actual hair line
Va	Most advanced degree of alopecia; however, the bald area does not reach the vertex

Figure 3: Modified Hamilton Norwood classification of AGA



Lee et al suggested a new, universal and systematic classification known as the Basic and Specific Classification (BASP).[75] The shape of the anterior hairline is the basic type represented by (BA), which is of four types (L, M, C and U) and the density of hair on specific areas like on frontal and vertex region is the specific type represented by (SP), which is of two types (F and V). The final type is determined by the combination of these two entities. (Figure 4).

Type L: No recession is observed along the anterior border in the FT region.

Type M: Recession in the FT hairline is more prominent than the mid-anterior hairline. The hairline resembles the letter M.

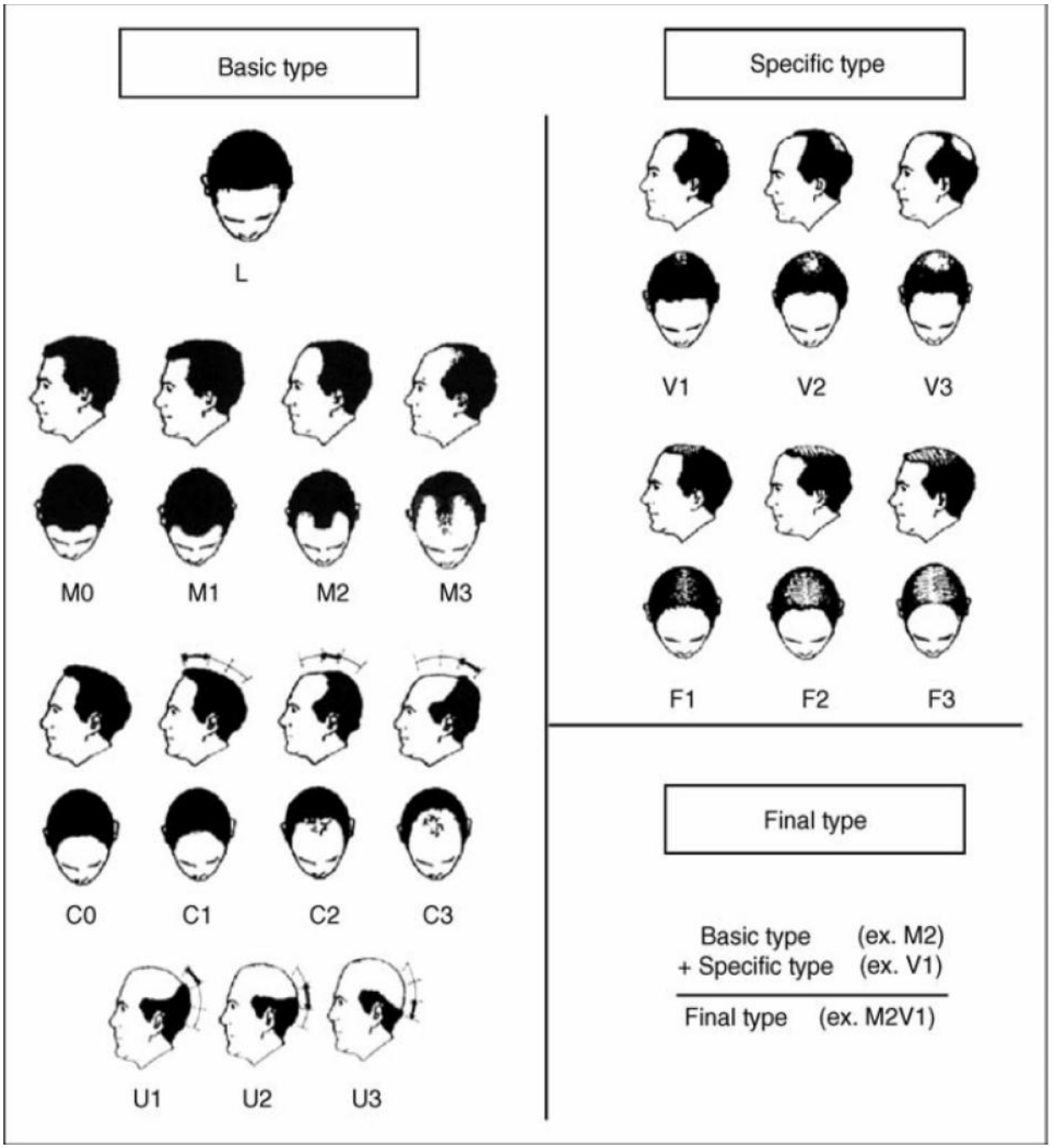
Type C: Recession in the mid-anterior hairline is more prominent than the FT hairline. The entire anterior hairline regresses posteriorly in the shape of half-circle, resembling the letter C.

Type U: The anterior hairline recedes posteriorly beyond the vertex forming a horseshoe shape, resembling the letter U.

Type F: General decrease in the density of hair over the entire scalp, regardless of the anterior hairline. It is more marked over the frontal area.

Type V: Hair loss is seen more distinctly in the vertex than in the frontal area.[75]

Figure 4: The basic and specific classification system



DIAGNOSIS

History

Other causes of hairloss can be ruled out by taking proper history. Chronic hairloss with thinning predominantly over the frontal, parietal or vertex areas is the typical history. Past history of any systemic diseases, intake of new medications within the previous year. Family history of AGA will be usually positive. To rule out nutrition related effluvium, diet history is another important aspect.[76] Effect of smoking and ultraviolet exposure on AGA, which have been implicated as aggravating factors should be enquired in personal history.[77,78]

General scalp and hair examination

Aggravating factors for AGA like seborrheic dermatitis[79] and photo-damage[78] should be looked for, otherwise in AGA scalp is usually normal.

Hair pull test

An easy method for testing the severity of hair loss is the hair pull test.[76,80,81] Around 60 hair are held between the thumb, index and middle finger. Hair are firmly but gently pulled. Normal shedding is indicated by a negative test where 6 or less hair are obtained on pulling, whereas active shedding of hair is indicated by a positive test where 6 or more hair are obtained on pulling. 24hrs prior to the test hair wash should be avoided. Usually test is negative in AGA except during the active phase and only on the affected sites like frontal region.

Trichoscopy

Recently, trichoscopy has emerged as an important diagnostic tool in the diagnosis of AGA. Characteristic features of AGA on trichoscopy are hair diameter diversity (HDD) more than 20% which corresponds to vellus transformation, peripilar

sign or perifollicular pigmentation which is the commonest change seen in Asians and yellow dot.[82] The HDD seen in AGA has been termed as 'anisotrichosis'.[83]

