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Assessment of cardiovascular risk factors in male androgenetic alopecia: A case control study in a tertiary care hospital of western Odisha

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Abstract: Androgenic alopecia (AGA) is the most common cause of patterned hair loss among males which is characterized by progressive hair loss from the bi-temporal and vertex regions of the scalp. Although previous epidemiological studies found an association between metabolic syndrome (MetS), and cardiovascular disease (CVD) risk among adult AGA male patients, there has been no comprehensive research till now to establish this correlation between AGA and cardiovascular risk and there is a paucity of data regarding this association. Two hundred men were included in the study, N = 100 AGA patients included in the patient group, and the rest in the control group. In both groups, the parameters for MetS such as family history, socioeconomic status, obesity, blood pressure, and lipid profile), and in the presence of the CAA plaques and carotid intima-media thickness (CIMT) using Doppler ultrasonography were established. The degree of AGA was assessed by using the Hamilton-Norwood grade (I-VII) system for males. Statistical analysis was performed using the Chi-square test. AGA was found in 11.6% of OPD patients, whereas 3 patients have CAA plaque and 6 cases have C-IMT from the patient's group. There was a statistical association between male AGA with MetS, and insulin-resistant patients (P = 0.001 and 0.0004, respectively). A positive family history of AGA patients, hypertension, DM, and CVD was found to be significantly more frequent in study cases than in the controls (P <0.05). Patients with AGA appear to have a highly prevalent risk of developing CVD and CAA plaque. Therefore, clinical evaluation of each AGA patient's cases is needed, especially for grade III and above which may help prevent CVD in the future. Timely intervention and lifestyle changes in male AGA patients can fulfil the ultimate objective of reducing cardiovascular complications in the future.

Introduction

Androgenetic alopecia (AGA) is considered to be the most prevalent form of baldness in genetically susceptible individuals, characterized by progressive hair loss in a patterned manner (bitemporal and vertex recession). It has a polygenic pattern, and dihydrotestosterone binding to androgenic receptors in hair follicles of the scalp triggers the genes accountable for the gradual transformation of large terminal follicles to miniature ones (Asfour et al., 2023; Glickman et al., 2021; Vinay et al., 2023; Hamed et al., 2022; Sözen et al., 2022). However, the exact etiology remains undetermined. Etiology believes that androgen-stimulated hair follicle miniaturization targets the genetically predisposed hair follicles, which causes the gradual replacement of large, terminal hairs with barely perceptible, vellus hairs in affected areas (Asfour et al., 2023; Glickman et al., 2021; Vinay et al., 2023; Hamed et

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al., 2022; Sözen et al., 2022). The etiology of the AGA causes an imbalanced control of hair growth due to the intra- and peri-follicular expression of particular regulatory molecules and their receptors (Hamed et al., 2022; Sözen et al., 2022; Qiu et al., 2022). Another pathological factor is the catagen, which occurs as a consequence of decreased levels of anagen due to the basic fibroblast growth factor (GF), insulin-like GF-1, and vascular endothelial GF simultaneously because of high expression of cytokines such as tumor necrosis factor-alpha (TNF-α), transforming growth factor beta-1 (TGFβ-1), interleukin-1alpha (IL-1α), chemokines, etc (Arefi et al., 2020; Sözen et al., 2022). The age prevalence rate for developing AGA in male cases is 50 years (30 to 50%) (Elhabak and Abdel Halim, 2020; Sheikh et al., 2021). With advancing age, cardiovascular disease (CVD) is the most important cause of morbidity and mortality worldwide, hence assessment of risk factors is of great importance. Metabolic syndrome (MetS) is a group of metabolic disorders such as glucose intolerance, insulin resistance (IR), central obesity, dyslipidemia, and hypertension that are associated with an increased risk of cardiovascular disease (Chen et al., 2022; Krysiak et al., 2022; Saafan et al., 2021; Vora et al., 2019). Many diseases like cardiovascular disease (CVD), hypertension, benign prostate hyperplasia, and prostate cancer have been reported to have concurrency with AGA (Vora et al., 2019). Insulin resistance (IR) is the underlying pathophysiology of MetS, characterized by a cluster of conventional and nonconventional cardiovascular risk factors that increase lipid profiles and their receptors. Which is considered to be a positive marker for the early onset of AGA development (Krysiak et al., 2022; Roohaninasab et al., 2022).

