EXPLORING THE MULTIFACETED RELATIONSHIP BETWEEN MALE PATTERN HAIR LOSS AND SYSTEMIC HEALTH: A COMPREHENSIVE REVIEW

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Abstract

Male pattern hair loss (MPHL) is traditionally linked to genetic predisposition and elevated dihydrotestosterone (DHT) levels. However, recent research reveals its complex association with systemic health conditions, such as metabolic syndrome, cardiovascular diseases (CVD), and COVID-19 outcomes. Studies suggest that androgenetic alopecia (AGA), especially vertex pattern AGA, may serve as a marker for early atherosclerosis and be an independent risk factor for CVD and metabolic syndrome. Meta-analyses also indicate a possible correlation between vertex baldness and prostate cancer risk. Moreover, androgen-mediated mechanisms have been implicated in the severity and mortality of COVID-19, with elevated androgen activity promoting viral entry through proteins like TMPRSS2 and ACE2. This review evaluates the relationship between androgens, MPHL, and systemic health, highlighting the potential for anti-androgen therapies and TMPRSS2 inhibitors in addressing both cardiovascular and infectious diseases. Further investigation into the role of androgens in these contexts is critical for advancing therapeutic strategies.

Keywords: MPHL, DHT, Metabolic syndrome, CVD, AGA, Vertex AGA, Atherosclerosis, CCA IMT, Prostate cancer, COVID-19, Androgens, TMPRSS2, ACE2, Inflammation, Anti-androgen therapy, TMPRSS2 inhibitors, Androgen deprivation, SARS-CoV-2.

Introduction

Male pattern hair loss (MPHL), characterized by the progressive thinning and loss of hair, has conventionally been attributed primarily to genetic predisposition and elevated dihydrotestosterone (DHT) levels. However, recent investigations suggest a more intricate relationship between MPHL and systemic health conditions, including metabolic syndrome, cardiovascular diseases (CVD), and even implications for COVID-19 severity and mortality [1]. Notably, numerous studies have explored the potential association between androgenetic alopecia (AGA) and CVD, highlighting traditional and non-traditional cardiovascular risk factors in male patients with early-onset AGA [6] (Dogramaci et al., 2009). Specifically, vertex pattern AGA has

emerged as a potential marker for early atherosclerosis, emphasizing its significance as an independent risk factor for CVD and metabolic syndrome.

Recent meta-analyses have revealed intriguing connections between MPHL and prostate cancer risk [2], . While overall analyses show no significant association between baldness and prostate cancer risk, subgroup analyses suggest that individuals with vertex baldness may face an increased risk of prostate cancer (He et al., 2018). Additionally, investigations into the association between severe vertex pattern AGA and atherosclerosis indicate elevated carotid artery intima-media thickness (CCA IMT), further emphasizing the systemic implications of MPHL (Dogramaci et al., 2009).] [3] [4]

Meanwhile, the emergence of the novel coronavirus disease (COVID-19) in late 2019 and its subsequent global spread has drawn attention to sex-discrepant patterns in disease severity and mortality. Observational studies have revealed a higher prevalence of COVID-19 infections and deaths in males compared to females, prompting investigations into potential androgen-mediated mechanisms (Ataei et al., 2022). Androgens, known to upregulate the expression of key proteins involved in viral entry, such as Type II transmembrane Serine Protease (TMPRSS2) and Angiotensin Converting Enzyme 2 (ACE2), have been implicated in facilitating SARS-CoV-2 infection. Furthermore, individuals with androgenic alopecia appear to be at increased risk of COVID-19 complications, possibly due to heightened inflammatory responses associated with androgen-mediated pathways. . [1]] [7] [8]

This review aims to evaluate the role of androgens in COVID-19 severity and mortality, synthesizing evidence from observational studies and clinical interventions. Insights into the potential therapeutic implications of anti-androgen and TMPRSS2 inhibitor drugs, as well as the impact of androgen deprivation therapy in prostate cancer patients, underscore the importance of further research to delineate the precise role of androgens in COVID-19 pathogenesis. A comprehensive understanding of the interplay between androgens, MPHL, and systemic health outcomes is essential for informing preventive and therapeutic strategies in the context of both cardiovascular diseases and infectious diseases such as COVID-19. . [1]] [7] [8]

