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Hypogonadism Prevalence and Correlation with Aging Male Symptoms and International Index of Erectile Function Scores

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What's known on the subject? and What does the study add?

With a high prevalence rate of Hypogonadism (HG), particularly pronounced in obese individuals, the research emphasizes the lack of a clear correlation between T levels, age, and symptom scores. It underscores the complexity of HG's diagnosis, given the absence of a universal T level threshold and the variable symptom presentation. By integrating commonly used symptom scores (IIEF-5 and AMS) for evaluation, the study contributes critical insights into the nuanced relationship between HG and obesity, advocating for targeted screening and management strategies in older males with high BMI. This research bridges existing knowledge gaps by clarifying the role of obesity as a key risk factor and questioning the reliance on age as a determinant of HG, thereby guiding more effective clinical assessments and interventions.

Abstract

Objective: To detect the prevalence and associated factors of hypogonadism (HG) among men, who were admitted to urology outpatient clinics for reasons other than sexual dysfunction.

Materials and Methods: This is a multicentric study designed and conducted by the Turkish Society of Urological Surgery, Andrology Study Group. Male patients between 50 and 75 years of age who were admitted to the urology outpatient clinic for complaints other than sexual dysfunction and whose total testosterone value was measured were included in the study. The correlation between testosterone value and aging male symptoms (AMS) and the international index of erectile function (IIEF) were evaluated. Patient-related factors such as age and comorbidities were also compared between patients with low testosterone values and normal testosterone values.

Results: A total of 1021 patients were included in the study. The mean patient age was 69.9±8.6. The most common complaint was non-neurogenic male lower urinary tract symptoms (52.3%). HG prevalence was 38.5% according to the threshold provided in the European Association of Urology guidelines (<12 nmol/L) There was no statistically significant correlation between HG and AMS or IIEF scores. In our study, the body mass index (BMI) was found to be the most strongly correlated factor with serum testosterone levels (r=-0.183, p<0.001) Subgroup analysis revealed the prevalence of HG as 44.9% in men with BMI ≥30 kg/m^2.

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Abstract

Conclusion: Our results suggest that BMI may be a risk factor for HG, and obese patients may require routine assessment of HG, including serum testosterone measurement and application of symptom questionnaires.

Keywords: Andrology, testosterone, hypogonadism, IIEF, AMS

Introduction

Hypogonadism (HG) is defined as low blood testosterone (T) level. Although there is no well-defined cut-off level for normal total T values, it is known that low T levels could be the cause of sexual disorders, increased cardiac risk, diminished bone density, and many other medical conditions (1-3). Also it is a known fact that advanced age is associated with HG, which is also defined as late-onset HG, and HG-related symptoms (4).

With the increased mean age and life expectancy of males management of low T had become important on which all the physicians should be aware of the general principles. Since not all of the senior male population experience a decrease in T levels and not all low T levels do cause symptoms (5), it could be challenging for a physician to decide when to start T replacement therapy.

To assess patients in a more objective manner, some symptom scores can be used in outpatient clinics for evaluating symptoms caused by low T levels. Those symptom scores could be specialized in one symptom group such as erectile functions [i.e., The international index of erectile function (IIEF)] or could be general-purpose [i.e., aging male symptoms (AMS), androgen deficiency in aging males] The aim of this multi-institutional study is to investigate the prevalence of low T levels in the senior male population in Turkiye and to determine the association of T levels with two commonly used symptom scores, which are IIEF and AMS.

Materials and Methods

This study is conducted by the Andrology Working Group of the Society of Urological Surgery in Türkiye. The study was designed as a retrospective case series, and patients who were investigated with morning total T on their primary admission to the urology outpatient clinic were included in the study. Patients who were younger than 50 years of age and whose primary complaint was sexual function disorders were excluded from the study. All participating centers were regarded as referral centers in their region with an on-site laboratory for blood work.

General patient characteristics and routine symptom scores evaluated in the outpatient clinic were also recorded, and their relationship with T levels was investigated. Total T values less than 12 nmol/L, which was suggested as the threshold for T replacement treatment in the European Association of Urology (EAU) guidelines, were regarded as low T values. For symptom score comparison Turkish validated form of the IIEF-5 and AMS were chosen as they were the most frequently used symptom scores in the study cohort (6).

The study was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee with the decision number: 09.2022.1498 and date: 04.11.2022.

