ORIGINAL ARTICLE

Association of Early-onset Androgenetic Alopecia and Metabolic Syndrome

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ABSTRACT
Objective: To evaluate the association of early-onset AGA (androgenetic alopecia) and metabolic syndrome in the younger male population.
Study Design: Case-control study.
Place and Duration of Study: Department of Dermatology, Mayo Hospital Lahore, from October 2017 to March 2018.
Methodology: A total of 202 patients were enrolled, 101 male patients with early-onset AGA (cases with a alopecia between 20-36 years of age), and were matched with 101 controls. All measurements regarding BMI, metabolic syndrome, and grades of alopecia were recorded on a pre-designed proforma.
Results: Of the 101 cases (mean age 27.77 ± 5.04 years), 27 (26.7%) had grade 3, 41 (40.6%) had grade 4, 29 (28.7%) had grade 5 and 4 (4%) had grade 6 AGA. Patients of AGA had an approximate four times increased frequency of metabolic syndrome. Of the cases 12 (11.9%) had metabolic syndrome whereas it was found in 3 (3%) of the control group. A significant association was found between cases of AGA and metabolic syndrome (p=0.016).
Conclusion: This study suggests a significant association of AGA with metabolic syndrome.

Key Words: *Androgenetic alopecia, Metabolic syndrome, Early-onset alopecia, Cardiovascular disease.*

INTRODUCTION

Male pattern baldness or androgenetic alopecia (AGA) is the most common cause of hair loss affecting approximately 30-50% of men by the age of fifty.[1] AGA is more common in Caucasians than in the Mongolian population.[1] Apart from the apparent psychological effects of AGA, it has also been linked to certain pathological processes including increased risk of cardiovascular disease,[2,3] metabolic syndrome,[4] an increased risk of benign prostatic hypertrophy; and in males, with the phenotypic equivalent of female polycystic ovarian syndrome presenting with features of obesity, insulin resistance, cardiovascular disease and infertility.[5,6]

The association of AGA with metabolic syndrome has been so striking that some studies have labelled AGA as an independent risk factor for cardiovascular disease and metabolic syndrome.[4] On the other hand, there are studies negating any such association.[7]

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Some studies have shown metabolic syndrome to be more specifically linked to early-onset AGA.[8] Early-onset AGA refers to AGA developing before the age of 36 years; and being at least at stage 3 on the Hamilton-Norwood classification.

Metabolic syndrome is the combination of abdominal obesity, dyslipidemia, elevated blood pressure and abnormal glucose tolerance.[9] For the diagnosis of this syndrome, a unified criteria by the International Diabetic Foundation (IDF)[10] considers various factors including waist circumference, triglyceride levels, high density cholesterol lipoprotein (HDL-C) levels , blood pressure, and blood glucose levels.[11]

Due to the controversy on the association between AGA and metabolic syndrome, there is a need for further studies to verify this association. More importantly, as metabolic syndrome is known to be linked to cardiovascular disease, identifying this association could lead to an earlier management of the population at risk. Since cardiovascular disease accounts for 30% of all global deaths, with 80% of deaths occurring in the low and middle income countries.[12] If this association of AGA and metabolic syndrome could be verified, AGA itself might be considered as a risk factor for cardiovascular disease; and such individual may be brought to notice earlier with earlier evaluation and management. This could contribute to a decrease in the global incidence and mortality of cardiovascular disease.

The objective of this study was to evaluate the association of

early-onset AGA and metabolic syndrome in the younger male population, that is between 20-36 years.

METHODOLOGY

This case-control study was done in the Department of Dermatology, Mayo Hospital, Lahore. The duration of study was six months from October 2017 to March 2018. Two hundred and two patients (101 patients in each group) were enrolled after their informed consent. Inclusion criteria for patients with early-onset androgenetic alopecia clinically were: males between 20 and 36 years and at least at stage 3 alopecia on the Hamilton-Norwood scale. Inclusion criteria for controls were males between 20 and 36 years and absence of androgenetic alopecia, clinically. Exclusion criteria for both groups were: known glucose metabolism disease, coronary artery disease, hypertension, current smoker or history of smoking in the last 8 years, deranged hepatic or renal profile (Bilirubin >1.2 mg/dL; ALT >40 U/L; AST >35 U/L; Creatinine >1.4mg/dL), history of medicines affecting carbohydrate metabolism, e.g. glucocorticoids and any other type of alopecia, e.g. alopecia areata. All subjects were selected from the Outpatient Department after approval from the Ethical Committee. After informed consent, subjects were examined and evaluated for alopecia and its scale. They were divided into two groups by lottery method. Group A to include patients of androgenetic alopecia and Group B to include age and gender-matched male patients, who fulfill the inclusion criteria and presented to the Outpatient Department for various dermatological complaints other than alopecia. Later, all subjects were evaluated for metabolic syndrome. A measuring tape was used to assess waist circumference, mercury sphygmomanometer was used to assess blood pressure. For fasting lipid profile and blood sugar level after a 12-hour fast, 5 cc syringe for 3 ml blood withdrawal from the antecubital/dorsum of hand vein.

