Original Article

Prevalence and Risk Factors of Testosterone Deficiency in Aging Thai Male Outpatients

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Background: Testosterone deficiency in men, characterized by a reduced concentration of serum testosterone, causes a constellation of signs and symptoms that may include decreased libido, erectile dysfunction, increased body fat, fatigue, and psychological problem. Testosterone deficiency in adult men is often overlooked, because they ignore their symptoms or attribute them to alternate causes, including aging and underlying diseases that made them lose the opportunity for treatment. The present study aimed to describe the prevalence of testosterone deficiency and to study potential risk factors associated with testosterone deficiency among Thai men in Phramongutklao Hospital.

Objective: To determine the prevalence of testosterone deficiency and potential risk factors associated with testosterone deficiency in Thai men.

Materials and Methods: Thai male older than 40 years old who visited in urological outpatient unit at Phramongkutklao Hospital between July and October 2018 were included. Demographic data, medical information, and the androgen deficiency in the aging male (ADAM) questionnaires were collected. The participants having symptoms of testosterone deficiency from ADAM questionnaires were requested to measure serum total testosterone levels and were repeated if serum testosterone level was less than 300 ng/dL.

Results: Data from 156 men were collected. The mean age of the participants was 67±8.73 years. Prevalence of testosterone deficiency was 5.8%. Obesity, waist circumference at or greater than 90 cm, diabetes mellitus, and dyslipidemia were identified as risk factors of testosterone deficiency. There was an association between three symptoms of ADAM questionnaires, which were decreased libido, erectile dysfunction, and decreased enjoyment of life, with testosterone deficiency.

Conclusion: Prevalence of testosterone deficiency among Thai men at Phramongkutklao Hospital is about 5.8%. Clarification of the underlying causes for the changes in testosterone level may provide helpful information so that preventive action can be taken. Low libido, erectile dysfunction, and decreased enjoyment of life may be specific symptoms of testosterone deficiency and should be the questions to ask the suspected patients.

Keywords: Testosterone deficiency; Total testosterone; Prevalence; ADAM questionnaires

Received 14 May 2020 | Revised 20 April 2021 | Accepted 21 April 2021

J Med Assoc Thai 2021;104(6):921-6

Website: http://www.jmatonline.com

Testosterone deficiency in men, characterized by a reduced concentration of serum testosterone[1], causes a constellation of signs and symptoms that may include decreased libido, erectile dysfunction, decreased volume of ejaculate[2], weakness, decreased lean body mass[3], decreased bone density[4], increased body fat, fatigue, and anemia.

It is estimated that testosterone levels in men older than 40 years decrease at a rate of 1% to 2% per year[5]. Because of the slow decrease, this is often overlooked, even in the presence of associated symptoms, because the patients often ignore their symptoms or attribute them to alternate causes[1].

Testosterone deficiency has been associated with mortality in men and a significant decrease in quality of life from sexual dysfunction to metabolic and musculoskeletal complication, higher prevalence of depression[6], osteoporotic fracture, and frailty[5].

Not all aging men become testosterone deficiency, unlike female menopause that have this normal abrupt hormonal process with advance age. A significant number of men remain eugonadal even with advanced age[7]. However, some conditions that likely to have in male aging such as cardiovascular disease, depression, osteoporosis, and diabetes may associate with decreased testosterone levels[8].

Although the epidemiology of testosterone deficiency was studied in many populations, the epidemiology of testosterone deficiency in Thai men has never been described. The purpose of the present study was to describe the prevalence of testosterone deficiency and to study potential risk

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How to cite this article:

Huengsri A, Wiriyabanditkul W, Binsri N. