Original Research Article

Severe androgenetic alopecia as a maker of metabolic syndrome in male patients of androgenetic alopecia: a hospital based case control study

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ABSTRACT

Background: Several previous studies have investigated the association between androgenetic alopecia (AGA) and metabolic syndrome (MS), with inconsistent results. Objectives of the study were to study the prevalence of metabolic syndrome in male patients of androgenetic alopecia and compare with control population and study the relationship of metabolic syndrome with different grades of AGA.
Methods: This prospective hospital based case control study included 100 new clinically diagnosed males of androgenetic alopecia, and age and sex matched control group. Assessment for presence of various components of metabolic syndrome was done following a uniform protocol in cases and controls. AGA was classified as per Hamilton –Narwood classification, grade I to III was classified as mild –moderate and grade IV and higher as severe AGA.
Results: Of the 100 male AGA patients (age range 21-50, mean 34.49), 36 had grade II AGA, 24 had grade III AGA, 20 had grade IV AGA, 15 had grade V AGA and 5 had grade VI AGA. Among AGA patients, 60 of patients had mild-moderate AGA and 40 patients had severe AGA. Metabolic syndrome was statistically significantly more common in patients with AGA compared to controls. Among patients of AGA, metabolic syndrome was statistically significantly present in severe AGA compared to mild-moderate AGA. Among the evaluated parameters, like blood pressure, fasting blood sugar, dyslipedemia, abdominal obesity, all were significantly more common in AGA patients compared to controls except abdominal obesity.
Conclusions: In the present study, metabolic syndrome was found to be 4.6 times more common in patients of androgenetic alopecia as compared to controls, being statistically significant, and more common in those with severe grades. This suggests that androgenetic alopecia patients especially with severe grades are at risk of metabolic syndrome and other cardiovascular diseases.

Keywords: Androgenetic alopecia, Cardiovascular disease, Metabolic syndrome

INTRODUCTION

Androgenetic alopecia (AGA), a common cause of non-cicatricial alopecia, is characterized by a gradually progressive transformation of terminal hair follicles to miniaturized hair in genetically predisposed males and females, defined by various patterns, and being more common in males.[1,2] In androgenetic alopecia, the duration of anagen phase gradually decreases and that of telogen phase increases, leading to miniaturization and eventually a bald appearance, as the duration of anagen phase determines the hair length.[3]

It has long been recognized that male pattern baldness runs in families and has a polygenic mode of inheritance and previous studies confirm a strong genetic element

associated with it, with concordance rates of 80-90% in monozygotic twins and consistently lower rates in dizygotic twins.[4] Although generally regarded as an androgen mediated process, the contribution from other coexisting risk factors is likely based on the observation of different patterns of androgenetic alopecia and lack of responsiveness to antiandrogen therapy in a group of subjects.[1,5-7]

Over the past two decades, there is evidence showing the association between androgenetic alopecia and metabolic syndrome or its associated diseases including cardiovascular diseases, hypertension and insulin resistance.[8] Metabolic syndrome is the combination of hypertension, abdominal obesity, dyslipidemia, impaired fasting glycemia and insulin resistance which has been associated with increased risk of cardiovascular diseases.[9]

There is a need to approach the disease as potentially multisystem disorder, so that such patients may be advised timely screening and treatment. Keeping this in mind, we undertook a study to assess the prevalence of metabolic syndrome in male patients of androgenetic alopecia, the first of its kind from Jammu region of North India.

METHODS

This prospective hospital based case control study was conducted in department of dermatology in a tertiary care center in Jammu over a period of one year from November 2014 to October 2015. Cases included clinically diagnosed male patients of Androgenetic alopecia with age more than 18 years.

Exclusion criteria

- Age less than 18 years; females
- Other types of alopecia like alopecia areata, scarring alopecia
- Other skin diseases associated with metabolic syndrome like Psoriasis;
- Patients with thyroid diseases, familial hyperlipidemia, nephritic syndrome, chronic renal failure;
- Patients on drugs that are known to cause hyperglycemia, hyperlipedimia, hypertension.

