Relation between Androgenic Alopecia with Metabolic Syndrome: Review Article
Ahmed Mohammed Hamed 1, Haider Ismail Ibrahim 1*, Nader Nasr Nazmy 1, and Doaa Abdallah Shaker 2
Departments of 1 Dermatology, Venereology and Andrology,
2 Medical Microbiology and Immunology, Faculty of Medicine, Benha University, Egypt
* Corresponding author: Haider Ismail Ibrahim, E-mail: Haidernazmy90@gmail.com, Phone: 01599773831

ABSTRACT
Background: Androgenetic alopecia (AGA) is the most prevalent form of hair loss in men and women, characterized by a progressive thinning of hair influenced by androgens and genetic predisposition. Recent studies suggest a potential link between AGA and metabolic syndrome (MetS), a cluster of conditions that increase the risk for heart disease and other health problems. Understanding the association between AGA and MetS could lead to improved screening and management strategies, potentially mitigating cardiovascular risk in affected individuals.

Objective: This review aimed to synthesize current knowledge on the pathophysiology, genetic basis, and treatment options for AGA, with a focus on the relationship between AGA and MetS. The objective was to highlight the importance of early detection and comprehensive management of AGA, considering its association with systemic health issues.

Methods: A thorough literature review was conducted, analyzing studies from PubMed, Cochrane Library, and Google Scholar databases. Articles published up to April 2023 were included, with a focus on those providing insights into the pathophysiology of AGA, its treatment, and its association with MetS. Cross-sectional, cohort, and case-control studies were reviewed to assess the strength of the relationship between AGA and MetS.

Conclusions: AGA is not only a cosmetic concern but also a potential marker for underlying metabolic dysregulation. The evidence suggested a strong association between AGA and MetS, emphasizing the role of androgens and genetic predisposition in both conditions. Early intervention in patients with AGA could serve as a preventive strategy for MetS and related cardiovascular diseases. Healthcare providers should consider screening for MetS components in patients presenting with AGA, particularly in those with a family history of metabolic or cardiovascular disorders.

Keyword: Androgenetic alopecia, Metabolic syndrome, Pathophysiology, Genetic predisposition, Cardiovascular risk.

INTRODUCTION
The majority of men and women experience hair thinning due to androgenetic alopecia (AGA), a dermatological disorder [1]. Among males, the prevalence increases to 30% after the age of 30 and 50% after the age of 50 years. At menopause, the occurrence rises in women, despite the fact that the clinical symptoms are often less severe and linked to scattered hair loss on the scalp [2].

Etiology: An overreaction to androgens is the main cause of androgenetic alopecia, which has a clear hereditary component as its name suggests. This disorder is inherited from both parents and is polygenic, meaning that the degree to which it manifests in an individual might vary. Androgenetic alopecia runs in families; if a father has baldness, his sons are five to six times more likely to do so as well [3].

Once the androgen receptors are activated, pattern alopecia may begin, which usually happens during puberty. People who have androgen insensitivity syndrome or who have prepubertal castration do not experience pattern baldness. In the development of pattern alopecia, both androgen receptors and hormone metabolism are crucial [4].

Pathogenesis:
In AGA, the ratio of anagen to telogen time declines as the hair cycle progresses because telogen time stays the same or becomes longer and anagen time gets shorter. The maximal length of newly grown anagen hair is less than that of previously grown hair since the period of anagen is the primary factor determining hair length [5]. The sole evidence of a functional follicle is a pore since the anagen period is too brief for the developing hair to reach the skin surface. An increase in the number of telogen hairs, which are easier to pluck than anagen hair, explains why people often notice more hair falling out when they wash and comb their hair [6].

As a result of these changes in the hair cycle, the papilla, matrix, and shaft of the hair are all affected by the miniaturisation of the follicles. Because of its central role in hair growth maintenance, the dermal papilla is likely the site of androgen-mediated alterations to the hair cycle, such as the shrinkage of the follicle [7].

Clinical presentation
In men: The modified Norwood-Hamilton classification, which evolved from the older Hamilton classification and has seven general categories and four distinct variation kinds, is the most often used grading system for AGA, but others exist [8].

Modified Norwood-Hamilton classification
Classification description:
Type I: Frontotemporal (FT) hairline receding somewhat along the frontal border [9];
Type II: symmetrical triangles of receding hairline in the frontal lobe of the ear that do not extend beyond about 2 centimeters in front of a line connecting the external auditory meatus on each side. The mid-frontal boundary may show signs of hair loss or sparsity. Extending more than around 2 cm anterior to a line drawn between the external auditory meatus on both sides.

