Female pattern hair loss: the relation to metabolic syndrome in premenopausal women

Marwa S. Zaki[a] and Iman Z. Ahmed[b]

[a]Departments of Dermatology and Venereology and [b]Internal Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Correspondence to Marwa S. Zaki, Department of Dermatology and Venereology, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Tel: +20 119 314 861; fax: +20 226 830 767; e-mail: marwasz1973@yahoo.com

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Background
Androgenetic alopecia and its female counterpart, female pattern hair loss (FPHL), are commonly associated with underlying clinical and metabolic abnormalities. Although there are several studies addressing the association of androgenetic alopecia with individual components of the metabolic syndrome (MS) (abdominal obesity, dyslipidemia, hypertension, and hyperglycemia), there are little data available regarding the association between FPHL and the MS as a whole.

Objective
To examine the association of FPHL with MS, diagnosed according to the Adult Treatment Panel-III criteria in premenopausal women, aiming at early identification and management of their modifiable cardiovascular risk factors.

Participants and methods
Thirty-three premenopausal women with Ludwig's stage II and III FPHL and 33 healthy controls were included. For each participant, fasting insulin, fasting blood glucose, homeostasis model assessment of insulin resistance index, lipid profile, waist circumference, and blood pressure were evaluated.

Results
The patients were found to have a significantly higher prevalence of MS compared with the controls (39.4 vs. 9.1%; $P<0.01$), with an odds ratio of 5.95 (95% confidence interval 0.58–61.2). The most common feature in the patients was an increased waist circumference, which occurred at a significantly higher frequency compared with the controls (75.8 vs. 30.3%; $P<0.01$). Patients had a significantly higher waist circumference ($P<0.01$), fasting insulin, fasting blood glucose, homeostasis model assessment of insulin resistance, and lower HDL cholesterol ($P<0.05$) compared with controls.

Conclusion
Women with FPHL have an increased prevalence of the MS, and should be screened and treated for the underlying clinical and metabolic abnormalities.

Keywords:
female pattern hair loss, insulin resistance, metabolic syndrome

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Introduction

Androgenetic alopecia (AGA) is the most common type of hair loss encountered in men and women [1]. As the role of androgens is not fully established, the term 'female pattern hair loss (FPHL)' is preferred to describe the condition in women [2].

Although essentially a cosmetic disorder, associations with underlying clinical and biochemical abnormalities have made AGA of greater clinical significance. Early-onset AGA in men may be associated with obesity, insulin resistance, hypertension, dyslipidemia, metabolic syndrome (MS), and early-onset coronary heart disease [3–7]. However, there are only a few studies addressing these associations in women, most of which included postmenopausal women [1,8,9]. Moreover, previous studies have studied the link between FPHL and individual components of the MS or other related criteria (e.g. insulin resistance) [1,8,10]. There are few data available regarding the association between FPHL and the MS defined according to the standard criteria.

The MS consists of several risk correlates of metabolic origin: abdominal obesity, dyslipidemia, hypertension, and hyperglycemia. MS is a stronger predictor of cardiovascular diseases, diabetes, and stroke compared with its individual components [11]. Individuals with MS have twice the risk for cardiovascular disease and a five-fold risk for type-2 diabetes [12].

The aim of this study was, to examine the association of FPHL with MS according to the Adult Treatment Panel (ATP)-III criteria [13] in Egyptian women, to determine whether FPHL could help in early detection and intervention. As the prevalence of the MS increases with menopause [14], we conducted this study on premenopausal women to avoid the influence of menopausal hormonal changes.

Participants and methods

We conducted a case-control study that included 33 premenopausal female patients (age range 18–40 years) with

Ludwig's stage II or III FPHL [15]. Patients were randomly selected from the Dermatology Outpatient Clinic, Ain Shams University Hospitals, Cairo. Thirty-three premenopausal female volunteers without FPHL were included as controls. For all recruited participants, a thorough history and examination for symptoms and signs of hyperandrogenism and other dermatologic or systemic diseases were performed. Participants were also asked about their smoking habits.

The diagnosis of FPHL was based on the findings of increased hair thinning over the frontal/parietal scalp with a greater hair density over the occipital scalp, retention of the frontal hairline, and the presence of miniaturized hair (seen with the aid of a magnifying loupe). Participants with symptoms and signs of androgen excess such as menstrual irregularities, history of infertility, hirsutism, severe unresponsive cystic acne, virilization, or galactorrhea; previous diagnosis of polycystic ovary syndrome or other endocrinal disorders; and those receiving hormonal treatment or hormone-releasing intrauterine contraceptive device or drugs that may affect blood glucose levels were excluded from the study. None of the patients had other types of alopecia or systemic diseases that may lead to hair fall.

