

A systematic review and meta-analysis on the association between androgenic alopecia and the risk of metabolic syndrome

Uma revisão sistemática e metanálise sobre a associação entre alopecia androgenética e o risco de síndrome metabólica

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ABSTRACT

This study conducted a systematic review of studies on the relationship between androgenic alopecia and metabolic syndrome. We performed a comprehensive review of databases including PubMed, Web of Knowledge, Google Scholar, Scopus, and Embase, and extracted relevant articles published from 2010 to 2018. The case reports, review articles, or studies lacking full-text articles were excluded. We examined nine studies for the meta-analysis step. The results showed a significant relationship between alopecia and metabolic syndrome (OR = 2.81; CI 95% = 2.16-3.66; I² = 73%; P = 0.0003). There is a significant correlation between androgenic alopecia and metabolic syndrome.

Keywords: Alopecia; Systematic review; Metabolic syndrome; Hair diseases; Insulin resistance; Review hair

RESUMO

Este estudo conduziu uma revisão sistemática de estudos sobre a relação entre alopecia androgênica e síndrome metabólica. Realizamos uma revisão abrangente de bancos de dados, incluindo PubMed, Web of Knowledge, Google Scholar, Scopus e Embase, e extraímos artigos relevantes publicados de 2010 a 2018. Os relatos de caso, artigos de revisão ou artigos sem textos completos foram excluídos. Nove estudos foram examinados para a etapa de metanálise. Os resultados mostraram uma relação significativa entre alopecia e síndrome metabólica (OR = 2,81; IC 95% = 2,16-3,66; I² = 73%; P = 0,0003). Existe uma correlação significativa entre a alopecia androgênica e a síndrome metabólica.

Palavras-chave: Alopecia; Revisão sistemática; Síndrome metabólica

Review Article

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INTRODUCTION

Androgenetic Alopecia (AGA) is a type of alopecia that shows hair thinning and loss in the frontal and central regions of the head or the vertex.¹

According to evidence, 50% of men and women suffer from androgenic alopecia.² AGA mainly affects people in the third and fourth decades of life but can occur any time after puberty and is more common in men than women. Also, the pattern of hair loss is different between the sexes.³

The etiology of AGA is multifactorial. Two fundamental changes occur in the hair cycle causing the condition: first, the hair anagen phase decreases, producing vellus and miniaturized hairs; second, the distance between the telogen and anagen phases increases, resulting in an increased number of empty hair follicles.⁴ Dihydrotestosterone (DHT) is a major factor in AGA pathogenesis. Five-alpha reductase enzyme converts testosterone to DHT. There are two types of 5-alpha reductase enzymes: type 1 and type 2. Type-2 5-alpha reductase plays an essential role in AGA. DHT binds to androgen receptors in the dermal papilla of the hair follicle, inhibits adenyl cyclase, and activates the genes responsible for transforming terminal hair to vellus hair in the anagen phase, resulting in empty follicles.^{5,6} Excess insulin and insulin resistance decrease the sex hormone-binding globulin levels and lead high free testosterone levels.⁷⁻⁹ An increased serum androgen level also causes hypertension through the androgen receptors in the arterial endothelium, causing the proliferation and hyperplasia of smooth muscle cells in the arteries and contracting the lumen leading to high blood pressure.^{10,11} Also, microvascular disorders and follicular hypoxia decrease the number of hair follicles.¹²

Studies on the effects of androgens on the serum lipid index show that anabolic steroids such as testosterone cause decreased HDL, increased LDL, hyperlipidemia, and coronary artery disease.¹³ Research show that androgenic alopecia is a risk factor for insulin resistance and type-2 *diabetes mellitus* in men.^{13,14} Insulin resistance and high blood insulin levels are also risk factors for cardiovascular disease.¹⁵ Metabolic syndrome consists of insulin resistance, obesity, dyslipidemia, and hypertension, increasing the risk of cardiovascular diseases, stroke, and diabetes.¹⁶⁻¹⁸ Studies show that some dermatologic conditions and metabolic syndrome are correlated,¹⁹ but there is still controversy about the association between AGA and metabolic syndrome.^{7,8}

The classic pattern of hair loss in men involves the frontal, temporal, and vertex regions of the scalp, while the hair on the parietal and occipital areas remains.¹ Female Pattern Hair Loss (FPHL) appears first as thinning and then as hair loss around the ear. However, some women experience other configurations, such as centralized, Christmas tree, or male patterns. The scattered pattern is graded using the Ludwig scale, the centralized pattern using the Olsen scale, and the male pattern using the Hamilton-Norwood scale to assess AGA.³

The present study systematically reviewed studies on the relationship between AGA and metabolic syndrome.