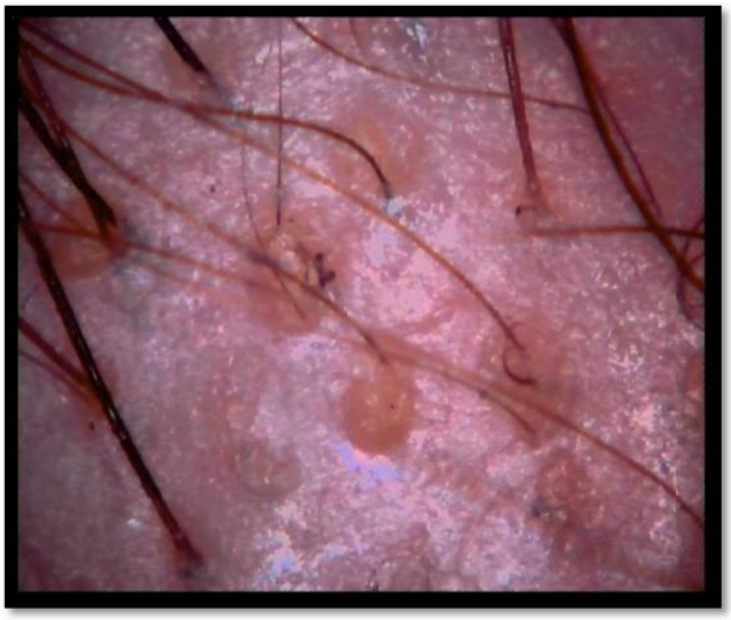


Figure 5: Yellow dots

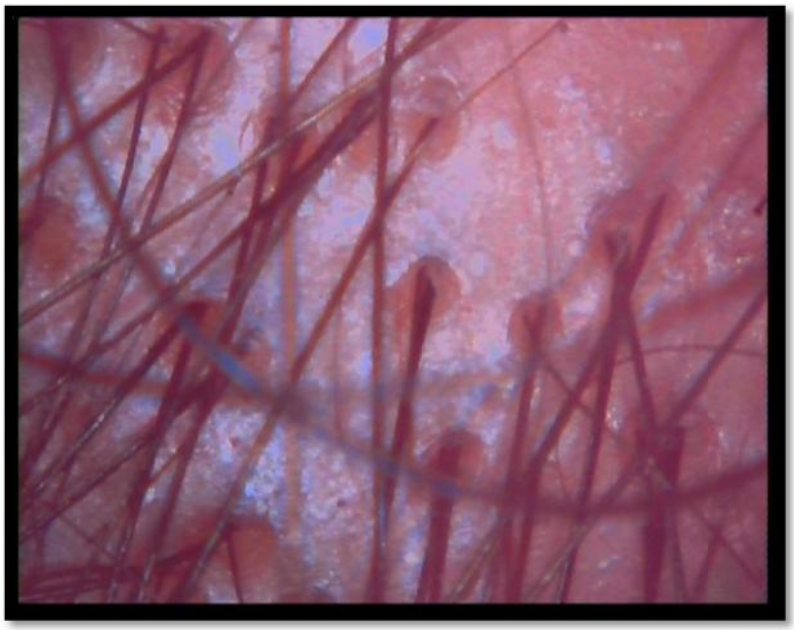


Figure 6 :Peripilar sign

Figure 7: Vellus hair

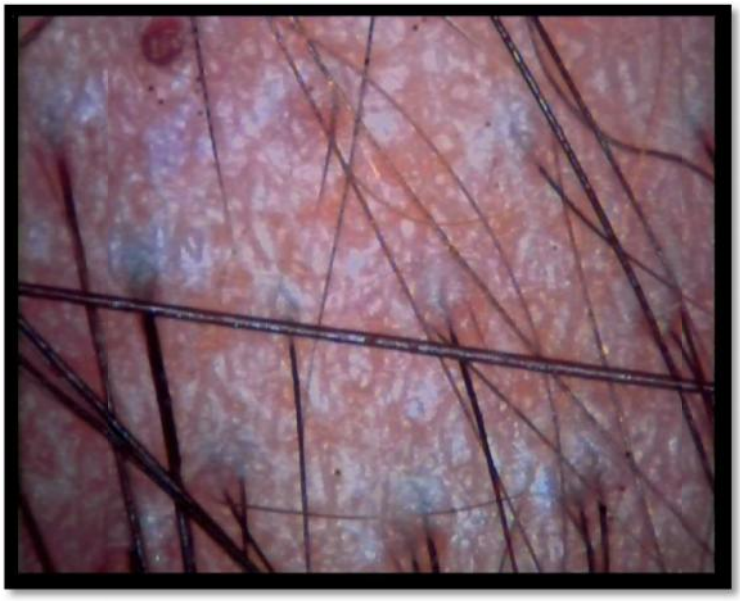


Figure 8 : Variation in hair density diameter

Trichogram and Photo-trichogram

To differentiate between different types of hairloss, trichograms are used, however they have minimal application in AGA. For valid and reliable results this procedure requires technical expertise and experience. Hair wash is avoided for 5 days, then using a rubber tipped forceps, 60-80 hairs are pulled. Examination of hair roots is done immediately. After pulling hair from a specific area usually 30 mm^2, unit area trichogram, hair follicle density, proportion of anagen fibers and hair shaft diameter are estimated.

Phototrichogram (PTG) involves taking serial, close up photographs of specific areas to evaluate rate of hair growth, hair follicle density and thickness of hair shaft. Contrast enhanced PTG and automated PTG are the variants of this technique. Trimming of hair over the selected area is one of the important components of this procedure.[76,81]

Hair wash test

To distinguish between AGA and telogen effluvium, Rebora et al proposed the hair wash test. This test is based on the count of vellus and terminal telogen hair that are rinsed out on hair wash following a five days abstinence from hair wash and shampooing. Results are interpreted based on total telogen hair and percentage of telogen vellus hair. There are many disadvantages to this method such as, double counting can occur due to hair breakage, not useful in curly hair patients and is time consuming.[81,84]

Laboratory investigations

Investigations for AGA are usually not required. Testing for PSA prior to onset of Finasteride has been recommended especially in men above 45 years of age as it causes decrease in PSA levels. A negligible decrease in serum PSA level is seen in men between 18-40 years.[85-87]

Scalp biopsy

As it is an invasive procedure scalp biopsy is not done routinely in AGA patients. Sample has to be taken from the centre of the most affected areas. Bitemporal regions tend to have miniaturized hair even in the absence of AGA, hence samples are avoided form these regions.[76,81] Ideal specimens are 4mm vertex punch scalp biopsies. Maximum diagnostic information is with horizontal biopsies than vertical biopsies.[88]

Reduction in terminal anagen hair count is a significant feature found on scalp biopsies. Secondary pseudo-vellus hair with residual angiofibrotic tracts replace the terminal hair progressively resulting in decrease in the number of terminal hair.[89] Ratio of terminal to vellus hair which is usually greater than 6:1 is changed to less than 4:1. A reduction in the ratio of anagen to telogen hair from 12:1 to 5:1 is also seen.[74] Increased follicular steleae and a minimal perifollicular lymphohistiocytic infiltrate with or without mild fibrosis around the upper part of the follicle may be the other findings in AGA.[90]

Global photography

It is an useful tool for follow up and evaluation of response to treatment in hair loss patients. Requirements include a co-operative patient with dry, clean hair and a technician who has the precision to comb and prepare the hair similarly at each visit

to the clinic. Maintenance of same hair style and colour should be counseled to the patient. All areas of scalp should be covered by shooting multiple images. The vertex, mid-pattern, frontal, and temporal views are the four specified views. Standardization of image with respect to magnification, position and lighting are the main aspects of good global photography. Use of stereotactic imaging apparatus can help in obtaining the best standardization.[76,91,92] As there is a standardized evaluation of whole scalp hair, global photography is one of the most effective methods of hair growth evaluation.[93]

MANAGEMENT

Efficacy, practicability, risks and cost involved are the important factors on which the choice of treatment for AGA is based. All these aspects in the treatment of AGA was addressed in a comprehensive evidence based S3 guideline developed by the European Dermatology Forum.[93]

Camouflage and Wigs

Easiest and simplest way of managing mild AGA is camouflage. Cosmetic satisfaction can be achieved by changing hair style to cover the bald areas, addition of electrostatistically held small fibers and dyeing of scalp similar to hair colour are some of the important and cheap measures. A natural look can be obtained by use of modern wigs which can be washed and styled as well.

Medical management

Minoxidil

Since 1960's, minoxidil was used orally for treatment of hypertension. Shortly following treatment with minoxidil, in nearly 100% of the users, hypertrichosis was

observed.[94-96] This led to the use of topical minoxidil for hair loss treatment.[97] In 1984 it got FDA approval for use in male AGA.

Many hypothesis were put forth to explain the mechanism of action of minoxidil. One of the hypotheses suggests its vasodilatory properties. 10-15 minutes following application of topical minoxidil an increase in cutaneous blood flow was observed.[98] Another important action of minoxidil helping in maintenance of dermal papilla vasculature and hair growth is the up-regulation of vascular endothelial growth factor (VEGF).[99] Promotion of regrowth of hair by action on open potassium channels is the current view on minoxidil.[100,101] An active metabolite, minoxidil sulfate opens the adenosine triphosphate (ATP) sensitive potassium channels which have a relaxing effect on vascular smooth muscle and makes the intracellular potential more negative which in turn promotes decrease in intracellular calcium. Epidermal growth factor in the presence of calcium has shown to inhibit the growth of hair follicle in vitro. This is suppressed by minoxidil resulting in increase in the duration of anagen phase of hair follicles.[102]

Result of use of topical minoxidil on hair growth has been shown by various studies.[103-105] Topical preparations of minoxidil are available as 2%, 5% and 10% solutions.

Even though both strengths are used in the treatment of AGA, 5% solution has been observed to be more efficacious than 2% solution.[106] Twice daily application of 1 ml of solution is effective in AGA patients above 18 years of age. The topical solutions have a liquid vehicle which is highly concentrated with propylene glycol which is a potent irritant. Minoxidil as a 5% topical foam is a recent development which is easy to apply and free of propylene glycol. Efficacy, safety and acceptance

of foam by patients has been demonstrated by placebo-controlled double blind trials.[107]

After treatment initiation, minoxidil produces an increase in the growth of miniaturized hair and induces anagen in the resting hair follicles which results in rapid shedding of previous telogen hair for 2-8 weeks. This shedding is temporary and an indicator of the positive effect of the treatment which resolves after few weeks.

Common side effects observed with the use of minoxidil include hypertrichosis, itching of scalp, erythema, increase in dandruff and allergic contact dermatitis secondary to either minoxidil or the vehicle propylene glycol.[108]

Finasteride

Finasteride is a potent and highly selective antagonist of 5-AR2 and is a synthetic azo-steroid, which inhibits conversion of testosterone to DHT. It was initially approved by FDA for use in BPH but in 1997 was approved for use in AGA as it inhibits formation of DHT and limits its action on hair follicles.

Maximum benefits with finasteride have been observed in various studies in AGA patients with type III and type IV hair loss.[106,109-116] Progression of AGA is slowed by finasteride and it also produces partial regrowth in around two thirds of men.[109] An increase in both total hair growth and anagen hair growth was observed in a study that used macro photographs to calculate the hair count.[110] A study of scalp biopsies also showed that use of finasteride results in decrease in vellus hair with increase in terminal hair.[111]

A 64% reduction in scalp DHT and 68% reduction in serum DHT was observed with once daily administration of 1 mg of finasteride.[113] The superiority of

finasteride over placebo was demonstrated by a 5 year multinational study in patients with AGA.[117] A progressive decrease in terminal hair count by 26% from baseline counts was observed at the end of the 5 year study. However patients on finasteride showed a 10% increase in hair count at the end of 1 year. Thereafter a decrease in hair count was seen which remained constantly 5% above baseline hair count after 5 years of treatment. Adverse effects associated with finasteride include gynecomastia, loss of libido, erectile dysfunction and a reduction in serum PSA level.[93]

Investigations have been carried out for using finasteride topically. On application of 0.05% solution to the scalp absorption of drug was better and a 40% reduction in serum DHT was observed, however no effect was seen on regrowth of hair. This was explained based on an observation that an important factor in preventing hair loss is inhibition of production of prostatic DHT i.e. a significant decrease in circulating DHT is necessary along with local blockade of 5-AR at the hair follicles.[4] Similar results were observed with the use of oral and topical finasteride after 18 months in a double blind, randomized clinical study.[118] Further studies are required to establish the efficacy of topical finasteride.

Dutasteride

Both 5-AR1 and 5-AR2 are inhibited by dutasteride. Inhibition of 5-AR1 is approximately 3 times more and of 5-AR2 is 100 times more than that of finasteride.[119] More than 90% reduction in serum DHT is observed with use of dutesteride when compared to the 70% reduction with finasteride.[120]

FDA has approved use of 0.5 mg of dutasteride in BPH while use in AGA is off label. The effect of 2.5 mg of dutasteride was more superior to 5 mg of finasteride in producing hair growth in men between the age group of 21 to 45 years in a

randomized placebo controlled study.[121] It also produced faster hair growth than finasteride. Side effects such as loss of libido, impotency, gynecomastia are more common with dutasteride than finasteride.[121,122] Reports of decrease in sperm count and volume have been seen with dutasteride.[123-126]

Topical antiandrogens

In women with AGA, oral antiandrogens such as spironolactone, cyproterone acetate have been used which have been contraindicated in men due to their feminizing effects. Fluridil, a topical antiandrogen was developed for use in AGA. It was developed to only undergo local metabolism, no systemic reabsorption and degrade into inactive metabolites without any systemic antiandrogen activity.[127] Increase in anagen to telogen ratio with maximum effect was seen within the first 90 days of daily use of topical fluridil in a double blind placebo controlled study. Side effects on libido and sexual performance was not observed, however long term studies are required to establish its safety and efficacy in AGA.