Statistical Analysis

Statistical analyses were performed with a python programming language using pandas, (7,8) NumPy (9), and SciPy (9) libraries. JupyterLab (10) was used as the coding interface. The scaler variables were investigated using visual (Histograms, QQ Plots) and analytical methods (Kolmogorov-Smirnov, Shapiro-Wilk, D'Agostino's K2 tests) to determine whether they are normally distributed. Independent samples t-test was used for the comparison of two groups if the variable is normally distributed in each group; otherwise, the Mann-Whitney U test was used. Categorical variables were compared with the chi-square test if the assumptions of the test are met. When the assumptions of the chi-square do not hold, for two groups Fisher's Exact test and for more than

Table 1. Comparison of general patient characteristics and symptom scores between groups

		HG (+)	HG (-)	p-value[1]
IIEF-5 score	**Median (IQR)**	15.0 (11.0-20.0)	16.0 (12.0-20.0)	0.167
AMS score	**Median (IQR)**	33.5 (26.0-43.0)	32.0 (25.0-42.0)	0.139
Patient age	**Median (IQR)**	60.0 (55.0-66.0)	59.0 (54.0-65.0)	0.145
AACCI	**Median (IQR)**	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.137

IIEF: International index of erectile function, AMS: Aging male symptoms, HG: Hypogonadism (total T <12 nmol/L), IQR: Interquartile range, AACCI: Age-adjusted Charlson comorbidity index, [1]: Mann-Whitney U

Table 2. Comparison of comorbidities between groups

		HG (+) n (%)	HG (-) n (%)	p-value[1]
Diabetes mellitus	-	305 (80.47)	511 (84.46)	0.106
	+	74 (19.53)	94 (15.54)	
Chronic liver disease	-	375 (98.94)	593 (98.02)	0.263
	+	4 (1.06)	12 (1.98)	
Chronic renal disease	-	370 (97.63)	588 (97.19)	0.679
	+	9 (2.37)	17 (2.81)	
Hypertension	-	358 (94.46)	583 (96.36)	0.155
	+	21 (5.54)	22 (3.64)	
Coronary artery disease	-	330 (87.07)	537 (88.76)	0.426
	+	49 (12.93)	68 (11.24)	
Malignancy	-	353 (93.14)	574 (94.88)	0.257
	+	26 (6.86)	31 (5.12)	
Cigarette	-	273 (72.03)	434 (71.74)	0.920
	+	106 (27.97)	171 (28.26)	
Obesity (BMI ≥30 kg/m²)	-	199 (69.34)	382 (77.96)	0.008
	+	88 (30.66)	108 (22.04)	

HG: Hypogonadism (total T <12 nmol/L), BMI: Body mass index, [1]: Chi-square

two groups likelihood ratio was used to compare categorical variables. Numbers are given in mean and standard deviation for normally distributed variables and median and interquartile range for non-normally distributed variables. For categorical variables, case number and percentage were given for each category. The correlation between scaler variables is investigated with Spearman correlation. For all statistical analyses, p-values, less than 0.05 were regarded as statistically significant.

Results

In total, 1.021 patients from all regions of Turkiye were included in this study. The mean patient age was 59.9±8.6. The most frequent symptom of patients on admission was lower urinary tract symptoms (52.3%). The prevalence of patients whose total T level was lower than 8 nmol/L and who were candidates for medical treatment based on EAU guidelines was 13.0%. If the total T threshold is taken as 12 nmol/L and HG prevalence is calculated including patients who are deemed in the gray zone for treatment, the HG prevalence would be 38.5%. Obesity was higher in patients with HG (total T <12 nmol/L) compared to patients with normal T values (p=0.008). Other comorbidities, age of patients, and symptom scores were similar between the two groups (Tables 1, 2). The prevalence of HG was even higher (44.9%) in obese patients.

The total T value of the patients had a statistically significant positive correlation with body mass index (BMI). On the other hand, there was no statistically significant correlation between total T levels and age, age-adjusted Charlson comorbidity index, IIEF-5 and AMS score, and subdomains of the AMS score (Figure 1).

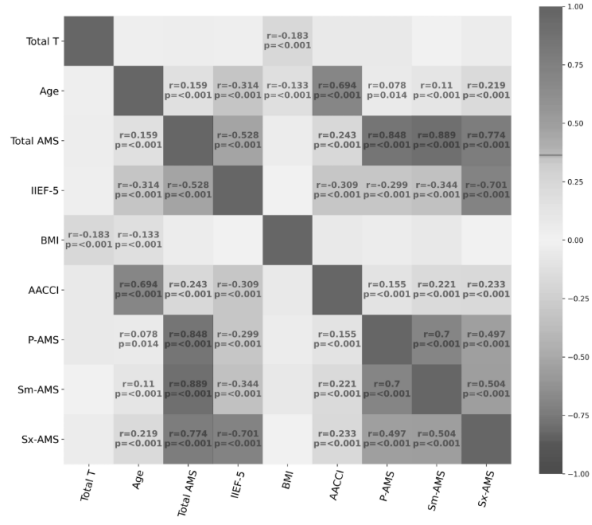

Figure 1. Correlation of total T levels with symptom scores, BMI, age, and comorbidity index

T: Testosterone, AMS: Aging male symptoms, IIEF: International index of erectile function, BMI: Body mass index, AACCI: Age-adjusted Charlson comorbidity index, P-AMS: AMS score psychological subdomain, Sm-AMS: AMS score somatic subdomain, Sx-AMS: AMS score sexual subdomain, r: Spearman correlation coefficient

Discussion

Studies show that the prevalence of HG increases with age, especially in obese and men with diabetes with overall poor health (11). Mulligan et al. reported the prevalence of HG in the United States as 38.7% for the general population. The HG prevalence in our study was 38.5% and was quite similar to their study. Although HG prevalence is seen as higher if the total T value is taken as the only determining factor for the diagnosis, it is known that the prevalence of symptomatic HG ranges between 2.1-5.7% (3,12). We also observed that not every man with HG exhibits symptoms, in our study, which was consistent with previous studies.