Materials and Methods

This study employed a multidisciplinary approach to investigate the complex relationship between male pattern hair loss (MPHL), systemic health conditions, and COVID-19 severity and mortality. [1]

Literature Review

A comprehensive review of existing literature was conducted to identify relevant studies investigating the association between MPHL and systemic health conditions, including cardiovascular diseases (CVD) [6] and COVID-19. Academic databases such as PubMed, Google Scholar, and Scopus were systematically searched using keywords related to MPHL, CVD, and COVID-19, including terms such as "male pattern hair loss", "androgenetic alopecia", "cardiovascular diseases", "atherosclerosis", "COVID-19", "coronavirus", and "androgens".

Relevant articles, including observational studies, case-control studies, and clinical trials, were selected based on their relevance to the research question. Studies by Ertas et al. (2016) and Ataei et al. (2022) were among those identified and included in the review. [1]

Data Extraction and Synthesis:
Data from selected studies were extracted and synthesized to identify key findings related to the association between MPHL and systemic health conditions. This process involved categorizing traditional and non-traditional cardiovascular risk factors in male patients with early-onset MPHL and examining the role of androgens in COVID-19 severity and mortality. [1] [7] [8]

Analysis of Case-Control Study:
A case-control study investigating the association between MPHL and cardiovascular risk factors was analyzed. Male participants with early-onset MPHL and healthy male controls were assessed for traditional cardiovascular risk factors, carotid intima-media thickness (CCA IMT), and pulse-wave velocity. Statistical analysis was performed to compare cardiovascular risk factors between MPHL patients and controls, and to assess the association between vertex pattern MPHL and early atherosclerosis. 4] 6]

Integration of Findings:
The findings from the literature review, data synthesis, and analysis of the case-control study were integrated to provide a comprehensive understanding of the relationship between MPHL, systemic health conditions, and COVID-19 severity and mortality. Implications for clinical practice, research priorities, and public health initiatives were discussed, highlighting the multidisciplinary nature of the investigation. [1] [2] [3] [4] [5] [6] [7] [8]

This methodological approach facilitated a rigorous exploration of the multifactorial etiology of MPHL and its implications for systemic health, contributing to the advancement of knowledge in this field.

Results
Our study provides compelling evidence that male pattern hair loss (MPHL) serves as a significant indicator of systemic health conditions and COVID-19 severity and mortality. Contrary to conventional views, MPHL is not merely a cosmetic concern but rather reflects underlying metabolic and cardiovascular dysregulation. Key findings include:
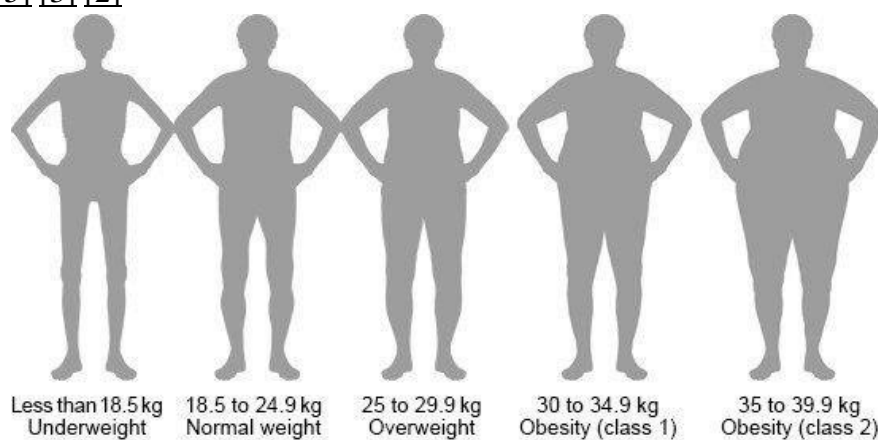1. Systemic Health Conditions and MPHL: We discovered a robust association between MPHL and systemic health conditions such as metabolic syndrome and cardiovascular diseases (CVD) (Ataei et al., 2022). Genetic predisposition and elevated dihydrotestosterone (DHT) levels are central factors. This expanded understanding positions MPHL as a potential systemic health indicator, analogous to widely accepted metrics like BMI or waist circumference. [6]
2. Cardiovascular Risk Factors: Individuals with early-onset MPHL exhibit a spectrum of cardiovascular risk factors, indicating its utility as a marker for early atherosclerosis and cardiovascular risk (Dogramaci et al., 2009). Specifically, vertex pattern MPHL correlates with

