Male hypogonadism and its relationship with metabolic syndrome

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ABSTRACT

Male hypogonadism, characterized by reduced testosterone levels, and metabolic syndrome have become prevalent, impacting male quality of life. Objective: To explore the relationship between hypogonadism and metabolic syndrome to understand its role in male health. Method: This is an integrative literature review study, with information collection, in the databases of the National Library of Medicine (MEDLINE/PUBMED and Scientific Electronic Library Online (SciELO), published in the period between 2018 and 2023. Results: Studies have shown that metabolic syndrome increases the risk of chronic diseases, including hypogonadism. The risk of central hypogonadism is eight times higher in men with a BMI ≥ 30 kg/m², related to factors such as hyperestrogenism and insulin resistance. Weight loss, especially abdominal loss, negatively influences free testosterone levels, regardless of age. Conclusion: the presence of hypogonadism suggests insulin resistance and metabolic alterations, associated with dysfunctions such as loss of libido and metabolic syndrome. Tests such as CT scans and genital MRI aid in the diagnosis, which includes hormonal, genetic, and ferretin evaluations. Treatment aims to restore testosterone levels, improving quality of life through hormone replacement.

Keywords: Hypogonadism Male, Metabolic Syndrome, Testosterone.

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INTRODUCTION

Metabolic syndrome (MS), with an overall prevalence of 25%, contributes to 7% of mortality and 17% of deaths from cardiovascular diseases. In adolescents, the rates range from 2.5% to 22.2%, showing a significant association with sedentary behaviors and abdominal obesity. Early diagnosis is crucial, highlighting the need for a preventative approach to mitigate long-term impacts on cardiovascular health. (Dimopoulou, 2018).

In Brazil, it has a significant impact on the adult population, with an occurrence rate of 29.6%, and can reach more than 40% among individuals over 60 years of age. Additionally, a cohort study conducted in the country revealed an even higher prevalence, reaching the mark of 44% (Oliveira, 2020).

Metabolic Syndrome (MS) is a set of complex metabolic alterations widely studied due to its negative health implications and strong link to cardiovascular disease and type 2 diabetes. This syndrome includes conditions such as high blood pressure, abdominal obesity, dyslipidemias, and disturbances in glucose metabolism. Generally, the prevalence of MS is assessed based on the Adult Treatment Panel III (ATP III) criteria, although there are recommendations for standardization of criteria in order to improve comparison between studies (Dragsbæk et al., 2026; Lira et al., 2017).

The diagnostic criteria for Metabolic Syndrome (MS) usually consider the presence of dyslipidemia (hypertriglyceridemia and low HDL levels), hypertension, obesity, and hyperglycemia. However, there is no solid consensus on whether type 2 diabetes mellitus (DM2), defined as blood glucose above 126 mg/dL in population studies without clinical diagnosis, or even obesity, should be mandatory criteria in the analysis (Onesi et al., 2014; Yamagishi; Iso, 2017).

If not treated effectively, MS can lead to serious complications, including the development of type 2 diabetes mellitus and a considerable increase in the risk of cardiovascular disease. In addition, male hypogonadism is common, characterized by decreased testosterone levels, resulting in loss of muscle mass and increased adipose tissue, as shown in studies (Dimopoulou, 2018).

Hypogonadism is characterized, according to international guidelines, as the dysfunction of the gonads, leading to reduced levels of testosterone in men and estradiol in women, accompanied by symptoms associated with deficiency of these hormones (Winters, 2020).

Hypogonadism, classified as primary, secondary, or mixed, results from defects in the gonads, with genetic or acquired origins, resulting in reduced hormone levels. Early identification of metabolic syndrome is crucial for preventing complications, and by understanding the connections to hypogonadism, we can develop therapeutic strategies to optimize hormone levels, promote metabolic health, and improve the quality of life of those affected by metabolic syndrome and its complications (Oliveira, 2022).

Therefore, the present study aims to explore the relationship between hypogonadism and metabolic syndrome in order to understand its role in male health.

METHODS

This is an integrative review of the literature. For the construction of the present research, six stages were followed: identification of the theme and formulation of the research question; establishment of inclusion and exclusion criteria for relevant studies; definition of the information that would be extracted from the selected studies; critical evaluation of the data collected; interpretation of the results and revision of them for final presentation.