Normal levels of T and threshold T values for the diagnosis of HG are still not clearly defined in the literature. Different organizations such as the EAU and the American Urological Association have different approaches to the cut-off value of T for the diagnosis of HG (13,14). Some studies demonstrate that total T values decrease with age, making HG a primary healthcare concern in aging populations (11). Although the relationship between age and total T values is well defined, all patients with low T values do not have symptoms related to this and they do not need treatment. In the Massachusetts male ageing study, it is demonstrated that total T levels are decreased with chronic disease and obesity, and the healthy men had significantly higher hormone levels (15). In this study, we could not demonstrate a definitive correlation between age and T levels. Since our study has a high patient number with a vast geographic distribution, it clearly shows that age may not be the only determining factor for T levels, which was also emphasized by past studies (5).

One of the main challenges in a patient with a low T value is the timing of the replacement therapy. A symptomatic patient with a total T level below 12 nmol/L is considered a good candidate for testosterone replacement therapy (TRT) (13). In order to evaluate the symptoms of the patients in a more objective manner some questionnaires have been developed and used for both diagnosis and follow-up of HG patients (16,17). The studies of these questionnaires also demonstrated that there is no definitive correlation between symptom scores and T levels and these questionaries are not specific tools for the diagnosis of HG (18). In our study most of the patients were evaluated with the AMS questionnaire which is also considered a suitable screening tool for the evaluation of HG symptoms in previous studies (18) and in concordance with previous studies there was no statistically significant correlation between symptom score and T level.

The effect of body fat and thus BMI on T metabolism is well documented (19). Studies highlight obesity with or without metabolic syndrome as a major risk factor for HG (20,21). Studies also confirm that with TRT, the percentage of body fat, BMI, and waist circumference decreases (22,23). These findings also confirm that high BMI is not only a cause of low T but also a result of it. The results of this multi-institutional population-based study also confirmed previous studies and demonstrated obesity as the major risk factor for low T levels.

T has a critical role in every aspect of male sexual function. The European aging male study demonstrated that low T values with advanced age caused decreased libido, erectile dysfunction, and decreased frequency of morning erections (3). In another study, patients admitted to urology outpatient clinics for erectile dysfunction are found to have lower sexual desire and less frequent morning erections (24). In this study, we were unable to demonstrate a close correlation between total T levels and sexual function. This is mainly because in our research, we tried having a more population-based approach and included patients with non-sexual function-related symptoms.

Study Limitations

Our study is not without limitation. This is a retrospective study conducted on the data of patients admitted to urology outpatient clinics. Since the study population is selected from a limited group, this may make it difficult to generalize the results of the study to the entire population. To overcome these authors included as many patients as possible in the study and the study population had a wide variety of geographic distributions. It is known that liquid chromatography-tandem mass spectrometry is the gold standard technique for sex steroid evaluation (25). Since this is a multi-centric study and the T values are evaluated in different laboratories, it was possible to standardize the T measurement procedure. Unfortunately, there is no way to overcome this in a multicentric retrospective study, but the authors paid great attention to ensuring all tests are taken in the morning, which could provide some level of standardization.

Conclusion

Our study showed that HG in the male population over the age of 50 is a frequent condition with 38.5 prevalence. All the patients with low T levels do not show symptoms, but our study clearly demonstrates that obesity is a major risk factor for HG, and elder males with high BMI should be carefully evaluated for HG and related symptoms. This patient group may require routine assessment of HG, including serum T measurement and application of symptom questionnaires.

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Ethics

Ethics Committee Approval: The study was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee with the decision number: 09.2022.1498 and date: 04.11.2022.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: B.Ş., Concept: B.Ş., Y.K., Ö.Y., C.Ş., İ.O.K., A.C., B.D., Ş.O., İ.Ü., H.D., Ö.Ç., Ü.G., T.T., H.Ö., Design: B.Ş., Y.K., Ö.Y., C.Ş., İ.O.K., A.C., B.D., Ş.O., İ.Ü., H.D., Ö.Ç., Ü.G., T.T., H.Ö., Data Collection or Processing: B.Ş., Analysis or Interpretation: B.Ş., Y.K., Ö.Y., C.Ş., İ.O.K., A.C., B.D., Ş.O., İ.Ü., H.D., Ö.Ç., Ü.G., T.T., H.Ö., Literature Search: B.Ş., Y.K., Ö.Y., C.Ş., İ.O.K., A.C., B.D., Ş.O., İ.Ü., H.D., Ö.Ç., Ü.G., T.T., H.Ö., Writing: B.Ş., Y.K., Ö.Y.

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