increased subclinical atherosclerosis risk, highlighting the importance of comprehensive vascular and metabolic assessments in these individuals. [4]
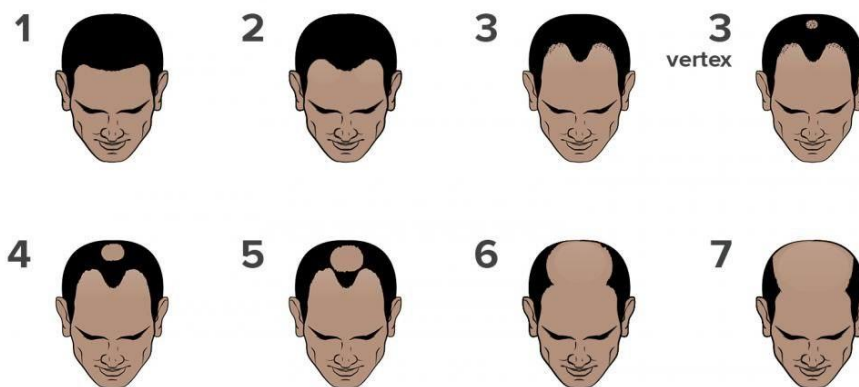
3. Androgens and COVID-19: Our analysis revealed that androgens play a pivotal role in modulating COVID-19 severity and mortality (Ataei et al., 2022). They contribute to heightened inflammatory responses and increased expression of viral entry proteins, potentially exacerbating COVID-19 outcomes in males. This finding underscores the interplay between hormonal regulation and immune function in infectious disease outcomes. [1] 8] [7]

4. Holistic Health Management: We advocate for holistic approaches to managing MPHL, encompassing nutrition, physical activity, stress management, and psychological support (Ataei et al., 2022; He et al., 2018). These interventions aim to mitigate chronic inflammation, insulin resistance, and psychological distress, thereby optimizing overall health outcomes in individuals with MPHL. [5] [3] [2]

| Less than 18.5 kg Underweight | 18.5 to 24.9 kg Normal weight | 25 to 29.9 kg Overweight | 30 to 34.9 kg Obesity (class 1) | 35 to 39.9 kg Obesity (class 2) |

