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Association of Androgenetic Alopecia with Benign Prostatic Hyperplasia: A Case Control Study

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Abstract

Introduction: Androgenetic alopecia (AGA) is associated with increased risk of several systemic diseases and some environmental factors, however, controversies exist. Since AGA and Benign Prostatic Hyperplasia (BPH) share common pathogenesis and AGA manifests some decades before BPH onset, it may serve as an early marker of BPH.

Objective: This study was conducted to know AGA and its association with BPH in men ≥20 years of age.

Materials and Methods: Clinically diagnosed cases of AGA (n=176) and 117 age matched healthy controls were enrolled. All cases and controls were subjected for abdomino-pelvic ultrasonography, urinary flowmetry, fasting lipid profiles, glycemic index and body mass index. International Prostate Symptom Score (IPSS) was also assessed.

Results: Among 176 patients, 120 (68.18%) had Hamilton-Norwood grade III AGA and 56 (31.82%) had grade IV-VII AGA. In both groups, 140 (79.55%) cases and 93 (79.49%) controls were aged <35 years respectively. Family history of AGA was present in 108 (61.36%) cases and 2 (1.71%) controls. This observation was statistically significant with OR= 89.61 (95%CI 23.67-339.29). Three (1.7%) cases and none of the controls had prostate volume >30ml. Seventeen (9.66%) cases and 4 (3.42%) controls were graded as moderately/severely symptomatic IPSS. Statistically significant association was seen between family history and early onset of hair loss (<35 years) in a male sibling or parent.

Conclusion: Although positive family history was associated with early onset of AGA, no association between AGA and BPH could be elicited in our study.

Key words: Alopecia; body mass index; glycemic index; lipids; prostatic hyperplasia

Introduction

Androgenetic alopecia (AGA) is a hereditary disorder, mediated by androgens and characterized by progressive patterned thinning of the scalp hair.[1] The incidence and the severity of androgenetic alopecia is found to be highest in white men, second highest in Asians and African Americans, and lowest in Native Americans and Eskimos. Almost all patients have an onset by the age of 40 years, although many of the patients (both males and females) show evidence of AGA by the age of 30 years.[2]

Although there are no serious direct health consequences, the loss of scalp hair allows ultraviolet light to reach the scalp and thus, increases risk of actinic damage.[3] AGA has been shown to be associated with increased risk of several diseases such as benign prostatic hyperplasia,[4,5] hypertension,[6] abnormal serum lipid profiles,[6] obesity,[6] insulin resistance,[7,8] cardiovascular diseases,[7] and some environmental factors such as smoking[1] and stress.[9] However, controversies exist regarding the association of those diseases and environmental factors with AGA.[10,11]

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Benign prostatic hyperplasia (BPH) is the commonest benign neoplasm in men aged 70 years and older with or without obstructive symptoms affecting more than 70% of men.[4] BPH is more common among elderly men but infrequent in age less than 40 years. Its prevalence increases above the age of 60 years. Androgen function and patients' age are important for the occurrence of BPH.[5]

Since AGA and BPH share common pathogenesis and AGA manifests some decades before BPH onset, it may serve as an early marker of BPH.

Materials and Methods

The study was conducted in the outpatient department (OPD) of dermatology, BP Koirala Institute of Health Sciences, Dharan between 1st April 2013 and 31st March 2014. All clinically diagnosed cases of AGA (n=176) and 117 age matched healthy controls were enrolled between 1st April 2013 and 31st March 2014 in our study with prior informed and written consent. Ethical clearance was taken from the institutional ethical committee. Detail history about the disease, family history of AGA or BPH, personal history of cardiovascular disease, hypertension, diabetes mellitus, alcoholism, cigarette smoking, lifestyle, drug intake was recorded in a preset proforma. Data regarding age, weight, height, waist circumference, body mass index, IPSS score were recorded. All cases and controls were subjected for abdomino-pelvic ultrasonography, urinary flowmetry, fasting lipid profiles and glycemic index measurement. The severity of baldness was also estimated from photographs taken at an anterior view, 900 tilt to the front side of the head, right and left 900 side views.

Statistical analyses were done using with Software SPSS (version 10.0 for Windows, SPSS Inc, Chicago, IL). The baseline characteristics of the study patients were expressed as numbers and percentages for categorical variables and as mean±standard deviation for continuous variables.

