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EARLY-ONSET OF ANDROGENETIC ALOPECIA AND IT'S ASSOCIATION WITH METABOLIC SYNDROME IN YOUNG MEN.

Dermatology

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ABSTRACT

Background: Androgenetic alopecia is the most common cause of patterned hair loss. Early-onset AGA has been reported to be associated with metabolic diseases. **Aim:** To study the association of early-onset androgenetic alopecia with metabolic syndrome and insulin resistance in young men. **Methodology:** We enrolled 100 male cases of AGA (15 to 35 years of age) and 100 age and gender matched controls. Metabolic syndrome and Insulin resistance were derived by NCEP ATP-III and HOMA-IR. **Results:** The most common grade of AGA was grade II and 57% cases had positive family history of AGA. The MS and IR were more in the AGA as compared to the control group, however, the difference between the two groups was statistically non-significant **Conclusions:** AGA associated with significantly higher mean value of serum triglyceride, systolic and diastolic BP, waist circumference and low HDL-Cholesterol. This may contribute towards developing cardiovascular disease in patients with early-onset AGA.

KEYWORDS

Androgenetic alopecia; Insulin resistance; Metabolic syndrome.

INTRODUCTION

The term "androgenetic alopecia" (AGA) was coined by Orentreich in 1960. Pattern hair loss in men is predominantly due to the combination of genetic predisposition and the effect of androgens. Early-onset AGA can be defined as if it developing before 35 years of the age. Metabolic syndrome (MS) is a constellation of various risk factors includes central obesity, hypertension, dyslipidemia, elevated blood sugar that leads to an increased risk of cardiovascular diseases and diabetes. Insulin resistance (IR) plays a major role in the pathophysiology of MS and could play an additional pathogenic role in the extreme miniaturization of hair follicles [1, 2]. The current study aims to see the association of early-onset AGA with MS and IR in young men.

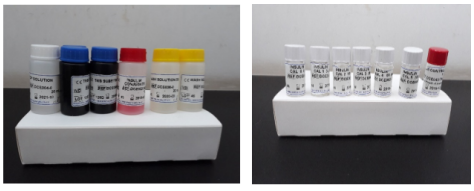
METHODS

We undersigned a single-center hospital based cross-sectional study of total 200 male participants in which 100 cases and 100 controls with the same age and gender attending the out-patient department of dermatology, venereology and leprosy (DVL) of a tertiary care hospital between April 2018 to March 2019 after taking approval from institutional review board (IRB). We included 100 new cases, clinically diagnosed for androgenetic alopecia and they were between the age group of 15-35 years. These were graded I to VII according to Norwood-Hamilton classification while healthy, same age and gender-matched subjects were taken as controls. Patients with history of thyroid, cardiovascular, renal disease, diabetes mellitus, familial hyperlipidemia, cancer, other immune related causes of alopecia and who receiving any treatment for androgenetic alopecia, local vasodilators (minoxidil), corticosteroid therapy were excluded in this study. After obtaining written informed consent, detailed clinical and family history of AGA were recorded in pre-structured performa.

A detailed dermatological and anthropometric examinations were carried out to determine the grading of AGA (according to Hamilton–Norwood classification of hair loss) [3] and metabolic syndrome (according to NCEP ATP-III criteria).

Body Mass Index (BMI) was calculated as the ratio of weight in kg to the square of height in m2 (Quetelet index). Waist circumference was measured at the midpoint between the lower margin of last palpable rib and top of the iliac crest, using non-stretchable measuring tape without causing compression of the skin, ensuring that the tape was horizontal. Blood pressure was recorded in the sitting position after rest for at least 20 minutes. The mean value for systolic and diastolic BP was calculated from the average of two readings.

A venous blood sample was taken in all cases and controls after 12 hours of overnight fasting, to estimate the serum level of fasting blood sugar, total cholesterol level, serum triglyceride, high density lipoprotein cholesterol, fasting insulin level by Insulin ELISA kit [Figure:1(a) reagent and (b) calibrators].



(a) (b)

Figure:1 Insulin ELISA kit [(a) reagent and (b) calibrators]

Modified National Cholesterol Education Program's Adult Treatment Panel III criteria (NCEP ATP III) was used to define metabolic syndrome, based on the presence of ≥3 criteria which include: (1) Waist circumference ≥ 102cm. (2) Triglyceride value ≥ 150mg/dl. (3) HDL-C <40mg/dl. (4) FBS ≥ 100mg/dl. (5) BP ≥ 130/85mm of Hg [4]. Insulin resistance – HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) was calculated using the updated model (fasting insulin (μIU/mL) x fasting glucose (mg/dl)/ 405) and value above 2.5 was considered to insulin resistance (IR) [5].

