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Prevalence of Metabolic Syndrome and its Components in Early Onset Androgenetic Alopecia: A Case Control Study from a North Indian Tertiary Care Hospital

Erken Başlangıçlı Androgenetik Alopeside Metabolik Sendrom ve Bileşenlerinin Görülme Sıklığı: Kuzey Hindistan Üçüncü Basamak Bakım Hastanesinden Bir Olgu Kontrol Çalışması

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ABSTRACT Objective: Androgenetic alopecia is the commonest cause of hair loss in males and has been associated with coronary heart disease. This study aims to find relationship between androgenetic alopecia and metabolic syndrome. **Materials and Methods:** This hospital based case-control study was conducted on 50 clinically diagnosed male patients of early onset androgenetic alopecia (<30 years) with Norwood grade ≥ II. 50 age matched patients attending the outpatient department for other unrelated complaints were taken as controls. The patients were enquired regarding age, age of onset, occupation, family history of androgenetic alopecia and smoking habit. Examination for grade of disease, body mass index, blood pressure and waist circumference was done and patients investigated for hyperglycemia and dyslipidemia. Metabolic syndrome was diagnosed as per the National cholesterol education program's adult treatment panel III (NCEP ATP III) criteria. **Results:** Both the groups were statistically comparable in terms of age. Metabolic syndrome was found in 15 (30%) patients and 6 (12%) controls. 29 patients in case group and 16 in controls were dyslipidemic. Family history of androgenetic alopecia was found in 23 patients of case group and 12 patients of control group. However, we found no difference in increased blood pressure (>130/85) and hyperglycemia (FBS>100 mg/dL) between the two groups. **Conclusion:** Patients of early onset androgenetic alopecia appear to have greater frequency of metabolic syndrome especially dyslipidemia. Therefore, androgenetic alopecia patients may be evaluated for metabolic syndrome especially dyslipidemia.

Keywords: Androgenetic alopecia; metabolic syndrome; dyslipidemia

ÖZET Amaç: Androgenetik alopesi erkeklerde saç kaybının en yaygın nedeni olup, koroner kalp hastalığı ile de birliktelik gösterir. Bu çalışmanın amacı androgenetik alopesi ile metabolik sendrom arasında bir ilişki olup olmadığını incelemektir. **Gereç ve Yöntemler:** Hastane bazlı vaka-kontrol çalışmamızda klinik olarak erken androgenetik alopesi (<30 yaş) tanılı, Norwood ≥ II evresinde 50 erkek hasta incelendi. Diğer polikliniklere başvurmuş, farklı şikayetleri olan, yaşları eşlenik 50 kişi kontrol grubu olarak alındı. Hastalar yaşları, meslekleri, sigara içimi, hastalıklarının ailesel öyküsü ve ilk ortaya çıktığı dönemlerine göre gruplandırıldı. Hastalıklarının şiddeti, beden kitle indeksleri, kan basınçları, bel çevresi ölçümleri, hiperglisemik ve dislipidemik olup olmadıkları incelenip kaydedildi. Metabolik sendrom tanıları ise "Ulusal Kolesterol Yetişkinler Eğitimi Panel III (NCEP ATP III)" kriterlerine göre yapıldı. **Bulgular:** Grupların yaşları istatistiki olarak karşılaştırılabilir dönemlerdeydi. 15 hastada (%30) ve 6 kontrol kişisinde (%12) metabolik sendrom tespit edildi. Hasta grubundan 29, kontrol grubundan ise 16 kişide dislipidemi saptandı. Hasta gruptan 23 kişide kontrol gruptan ise 12 kişide ailesel androgenetik alopesi öyküsü mevcut idi. Bununla birlikte, 2 grup arasında yüksek kan basıncı (>130/85) ve hiperglisemi (FBS>100 mg/dL) yönünden farklılık saptamadık. **Sonuç:** Erken androgenetik alopesi hastalarında metabolik sendrom ve özellikle dislipidemi açısından sıklık yüksekti. Bu nedenle, androgenetik alopesi hastaları metabolik sendrom, özellikle de dislipidemi yönünden dikkatle incelenmelidir.