- **Type III:** Deep FT hair recession is often symmetrical. Baldness or very little hair is seen in these spots.

- **Type IV:** The hair loss is mostly located in the vertex, but it may also occur in the front, although it is not as severe as in type III. Hair loss in the vertex region and frontal and temporal lobes is more pronounced in type IV compared to type III. On each side of the completely hairy fringe is a strip of relatively thick hair that serves to divide the large bald patches.

- **Type V:** It is characterised by more extensive thinning around the crown and temples than type IV, with a thinner and less dense transitional hairline.

- **Type VI:** This kind of alopecia is characterized by a lack of a hair bridge over the head and a loss of hair in both the frontal and lateral areas.

- **Type VII:** A narrow band of hair that resembles a horseshoe, starting from the side right in front of the ear and continuing behind the sides and quite low on the occipital region.

Different kinds make for three percent of all AGA cases: (I) A complete receding of the hairline appears without the typical mid-frontal hair island, (II) A patch of baldness does not appear on the vertex at the same time. The anterior recession, on the other hand, just moves behind the vertex. (III) The frontal hairline is perfectly horizontal and rests high on the forehead. There are only a handful of thin hairs that make up the typical mid-frontal island of hair. No more than 2 centimeters beyond the frontal line does the denudation region extend? (IV) The denuded region extends to the mid-coronal direction. (V) There is denudation that goes beyond the mid-coronal line and a lot of hair thinning below the real hair line. (VI) Alopecia in its most severe stage, when the bald spot does not extend to the scalp's vertebrae.

**In women,**

**Typically, three patterns have been described:**

There are three levels of female pattern genetic hair loss, as described by the Ludwig classification: mild, moderate, and extensive. The frontal hairline is mostly unaffected by the hair loss that occurs during all three Ludwig phases, although the top and frontal scalps do. It is unclear if the sides and back are implicated.

A study proposed a basic and specific classification (BASP) as a more recent, systematic, and universal method of categorization. There are two main categories of hairstyles: basic (BA) and particular (SP). The former describes the general contour of the front hairline, while the latter describes the density of hair on different parts of the body. L, M, C, and U are the four general kinds, whereas F and V are the two distinct kinds.

A combination of the shapes of the front hairline, as described by the English alphabet, determines the final form, with the exception of the linear L type.

If the frontotemporal area shows no signs of recession along its anterior boundary, then the lesion is classified as type L. Recession is more noticeable in the frontotemporal hairline than in the mid-anterior hairline in Type M. An M-shaped pattern emerges from the hairline. C type receding hairlines are more noticeable than F type receding hairlines in the frontotemporal region. The front part of the hairline falls back in a half-circle shape, like the letter C, as seen from the front. The front part of the hairline falls back behind the crown, creating a horseshoe shape that looks like the letter U. In Type F, the loss of hair density is widespread and affects the whole scalp, not just the front hairline. On most people, the front of the scalp will show it more prominently. The vertex, rather than the frontal region, shows more noticeable hair loss in Type V.

**Diagnosis**

**General scalp and hair examination**

In AGA, the scalp often looks normal, but you should be on the lookout for things that might make it worse, such as seborrheic dermatitis or photodamage. Finding out whether the hair loss is patterned is the primary goal of the clinical assessment.

The "pull test" is an easy way to gauge how bad your hair loss is. Roughly sixty hairs exist, the trichogram is. There is minimal value for trichograms in AGA, however they may be used to distinguish between other forms of hair loss.

When a definite diagnosis cannot be made by clinical examination, trichotoxin testing might be helpful in ruling out cicatricial alopecias or alopecia areata.

It is possible to determine the density of hairs per field of vision by histopathologically analysing horizontal sections. More little hairs, resembling vellus, are present in AGA. In women suffering from this illness, the ratio of terminal to vellus-like hair follicles is usually less than 3:1, compared to a normal scalp where the ratio is more than 7:1.

**Treatment/Management**

Topical minoxidil and finasteride are the two main drugs that may be used to treat pattern baldness, according to the Food and Drug Administration. Both work best when used together over the long-term and need regular application to see effects. Minoxidil, an over-the-counter drug, helps nourish hair follicles by widening blood vessels. In contrast, finasteride promotes hair growth.
regeneration, especially in the vertex area, by inhibiting the 5 alpha-reductase enzyme. The dangers to foetal development make it inappropriate for use by women who are pregnant or planning to become pregnant [17].

