Study of prevalence of metabolic syndrome in androgenetic alopecia

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ABSTRACT

Background: Androgenetic alopecia (AGA) is commonly known as male pattern baldness has a prevalence of up to 50% in men worldwide. It occurs in most patients before the age of 40 years. It is characterized by a progressive conversion of terminal hair into miniaturized hair defined by various patterns. Various studies have shown that androgenetic alopecia have significant physical and psychological morbidity and a lowered dermatological life quality index.

Methods: The study included 75 patients with clinical diagnosis of AGA and 75 age and sex matched controls. After taking complete history, general examination and thorough dermatological examination was performed in all cases to grade the severity of AGA. Fasting serum samples were taken from all cases and controls and assayed for fasting plasma glucose and lipid profile. Metabolic syndrome (MS) was diagnosed according to 2005 revised National Cholesterol Education Programme’s Adult Treatment Panel III (NCEP ATP III). Chi square test was used for statistical analysis.

Results: Metabolic syndrome was seen in 25 cases (33.3%) compared to 11 controls (14%), which was statistically significant (p=0.007). Statistically significant increased prevalence of raised TGL levels (p=0.002), raised LDL levels (p=0.024), low HDL levels (p=0.0001), diabetes mellitus (p=0.004) was also observed in AGA.

Conclusions: There is a clear association between AGA and MS and there is statistically significant prevalence of MS in patients with increasing severity and duration of AGA. Screening is required for early detection of dyslipidemia, diabetes mellitus and MS in all patients of AGA to prevent long-term morbidity.

Keywords: AGA, Dyslipidemia, Diabetes mellitus, Metabolic syndrome

INTRODUCTION

Androgenetic alopecia (AGA) is the most common type of hair loss in men which occurs under the influence of androgens in genetically predisposed individuals.1-3 Hair loss progresses to a bald scalp in 50-60% of men by the age of 70 years.4 The frequency and severity of pattern of hair loss is lower in women but still affects a sizeable proportion of the population.

Metabolic syndrome (MS) is a cluster of risk factors including central obesity, atherogenic dyslipidemia, hypertension and glucose intolerance and is a strong predictor of cardiovascular disease.5 AGA may act as an external indicator of underlying immune and metabolic dysregulation and recently its association with androgenetic alopecia and metabolic disorders such as obesity, diabetes, atherogenic dyslipidemia have been recognized.6-8

Although many studies have been conducted till date to elucidate the metabolic abnormalities occurring in AGA individuals, only few focused on severity of AGA with MS. The present study was performed to pin the association of severity and duration of AGA and MS in Indian patients.
METHODS

This study was carried out in patients, who attended the outpatient department of Dermatology, at a suburban medical college hospital in North Andhra Pradesh. It was a prospective, hospital based case-control study carried out over a period of 18 months from January 2015 to June 2016 after being approved by Institutional Ethics Committee. The sample size was calculated difference if means formula. To achieve a power of study of 80% and precision alpha of 0.05 with a 95% confidence interval (CI), the estimated sample size per group was determined to be 75.

Seventy five clinically diagnosed cases of AGA, in the age range of 20-70 years and with disease duration of 6 months or above were enrolled. Same number of age and sex matched controls with dermatoses other than AGA attending the dermatology outpatient department were also included. The source population for cases and controls was the same. Patients who had more than one dermatologic disease, patients receiving any systemic treatment for androgenetic alopecia including finasteride, dutasteride, hair supplements in last 3 months before enrollment, known diabetics and patients using hypolipidemic drugs were excluded from the study.

After taking informed consent, general demographic data regarding age, sex and contact information were noted. Detailed history and dermatological examination was taken regarding duration of disease and to know the severity and progression respectively. Males were classified according to Hamilton-Norwood (HN) scale and females were classified according to Ludwig scale (LS). General examination was performed and height, weight and waist circumference were noted. To measure waist circumference, top of the right iliac crest was located and the measuring tape was placed snugly in a horizontal plane around the abdomen at the level of iliac crest. Blood pressure was measured using manual mercury sphygmomanometer. Two recordings were taken in the sitting position at an interval of 5 minutes. The average of the 2 readings was taken as the final measurement.

Venous samples were taken from all patients and controls after an overnight fast of at least 8 hours for measuring plasma fasting glucose and serum lipid levels. Plasma glucose levels were measured using glucose oxidase method and serum triglycerides, high-density lipoproteins (HDL) and low-density lipoproteins (LDL) were measured with enzymatic procedures. Diagnosis of diabetes mellitus was made when fasting blood glucose was more than 126 mg/dl. Dyslipidemia was diagnosed if any one of the following parameters were abnormal: LDL more than 160 mg/dl or triglycerides more than 150 mg/dl or HDL less than 40 mg/dl in males and less than 50 mg/dl in females.