The control group included male patients attending the department for skin diseases other than androgenetic alopecia, and male attendants of patients matched by age and other risk factors.

A detailed history was taken regarding name, age, occupation, age of onset and duration of disease, family history of alopecia, family history of cardiovascular disease, diabetes, hypertension, personal habits like smoking, alcohol intake and tobacco consumption. General physical and systemic examination was performed. The diagnosis of male pattern Androgenetic

alopecia was made clinically based on characteristic pattern showing recession of the frontotemporal hair line and hair thinning over the frontal and/ or vertex areas. The grading of male pattern androgenetic alopecia was done according to modified Norwood- Hamilton classification – Norwood - Hamilton grade I-III was taken mild to moderate male pattern androgenetic alopecia and grade IV and higher as severe. Early onset androgenetic alopecia was taken grade III male pattern androgenetic alopecia before 30 years of age.[10]

Biometric data such as weight, height, waist and hip circumference was taken. Height measurement was taken twice and average was considered. Weight measurement was taken in participants with light clothes and without shoes.

To determine waist circumference, a non-extendable measuring tape was placed at the level of the umbilicus and the widest part of hip for hip circumference. Body Mass Index or BMI was calculated by weight in kilograms /Height in meters^2 (Quetelet's Index). Blood pressure was taken as average of two measurements taken 5 minutes apart after subjects have been sitting for 5 minutes.

Besides routine investigations like haemogram, liver function test and renal function, the following investigations were carried out in both cases and controls after 12 hours of overnight fasting using enzymatic methods: Serum levels of fasting blood sugar, Total cholesterol, Triglycerides (TG), Low –density lipoprotein cholesterol (LDL), High density lipoprotein cholesterol (HDL), Very low density lipoprotein cholesterol (VLDL).

Thyroid profile, serum ferritin and fasting insulin levels were done in some patients. Metabolic Syndrome was defined according to National Cholesterol Education Programe (NCEP) adult treatment panel 3 (ATP3) by the presence of 3 of following

- Abdominal circumference greater than 102 cm in men and 88 cm in women.
- Hyper-triglyceridemia greater than 150mg/dl.
- High density lipoprotein cholesterol (HDL-C) less than 40mg/dl in men and less than 50mg/dl in women.
- Blood pressure greater than 130/85 mmHg.
- Glycemia greater than 100 mg/dl.

A BMI greater than or equal to 25 was taken as overweight and BMI greater than or equal to 30 as obesity, as per WHO definition.

Statistical analysis

Appropriate statistical techniques was used to find out prevalence and significance of any apparent association by using Fischer exact test based on the type of data available.

RESULTS

100 male patients of AGA patients (age range 21-50, mean 34.39) and 100 controls (age range 20-50, mean 34.14) were studied. Of the 100 AGA patients 36 (36%) had grade II AGA, 24 (24%) had grade III AGA, 20 (20%) had grade IV AGA, 15 (15%) had grade V AGA and 5 (5%) had grade VI AGA according to Hamilton-Narwood classification. According to severity 60 patients (60%) had mild - moderate AGA and 40 (40%) severe AGA.

Table 1: Prevalence of metabolic syndrome among cases and controls.

Metabolic syndrome (MS)	Patients (n=100)	Controls (n=100)	P value (<0.05)
Present	14	03	0.0093
Absent	86	97	

Metabolic syndrome was found to be statistically significantly more common in AGA patients as compared to controls (p=0.0093) (Table 1). Among the patients, metabolic syndrome was found to be statistically significantly more common in patients with severe AGA as compared to patients with mild-moderate AGA (p=0.0002) (Table 2).

Table 2: Prevalence of metabolic syndrome as per the disease severity.

Severity of AGA	No of patients (n=100)	Percentage (%)
Mild-moderate AGA	2/60	3.3%
severe AGA	12/40	30%
P value	0.0002	

Hypertension, impaired fasting glucose and dyslipedemia was found to be statistically significantly more common in AGA patients as compared to controls (Table 3). Among the patients of AGA these parameters were statistically significantly more common in patients with severe AGA as compared to patients with mild- moderate AGA (Table 4).

