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Metabolic Syndrome in Androgenetic Alopecia in a Tertiary Care Centre in Goa: A Case Control Study During COVID-19 Pandemic

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Abstract:

Background: Androgenetic alopecia (AGA) is a hereditary condition that results in the transformation of terminal hair on the scalp into smaller vellus hair in a distinct pattern. This condition affects nearly 80% of Caucasian men and 40% of Caucasian women. Although it can start during puberty, its prevalence increases with age. Circulating androgens, such as dihydrotestosterone (DHT), penetrate the follicle via the capillaries of the dermal papilla (DP), attach to the androgen receptor within the DP cells, and subsequently activate or inhibit molecular signalling pathways that lead to follicular miniaturization and an early shift from anagen to catagen. Symptoms of metabolic syndrome (MetS) include increased waist circumference, elevated triglycerides (TG), reduced high-density lipoprotein-C (HDL-C), heightened fasting blood glucose, and increased blood pressure. Despite the high prevalence of AGA and MetS in India, there is a lack of accurate data on the issue. The medical literature contains only a few studies, and there is no precise information regarding this association within the Indian population.

Aims & Objectives: The objective of this study was to investigate the relationship between androgenetic alopecia and metabolic syndrome, as well as to compare it with a healthy control group.

Methods: This was a prospective case control study done over a period of 3 months from patients visiting the Outpatient Department of Dermatology, Venereology and Leprosy of a tertiary care centre in western India during COVID-19 pandemic with 54 cases of AGA and 54 age and sex-matched controls. The criteria updated according to the joint consensus of 2009 were employed for the diagnosis of MetS. We categorized the patients of androgenetic alopecia into two categories in our study as normal to mild AGA and moderate to severe AGA.

Results: Out of 54 cases, 16.7% (n=9) were females & remainder were males. The most commonly affected age group was less than 30 years. Family history was positive in 88.9% of the patients out of which 38.9% (n=21) of the patients had only positive paternal history of AGA. Sedentary behaviour (physical activity less than 30 minutes daily) was present in 24.1% (n=13) of the patients. Norwood Hamilton grade V was the most common grade of AGA among male patients. Prevalence of metabolic syndrome in patients with AGA i.e., the cases group was 40.7% & that in the control group was 14.8%. Comparison of prevalence of metabolic syndrome between two groups showed higher prevalence in the cases group which was statistically significant with a p value of 0.003 ($p<0.05$).

Conclusion: We believe that by finding positive association of metabolic syndrome with androgenetic alopecia we can emphasize the patients with androgenetic alopecia to screen themselves for components of metabolic syndrome as well as metabolic syndrome in order to prevent or delay the adverse future

outcomes occurring as a consequence of metabolic syndrome or its components by undertaking in necessary lifestyle modifications & treatment wherever necessary.

Keywords: Androgenetic Alopecia, Metabolic Syndrome, COVID-19 Pandemic.

Introduction

Alopecia is taken from the Greek term Alopekia, which is derived from the word Alopek, which means fox. Hair loss, miniaturization, involution, or increased fragility at all hair-bearing sites such as the scalp, face, eyebrows, eyelashes, and body are all examples [1]. The phrase 'pattern hair loss' refers to a type of hair loss that follows a recognizable pattern and is defined by a gradual decrease in hair fibre synthesis by scalp hair follicles and eventual shrinkage [1]. Androgenetic alopecia (AGA) is a hereditary physical feature caused by the conversion of terminal hair on the scalp into shrunken vellus hair in a specific pattern [2]. It affects up to 80% of Caucasian men and 40% of Caucasian women [3]. Despite the fact that it can begin at puberty, its frequency rises with age [2,3]. Circulating androgens, such as dihydrotestosterone (DHT), enter the follicle through the dermal papilla's (DP) capillaries, bind to the androgen receptor within the DP cells, and then activate or repress molecular signalling pathways that cause follicular miniaturization and premature transition from anagen to catagen [4].