The weight, height, and waist circumference of the participants were measured, and their BMI (kg/m^2) was calculated. Blood pressure was measured after 20 min rest. After a 12-h fasting period, a venous blood sample was taken in the morning from all participants for the detection of fasting serum insulin (FI) levels (Diagnostic Systems Laboratories, Webster, Texas, USA), fasting blood glucose (FBG) levels (Beckman, Fullerton, California, USA), total cholesterol, triglycerides, HDL cholesterol (HDL-C), and LDL-C (Human, Germany).

The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated [glucose (mg/dl) × insulin (μU/ml)/405] to assess insulin resistance [16]. Prevalence of MS was calculated according to the ATP-III criteria; MS was defined by the presence of three of the following (in women) [13]: waist circumference equal to or greater than 88 cm, hypertriglyceridemia equal to or greater than 150 mg/dl, HDL-C less than 50 mg/dl, blood pressure greater than 130/85 mmHg, or FBG greater than 100 mg/dl. All participants included in the study gave their informed consent.

Statistical analysis

The Student *t*-test was applied to compare mean values of the quantitative variables. Qualitative variables were analyzed with the Fisher exact test. To test the independent association of individual MS criteria with FPHL, we performed multivariable conditional logistic regression analysis, adjusting for each of the individual confounding factors. Software (SPSS 16.0; SPSS Inc., Chicago, Illinois, USA) was used for the data analyses. A two-tailed $P<0.05$ was considered statistically significant, whereas $P<0.01$ was considered highly significant.

Results

There was no statistically significant difference in age between the cases and the controls (mean ± SD = 26.8 ± 8.3 vs. 29.9 ± 7.3; $P>0.05$). There was also no significant difference in the frequency of smoking among the two groups (15.2 vs. 12.1%; $P>0.05$). We compared the values of individual MS criteria and other criteria linked to MS (BMI, FI, and HOMA-IR) between the patients and the control participants. No significant difference in BMI between the cases and the controls was found ($P>0.05$). Patients were found to have a significantly higher waist circumference ($P<0.01$), FI, FBG, and HOMA-IR, and lower HDL-C ($P<0.05$) compared with the controls (Table 1).

Among patients with FPHL, prevalence of MS was 39.4% compared with 9.1% in the control participants ($P<0.01$). The most common feature of the MS encountered in patients was an increased waist circumference (75.8%), followed by low HDL-C (57.6%) and elevated FBG (33.3%). Apart from abdominal obesity and low HDL-C, there was no significant difference in the prevalence of any specific factor of MS between the two groups (Table 2).

Using the logistic regression, the odds ratio (OR) for MS was 5.95 [95% confidence interval (CI) 0.58–61.2] in patients with FPHL. There was also an increased tendency for patients with FPHL to have abdominal obesity and low HDL-C with ORs of 3.8 (95% CI 0.9–15.9) and 1.8 (95% CI 0.4–7.4), respectively.

In participants with an increased waist circumference, the OR for MS was 13.2 (95% CI 2.4–79.4), whereas it was 14.7 (95% CI 1.6–134) for patients with both FPHL and an increased waist circumference.

Discussion

In the era of a growing pandemic of MS, it is necessary to recognize and refer patients who are unaware of their increased risk of developing this syndrome, which may have serious cardiovascular consequences [11]. We conducted this study on premenopausal Egyptian women, to

Table 1. Comparison of values of the metabolic syndrome and other related criteria (mean ± SD) in patients with female pattern hair loss and control participants

Factor	Patients	Controls	*P*-value
BMI kg/m^2	28.1 ± 4.3	25.8 ± 5.4	0.06
Waist circumference (cm)	93.5 ± 9.7	85.9 ± 9.9	0.003*
Dyslipidemia (mg/dl)			
Cholesterol	167.9 ± 29.1	161.7 ± 26.3	0.36
Triglycerides	77.1 ± 24.4	65.3 ± 34.7	0.1
HDL-C	51.7 ± 21.3	61.5 ± 15.1	0.04†
LDL-C	109.5 ± 21.9	98.7 ± 29.7	0.097
Insulin resistance			
FI (μU/ml)	13.1 ± 7.7	9.4 ± 4.2	0.02†
FBG (mg/dl)	98.9 ± 15.3	92.2 ± 8.1	0.029†
HOMA-IR (μU/mg)	3.1 ± 2.3	2.1 ± 1.1	0.029†
Hypertension (mmHg)			
Systolic BP	122.2 ± 15.6	116.2 ± 14.6	0.111
Diastolic BP	74.1 ± 10.9	69.4 ± 12.8	0.12

BP, blood pressure; FBG, fasting blood glucose; FI, fasting insulin; HDL-C, HDL cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, LDL cholesterol.
*Highly significant ($P<0.01$).
†Significant ($P<0.05$).