METHODS

Protocol and Registration

All the design steps were based on the PRISMA guidelines and the study sought to answer the question of whether the prevalence of the metabolic syndrome is higher in androgenic alopecia patients than in healthy controls.

Information Sources

We conducted a comprehensive review of databases including PubMed, Web of Knowledge, Google Scholar, Scopus, and Embase, and extracted pertinent articles.

The keywords used to find the articles included: Metabolic syndrome, central obesity, high blood pressure, high blood sugar, high serum triglycerides, low serum high-density lipoprotein, and androgenic alopecia.

Search Strategy

The search strategy for PubMed was: (Metabolic syndrome) OR (central obesity) OR (high blood sugar) OR (high serum triglycerides) OR (low serum high density lipoprotein) AND (androgenic alopecia) AND ("2010/01/01" [PDat]: "2018/12/31" [PDat])

After extracting pertinent articles from the databases, we entered all of them into Endnote and removed the duplicates. Subsequently, two researchers selected the articles independently, and whenever there was disagreement about the selections for the final review, a third researcher was recruited to make the final decision.

Eligibility Criteria

This study included all articles published in English from 2010 to 2018 on patients with androgenic alopecia examined in terms of metabolic syndrome. Case reports, review articles, or studies lacking full-text articles were excluded.

Evidence Synthesis and Results

STATA version 13.2 and Metan software were used to determine the prevalence of the condition. The pooled odds ratio was finally calculated, and the result was determined based on a 95% confidence interval (CI). The heterogeneity of the results of the studies was determined based on I^2 statistics and P-value. Publication bias was also determined based on a funnel plot graph and Egger test.

RESULT

There was a significant relationship between metabolic syndrome and alopecia. This result is contrary to the findings of some studies, perhaps because these other studies had not appropriately examined the confounding factors. The odds ratio (OR) of 2.81 shows that androgenic alopecia is a risk factor for metabolic syndrome. The incidence of metabolic syndrome was 43% to 51% in the groups with androgenic alopecia and 20% to 28% in the healthy controls.

Figure 1 shows the selection process for the databases.

The meta-analysis included a total of nine studies. The total sample size of the studies was 1,452, and 880 cases had AGA. Table 1 presents the list of studies included in the meta-analysis. Table 2 shows the risk of bias in the studies. We used a forest plot chart to calculate the numerical results of the studies (Fig. 2). Based on this chart, the results showed a significant relationship between alopecia and metabolic syndrome (OR = 2.81; 95% CI = 2.16-3.66; $I^2 = 73%$; $P = 0.0003$).

Figure 2: The forest plot chart for examining the OR and significance of the relationship between alopecia and metabolic syndrome.

The funnel plot chart was used to investigate publication

bias. As shown in figure 3, the studies are reasonably accurate, and there is no significant publication bias.

Figure 3: The funnel plot investigating the symmetry between the studies

DISCUSSION

Just two review studies have been conducted on metabolic syndrome and endogenous alopecia, and both confirm the results of our analysis. According to these analyses, there is a significant correlation between androgenic alopecia and metabolic syndrome.