Classification with clinical overlap and gender-specific traits (Norwood–Hamilton classification for males and Ludwig classification for women) [5]. Increased waist circumference, higher triglycerides (TG), decreased high-density lipoprotein-C (HDL-C), elevated fasting blood glucose, and blood pressure are all symptoms of the metabolic syndrome (MetS). Despite the significant prevalence of AGA and MetS in India, there is a scarcity of precise data on the problem. There are only a few studies in the medical literature, and there is no exact data on this association in the Indian population. The goal of this study was to look at the link between androgenetic alopecia and metabolic syndrome, as well as compare it to a healthy control group.

Methods

Study Design and Setting

This was a single centre, prospective case control study done over a period of 3 months from patients visiting the Outpatient Department of Dermatology, Venereology and Leprosy of a tertiary care centre in western India during COVID-19 pandemic. The study period extended from March 2021 to May 2021.

Ethical Approval and Consent

The study protocol was reviewed and approved by the Institutional Ethics Committee of Goa Medical College (Approval No. GMCIEC/2020/15), in accordance with the ethical principles outlined in the Declaration of Helsinki (2013 revision). Written informed consent was obtained from all participants or their legally authorized representatives prior to enrolment. Strict confidentiality was maintained, and all data were anonymized prior to analysis to protect participant privacy.

Study Population

A detailed history was elicited, and thorough clinical examination was done of every patient, recorded in a specially prepared proforma. Informed consent was taken from all the patients included in the study.

Patients in age group 18-55, males as well as females who were clinically diagnosed AGA as per relevant grading system and were willing to do biochemical tests were included in the study. Patients above 55 years of age, patients receiving hormone replacement therapy with testosterone, those on systemic corticosteroid therapy, those with hypothyroidism & Psoriasis were excluded from the study. All patients had a full history obtained using the usual questionnaire, with an emphasis on the history of hair fall, its origin, duration, any related symptoms (itching, discomfort in the scalp, scaling of the scalp), and any exacerbating circumstances. Diabetes, hypertension, hypothyroidism, and hyperthyroidism were all mentioned in the history. History of taking any oral or topical medication was taken. Hair loss in the family was documented in the father/mother, brother/sister, uncle/aunt. A comprehensive clinical examination was performed. Pallor, icterus, cyanosis, clubbing, edema, lymphadenopathy, seborrheic dermatitis, folliculitis, or any other scalp disease or infection were all checked for. Acne, hirsutism, acanthosis nigricans, and other symptoms of hyperandrogenism were examined on the skin. The pattern of hair loss was documented and classified appropriately, using the Hamilton Norwood/Ludwig/Olsen classification system. Hamilton Norwood grade IV of AGA represents the starting grade of severe frontal AGA concurrent with vertex AGA. Therefore, AGA was divided into two categories, normal to mild AGA as severity 1 -Hamilton Norwood grades I-III and Ludwig classification grade I and moderate or severe AGA as severity 2 -Hamilton Norwood grades IV-VII and Ludwig classification grade II-III respectively, to assess its association with other potential risk factors. Each patient underwent a hair pull test, which was followed by trichoscopy using a contact non-polarized dermo scope at 10-fold magnification at hair loss sites in all patients, which was compared to the occipital region (served as control region). The frontal and occipital (control) regions of each patient's trichoscopic pictures were examined for typical distinguishing features. The relative dermoscopic difference in hair related factors in the frontal and occipital areas were solely recorded because pattern hair loss mostly affects the frontal scalp. Patients with identical occipital and frontal dermoscopic findings were assumed to have telogen effluvium rather than FPHL/MPHL and were therefore excluded from the study. From hospital patients and attendants, age-matched controls without a history of hair loss were recruited. The controls were enlisted at the same time as the patients and were subjected to the identical exclusion criteria.

Anthropometric data was recorded from all participants which included Height (in centimetres) Weight (in kilograms) and Waist Circumference (in centimetres) [At the end of a normal expiration, the waist circumference was measured at the midpoint between the lower edge of the last perceptible rib and the top of the iliac crest using a non-stretchable tape]. Blood pressure (BP) i.e., systolic blood pressure (SBP) & diastolic blood pressure (DBP) was measured of all participants using a mercury sphygmomanometer apparatus in sitting position after 5 min & 10 min rest mean blood pressure was then recorded in the study proforma. Blood samples were collected from all enrolled patients after an overnight fast and the following investigations were performed: Complete blood Counts, Fasting blood sugar levels (FBSL), Complete lipid profile.

