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Metabolic Syndrome in Patients with Androgenetic Alopecia in a Tertiary Care Hospital.

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Abstract

Background: Androgenetic alopecia (AGA) is a hereditary androgen-dependent disorder, characterized by a progressive decline in hair fibre production by scalp hair follicles and their eventual miniaturization. Metabolic syndrome is a cluster of inter-related risk factors that increase the risk of coronary artery disease. Despite the high burden of Androgenetic Alopecia and Metabolic Syndrome in India, specific data on the participants are relatively sparse.

Methods: A total of 126 patients of androgenetic alopecia (age range 18-55 years; mean age 30.83±10.37 years; 83.3% males) falling in sampling frame were enrolled in the study and were assessed clinically, anthropometrically and biochemically. Metabolic syndrome was diagnosed using Joint interim statement of International Diabetes Federation, National Heart, Lung and Blood Institute, American Heart Association, World Health Federation, International Atherosclerosis Society, and International Association of the Study of Obesity criteria.

Results: Prevalence of Metabolic Syndrome (MetS) was 29.4% in 126 cases of Androgenetic Alopecia. The P Value was <0.001 for obesity (52.4%), hypertension (35.7%), low HDL cholesterol (21.4%), hypertriglyceridemia (13.5%) and high fasting glucose (12.7%) respectively. Patients with higher severity grade of AGA had significantly higher prevalence of MetS and its components.

Conclusions: Metabolic Syndrome showed a positive relation with Androgenetic Alopecia. Early screening for Metabolic Syndrome is beneficial in patients with androgenic alopecia to prevent them from developing coronary artery disease.

Key words: Alopecia, Metabolic syndrome, Obesity, Hypertension, Diabetes, Sedentary.

Introduction

Androgenetic alopecia (AGA) is the most common cause of hair loss affecting both males and females. It is characterized by progressive loss of terminal hair of the scalp during the lifetime after the attainment of puberty. The most common age of onset remains to be the third and fourth decades of life. It is a disease of progressive nature[1,2,3]. Males have been reported to be affected almost four times higher as compared to females according to an Indian study[4].

The male-pattern hair loss is characterized by loss of hair in vertex and frontotemporal regions. On the other hand, in females, there is diffuse hair loss especially at the crown and top of the head affecting a wider central part whereas frontal hairline remains intact[2].

AGA is a genetic disorder in which miniaturization of hair follicle takes place under the influence of androgen[5,6]. According to Rebora, the pathogenesis of AGA could be considered to be guided by three mechanisms, viz., "miniaturization by a dihydrotestosterone-induced acceleration of the mitotic rate of the matrix that leaves less and less time for differentiation; an increased telogen shedding as a result of the shortening of the hair cycles that increases the telogen number per unit of time; and the increased number and duration of the lag phase or kenogen[7].

AGA patients have also been found to have a high prevalence of cardiovascular and metabolic risk factors like obesity, hypertension, lipid levels and insulin resistance[8,9]. These cardiovascular and metabolic risk factors together comprise a condition termed as metabolic syndrome.

Metabolic syndrome (MetS) is described as a combination of some clinical factors that together reflect metabolic disorders of different types. There are multiple criteria to define metabolic syndrome. Two widely used criteria for identifying metabolic syndrome are National Cholesterol Education Programme (NCEP) ATP-III[10], International Diabetic Federation (IDF)[11]. In the present study we have used Joint interim statement of International Diabetes Federation, National Heart, Lung and Blood Institute, American Heart Association, World Health Federation, International Atherosclerosis Society, and International Association of the Study of Obesity criteria for Metabolic Syndrome[12]. We used Joint statement criteria in order to make it more inclusive while taking into consideration waist circumference instead of body mass index, as waist circumference provides a better measure of central obesity.

The present study was planned to assess the prevalence of MetS among patients with AGA and to find out an association between different grades of AGA and MetS and its components at a tertiary care centre in North India.

Methods

After obtaining clearance from the Institutional Ethical Committee, Era's Lucknow Medical College & Hospital, Lucknow, the present study was carried out as a cross-sectional observational study on 126 patients attending the OPD of Dermatology department at Era's Lucknow Medical College & Hospital over a period of 24 months. All patients aged 18-55 years with a diagnosis of AGA were recruited in the study. Patients with AGA coexisting with other causes of alopecia, on hormonal therapy and pregnant or breastfeeding females were excluded from the study. The included patients of AGA were examined and graded as per Hamilton-Norwood grading for males and Ludwig grading for females. For assessment of all the patients a combined grading for AGA severity was formed where patients with grade < 2 on Ludwig and grade ≤ 3 on Norwood-Hamilton were classified as Low-grade severity and those with Ludwig grade ≥ 2 and Norwood-Hamilton grade ≥ 4 were classified as High-grade severity. Physical examination was done to assess waist circumference, height, weight, blood pressure. Collection of venous blood sample for fasting blood sugar and lipid profile after 12 hours overnight fast was done. Patients were defined as MetS by using the Joint interim statement of International Diabetes Federation, National Heart, Lung and Blood Institute, American Heart Association, World Health Federation, International Atherosclerosis Society, and International Association of the Study of Obesity criteria for MetS. Data was analyzed using SPSS 21.0 Software and has been represented as Mean±SD and Numbers (%). Chi-square test has been used for categorical and Independent 't'-test was used for comparison of continuous data.