Statistical analysis- Data were analyzed using Graph-pad instat3 statistics software. All the quantitative parameters were derived as mean ± standard deviation, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Whereas categorical data was given as number and percentage. Mann-Whitney U test was performed for quantitative nonparametric distribution. Chi-square test was performed for categorical variables. Fisher exact test was used for 2 × 2 tables when expected cell count of >25% of cases was <5. Statistical significance was set at p-value of $p<0.05$ (two-tailed).

Results: The maximum number of subjects were between the age of 21-25 years (Table 1) and the most common grade of AGA was II (30%) and the least common grade was VII (2%) (Table 1).

Table 1: - Distribution of cases according to grade and age of AGA patients.

Age Group (yrs)	Grade of Androgenetic alopecia							Total
	Grade I	Grade II	Grade III	Grade IV	Grade V	Grade VI	Grade VII	
15-20	03	05	05	01	0	0	0	14
21-25	07	20	11	06	01	0	0	45
26-30	0	03	08	05	03	04	02	25
31-35	0	02	01	08	03	02	0	16
Total	10	30	25	20	07	06	02	100

The mean value of demographic data, anthropometric measurement and laboratory value (including components of metabolic syndrome and insulin resistance) in both cases and control groups were given in Table 2.

Table 2: - Comparison of AGA cases and control groups with respect to Mean (SD) value of demographic data, anthropometric measurement and laboratory value (including components of metabolic syndrome and insulin resistance).

Parameters	Case group Mean ± SD	Control group Mean ± SD	P-value (Mann-Whitney test)
Age (Years)	25.39 (±4.601)	24.59 (±4.701)	0.1553
Weight(kg)	61.08 ±15.037	56.40 ±10.722	0.0027*
Height (cm)	168.82 ±11.399	170.28 ±6.128	0.5715
BMI (kg/m2)	21.01 ±3.659	19.44 ±3.191	0.0012*
S. Cholesterol(mg/dl)	182.08 ±44.869	162.61 ±34.676	0.0025*
S. Triglycerides (mg/dl)	111.77 ±49.224	95.78 ±49.930	0.0055*
HDL-C (mg/dl)	49.47 ±10.198	51.8 ±7.640	0.0241*
FBS (mg/dl)	90.3 ±12.135	89.27 ±9.179	0.6363
F. Insulin (µIU/ml)	5.8755 ±4.719	5.1216 ±3.456	0.4673
HOMA-IR	1.3248 ±1.156	1.134 ±0.80	0.4466
Systolic BP (mm of Hg)	123.79 ±13.270	116.28 ±10.111	0.0001*
Diastolic BP (mm of Hg)	81.58 ± 7.154	79.04 ±6.238	0.0176*
Waist circumference (cm)	82.845 ±9.581	78.16 ±8.91	0.0006*

*Denotes statistical significance

Among 100 cases of AGA, 57 cases were found with a positive family history of AGA (57%) whereas in controls it was 10%, the difference between the two groups was statistically significant (p<0.0001) (Table 3).

Table 3:- Family history of AGA in cases group and prevalence of metabolic syndrome and insulin resistance in positive and negative family history groups.

Family history		Metabolic syndrome present	Insulin resistance present
Positive	57	9	8
Negative	43	2	6
Total	100	11	14

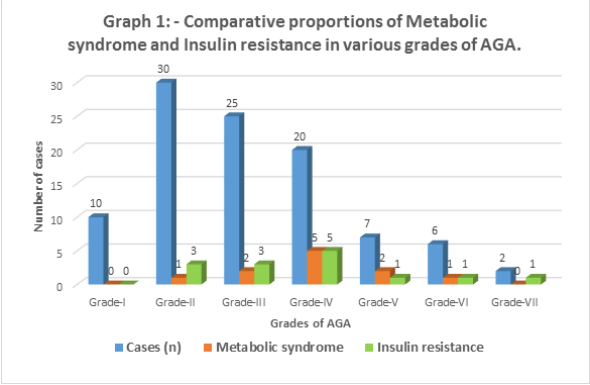
In our study, we found that the maximum number of AGA cases had ≤ 24 months duration of alopecia (65%) but the risk of metabolic syndrome was more with increased duration of alopecia (20%). In our study metabolic syndrome was more in the AGA group (11%) as compared to control group (5%), however, the difference between the two groups was statistically not significant (p=0.2585) (Table 4). In the present study insulin resistance was higher in cases (14%) as compared to control (8%) groups and here also the difference between both groups was statistically not significant (p=0.2585) (Table 4). Among all components of metabolic syndrome, hypertension was found most common component as well as statistically significant in AGA cases as compared to controls (Table 4).

