Dyslipidemia in patients with early onset androgenetic alopecia and risk of coronary artery disease

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ABSTRACT
Background: The association between androgenetic alopecia (AGA) and coronary artery disease (CAD) has been explored in serious studies.
Aim of the work: This study was designed to evaluate lipid profile in male patients with early onset AGA.
Patients and methods: This study included 60 male patients with AGA as case group and 40 males with a normal hair status as control group. The age of both groups ranged from 20-35. Lipid profile including total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), lipoprotein-a (Lp-a), apolipoprotein A1 (Apo A1), and apolipoprotein B (Apo B) were measured in both groups.
Results: There was a significant difference in serum LDL between patients and controls (147.40 ± 58.12 versus 100.20 ± 35.62, P < 0.05). Also, there was a significant difference in serum lipoprotein-a between patients and controls ((48.10 ± 52.53 versus 16.49 ± 12.12, P < 0.05 ). The difference in other lipid parameters between two groups was not significant.
The family history of androgenic alopecia and coronary heart disease was significantly higher in the cases than the controls (51 (85%) versus 15 (37.5%),18(30%) versus 4(10%), P < 0.05).
Conclusion: Disorder of lipid profile, especially low density lipoprotein and lipoprotein-a can be considered as a risk factor for coronary artery disease in patients with early onset AGA. Investigation of lipid profile mainly low density lipoprotein and lipoprotein-a should be done for every patient with early onset androgenetic alopecia. Early therapy with lipid lowering drugs and follow up with cardiologist is useful to reduce the risk of coronary artery disease.

KEY WORDS: Dyslipidemia, androgenetic alopecia, coronary artery disease

INTRODUCTION
Androgenetic alopecia (AGA) is a hereditary and androgen-dependent progressive thinning of the scalp hair in a defined pattern. It is a common dermatological disorder affecting more men and occasionally women, with significant negative impact on their social and psychological well being. AGA commonly begins by 20 years of age and affects nearly 50% of men by the age of 50 years.¹² Its etiopathogenesis is mainly androgen-dependent and modulated via the testosterone metabolite (dihydrotestosterone), the expression of hair follicle-related androgen receptor and genetic factors also have been implicated.³

Coronary artery disease (CAD) is a major cause of death and disability worldwide.⁴ Advanced obstructive CAD can exist in patients with minimal or no symptoms and can progress rapidly, so early detection is extremely important.⁵ Several studies have shown that baldness is associated with the risk of CAD. These studies have generally found a positive association between baldness and CAD,
although the strength of the association has varied.\textsuperscript{6-11} The effect of serum lipids, as a pathogenic factors for CAD in patients with AGA has been evaluated in various studies.\textsuperscript{12, 13}

In this study, lipid profile of men with early onset AGA (age from 20-35 years) was investigated and compared with controls. This age group was selected because coronary disease often does not occur in this age group and also, risk factor may be present but inapparent. So, early detection of risk factor is useful for early intervention to decrease the incidence of CAD.

**PATIENTS AND METHODS**

This study included 60 male patients with early onset AGA, aged between 20 and 35 years, from outpatient dermatology clinic, Al-Hussain University Hospital and enrolled in the study from March 2011 to November 2013. Forty age-matched healthy men with a normal hair status were also recruited. An informed written consent was taken from each individual in the case and control groups. Men who were on any medication which could affect lipid metabolism, smokers, alcohol drinkers and those with Diabetes Mellitus (DM), CAD, hypertension (HTN), familial hyperlipidemia, thyroid disease, chronic renal failure, liver disease, and cancer were excluded from both groups. The family history of DM, CAD, HTN, and androgenic alopecia was recorded. The baldness pattern was assessed by Hamilton Baldness Scale, as modified by Norwood scale.\textsuperscript{14, 15}

After 12-14 hours of fasting, a venous blood sample was taken for lipid profile including cholesterol, triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), lipoprotein-a (Lp-a), apolipoprotein A1 (Apo A1) and apolipoprotein B (Apo B). Biochemical assays on the serum were performed with a multi-autoanalyzer (Spicific Kone Ltd, Finland). The TG was estimated by using a kit employing enzymatic hydrolysis of TG with lipases, total cholesterol assay was done using a modified method of Liebermann-Burchard, HDL was estimated by precipitation method and LDL was calculated using the Friedwald’s formula.\textsuperscript{16-19} The immunoturbidimetric method was used to measure Apo A1, Apo B and LP-a levels.\textsuperscript{20} Statistical analysis was carried out using SPSS 16. Data was analyzed using t-test and Chi square. A P-value less than 0.05 was accepted as evidence of statistical significance.

**RESULTS**

This study included 60 male patients with early onset AGA and 40 males with a normal hair status. The mean age of the cases and controls was 26.7 ± 6.25 and 27.14 ± 6.42 years, respectively. There was no statistically significant difference between patient and control groups regarding age. In this study, a positive family history of AGA and CAD was significantly more frequent in cases than the controls (P< 0.05). But, there was no statistically significant difference between patient and control groups regarding family history of hypertension and diabetes mellitus (Table 1) and (Fig. 1). The pattern of hair loss was compatible with Hamilton-Norwood scale: 66.6% of patients had frontal recession and 33.4% of patients had vertex loss pattern. No correlation between family history of AGA among patients and their baldness pattern could be detected.