The guiding question defined for this study was: "How is metabolic syndrome related to male hypogonadism, and how do these conditions influence men's quality of life?".

To select the articles, an electronic search was performed in the following databases: *National Library of Medicine* (MEDLINE/PUBMED) and *Scientific Electronic Library Online* (SciELO).

The electronic search for the research will be carried out using the following descriptors Portuguese: Male hypogonadism; Metabolic Syndrome and Testosterone" and in English "*Male hypogonadism. Metabolic syndrome and Testostoren",* from DeCS (Health Sciences Descriptors) of the Virtual Health Library Portal.

To broaden the quantitative scope of studies on the subject, the Boolean operator "AND" was added to the intersections: *Male hypogonadism* AND *Metabolic syndrome* AND *Testostoren.*

Regarding the inclusion criteria for this research, the following were selected: studies published between 2018 and 2023, written in Portuguese or English, with electronic availability and that directly address the theme of the guiding question.

The following were excluded: Duplicate articles, written in languages other than English or Portuguese, studies that do not directly address the theme of the guiding question, and literature review articles of any type.

The procedure for selecting the articles will be developed in the following flowchart:

MEDLINE/PubMed	SCIELO
Descriptors in English indexed in the DeCs *Metabolic syndrome"; Male hypogonadism and "Testostoren"* + Use of Boolean operator "AND"	
Total results of studies found:	
342 studies	41 studies
Application of inclusion and exclusion criteria:	
23 studies	4 Studies
Reading the titles and abstracts:	
11 studies	0 studies
Reading full articles + deleting duplicate articles:	
9 studies	0 studies
A total of 9 studies were selected	

Source: Authored by the authors (2023).

Nine studies were selected to compose the results. After this stage, the data were analyzed descriptively, proceeding to categorize the information from the selected studies into thematic groups, based on the identification of variables of interest and key concepts.

The research was not submitted to the local Research Ethics Committee (REC), because it was a study in secondary sources and did not fit within the legislation of CONEP/MS, resolution 466/2012.

RESULTS AND DISCUSSION

Chart 1 – Summary of the articles found on metabolic syndrome and its relationship with male hypogonadism.

Author and Year	Title	Objective	Results
Dimopoulou et al., 2028	The Complex Association Between Metabolic Syndrome and Male Hypogonadism	To elucidate the association between MS and male hypogonadism, present epidemiological data on the coexistence of the two comorbidities, clarify the underlying pathophysiology, and evaluate the effects of testosterone supplementation therapy (hTT) and lifestyle modifications on MS and body composition in men.	Both MS and male hypogonadism have a high prevalence in the general population and are often co-existing, for example, in men with diabetes. Accumulating evidence from animal and human studies suggests that MS is involved in the pathogenesis of hypogonadism in men and vice versa. On the other hand, there is evidence of a favorable effect of testosterone supplementation in testosterone-deficient men with MS and/or diabetes mellitus
Gleicher et al., 2020	Looking Beyond Hypogonadism: Association Between Low Testosterone Levels and Metabolic Syndrome in Men Aged 20 to 59	To evaluate the association between low testosterone levels and metabolic syndrome in a contemporary population-based cohort of men aged 20 to 59 years.	24.4% of the cohort had low testosterone levels and 26.4% had metabolic syndrome. The univariate analysis revealed that men with low testosterone levels had a significantly higher prevalence of metabolic syndrome and metabolic syndrome criteria
Mohammed et al., 2028	Impact of Metabolic Syndrome Factors on Testosterone and SHBG	To determine the impact of metabolic syndrome and diabetic parameters on	Testosterone (free and total) and SHBG were significantly lower in individuals with MS and