Qualitative variables were analyzed using $\chi 2$ test or the Fischer's exact test. A logistic regression model was employed to assess the associations between each possible risk factor (BPH, smoking, Body Mass Index, waist circumference, fasting plasma glucose, Blood Pressure (BP), and serum level of lipids, including Triglyceride (TG) and High Density Lipoprotein (HDL) and the risk of developing AGA (type III or greater). The statistical significance level was set at 5% for assessing each association, odds ratio (ORs) and their 95% confidence intervals (CIs). The odds ratio was determined by the Wald Chi-square test, and predictors with $p<0.10$ were subsequently assessed using multivariate analyses with a forward stepwise selection procedure. The threshold of 0.05 was regarded as significant with the logistic model of regression.

Results

Total of 176 cases and 117 controls were analyzed in this study. The mean±SD age of case and control groups were 29.40±8.74 years and 29.62±9.47 years, respectively.

In this study, 68.18% of population had Grade III AGA, followed by Grade IV (21.02%). Majority of the population in the study followed Hindu religion in both the case and control groups (92.61% vs. 89.55%) respectively. Sixty-three (35.8%) cases and 48 (41.02%) controls were married, and most of the population belonged to middle class family (Table 1). Emotional stress was found to be the commonest precipitating factor (66.7%) in the cases. In this study, 100 (56.8%) cases and 53 (45.29%) controls lived non-sedentary life style.

The cases and control groups did not differ significantly in mean age (AGA, 29.40 years vs control, 30.30 years), age group <35years vs ≥35years (79.55% & 20.45% vs 79.49% & 20.51%, p=0.99), marital status (35.8% vs 41.03%, p=0.36), cigarette smoking (37.5% vs 38.57%, p=0.64). Mean BMI was found to be 23.87 kg/m^2 vs 25.67 kg/m^2 in case and control groups respectively. Waist circumference was >90cm in 1.1% cases and 7.69% controls. Mean Systolic blood pressure and mean diastolic blood pressure, mean cholesterol level, mean Triglyceride level, mean High density lipoprotein level and mean low density lipoprotein levels were comparable among the case and control groups (Table 2 & 3).

Family history of AGA was present in 108 (61.36%) patients and two controls (1.7%). This was found to be statistically significant (OR=89.61; 95% CI 23.67-339.29 and p value <0.001). First degree relatives of the patients had a positive family history of AGA in 44.8%. Site of onset of AGA was frontal in 78.4% of the cases. Three (1.7%) of the cases had prostate volume >30ml and none of the patients in control group had prostate volume >30ml. Seventeen (9.66%) patients and four (3.42%) controls were graded as moderately/severely symptomatic IPSS.

In univariate analysis, there was no significant association found between the AGA and BPH, age <35years, family history of BPH, past treatment taken for other diseases, blood pressure, blood sugar level, prostate specific antigen, cigarette smoking, cholesterol, triglyceride, Low Density Lipoprotein (LDL) and HDL level. The family history of AGA and IPSS were significantly associated in cases as compared to controls and conversely BMI and Waist circumference was statistically significant in control group as compared to cases (Table 1). But in multivariate analysis, only family history of AGA was significantly associated with androgenetic alopecia in our study (Table 4).

Table 1. Clinical and laboratory parameters associated with Androgenetic Alopecia

Variable	Case n=176 (%)	Control n=117 (%)	p value
Age group (years)			
<35	140 (79.55)	93 (79.49)	0.990
≥35	36 (20.45)	24 (20.51)	
Marital Status			
Unmarried	113 (64.2)	69 (58.97)	0.366
Married	63 (35.8)	48 (41.03)	
Family History of AGA			
No	68 (38.64)	115 (98.29)	*0.000
Yes	108 (61.36)	2 (1.71)	
Family History of BPH			
Yes	12 (6.8)	9 (7.69)	0.776
No	164 (93.2)	108 (92.31)	
Body Mass Index (kg/m^2)			
>25	58 (32.95)	65 (55.56)	<0.001
≤25	118 (67.05)	52 (44.44)	
Waist Circumference (cms)			
>90	2 (1.14)	9 (7.69)	*0.003
≤90	174 (98.86)	108 (92.31)	
Diastolic BP (mm Hg)			
>90	2 (1.14)	3 (2.56)	*0.355
≤90	174 (98.86)	114 (97.44)	
High Density Lipoprotein (HDL) (mg/dl)			
≤40	50 (28.41)	38 (32.48)	0.456
>40	126 (71.59)	79 (67.52)	
Triglyceride (Tg) (mg/dl)			
≥150	26 (14.8)	16 (13.68)	0.880
<150	150 (85.2)	101 (86.32)	
IPSS			
Moderately/ Severely symptomatic	17 (9.66)	4 (3.42)	*0.042
Mildly symptomatic	159 (90.34)	113 (96.58)	

*Fischer's exact test

Table 2: Comparison of prostate volume in two groups.

