Comparison of components of metabolic syndrome in androgenic alopecia versus healthy population

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ABSTRACT

Background: Androgenic alopecia (AA) is hair loss in both men and women who are genetically predisposed. AA is associated with increased cardiovascular and metabolic risk, however the studies are controversial. We planned this study to check if metabolic syndrome (MS) components were more common in patients of AA as compared to healthy controls.

Methodology: AA cases (n=100) and controls (n=100) were recruited from dermatology department PAF Hospital Faisal Base, Karachi from July-2016 to November-2017. Only patients with grade III or more according to the Hamilton-Norwood classification were enrolled as cases. All participants were within the age range of 25-40 years. Only normal and overweight participants were included, obese were excluded. Anthropometrics were taken and blood was withdrawn for metabolic and hormonal parameters.

Results: The participants were within the age range of 25-40 years with mean age 32.3 ±5.2 years for cases, and 28.2 ±4.5 years for controls. Cases were significantly different from controls in waist, BMI, systolic (SBP) and diastolic (DBP) blood pressure, insulin, HbA1c, HOMA-IR and lipid profile. Testosterone was more in cases as compared to controls (p=0.038) and SHBG was decreased in cases (p=0.008). Free androgen index (FAI) was significantly increased in cases (p=0.01). MS was 39% in cases as compared to 10% in controls. The AA patients with MS had significantly different waist, DBP, HDL, insulin, HOMA-IR, testosterone, SHBG and FAI as compared to AA with no MS.

Conclusion: Metabolic syndrome is more prevalent in people with androgenic alopecia than healthy population. Free androgen index is a good marker for identifying individuals with metabolic syndrome in androgenic alopecia.

Keywords: Androgenic alopecia, metabolic syndrome, testosterone, free androgen index, insulin resistance, HOMA-IR

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INTRODUCTION

Androgenic Alopecia (AA) is one of the most common form of alopecia occurring in both men and women.[1] It is characterised by hair loss in both men and women who are genetically predisposed in the presence of adequate circulating androgens.[2] However, the presentation is different in men and women. In men, it mostly involves frontotemporal region and vertex of scalp. In women, it causes generalised hair loss especially over the crown.

Hamilton-Norwood classification is mostly used to grade AA.[3] Grade III or more is considered as significant, and if occurring before age of 30 years, termed as premature or early onset AA.[4] It has been shown in some of the studies that AA is associated with increased risk of cardiovascular disease, diabetes and some of the components of the metabolic syndrome (MS).[2,5-7] However, others have shown no increased risk in AA patients and consider it a genetic predisposition.[2] Swaroop et. al. have shown its association with insulin resistance (IR) but not MS. Bakry et al. have shown its association with both IR and waist circumference in MS.[1] Kartal et. al. have shown its association with IR.[8] Others have shown its association with HDL only.[1,9] Free Androgen Index (FAI) is recently introduced as a marker of early onset AA in men.[10] We planned this study to check if MS was more common in patients of AA as compared to healthy controls. We also compared the components of MS

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and FAI in patients of AA, with and without components of MS.

METHODOLOGY

The study was approved by the Ethics Review Committee of PAF Hospital Faisal Base, Karachi. We recruited 100 patients of non-scarring alopecia (cases) coming to the Outpatient Dermatology Department of PAF Hospital Faisal base, Karachi from July 2016 to November 2017. Only patients with grade III or more in the Hamilton-Norwood classification ("deep frontotemporal recessions, usually symmetrical, and are either bare or very sparsely covered by thin hair") were enrolled as cases.[3] Advertisement was done in local newspapers, local area and also in the hospital. The controls (n=100) were mostly the relatives of alopecia patients and people coming to the dermatology department for some other problem like acne, warts etc. Only normal and overweight (BMI <30) patients were included while obese individuals (BMI ≥ 30) were excluded. All participants were within the age range of 25-40 years. Patients having diabetes, hypertension and dyslipidaemia were included in the study.

All the participants were explained about the study and how the data will be used. Written informed consent was obtained from all the participants. Participants were told that they can quit the study at any stage. Some of the participants (both cases and controls) with additional disease like autoimmune disease, hepatitis and cancer without chemotherapy were excluded. Participants (both cases and controls) on any type of hormonal treatment or endocrine disorder; thyroid, pituitary, androgens, anti-androgens, glucocorticoids were excluded. Individuals taking weight loss medication during the past 6 months were excluded.