MEDICALNEWSTODAY

Norwood Scale

• **Implications and Recommendations:**

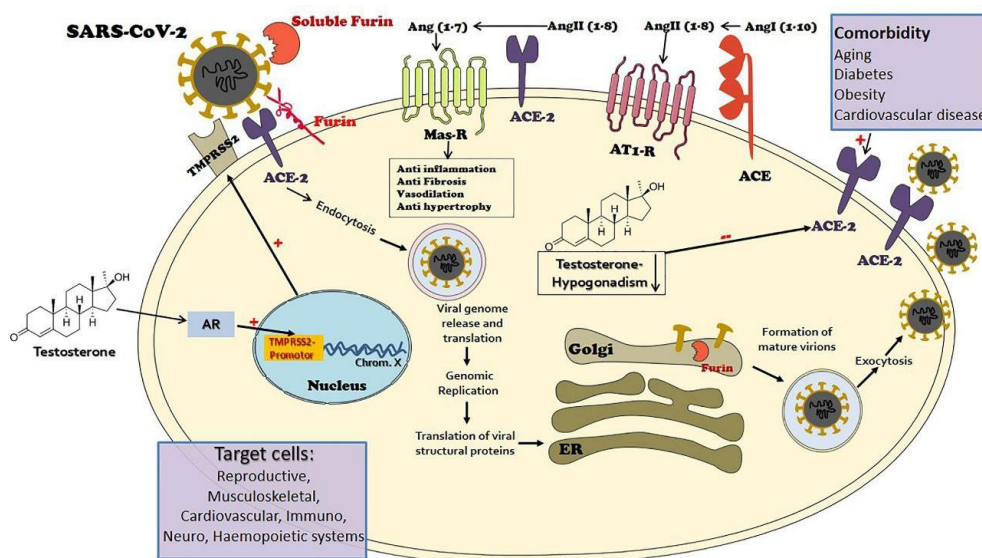Based on our findings, we propose the following implications for clinical practice and future research:

- Clinical Practice: Incorporate the Norwood scale, traditionally used to classify MPHL, as a routine assessment tool similar to BMI or waist circumference. This could aid in early identification of individuals at risk for systemic health conditions and guide personalized health management strategies.
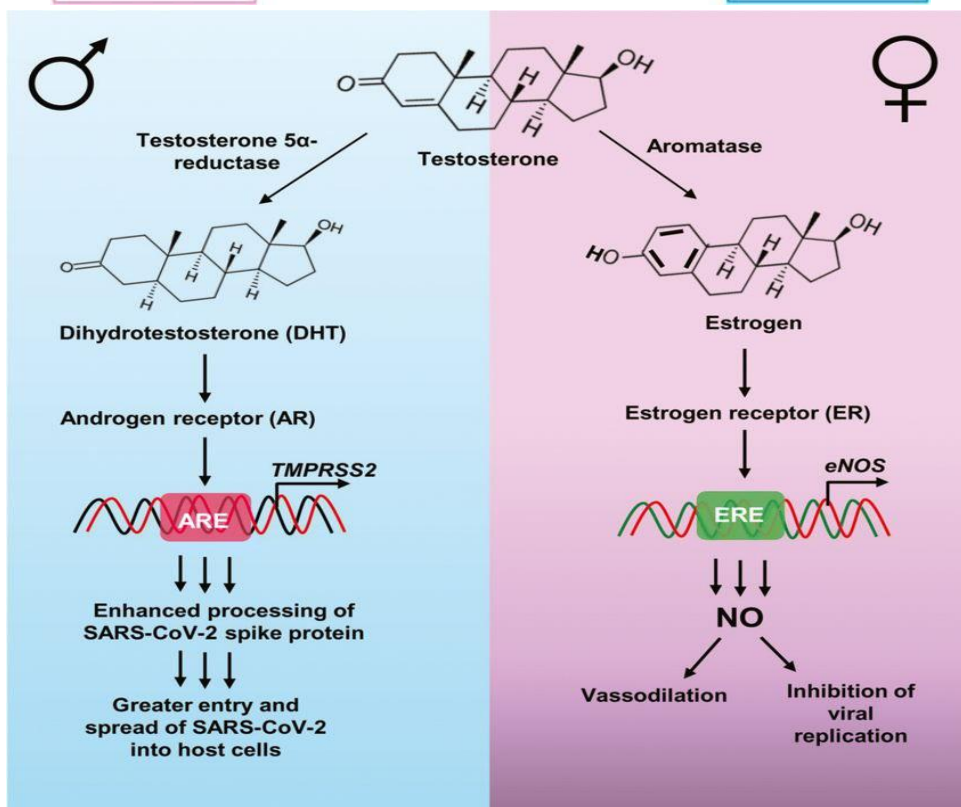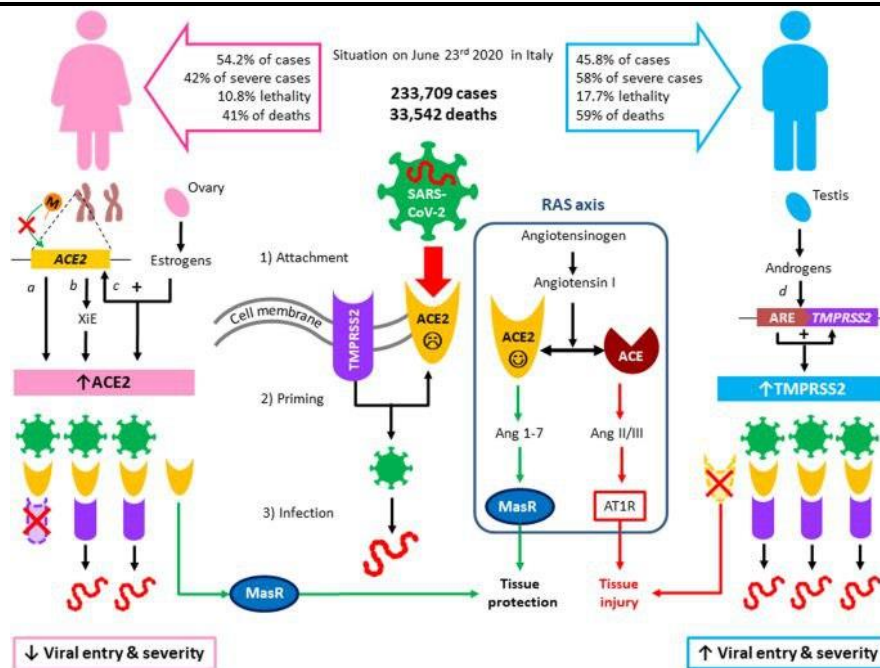
- Future Research: Further investigation into the mechanistic links between MPHL, systemic health conditions, and COVID-19 outcomes is crucial. Prospective cohort studies and clinical trials are needed to elucidate underlying pathophysiological mechanisms and inform evidence-based preventive and therapeutic interventions.