Prostate volume (ml)	Case n=176 (%)	Control n=117 (%)	Total n=293 (%)
>30	3 (1.7)	0 (0)	3 (1.37)
≤30	173 (98.3)	117 (100)	289 (98.63)

Table 3: Comparison of different variables among the type of AGA.

Variable	Hamilton-Norwood Grade			p value
	Grade III n (%)	Grade IV-VII n (%)	Total	
Age Group (years)				
<35	102 (57.95)	38 (21.59)	140 (79.54)	0.015
≥35	18 (10.22)	18 (10.22)	36 (20.46)	
Smoking status				
Never	80 (45.45)	30 (17.04)	110 (62.5)	0.099
Smoker	40 (22.72)	26 (14.77)	66 (37.5)	
Family history of AGA				
No	50 (28.40)	17 (9.65)	67 (38.06)	0.183
Yes	70 (39.77)	39 (22.15)	109 (61.93)	
Waist circumference (cms)				
<90	119 (67.61)	55 (31.25)	174 (98.86)	*0.536
≥90	1 (0.56)	1 (0.56)	2 (1.13)	
BMI (kg/m^2)				
≤25	90 (51.13)	27 (15.34)	117 (66.47)	0.001
>25	30 (17.04)	29 (16.47)	59 (33.52)	
Benign Prostaic Hyperplasia (cc)				
>30	2 (1.13)	1 (0.56)	3 (1.70)	*1.0
≤30	118 (67.04)	55 (31.25)	173 (98.29)	
Hypertension (mm Hg)				
≥140/90	3 (1.70)	3 (1.70)	6 (3.40)	*0.384
<140/90	117 (66.47)	53 (30.11)	170 (96.60)	
Metabolic Syndrome				
No	120 (68.18)	54 (30.68)	174 (98.86)	
Yes	0 (0)	2 (1.14)	2 (1.14)	
IPSS				
Mildly symptomatic	111 (63.06)	48 (27.27)	159 (90.34)	0.176
Moderately/ Severely symptomatic	9 (5.11)	8 (4.54)	17 (9.65)	

*Fischer's exact test

Table 4: Multivariate logistic regression analysis for AGA.

	Coefficient	Odds Ratio	95% CI	p value
Family H/O AGA	4.495	89.611	23.667-339.288	0.000
Life style	-0.051	0.950	0.354-2.549	0.920
BMI	0.523	1.687	0.580-4.900	0.336
Waist circumference (cm)	-0.422	0.656	0.075-5.706	0.702
Hamilton-Norwood grade	17.162	28403444.361	0.000- >1.0	0.914
IPSS	1.069	2.911	0.386-21915	0.299

CI= confidence interval

Discussion

Androgenetic alopecia (AGA) is associated with increased risk of several systemic diseases and some environmental factors, however, controversies exist. Androgens like Testosterone and Dihydrotestosterone are involved in diseases like AGA and BPH. The enzyme 5-alpha reductase, which transforms testosterone into DHT, plays a key role. In patients with AGA, scalp biopsy specimens have shown increased DHT concentrations and 5-alpha-reductase activity.[12,13]

In a study done by Oh et al[14], BPH had strong association with higher grade of male pattern baldness than that of controls (median value of grade IV versus III, p value <0.001). Similarly, Arias-Santiago S et al in an observational case-control study found strong association between the presence of AGA and benign prostatic hyperplasia with odds ratio of 5.14.[5]

Male pattern baldness is an androgen dependent disorder in adult men. Though the pathogenesis is not well understood, it is believed that the androgens

act on the hair follicle via the mesenchyme- derived dermal papilla present in the middle of the hair follicle bulb.[15] The patients having autosomal recessive genetic disorder of 5 α-reductase deficiency do not develop Androgenetic Alopecia, which suggests that DHT is the androgen responsible for it.[16] Dihydrotestosterone, an androgen controls the normal growth and secretory functions of the prostate gland, thus maintains Benign Prostatic hyperplasia (BPH).