Table 4:- Comparison of AGA cases and control groups with respect to metabolic syndrome, insulin resistance and components of metabolic syndrome.

Component	Case(n=100)	Control(n=100)	P-value
MS Present	11	5	0.1925
IR Present	14	8	0.2585
Hypertriglyceridemia	20	13	0.253
Reduced HDL-C	16	15	0.845
Impaired fasting glucose	14	09	0.375
Component	Case(n=100)	Control(n=100)	P-value
MS Present	11	5	0.1925
IR Present	14	8	0.2585
Hypertriglyceridemia	20	13	0.253
Reduced HDL-C	16	15	0.845
Impaired fasting glucose	14	09	0.375

*Denotes statistical significance

In the present study metabolic syndrome was more common (28.57%) in AGA grade V and insulin resistance was more common (50%) in AGA grade VII (Graph 1).



DISCUSSION

Androgenetic alopecia (AGA), is the most common cause of non-scarring alopecia in genetically predisposed men and women in which androgen-mediated gradual miniaturization of terminal hairs into vellus hairs with a significant negative impact on social and psychological life of an individual [6]. The comparison of demographic details, metabolic syndrome and insulin resistance between various studies were shown in Table 5 [7-9].

Table-5:- Literature study showing Mean of demographics data and prevalence (%) of Metabolic syndrome and Insulin resistance in cases and control group.

Parameters	Study group	Our study	Chakrabarty S et al	M. RangaSwaroop et al	Acibucu et al	SeyranOzbasGok et al
Age (Yrs)	Case	25.39	26.44	25.12	36.28	32.14
	Control	24.59	25.65	24.18	35.14	34.40
Family history (%)	Case	57	-	31.1	-	-
	Control	10	-	14	-	-
Metabolic syndrome (%)	Case	11	43	30	25	14.9
	Control	5	2.4	8	10.4	26.2
Insulin resistance (%)	Case	14	-	10	31.3	-
	Control	8	-	4	12.5	-

Family history plays an important role in the development of androgenetic alopecia [10]. In the present study, 57% of cases and 10% of control had a positive family history of AGA with a statistically significant p-value (p<0.0001). Our results were in concordance with the study done by M. Ranga Swaroop et al [8] (Table 5), but here interesting observation is that 9 out of 11 cases (81.8%) of MS in AGA group, whereas only 1 out of 5 control (20%) of MS had a positive family history. Thus it signifies the role of family history in causing metabolic syndrome in early-onset AGA.

In the present study, we observed grade II was the most common grade of hair loss (30%) followed by grade III (25%) and the least common grade was grade VII (02%) and similar observations showed by many other studies [11-14].

Metabolic syndrome (MS) with AGA: Many studies have reported a relationship between AGA and metabolic syndrome with conflicting results [9, 15-20].

In our study metabolic syndrome was more in the AGA group (11/100) as compared to the control group (5/100), however, the difference between the two groups was statistically not significant (p=0.1925). Our observations were similar to the study done by Seyran OzbasGok et al, who did not found the relationship between AGA and metabolic syndrome (Table 5) [20].

In the present study Mean level of the S. cholesterol, S. triglyceride, systolic and diastolic blood pressure, waist circumference, BMI and weight were significantly higher in the AGA group as compared to the control group. The Mean level of HDL-C was significantly lower in the AGA group as compared to the control group. Similar observations were seen in other published studies [7, 15, 21].

Insulin resistance (IR) with AGA: An association between insulin

resistance and early-onset AGA has been reported in many studies. Hyperinsulinemia plays a pathogenic role in local androgen production and miniaturization of hair follicles [21]. In our study, Patients with AGA were found with a higher level of the mean of fasting serum insulin (5.875 ±4.72) as compared to the control group (5.123±3.46), however, the difference between the two groups was statistically non-significant (p=0.1991). When the groups were compared concerning IR based on the HOMA-IR, only 14% of cases with early-onset AGA and 8% controls had insulin resistance, the difference between both groups was non-significant (p=0.2585). Similar findings were observed by M. RangaSwaroop et al [8], Acibucu et al [9] and Nabaie et al [17] who found higher levels of insulin in the case group than in the control group, but the difference was statistically non-significant (Table 5). Few studies showed a statistically significant relationship between IR and early-onset AGA [9, 15, 21].

In the present study it concluded that, among the components of metabolic syndrome like serum triglyceride, blood pressure, waist circumference showed a higher value in cases as compared to controls whereas a decreased value of serum HDL was observed in AGA cases. Furthermore, AGA cases were found to have higher insulin resistance. So the present study highlight that patients with early-onset androgenetic alopecia even from grade I should be evaluated for the screening of metabolic syndrome and early intervention for management of glucose intolerance, type 2 diabetes mellitus, and cardiovascular diseases.

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