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Original Article

The Prevalence of Late-Onset Hypogonadism in Middle and Old Aged Men and Its Impact on Erectile Function

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ABSTRACT

Background: Late-onset hypogonadism (LOH) has a significant impact on the quality of life of aging men. It is linked to lower testosterone levels and various associated symptoms. Erectile dysfunction is a common manifestation of LOH, impacting men's sexual health and overall well-being. Estimating the LOH prevalence and its effects on sexual function is critical to inform clinical practice and develop effective treatment. This study aimed to determine the prevalence of LOH and its impact on erectile function among Egyptian men aged 40 or older

Methodology: A total of 400 men aged 40 or older were recruited between July 2023 and March 2024. Participants completed the Male Andropause Symptoms Self-Assessment Questionnaire (MASSQ) to assess LOH symptoms and the International Index of Erectile Function (IIEF) to evaluate erectile function. Levels of serum total testosterone (TT) and free testosterone (FT) were determined and results were correlated with different scores and demographics.

Results: The average age of the participants was 56.5, with 48.2% being younger than 58 years old. 28.5% of the participants had TT levels below the normal threshold, indicating late-onset hypogonadism (LOH). The MASSQ scores for subjects with normal TT levels were analyzed and results show that the majority of subjects with normal TT levels might benefit from testosterone replacement therapy (TRT), with 77.97% possibly benefiting and 6.3% needing TRT based on their MASSQ scores. Correlation analyses revealed a relatively strong positive relationship between free and total testosterone with IIEF scores, while a moderate negative correlation was found between MASSQ and TT levels.

Conclusion: This study sheds light on the prevalence of LOH among middle and old-aged Egyptian men. MASSQ and IIEF scores work better than testosterone levels (free or total) for diagnosis of LOH. The clinical LOH have substantial implications for sexual health and quality of life, reflecting the importance of early diagnosis and treatment.

Keywords: Hypogonadism; Erectile dysfunction; Andropause; Testosterone; Male Andropause Symptoms Self-Assessment Questionnaire.

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INTRODUCTION

The term Late-onset hypogonadism (LOH) is defined as a clinical and biochemical decline in the testosterone levels with advancing male age. Other physical, sexual and mental changes are usually associated with the condition [1,2]. World health organization (WHO) adopted the term "late-onset hypogonadism" for reduced levels of testosterone with advanced age. However, other synonyms were adopted to describe the same condition. These include "partial androgen decline in aging males (PADAM), androgen decline in aging males (ADAM), and low testosterone syndrome" [3-6].

The issue of age at which testosterone deficiency can be recognized as late onset is a matter of debate. The WHO defined middle aged populations as those 40 years or older, while older population segment was started at the age of 60 [2].

The LOH initially showed a general (non-specific, clear) clinical manifestations. However, the physical, sexual, and mental health, as well as the quality of life are adversely affected. The clinical manifestations are diverse and may include negative mood, disturbed sleep, hot flashes, prostate enlargement, anxiety, frequent urination, generalized aches (especially for muscles and bones), decrease memory and mental concentrations, reduced stress-coping capacity, decreased libido, erectile dysfunction, and lack of interest or motivation for work [7-9].

It is well-established that, in aging men between 40 and 70 years, the total testosterone reduced by 1.0%, while free testosterone reduced by 1.2% per year. This was described as modest reduction and does not affect every man [10,11].

The decline in testosterone levels with age is due to different etiologies and multiple risk factors. The possible causes are the changes in the hypothalamic-pituitary-gonadal (HPG) axis dynamics and reduced Leydig cells. Other associated factors include genetics, obesity, stress, depression, chronic metabolic or liver disease, obstructive sleep apnea syndrome, rheumatic diseases, smoking, drinking and medications (e.g., gluco-corticoids). All these factors share in the reduced production of testosterone [12-18].

The current study was designed to determine the prevalence of late-onset hypogonadism among Egyptian men, 40 years or older and its impact on erectile function.

SUBJECTS AND METHODS

The study included a total of 400 men aged 40 years or older were randomly recruited during the period from July 2023 to March 2024. The inclusion criteria were 1) males, 40 years or older. On the other side, men below 49 years of age, those who do not provide their consent or those who not provide sufficient answers to the questions of the stud questionnaire were excluded from the study.

