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The association of metabolic syndrome and insulin resistance in early-onset androgenetic alopecia in males: a case-control study

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Abstract

Introduction: Men with premature androgenetic alopecia (AGA) are found to be susceptible to cardiovascular diseases, metabolic syndrome, diabetes mellitus and hypertension and also premature baldness can have a definite negative impact on self-image and self-esteem in these patients. Insulin resistance (IR), metabolic syndrome (MS) are known to be independent risk factors for coronary heart disease (CHD). The aim of this study was to assess the strength of association between MS and/or insulin resistance in males with early-onset Androgenetic alopecia (AGA).

Methods: A total of 50 male patients with premature AGA attending the dermatology out-patient department and satisfying the inclusion and exclusion criteria were recruited in the study. Equal number of normal age and gender matched patients attending the dermatology OPD were taken as control group. A detailed history of the patients as per the prepared questionnaire was taken. Elaborate general, physical and systemic examination were carried out and recorded in standard proforma. Complete examination of scalp was done with emphasis on pattern and severity of hair loss. Hair loss was graded according to Hamilton-Norwood scale. Anthropometric and blood pressure measurement was done according to structured proforma. Fasting blood samples were collected and fasting insulin level, fasting blood sugar levels, high density lipoproteins, triglycerides were determined.

Results: In this study, majority of patients with early onset AGA were in the age group of 22-24 years. Most common grade of hair loss was grade III a (32%) of Hamilton- Norwood scale of hair loss. 5 out of 50 cases (10%) and 2 out of 50 controls (4%) had shown association with insulin resistance and the difference between the groups was statistically insignificant (p= 0.23). 15 out of 50 cases (30%) and 4 out of 50 controls had shown association with metabolic syndrome and the difference between the group was statistically significant (p= 0.005).

Conclusion: In our study, majority of patients with early onset AGA were in age group 22-24 years. 31% of cases had family history of AGA. Majority of the patients had stage III of Hamilton-Norwood scale of hair loss. Male patients with early onset AGA were not associated with IR. Metabolic syndrome was associated with male patients with early onset AGA.

Keywords: Early-onset androgenetic alopecia, Insulin resistance, Metabolic syndrome.

Introduction

Androgenetic alopecia (AGA), the commonest non scarring alopecia, is an androgen induced disorder characterised by hair loss in genetically predisposed men and women. In AGA, androgens induce miniaturisation in hair follicles, especially in the fronto-temporal area and vertex of scalp in men; over the crown in women.(1)

AGA in males developing before 30 years of age with at least grade III of Hamilton-Norwood classification is termed as early onset or premature AGA. Men with premature AGA are found to be susceptible to cardiovascular diseases, metabolic syndrome, diabetes mellitus, hypertension and also premature baldness can have a definite negative impact on self-image and self-esteem in these patients(2). In-spite of emerging evidences for the association between premature AGA and metabolic syndrome, it is highly inconsistent, with very few studies being reported in Indian population. Since the pathophysiological link between metabolic syndrome, insulin resistance and premature AGA is not yet fully understood, we conducted the present study to evaluate their association.

Methods

This study was conducted in the Out-patient Department of Dermatology, Venereology and Leprosy, Adichunchanagiri Institute of Medical Sciences, Balagangadharanatha Nagara, Nagmangala taluk, Karnataka during Dec 2014-May 2016. This was a case control study. 50 male patients aged between 18-30 years with early onset AGA were enrolled in the study as cases and equal number of age matched participants who presented to out-patient department were enrolled in the study as controls.

Approval was obtained from the Institutional ethical committee and an informed consent was taken from all the patients before enrolling them in the study. Those who presented with AGA after age 30 years, had cardiovascular disease or glucose metabolism disorder, presented with other patterns of non-scarring alopecia (like alopecia areata, telogen effluvium, anagen effluvium), were taking androgen or anti-androgen therapy, insulin treatment, glucocorticoid treatment within the previous 6 months were excluded from the study.

Clinical history: A detailed history of the patients as per the prepared questionnaire was taken with emphasis on history of hair-fall, onset, duration, any associated symptoms (itching, pain in scalp, scaling of the scalp) and history of exacerbating factors if any. Family history of hair-loss was also taken. All were documented in a structured proforma.