In both groups, the participants waist circumference (in cm) was measured using non-extendable metric tape, at the level between the 12th costal lower boundary and iliac crest. It was measured twice, with a maximum variation of 1cm and average was calculated. Blood pressure was measured using a sphygmomanometer after a 20 min rest in the mid-supine position. Triglycerides, HDL-C and fasting blood glucose were obtained from blood samples drawn after a 12-hour fast. A combination of abdominal obesity, hypertension, diabetes and hyperlipidemia was diagnosed as having metabolic syndrome using the National Cholesterol Education Program Adult Treatment Panel III criteria. This required at least 3 out of the criteria waist circumference (Men) $\geq$102 cm, triglycerides level of $\geq$150 mg/dL, high density cholesterol at <40 mg/dL, blood pressure at $\geq$130 / $\geq$85 mmHg, and fasting glucose at $\geq$110 mg/dL. All this information was recorded in a pre-designed proforma. Data was entered and analysed in SPSS-23. Quantitative variables were presented as mean ± standard deviation. Qualitative variables were presented as frequencies and percentages. Data was stratified for age, BMI and economic status to address effect modifiers. Strength of association between qualitative variables was tested by calculating the odds ratio. OR >1 was considered as statistically significant. Independant sample t-test was applied to determine the differences between means. Chi-square or Fisher's Exact test were applied with p-value $\leq$0.05 considered as significant.

RESULTS

Two hundred and two patients were enrolled. In Group A, 27 (26.7%) had grade 3, 41 (40.6%) had grade 4, 29 (28.7%) had type 5 and four (4.0%) had type 6 AGA. There was a significant association between the grade of alopecia and metabolic syndrome in Group A (p <0.001). The mean age for both groups was almost similar i.e. 27.77 ± 5.04 years in cases and 27.38 ± 4.91 in controls. There was no statistically significant difference in means of BMI in both groups. (p = 0.958, Table I). There were statistically significant differences in the mean values of serum triglycerides (143.75±48.16 mg/dL in cases vs. 129.6 ±14.59 mg/dL in controls, (p = 0.006) and waist circumference (89.64 ± 6.50 cm in cases vs. 86.85 ±6.13 cm in controls, (p = 0.002 Table I).

Of the 101 cases with AGA 12 (11.9%) patients and among 101 healthy controls 3 (3%) fulfilled the criteria for metabolic syndrome and on performing the Chi-square test of association this difference was found to be significant (p = 0.016). The odds ratio of cases with AGA having metabolic syndrome was OR=4.00, 95% C.I: 1.16-13.75, which was found to be significant when compared to controls. The stratification of cases and controls in terms of BMI is shown in Table II. The differences in the different parameters that make up metabolic syndrome and their statistical significance are shown in Table III. Serum triglycerides (p = 0.014) and HDL-C (p = 0.03) were found to have a statistical association with AGA after applying the chi square test of association.

DISCUSSION

There was a significant difference in the frequency of metabolic syndrome between cases and controls in this study. Cases of AGA had a 4-fold increased risk of metabolic syndrome compared to controls and this was found to be significant. Some studies have shown a definite link between AGA and cardiovascular disease.[13,14] Some studies have shown the link with cardiovascular disease to be more specifically related to early-onset AGA.[7,8,15] Others show vertex pattern baldness to be more significantly linked to myocardial infarction.[14] There are other studies linking AGA to insulin resistance,[14,16] and its associated systemic disorders including hyperinsulinaemia, obesity, hypertension and dyslipidaemia, i.e various components of the metabolic syndrome. A study by Acibucu et al. showed the rate of insulin resistance and metabolic syndrome to be significantly higher in 80 patients with early-onset AGA.[17]

The present findings are consistent with studies by Behrangi et al., who found that 64% of cases and 53% of controls had co-existant metabolic syndrome, respectively.[18] Although this study did not find such a high frequency of metabolic syndrome (11.9% of cases and 3% of controls had metabolic syndrome, respectively).

Table I: Comparison between means of different variables of metabolic syndrome.

Parameters	Cases	Controls	p-value
BMI	21.01 ± 2.85	21.03 ± 2.35	0.958
Triglycerides	143.75 ± 48.16	129.6 ± 14.59	0.006
Waist circumference	89.64 ± 6.50	86.85 ± 6.13	0.002
Systolic BP	119.31 ± 8.66	118.42 ± 8.45	0.460
Diastolic BP	76.44 ± 9.65	76.14 ± 5.47	0.788
HDL-C	44.0 ± 4.41	44.64 ± 3.33	0.243
Fasting Blood Sugar	88.13 ± 11.78	84.41 ± 18.63	0.091

Table II: Metabolic syndrome in cases and controls stratified in terms of BMI.