All recruited men were subjected to standard assessment in the form of history taking (demographic data, medical history, special habits and symptoms suggestive of andropause). In addition, assessment of total and free testosterone levels was measured.

The assessment of LOH: It was performed using the Male Andropause Symptoms Self-assessment questionnaire (MASSQ) and International Index of Erectile Function (IIEF-5).

MASSQ consisted of 25 items regarding the disability and symptoms of andropause. Each item is given a score from 1 (none) to 5 (severe). The overall scores of this scale ranges from 25 to 125 which indicate no symptoms to most severe symptoms, respectively. The values more than or equal to 40 and less than or equal to 84 might benefit from replacement therapy. However, values above 85 need replacement therapy [1].

On the other side, IIEF-5, is a widely used patient-reported outcome measure (PROM) for the assessment of male sexual disorders. It comprises five main domains: erectile function (6 items), orgasmic function (2 items), sexual desire (2 items), intercourse satisfaction (3 items), and overall satisfaction (2 items). It can clearly distinguish between patients with erectile dysfunction (ED) and those without. The IIEF-5 score ranges from 5 to 25, and ED was classified into five categories based on the scores: severe (5-7), moderate (8-11), mild to moderate (12-16), mild (17-21), and no ED (22-25) (19).

Ethical consideration:

Informed consent was signed by each participant before enrollment in the study and after approval of the Medical Research Ethics Committee. The patient's data were only disclosed to the main researcher. The anonymity of subjects was assured through coding of data.

Statistical analysis:

The collected data were analyzed using the Statistical Program for Social Science (IBM® Inc., Chicago, Illinois), Version 22.0. The collected data were tabulated and presented by relative frequency and percentages for qualitative variables and mean and standard deviation for continuous variables. The prevalence of late-onset hypogonadism (LOH) was calculated and subjects were categorized accordingly. One-way ANOVA (Analysis of Variance) was used to compare the mean IIEF scores according to the category of LOH. Correlation between IEEF scores and MASSQ scores were performed using Pearson's and Spearman's correlation coefficients as appropriate. The correlation analysis was also used to examine the relationship between IIEF scores and free and total testosterone levels. P value < 0.05 was considered significant.

RESULTS

The analysis included the data from 400 male subjects during the period from July 2023 to March 2024. The characteristics of the studied subjects are presented in Table 1. The age ranged

between 40 and 70 years and the mean age was 56.5 years. About 48.2% were lower than 58 years, while 51.8% were 58 years or older. Smokers represented 17.2% and 5.0%, 13.8% and 19.7% had cardiac disease, hypertension and diabetes mellitus respectively. Finally, 48% receive medical therapy for LOH in the form of Phosphodiesterase Inhibitor (PDEI). The mean free testosterone level among the subjects was 84.9 ± 27.3 pg/mL, and the mean total testosterone level was 5.3 ± 2.1 ng/mL.

Figure (1) presents the prevalence of LOH among the studied subjects based on their total testosterone (TT) levels. Hypogonadism was determined based on a TT level of less than 350 ng/dl (3.5 ng/ml). The results indicated that 28.5% of the subjects exhibited TT levels below this threshold, thereby classifying them as having LOH. Table (2) presented the results of the scores obtained from both the Male Andropause Symptoms Self-Assessment Questionnaire (MASSQ) and the International Index of Erectile Function (IIEF) among the 400 studied subjects. The mean MASSQ score was 60.4 ± 9.5. The mean IIEF Erection and Satisfaction scores were 13.1 ± 3.5 and 2.5 ± 1.1 respectively. Additionally, the mean Total score from the IIEF was 15.6 ± 4.5.

The analysis of MASSQ scores showed that, 12.25% of subjects do not need replacement therapy (score < 40), while 71.50% might benefit from replacement therapy (score between 40 and 84) and finally 16.50% need replacement therapy (scores > 85) (Figure 2). These results provide insight into the prevalence of symptoms based on MASSQ scores.

The Analysis of MASSQ Scores for Subjects with Normal TT Levels (n=286) showed that, 15.73% do not need replacement therapy, while 77.97% might benefit from replacement therapy and 6.3% need replacement therapy (Figure 3). These results highlight that a substantial proportion of participants display LOH symptoms according to their MASSQ scores, even though their TT levels remain within the normal range.