Latanoprost

Latanoprost is a prostaglandin analogue which prolongs anagen phase of hair cycle thus stimulating hair growth. With topical use of latanoprost for glaucoma an increase in the length of eyelash and eyebrows was seen.[128] Significant increase in hair density in comparison with baseline and placebo was seen in a placebo controlled study.[126]

Topical antibiotics and antifungal

In pathogenesis of AGA role of inflammation is not well established. In follicular infra infundibular and isthmus region, a decrease in density of activated T cells was observed in a study of 20 men who were using topical lotion containing

antimicrobials piroctoneolamine and triclosan regularly for 18 months.[129] Signs of hair regrowth with moderate increase in transitional hair density were observed on trichograms taken at 3 months intervals. Use of topical antimicrobials for treatment of AGA requires further studies for confirmation.

Increased hair growth in humans as well as rodents was seen with use of topical ketaconazole shampoo when compared with a placebo.[130] Due to its anti inflammatory and anti androgenic activity and also on seborrheic dermatitis, ketoconazole shampoo can be added as an adjuvant treatment.[131]

Growth factors

Number of cytokines and growth factors play a role in growth and development of hair follicles. Topical or subcutaneous use of such growth factors can be done for promotion of hair growth. To evaluate the efficacy in promotion of hair growth, the safety of a bioengineered, non-recombinant, human cell–derived formulation containing follistatin, keratinocyte growth factor (KGF), and VEGF was assessed in a phase I, double blind clinical trial.[132] A statistically significant increase in total hair count was observed in 26 patients enrolled in the study without any side effect to the single intradermal injection.

For growth factors and stimulatory mediators platelet rich plasma (PRP) isolated from whole blood can be used. This is widely used by surgeons for promoting growth of transplanted grafts. [133] It is an emerging treatment of AGA suggested by recent data due to its positive effects on hair regrowth and minimal side effects.[134,135]

Lasers

Popularity of laser/light treatment in hair loss has been increasing over past few years. Even though there is evidence of stimulation of hair growth at some wavelengths by laser light, the mechanism by which it occurs is not clear and proof from large scale placebo controlled trials is lacking.[136-138]

Surgical management

Hair transplantation is a process where hair from the occipital region are removed and re- implanted into the bald vertex or frontal region. More than 90% of graft survival can be achieved with the use of modern techniques. Stabilization of hair loss with adequate medical treatment and good population of donor hair on the occipital region are the pre requisites for this procedure.

In 1930's modern hair transplant technique was started in Japan, where damaged eyebrows and eyelashes were covered with small punch grafts.[139] Donor dominance was a term proposed by Norman Orentreich to describe the hair taken from androgen resistant occipital region remain androgen resistant when implanted into androgen sensitive areas of scalp.[59]

Follicular unit transplantation (FUT) was introduced in 1995 by Bernstein, Rassman et al where naturally occurring units of 1-4 hair are transplanted.[140] Donor hair are harvested in two different methods in FUT :

Strip harvesting: Under local anesthesia, a strip of 8-14 mm and 20-30cm scalp is taken from the occipital region and the wound is sutured back. The donor hair is then transplanted to the bald areas after separating it into follicular units. A linear scar in the donor occipital area is the main disadvantage with this method.

Follicular unit extraction (FUE) harvesting: With 1mm punch biopsy individual follicles of hair from occipital region are removed under local anesthesia. Using a micro blade each unit of hair is re-inserted into the balding areas. The advantages with this method are that there are no visible scars and the time taken for healing is also less.

Good results can be achieved with both these methods, but FUT have the advantage of achieving greater hair density. Requisites for these methods include presence of frontal or mid-frontal hair loss and adequate donor hair density for the procedure i.e. >40 follicular units/cm^2. Disadvantages of these methods include increased time and labour requirements and high cost for the patient. After insertion the transplanted hair immediately go into telogen resting phase. Thus results of the procedure can be assessed after 3 months. Chances of graft failure are present and reasons include skill of surgeon, density of graft placed, careless handling and preparation of graft units.

Combination of medical, medical and surgical treatment

Finasteride in combination with either topical minoxidil or ketaconazole showed better hair growth than with finasteride as monotherapy in an open, randomized, parallel group study which compared the efficacy of available medications as monotherapy or combined therapy. This study concluded that efficacy is enhanced with use of combination of medications with different mechanisms of action.[141] In a recent case study marked improvement in hair loss was observed when a patient was started on 0.5 mg of dutasteride who was unresponsive to finasteride.[142] Useful adjuvant treatment following hair transplant is the combination of minoxidil and finasteride which prevent the progression of balding process and also unnatural

appearance which may occur over time. Studies have shown that the usual shedding that occurs 1-2 weeks after transplantation and fast regrowth can be achieved by using minoxidil in perioperative period.[143] A double blind trial also confirmed these findings which showed less loss of grafted hair during the shedding period.[144] Stabilization of hair loss, increase in number of anagen hair and reduction in post procedure telogen effluvium can be achieved with use of topical minoxidil as a pre-medication in hair transplant procedures. 2-3 days prior to surgery use of minoxidil should be stopped to reduce skin irritation and intra operative bleeding caused by vasodilatation. It should be restarted 1-2 weeks after the procedure. In a randomized double blind trial of 79 men with AGA using 1mg of finasteride daily or a placebo 4 weeks prior and 48 weeks post hair transplantation procedure showed a significant improvement in the treatment group from baseline when compared with the placebo group.[145]

Associated findings with AGA

Several diseases have been shown to be associated with AGA as follows:

Coronary artery disease

A relationship between coronary artery disease (CAD) and AGA has been seen in various studies.[146-153] Early onset AGA has been implicated as a risk factor for development of early onset of severe CAD.[147] Vertex pattern baldness has been seen as a marker for increased risk of CAD in few studies.[149,151] However this association was not seen in a cross sectional study.[154]

Insulin resistance

An increased risk of hyperinsulinemia and insulin-resistance associated disorders such as obesity, hypertension and dyslipidemia has been observed with early onset AGA. [155,156] Increased tendency of developing insulin related disturbances like hypertension and diabetes has also been observed in elderly men with AGA.[157]

Hypertension

A strong association of hypertension with AGA was observed in a prospective study of 250 men aged between 35-65 years.[158]

Prostate cancer

Few studies showed that AGA is a risk factor for developing prostate cancer [159] whereas few studies did not find any associations between the two.[160,161] An association between AGA and vertex baldness only but not with frontal and frontal-vertex baldness was reported by Giles et al.[162]

Benign prostatic hyperplasia

Progressive enlargement of prostate associated with symptoms of impaired bladder emptying with gradual progression of symptoms and complications is BPH. It has a prevalence rate and is the fourth most common condition after CAD, hypertension and diabetes. Patients with BPH in 2010 comprised of 210 million men or 6% of the general population.[163,164]

Androgens help in maintaining the normal metabolic and secretary functions of prostate and is also implicated in development of BPH and prostatic cancer. For maintenance of normal prostate physiology an adequate balance between testosterone and 5-AR is required. The main event in response of prostate to androgens is

conversion of testosterone to DHT and its aromatization to estradiol. This conversion is mediated by 5-AR.[7]

In the diagnosis and management of BPH serum PSA has many applications such as prediction of prostate volume, prediction of the course of disease and providing risk assessment for prostatic cancer.

Both AGA and BPH are androgen-dependent diseases in which the enzyme 5-AR plays a key role in conversion of testosterone to DHT.[7] Various studies were carried out to evaluate the association between AGA and BPH with varying results.[10, 165-168]

This study was done to evaluate association between AGA, the prostate volume and serum PSA level.

METHODOLOGY

The details of our study methodology are as follows:

Study source: All male patients with AGA attending the Department of Dermatology, Venereology and Leprosy, KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Study duration: The study was conducted between January 2015 to December 2015.

Ethical clearance: It was granted by the J.N.M.C Institutional Ethics Committee of Human Subjects Research.

Study design: Cross sectional study

Sample size: 64 cases were enrolled in the study according to the formula sample size, $n= z_{\alpha}^2 pq/d^{2,}$ *(z_{α} = 1.96,p = 60,q= 40, d = 12)*

Sample selection criteria: All male patients with AGA attending the Department of Dermatology, Venereology and Leprosy, KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belgaum were recruited as per the Inclusion and Exclusion criteria.

Inclusion criteria:

- All consenting male patients with AGA between the age of 25 to 45 years attending the Department of Dermatology, Venereology and Leprosy between January to December 2015.
- Male patients having androgenic alopecia of type III and above as per Hamilton - Norwood classification.

Exclusion criteria:

- Subjects who are on treatment with minoxidil, finasteride or any medication which has an effect on size of prostate or hair growth.
- Subjects who had history of hair transplantation.
- Subjects should not be on androgenic supplements.
- Subjects who do not comply with the protocol.

Data collection:

- Informed consent will be taken from all the patients included in the study. All patients in study will undergo a detailed history taking, general physical, systemic and dermatological examination.
- Patients will be asked about any family history of AGA or prostatic cancer, personal history of systemic diseases and drug intake (antihypertensives, diuretics, hypocholesterolemics, and oral antidiabetics).
- Data will be collected by a single examiner.
- Blood samples will be drawn between 8 AM and 9 AM after a 12-hour fasting period for serum PSA.
- All participants will undergo transabdominal ultrasound examination at the Urology department (examiner who do not know the purpose of the study) to determine the prostate volume.
- Records will be maintained and analyzed statistically.

Statistical method for data analysis:

ANOVA and Spearman's Rank correlation.

RESULTS

A total of 64 patients with AGA who fulfilled the inclusion and exclusion criteria were enrolled in this study.