In cases when finasteride is not producing the desired effects, dutasteride may be prescribed to patients, despite the fact that it has not yet been approved by the FDA. Spironolactone and other oral antiandrogens are often prescribed to women. Hyperkalemia and menstrual abnormalities are among the possible adverse effects of spironolactone, which suppresses powerful androgens. Hair transplantation, which requires a sufficient amount of donor hair for excellent outcomes, and laser treatment at 660 nm are also other possible choices [18].

Additional therapies include growth factors, prostaglandin analogues, and saw palmetto extract. Along with well-established therapies, they are often used. While the exact relationship between pattern baldness and the peptide hormone adropin, which plays a role in energy homeostasis, is yet unknown, it has shown promise in metabolic control. Ongoing studies, however, may reveal its promise in treating a range of metabolic diseases [19].

The importance of metabolic syndrome (MetS), also known as insulin resistance syndrome, syndrome X, hypertriglyceridemic waist, and "the deadly quartet," as a risk factor for cardiovascular disease is becoming more acknowledged. As early as 1998, the World Health Organization's diabetic consulting committee came up with the first globally accepted definition of MetS. Insulin resistance (low fasting glucose, impaired glucose tolerance, or type 2 diabetes mellitus) plus two risk factors; obesity (waist-hip ratio or body mass index), hyperlipidemia (hypertriglyceridemia, low high-density lipoprotein [HDL] cholesterol), hypertension, or microalbuminuria, was said to be the definition of MetS.

Several revisions to this concept have been suggested since MetS was first described (………………………………………)

---

Table (1): Definitions of metabolic syndrome [20].

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria</td>
<td>IR + any other 2</td>
<td>IR + any other 2</td>
<td>Any 3 of 5</td>
<td>Increased WC (population specific) + any other 2</td>
<td>Any 3 of 5</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>IGT/IFG IR</td>
<td>Plasma insulin &gt; 75th percentile</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>IFG/IGT/T2DM (excludes diabetes)</td>
<td>IFG/IGT</td>
<td>≥ 110 mg/dL (includes diabetes)</td>
<td>≥ 100 mg/dL</td>
<td>≥ 100 mg/dL (includes diabetes)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>TG ≥ 1.69 mmol/L and HDL-C men &lt; 0.90 mmol/L, women &lt; 1.01 mmol/L</td>
<td>TG ≥ 1.69 mmol/L and HDL-C men &lt; 1.03 mmol/L, women &lt; 1.29 mmol/L</td>
<td>TG ≥ 1.69 mmol/L or on TG treatment HDL-C men &lt; 1.03 mmol/L, women &lt; 1.29 mmol/L Or HDL treatment</td>
<td>TG ≥ 1.69 mmol/L or on TG treatment HDL-C men &lt; 1.03 mmol/L, women &lt; 1.29 mmol/L Or HDL treatment</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>≥ 140/90 mmHg</td>
<td>≥ 140/90 mmHg or on antihypertensive medications</td>
<td>≥ 130/85 mmHg or on antihypertensive medications</td>
<td>≥ 130/85 mmHg or on antihypertensive medications</td>
<td>≥ 130/85 mmHg or on antihypertensive medications</td>
</tr>
<tr>
<td>Obesity</td>
<td>Waist: hip ratio men &gt; 0.9 women &gt; 0.85 and/or BMI &gt; 30 kg/m²</td>
<td>WC men ≥ 94 cm, women ≥ 80 cm</td>
<td>WC ≥ 94 cm</td>
<td>WC men ≥ 102 cm, women ≥ 88 cm</td>
<td>WC ≥ 94 cm</td>
</tr>
<tr>
<td>Other</td>
<td>Microalbuminuria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

https://ejhm.journals.ekb.eg/
HDL-C stands for high-density lipoprotein cholesterol; BMI is for body mass index; Impairment in glucose tolerance (IGT) and impaired fasting glucose (IFG) IR, hyperinsulinemia; Diabetes mellitus type 2 (T2DM); It stands for triglycerides. Waist size, abbreviated as WC.

Figure (1): The pathophysiology of metabolic syndrome. The acronyms AT2, CRP, IL-6, LOX, RAAS, ROS, and TNF stand for renin, angiotensin II type 2, interleukin 6, lectin-like oxidised low-density lipoprotein, and tumour necrosis factor, respectively [20].

CONCLUSION
There is tremendous significance in the link between AGA and MetS. Conditions linked to metabolism and MetS are most significantly connected with AGA.

Financial support and sponsorship: Nil.
Conflict of Interest: Nil.

REFERENCES
5. Nestor M, Ablon G, Gade A et al. (2021): Treatment options for androgenetic alopecia: Efficacy, side effects, compliance,