Figure (4) shows the free testosterone (FT) levels among participants who have normal total testosterone (TT) levels but display symptoms of late-onset hypogonadism (LOH) according to their MASSQ scores. The FT levels were categorized as low if they were below 225 pmol/L or 65 pg/mL. Among these participants, 10 (3.5%) had low FT levels, while 231 (96.5%) had normal FT levels.

Table (3) displays the MASSQ scores of participants with low total testosterone (TT) levels (n=114) who were classified as having late-onset hypogonadism (LOH) based on their TT levels. This analysis aims to identify individuals who exhibit LOH symptoms according to MASSQ in addition to having low TT levels. The results revealed 3.51% do not need replacement therapy, 79.82% with mild symptoms and potentially benefiting from replacement therapy. Finally, 16.67% scored 85 or higher, demonstrating significant symptoms and likely requiring replacement therapy. Table (4) showed the results of a correlation analysis exploring the relationship between MASSQ scores and testosterone (TT) levels among all studied subjects. The analysis revealed a moderate negative and statistically significant correlation between MASSQ scores and overall TT levels, with a correlation coefficient of -0.35 and a p-value of <0.0001, indicating that lower TT levels are associated with higher MASSQ scores. In contrast, the correlation between MASSQ scores and TT levels among participants with low TT, indicative of LOH, was negligible, with a coefficient of -0.08 and a p-value of 0.77, suggesting no significant relationship. Additionally, the correlation between MASSQ scores and TT levels among subjects with normal TT was also moderate and statistically significant, with a coefficient of -0.24 and a p-value of <0.0001.

Table (5) compares the mean International Index of Erectile Function (IIEF) scores between subjects with low TT levels (indicative of LOH) and those with normal TT levels. Subjects with low TT levels had significantly lower mean scores across all three IIEF categories—Erection, Satisfaction, and Total—with p-values <.0001 for each comparison, indicating statistically significant differences. In summary, lower TT levels are associated with markedly reduced IIEF scores, highlighting the impact of low testosterone on erectile function and overall sexual satisfaction.

Table (6) presents the results of a correlation analysis between IIEF scores and testosterone levels among 400 patients. The analysis revealed a relatively strong positive correlation between IIEF scores and total testosterone levels. Specifically, the correlation coefficient for the IIEF Erection score, IIEF Satisfaction score, and the total IIEF score is 0.39, 0.41, and 0.40 respectively. All p-values were less than 0.0001, indicating statistical significance for all three associations. In addition, there was a relatively positive and statistically significant correlation between IIEF scores and free testosterone levels, indicating that higher levels of free testosterone are associated with increased IIEF scores. The correlation coefficients were 0.41 for the IIEF Erection score, 0.41 for the IIEF Satisfaction score, and 0.42 for the total IIEF score. All p-values were less than 0.0001, confirming the statistical significance of these findings.

Table (1): Characteristics of the Studied Subjects

Variables		N= 400
Age in years	mean ± SD	56.5 ± 6.9
	Min. – Max.	40-71
Age categories	< 58 years	193 (48.2)
	≥ 58 years	207(51.8)
Smoking		69 (17.2)
Medical history	Negative	246 (61.5)
	Cardiac	20 (5.0)
	Hypertension	55 (13.8)
	Diabetes mellitus	79 (19.7)
Medications	none	208 (52.0)
	Phosphodiesterase Inhibitor (PDEI)	192 (48.0)
Free T (pg/ml)		84.9±27.3
Total T (ng/ml)		5.3 ± 2.1

Table (2): Summary Statistics of the Studied MASSQ and IIEF Scores Among the Studied Subjects (n=400)

Study scores			N (%)
MASSQ (25-125)	**Mean± SD**		60.4±9.5
	Min. – Max.		37-87
IIEF	**Erection score (4-20)**	**Mean± SD**	13.1 ± 3.5
		Min. – Max.	4-20
	Satisfaction score (1-5)	**Mean± SD**	2.5 ± 1.1
		Min. – Max.	1-5
	Total score (5-25)	**Mean± SD**	15.6 ± 4.5
		Min. – Max.	5-25

Table (3): Analysis of MASSQ Scores Among Subjects with Low TT Levels (n=114)

MASSQ score	N (%)
Don't Need Replacement Therapy (<40)	4 (3.51)
Might Benefit from Replacement Therapy (>=40 and <=84)	91 (79.82)
Need Replacement Therapy (>=85)	19 (16.67)

Table (4): Correlation between MASSQ Scores and TT levels Among Studied Subjects

	Total testosterone	
	Correlation coefficient (r)	**P value**
MASSQ – TT (All subjects)	-0.35	<.0001*
MASSQ – Low TT (LOH subjects)	-0.08	0.77
MASSQ – Normal TT	-0.24	<.0001*

Table (5): Comparison of the Average IIEF scores by TT Levels.