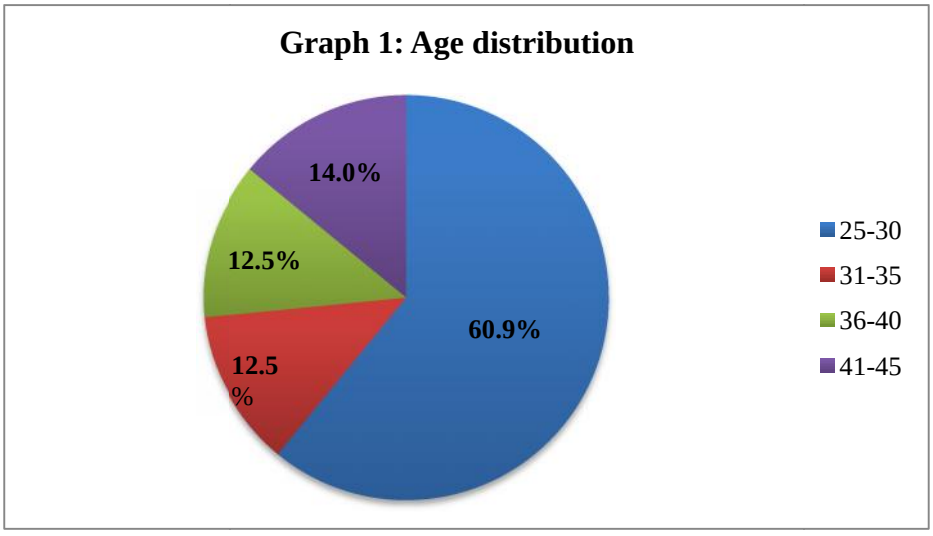
Age distribution

The youngest patients in the study were 25 years old, whereas the oldest were 45 years old.

Table 2: Age distribution

Age (years)	Number of patients	%
25-30	39	60.9
31-35	8	12.5
36-40	8	12.5
41-45	9	14.0

Graph 1: Age distribution



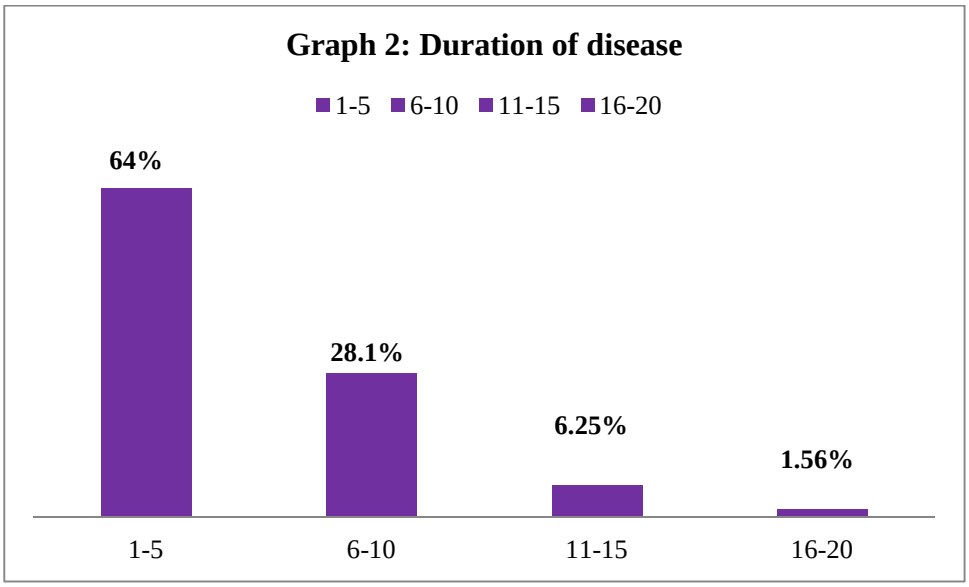
The above data suggests that out of 64 patients of AGA, 39 (60.9%) of patients were between the age group of 25-30 years, 8 (12.5%) in 31-35 years, 8 (12.5%) in 36-40 years and 9(14.0%) in 41-45 years. So the maximum number of patients were in the age group of 25-30 years. Mean age of the patients was30.9 years with a standard deviation of 6.62 years.

Duration of disease

The shortest duration of disease was 1 year, whereas the longest duration was 20 years.

Table 3: Duration of disease

Duration of disease (years)	Number of patients	%
1-5	41	64.0
6-10	18	28.1
11-15	4	6.25
16-20	1	1.56



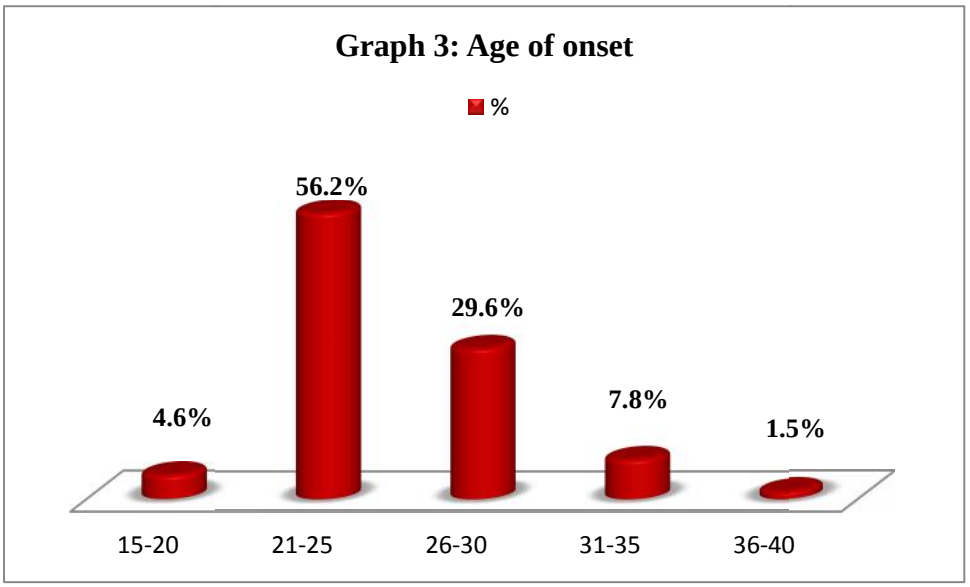
The above data suggests that out of 64 patients of AGA, the duration of disease in 41(64%) of patients was between 1-5 years, 18 (28.1%) was 6-10 years, 4(6.25%) was 11-15 years and 1(1.56%) was 16-20 years. The maximum number of patients were in the group of 1-5 years. The mean duration of the disease was 5.5 years with a standard deviation of 4.17 years.

Age of onset

The lowest age of onset in the study was 18 years old, whereas the highest was 37 years old.

Table 4: Age of onset

Age of onset (years)	Number of patients	%
15-20	3	4.6
21-25	36	56.2
26-30	19	29.6
31-35	5	7.8
36-40	1	1.5



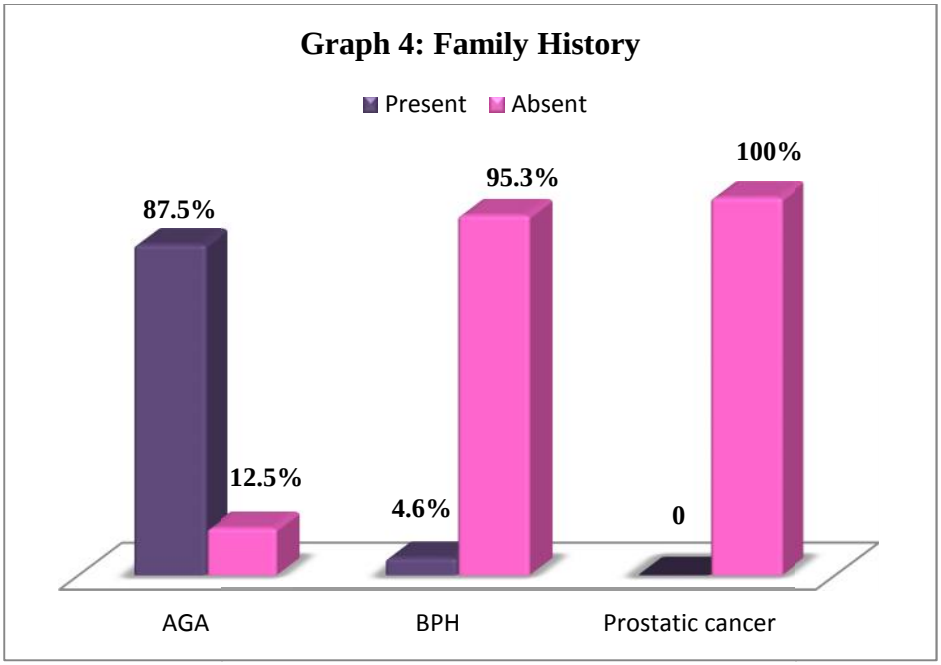
The above data suggests that out of 64 patients of AGA, the age of onset in 3 (4.6%) patients was between 15-20 years, 36(56.2%) was between 21-25 years, 19(29.6%) was between 26-30 years, 5(7.8%) was between 31-35 years and 1(1.5%) was between 26-40 years. The maximum number of patients were in the group of 21-25 years. The mean age of onset was 25.4 years with a standard deviation of 4.01 years.

Family history of AGA, BPH and prostatic cancer

Positive family history of AGA was present in 56 patients, of BPH in 3 patients and no history of prostatic cancer in any patient.