Anahtar Kelimeler: Androgenetik alopesi; metabolik sendrom; dislipidemi

Androgenetic alopecia is also called as 'Common baldness' because of being the most frequent cause of hair loss in men. The disease has a polygenic inheritance and miniaturization of hair follicle is the central event in the pathogenesis of this disease.[1] At least physiological levels of circulating androgens are needed to produce androgenetic alopecia but androgen levels are usually normal, proving a role of end organ hyperreactivity to androgen.[2] Metabolic syndrome (MS) is a constellation of risk factors including abdominal obesity, dyslipidemia and hypertension.[3] Androgenetic alopecia is found to be associated with coronary artery disease in a number of studies and metabolic syndrome is the preceding event in a majority of such patients.[4-6] Metabolic syndrome adds to the damage to the self esteem that androgenetic alopecia usually produces.[7] Our study aims to find an association between early onset androgenetic alopecia and metabolic syndrome.

MATERIAL AND METHODS

This was a hospital based analytical cross-sectional study, carried out on 50 cases and 50 age matched controls, attending the Outpatient Department (OPD) of Dermatology, over a period of one year from September 2016 to August 2017. Male patients of age ranging from 18 years to 50 years, having clinically diagnosed androgenetic alopecia of early onset (before 30 years of age) and Norwood grade > II were taken as cases. Similar age matched 50 controls attending the outpatient department for disease other than androgenetic alopecia (mostly dermatophytic infection and wart patients) were taken as controls. This study was limited to 50 years of age because of increased prevalence of metabolic syndrome with increasing age.[8] Because of the controversial role of androgen and differences in pathogenesis of female pattern hair loss, females were excluded from the study.[9] Patients receiving oral corticosteroid therapy, hormone replacement therapy with testosterone, psoriasis and hypothyroidism were excluded from the study to minimize the confounding factors of metabolic syndrome. Ethical approval for conducting the study was taken from Institutional ethics committee.

Diagnosis of androgenetic alopecia was made based on the characteristic pattern of hair loss involving mainly frontal and parietal scalp area. Patients were classified as per Norwood grade system. After obtaining informed consent from the patients, a detailed history including age of patient, age of onset of androgenetic alopecia, family history of androgenetic alopecia and other co-morbidities were taken. Personal history and any drug history especially related to hypertension and dyslipidemia was enquired. All patients were then examined and weight, height and waist circum ference was recorded. Waist circumference was measured by the standard non-stretchable standard plastic measuring tape, at the midpoint between lower margin of the last palpable rib and top of the iliac crest at the end of a normal expiration. Systolic and diastolic blood pressure were measured using standard oscillometric method with standard cuff size after five minutes of rest and one more reading taken ten minutes apart and mean value of two readings was recorded. All patients were then investigated for plasma sugar and complete lipid profile in a blood sample drawn between 8 and 10 am after a 12 hour fast.

The diagnosis of metabolic syndrome was made as per revised NCEP ATP III (National Cholesterol Education Program, Adult Treatment Panel III) criteria that mandates the presence of at least three out of the five factors: (1) waist circumference ≥ 90 cm for Indian men (ethnicity-specific value) (2) raised triglycerides ≥ 150 mg/dl (1.7 mmol/l), (3) reduced high-density lipoprotein (HDL) cholesterol < 40 mg/dl (1.03 mmol/l) in men and < 50 mg/dl (1.29 mmol/L) in women, (4) raised BP: Systolic BP ≥ 130 or diastolic BP ≥ 85 mm of Hg, and (5) raised fasting plasma glucose (FPG) ≥ 100 mg/dl (5.6 mmol/l).[10]

STATISTICAL ANALYSIS

Analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 18.00. The Student's t-test was applied to compare mean values of quantitative variables. Qualitative variables were analyzed with a Chi-square test. $P<0.05$ was considered significant.