Clinical examination: Elaborate general, physical and systemic examination were carried out and recorded in standard proforma. Complete examination of scalp was done with emphasis on pattern and severity of hair loss. Hair loss was graded according to Hamilton-Norwood scale.

Anthropometric and blood pressure measurement

Height: Measured against vertical board with an attached metric rule and bringing horizontal head board in contact with the uppermost point on the head. Recorded in bare foot, full erect position and deep inspiration.

Weight: Recorded without foot wear and light clothes on ISI (Indian standards institute) certified weighing machine to the nearest of 100 gm.

Body mass index: Calculated as weight in kg/ height in m^2 (kilo gram/meter). In adults overweight is defined as BMI between 25-29.9 and obese is defined as BMI ≥30.

Waist circumference: Measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, using a stretch-resistant tape that provides a constant 100 g tension.

Blood pressure measurement: Blood pressure (BP) was recorded with sphygmomanometer on the right arm in a sitting position after 20 minutes rest. The mean value for systolic and diastolic BP was calculated from average of three readings.

Systolic BP ≥130 mmHg and diastolic BP ≥85 mmHg were taken as cut off points for hypertension.

Investigations: Blood samples were collected from all enrolled patients after 12-hour fast and the following investigations were performed.

1. Fasting serum insulin levels,
2. Fasting blood sugar levels (FBS),
3. Triglycerides (TGs),
4. High-density lipoprotein (HDL).

Diagnosis of Metabolic Syndrome (MS):

Diagnosis of Metabolic syndrome will be done based on the National Cholesterol Education Programme (NCEP) Adult treatment Panel III by the presence of three or more of the following criteria.[3]

a. Waist circumference ≥102 cm in males.
b. Triglycerides value ≥150 mg/dl.
c. HDL<40 mg/dl.
d. FBS ≥ 110 mg/dl.
e. BP ≥130/85 mmHg.

Diagnosis of Insulin Resistance (IR)

Diagnosis of insulin resistance will be done by using the Homeostasis model assessment of Insulin resistance (HOMA-IR) according to the following formula:

Insulin resistance = [Fasting insulin level (μIU/mL) x fasting glucose level (mmol/L)/22.5]

A value above 2.7 is considered to indicate Insulin resistance.[3]

Fasting blood samples were collected from all enrolled patients for the above investigations.

For measurement of fasting insulin level, Microplate chemiluminescence Assay using the instrument Alpha prime light was used. Normal values ranged from 2.6-24.9 μIU/mL.

Serum lipid profile: HDL was estimated with Auto-aqant 400 analyzer using direct method and TGs measurement was performed by GPO-Trinder endpoint technique. HDL < 35 mg% and TGs > 150 mg% was considered as raised.

Venous plasma glucose was measured by glucose oxidase method. Fasting blood glucose 110 mg% was considered as raised.

Statistical Analysis: The statistical software namely SAS9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurement was presented on Mean±SD and results on categorical measurements was presented in Number (%). Significance was assessed at 5% level of significance. The following assumption on data was made, Assumption were:

1. Dependent variables should be normally distributed.
2. Samples drawn from the population should be random. Cases of the samples should be independent.

Chi-square/Fisher Exact test had been used to find the significance of study parameters on categorical scale between two or more groups.

A p-value < 0.05 was considered to be statistically significant.

Results

The patient group consisted of 50 male subjects in the age group between 18-30 years and the same number of age and gender matched subjects were taken as controls. In the present study majority of patients with early onset AGA were in the age group of 18-24 years (68%). The mean age of patients with early onset AGA was 25.12±2.344 years and that of participants in control group was 24.18±2.663 years. The age difference between the groups was insignificant (p= 0.94). Majority of patients had insidious onset of hair loss (58%). 31% among the cases and 14% in controls had family history of baldness and the difference between the groups was statistically significant (p=0.001). On scalp

examination, 23 (46%) patients were classified as stage III, 12 (24%) as stage IV, 10 (20%) as stage V, and 5 (10%) as stage VI based on Norwood-Hamilton scale of hair loss.