Table 5: Family history of AGA, BPH and prostatic cancer

Family history	Present	%	Absent	%
AGA	56	87.5	8	12.5
BPH	3	4.6%	61	95.3
Prostatic cancer	0	0	64	100



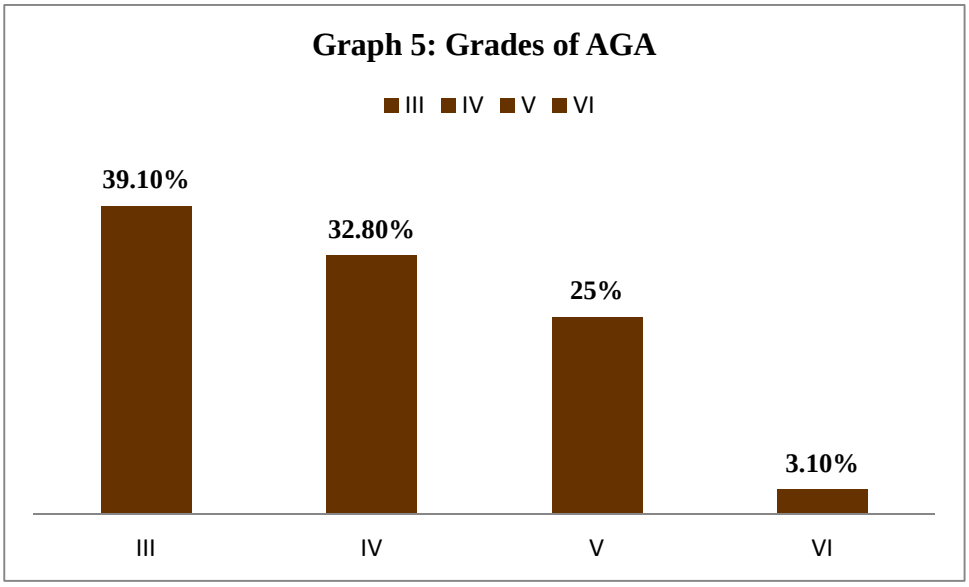
The above data showed that out of 64 AGA patients, 56(87.5%) patients had a positive family history for AGA, whereas in 3(4.6%) patients had positive family history for BPH and in prostatic cancer family history was negative in all patients, 64(100%).

Grades of AGA

All 64 patients of AGA were classified into different grades based on Hamilton- Norwood classification. Maximum number of patients had Grade III AGA, whereas Grade VI was seen in minimum number of patients.

Table 6: Grades of AGA

Grade of AGA	Number of patients	%
III	25	39.1%
IV	21	32.8%
V	16	25%
VI	2	3.1%



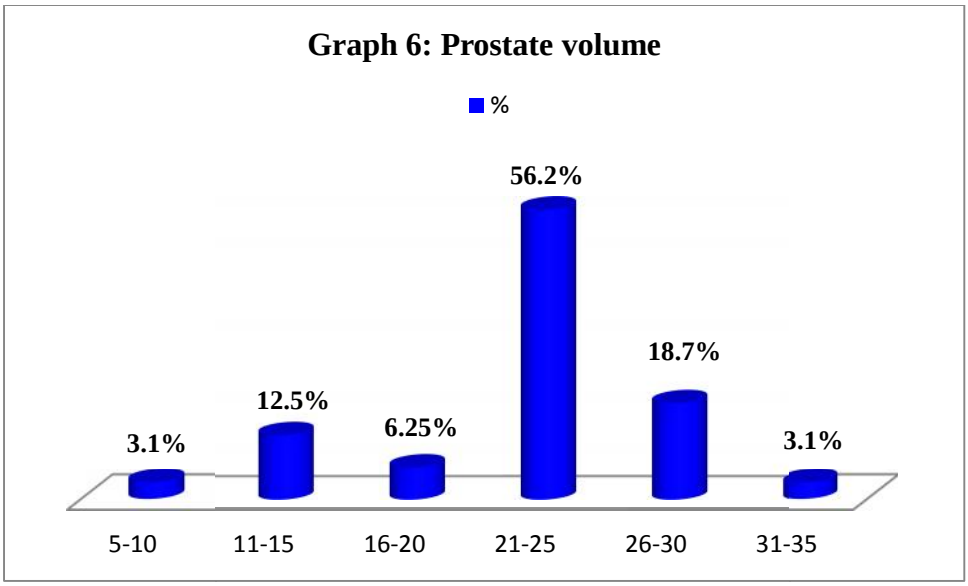
The above data showed that in 64 patients of AGA, 25(39.1%) of patients had Grade III AGA, 21(32.8%) had Grade IV AGA, 16(25%) had Grade V AGA and 2 (3.1%) had Grade VI AGA.

Prostate volume

All 64 patients of AGA underwent Trans -abdominal ultrasound which showed maximum number of patients had prostate volume ranging between 21-25 ml.

Table 7: Prostate volume

Prostate volume (ml)	Number of patients	%
5-10	2	3.1
11-15	8	12.5
16-20	4	6.25
21-25	36	56.2
26-30	12	18.7
31-35	2	3.1



The above data showed that in 64 patients, 2 (3.1%) patients had prostate volume between 5-10 ml, 8(12.5%) had between 11-15 ml, 4(6.25%) between 16-20 ml, 36(56.2%) between 21-25 ml, 12(18.7%) between 26-30 ml and 2 (3.1%) between 31-35 ml.

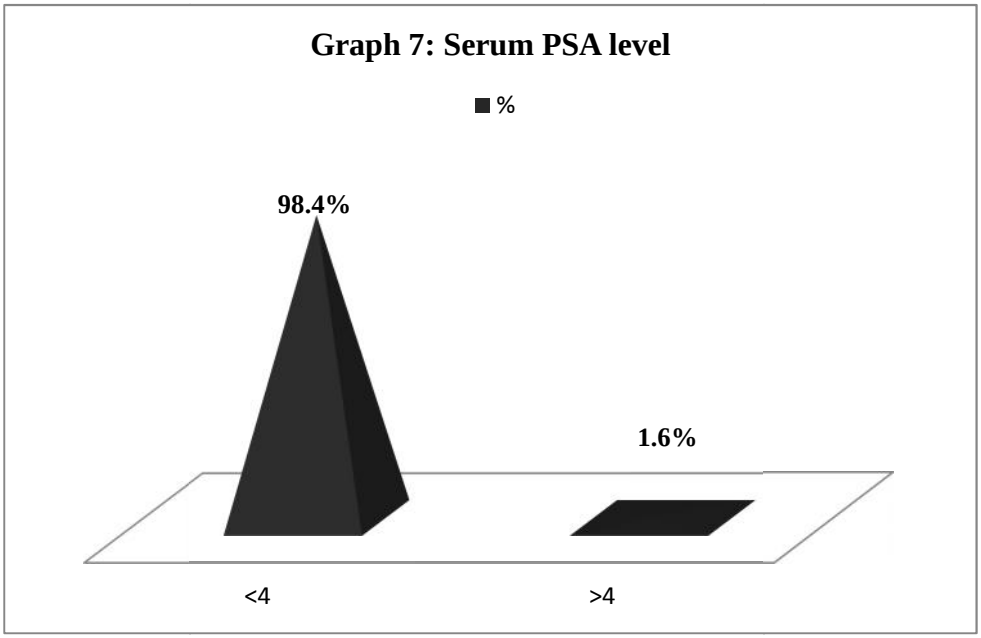
Serum PSA level

Out of 64 patients, 63 (98.4%) had serum PSA level <4 ng/ml and 1 (1.6%) had serum PSA level >4ng/ml.

Table 8: Serum PSA level

Serum PSA level (ng/ml)	Number of patients	%
<4	63	98.4
>4	1	1.6

Graph 7: Serum PSA level

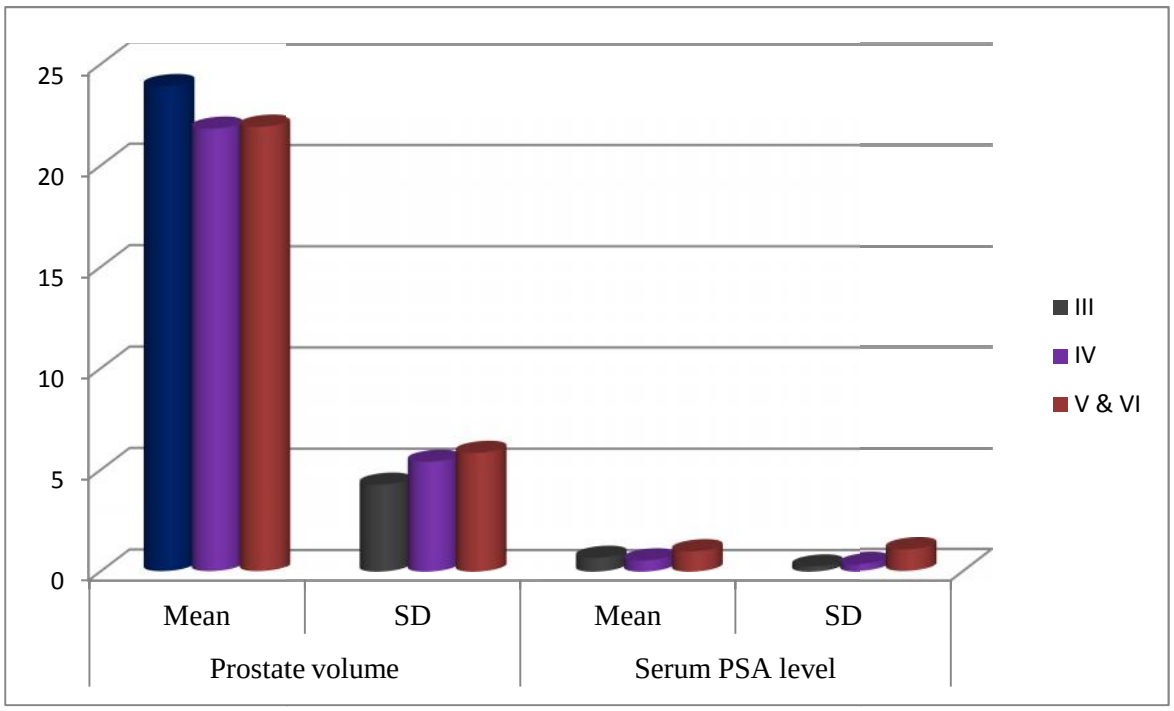


Comparison of prostate volume and serum PSA level among patients with different AGA grades

Table 9: Comparison of prostate volume and serum PSA level among patients with different AGA grades

AGA grade	Prostate volume		Serum PSA level	
	Mean	SD	Mean	SD
III	23.9	4.29	0.68	0.25
IV	21.8	5.42	0.55	0.33
V & VI	21.9	5.86	1	1.04

Graph 8: Comparison of prostate volume and serum PSA level among patients with different AGA grades



As the Grade of AGA increased there was reduction in prostate volume in patients.