The metabolic syndrome (MetS) was diagnosed according to Harmonized Definition [6] i.e. presence of three or more of following: Obesity based on waist circumference based on geographic & ethnic specific i.e., ≥ 90cm for males & ≥80 cm for females, Dyslipidaemia based on either HDL-C <40 mg/dl in males, <50 mg/dl in females; TG ≥150 mg/dl or treated, Hyperglycaemia based on FBSL ≥ 100 mg/dl or treated and Hypertension based on SBP ≥130 mmhg & DBP ≥85 mmhg or treated

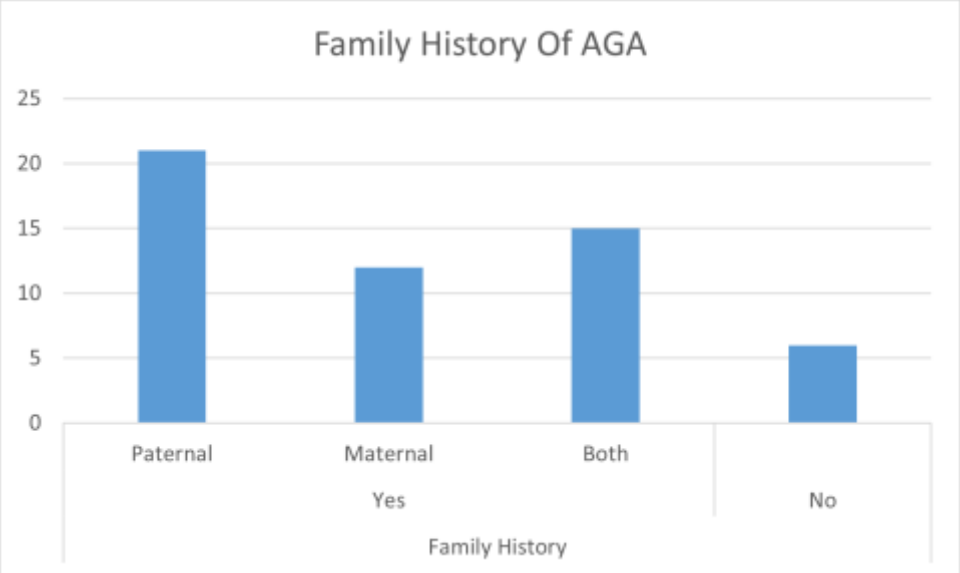
We categorized the patients of androgenetic alopecia into two categories in our study similar to a study done by KCD Kumar et al [7], Yi et al [8] & Tilwani MR et al [9]: normal to mild AGA and moderate to

severe AGA. Severity 1 is determined by Hamilton Norwood grades I-III and Ludwig categorization grade I& moderate to severe AGA i.e., severity 2 by Hamilton Norwood grades IV-VII and Ludwig classification grades II-III, respectively, to see if it's linked to other risk factors as well as to determine relationship of metabolic syndrome with severity of androgenetic alopecia.
Results were tabulated in excel sheet and statistical analysis was performed using SPSS version 26, using chi square test for categorical data & independent t test for continuous variables. Statistical significance was set at P value of < 0.05.

Results

In our research, the number of males exceeded that of females. Approximately 83.3% of both the cases and controls examined were males, while 16.7% were females. The male to female ratio among cases and controls was 5:1.
The largest proportion of cases and controls were from the age group of under 30 years (35.2%). The average age of the patients involved in the study was 36±10.07 years, and the average age at which symptoms began was 28.44±7.53 years. Almost 68.5% of the cases fell into severity category 2 (moderate or severe AGA), while 31.5% were classified as severity category 1 (normal-to-mild AGA).