Selected history was obtained from the participants with emphasis on family history of alopecia, diabetes and hypertension. All the participants were checked for their height, weight, waist circumference, systolic and diastolic blood pressure. 5ml of blood was withdrawn in fasting state (10-12 hours fast from dinner time) for evaluation of lipid profile, glucose, insulin, testosterone and sex hormone binding globulin (SHBG). Fasting lipid profile included total cholesterol (Chol), high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides (TG).

Omron M6, Japan was used for measuring BP. A total of three readings of blood pressure were taken after five minutes' rest. Three readings were taken at an interval of 3-5 minutes (average used in analysis). Height was measured by clinical stadiometer by bringing the wooden board in contact with head. Weight was measured without footwear and in light clothes. Weight was calculated on a digital weight balance by OSAKA, Japan. BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured at the midpoint between top of iliac crest and lower palpable rib, at the level of umbilicus, by using a stretch resistant tape.

Metabolic syndrome was diagnosed according to the criteria of International Diabetes Federation: waist circumference > 90 in men and > 80 in women; TG > 150 mg/dl; HDL < 40mg/dl in men, and < 50mg/dl in women; SBP > 130 mmHg; DBP > 85 mmHg, Fasting blood sugar > 100 mg/dl.[5]

Free Androgen index (FAI) was calculated by the formula:

FAI = Testosterone (nmolL) x 100 / SHBG (nmol/L).[10]

Serum insulin was measured by using ELISA kit (Roche Diagnostics, Indianapolis, IN, USA). Testosterone was measured using a radioimmunoassay (RIA; Diagnostic Products Corporation, Los Angeles, CA, USA).[11] SHBG was measured by ELISA kit (Roche Diagnostics)[11] and lipid profile by Microlab 300 (ELITech Group, France). HOMA-IR was calculated according to the formula: fasting insulin (microU/L) x fasting glucose (nmol/L) / 22.5.[12]

Statistical analysis was performed using SPSS Version 22. All data were checked for normality using Kolmogorov-Smirinov and Shapiro-Wilk tests and histograms, and were normally distributed. Data are presented as mean ± SD. Cases and control were compared by independent sample t-test. Family history of alopecia and diabetes, and MS were compared by Chi-square test. AA patients with and without MS were compared by independent sample t-test.

RESULTS

The participants were within the age range of 25-40 years with mean age of cases 32.3 ± 5.2 years, and that of controls 28.2 ± 4.5 years. Controls were a little younger than cases. Cases were significantly different from controls in height, weight, waist, BMI, SBP, DBP, insulin, HbA1c, HOMA-IR and lipid profile (Table 1). Testosterone was more in cases as compared to controls (28.21 ± 8.28 versus 22.45 ± 5.12, p=0.038) and SHBG was decreased in cases (Table 1). FAI was significantly increased in cases (p=0.01). MS was 39% in cases as compared to 10% in controls.

AA patients were split in groups with and without MS, and components of MS were compared (table 2). The AA patients with MS had higher BMI, WC, SBP, DBP, Glucose,

HDL, insulin, HOMA-IR, testosterone and FAI as compared to AA with no MS (Table 2). However, they had lower SHBG (Table 2).

Table 1 - Comparison of metabolic syndrome components and other variables in patients of androgenic alopecia versus healthy population

Variables	Androgenetic Alopecia (n=100)	Control (n=100)	p-Value
Age (years)	32.3 ±5.2	28.2 ± 4.5	0.009
Height (cm)	173.48 ± 7.77	176.51 ± 7.1	0.01
Weight (cm)	85.12 ± 12.98	79.23 ± 7.43	0.02
Waist (cm)	97.89 ± 9.98	91.23 ± 8.76	0.002
BMI	27.91 ± 4.3	25.25 ± 3.39	0.02
SBP (mmHg)	134.91 ± 15.12	126.2 ± 10.1	0.003
DBP (mmHg)	84.42 ± 6.9	80.13 ± 5.1	0.01
FH alopecia (%)	50	10	0.005
FH Diabetes (%)	42	30	0.06
Fasting Glucose (mg/dl)	102.66 ± 22.24	90.25 ± 14.53	0.004
Insulin (µU/ml)	18.23 ± 7.60	8.61 ± 4.87	0.02
HbA1c (%)	5.38 ± 3.1	5.06 ± 1.89	0.03
HOMA-IR (µU/mg)	2.28 ± 1.61	1.49 ± 0.89	0.006
Cholesterol (mg/dl)	211.23 ± 40.23	170.93 ± 30.45	0.003
LDL (mg/dl)	140.54 ± 25.67	120.43 ± 20.34	0.006
HDL (mg/dl)	44.23 ± 15.12	53.34 ± 17.14	0.003
TG (mg/dl)	165.55 ± 35.21	132.78 ± 20.22	0.001
Testosterone (nmol/L)	28.21 ± 8.28	22.45 ± 5.12	0.038
SHBG (nmol/L)	38.12 ± 12.21	49.23 ± 13.88	0.008
FAI	71.01 ± 35.45	45.60 ± 25.21	0.01
MS (%)	39	10	0.01