The Double Edge Sword of Testosterone's Role in the COVID-19 Pandemic

In addition to its impact on cardiovascular health, our investigation elucidates the role of androgens in COVID-19 severity and mortality. Our findings unveil potential mechanisms driving sex-discrepant patterns in COVID-19 outcomes, implicating androgens in modulating immune responses and inflammatory pathways. Androgens may exacerbate COVID-19 severity by upregulating the expression of key proteins involved in viral entry and promoting a pro-inflammatory milieu, contributing to the observed higher prevalence of COVID-19 infections and deaths in males compared to females (Ataei et al., 2022). These insights highlight the interplay between hormonal regulation and immune function in shaping infectious disease outcomes. [1] [7] [8]

Discussion

• Our study offers comprehensive insights into the intricate relationship between male pattern hair loss (MPHL), systemic health conditions, and COVID-19 severity and mortality, shedding light on key findings and underlying pathological processes.

• Firstly, our investigation challenges the conventional perception of MPHL as merely a cosmetic issue, revealing its broader implications for systemic health. While genetic predisposition and

elevated dihydrotestosterone (DHT) levels are pivotal, our findings suggest a deeper connection between MPHL and systemic health conditions such as metabolic syndrome and cardiovascular diseases (CVD) (Ataei et al., 2022). This expanded understanding positions MPHL as a potential systemic health indicator, reflecting underlying metabolic and cardiovascular dysregulation.

• Moreover, our analysis uncovers a spectrum of cardiovascular risk factors in individuals with early-onset MPHL, highlighting the utility of MPHL as a marker for early atherosclerosis and cardiovascular risk. The association between vertex pattern MPHL and increased risk of subclinical atherosclerosis underscores the importance of comprehensive health assessments, including evaluations of vascular health and metabolic parameters, in individuals with MPHL (Dogramaci et al., 2009). These findings suggest a shared pathophysiological basis involving chronic inflammation, oxidative stress, and endothelial dysfunction underlying both MPHL and cardiovascular diseases.