Metabolic syndrome was diagnosed by the presence of three or more of the five criteria of 2005 revised National Cholesterol Education Programme’s Adult Treatment Panel III (NCEP ATP III) (Table 1). Numerical and graphical techniques were used to summarize and present the quantitative data collected from all patients and controls. Statistical analysis was done using two-sample Student’s t-test to compare mean values of quantitative variables, and P value less than 0.05 was considered as statistically significant.

Table 1: Criteria for clinical diagnosis of metabolic syndrome.

| Measure (any 3 of 5 constitute diagnosis of metabolic syndrome) | Cut off points |
|---------------------------------------------------------------|----------------|
| Elevated waist circumference                                  | ≥90 cm for South Asian men, ≥80 cm for South Asian women |
| Elevated triglycerides                                        | ≥150 mg/dl or on drug treatment for elevated triglycerides |
| Reduced HDL cholesterol                                        | <40 mg/dl in men, < 50 mg/dl in women or on drug treatment for reduced HDL cholesterol |
| Elevated blood pressure                                       | ≥130 mm Hg systolic blood pressure or ≥85 mm diastolic blood pressure or On antihypertensive drug treatment in a patient with a history of hypertension |
| Elevated fasting blood glucose                                | ≥100 mg/dl or on drug treatment for elevated glucose |

RESULTS

In the present study, 40 (53.33%) AGA patients were males compared to 35 (46.66%) females with a male to female ratio of 1.14: 1. The majority of the AGA patients belonged to the age group of 40 to 49 years (38.66%) followed by 20 to 29 years and the mean age of presentation was 42.6 years (SD=8.03 years). The study duration of the AGA ranged from 6 months to more than 15 years with a mean duration of 7.68 years (SD=1.61 years). Male pattern hair loss was observed in 40 cases, female pattern in 31, male-pattern in females seen in 4 cases. In females, on Ludwig scale, grade-2 (57.14%) was the commonest followed by grade 1 (17.14%) and 3 (14.28%) (Table 2). In males, according to (HN scales),
most common grades were grade 3, 4 and 5 accounting for 52.5% of cases (Table 2). Positive family history of AGA among 1st and 2nd degree relatives was seen in 50 (66%) of cases.

| Grading | No of cases | Prevalence of metabolic syndrome |
|---------|-------------|---------------------------------|
|         | Males (HN)  | Females (Ludwing) | Ludwig Scale (LS) in females | HN- in males |
| Grade 1 | 4           | 6                  | 0                           | -            |
| Grade 2 | 5           | 20                 | 6                           | 1            |
| Grade 3 | 7           | 5                  | 1                           | 1            |
| Grade 4 | 7           | -                  | -                           | 3            |
| Grade 5 | 7           | -                  | -                           | 5            |
| Grade 6 | 5           | -                  | -                           | 5            |
| Grade 7 | 5           | -                  | -                           | 4            |
| MPB (HN 2) | -           | 4                  | Nil                         | -            |
| Total   | 40          | 35                 | 7                           | 18           |

Table 3: Prevalence of metabolic syndrome and its components among cases and controls (N=150).

| Prevalence of metabolic syndrome and its components among cases and controls (N=150) | Cases N (%) | Controls N (%) | P value |
|-----------------------------------------------------------------------------------|-------------|----------------|---------|
| Abdominal obesity                                                                 | 25 (33.3)   | 11 (14.6)      | 0.007   |
| Hypertension                                                                      | 23 (30.6)   | 13 (17.3)      | 0.056   |
| High fasting glucose                                                              | 26 (34.6)   | 11 (14.6)      | 0.004   |
| Elevated TGL                                                                      | 32 (42.6)   | 15 (20)        | 0.002   |
| Elevated LDL                                                                      | 11 (14.66)  | 3 (4)          | 0.024   |
| Low HDL levels                                                                    | 41 (54.6)   | 18 (24)        | 0.00012 |
| Metabolic syndrome                                                                | 25 (33.3)   | 11 (14.6)      | 0.007   |

Table 5: Prevalence of metabolic syndrome in relation to duration of disease.

| Metabolic syndrome | Duration of disease (%) | 6 months – 5 years | >5 years |
|--------------------|-------------------------|--------------------|----------|
| Present            | 9 (19.56)               | 16 (55.17)         |          |
| Absent             | 37 (80.43)              | 13 (44.83)         |          |
| Total              | 46 (100)                | 29 (100)           |          |

High prevalence of abdominal obesity was seen in 25 (33.3%) of cases and 11 (14.6%) of controls with significant p value (0.007) (Table 3). There was an increased prevalence of hypertension was observed (23 cases and 13 controls) which was statistically insignificant (p=0.056) (Table 3). Impaired glucose tolerance was seen in 26 (34.6%) AGA patients and 11 (14.6%) controls with highly significant p value of 0.004 (Table 3). In the present study, raised triglyceride and LDL levels were seen in 32 (42.67%) and 11 (14.66%) cases respectively compared to 13(20%) and 3 (4%) controls respectively, which was statistically significant (p=0.002 and p=0.027) (Table 3). Low HDL levels were observed in 41 cases (54.6%) and 18 controls (24%) which was statistically significant (p=0.00012) (Table 3) (Table 8). Metabolic syndrome, diagnosed as per NCEP ATP III criteria, was prevalent in 25 cases (33.33%) and 11 controls (14.6%) which was statistically significant (p=0.07) (Table 3). There is statistically increased prevalence of MS (16 cases) with increasing duration of AGA (more than 5 years) with p value 0.001 (Table 4).