The association between AG and metabolic syndrome was defined in a significant number of previous epidemiological studies (Dawoud et al., 2023; Qiu et al., 2022). Although some studies have found no relationship, the majority have supported the notion that suffering from AGA is correlated with cardiovascular health risk, with conflicting results (Arefi et al., 2020) and few pieces of literature also specified that cardiovascular risk (CVR) is associated with AGA as compared with normal individuals (Arefi et al., 2020; Saafan et al., 2021; Dawoud et al., 2023; Zhu et al., 2022).

An understanding of the relationship between male androgenetic alopecia and CVD may be important in improving primary prevention which can help to prevent cardiovascular mortalities and morbidities at an early stage (Arefi et al., 2020; Saafan et al., 2021; Dawoud et al., 2023; Wang et al., 2021). Keeping this in mind, we aimed to determine the association of cardiovascular risk factors in androgenetic alopecia, specifically in males, and to prove an association between male AGA and CVD. Our study also had the objective of creating awareness among people with AGA about the importance of early screening of parameters related to metabolic syndrome, IR, and CIMT which in turn helps to arrest future CVD. (Chen et al., 2022; Krysiak et al., 2021)

This study aimed to evaluate the association of cardiovascular risk factors in patients with male androgenetic alopecia. The secondary goal of utilizing various parameters is to demonstrate a connection between androgenetic alopecia and cardiovascular risk factors.

Materials and Methods

We undertook a single-center hospital-based case-control study of a total of 100 male AGA patients and 100 age-matched controls with normal hair status attending outdoor patients (OPD) at the Department of Dermatology, Veer Surendra Sai Institute of Medical Sciences and Research (VIMSAR), Burla from 1st October 2018 to 30th September 2019. The study was done after the approval of the institutional scientific review committee and followed under guidance of the ethics of the institution. All the patients had submitted a written informed consent form, detailed history and clinical examination were entered in a proforma. The AGA male patients in the age group between 20 to 50 years with clinically diagnosed with AGA were included in this study. For the control group, the male aged the same as the patient group with a dermatological disease other than AGA visit to the department.

Inclusion criteria

- Male patients with clinically diagnosed AGA, any grade included. That is reduced diameter and density of hair in the bitemporal, frontal area or vertex with greater density in the occipital area and the presence of miniaturized hairs of different diameter as observed using trichoscopy.
- Age from 20 to 50 years old.

Exclusion criteria

- Known cases of diabetes mellitus, hypertension, congenital adrenal hyperplasia, familial genetic syndrome, i.e., familial hypertriglyceridemia, thyroid disease, Cushing̓s disease, nephrotic syndrome.
- Patients who were receiving androgen, antiandrogens, slimming or insulin-sensitizing drugs or insulin treatment; had used glucocorticoid agents, weight gaining drugs during the previous 6 months.

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A detailed data were collected such as age, sex, area, occupational status, educational status, economic status, family history, previous medication, and duration of hair fall. Personal history of drugs for hypertension, diabetes mellitus, and dyslipidemia were obtained. Clinically examined AGA patterns of hair thinning on the frontal and parietal scalp with intact density on the occipital scalp were obtained. All the patients were measured for the degree of scalp involvement based on Hamilton-Norwood classification grading system by grade I to VII (Singdia et al., 2023). Laboratory investigation on body mass index (BMI), height, waist circumference (WC), fasting plasma sugar (FPS), lipid profile, blood pressure (BP), measurement of carotid intima-media thickness (CIMT) by ultrasonographic studies on common carotid artery on both the sides by using high-resolution Doppler ultrasound (USG) (ATL 5000) with a 5-12 MHz linear transducer (Figure 3 and 4) was also recorded.

Statistical analysis

All the Statistical analysis was carried out by using the IBM SPSS Statistic version 26.0. Continuous parameters were expressed in mean ± standard deviation and frequencies (%) for categorical variables. Quantitative variables were compared groups by using the Student's t-test and qualitative variables analyzed through Chi-square test. *P*-value <0.05 was considered statistically significant andthe margin of error was taken as a 95% confidence interval.