RESULTS

This study was carried out on a total of 100 patients, out of that 50 patients of androgenetic alopecia constituted the case group while 50 patients having some other unrelated disease were selected as controls. Both the groups were statistically comparable in terms of age (p = 0.833). The age distribution of patients is given in (Table 1). Out of 50, 22 patients (44%) were having Norwood grade III alopecia making it single largest group, followed by grade II (26% patients). The grade distribution of androgenetic alopecia of patients included in this study has been depicted in (Table 2). Dyslipidemia was seen in 29 cases (58%) compared to 16 controls (32%) (p=0.015). Abdominal obesity was found in 22 cases (44%) compared to 13 controls (26%) (p= 0.037). 19 patients (38%) from the case group were found to have blood pressure > 130/85, compared to 15 controls (30%) (p=0.149). Increased plasma glucose was seen in 9 patients (18%) in the case group compared to 6 controls (12%) (p=0.575). Family history of androgenetic alopecia was present in 23 cases (46%) compared to 12 patients (24%) among controls, making it a statistically significant (p= 0.036) association. Taking all factors into consideration, metabolic syndrome was diagnosed in 15 patients from case group and 6 patients from control group (Table 3). After statistical calculation, this association was found to be statistically significant (p = 0.049). Dyslipidemia and abdominal obesity were major contributory factor in satisfying the criteria of metabolic syndrome. However, prevalence of metabolic syndrome increased with the rise in severity of androgenetic alopecia but did not correlate statistically with the severity of androgenetic alopecia (p=0.876) (Figure 1).

TABLE 1: Age distribution of patients.

	Cases (n=50)		Controls (n=50)	
Age (in years)	Number of patients	Percentage	Number of patients	Percentage
18- 30	26	52	23	46
31- 40	18	36	20	40
41- 50	6	12	7	14
		p=0.833		

TABLE 2: Grade of androgenetic alopecia among cases.

Hamilton-Norwood grade	No. of patients
Grade II (including IIA)	13 (26%)
Grade III (including IIIA and IIIV)	22 (44%)
Grade IV (including IVA)	8 (16%)
Grade V (including VA)	5 (10%)
Grade VI	2 (4%)
Total	50 (100%)

DISCUSSION

Metabolic syndrome is a known risk factor for coronary heart disease and other cardiovascular diseases, and has been associated with higher mortality even after adjusting other risk factors for cardiac diseases. The morbidity and mortality risk increases with the increasing number of components of metabolic syndrome present in the individual.[11] As per aim of our study, we tried to find any association between early onset androgenetic alopecia and metabolic syndrome, in order to predict any future risk of cardiovascular morbidity and mortality. In spite of having a cross-sectional data supporting an association between coronary heart disease and high testosterone level in men, Wu et al. in his large prospective study didn't confirm any significant and independent association between endogenous testosterone levels and coronary events in men and women.[12] A high prevalence of androgenetic alopecia in the population and importance of cardiovascular disease as a leading cause of mortality in many countries mandate the study of the association between the two conditions.[13]

Our study has shown an increased prevalence of metabolic syndrome in patients of early onset androgenetic alopecia, when compared with healthy unrelated age matched controls (p=0.049). A few similar studies have been done in the past, which have found results similar to that of our study. Gopinath et al. conducted a similar study in a South Indian city, where he found metabolic syndrome in 19 (22.4%) cases of androgenetic alopecia and 8 (9.4%) controls (p=0.021).[14] A case-control study conducted by Arias-Santiago et al. in

TABLE 3: Comparison of metabolic syndrome and its components among patients.