In 1972, Cotton *et al.*²⁰ showed a significant relationship

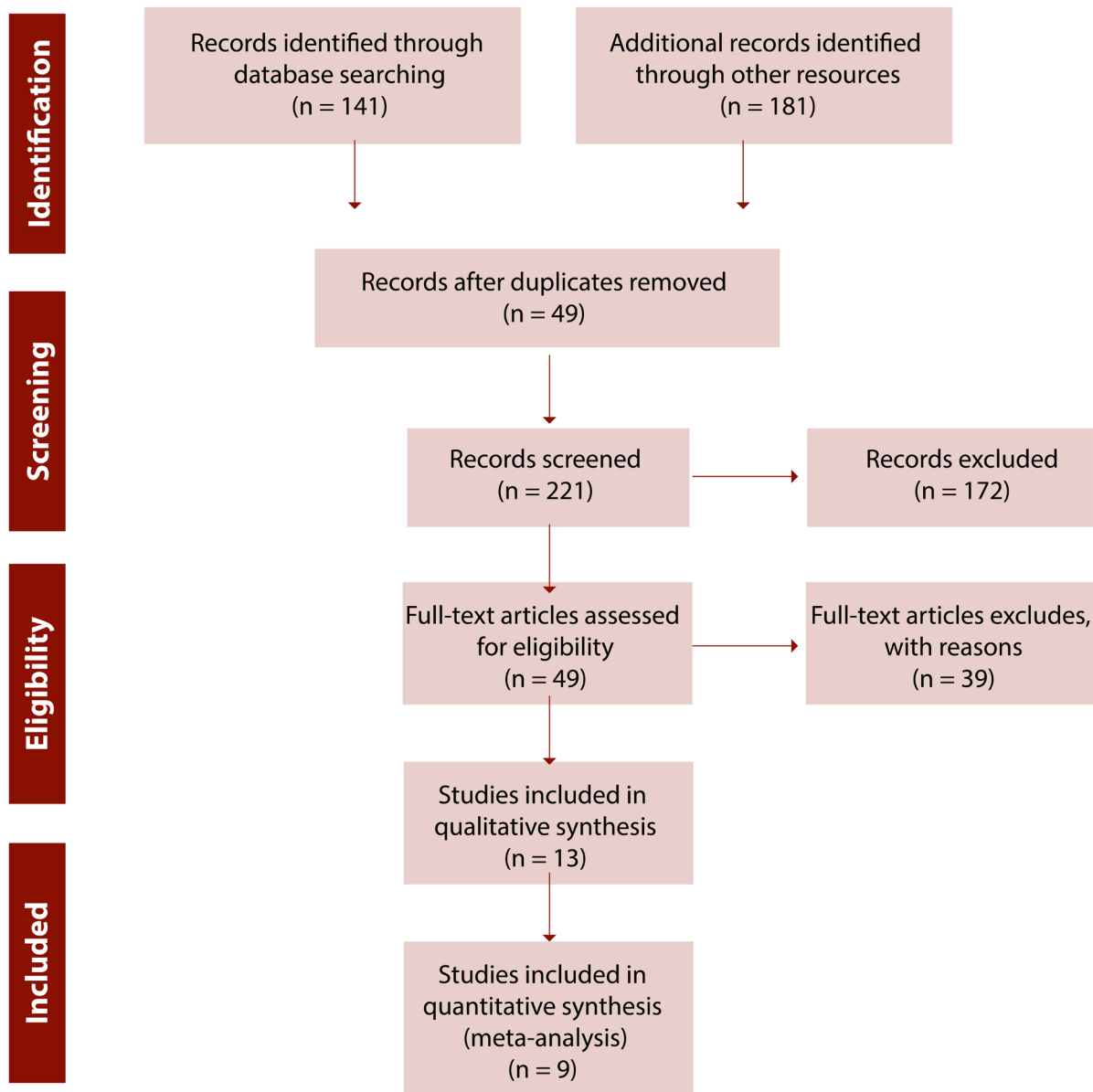


FIGURE 1: PRISMA diagrams examining the process of include and exclude studies to meta-analysis