Result and Discussion

In our present study, a total of 100 outdoor patients had androgenetic alopecia, out of 21638 male patients who visited the OPD. Among all patients attending our SKIN & V.D. OPD, AGA among males was 11.6% (Table 1). Most of the patients were in the age group of 31–35 years (26%) among cases, whereas most of the controls were between 36 and 40 years (25%), showing the highest age for AGA. The mean age of cases was found to be 33.12±7.13 years, and the mean age of controls was 32.84±7.18 years (*P*-value = 0.782). As we described the socio-demographic status in Table 1, out of 100 patients, 41 were from rural areas and 59 were from urban areas, whereas 38 in the control group belonged to rural areas and 62 non-AGA patients belonged to urban areas. Among various occupation statuses, office workers comprised 40% of cases, followed by students (32%), whereas among the control group, the maximum proportion, which is 35%, was businessmen, followed by students (25%). The majority of patients' group, that is, 80% had studied up to a higher level in cases, while 65% of controls had completed graduation or above. The majority of patients, 41% of cases, and 44% of controls belonged to the upper socio-economic group, followed by 31% of cases and 26% of controls who belonged to the upper middle class.

Table 1. Demographic and Socio-economic factors of AGA patients

Gender	AGA	No AGA/ Control group
OPD Male patients	100	100
Age distribution (in years)		
20 – 25	17	19
26 – 30	20	18
31 – 35	26	23
36 – 40	22	25
41 – 45	09	10
46 – 50	06	05
Rural / urban locality distribution		
Rural	41	38
Urban	59	62
Occupational status		
Farmer	2	3
Office worker	40	19
Student	32	25
Businessman	11	35
Unemployed	15	18
Educational status		
Illiterate	1	1
Primary	6	4
Secondary	13	30
Higher	80	65
Economic status		
Lower	2	4
Upper Lower	8	6
Lower middle	18	20
Upper middle	31	26
Upper	41	44

*SD, standard deviation; AGA, Androgenetic alopecia; OPD, outdoor patient.

In this study for the grading of AGA, we used a grading system called Hamilton-Norwood, which is defined by different morphological patterns (Figure 1 (a-g); Table 2). The patient group of grade-V alopecia (22%) constituted the highest number, followed by grade-IV (20%) and grade-III (18%). However, most of the patients with metabolic syndrome belonged to grade IV alopecia (26.31%), followed by grade V (23.68%).

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Figure 1. a. Clinical cases of AGA grade-I.
b. Clinical cases of AGA grade-II.
c. Clinical cases of AGA grade-III.
d. Clinical cases of AGA grade-IV.
e. Clinical cases of AGA grade-V.
f. Clinical cases of AGA grade-VI.
g. Clinical cases of AGA grade-VII.

Table 2. Grade system hamilton-norwood classification in AGA patients and MetS patients with or without AGA.

Grade system hamilton-norwood classification	No. of cases in AGA	MetS present	MetS absent
I	15	1	14
II	12	2	10
III	18	5	13
IV	20	10	10
V	22	9	13
VI	06	5	1
VII	07	6	1
***** MetS, Metabolic syndrome			

A positive family history of AGA patients, hypertension, DM, and CVD was found to be significantly more frequent in study cases than in controls (P <0.05) (Table 3).

The difference in waist circumference between the study and control groups was significant (P 0.05). However, no significant differences were observed in the mean values of BMI (P =0.09) (Table 3). There was a statistically highly significant difference in the mean±SD values of systolic and diastolic blood pressure, which is P <0.01. The differences in Mean±SD between cases and

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controls of serum LDL and HDL were found to be highly significant (P <0.01), whereas there was a significant difference in mean values of serum TG (P <0.05). But no significant difference in mean was found for serum cholesterol among cases and controls (P >0.05). The mean±SD values of FBG showed a statistically meaningful difference between the study and control groups, which is P <0.05 (Table 3; Fig. 2).