Table 3: Other risk factors associated with androgenetic alopecia between cases and controls.

Risk factor present	Patients (%)	Controls (%)	P value
Hypertension	18	5	0.0067
Impaired fasting glucose	15	3	0.0052
Triglycerides>150	16	6	0.04
HDL<40	15	3	0.0052
Total cholestrol>200	16	6	0.04
Abdominal obesity	15	7	0.112

Table 4: Association of risk factors as per the severity of disease.

Severity of AGA	HTN	IFG	Abdominal obesity	T.C	HDL	Triglycerides
Mild-moderate	3/60 (5%)	3/60 (5%)	3/60 (5%)	4/60 (6.67%)	3/60 (5%)	4/60 (6.67%)
Severe	15/40 (37%)	12/40 (30%)	12/40 (30%)	12/40 (30%)	12/40 (30%)	12/40 (30%)
P value	0.0002	0.0001	0.0001	0.0041	0.0001	0.0041

There was no statistically significant difference between age, weight, height, BMI, abdominal obesity between cases and controls.

DISCUSSION

In 1972 it was first suggested that androgenetic alopecia may be a risk factor for cardiovascular disease and an association between occurance of cardiovascular diseases and hair loss was demonstrated.[11] Over the past two decades, evidence has emerged showing the association between androgenetic alopecia and metabolic syndrome or its associated diseases including cardiovascular diseases, hypertension, dyslipidemia and insulin resistance.[8] The present study conducted in a tertiary care center was a prospective case control study, in which total of 100 male patients of androgenetic alopecia and equal number of age matched male controls were studied during study period of one year. The age distribution of cases and controls was comparable.

Maximum number of patients in this study had grade II (36%) and grade III (24%) Hamilton and Narwood classification of androgenetic alopecia, comparable to previous studies.[12-14]

Association of androgenetic alopecia with metabolic syndrome has been reported by many investigators in

literature. In present study metabolic syndrome was found in 14 (14%) patients out of 100 patients of androgenetic alopecia as compared to 3 (3%) patients in controls. The difference was statistically significant (p<0.05). Androgenetic alopecia patients were found to be 4.6 times more likely to have metabolic syndrome as compared to controls (RR=4.66). The results of our study were found to be comparable with many previous studies.[8,14-16] This was in contrast to other studies where no statistically significant difference was seen in the prevalence of metabolic syndrome between patients of androgenetic alopecia and control population.[17,18]

In present study, metabolic syndrome was found more commonly in patients of androgenetic alopecia with higher grade severity 12/40 (30%) as compared to the androgenetic alopecia patients with mild-moderate severity 2/60 (3.3%). Androgenetic alopecia patients with mild-moderate severity were 9 times less likely to have metabolic syndrome as compared to those with severe severity. The difference was statistically significant (P<0.05). This observation was similar to some multicenter studies.[19] In present study metabolic syndrome was seen more commonly in patients with age >40 years in both cases and controls, difference was statistically significant in cases (P<0.0001) but not in controls (P=0.09).

The mean values of systolic and diastolic blood pressure were higher in cases than controls in present study. Hypertension was found in 18/100 (18%) cases and 5/100 (5%) of controls. There was statistically significant difference (P<0.05) in the prevalence of hypertension between cases and controls, with androgenetic alopecia patients 3.6 times more likely to be hypertensive as compared to controls (RR=3.6). The results of our study were similar to many previous studies.[20,21] Raised aldosterone levels have been held responsible for both androgenetic alopecia and hypertension, paving way for the role of aldosterone antagonists for control of blood pressure and halt in progression of alopecia.[8,22] Aldosterone causes increase in the level of ROS, EGF beta and TGF beta which modulate fibrinolytic effects and inflammatory response which may be responsible, along with other factors in causing perifollicular fibrosis and inflammation in androgenetic alopecia. However Hissro et al did not find any statistically significant differences for systolic or diastolic blood pressure levels in patients aged less than 35 years, and likewise, Gok SO et al in a study found significant association between androgenetic alopecia and systolic blood pressure (P<0.05) but not with diastolic blood pressure.[18,23]