	Cases (n = 50)		Controls (n = 50)		
Factors	**Number of patients**	**Percentage**	**Number of patients**	**Percentage**	**p value**
Dyslipidemia (TG > 150 mg/dl, HDL < 40 mg/dl)	29	58	16	32	0.015
Abdominal obesity (WC > 90 cm)	22	44	13	26	0.037
Hypertension (BP > 130/85)	19	38	15	30	0.149
Fasting plasma sugar (> 100 mg/dl)	9	18	6	12	0.575
Metabolic syndrome	15	30	6	12	0.049

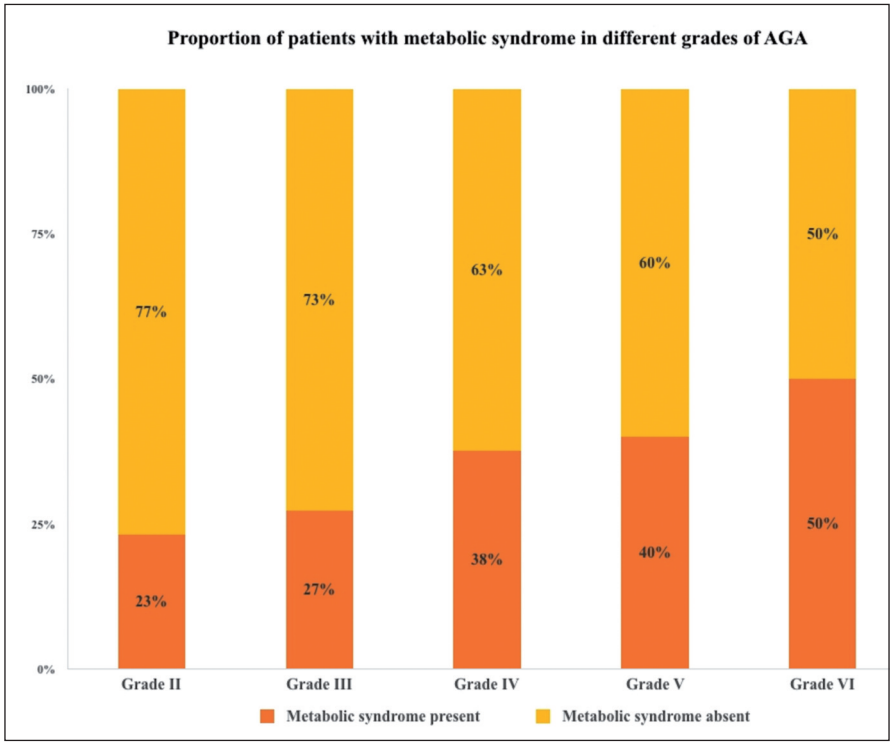

FIGURE 1: Proportion of patients with metabolic syndrome in different grades of androgenetic alopecia (AGA).

Spain involving 77 participants with early-onset androgenic alopecia and 77 controls, demonstrated metabolic syndrome in 60% of men with androgenic alopecia, 48.6% of women with androgenic alopecia, 12.5% of male control subjects and 8.1% of female control subjects (P<0.0001).[15] The lower incidence of metabolic syndrome in our study might be attributed to the ethnic and lifestyle variation of both countries. However, we found no statistically significant association between the severity of androgenetic alopecia (as determined by Norwood grade) and prevalence of metabolic syndrome (p=0.876).

In a community based survey in Taiwan, done by Su et al. they found a statistically significant association between androgenetic alopecia and presence of metabolic syndrome, after controlling for other confounding factors like age, family history of androgenetic alopecia and smoking status.[16] Among all metabolic syndrome components, high density lipoprotein cholesterol (HDL-C) was revealed as the most important factor associated with androgenetic alopecia in their study.