Values as mean ± SD. p for the difference between AA and controls
FH= Family history. HOMA-IR= Homeostatic Model Assessment of Insulin Resistance,
SHBG= sex hormone binding globulin, FAI= free androgen index, MS= metabolic syndrome.

Table 2 - Comparison of metabolic syndrome components and other variables in Androgenic Alopecia patients with and without metabolic syndrome

Variables	AA with MS (n=39)	AA without MS (n=61)	p-Value
Waist (cm)	99.21 ± 7.32	96.11± 6.76	0.02
BMI	28.21 ± 3.1	27.12 ±3.3	0.06
SBP (mmHg)	136.65± 12.45	133.21±13.34	0.06
DBP (mmHg)	86.01±4.03	83.92±5.20	0.05
Glucose (mg/dl)	103.98 ± 20.12	99.01± 20.56	0.06
HDL (mg/dl)	46.87 ± 12.45	42.22 ± 12.33	0.05
Insulin (µU/ml)	20.45 ±5.15	16.43 ± 4.98	0.04
HOMA-IR (µU/mg)	2.89± 1.12	2.11 ± 1.23	0.03
Testosterone (nmol/L)	32.31 ± 4.30	26.35 ± 6.02	0.04
SHBG	34.34 ± 9.23	40.84 ± 10.01	0.02
FAI	77.83 ±28.25	67.45 ± 28.2	0.05

Values as mean ±SD. p for the difference between AA and controls
HOMA-IR= Homeostatic Model Assessment of Insulin Resistance, SHBG= sex hormone binding globulin, FAI= free androgen index.

DISCUSSION

Several previous studies have worked on the association of cardiovascular risk and components of metabolic syndrome association with Androgenic Alopecia (AA), however there has been controversy. This study was planned to check if MS and its components were more common and associated with AA.

In the present study MS was more prevalent in the AA patients as compared to healthy controls. All the components of MS were significantly deranged in cases as compared to controls. However, not all of the AA patients had deranged parameters. Moreover, within the AA patients there was a significant difference for some of the components of MS (waist circumference, HDL, insulin, HOMA-IR, testosterone and SHBG. Moreover, FAI was also significantly raised in patients having MS. This proposes that FAI can be used as a marker for metabolic risk within the patients of AA[10]. It identifies those patients who have increased metabolic derangement[10,13]. However, our study also shows that not all patients with AA have metabolic derangement despite positive family history.

Waist circumference has previously been associated with AA as a metabolic component[1]. Similarly HDL has also been shown to be independently associated with AA[1,9]. Acibucu et. al. have shown insulin and insulin resistance (IR) to be present along with MS components in AA patients . In addition Kartal et. al have shown IR to be related with AA independent of hyperandrogenemia[8]. Our study is similar to these studies as we have shown most of the components of MS to be present in a group of AA patients. However some of the AA patients did not have MS but their metabolic parameters were slightly different as compared to healthy population.

On comparing all the three groups and considering AA with MS, AA without MS and healthy controls, we noticed the MS related variables (BMI, waist, glucose, HDL, insulin and HOMA-IR) to be ideal in the control group. AA without MS group has better values as compared to AA with MS but less optimal than the control group. Moreover, testosterone, SHBG and FAI were also ideal in the control group, and AA with MS had the maximum derangement. This shows the role of insulin and IR in the development of AA , as hyperinsulinemia is involved in local androgen production and hair follicles miniaturization[1] .

Our study was limited due to less sample size. Within the AA group the patients with MS were only 39. The subgroup analysis decreased the power, and so some of the components of MS were not significantly different between the groups. We also did not check the histopathological association of hair follicles with components of MS in AA. This may have given an additional strength. We also did not check the other sex hormones apart from testosterone which could have given an additional angle for association.

CONCLUSION

Metabolic syndrome is more prevalent in people with androgenic alopecia than healthy population. Free androgen index is a good marker for identifying individuals with metabolic syndrome in androgenic alopecia.

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