In the present study, there was no statistically significant difference(P>0.05) in abdominal obesity (WC>102cm) between case 15/100 (15%) and controls 7/100 (7%), similar to some of previous studies; and in contrast to some.[8,14,15,18,19] Abdominal fat tissue is associated with serious metabolic disorders, such as insulin resistance, hyper-insulinemia, hypertension, increased triglycerides, glucose intolerance, diabetes and metabolic syndrome, coronary heart disease.[15,24] The absence of association in our study could be because of predominance of patients with younger age group in present study.

There was statistically significant (P<0.05) difference in the prevalence of dyslipidemia between cases and controls in present study. There was statistically significant (P<0.05) decrease in HDL and statistically significant increase in LDL, cholesterol and triglyceride level in patients with androgenetic alopecia as compared to controls (P<0.05). Increased LDL was seen in 14% cases as compared to 3% in controls (P=0.0052). HDL was decreased in 14% cases and controls (P=0.0052). Serum cholesterol and triglyceride level was increased in 16% cases and 6% controls (P=0.04). Among the patients of androgenetic alopecia HDL was decreased in 30% patients with severe androgenetic alopecia as compared to 5% in mild-moderate androgenetic alopecia (P=0.0011). LDL was increased in 30% patients with severe androgenetic alopecia as compared to 5% in mild-moderate androgenetic alopecia (P=0.0011). Serum cholesterol and triglyceride level was increased in 30% androgenetic alopecia patients with severe AGA as compared 6.67%in patients with mild-moderate AGA (0.0041). The results of our study were similar to many previous studies.[8,19,25] In contrast, Guzzo et al found no statistically significant difference in lipid indices of cases and controls.[26]

The elevated lipid values in androgenetic alopecia patients may contribute, alongside other mechanisms, to the development of cardiovascular disease (CVD).[27,28]

In present study the mean values of fasting blood glucose was higher in cases as compared to controls, and the prevalence of impaired fasting glucose (IFG) (>100mg/dl) was found statistically significantly higher in cases (15%) as compared to controls (3%) (P=0.0052). Androgenetic alopecia patients were found to be 5 times more likely to have impaired fasting glucose as compared to controls (RR=5). Among the patients of androgenetic alopecia impaired fasting glucose was seen in 30% patients with severe AGA as compared to 5% of patients with mild –moderate AGA (P=0.0011). Androgenetic alopecia patients with severe AGA were found to be 6 times more likely to have impaired fasting glucose as compared to AGA patients with mild-moderate AGA (RR=6). These observations were similar to previous studies.[14,19,20] This was in contrast to other studies.[15,29]

Limitations

The limitations of the study were small sample size, non-measurement of Insulin level.

CONCLUSION

In the present study, metabolic syndrome was found to be 4.6 times more common in patients of androgenetic

alopecia as compared to controls, which was statistically significant, with metabolic syndrome being more common in those with severe androgenetic alopecia as compared to those with mild-moderate androgenetic alopecia. Metabolic syndrome was also found to be more common in age group >40 years in both cases and controls.

Along with increased prevalence of metabolic syndrome, its various components including, abdominal obesity, hypertension, impaired fasting glucose and dyslipidemia were found more in patients of androgenetic alopecia especially those with severe androgenetic alopecia. This suggests that androgenetic alopecia patients are at risk of metabolic syndrome and other cardiovascular diseases. It is important to ascertain the risk of co-morbidities across the whole spectrum of androgenetic alopecia so that patients with significant disease or associated risk factors can be timely screened, educated/counseled and managed accordingly. This lays emphasis to the fact that androgenetic alopecia should be taken as a potentially multisystem disorder and patients should be warned accordingly about the possible negative consequences of their disease and counseling for healthy life style in order to correct their modifiable risk factors.

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