

ORIGINAL RESEARCH

High Rates of Depression and Depressive Symptoms among Men Referred for Borderline Testosterone Levels

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ABSTRACT

Introduction. Men referred for borderline testosterone levels represent an increasingly common clinical scenario, yet there is little literature on this population.

Aim. We hypothesized that men referred for borderline testosterone levels would have higher rates of depression and depressive symptoms than the general population.

Methods. Subjects included 200 adult men (mean age of 48 years old) referred for borderline total testosterone levels between 200 and 350 ng/dL (6.9–12 nmol/L). Collected data included demographic information, medical histories, medication use, signs and symptoms of hypogonadism, and assessments of depressive symptoms and/or a known diagnosis of depression or use of an antidepressant.

Main Outcome Measures. The main outcome measure was a combination of known depression, current use of an antidepressant, and/or depressive symptoms according to the Patient Health Questionnaire 9 (PHQ-9) with scores ≥ 10 considered positive.

Results. Depression and/or depressive symptoms were present in 56% of the subjects. This rate was significantly higher than rates of 6–23% (PHQ-9 scores ≥ 10) seen in general populations. Antidepressant use was 25%. The population was notable for high rates of overweight/obesity and physical inactivity. Common symptoms were erectile dysfunction, decreased libido, fewer AM erections, low energy, and sleep disturbances.

Conclusions. While sexual and nonspecific symptoms (i.e., fatigue) likely prompted measurements of testosterone in this selected population, clinicians should recognize the high rates of depression and depressive symptoms in men referred for borderline testosterone levels. Clinicians should consider screening for depression/depressive symptoms and overweight and unhealthy lifestyle risk factors in men referred for tertiary care for potential hypogonadism. **Westley CJ, Amdur RL, and Irwig MS. High rates of depression and depressive symptoms among men referred for borderline testosterone levels. J Sex Med 2015;12:1753–1760.**

Key Words. Depression; Erectile Dysfunction; Libido; Obesity; Testosterone

Introduction

Over the past decade, there has been a dramatic increase in the frequency of measuring testosterone levels in men and in testosterone supplementation. This trend corresponds to increased direct-to-consumer marketing in which a disease awareness campaign for “Low T” leads

men to believe that their low energy and decline in sexual function are due to lower levels of testosterone [1]. Not surprisingly, from 2001 to 2011, prescriptions for testosterone tripled among one of the largest commercial health insurance populations in the United States [2].

Among the many men who have their testosterone levels checked, a substantial number will have

borderline levels close to the lower limit of the reference range. What constitutes a “low testosterone” is unclear as the effects of testosterone in various target tissues such as the brain, muscle, bone and reproductive organs are more important than serum testosterone levels. There is no universally accepted lower limit of normal for serum testosterone which reflects different opinions by experts, different assay methodologies, and a lack of standardization among the assays [3]. Furthermore, the signs and symptoms of male hypogonadism are quite nonspecific and overlap with many signs and symptoms of depression. A bidirectional association exists between sexual dysfunction and depression among middle-aged men [4]. A clinical practice guideline and a consensus statement on late-onset hypogonadism therefore recommend against using case-finding instruments for the detection of hypogonadism [3,5].

In the European Male Aging Study (EMAS), the authors suggest that borderline total testosterone levels range between 8 and 11 nmol/L (230–320 ng/dL) [6]. In this population-based study, men with borderline testosterone levels had adjusted mean scores which showed poorer general health, decreased physical function, decreased hemoglobin, and a slight increase in the risk of cardiovascular disease as compared with the normal testosterone group [7]. It is well established that decreased levels of testosterone are associated with aging, development of comorbid health conditions, and lifestyle factors [8,9].

Large studies examining the relationship between testosterone levels and depression or depressive symptoms have shown no association. In the Massachusetts Male Aging Study (MMAS) and Tromso study, total testosterone levels were not associated with depressive symptoms as assessed by the Center for Epidemiologic Studies-Depression Scale and Hopkins Symptom Checklist-10, respectively [10,11]. In the Coronary Artery Risk Development in young Adults (CARDIA) Male Hormone Study, only black men in the lowest quartile of total testosterone had a higher adjusted odds ratio of depressive symptoms as assessed by the Center for Epidemiologic Studies-Depression Scale [12].

There is little published literature on adult men referred for management of borderline testosterone levels, although this is a very common clinical scenario. Clinicians face a difficult challenge in how best to manage these men in the absence of data from large randomized controlled trials. This study seeks to compare the rates of depression and

depressive symptoms in men referred for borderline testosterone levels with large reference populations that used the same validated instrument. Based on clinical observation, we hypothesized that men referred for borderline testosterone levels would have higher rates of depression and depressive symptoms than the general population.

Subjects and Methods

Subjects and Study Design

A chart review was performed on adult men 18 years and older who were referred to the senior author's tertiary academic endocrinology practice from September 2007 to August 2014 for management of borderline testosterone levels. Patients were typically referred for interpretation of ambiguous levels of testosterone and for assessment of potential hypogonadism. Inclusion criteria were a baseline total testosterone between 6.9 and 12 nmol/L (200–350 ng/dL), a repeat measurement of total testosterone, and an assessment of depressive symptoms and/or an established self-reported diagnosis of depression or current use of an antidepressant. We defined the borderline total testosterone range as 6.9–12 nmol/L as it included the lower limit of the reference interval for most major commercial assays and it was similar to the 8–12 nmol/L range from a consensus statement [5]. Exclusion criteria included exogenous testosterone within the prior 3 months, medications that lower testosterone (i.e., GnRH agonists), or clearly documented causes of hypogonadism (i.e., Klinefelters' Syndrome, hypopituitarism, etc).

Collected Data

Medical histories were obtained by self-report and by chart review during the initial clinic visit. An inventory of medical conditions and medication use was collected as chronic conditions are associated with depression and many medications are associated with adverse sexual effects and other nonspecific symptoms. Self-identified race or ethnicity was not assessed, but the clinic population is primarily Caucasian and African-American. Exercise amount was reported as the number of nonwalking exercise sessions per week. The five-item abridged international index of erectile function assessed for the presence of erectile dysfunction with scores 21 and under indicative of this condition [13]. Two blood pressure readings were averaged over two separate visits. Metabolic syndrome was defined according to the criteria of the

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