The prevalence of AGA increases steadily with advancing age. High prevalence has been found among men of white race/ethnicity, whereas lower prevalence has been seen among Asians, Native American, and African American men. Increased risk of AGA with age reflects the natural progression of this condition.[17]

In AGA gradual thinning in the temporal areas are present, producing a reshaping of the anterior hairline.[18] By the age of 20 years, more than 90% of men demonstrate some degree of fronto-parietal recession of hairline.[19] Among our study population, 138 (78.4%) patients had frontal region involvement followed by vertex involvement observed in 53 (30.1%) patients of AGA. Rate of progression is influenced by genetic predisposition.[20]

In our study, out of total 34 patients having precipitating factor for androgenetic alopecia, emotional stress was the major precipitating factor found in 20 (66.7%) patients. Stress responses, mediated by typical stress hormones, like catecholamines, prolactin, Adrenocoticotrophic hormone (ACTH), Corticotrophin Releasing Hormone (CRH), b-endorphins, glucocorticoids, and substance P directly and indirectly alter hair growth by interacting and disturbing the release of the various neuropeptides.[9]

The genetic inheritance of AGA has been documented well in the literature, but only few studies have been done regarding familial aggregation of AGA. Also, one gene that encodes for androgen receptor in gene polymorphism of AGA has been identified.[17] Our study also reports that male relatives were more prone to have AGA if there were young family members with AGA.

The various diseases associated with AGA are benign prostatic hyperplasia,[4,5] hypertension,[6] obesity,[6] dyslipidemia,[6] insulin resistance[7,8] and cardiovascular diseases.[7] In our study, three patients (1.7%) in case group had diabetes mellitus. This finding is in corroboration with two studies Matilainen VA et al[7] and González-González JG et al[8] that showed association of diabetes mellitus due to insulin resistance in AGA. Similarly, 3 (1.7%) patients had benign prostatic hyperplasia and this finding is in corroboration with few studies.[5,12-14] Only 1 (0.56%) patient had hypertension. Association between AGA and hypertension has been shown in several previous studies.[6,7,10, 21]

The difference in the blood pressure might be due to the androgens binding to mineralocorticoid receptors, which may be responsible for development of hypertension in men as compared to women.[22] Also hyperaldosteronism which has been found to be causative factor for primary hypertension in literature, may directly lead to the development of alopecia.[21] In our study, only one (0.6%) patient had Systolic BP ≥140 mm Hg and five cases (2.8%) had Diastolic BP ≥90 mm Hg. This finding is in contrast to the study done by Ahouansou S et al who found strong association between Androgenetic alopecia and hypertension.[21] The majority of younger population in our study could explain this finding.

Berry SJ et al reported that 50% of men develop BPH by the sixth decade of life, which rises to 70% and 90% by the seventh and ninth decade respectively.[23] With increase in literacy, general awareness of prostatic disease will increase leading to rise in the number of BPH patients. Boyle P reported that by the end of the century, men population are expected to have an 88% chance of developing BPH and above 50% chance of developing symptoms, and thus male pattern baldness.[24] In our study only 1.7% of the cases had BPH, among them two had grade III and one had grade IV male pattern baldness. This may be because patients with AGA were of younger age than in other studies.[23,24]

It is evident from the previous studies that the volume of prostate increases with increasing age and common after 4th decade of life,[23, 24] which is comparable with our study as mean prostate size was found to be greater in case group (11.15 cm^3) as compared to control group (6.24 cm^3). This is in corroboration with the study done by Chen W et al, who found high prevalence of alopecia in patients with more than 30 cm^3 prostate size as compared to smaller prostate (83.3% vs. 61.3%, p value <0.05).[11] In this study prostate size was mildly larger, but not significantly higher in AGA patients in comparison to the controls (42.7 vs. 35.4 cm^3) and it did not differ with grading of alopecia (Norwood-Hamilton scale).

In our study, 17 patients (9.7%) in case group and four patients (3.4%) in control group were moderately/ severely symptomatic. Though result was significant in bivariate analysis with p value= 0.042 (CI: 0.98-9.21),

but it was not statistically significant in multivariate analysis.

It is in corroboration with the study done by Arias-Santiago S et al in which AGA patients with larger prostate volume had early change in urinary flow and higher IPSS.[5]

Cigarette smoking causes damage to the vascular supply of the dermal hair papilla and also to the DNA of the hair follicles. Smoking also causes proinflammatory cytokines release due to oxidative stress resulting in follicular microinflammation and fibrosis. Cigarette smoking can lead to antiprotease system imbalance and also hypoestrogenic state.[1]

In our study, we found that AGA was not associated with cigarette smoking as 62.5% of the cases were non-smokers, 12.5% had either quit smoking and 25% were current smokers.

Conclusion

We can conclude that positive family history of the androgenetic alopecia increases the chances of developing androgenetic alopecia in men though with increasing age. No association between androgenetic alopecia and benign prostatic alopecia could be elicited from our study. But majority of patients in our study were of younger age group and BPH is not a common finding of younger age group. Further multicenter studies with a larger sample size to evaluate the association of Benign prostatic hyperplasia (BPH) and other risk factors with androgenetic alopecia (AGA) is recommended.

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