Figure 2. Dermoscopy images of AGA, Short vellus hairs (red arrowhead), White dot (black arrow), Peripilar sign (yellow solid arrow)

Table 4. CAA plaque and CIMT were compared between AGA patients and the control group

CAA Plaque	Present	Absent	*P* Value
Case	3	97	>0.05, 0.31
Control	1	99	
CIMT	**CIMT > 1mm**	**CIMT < 0.8mm (normal range)**	***P* Value**
Case	6	94	0.05
Control	1	99	

*CAA, Carotid artery atherosclerotic plaque; CIMT, Carotid–intima media thickness

Additionally, Mean±SD values of fasting insulin and HOMA-IR showed a highly significant difference (P <0.0001) with a positive correlation between AGA and IR. IR was diagnosed in 41 AGA patient groups and 18 control groups, with a significant difference in both groups (P = 0.0004) (Table 3). Based on the diagnostic criteria of MetS, it was diagnosed in 38 cases and 17 controls, with a significant difference between both groups (P = 0.001). MetS was found to be present in 38% of cases and 17% of controls, whereas IR was detected in 41% of cases and only 18% of controls. There was no specific trend in the association between MetS and grades of AGA. CAA plaque was found to be present in 3 cases and only 1 control, with no significant difference between the two groups (P =0.31). Raised CIMT (>1mm) was detected in four cases and only one control, without any significant difference between the two groups (P =0.05) (Table 4; Figures 3, 4 and 5).

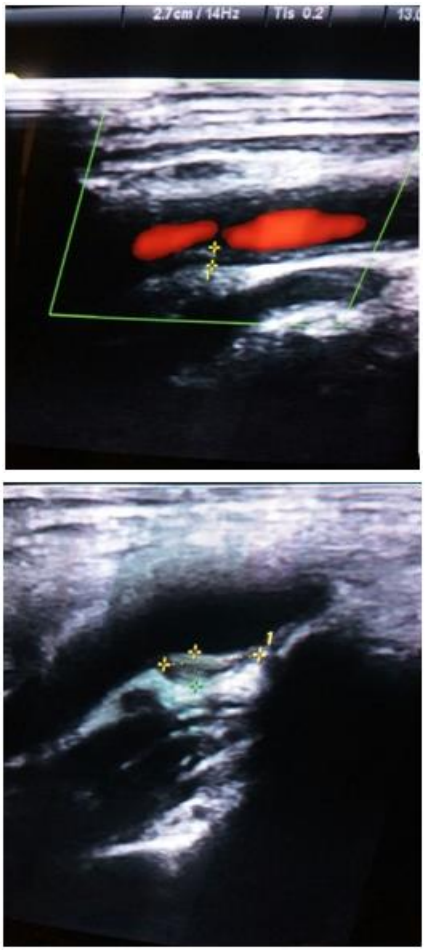
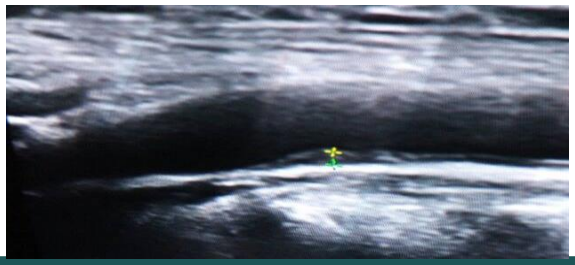


Figure 3. Doppler USG of carotid artery showing atherosclerosis plaque (measured using yellow cross)



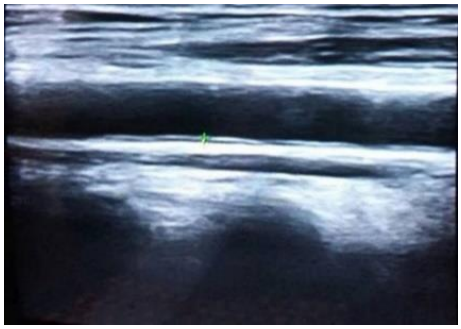


Figure 4. USG of carotid artery showing increased carotid intima-media thickness test (CIMT) (yellow and green cross)

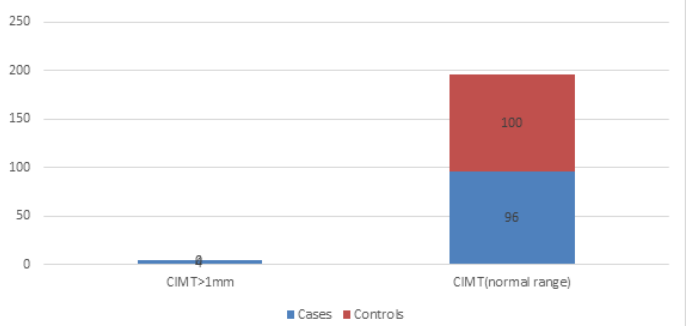


Figure 5. Comparative proportion of increased CIMT in case and control

100 male patients with AGA and 100 control participants who appeared to be in good health were included in this study. All of the patients were selected from the dermatology OPD at VIMSAR. Our results showed that the co-morbidity of MetS was highly prevalent in grade IV and grade V patients (Hamed et al., 2022; Sözen et al., 2022).