Results

A total of 126 diagnosed patients of AGA were enrolled in the study. Age of patients enrolled in the study ranged between 18 to 55 years, with a mean age of 30.83±10.37 years. Majority of the patients were aged 21-40 years (72.3%). Only

7.9% were aged ≤20 years and 6.3% were aged >50 years (Table 1). Out of 126 patients, 105 (83.3%) were males, rest 21 (16.7%) were females. Majority of the patients were engaged in active occupations, 24.6% had sedentary occupation and rest 21.4% were engaged in occupations with moderate activity. Out of 21 females enrolled in the study, majority of females (81.0%) reported abnormal menstrual status (Table 2).

Receding hairline (82.5%) was the most common presenting complaint, 35.7% presented with complaints of hair thinning, 17.5% had partial baldness. Few patients presented with combination of above presenting complaints (Table 3).

Female patients were assessed using Ludwig Grade and it was found that 57.1% had Grade 1 AGA, 33.3% had Grade 2 AGA and 9.5% had Grade 3 AGA (Table 4). Among the male patients using Norwood-Hamilton grading, 71.4% had Grade ≤3 and 28.6% patients had Grade >3 (Table 5). As per the combined grading of AGA severity of the patients, 69% had low-grade while 31% had high-grade AGA severity (Table 6).

Most common MetS component in the present study was Obesity (52.4%) followed by Hypertension (35.7%). Low HDL cholesterol, high fasting blood glucose and hypertriglyceridemia were observed in 21.4%, 12.7% and 13.5% respectively (Table 7). Out of 126 patients, 37 (29.4%) patients had MetS, rest of the 89 patients did not fulfil the defined criteria of MetS (Table 8).

Upon comparing the variables of patients with MetS and those without Mets it was found that the anthropometric characteristics significantly associated with MetS patients was larger waist circumference (100.19±7.81 vs. 87.74±8.31 cm), and higher BMI (27.68±2.77 vs. 23.20±3.16 kg/m^2) (Table 9). Hemodynamic parameters significantly associated with MetS were higher systolic and diastolic blood pressure. Biochemical/lipid parameters showing significant association were higher fasting blood glucose, triglyceride levels, lower HDL levels in quantitative terms as well as raised total cholesterol (21.6% vs. 6.7%), raised LDL (16.2% vs. 2.2%), VLDL (18.9% vs. 3.4%), dyslipidemia (8.1% vs. 0.0%) in qualitative terms (Table 10). MetS also showed significant association with presence of type 2 diabetes (21.6%). Significantly higher proportion of High-Grade AGA patients as compared to Low-Grade had metabolic syndrome (46.2% vs. 21.8%).

Table 1: Age, Sex and other Demographic Profile of study population

SN	Variable	No. of cases	Percentage
1.	Age (in years)		
	≤20	10	7.9
	21-30	68	54.0
	31-40	23	18.3
	41-50	17	13.5
	>50	8	6.3
2.	Sex		
	Males	105	83.3
	Female	21	16.7
3.	Occupation		
	Sedentary activity	31	24.6
	Moderate activity	27	21.4
	Active	68	54.0

Table 2: Distribution of female patients according to complaints of menstrual irregularity (n=21)

SN	Menstrual irregularity	No. of cases	Percentage
1.	Yes	17	81.0
2.	No	4	19.0

Table 3: Distribution of Cases according to presenting complaints (n=126)

SN	Complaints	No. of cases	Percentage
1.	Receding hairline	104	82.5
2.	Hair thinning	45	35.7
3.	Partial baldness	22	17.5

Table 4: Distribution of Cases according to AGA Severity – Ludwig Grade among females (n=21)

SN	Ludwig Grade	No. of cases	Percentage
1.	Grade 1	12	57.1
2.	Grade 2	7	33.3
3.	Grade 3	2	9.5

Table 5: Distribution of Cases according to AGA Severity – Norwood-Hamilton grade in males (n=105)

SN	NH Grade	No. of cases	Percentage
1.	NH Grade ≤3	75	71.4
2.	NH Grade >3	30	28.6