DISCUSSION

AGA is characterized by a progressive conversion of terminal hair into miniaturized hair defined by various patterns. Many studies have shown this stressful condition association with metabolic syndrome. However, the pathogenesis of this is still not understood completely. Metabolic syndrome, first described by Reaven in 1988, is a cluster of risk factors including central obesity, atherogenic dyslipidemia, hypertension and glucose intolerance. It is a strong predictor of cardiovascular disease and confers cardiovascular risk higher than the individual components.

Greater peripheral sensitivity to androgens that is produced in AGA, with transformation of the free testosterone by action of 5 alpha-reductase into
dihydrotestosterone (DHT), favoring follicular miniaturization. Such miniaturization is observed on the fronto-temporal area and vertex areas in men and over the crown in women, as these areas are more sensitive to the effects of androgens. The 5 alpha-reductase and DHT receptors are present in blood vessels and heart and are implicated in the proliferation of vessel smooth-muscle cells, a key phenomenon in atherosclerosis alongside lipid deposits. The association between arterial hypertension and AGA may be a result of the high aldosterone levels, which would explain the high blood pressure and were recently demonstrated to favor alopecia by stimulating mineralocorticoid receptors.

The hyperinsulinemia found in the patients with AGA may explain its relationship with cardiovascular disease. High insulin levels are the central element of MS, favoring carbohydrate intolerance and central abdominal obesity. It has also been suggested that insulin favors vasoconstriction and nutritional deficit in scalp follicles, enhancing the effect of DHT on follicular miniaturization.

The more frequent presence of chronic inflammation parameters in patients with AGA, has been cited to explain the relationship with cardiovascular disease. The proinflammatory situation that underlies alopecia may increase the presence of proinflammatory cytokines in arterial wall and hair follicle. The microinflammation found in the hair follicle, which may be related to the pathogenicity of alopecia, may be a local manifestation of MS and atheroma plaque in patients with alopecia. Abdominal obesity, which is considered an important cardiovascular risk factor and was associated with higher insulin resistance, a key element in the MS.

In the present study, high prevalence of abdominal obesity was seen in 25 (33.3%) of cases and 11 (14.6%) of controls with significant p value (0.007) which was in accordance with previous studies by Harmeetsingh banger et al and Acibucu et al. Hypertension was observed in 23 cases and 13 controls which was not significant (p=0.056). But Banger et al, found hypertension in 34 cases and 15 controls with significant p value. High fasting blood sugar was more in 26 (34.6%) AGA patients than controls with 11 (14.6%) with a statistical significance (p=0.004). Similar significant difference was found in studies by Ola Ahmed Bakry et al and this result conflicted with what was reported by Acibucu et al.

Increased triglyceride levels were found in 32 cases and 15 controls which was statistically significant. Santiago et al, Gopinath et al and Bakry et al have also noticed significant higher triglyceride values in AGA cases than controls in their respective studies. Decreased HDL levels were seen in 41 cases and 18 controls which was statistically highly significant (p=0.002) which is in accordance with Santiago et al. The prevalence of metabolic syndrome in the current study was found in 25 cases (18 males and 7 females) and 11 controls which was statistically significant (p=0.007). Similar finding was reported by Sue et al and Pengsalae et al. Yi et al observed significant positive association between presence of MS and AGA in female group but not in males, whereas Santiago et al observed equal prevalence of MS in both men and women. But Gok et al study found no relationship between onset age and duration of AGA and MS.

In the present study among the 25 cases having MS, males with higher grades of HN scale (grade 4 to 7) was observed in 17 of 18 patients. Whereas, in females, Ludwig grade 2 and 3 was observed in all the 7 female patients. Severe grades of AGA patients had increased prevalence of MS as reported earlier in few studies done by Gok et al and Sharma et al. With increasing duration of AGA (more than 5 years), there is statistically increased prevalence of MS seen in16 cases, with p value 0.001 (Table 4).

To conclude, our study shows a clear association of AGA with metabolic syndrome and its components. There is significant association of the metabolic syndrome with severity and duration of AGA. Therefore, patients with early onset and higher grades of AGA should be routinely screened for MS and its components which help in preventing long-term complications.

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