BMI	Metabolic syndrome	Group		p-value	OR (CI)
		Cases	Controls		
Underweight BMI<18.5kg/m^2	Yes	2 (8.3%)	0 (0%)	0.532	0.98 (0.87-1.022)
	No	22 (91.7%)	13 (100%)		
Normal weight BMI 18.5-24.9kg/m^2	Yes	5 (7.8%)	1 (1.3%)	0.091	0.15 (0.02-1.35)
	No	59 (92.2%)	77 (98.7%)		
Overweight BMI 25.0-29.9kg/m^2	Yes	5 (38.5%)	2 (20%)	0.405	0.40 (0.06-2.70)
	No	8 (61.5%)	8 (80%)		

Table III: Values of the parameters of metabolic syndrome in cases and controls.

Parameters	Cut-off values	Controls	Cases	p-value	OR (95% CI)
Waist circumference (cm)	<102	93 (92.1%)	94 (93.1%)	0.788	1.16 (0.40-3.32)
	>102	8 (7.9%)	7 (6.9%)		
Triglycerides (mg/dL)	<150	97 (96.0%)	87 (86.1%)	0.014	0.26 (0.08-0.81)
	≥150	4 (4.0%)	14 (13.9%)		
HDL-C (mg/dL)	≥40	99 (98.0%)	92 (91.1%)	0.03	0.21 (0.04-0.98)
	<40	2 (2%)	9 (8.9%)		
Systolic BP (mmHg)	<130	90 (89.1%)	90 (89.1%)	>0.999	1.0 (0.41-2.42)
	≥130	11 (10.9%)	11 (10.9%)		
Diastolic BP (mmHg)	<85	98 (97.0%)	94 (93.1%)	0.194	0.41 (0.10-1.64)
	≥85	3 (3%)	7 (6.9%)		
Fasting blood sugar (mg/dL)	<110	97 (96.0%)	98 (97%)	>0.999	1.35 (0.29-6.18)
	≥110	4 (4.0%)	3 (3%)		

The differences in the frequencies between this study and that by Behrangi et al. may be due to the different study population.[18] In the present study, only the younger male population was included, while that by Behrangi et al., included both males and females with no limitations on age. A study by Banger et al. to determine the association between early-onset AGA and metabolic syndrome had similar lower frequencies (22% of cases and 9% of controls had metabolic syndrome respectively).[12] Another study by Bakry et al. in Egypt had similar results although they also determined whether the underlying link was related to insulin resistance.[19] Both Behrangi et al. and Bakry et al. evaluated the association in both males and females, the present study was gender specific and limited to males.[18,19]

This study also showed no significant differences in BMI of cases and controls (p = 0.958) consistent with a study conducted by Arias-Santiago et al.[20] On the other hand, Matilainen et al. found a significant difference in BMI.[15] These differences may be related to the fact that this study evaluated a younger population, while Matilainen et al. targeted a more middle aged population where both prevalence of AGA and obesity is higher.[15] The present authors also found no link between individuals with an above-average income and BMI (p = 0.584) in cases and controls.

A study by Su et al. found that the link was not limited to metabolic syndrome itself but also to its individual components.[21] They found a significant association with all components of metabolic syndrome. Similar results were obtained by Behrangi et al.[18] However, although the present result showed significant differences in means of serum triglycerides and waist circumference between cases of AGA and controls, on applying the Chi-square test of association, a significant association was found with serum triglycerides (p = 0.014) and HDL-C (p = 0.03). Similar results were obtained by Chakrabaty et al.[22] In their study, as compared to controls with a significant manner, the patients with AGA had higher serum triglycerides, diastolic blood pressure, systolic blood pressure, and lower HDL cholesterol levels. Although this study does not show a significant association with all parameters, this may be related to the younger population and smaller size of this study group.

The present study did not find any significant differences between fasting blood sugar in cases or controls consistent with observations by other.[17,23] A significant association was found by other researchers.[18,19,24] The discrepancies in the results may either be incidental or due to differences in the study populations. A larger study population with no limitations on age may show similar results. Contrary to observations by Pengsalae et al.,[25] the results of this study found a relationship between severity of AGA and metabolic syndrome (p = <0.001).

Due to certain discrepancies in the results more prospective studies are required to more objectively clarify this association. The underlying pathophysiological link, if related to insulin resistance should be investigated further. This study was a gender specific study and further gender non- specific and large population studies are required.

This study does, however, suggest that an association of AGA with metabolic syndrome exists, and early screening for metabolic syndrome is beneficial in patients with androgenetic alopecia to prevent future unforeseen complications by early lifestyle modifications.

CONCLUSION

There is significant association between early onset androgenetic alopecia in younger male population and metabolic syndrome.

ETHICAL APPROVAL:
This study was conducted with the approval from the Ethics Committee of the Mayo Hospital Lahore.

PATIENTS' CONSENT:
Informed consents were obtained from all patients.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS´ CONTRIBUTION:
FZS: Data acquisition, interpretation and drafting.
GB: Analysis, critical revision and final approval.
RH: Conception and design.
AM: Analysis and interpretation.
FA: Interpretation and critical revision.
IH: Final approval.

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