ANOVA was performed to compare mean prostate volume among AGA grades which was not statistically significant. (F=1.215, p=0.304)

Serum PSA level also decreased with AGA grades and difference between the grades was not statistically significant. (F=2.748, p=0.072)

Spearman's rank correlation between grades of AGA and prostate volume was found to be -0.147 indicating that as grades of AGA increased prostate volume was reduced. However, this correlation was not statistically significant.(p=0.247).

There was poor correlation between AGA grades and serum PSA level, Spearman's rank correlation being 0.016, statistically not significant. (p=0.902)

DISCUSSION

The association between AGA and BPH has been evaluated by very few studies, where studies were conducted on patients already having BPH. Present study was performed on AGA patients who had no history of BPH to determine the association between AGA, prostate volume and serum PSA levels. It is a cross sectional study in which a total of 64 patients were studied. Here we have compared the present study with a few related studies.

Comparison of sample size of various studies

The sample size of the present study was 64 patients. In a study done by Chen et al[10] the sample size was 62 patients, Arias Santiago et al[166] had 87 patients, Oh et al[165] had 225 patients and Dastgheib et al[168] had 150 patients.

Table 10: Comparison of sample size of various studies

Studies	Sample size
Present study	64
Chen et al	62
Arias Santiago et al	87
Oh et al	225
Dastgheib et al	150

Age distribution

The age distribution in present study was 25-45 years, whereas the other studies were all conducted on elderly males.

Table 11: Comparison of age distribution in various studies

Studies	Age distribution (years)
Present study	25-45
Chen et al	56-87
Arias Santiago et al	35-65
Oh et al	>60
Dastgheib et al	50-83

Family history

In present study 87.5% of the patients had positive family history of AGA whereas only 4.6% had positive family history of BPH. In most of the studies, patients had a positive family history of AGA and two studies also had a positive family history of BPH.

Table 12: Comparison of family history in various studies

Studies	Family history (%)	
	AGA	**BPH**
Present study	87.5	4.6
Oh et al	12.5	31.6
Dastgheib et al	57.3	-
Arias Santiago et al	88	12.5

Grades of AGA

Table 13: Comparison of grades of AGA in various studies

Studies	Grades of AGA (%)			
	III	**IV**	**V**	**VI**
Present	39.1	32.8	25	3.1
Oh et al	23.9	14.3	13.2	12.5
Arias Santiago et al	36.5	31.1	33.3	
Dastgheib et al	59.6	34.1	6.3	

In almost all studies Grade III was found to be the most common grade of AGA. In present study 39.1% of the patients had Grade III AGA comparable with other studies done by Oh et al, Arias Santiago et al, Dastgheib et al where Grade III was observed in maximum number of patients.

Prostate volume

In present study the prostate volume ranged between 8-32 ml whereas in study done by Dastgheib et al the range was 10-173 ml. Other studies done by Chen et al and Arias Santiagoet al had enrolled patients with prostate volume >30 ml.

Serum PSA level

In present study the range on serum PSA level was between 0.1 to 4.8 ng/ml whereas in study done by Dastgheib et al the range was 0.1 to 6.8 ng/ml. Studies done by Chen et al and Arias Santiago et al had enrolled patients with serum PSA levels <10 ng/ml.

Comparison of association between AGA and BPH in various studies

The present study did not show any relation between AGA, prostate volume and serum PSA level, however it showed an increase in prostate volume in most of the AGA patients which was not statistically significant. This conclusion was similar to the conclusion of Dastgheib et al's study. Studies done by Chen et al, Oh et al and Arias Santiago et al concluded a positive association between AGA and BPH.

CONCLUSION

This study showed that among 64 patients with AGA, prostate volume more than 20 ml was present in 51 (79.6%) patients and absent in 13 (20.4) patients. Serum PSA level >4 ng/ml was seen in only 1(1.6%) patient and <4 ng/ml in 63 (98.4%) patients.

Maximum number of patients 39(60.9%) were in the age group of 25-30 years.

The duration of illness in most of the patients 41(64%) was between 1-5 years.

The age of onset in maximum number of patients 36(56.2%) was between 21-25 years.

Total number of patients with positive history of AGA were 56 (87.5%) and those with positive family history of BPH were 3(4.6%).

The most commonly observed grade of AGA was Grade III in 25(39.1%) followed by Grade IV 21(32.8%), Grade V 16(25%) and Grade VI 2(3.1%).

On comparison of prostate volume and serum PSA levels in different grades of AGA no significance was found between them.

Even though there was an increase in the prostate volume among AGA patients it was not statistically significant. The study of larger sample sizes of AGA patients with a control group from the general population who can be followed up for a considerable amount of time, would further strengthen this association.

Patients with early onset AGA had an increase in prostate volume. This association has been explained by the common pathophysiology of these two entities where androgens play an important role. If this observation is further confirmed in

additional studies, dermatologists and physicians can monitor patients with early onset AGA for development of any urinary symptoms which permits for an early diagnosis of BPH. Additional studies may also confirm if treatment of AGA patients can prove beneficial to BPH which might be present in its initial stage of development.

SUMMARY

- Our study was a cross sectional study which was carried out from January 2015 to December 2015
- The source of data were androgenetic alopecia patients attending the Dermatology OPD at KLE'S Dr Prabhakar Kore Hospital & MRC, Belgaum.
- The objectives of the study were to evaluate the association between androgenetic alopecia with benign prostatic hyperplasia and association of androgenetic alopecia with serum PSA level.
- The youngest patients in the study were 25 years old, whereas the oldest were 45 years old. The average age of all patients enrolled in the study was 30.9 years.
- The shortest duration of disease was 1 year, whereas the longest duration was 20 years. The mean duration of the disease was 5.5 years.
- The lowest age of onset in the study was 18 years old, whereas the highest was 37 years old. The mean age of onset was 25.4 years.
- Positive family history of AGA was present in 56 patients, of BPH in 3 patients and no history of prostatic cancer in any patient.
- All 64 patients of AGA were classified into different grades based on Hamilton- Norwood classification. Maximum number of patients had Grade III AGA, whereas Grade VI was seen in minimum number of patients. In 64 patients of AGA, 25(39.1%) of patients had Grade III AGA, 21(32.8%) had Grade IV AGA, 16(25%) had Grade V AGA and 2 (3.1%) had Grade VI AGA.

- All 64 patients of AGA underwent Trans -abdominal ultrasound which showed maximum number of patients had prostate volume ranging between 21-25 ml. In 64 patients, 2 (3.1%) patients had prostate volume between 5-10 ml, 8(12.5%) had between 11-15 ml, 4(6.25%) between 16-20 ml, 36(56.2%) between 21-25 ml, 12(18.7%) between 26-30 ml and 2 (3.1%) between 31-35 ml.
- Out of 64 patients, 63 (98.4%) had serum PSA level <4 ng/ml and 1 (1.6%) had serum PSA level >4ng/ml.
- Though maximum number of AGA patients showed a larger prostate volume, the values were not statistically significant.
- Spearman's rank correlation between grades of AGA and prostate volume was found to be -0.147 indicating that as grades of AGA increased prostate volume was reduced. However, this correlation was not statistically significant. (p=0.247).
- There was poor correlation between AGA grades and serum PSA level, Spearman's rank correlation being 0.016, statistically not significant. (p=0.902)

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ANNEXURE – I - INFORMED CONSENT FORM

I.D.NO. | | | |

"ONE YEAR CROSS SECTIONAL STUDY OF ASSOCIATION BETWEEN ANDROGENETIC ALOPECIA AND BENIGN PROSTATIC HYPERPLASIA IN MALE PATIENTS VISITING KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"

The study is conducted by Dr. _____, Post graduate student in M.D Dermatology under guidance of Dr. _____, Professor of Dermatology, J N Medical College, Belgaum.

Respected Sir, we invite you to participate in our study as, you are eligible for the same. During the study you will be asked some questions in detail regarding your present complaints.

Purpose of the study:

Androgenetic alopecia is a progressive, patterned hair loss that occurs in genetically predisposed individuals and is the most common cause of hair loss among males. Both AGA and BPH are androgen-dependent diseases. Purpose of the study is to find out the relation between baldness in men and prostate size and prostate specific antigen level in blood. All patients attending the outpatient department, who are diagnosed to have this disease, will be requested to participate in this study during the period of one year.

Procedure and treatment:

If you agree to participate in the study the basic data about you and history related to AGA will be recorded in a proforma. The grade of your baldness will be documented in your proforma. Digital photographs may be taken for documentation.

You will undergo special investigations like serum PSA level and trans abdominal ultrasonography. All your basic data will be kept confidential.

Risks and benefits:

There is no undue potential risk and discomfort foreseen by getting enrolled in this study. However all necessary steps and precautions will be taken to ensure your safety. By getting enrolled in the study, you will get the chance to get examined by the doctor in general with benefits of blood investigations and the early diagnosis of increase in size of prostate gland if any.

Alternatives:

If you decide not to participate in this study, you will still be receiving the usual standard care for your disease.

Privacy and confidentiality:

Your privacy will be respected and all information collected about you during the course of this study will be kept confidential. Your identity will remain undisclosed.

Financial incentives:

You shall not be receiving any payment or any financial incentives for participating in this study.

Authorization to publish results:

The results of this study may be published for scientific purpose or presented to a scientific group. Your identity, however, will be maintained confidential at all times.

Voluntary participation:

Your participation in this study is voluntary. Your decision whether or not to participate will neither affect the care of your current disease, nor your future relations with the doctor or the hospital. . In the event if you suffer any physical injury as the result of your participation in this study, you may contact Dr. _____ Telephone No._____ or Dr. _____, Telephone No._____. In the event of an emergency, you should contact KLE'S Dr. Prabhakar Kore Hospital and MRC on Telephone No. 08312473777.

In case you need further information regarding your rights as a study participant, you may please contact Dr. _____ chairman of the ethical committee, J N Medical College, Belgaum. Telephone No _____ .