Figure 1: Family History of Androgenetic Alopecia in Cases



AGA: Androgenetic Alopecia
Y axis: Number of Cases, X axis: Family History

The differences in diastolic blood pressure, triglyceride levels, and fasting blood sugar levels were statistically significant between the cases and controls, as illustrated in Table 1. The occurrence of MetS in the cases (40.7%) was statistically significant when compared to the controls (14.8%) (P < 0.003).

Table 1: Mean ± Standard Deviation and P Value of Metabolic Syndrome Parameters in Cases and Controls

Parameter	Cases	Controls	P Value
SBP	121.04 ± 10.3	125.04 ± 11.27	0.057
DBP	79.44 ± 8.36	82.89 ± 7.09	**0.023**
TG	107.59 ± 29.09	149.65 ± 80.37	**0.001**
HDL	46.7 ± 10.11	43.56 ± 9.38	0.096
FBSL	87.63 ± 12.3	95.43 ± 21.02	**0.02**
WC	82.74 ± 7.93	85.65 ± 8.63	0.071

Metabolic Syndrome parameters compared using Independent Samples t-test (Two-Sample t-test), threshold for statistical significance p value < 0.05
SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, TG: Triglycerides, HDL: High-density lipoproteins, FBSL: Fasting blood sugar levels, WC: Waist Circumference.
The systolic blood pressure, diastolic blood pressure, TG levels, HDL levels, and FBSL values in severity 2 cases were found to be statistically non-significant when compared to severity 1 cases, as illustrated in Table 2. The occurrence of MetS in severity 2 cases (72.7%) was also statistically non-significant in comparison to severity 1 cases (27.3%) (P = 0.581, P < 0.05).

Table 2. Mean ± Standard Deviation and P value of Metabolic Syndrome Parameters in Severity 1 Cases and Severity 2 Cases

Parameter	Cases		P Value
	Severity 1	Severity 2	
SBP	123.06 ± 12.77	125.95 ± 10.57	0.387
DBP	81.53 ± 7.95	83.51 ± 6.67	0.344
TG	145.94 ± 54.85	151.35 ± 90.35	0.319
HDL - males	43.29 ± 8.36	42.90 ± 10.00	0.901
HDL - females	48.33 ± 7.51	45.17 ± 10.44	0.745
FBSL	91.18 ± 11.30	97.38 ± 24.11	0.821
WC - males	84.79 ± 9.31	87.52 ± 8.14	0.698
WC - females	79.00 ± 5.57	81.33 ± 9.00	0.324

Metabolic Syndrome parameters compared using Independent Samples t-test (Two-Sample t-test), threshold for statistical significance p value < 0.05
SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, TG: Triglycerides, HDL: High-density lipoproteins, FBSL: Fasting blood sugar levels, WC: Waist Circumference.

Discussion

The link between androgenetic alopecia and metabolic syndrome has been studied extensively within the past. However, the outcomes were mixed. The aim of our study was to work out whether patients with androgenetic alopecia had metabolic syndrome, also to examine metabolic syndrome parameters in cases and controls & compare the same with severity of androgenetic alopecia.

In this study, hypertension, hyperlipidaemia, fasting blood glucose levels, and the various grades of androgenetic alopecia according to the Hamilton Norwood classification in males and the Ludwig classification in females were investigated in 54 cases diagnosed with androgenetic alopecia and 54 controls without androgenetic alopecia. Blood investigations were performed on both the cases and the controls to determine HDL levels, triglyceride levels, and fasting blood sugar levels, as well as anthropometric measurements.

The age of onset of hair loss in our study was roughly 28.44±7.53 and the age group involved was 36±10.07, which was close to the age group in the study by Acibucu F et al [10], which was 36.280 ± 7.74. Males outnumbered females in our study. Males made up 83.3 percent of the cases and controls analysed, while females made up 16.7%. In all cases and controls, the male to female ratio was 5:1. KCD Kumar et al [7] had reported a male participant of 64% & female participants of 36% with male to female ratio of 1.78:1. The reason for higher ratio in our study could be hypothesized mainly due to smaller sample participants in our study which could be attributed to lack on part of patients to visit healthcare facilities for nonemergency conditions owing to covid 19 pandemic which was rampant in the country during the study period & also non-willingness on part of patients to follow up with biochemical investigations due to the same.

