# Obesity Associated Reproductive and Sexual Syndrome(OARS) in Men

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## Abstract

Obesity, which has emerged as a major global public health challenge, is associated with myriad medical and multisystemic complications. Obesity impacts the male reproductive and sexual function in multiple ways as well. However, perhaps because of the focus on cardiovascular and metabolic health, the gonadal aspects of obesity medicine have not been given due attention. We propose the term OARS to describe obesity-associated reproductive and sexual syndrome in men living with obesity. OARS can be defined as a constellation of functional, hormonal, and structural abnormalities that affect the reproductive and sexual health of such men. The term OARS should attract attention to this neglected field and prompt efforts to prevent and address the needs of men living with obesity.


**Keywords:** hypogonadism, infertility, obesity, overweight, sexual dysfunction, sexuality, spermatogenesis, subfertility

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## Introduction

Obesity is a major clinical as well as public health problem. Estimates suggest that nearly 3.3 billion adults may have a high body mass index by 2035, compared with 2.2 billion in 2020. This reflects an increase from 42% of adults in 2020 to over 54% by 2035. For young people aged 5 to 19 years, the figure rises from 22% experiencing high BMI (430 million) to over 39% (770 million) by 2035.[1]

### Physiology

Male gonadal physiology is governed by the hypothalamic-pituitary-testicular axis. Pulsatile secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus triggers puberty and leads to the production of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). These, in turn, stimulate the Sertoli and Leydig cells to produce sperm and testosterone, respectively. Paracrine and autocrine mechanisms contribute to the optimization of testicular function as well. The aromatase enzyme breaks down testosterone released into circulation to produce estrogen.[2]

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### Impact of Obesity

Obesity leads to various complications related to reproductive and sexual health (Table 1).[3-5] These are mediated by multiple mechanisms (Tables 2,3), which are still being delineated and deciphered.[6,7] While not all of these functional, structural, biochemical, or seminal abnormalities may be noted in every obese individual, they are sufficiently linked to justify the existence of a syndrome. We term this as obesity-associated reproductive and sexual syndrome (OARS).

**Table-1:** FComponents of obesity-associated reproductive and sexual syndrome (OARS).

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|---|
| **Reproductive** |
| • Low testosterone |
| • Relative low FSH and LH |
| • Impaired spermatogenesis |
| • Reduced structural integrity of sperms |
| • Reduced sperm motility and viability |
| **Sexual** |
| • Reduced sexual drive/ libido |
| • Erectile dysfunction |
| • Mechanical challenge to sexual intercourse |
| **In Children/Adolescents** |
| • Buried penis syndrome |
| • Precocious puberty |
| • Delayed puberty |

**Table-2:** Mechanism of Hypogonadism in Obese Men.

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|---|
| **Hypothalamic** |
| • Reduced kisspeptin mRNA and KISS 1 secretion, due to leptin resistance |
| • Impaired GnRH pulsatility |
| • Reduced LH, FSH secretion, due to GnRH pulse dysfunction and inhibin B |
| **Testicular** |
| • Impaired testosterone synthesis* due to high levels of estrogen, leptin, ghrelin |
| • Impaired testosterone synthesis due to chronic low-grade inflammation; low levels of orexin |
| **Peripheral** |
| • Increased lipogenesis and reduced lipolysis due to impaired Kisspeptin secretion |
| • Reduced testosterone due to reduced SHBG, due to hyperinsulinaemia |
| • Increased conversion of testosterone to estrogen, by aromatase |

*Steroidogenic acute regulatory (StAR) protein, steroidogenic enzymes (p450SCC, 3β hydroxysteroid dehydrogenase, 17β hydroxysteroid dehydrogenase) suppression; FSH= follicle stimulating hormone; GnRH= gonadotropin releasing hormone; LH= Luteinizing hormone; MRNA= m ribonucleic acid, SHBG= sex hormone binding globulin.

**Table-3:** Mechanisms of subfertility in obese men.

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|---|
| **Defects in Spermatogenesis** |
| • Endoplasmic reticulum stress due to hyperglycaemia, hyperlipidaemia |
| • High scrotal temperature |
| • Increased apoptosis of spermatogenic cells |
| • Reduce sperm count |
| • Increased sperm DNA fragmentation |
| • Epigenetic regulation of sperm DNA |
| **Defects in Sexuality** |
| • Low testosterone |
| • Loss of libido |
| • Erectile dysfunction |
| • Mechanical challenges in sexuality |

### Proposed Definition and Diagnostic Criteria

Each syndrome needs a definition, as well as criteria for diagnosis. OARS may be defined as a constellation of symptoms, signs, and laboratory abnormalities related to reproductive and sexual health in men living with obesity. At least two of the following three criteria: male sexual dysfunction (MSD), hypogonadism (low testosterone), and impaired sperm quantity/morphology/function must be present to diagnose OARS. MSD should be diagnosed by well-laid criteria, as in International Classification of Disease (ICD) or Diagnostic and Statistical Manual 5 (DSM5). Hypogonadism, which may be primary or secondary, should be confirmed by diagnostic thresholds laid down by leading professional endocrine societies while keeping possible differential diagnoses in mind. Sperm parameters should be evaluated as per internationally accepted guidance of the World Health Organization.[7,8]

### Clinical Relevance

While OARS has not been studied as a combined entity, the prevalence of reproductive and sexual dysfunction in obesity is significant. These issues are linked with body mass index.[9] This suggests that OARS is a significant clinical challenge.

Combined and comprehensive strategies are required to optimize reproductive and sexual health in men living with obesity. These include strategies for weight loss, such as intensive behavioural therapy, lifestyle modification, drugs, and bariatric surgery.[10] Aromatase inhibitors (letrozole, anastrozole), testosterone supplementation in select cases, and nutraceutical support for spermatogenesis may also be necessary. All health care professionals who manage men living with obesity should assess the reproductive and sexual history, acknowledge and address the patient's concerns, and manage them appropriately. Referral to qualified endocrinologists may be sought if necessary.

## Summary

This paper highlights the existence of a distinct syndrome, OARS, which highlights the reproductive and sexual dysfunction faced by men living with obesity. It proposes a working definition and diagnostic criteria that can help clinical evaluation. Screening, diagnosis and management of OARS is important to optimize health of men living with obesity.

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