Table 1: Details of the reviewed studies

Reference	Title	Year of Publication	Country	Patient Size	Alopecia Grading Scale	Result
Acibucu <i>et al.</i> ²¹	The association of insulin resistance and metabolic syndrome in early androgenetic alopecia	2010	Turkey	128	Hamilton-Norwood Scale	Significant in the alopecia group
Mumcuoglu <i>et al.</i> ²²	The investigation of insulin resistance and metabolic syndrome in male patients with early-onset androgenetic alopecia	2011	Turkey	90	Hamilton-Norwood Scale	Significant in the alopecia group
Chakrabarty <i>et al.</i> ²³	Association of premature androgenetic alopecia and metabolic syndrome in a young Indian population	2014	India	170	Norwood-Hamilton Scale	Significant in the alopecia group
Bakry <i>et al.</i> ³⁸	Androgenetic alopecia, metabolic syndrome, and insulin resistance: Is there any association? A case-control study.	2014	India	200	Hamilton-Norwood Scale	Significant in the alopecia group
Ozbas Gok <i>et al.</i> ²⁴	Is there really relationship between androgenetic alopecia and metabolic syndrome?	2015	Turkey	116	Hamilton-Norwood Scale	Not significant between the two groups
Ertas ³⁹	Androgenetic alopecia as an indicator of metabolic syndrome and cardiovascular risk.	2016	Turkey	68	Hamilton-Norwood scale and the presence of vertex hair loss	Significant in the alopecia group
Agamia <i>et al.</i> ²⁵	Benign prostatic hyperplasia, metabolic syndrome and androgenic alopecia: Is there a possible relationship?	2016	Egypt	68	Hamilton-Norwood Scale	Significant in the alopecia group
Pengsalae <i>et al.</i> ²⁶	Association of early-onset androgenetic alopecia and metabolic syndrome in Thai men: a case-control study	2013	Thailand	400	Hamilton-Norwood Scale	Significant in the alopecia group
Banger <i>et al.</i> ¹⁸	Is early onset androgenic alopecia a marker of metabolic syndrome and carotid artery atherosclerosis in young Indian male patients?	2015	India	200	Hamilton-Norwood Scale	Significant in the alopecia group

between hair loss and cardiovascular diseases for the first time. In 2010, Acibucu *et al.*²¹ revealed, assessing 168 patients, that the probability of metabolic syndrome was 2.7 times higher in the AGA group than in the control group. The main problem of their study was the small sample size in the control group, although they showed significant intergroup correlations.²¹ In 2011, in Turkey, Mumcuoglu *et al.*²² examined insulin resistance and metabolic syndrome in men with early androgenic alopecia and showed that insulin resistance-related diseases and coronary artery diseases are more common in men with androgenic alopecia. This study included 50 men (18-30 years) with AGA ≥ 3

on the Hamilton-Norwood scale and BMI <27 and 40 men matched in weight and age. According to the results, high Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and Fasting Insulin Resistance Index (FIRI) scores indicate that men with AGA have insulin resistance.²² In a 2014 case-control study, Chakrabarty *et al.*²³ examined the frequency of metabolic syndrome in people with primary AGA at a cognitive therapy clinic in Bangalore, India. They assessed 85 cases of AGA and 85 matched controls using the Norwood-Hamilton scale to evaluate the degree of AGA. The study used the Chi-square test to compare the ratios between the groups and compared the

TABLE 2: The risk of bias in the reviewed studies

	Random Sequence Allocation	Selection Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Biases
Acibucu <i>et al.</i> ²¹	+	?	–	–	?	+
Mumcuoglu <i>et al.</i> ²²	?	?	?	–	+	?
Chakrabarty <i>et al.</i> ²³	?	?	?	–	?	+
Bakry <i>et al.</i> ³⁸	?	?	?	+	–	+
Banger <i>et al.</i> ¹⁸	+	+	+	+	+	–
Ozbas Gok <i>et al.</i> ²⁴	?	?	–	–	?	+
Ertas <i>et al.</i> ³⁹	+	?	?	+	?	+
Agamia <i>et al.</i> ²⁵	?	?	?	–	?	?
Pengsalae <i>et al.</i> ²⁶	?	–	+	–	–	?