Statement of Consent:

I.D.NO: | | | |

I, Mr _____

Volunteer and consent to participate in this study. I have read the consent document or it has been read to me in my vernacular language. I accept to participate in the study. All the information regarding this study is provided to me and I have understood the same. I have been given the opportunity to ask questions and obtain appropriate answers.

Participant's name:

Signature or left thumb print of participant:

Witness name:

Signature of witness:

Signature of the investigator:

Date:

ANNEXURE - II - PROFORMA

"ONE YEAR CROSS SECTIONAL STUDY OF ASSOCIATION BETWEEN ANDROGENETIC ALOPECIA AND BENIGN PROSTATIC HYPERPLASIA IN MALE PATIENTS VISITING KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELGAUM"

Case no: | | | | **IP/OP no:** | | | | | | | |

Name:

Age:

Sex:

Address:

Contact no: | | | | | | | | | | |

Occupation:

Chief Complaints:

History of Present Illness:

Age at onset of Illness:

Past History:

Treatment History:

Personal History: Diet : Veg / Non-veg

Smoking: Yes / No Duration:

Alcohol: Yes / No Duration:

Bowel habits: Bladder habits:

Family History: Diabetes: Yes / No

Asthma: Yes/ No

Hypertension: Yes / No

AGA: Yes/ No

Prostatic cancer: Yes/ No

General Examination:

Height: Weight: BMI:

Pulse: /min

BP: mmHG

RR: /min

Temperature:

Pallor: Present/Absent

Icterus: Present/Absent

Cyanosis: Present/Absent

Clubbing: Present/Absent

Pedal oedema: Present/Absent

Lymphadenopathy: Present/Absent

Systemic Examination: CVS:

RS:

P/A:

CNS:

Dermatological Examination

Skin:

Fitzpatrick Skin type**:** | I | | II | | III | | IV | | V | | VI |

Palms and Soles:

Oral Mucosa:

Genitalia:

Nails:

Hair:

Grade of baldness as per Hamilton Norwood classification:

I	II	III	IV	V	VI	VI	VIII

Investigations:

Trans abdominal USG :

Prostate volume - _____ ml

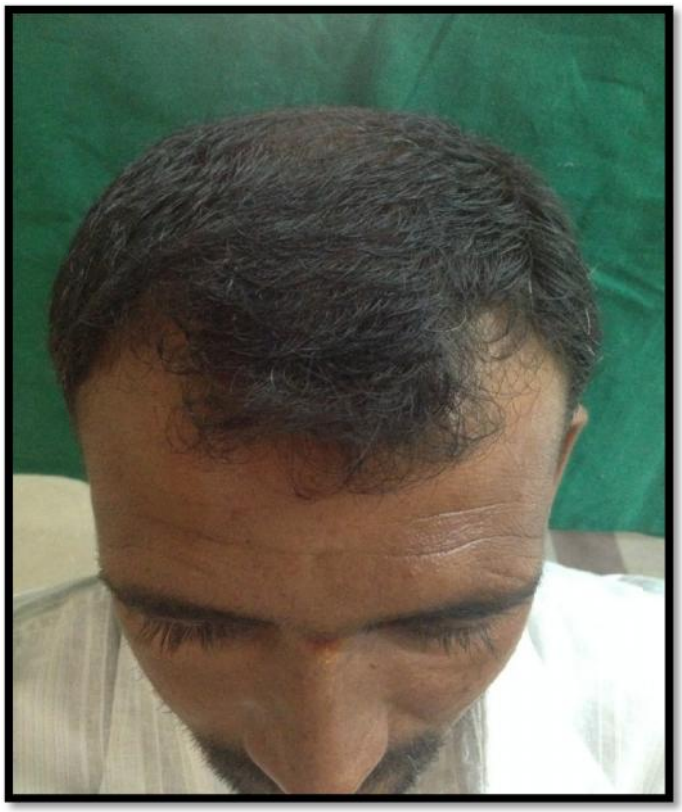
BPH Grade: | I | | II | | III | | IV |

Serum PSA : _____ng/ml

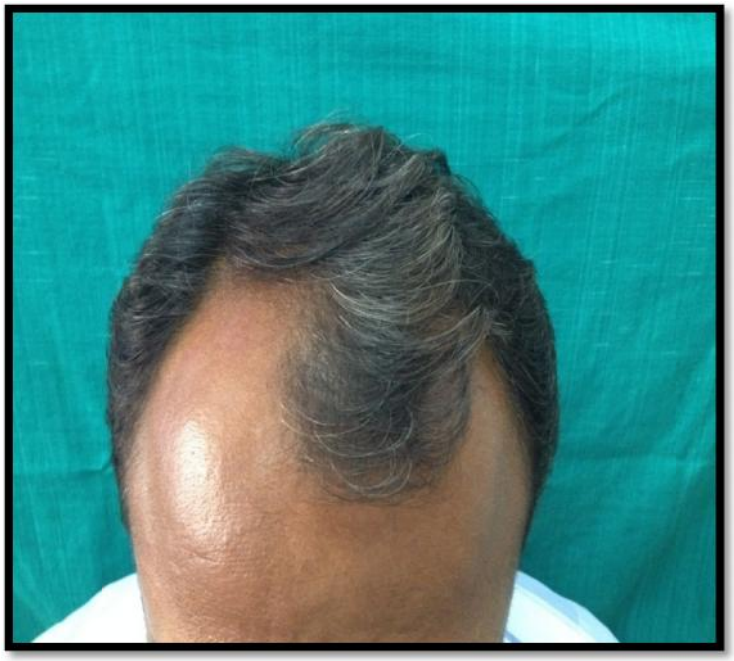
DIAGNOSIS: ANDROGENETIC ALOPECIA GRADE –