Table 2. Prevalence of the metabolic syndrome criteria in patients and controls

	Patients (%)	Controls (%)	*P*-value
Waist circumference ≥88 cm	75.8	30.3	0.0001*
Blood pressure ≥130/85 mmHg	18.2	9.1	0.09
Triglycerides ≥150 mg/dl	12.1	9.1	0.1
HDL-C <50 mg/dl	51.5	15.2	0.001*
FBG ≥100 mg/dl	33.3	15.2	0.08
Prevalence of MS (≥3 of above factors).	39.4	9.1	0.002*

FBG, fasting blood glucose; HDL-C, HDL cholesterol; MS, metabolic syndrome.
*Highly significant ($P<0.01$).

investigate the association of FPHL with the MS diagnosed according to the ATP-III criteria.

We found that, a significantly larger number of patients in comparison with the controls fulfilled the criteria of MS. Patients with FPHL had a 5.95 times greater probability of having MS compared with those without FPHL. The most common feature of MS encountered in patients was an increased waist circumference, which occurred at a significantly higher frequency and showed higher mean values in relation to the controls. This occurred despite a nonsignificant difference in BMI between the two groups, indicating that visceral accumulation of fat may be independent of obesity and may have an important association with FPHL. Furthermore, patients with FPHL and an increased waist circumference had the greatest probability of having MS (OR = 14.7).

Arias-Santiago *et al.* [9] recently described an increased prevalence of MS in patients with AGA (60% in men and 48.6% in women). Patients included in their study, however, ranged in age from 35 to 55 years, i.e. perimenopausal and postmenopausal women were included, making it difficult to compare their results with ours. Furthermore, ethnic differences play an important role in the susceptibility to various components of the MS [17].

Increased waist circumference (abdominal obesity) has been found to accurately reflect the increase in visceral adipose tissue [18], and is now recognized as a central component of the MS [13]. Visceral accumulation of fat is associated with insulin resistance leading to the development of hyperinsulinemia. The association of insulin resistance and AGA has been reported previously in men [4,7] and in postmenopausal women [1], whereas other studies found no association between AGA in men and insulin resistance [19]. In our study, patients demonstrated significantly higher levels of FI and HOMA-IR, supporting the speculation that insulin resistance may be the pathological link between FPHL and the different features of MS.

The finding that early-onset AGA in men may be associated with early-onset coronary heart disease [3] has led several authors to investigate the association of AGA with dyslipidemias. A higher prevalence of dyslipidemia in men [3,6] with AGA has been reported, whereas no such association was found in women [1]. Recently, Arias-Santiago *et al.* [9] found significantly higher lipid levels in women but not in men with AGA in comparison with their healthy counterparts. The current study adds to the previous studies, in which we demonstrated a significantly lower mean HDL-C values and a higher prevalence of decreased HDL-C in patients in relation to the controls.

It is hypothesized that, differences in endogenous sex steroids and insulin resistance might explain the differences in coronary artery disease between men and women, where women with normal estrogen/androgen profiles have less insulin resistance and favorable (i.e. 'female') lipid profiles. In contrast, women with insulin resistance as a result of obesity (or, more importantly, adipose distribution) and (or) abnormal androgen/estrogen profiles (as in postmenopausal women) lose their favored cardiovascular low-risk status [14]. Mansouri *et al.* [20] demonstrated that the loss of this favored low-risk status may account for the increased cardiovascular risk in patients with FPHL.

Apart from their association in polycystic ovary syndrome, androgen and insulin pathways appear to be closely linked in both women and men [21]. It has been suggested that insulin plays an important role in the development of ovarian hyperandrogenism and related metabolic abnormalities [22]. Hyperinsulinemia may contribute to hyperandrogenism, both directly (through stimulation of androgen biosynthesis in the ovarian theca cell and the adrenal zonafasciculata) and indirectly (through its suppressive effects on sex hormone-binding globulin and insulin-like growth factor-binding protein-1 production by the liver) [23]. Hyperinsulinemia may also induce 5-α reductase activity, leading to an increased conversion of testosterone to dihydrotestosterone [24]. As the majority of women with FPHL have no biochemical evidence of androgen excess [25], but rather have higher levels of 5-α reductase, more androgen receptors, and lower levels of cytochrome P450-aromatase (which converts testosterone to estrogen) in hair follicles of frontal balding areas [26], it seems reasonable to suggest that these may be the sites of action where insulin contributes to the clinical manifestations of hyperandrogenism.

In conclusion, we have found a higher prevalence of MS in premenopausal women with FPHL, which could have severe cardiovascular consequences. We recommend that patients with FPHL, especially if associated with an increased waist circumference, should be screened for components of MS for early identification and management.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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