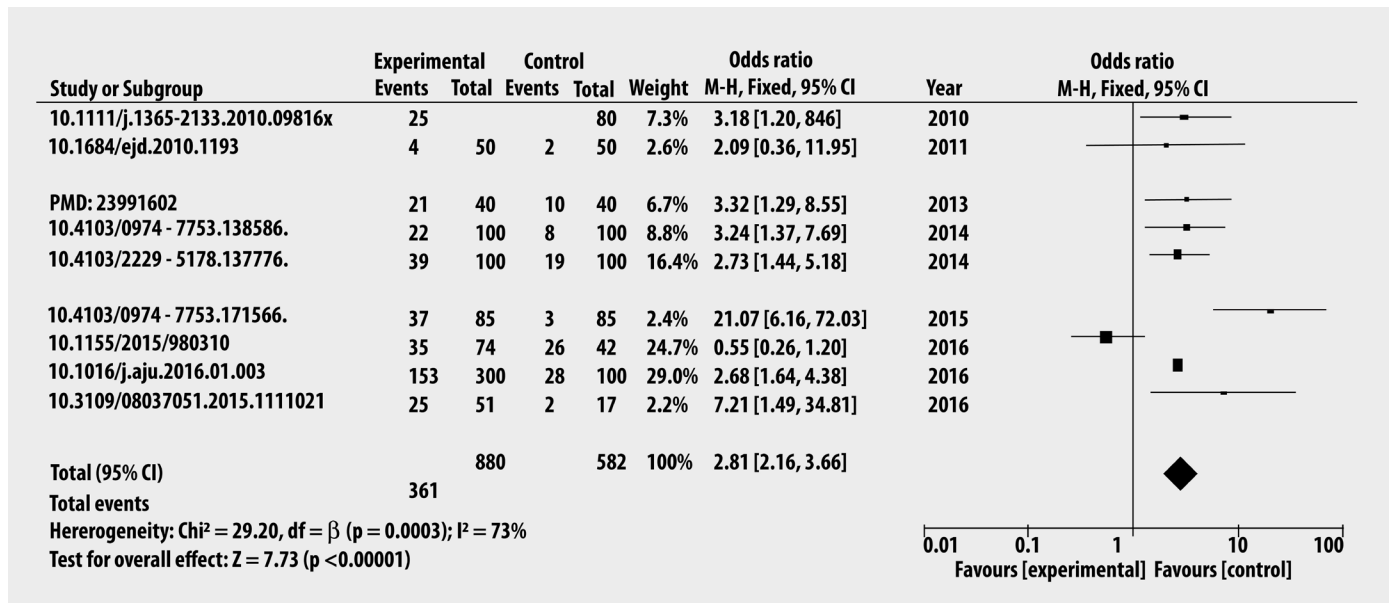


FIGURE 2: Forest Plot Chart, checking OR and Significant Relationship Between Alopecia and Metabolic Syndrome

means between the subjects with metabolic syndrome and the controls using the independent t-test.

AGA was associated with metabolic syndrome in Indian men younger than 30 years old ($P < 0.001$), but the severity of AGA was not correlated with metabolic syndrome. A 2015 case-control study by Banger *et al.*¹⁸ in India examined the clinical characteristics of AGA and the presence of metabolic syndrome and carotid artery atherosclerosis in men with early AGA and compared the results against a control group. The samples consisted of 100 men aged 18–35 years with AGA and several healthy controls; 22% of the patients with early androgenic alopecia

met the criteria for metabolic syndrome compared to 8% in the control group. Nonetheless, there was no significant difference in the mean cholesterol levels. The research found an atherosclerotic plaque in two patients in the case group and no plaque in the control group.

Another case-control study by Ozbas Gok S. *et al.*²⁴ in 2015 in Turkey assessed 74 men with AGA and 42 male controls. Of the 74 male AGA patients (age range of 20–50 years, mean age of 32.14 years), 24 were in stage 2, 26 in stage 3, 17 in stage 4, 1 in stage 5, and 5 were in stage 7. In the case group, 35 out of 74 individuals had metabolic syndrome. However, 26 out of the