The groups were compared in terms of height, weight, Body Mass Index(BMI), waist circumference(WC)C, systolic and diastolic BP, HDL, TGs, FBS. The difference between the groups with respect to weight, BMI, WC, HDL, TGs and FBS were statistically significant ($p < 0.05$). However, the difference between the groups with respect to height, systolic and diastolic BP were not found to be statistically significant ($p > 0.05$) [Table 1].

Table 1: Distribution of demographic and laboratory parameters of the two groups in the study

Parameters	Group	Mean	SD	P Value
Age	Controls	24.18	2.663	0.94
	Cases	25.12	2.344	
Height	Controls	158.56	8.711	0.106
	Cases	161.53	9.513	
Weight	Controls	61.87	7.494	0.008*
	Cases	67.58	12.721	
BMI	Controls	24.51	1.756	0.016*
	Cases	25.65	2.752	
WC	Controls	80.93	5.552	<0.0001*
	Cases	86.86	9.282	
Systolic	Controls	112.74	11.333	0.148
	Cases	116.28	12.873	
Diastolic	Controls	75.98	8.055	0.181
	Cases	78.34	9.410	
Fasting INSU	Controls	3.32	1.341	0.020*
	Cases	4.21	2.285	
TGs	Controls	125.64	19.537	0.040*
	Cases	135.06	25.278	
HDL	Controls	46.48	5.448	0.008*
	Cases	43.40	5.938	
FBS	Controls	90.18	13.428	0.043*
	Cases	97.28	20.427	

*Denotes statistical significance
SD: standard deviation;

The fasting insulin levels was 4.21±2.285 μIU/mL in the cases and 3.32±1.341 μIU/mL in the control group. The values in the cases were higher than controls and the difference between the two groups was statistically significant (p= 0.020).

When the patients were grouped according to the HOMA-IR > 2.7 cut-off value and IR was compared, 5 out of 50 (10%) patients in the early AGA group were found to have IR, whereas only 2 out of 50 (4%) patients in the control group were observed to have IR. The difference between the groups was statistically not significant (p= 0.23) [Table 2].

Table 2: Comparison of the groups with respect to Insulin resistance

Group	IR	No IR	Total	p-value
Cases	5 (10%)	45 (90%)	50 (100%)	0.23
Controls	2 (4%)	48 (96%)	50 (100%)	
Total	7 (14%)	93 (86%)	100 (100%)	

When the stages of hair loss in patients with early onset AGA were compared with regard to IR, the difference was statistically not significant (p= 0.185) [Table 3].

Table 3: Comparison of Androgenetic alopecia stages with respect to Insulin resistance

Alopecia stage	IR	No IR	Total	p-value
Stage III	0 (0%)	23 (100%)	23 (100%)	0.185
Stage IV	2 (16.7%)	10 (83.3%)	12 (100%)	
Stage V	2 (20%)	8 (80%)	10 (100%)	
Stage VI	1(20%)	4 (80%)	5 (100%)	
Total	5 (10%)	45 (90%)	50 (100%)	

When the groups were compared with respect to MS frequency, 15 (30%) patients in early AGA group and 4 (8%) participants in control group were found to have MS and the difference between the groups was statistically significant (p= 0.005) [Table 4].

Table 4: Comparison of the groups with respect to Metabolic syndrome

Group	MS	No MS	Total	p-value
Cases	15 (30%)	35 (70%)	50 (100%)	0.005
Controls	4 (8%)	46 (92%)	50 (100%)	
Total	19 (38%)	81 (162%)	100 (100%)	

Discussion

AGA in males developing before 30 years of age with at least grade III of Hamilton-Norwood classification is termed as early onset or premature AGA. In present study, 50 cases and 50 age and gender matched controls were recruited in the study. In our study, the most common age group was between 22-24 years. The mean age of cases and controls in our study were 25.12±2.344 and 24.18±2.663 respectively and the difference between the groups was statistically not significant (p=0.94). Our observation was similar to studies done by Chakrabarty S et al[6] (26.44±2.64 and 25.65±3.19) and Acibucu F et al[3] (36.28±7.74 and 35±6.54).