IIEF scores	Low	Normal	P value
Erection score	11.3±2.8	13.8±3.5	<.0001*
Satisfaction score	**2.0 ±1.0**	**2.8 ± 1.1**	**<.0001***
Total score	**13.3±3.6**	**16.6±4.5**	**<.0001***

Table (6): Correlation between IIEF Scores with Total and free testosterone levels Among the Studied Subjects (n= 400)

	Total testosterone		Free testosterone	
	(r)	**P**	**(r)**	**P**
IIEF, Erection score	0.39	<.0001*	0.41	<.0001*
IIEF, Satisfaction score	0.41	<.0001*	0.41	<.0001*
IIEF, Total score	0.40	<.0001*	0.42	<.0001*

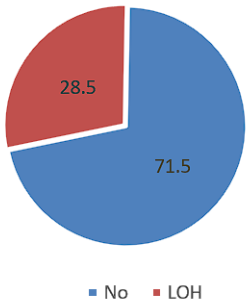

Figure (1): Prevalence of LOH among the Studied Subjects based on TT Levels (n= 400)

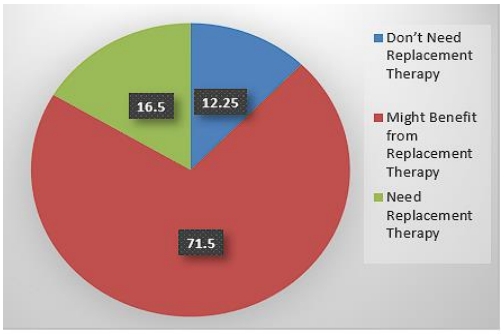

Figure (2): Analysis of MASSQ Scores among Studied Subjects (n=400)

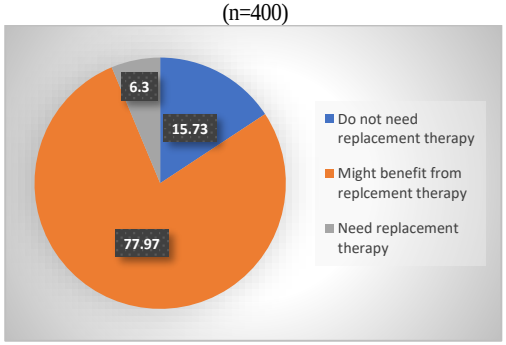

Figure (3): Analysis of MASSQ Scores for Subjects with Normal TT Levels

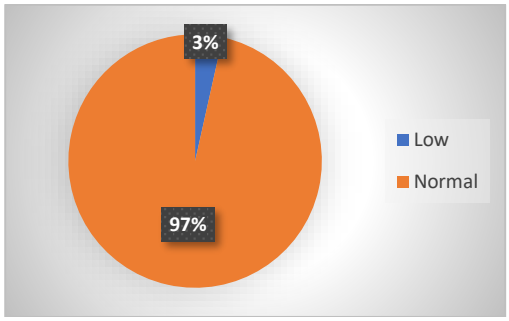

Figure (4): Analysis of FT Levels Among Subjects with Normal TT Levels and LOH Symptoms Based on Their MASSQ Scores

DISCUSSION

The current study aimed to shed light on the prevalence and implications of LOH among Egyptian men aged 40 years or older. The study's findings indicate that LOH is quite prevalent with approximately 29% of subjects having total testosterone (LOH) levels below the normal threshold (the accepted threshold of 12 nmol/L (350 ng/dL).

The reported prevalence lies within the reported prevalence in previous literature. For example, the reported prevalence of LOH in men aged 40 to 70 years was 30.0% to 40%, while the subclinical LOH affecting 23–38% of patients [20, 21]. However, the prevalence of LOH was increased up to 48.21% in patients with benign prostatic hyperplasia (BHP) but remains closer to reported prevalence in patients with no BPH (41.30%) as reported in a recent study [22].