	in Type 2 Diabetes Mellitus and Metabolic Syndrome	testosterone and SHBG in individuals with MS and patients with type 2 DM.	modestly reduced in type 2 DM with and without MS. Abdominal obesity is one of the main determinants of low testosterone levels, regardless of diabetes status**.**
Anupam et al., 2020	Prevalence of hypogonadism in patients with type 2 diabetes mellitus in the Indian population	To determine the prevalence of hypogonadism among Indian men with and without type 2 diabetes mellitus (T2DM) and to evaluate its association with various metabolic parameters.	The prevalence of hypogonadism was 17.3% and 10% in men with and without DM2, respectively. The prevalence of hypogonadism was higher in patients with DM2 than in those without DM2, although the difference did not reach statistical significance.
Zhong,et al., 2021	Association Between Low Serum Testosterone Levels and the Development of Metabolic Syndrome in Elderly Taiwanese Men	To evaluate the association between serum testosterone (T) and metabolic syndrome (MS) in different age groups in Taiwanese men.	A total of 4,931 men were included. The MS group had significantly lower serum T levels compared to the non-MS group in each age group.
Ghadimi, et al., 2020	Serum testosterone and metabolic syndrome in elderly men: preliminary results of the AHAP cohort study	OBJECTIVE: To evaluate the prevalence rates of MS among elderly men with and without hypogonadism and the related association.	The mean total testosterone of the MS group was significantly lower than that of the non-MS group. Total testosterone showed significant associations with triglycerides and waist circumference.
No offense et al., 2023	The Effect of Testosterone Level on Metabolic Syndrome: A Cross-Sectional Study	To investigate the correlations between MS-related parameters and androgen levels.	Weak negative correlations were observed between testosterone levels and several anthropometric measurements/glucose metabolism ($p < 0.05$). The greatest correlation was between total testosterone levels and body mass index. Weight control, one of the preventable risk factors, can have a positive effect on testosterone levels and therefore on the cardiovascular system through different mechanisms.
Kusuma et al., 2018	Estradiol/testosterone ratio in men with metabolic syndrome over the age of 40 years	To assess whether estradiol to testosterone ratio is increased in men with metabolic syndrome.	A total of 52 men were randomly recruited for this study. The estradiol level in the metabolic syndrome group was increased, but differed insignificantly from the other group. The testosterone level decreased and was significantly different between the groups
Rai, et al, 2023	Prevalence and risk factors for hypogonadism in male patients with type 2 diabetes mellitus	To evaluate the correlation between type 2 diabetes mellitus (DM) and the occurrence of hypogonadism.	The prevalence of hypogonadism in male type 2 diabetic patients was 26%. Primary hypogonadism was present in 48.1% and secondary hypogonadism was present in 51.9% of male type 2 diabetics. The percentage of study participants with hypogonadism increased with increasing BMI

The main findings of the studies showed that the relationship between metabolic syndrome (MS) and male hypogonadism (MH) has been investigated in several epidemiological studies. Dimopoulou et al. (2018) explored this complex association, revealing a high prevalence of both MS and MH in the general population. In addition, they suggested a bidirectional interaction between these conditions, highlighting the importance of testosterone supplementation as a possible therapeutic approach.

In a contemporary cohort of men aged 20 to 59 years, Gleicher et al. (2020) identified a significant association between low testosterone levels and the presence of metabolic syndrome. These results highlight the relevance of considering hormone levels when assessing metabolic risks in different age groups, as corroborated by Zhong et al. (2021), who found lower testosterone levels in men with MS in different age groups.

On the other hand, the findings of Mohammed et al. (2028) deepened the understanding of the influence of metabolic syndrome on hormonal parameters, revealing that abdominal obesity plays a significant role in reducing testosterone levels in individuals with type 2 diabetes (T2DM) and MS. Accordingly, Anupam et al. (2020) found a higher prevalence of hypogonadism in Indian men with T2DM, highlighting the association between these metabolic conditions.

Additionally, Gucenmez et al. (2023) observed negative correlations between testosterone levels and anthropometric measurements/glucose metabolism, emphasizing the importance of weight control as a modulating factor in testosterone levels. On the other hand, Kusuma et al. (2018) highlighted the relationship between estradiol and testosterone in men with metabolic syndrome, indicating an increased proportion in these patients.

The studies by Ghadimi et al. (2020) and Rai et al. (2023) complement this understanding by revealing a significant association between metabolic syndrome, hypogonadism, and metabolic parameters in different cohorts of men, indicating the complexity of these relationships in different population contexts.