Table 6: Distribution of Cases according to Combined Grading of AGA severity (n=126)

SN	Combined AGA grade	No. of cases	Percentage
1.	Low (Ludwig grade 1 or NH grade ≤3)	87	69.0
2.	High (Ludwig grade ≥2 or NH grade ≥4)	39	31.0

Table 7: Distribution of cases according to Prevalence of different metabolic syndrome components (n=126)

SN	Component	No. of cases	Percentage
1.	Obesity	66	52.4
2.	Hypertension	45	35.7
3.	High fasting blood glucose	16	12.7
4.	Hypertriglyceridemia	17	13.5
5.	Low HDL cholesterol	27	21.4

Table 8: Distribution of cases according to Metabolic Syndrome (MetS) status (n=126)

SN	Group	No. of cases	Percentage
1.	No MetS	89	70.6
2.	MetS	37	29.4

Table 9: Comparison of MetS and Non-MetS patients for different demographic and clinical variables

SN	Variable/ Parameter	MetS (n=37)		Non-MetS (n=89)		Statistical significance	
		Mean	**SD**	**Mean**	**SD**	**'t'**	**'p'**
1.	Mean age	39.11	10.47	27.38	8.19	6.723	**<0.001**
2.	Male:Female	29 (78.4%): 8 (21.6%)		76 (85.4%): 13 (14.6%)		χ^2=0.926; p=0.336	
3.	Marital status Married	31 (83.8%)		35 (39.3%)		χ^2=20.71; **p<0.001**	
4.	Rural:Urban	29 (78.4%): 8 (21.6%)		51 (57.3%): 38 (42.7%)		χ^2=5.008; **p=0.025**	
4.	Sedentary occupation	10 (27.0%)		21 (23.6%)		χ^2=0.424; p=0.515	
5.	Irregular menstrual history	8/8 (100%)		9/13 (69.2%)		χ^2=3.041; p=0.081	
6.	Chief complaint						
	Receding hairline	29 (78.4%)		73 (82.0%)		χ^2=0.225; p=0.635	
	Hair thinning	20 (54.1%)		35(39.3%)		χ^2=2.010; p=0.156	
	Partial baldness	10 (27.0%)		12 (13.5%)		χ^2=3.327; p=0.068	
7.	WC (cm)	100.19	7.81	87.74	8.31	7.793	**<0.001**
8.	SBP (mmHg)	134.30	14.39	118.76	9.75	7.030	**<0.001**
9.	DBP (mmHg)	86.32	6.36	77.13	5.62	8.037	**<0.001**
10.	FBS (mg/dl)	97.93	17.45	87.27	5.23	5.247	**<0.001**
11.	TG (mg/dl)	139.62	19.46	113.88	25.91	5.435	**<0.001**
12.	HDL (mg/dl)	45.60	10.61	54.55	10.30	4.387	**<0.001**
13.	Raised TC	8 (21.6%)		6 (6.7%)		χ^2=5.86; **p=0.015**	
14.	Raised LDL	6 (16.2%)		2 (2.2%)		χ^2=8.577; **p=0.003**	
15.	Raised VLDL	7 (18.9%)		3 (3.4%)		χ^2=8.65; **p=0.003**	
16.	Diabetic history	8 (21.6%)		0		χ^2=20.55; **p<0.001**	
17.	Dyslipidemia	3 (8.1%)		0		χ^2=7.39; **p=0.007**	
18.	AGA Severity Low grade	19 (51.4%)		68 (76.4%)		χ^2=7.675; **p=0.006**	
19.	AGA Severity High grade	18 (48.6%)		21 (23.6%)		χ^2=7.675; **p=0.006**	
20.	Smoking/Alcohol/ Tobacco use	8 (21.6%)		19 (21.3%)		χ^2=0.001; p=0.979	
21.	Family history	21 (56.8%)		56 (62.9%)		χ^2=0.418; p=0.518	
22.	Mean BMI±SD (kg/m^2)	27.68±2.77		23.20±3.16		t=7.502;**p<0.001**	

Table 10: Association of AGA Grades with MetS and its components

SN	Factor	Low AGA Grade (n=87)	High AGA Grade (n=39)	Statistical significance
1.	Metabolic syndrome	19 (21.8%)	18 (46.2%)	χ^2=7.675; p=0.006
2.	Central obesity	40 (46.0%)	26 (66.7%)	χ^2=4.621; p=0.032
3.	Hypertriglyceridemia or under medication for Dyslipidemia	22 (25.3%)	23 (59.0%)	χ^2=13.31; p=0.001
4.	Low HDL cholesterol	6 (6.9%)	10 (25.6%)	χ^2=8.535; p=0.003
5.	Hypertension	8 (9.2%)	9 (23.1%)	χ^2=4.446; p=0.035
6.	Fasting blood glucose or under medication or previously diagnosed Type 2 Diabetes	19 (21.8%)	8 (20.5%)	χ^2=0.028; p=0.867

Discussion

Androgenetic alopecia (AGA) is a common form of hair loss that affects both men and women. Androgens, particularly dihydrotestosterone (DHT), have been implicated in the pathogenesis of AGA. Androgens are known to have versatile roles including a participative role in generating chronic inflammation, oxidative stress, and adipokines. Comorbidities, particularly metabolic comorbidities have been reported to be very common in AGA patients[8,9].