The level of LDL was significantly higher in patients than controls (147.40 ± 58.12 versus 100.20 ± 35.62, P < 0.05). Also, the level of LP-a was significantly higher in patients than controls.
Lipid profile

<table>
<thead>
<tr>
<th>Patient (Mean ± SD)</th>
<th>Controls (Mean ± SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG 91.65 ± 42.93</td>
<td>102 ± 36.92</td>
<td>0.103</td>
</tr>
<tr>
<td>Total cholesterol  163.67 ± 33.21</td>
<td>160.96 ± 49.15</td>
<td>0.835</td>
</tr>
<tr>
<td>LDL 147.40 ± 58.12</td>
<td>100.20 ± 35.62</td>
<td>0.002</td>
</tr>
<tr>
<td>HDL 55.48 ± 34.42</td>
<td>48.95 ± 15.22</td>
<td>0.102</td>
</tr>
<tr>
<td>Apo A 120.27 ± 40.37</td>
<td>117±15.91</td>
<td>0.131</td>
</tr>
<tr>
<td>Apo B 81.22 ± 78.19</td>
<td>83.52 ± 19.21</td>
<td>0.831</td>
</tr>
<tr>
<td>Lp-a 48.10 ± 52.53</td>
<td>16.49 ± 12.12</td>
<td>0.001</td>
</tr>
</tbody>
</table>

DISCUSSION

Androgenetic alopecia (AGA) is considered as a genetically determined disorder characterized by increased level of local androgen metabolite and increased androgen receptor binding in genetically predisposed men. AGA developed before 36 years of age and reached at least stage 3 of Hamilton-Norwood classification is termed as early onset AGA. Early onset AGA not only leads to psychological stress but also reported as the risk factor of carcinoma of prostate, cardiovascular diseases and metabolic syndromes. Dyslipidemia [elevated levels of serum total cholesterol (TC), triglycerides (TG) and low-density lipoprotein (LDL) and low levels of high-density lipoprotein (HDL)] is a major risk factor for coronary disease. In this study we evaluated serum lipid parameters in a trial to elucidate role of dyslipidemia as a risk factor for CAD in patients with early onset AGA.

In current study and as reported in similar studies, family history of both AGA and CAD was significantly high in patients than controls. The frequency of AGA in the fathers of men with AGA is higher than the fathers of men without AGA. A genetic factors are said to play a role in causing AGA. Androgen receptor gene which is X-linked recessive has been mentioned to be the cardinal prerequisite for balding but other genes are also involved. Genetic sensitivity of hair follicles to dihydrotestosterone (DHT) causes them to shrink when exposed to it. 5 α-reductase is responsible for converting free testosterone (a major circulating androgen in men) into DHT. Hair growth inhibitory factor-β, released from androgen-stimulated fibroblasts of the follicular dermal papilla may cause hair growth inhibition and hair follicle miniaturization, short lifespan,
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thereby preventing normal hair production.27 It has been reported that 5-α-reductase exists in the blood vessels and the heart. Also, DHT receptors are involved in vascular smooth muscle proliferation that represents a fundamental feature of atherosclerosis along with deposition of lipids.28 The association between AGA and CAD was first suggested in 1972 by Cotton et al.29 Several subsequent studies appeared to support the early findings.7,30,31 Serious studies have investigated the serum lipid profile in patient with AGA. Sharma et al23 and Smaz et al12 showed that the triglyceride, LDL and lipoprotein-a levels in patients with AGA were significantly higher than controls. Acibucu et al,32 found that male patients with AGA had significantly higher levels of serum triglyceride and total cholesterol compared to male individuals with no AGA. Lotufo et al,8 found a significant difference in serum total cholesterol, LDL and LP (a) between patients and controls. Nassiri et al,33 showed a higher triglyceride and lower HDL levels in cases than the controls. Aerius et al,34 found that men with AGA had significantly higher levels of serum triglyceride, total cholesterol and LDL compared to men without AGA.

In this study, there was a significant difference in serum LDL and lipoprotein-a in patients than controls. But there was no a significant difference in other lipid parameters between patients and controls. In current study and as reported in previous study,8 there was no correlation between pattern of AGA and lipid parameters, but this findings was in contrast with other studies.6,9,31 The discrepancy in the results in-between the studies can be explained by that serum lipid parameters are related to various factors such age, gender, genetics, environment etc.

The risk of coronary artery disease is directly related to the level of LDL and inversely related to the level of HDL. The protective effect of HDL is at least as strong as the atherogenic effect of LDL and is independent of lipids and other risk factors. The risk of CAD varies widely depending on the LDL/HDL ratio. Normally LDL (“bad”) cholesterol should be as low as possible, and HDL (“good”) cholesterol should be as high as possible.35 Increased level of serum lipoprotein-a is said to be associated with endothelial dysfunction and CAD as it has a structure similar to LDL but is attached to a glycoprotein called apolipoprotein-a. It has sticky adhesive nature and can easily attach to LDL, calcium, and other components in an atherosclerotic plaque on the blood vessel wall. Due to its similarity with plasminogen, it competes for binding with fibrin inhibiting its breakdown and may promote blood clot formation. It also activates immune cells including monocytes and macrophages which help in inducing inflammation. These effects may help in inducing plaque formation and promote clot formation after the plaque is ruptured.36 Disorder of lipid profile in patients with early onset AGA could explain its association with CAD.

CONCLUSION
This study showed that, dyslipidemia in patients with early onset AGA could explain its correlation with CAD. Lipid parameters especially LDL and lipoprotein-a should be investigated in every patient with AGA. Early treatment with lipid lowering drugs and follow up with cardiologist can help in reducing risk of CAD.

REFERENCES
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