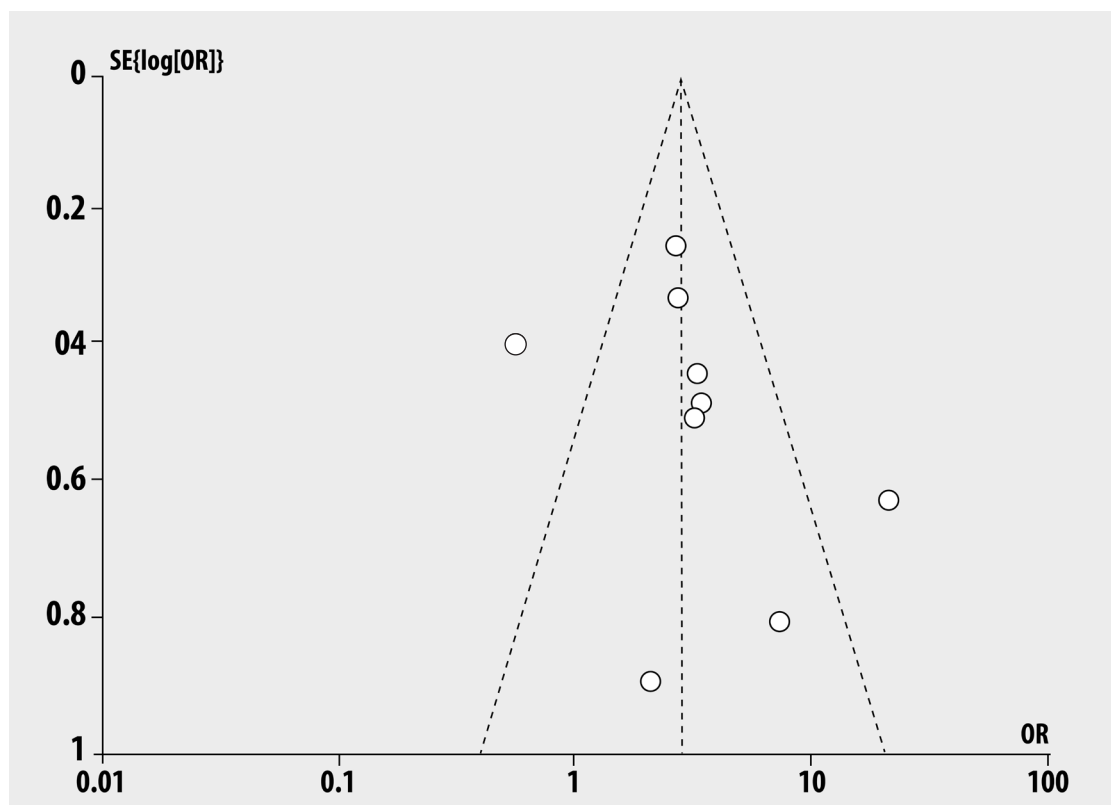


FIGURE 3: Funnel plot, investigating the symmetry of Existing Studies

42 subjects in the control group were affected. There was no significant difference in metabolic syndrome prevalence between the AGA patients and the control group ($P=0.135$). Among the studied parameters, only systolic blood pressure was significantly higher in the AGA group than in the control group.²⁴ A study by Agamia *et al.*²⁵ in Egypt in 2016 found a significant association between benign prostatic hyperplasia (BPH) and metabolic syndrome with AGA: the risk of metabolic syndrome was 2.68 times higher in the patients with androgenic alopecia. Androgenic changes in men's bodies also increase the chance of developing prostate cancer.²⁵ A study by Pengsalae *et al.*²⁶ in Thailand in 2013 evaluated the association between androgenic alopecia and metabolic syndrome in Thai men. The research selected 80 male subjects, including 40 with early diagnosis of AGA (before 35 years of age) and 40 controls without alopecia. The patients with early androgenic alopecia were 3.48 times more likely to have metabolic syndrome than the control group ($P=0.015$, $OR=3.48$, $95\% CI=1.25-9.75$). Pengsalae *et al.*²⁶ found a significant association between androgenic alopecia and metabolic syndrome. Also, they observed a correlation between the severity of AGA and metabolic syndrome ($P=0.629$). They concluded that the early detection of metabolic syndrome in this population might be helpful in preventing cardiovascular diseases.²⁶ A study in South Korea by Yi *et al.*²⁷ in 2012 using the Norwood scale for men and the Ludwig scale for women examined a total of

3,408 individuals (1,707 men and 1,701 women) from January 2008 to February 2010. The relationship between AGA and all five metabolic syndrome components (waist circumference, triglycerides, high-density lipoprotein, blood glucose, and blood pressure) was statistically non-significant.