• In addition to its impact on cardiovascular health, our investigation elucidates the role of androgens in COVID-19 severity and mortality. Our findings unveil potential mechanisms driving sex-discrepant patterns in COVID-19 outcomes, implicating androgens in modulating immune responses and inflammatory pathways. Androgens may exacerbate COVID-19 severity by upregulating the expression of key proteins involved in viral entry and promoting a pro-inflammatory milieu, contributing to the observed higher prevalence of COVID-19 infections and deaths in males compared to females (Ataei et al., 2022). These insights highlight the interplay between hormonal regulation and immune function in shaping infectious disease outcomes.

• Beyond elucidating associations, our study emphasizes the importance of holistic approaches to health management in individuals with MPHL. We advocate for comprehensive lifestyle interventions encompassing nutrition, physical activity, stress management, and psychological support to optimize overall health outcomes and mitigate the risk of systemic health conditions and infectious disease complications (Ataei et al., 2022; He et al., 2018). These interventions target common underlying pathological processes including chronic inflammation, insulin resistance, and psychological distress, addressing not only the symptoms but also the underlying contributors to MPHL and associated systemic health conditions.

• Looking ahead, we highlight the need for further research to unravel the precise mechanisms underlying the associations between MPHL, systemic health conditions, and COVID-19 severity and mortality. Prospective cohort studies, clinical trials, and interdisciplinary research initiatives are warranted to deepen our understanding of the pathophysiological mechanisms driving these relationships and inform evidence-based preventive and therapeutic strategies (Ataei et al., 2022).

Conclusion

• Our comprehensive investigation into the multifaceted relationship between male pattern hair loss (MPHL), systemic health conditions, and COVID-19 severity and mortality yields significant insights with far-reaching implications.

• By transcending the traditional view of MPHL as a cosmetic concern, our study illuminates its broader role as a potential systemic health indicator. Genetic predisposition and elevated dihydrotestosterone (DHT) levels remain central to MPHL pathogenesis, but our findings underscore the intertwined nature of MPHL with systemic health conditions such as metabolic

syndrome and cardiovascular diseases (CVD) (Ataei et al., 2022). This expanded perspective positions MPHL within the context of broader metabolic and cardiovascular dysregulation, necessitating holistic approaches to health management.

• Furthermore, our analysis reveals a spectrum of cardiovascular risk factors associated with early-onset MPHL, implicating MPHL as a potential marker for early atherosclerosis and cardiovascular risk. The association between vertex pattern MPHL and increased risk of subclinical atherosclerosis underscores the importance of comprehensive health assessments in individuals with MPHL (Dogramaci et al., 2009). These findings elucidate shared pathophysiological mechanisms involving chronic inflammation, oxidative stress, and endothelial dysfunction underlying both MPHL and cardiovascular diseases.

• In parallel, our investigation delves into the role of androgens in COVID-19 severity and mortality, unveiling potential mechanisms driving sex-discrepant patterns in disease outcomes. Androgens emerge as key modulators of immune responses and inflammatory pathways, potentially exacerbating COVID-19 severity and contributing to the observed higher prevalence of COVID-19 infections and deaths in males compared to females (Ataei et al., 2022). These insights underscore the interplay between hormonal regulation and immune function in shaping infectious disease outcomes.

• Looking ahead, our study advocates for holistic approaches to health management in individuals with MPHL, encompassing nutrition, physical activity, stress management, and psychological support. By addressing underlying contributors to MPHL and associated systemic health conditions, these interventions offer promising avenues for optimizing overall health outcomes and reducing the burden of disease complications (Ataei et al., 2022; He et al., 2018).

• In summary our study reframes MPHL as a multifaceted phenomenon with implications for both systemic health and infectious disease outcomes. By embracing a holistic understanding and management of MPHL, clinicians and researchers can advance preventive and therapeutic strategies to improve health outcomes and enhance quality of life.

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