Although, relationship between AGA and MetS has been well established in many clinical studies yet its clinical presentation and association with severity of AGA has not been widely studied. Hence the present study was planned to find out the prevalence of Metabolic Syndrome and its components in patients of Androgenetic Alopecia and to associate it with severity grades of AGA apart from identifying the potential risk factors responsible for this.

A cross-sectional study was carried out in which a total of 126 patients with AGA (both males as well as females) were enrolled. Mean age of patients in the present study was 30.83±10.37 years. Majority of them (83.3%) were males. Sex-ratio (M:F) was 5:1.

In the present study we used the Joint interim statement of International Diabetes Federation, National Heart, Lung and Blood Institute, American Heart Association, World Health Federation, International Atherosclerosis Society, and International Association of the Study of Obesity criteria for MetS. Most of the earlier studies have instead used NCEP ATP III criteria for this purpose[13,14]. Tomar *et al.*[15], however, preferred to use IDF criteria. We used Joint statement criteria in order to make it more inclusive while taking into consideration waist circumference instead of body mass index, as waist circumference provides a better measure of central obesity.

Prevalence of metabolic syndrome in the study population was 29.4% using Joint criteria. This is close to the MetS prevalence reported by Mustafa *et al.*[13] who reported it to be 30% using NCEP-ATP-III criteria. Most of the other workers also reported the prevalence of MetS in nearly one-quarter to one-third of AGA patients in their studies[14,15]. However, Sheikh *et al.*[16] in their study found the prevalence of MetS to be 11.9% only which is much lower than that in the present study but could be attributed to a relatively younger age profile (mean age 27.77 years) and male dominance (100%) in their study. Some other workers who also targeted male patients aged <30 years have reported the prevalence of MetS to be <15% in their studies[17]. A much higher prevalence of MetS in the study of Thakare and Singh[18] (50%) was reported despite a much younger age profile (mean age 24.04 years) which could be attributable to a relatively higher severity of disease (all patients AGA $\geq$3). Compared to these studies, in the present study majority of patients were of lower AGA severity grades (Ludwig grade 1 or Norwood-Hamilton grade 3 or less).

In the present study, obesity (52.4%) was the most common metabolic syndrome component followed by hypertension (35.7%), low HDL cholesterol (21.4%), hypertriglyceridemia (13.5%) and high fasting glucose (12.7%) respectively. Compared to the present study, Sheikh *et al.*[16] in their study found obesity (6.9%) and high fasting blood sugar (3%) as the least common metabolic syndrome factors whereas hypertriglyceridemia (13.9%), high blood pressure (10.9%) and low HDL (8.9%) were more common metabolic syndrome factors. Interestingly, despite overall low prevalence of different metabolic syndrome factors in their study as compared to the present study, the prevalence of hypertriglyceridemia in their study (13.9%) was comparable to the present study (13.7%). Compared to their study, higher prevalence of MetS factors, particularly obesity in the present study could be attributed to an older age profile and a mixed-gender study population in our study.

Older age, marriage and rural residence were found to be the sociodemographic variables significantly associated with MetS. However, we did not find a significant association of patient's sex and occupation/activity level with MetS prevalence.

Majority of male patients (n=60/105; 57.1%) had Norwood-Hamilton grade 3 or above whereas majority of female patients (n=12/21; 57.1%) had Ludwig grade 2. Overall majority of cases were either Ludwig Grade 1 or Norwood-Hamilton grade $\leq$3 (n=87; 69%). There was a significant association of higher AGA grade with MetS prevalence.

Conclusion

The findings of the study showed a high prevalence of metabolic syndrome and its components in AGA patients. The study identified older age, married life, rural residence, higher BMI, diabetes and dyslipidemia history and higher severity grade as the risk factors associated with it. The findings of the study showed the need to assess the AGA patients for metabolic disorders. Further studies on a larger sample size with inclusion of a control group of non-AGA patients are also recommended to assess the increased risk of MetS in AGA patients as compared to that in the non-AGA population in relative terms.

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