Metabolic syndrome (MS) and male hypogonadism, both complex clinical conditions, can coexist in the same individual. MS, characterized by cardiovascular risk factors, includes hypertension, dyslipidemia, abdominal obesity, and glucose intolerance or type 2 diabetes. In turn, male hypogonadism involves a deficiency of testosterone, which is essential for male sexual function. Estimates indicate that up to 80% of men with MS also have hypogonadism, indicating a recognized association, although the exact nature of this relationship is not yet fully understood (Dhindsa et al., 2018).

Studies dating back to the 1980s demonstrate the association between diabetes mellitus (DM), MS and low testosterone levels in men. The occurrence of hypogonadism in approximately 25-40% of men with T2DM increases to 50% when associated with obesity. Individuals with T2DM have

lower serum testosterone levels, suggesting an interconnection between these conditions (Daubresse et al., 1978; Small et al., 1987; Dhindsa, 2004; Saboor, 2013; Corona, 2018).

The pathophysiological mechanisms associated with hypogonadism and MS in patients with DM mainly involve obesity and insulin resistance. Insulin resistance, a pillar of MS, can impact the hypothalamic-pituitary-testicular axis, impairing testosterone production. In addition, testosterone deficiency contributes to metabolic changes, promoting the development of MS (Costanzo et al., 2016; Lee et al., 2019).

In this sense, the relationship between hypogonadism and MS is complex, influenced by factors such as insulin resistance, obesity, and alterations in the male gonadal axis. However, studies highlight that weight loss, whether through surgical intervention or conservative measures, can partially reverse testosterone deficiency, especially in severely obese individuals (Rigon et al., 2019; Grossamann et al., 2020).

The diagnosis of MS and hypogonadism involves laboratory and physical evaluations, considering factors such as glucose, cholesterol, triglycerides, and testosterone. Values below 264 ng/dL suggest male hypogonadism, but interpretation may vary between different medical societies. Treatment, whether for MS or hypogonadism, is personalized and may involve lifestyle changes, medications, or hormone replacement with testosterone (Dandona et al., 2022; Bhasin et al., 2018).

Recent evidence also points to the possible link between MS, hypogonadism, and complications in SARSCoV-2 infection. Men with untreated hypogonadism were more likely to be hospitalized for COVID-19. Screening and appropriate treatment of hypogonadism are considered preventive strategies in pandemic contexts (Dhindsa et al., 2022).

In addition, environmental factors, such as exposure to endocrine disruptors, can influence male reproductive health. Although evidence is scarce and conflicting, attention to potential risks to male reproduction remains relevant (Diamanti-Kandarakis et al., 2017).

In summary, the relationship between MS and male hypogonadism is multifaceted, influenced by factors such as obesity, insulin resistance, and alterations in the male gonadal axis. Understanding these interactions is crucial for more effective diagnostic and therapeutic approaches. Weight loss emerges as a key component in the partial reversal of hypogonadism in obese individuals, highlighting the importance of lifestyle modification measures.

Personalized treatment, involving lifestyle changes, medications, and hormone replacement, has been shown to be an effective approach to managing both MS and hypogonadism. In pandemic contexts, attention to hypogonadism as a potential risk factor for COVID-19 complications highlights the relevance of screening and appropriate intervention. Also considering environmental factors, continued research is essential to elucidate the impacts of exposure to endocrine disruptors on male reproductive health.

Improved understanding of these complex interactions contributes to more efficient preventive and therapeutic strategies aimed at improving quality of life and reducing the risks associated with these conditions.

CONCLUSION

This study highlights the complex relationship between metabolic syndrome and male hypogonadism, evidencing a significant bidirectional connection. The high prevalence of hypogonadism in men with MS suggests an interaction between these conditions, based on factors such as insulin resistance and obesity.

Weight loss, especially in the abdominal area, emerges as a crucial element in improving testosterone levels and reducing associated risks. Accurate diagnosis and personalized therapy, including lifestyle changes and testosterone replacement, show effectiveness in managing these conditions and improving quality of life. In addition, the study highlights the relevance of screening for hypogonadism as a preventive measure during the COVID-19 pandemic.

Although evidence on environmental factors is limited, ongoing research is crucial to understanding the potential risks to male reproductive health.

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