Of the 54 patients with AGA 6 patients (11.1%) did not have any family history of AGA whereas the remaining patients had family history of AGA 48 (88.9%) which was statistically significant similar to findings reported by Bakry et al [11] and Arias-Santiago et al [12] in their study. We found a higher percentage of paternal history of AGA (38.9%) followed by combined paternal along with maternal history of AGA (27.8%) with maternal history of AGA being positive in 22.2% of patients. This was contrary to the findings of Chumlea et al [13] where they had found a higher percentage in the combined group followed by maternal & then paternal history of AGA. The reason for such contrary findings in our study we believe could be due to a limited sample size when compared to their study & also could be due to the difference in ethnicity in our study population.

In our study the value of systolic blood pressure was statistically non-significant between cases & controls. In contrast to our findings, Arias-Santiago et al [12], S Chakrabarty et al [14], Ola Ahmed Bakry et al [11] & KCD Kumar et al. [7] had found statistical significance when cases were compared to controls. The reason for statistical non-significance in our study could be attributed to mainly to a lower sample size in our study due to covid 19 pandemic as well as also due to major clustering of cases & controls below 30 years of age followed by below 40 years of age as it is a well-known fact that risk of hypertension increases progressively with age due to other risk factors as well as confounding factors acting in synergism to lead to development of systemic hypertension. However, the difference in diastolic blood pressure between

patients and controls was statistically significant in our study. Regarding diastolic BP, Arias-Santiago et al [12], S Chakrabarty et al [14], and Ola Ahmed Bakry et al [11] all showed similar findings. Hirsso et al. [15] observed a strong link between AGA and hypertension in a population-based study of AGA patients. The endothelium of the arterial wall contains androgen-mediated receptors. Increased serum testosterone levels in AGA patients [16] contribute to smooth muscle cell proliferation in Vessels [17] and raise the risk of hypertension [18]. Another reason for this link is androgen binding to mineralocorticoid receptors, which raises blood pressure [19] or enhances peripheral sensitivity to androgens despite normal circulating levels [20]. When compared to the controls, the value of fasting blood sugar levels in cases was statistically significant. Ola Ahmed Bakry et al [11] found a similar outcome in their study. When compared to controls, the value of triglycerides in cases was statistically significant in our study. Acibucu F et al [10], S Chakrabarty et al [14], Ola Ahmed Bakry et al [11] & KCD Kumar et al. [7] all found similar results.

When compared to controls, the value of high-density lipoprotein in cases was statistically significant in our sample of males, which was similar to study by S Chakrabarty et al [14], Ola Ahmed Bakry et al. [11]. When cases were compared to controls, Arias-Santiago et Al [12] did not find statistical significance, contrary to the findings of Acibucu F et al [10] & KCD Kumar et al. [7]. Many experimental studies have shown that androgens lower HDL-C levels [21]. The transition from atheroma to atherothrombosis was related with higher TGs and lower HDL-C levels. As a result, early assessment and adjustment of lipid profiles in individuals with AGA is critical in lowering this risk [22]. The value of high-density lipoprotein in cases was statistically non-significant in females when compared to controls. Similar findings were reported by Arias-Santiago et al [12] in their study when cases were compared to controls, there was no statistical significance. The reason for statistical non-significance for value of high-density lipoprotein in case of females could be attributed to lesser number of female participants in our study as well as it is well-known fact that females tend to have higher HDL levels in general due to effects of estrogen which are in higher amounts in females when compared to males.

When compared to the controls, the value of waist circumference in cases was statistically non-significant in men in our study.