In present study out of 50 cases with early onset AGA, 31 (62%) patients had family history of hair loss. Out of 50 controls 14 (28%) patients had family history of hair loss. The difference between the groups was statistically significant (p= 0.001). Our results were in concordance with study done by Arias-santiago S et al.[13]

In present study, grade III of Norwood- Hamilton scale was the most common grade of hair loss (46%) observed. The lowest stage found among cases was stage III and the highest was stage VI. Stage IV was identified as the mean stage. Our observation was similar to study done by Acibucu F et al.[3]

Evaluation of IR in studied groups: Insulin resistance (IR) plays a major role in pathophysiology of metabolic syndrome (MS) and hyperinsulinaemia is an independent risk factor for coronary artery diseases (CAD) wherein it accelerates the development of atherosclerosis and prevents the resorption of atherosclerotic plaque.[3] Association between IR and early onset AGA have been reported and hyperinsulinemia plays a pathogenic role in local androgen production and miniaturisation of hair follicles.[4]

In our study, when the groups were assessed with respect to their fasting insulin levels, men in AGA were found to have higher level (4.21+2.28) than those in the control group, the difference was statistically significant (p=0.020). However, when the groups were compared with respect to IR based on the HOMA-IR, only 5cases out of 50 patients with early onset AGA and 2 patients among control group had insulin resistance, the difference between both groups was not significant (p=0.23).

In contrary, studies done by Acibucu F et al,[3] Matilainen et al,[11] Pengsalae N et al,[9] and Gonzalez-Gonzalez et al[5] found that a significant relationship exists between IR and early onset AGA.

In present study, when the stages of hair loss according to Hamilton-norwood scale were compared with respect to IR, the difference between the groups was statistically insignificant (p =0.185) which was in accordance with study done by Acibucu F et al[3].

Evaluation of metabolic syndrome in studied cases: The NCEP ATP III mentions MS as a major cardiovascular risk factor. Individuals with MS are at an increased risk of coronary arterial calcification. The presence of MS has been associated with a three-fold risk increase for coronary artery diseases and five-fold increase for cardiovascular mortality.[3]

The groups were compared in terms of Height, Weight, BMI, WC, Systolic and Diastolic blood pressure, TGs, HDL, FBS.

In the present study, there were significant differences between the cases and control subjects regarding body weight and waist circumference [WC] (p< 0.05). Similar results were reported in the study done by Bakry OA et al.[4]

Abdominal fat tissue is associated with serious metabolic disorders such as IR, hyperinsulinaemia, hypertension, increased TG, glucose intolerance and diabetes mellitus.[3]

In present study, there was significant difference between the cases and control subjects with respect to BMI (p< 0.05). Similar observations were reported in studies done by Bakry OA et al[4] and Matilainen et al.[11] However, Arias-Santiago et al[13] found that BMI did not differ between AGA cases and normal controls.

In the present study, there were no significant difference between cases and controls regarding the mean values of systolic and diastolic BP. Contrary to our results, Bakry OA et al,[4] Hirsso et al,[12] Matilainen et al[11] and Arias-Santiago et al[13] found significant differences between cases and controls regarding systolic and diastolic BP.

In the present study, the difference between the groups with respect to the mean value of FBS was statistically significant which was in concordance with studies done by Bakry OA et al,[4] Nabaie et al[14] and Acibucu et al.[3]

In the present study, mean value of HDL-C and TGs were found to be significantly higher in cases than controls. In a similar study done by Bakry OA et al, mean value of TGs was significantly higher in cases, whereas the mean value of HDL-C was significantly lower in cases than in control subjects. Contrary to our results, Guzzo et al[15] found no difference in mean values of HDL-C and TGs between cases and controls.

In the present study, MS was significantly associated with early onset AGA group when compared with control group (p =0.005). Similar results were observed by Acibucu et al[3] and Bakry OA et al.[4]

To conclude, in present study MS was significantly associated with early onset AGA. There was no association between insulin resistance and premature AGA. Early-onset AGA patients should be closely followed-up in the long term, particularly for cardiovascular disorders. The observations in present study may raise awareness in susceptible individuals that lifestyle changes (weight control, exercise diet with a low glycemic index) in early life can reduce the risk of coronary heart diseases (CHD).

Limitation

More Prospective studies with large sample sizes may be required to conclusively define any association between early onset AGA and Metabolic Syndrome.

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