On the extreme side, **Ye *et al.*** [23] reported a lower LOH prevalence (7.8%). This may be due to differences in geographical distributions, racial factors and different sample sizes. In addition, criteria of diagnosis (such as questionnaires versus hormone level assessments or a combination of both), and other factors may be

responsible. Moreover, it's essential to consider that the prevalence reported in studies can vary significantly depending on whether it includes subjects with comorbidities such as hypertension or diabetes, focuses on healthy individuals, or selects participants randomly, which plays a key role in influencing the reported prevalence of LOH. The current study included both healthy and those with comorbidities, as the selection of participants was done randomly.

In this study, the mean total and free testosterone levels suggested normal total and free testosterone values. However, the prevalence of LOH was 29%, indicating that the mean testosterone levels alone are not indicative of the presence or absence of LOH. Thus, MASSQ was administered to all subjects as part of this study and patients were categorized based on the likelihood of andropause.

This classification follows that of **Asadollahi *et al.*** [23] who studied the reliability and validity of the MASSQ. In the current work this classification showed that, 12.25% exhibited minimal symptoms, indicating they likely do not require TRT. Meanwhile, 71.50% had mild symptoms and a potential benefit from TRT, while 16.50% had higher scores, indicating significant symptoms and a likely need for TRT.

Comparable results were reported by **Rezaei *et al.*** [24], with a slightly lower mean (SD) MASSQ score of 57.46 (17.56) among their participants. In their study, 61 men (15.5%) were classified in the 'don't need testosterone' category, 303 men (71.1%) were identified as potentially benefiting from testosterone, and 29 men (7.4%) were categorized as certainly needing testosterone.

The analysis of MASSQ scores for participants with low TT levels reveals that the majority (79.82%) exhibit symptoms suggesting they might benefit from HRT. Additionally, 19% of participants have symptoms indicating a higher need for HRT, while 3.51% have scores indicative of no symptoms despite the low TT levels.

These results highlighting that almost all participants with low TT levels either might benefit from or need HRT according to their MASSQ scores. In patients with normal TT, the MASSQ analysis showed that, 15.73% of these individuals did not require TRT, while 77.97% might benefit from TRT, and 6.3% necessitate TRT. These results indicated that, the value of TT do not reflect the clinical andropause. The TT had a significant moderate negative correlation with MASSQ scores. These correlation decreased in patients with normal TT levels (-0.24, $p < 0.05$) and in low TT (-0.08, $p > 0.05$).

The comparison of IIEF scores based on TT levels among the studied subjects revealed statistically significant differences. For instance, subjects with low TT levels had significantly lower mean scores across all three IIEF domains (Erection, Satisfaction, and Total). The correlation between IIEF scores and TT levels revealed a relatively strong positive correlation between. Specifically, the correlation coefficients for the erection, satisfaction and the total score are 0.39, 0.41, and 0.40 respectively.

These results reflected better performance between IIEF scores and TT levels. The free testosterone showed similar correlation with IIEF scores.

The findings of this study agree with those of **Lisco *et al.*** [25], who examined the correlation between TT and IIEF scores. They reported an even stronger positive correlation. Their correlation coefficient was 0.67 with a p-value of <.0001, suggesting a stronger and statistically significant positive relationship between TT and total IIEF scores.

In addition, our results are consistent with those of **Brooke *et al.*** [26], who found a significant positive correlation between IIEF-5 scores and total testosterone ($r = 0.546$, $p = 0.001$) as well as free testosterone ($r = 0.532$, $p = 0.001$).

In conclusion, the current study sheds light on the problem of LOH in middle and old-age Egyptian men and its potential impact on sexual function. The testosterone levels (total or free) alone do not indicate the presence of LOH. The use of MASSQ and IIEF scores reflect the LOH better than the testosterone levels and correlate with it. Thus, the future diagnoses of LOH should consider both hormonal levels and these additional scores to provide a more comprehensive assessment.

Study limitations:

The interpretation of the results of the current work should be done in the light with the following limitations. First, the random selection of subjects within a limited set of cities, reflected issues in representation of the broader populations. In addition, the inclusion of different comorbidities with healthy subjects may impair the globalization of results. Thus, future studies including more representative sample for the whole country and categorization of subjects according their health or comorbid conditions are recommended.

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