BENIGN PROSTATIC HYPERPLASIA GRADE -

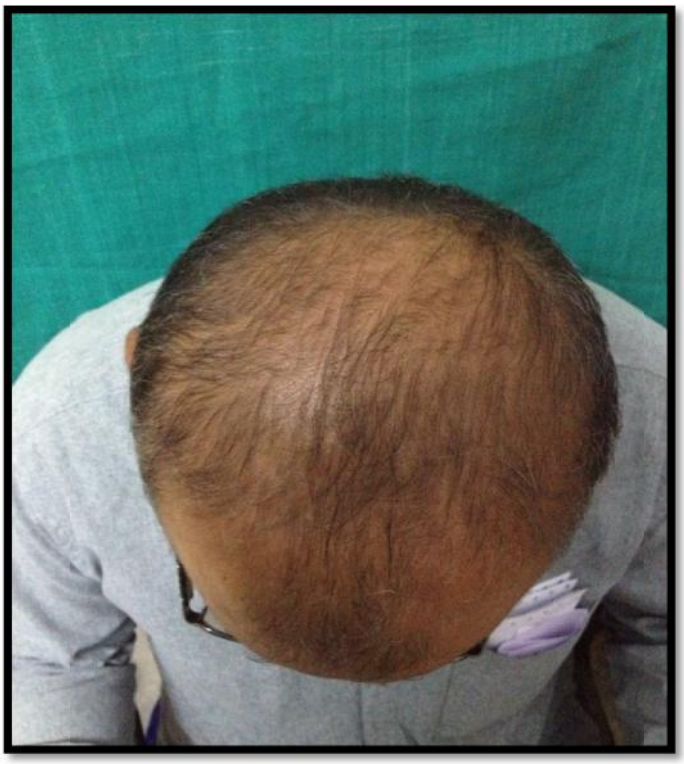
ANNEXURE- III - PHOTOGRAPHS



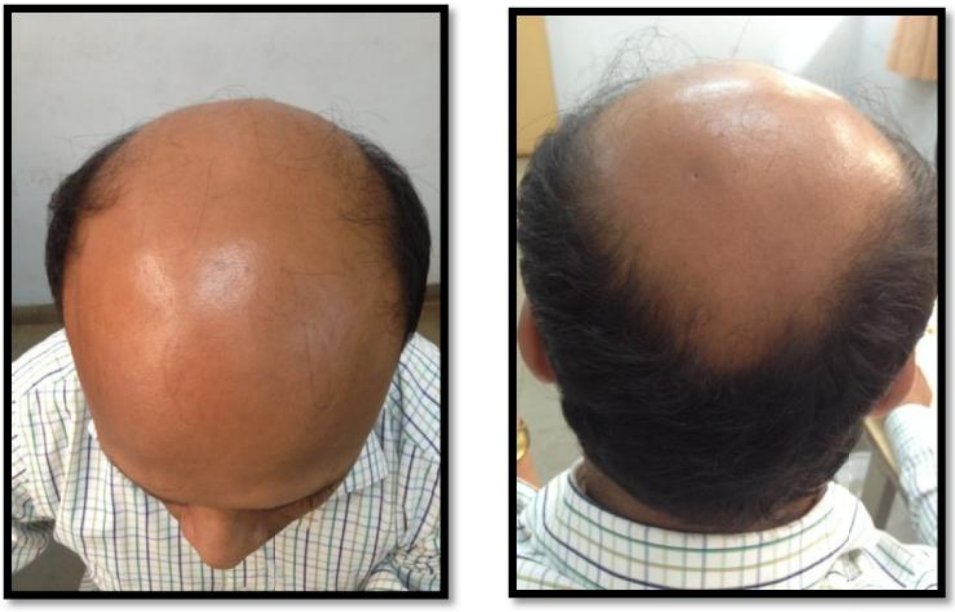
Photograph 1: Grade III AGA



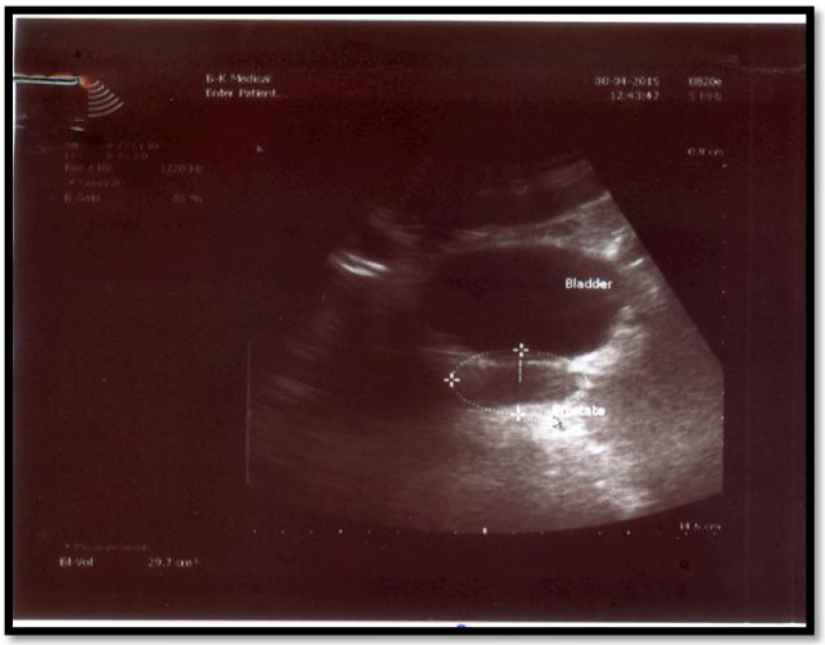
Photograph 2: Grade IV AGA



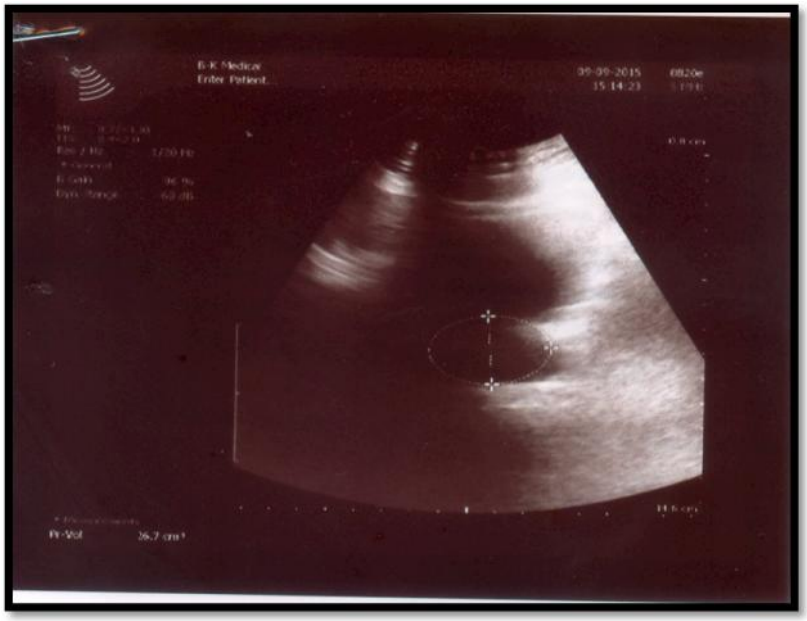
Photograph 3: Grade V AGA



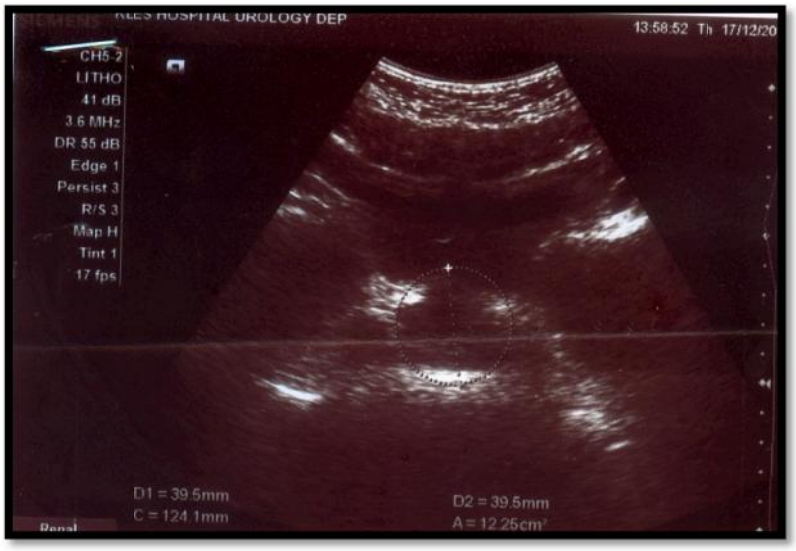
Photograph 4 : Grade VI AGA



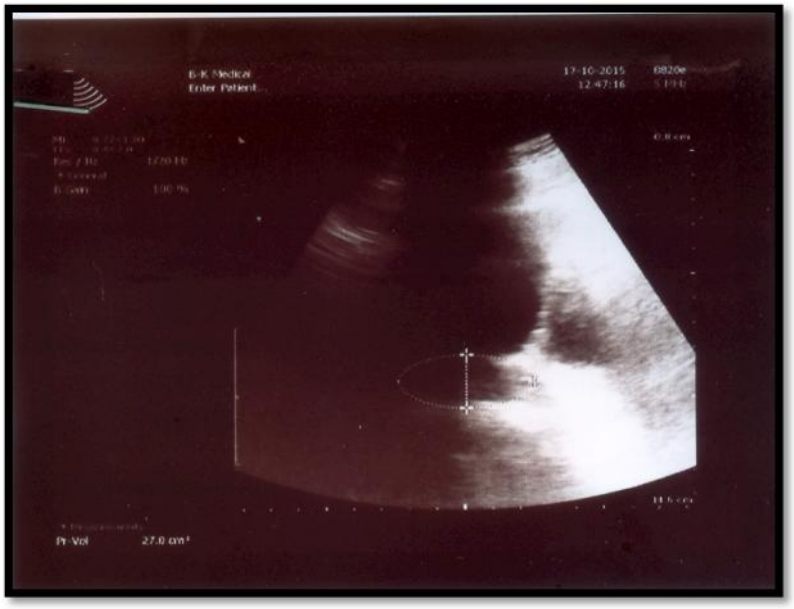
Photograph 5: Prostate volume 29 ml



Photograph 6: Prostate volume 26 ml



Photograph 7: Prostate volume 32 ml



Photograph 8: Prostate volume 27 ml

ANNEXURE- IV – MASTER CHART

SL No	Age (yrs)	Duration of illness (yrs)	Age at onset (yrs)	Family history of AGA	Family history of prostatic cancer	Family history of BPH	AGA grade	Prostate volume (ml)	Serum PSA level (ng/ml)
1	45	15	30	P	A	A	V	8.08	0.36
2	42	14	28	P	A	A	VI	15.2	1.16
3	27	4	23	P	A	A	IV	10.5	0.81
4	40	10	30	P	A	A	V	22.1	0.41
5	25	4	21	P	A	A	III	12.6	1
6	25	1	24	P	A	A	III	21	0.56
7	31	6	26	P	A	A	III	23.9	0.73
8	28	6	22	P	A	A	IV	18.3	0.26
9	31	10	21	P	A	A	IV	21.3	0.72
10	25	3	22	P	A	A	III	29.3	0.44
11	42	20	22	P	A	A	V	21.3	0.51
12	28	5	23	P	A	A	IV	12.5	0.37
13	41	5	37	P	A	A	IV	21.3	0.23
14	26	1	25	P	A	A	III	13.6	0.54
15	28	5	23	A	A	A	V	14.9	0.8
16	25	5	20	A	A	A	V	12.9	0.49
17	44	10	34	P	A	A	V	22	0.49
18	27	1	26	A	A	A	IV	13.6	0.9
19	27	5	22	A	A	A	IV	16.6	1.6
20	45	15	30	A	A	A	IV	25.1	0.61
21	40	10	30	A	A	P	IV	15.2	0.37
22	29	1	28	A	A	A	III	18	1.08
23	25	2	23	P	A	A	IV	23	0.39
24	45	15	30	P	A	A	V	24.6	0.89
25	25	3	22	P	A	A	III	25.8	0.59
26	27	1	26	P	A	A	III	23.2	0.8
27	39	4	35	P	A	A	IV	23.4	0.56
28	25	1	24	P	A	A	III	24.6	0.68
29	26	3	23	P	A	A	IV	25.8	0.67
30	28	3	25	A	A	A	III	23.2	0.89

31	25	2	23	P	A	A	III	23.2	0.52
32	25	3	22	P	A	A	IV	23.4	0.76
33	28	3	25	P	A	A	V	23.9	1.79
34	31	5	26	P	A	A	IV	24.5	0.5
35	25	3	22	P	A	A	IV	21.6	0.52
36	36	7	29	P	A	A	III	23.2	0.45
37	25	2	23	P	A	A	III	25.8	0.51
38	37	10	27	P	A	A	V	23.4	0.49
39	25	2	23	P	A	A	III	23.5	1.23
40	33	6	27	P	A	A	IV	24.5	0.13
41	28	5	33	P	A	A	III	23.2	0.38
42	43	10	33	P	A	A	V	20.1	1.54
43	30	5	25	P	A	A	IV	26.7	0.55
44	43	10	33	P	A	A	V	23.2	0.93
45	29	6	23	P	A	A	III	26.7	0.58
46	25	2	23	P	A	A	IV	24.5	0.5
47	30	5	25	P	A	A	III	23.2	0.71
48	40	10	30	P	A	P	V	25.7	0.56
49	37	10	27	P	A	A	VI	26.5	0.63
50	28	3	25	P	A	A	V	26.3	0.22
51	28	10	18	P	A	A	V	25.7	0.55
52	35	8	27	P	A	A	V	26.8	1.43
53	27	7	20	P	A	A	IV	27	0.19
54	27	4	23	P	A	A	III	26.5	0.59
55	25	4	21	P	A	A	III	25.7	0.49
56	25	4	21	P	A	A	III	27.1	0.76
57	25	2	23	P	A	P	III	30.2	0.71
58	31	6	25	P	A	A	III	23	0.47
59	26	3	23	P	A	A	IV	23.2	0.91
60	27	2	25	P	A	A	III	30.8	0.6
61	25	1	24	P	A	A	IV	32.2	0.18
62	30	2	28	P	A	A	III	23.2	1.35
63	31	3	29	P	A	A	V	32.2	4.8
64	25	2	23	P	A	A	III	27	0.39