When multiple regressions were used to adjust for age, family history, and smoking status, there was no significant relationship between the prevalence of metabolic syndrome and AGA in the male group. In contrast, there was a statistically significant relationship between the prevalence of metabolic syndrome and AGA in the female group. A 2010 study by Acibucu *et al.*²¹ in Singapore assessed the frequency of insulin resistance, hyperinsulinemia, and metabolic syndrome in patients with androgenic alopecia. The study analyzed 80 patients with primary AGA and 48 healthy controls. The results showed that the difference in insulin resistance between the groups was statistically significant, as this index was higher in patients with preterm AGA compared to the healthy controls. Also, the incidence of metabolic syndrome was significantly higher in the AGA group than in the control group. The study showed that the prevalence of insulin resistance and metabolic syndrome increases in patients with AGA.²¹ A 2010 study by Su L. H. *et al.* in Taiwan evaluated the relationship between metabolic syndrome and androgenic alopecia in 740 individuals aged 40 to 91 years.⁶ It used the Norwood scale to evaluate the rate of hair loss. The research

collected data on the components of metabolic syndrome and other possible risk factors, and the results showed a significant relationship between AGA and metabolic syndrome (OR= 1.67, 95% CI= 1.01–2.74) as well as a significant relationship between AGA and the number of components of the metabolic syndrome (OR= 1.21, 95% CI= 1.03–1.42). Among the components of the metabolic syndrome, high-density lipoprotein cholesterol (HDL-C) was identified as the most important factor associated with AGA (OR= 2.36, 95% CI= 1.41–3.95; P= 0.001). This finding may have significant implications for the detection of metabolic syndrome in patients with moderate or severe AGA.⁶ A 2016 cross-sectional study by Gopinath H. *et al.*¹⁷ in India, examined the association between metabolic syndrome and early androgenic alopecia in men aged 18–55 years. The research included 85 cases with clinically diagnosed early-onset (less than 35 years) androgenic alopecia (Norwood III) plus 85 controls without androgenic alopecia. Metabolic syndrome was observed in 19 (22.4%) patients with androgenic alopecia and eight (4.9%) controls (P = 0.021). Abdominal obesity, hypertension, and low-density lipoprotein levels were higher in patients with androgenic alopecia compared to the controls.¹⁷ A 2014 study by Eckel *et al.*²⁸ in India evaluated the link between metabolic syndrome and insulin resistance in patients with AGA. It recruited 100 men with stages III–VII AGA based on the Hamilton–Norwood scale and 100 controls of the same sex and age. They observed a significant correlation between AGA and metabolic syndrome (P = 0.002) and between AGA and IR (P<0.001).

There are many articles on the rise regarding the significant association between dermatologic disorders, metabolic syndrome, and its correlated laboratory markers and also possible logical adjunctive therapeutic options, especially psoriasis, acne, androgenic alopecia, acanthosis nigricans, hidradenitis suppurativa, and lichen planus.^{19,29–42} This systematic review and meta-analysis focused on the association between androgenic alopecia and metabolic syndrome. ●

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Abbreviations:

AGA: Androgenic Alopecia

DHT: Dihydrotestosterone

FPHL: Female Pattern Hair Loss

HOMA-IR: Homeostatic Model Assessment for Insulin Resistance

FIRI: Fasting Insulin Resistance Index; BPH: Benign Prostatic Hyperplasia

HDL-C: High-Density Lipoprotein Cholesterol

Review criteria:

- This systematic review was conducted using five databases to assess the relationship between androgenic alopecia (AGA) and metabolic syndrome.
- This systematic review adheres to the PRISMA guidelines. Two independent reviewers extracted data, and an expert epidemiologist performed the meta-analysis.

Implications for clinical practice:

- According to the results of this study, there was a significant relationship between metabolic syndrome and androgenic alopecia;
- Androgenic alopecia could be a risk factor for metabolic syndrome;
- The incidence of metabolic syndrome was 43% to 51% in the groups with androgenic alopecia and 20% to 28% in the healthy groups.

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