In our study, we found abdominal obesity (indicated by increased waist circumference) to be a

statistically significant (p=0.037) factor causing difference in metabolic syndrome prevalence among cases and controls. Hirsso et al. also found a similar result showing that men with moderate to extensive alopecia had larger waist circumference compared to controls without alopecia (p<0.05).[17] Increased waist circumference should be considered an independent risk factor for mortality, as depicted by Koster et al. in his study.[18] After adjustment for body mass index (BMI) and other covariates, they found that a large waist circumference was associated with an approximately 25% increased mortality risk.

Among all factors, our study has found dyslipidemia as the most important contributory factor in causation of metabolic syndrome in patients of androgenetic alopecia compared to controls (p= 0.015). A similar result was demonstrated by Sadighha et al. in their study.[19] They found lower high density lipoprotein cholesterol (HDL-C) and higher triglyceride levels in men with vertex type androgenetic alopecia compared with controls. Bakry et al. found a significant difference in the mean values of triglyceride and HDL-C between patients with androgenetic alopecia and controls.[20] Dyslipidemia is a known risk factor and important contributor towards cardiovascular disease related morbidity and mortality. Therefore, dyslipidemia acts as a bridge between androgenetic alopecia and increased coronary heart disease related mortality risk.

In contrast to the proposal of insulin resistance as the underlying pathophysiological cause of metabolic syndrome,[21] our study didn't reflect any significant association between elevated fasting plasma glucose and androgenetic alopecia. Insulin and insulin resistance related parameters were not evaluated in our study. A similar result was obtained by Ekmekci et al. who also didn't find any significant difference in fasting blood glucose in women with androgenetic alopecia compared with controls.[22] However, Matilainen et al. found a twofold risk of hyperinsulinemia in men with early onset androgenetic alopecia compared with controls.[23]

We found no statistically significant association between hypertension and early onset androgenetic alopecia in our study (p=0.575). Ahouansou et al. conducted a study in France and found a strong association between hypertension and androgenetic alopecia in 250 Caucasian men.[24] The difference in results can be explained by the age distribution of subjects taking part in study, as Ahouansou et al. in their study, included patients upto 65 years of age, while age limit in our study was 50 years. Moreover, ethnic variation and a very frequent self-administered injudicious use of minoxidil for androgenetic alopecia (which also have an antihypertensive action) in our setup can also be a cause of this conflict of result.

In our study, we found a statistically significant (p=0.036) association of family history in patients having androgenetic alopecia, when compared with age and sex matched controls. Gopinath et al. also found similar results in a study from South India.[14] This association of family history probably explains the genetic factors involved in the causation of the disease.

The limitation of our study was the small sample sizes in both the subgroups. Being a cross-sectional study, we were unable to find any temporal relationship between androgenetic alopecia and metabolic syndrome.

CONCLUSION

In our study, a significant association between early onset androgenetic alopecia and metabolic syndrome was seen. As metabolic syndrome may predispose a patient of early onset androgenetic alopecia to develop cardiovascular diseases in future, leading to an increased risk of morbidity and mortality. Therefore, a patient presenting with early onset androgenetic alopecia should be screened for metabolic syndrome and its components and intervened if necessary. Further studies with larger sample sizes are needed to establish the relationship between the grade or duration of androgenetic alopecia with metabolic syndrome, as well as its components.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Syed Suhail Amin, Mohammad Adil;* ***Design:*** *Mahtab Alam, Mohammad Adil, Mohd Mohtashim;* ***Control/Supervision:*** *Syed Suhail Amin, Mohammad Adil;* ***Data Collection and/or Processing:*** *Mahtab Alam, Annu Priya;* ***Analysis and/or Interpretation:*** *Mohd Mohtashim, Sabha Mushtaq;* ***Literature Review:*** *Mohd Mohtashim, Sabha Mushtaq;* ***Writing the Article:*** *Mahtab Alam, Annu Priya;* ***Critical Review:*** *Syed Suhail Amin, Mohammad Adil;* ***References and Fundings:*** *Mahtab Alam, Mohammad Adil;* ***Materials:*** *Mahtab Alam, Mohammad Adil.*

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