In contrast to the findings of Arias-Santiago et al. [9], Acibucu F et al. [10], Ola Ahmed Bakry et al. [11] & KCD Kumar et al. [7], where the mean waist circumference in patients was found to be statistically significant. In females also, the difference in waist circumference between cases and controls was not statistically significant in our study. Similar findings were reported by KCD Kumar et al. [7] in their study. In contrast to our findings, Arias-Santiago et al [12] found that the mean waist circumference in cases was statistically significant even in females. The reasons for non-significant waist circumference in our study in males as well as females we believe may be due to lack of sedentary behaviour in our participants i.e., only 13 (24.1%) patients of AGA & 5 (9.3%) controls had a sedentary behaviour (< 30 mins of daily physical activity) whereas rest had non-sedentary behaviour & it is a known fact that a sedentary behaviour has been linked to greater waist circumference values & higher BMI values. Metabolic syndrome was found to be strongly linked to AGA cases in our study. When compared to the control group (14.8 percent), the prevalence of metabolic syndrome in patients (40.7 percent) was statistically significant ($p = 0.003$, $p < 0.05$). Acibucu F et al. [9], S Chakrabarty et al. [14], Arias-Santiago et al. [12], Ola Ahmed Bakry et al. [11] & KCD Kumar et al. [7] all found similar results. There was no statistically significant difference between the cases and controls, in findings of Mumcuoglu C et al. [23].

To our knowledge, this is the first study in the Goan population to look at the relationship between metabolic syndrome and its characteristics and the severity of AGA. However, similar studies have been done in the Indian population & elsewhere [7,8,9]. We categorized the patients of androgenetic alopecia into two categories in our study similar to a study done by KCD Kumar et al [7], Yi et al [8] & Tilwani MR et al [9]: normal to mild AGA and moderate to severe AGA. Severity 1 is determined by Hamilton Norwood grades I–III and Ludwig categorization grade I& moderate to severe AGA i.e., severity 2 by Hamilton Norwood grades IV–VII and Ludwig classification grades II–III, respectively, to see if it's linked to other risk factors. 31.5% of the patients analysed were classified as severity 1(normal to mild AGA), whereas 68.5% were classified as severity 2. (Moderate to severe AGA). The reason for such categorization was to compare the severity of androgenetic alopecia with metabolic syndrome as well as to compare the severity of AGA with individual risk factors of metabolic syndrome to determine if severity of alopecia makes an individual at greater risk for developing metabolic syndrome or its components i.e., if greater severity of alopecia is linked to more likelihood of developing metabolic syndrome. We did not find statistically significant differences in values of Systolic blood pressure, diastolic blood pressure, triglycerides, high density lipoprotein, waist circumference & prevalence of metabolic syndrome between severity 1 & severity 2 in our study. Similar findings were reported by Yi et al [8] in their study in male participants however they had reported significant association in their female participants which we did not have in our study.

KCD Kumar et al [7] had however reported statistically significant association in systolic blood pressure, diastolic blood pressure, triglyceride & prevalence of metabolic syndrome. Tilwani MR et al [9] had reported statistically significant association in hypertension, fasting blood glucose, HDL & abdominal obesity in their study. We believe the reason for non-significance in the above parameters in our study could be attributable to a lower sample size owing to frequent shut down of OPDs due to COVID-19 pandemic during the timeframe of the study & lack of willingness on part of patients to follow up with biochemical investigations due to which the same did not fit into selection criteria & were excluded from the study.

Conclusion

Association of metabolic syndrome with androgenetic alopecia has been tested in various studies across the world with mixed outcome & with very few studies done in Indian setting involving both males as well as female participants. Through our study we intended to find if association exists between metabolic syndrome & androgenetic alopecia involving mixed participants i.e., male as well as female patients. Through our study we have found that a positive association exists between metabolic syndrome & androgenetic alopecia in context of Goan population presenting to our tertiary care centre.

However, we could not establish association between severity of androgenetic alopecia & metabolic syndrome due to constraints involved because of Covid-19 pandemic during study period.

We believe that by finding positive association of metabolic syndrome with androgenetic alopecia we can emphasise the patients with androgenetic alopecia to screen themselves for components of metabolic syndrome as well as metabolic syndrome in order to prevent or delay the adverse future outcomes occurring as a consequence of metabolic syndrome or its components by undertaking in necessary lifestyle modifications & treatment wherever necessary

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