Clinically the AGA shows features such as recession of the frontal hair line leading to the whole baldness of the vertex scalp. The hair loss progresses up to the rim of the normal hair growth at the back of the scalp which remains as such. Additionally, the hair thinning, and shortening, in the intermediate hairs and finally to the non-pigmented vellus hair-involved areas completely disappeared (Asfour et al., 2023; Glickman et al., 2021; Vinay et al., 2023; Sözen et al., 2022; Hamed et al., 2022).

In modern society, hair is an important cosmetic asset. Therefore, hair loss impairs self-confidence and leads to social stress and also affects individual economic status. AGA results in psychological depression and also affects quality of life by causing anxiety (Krysiak et al., 2022).

All the previous studies were conducted to display the link between MetS. Vora et al., in 2019; Singdia et al., 2023, revealed that the probability of having AGA with metabolic syndromes was higher than in the control groups. This is similar to our study result. But the main problem of their study was the small sample size in the control group (Vora et al., 2019; Singdia et al., 2023).

Abdollahimajd and his colleagues (2021) in Indian population study for AGA described the characteristics and relationship between MetS and CAA plaque. They concluded that there was no significant difference was found in the mean of the cholesterol levels, but two CAA plaques found in the case group which gives a high recommendation to rule out CAA in AGA patients group (Abdollahimajd et al., 2021).

Additionally, in 2021, Mumcuoglu and his colleagues examined IR and MetS in men with early AGA and also concluded that the IR-related disease and CAD are more common with prevalent in males with AGA. In his study group included 50 males with AGA>3 and BMI <27, and 40 control group males matched with age. This study is very similar to our study output by scoring in Fasting insulin resistance index for correlated with AGA (Mustafa et al., 2021).

Another case-control study done in 2021 by Mustafa and his co-worker in Turkey assessed included a total of 106 males (74 in AGA group and 42 in the Control group) with an age range between 20-50 years, mean age is 32.14, very close with our mean age result that is 32.84±7.18 years (*P*-value = 0.782). But in the case of Oiwoh et al., they found no significant relationship with MetS prevalence between the AGA patients and the control group (P = 0.135) which is the opposite in our study (Oiwoh et al., 2023).

Males with AGA should be made aware of an increased risk of metabolic syndrome, insulin resistance, carotid artery atherosclerosis and its consequences later in life for diseases such as cardiovascular diseases. AGA patients with abdominal obesity (suggested by higher WC) should be advised regarding lifestyle modifications for weight reduction.

More prospective studies are required in order to objectively clarify whether the increased risk of CVD in AGA can be attributed to dyslipidemia due to androgens, IR alone, or MS due to IR.

Limitations of the study

This was a cross-sectional case-control study in a tertiary care hospital which reflects the tip of the iceberg. It was a single center study with a small sample size. Multicentric studies with larger sample sizes at the community level should be carried out to establish the association between AGA and metabolic syndrome.

Future prospective

There is a lot of research, case-control studies, meta-analyses, and cross-sectional studies on the rise regarding the significant association between the AGA with MetS, CAD, CAA plaque, and its correlated laboratory markers. Our study also defines a systematic relationship between

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them to encourage highly preventive care at an early stage. Findings from this study should not only raise awareness among clinicians to screen AGA patients for metabolic and cardiovascular abnormalities but also encourage AGA patients to seek early measures to modify bad lifestyle habits to reduce the risk of future cardiovascular complications.

Conclusion

Patients with AGA appear to have a highly prevalent risk of developing CVD and CAA plaque. Therefore, clinical evaluation of each AGA patient's cases is needed, especially for grade III and above, which may help prevent CVD in the future. Statistical associations were found in waist circumference, mean values of systolic and diastolic blood pressure, serum HDL and LDL levels, mean serum triglyceride level, fasting blood sugar, and insulin resistance to AGA, but no association was found between severity of metabolic syndrome and grading of AGA. Timely intervention and lifestyle changes in male AGA patients can fulfil the ultimate objective of reducing cardiovascular complications in the future.

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Conflict of Interest

There are no conflicts of interest.

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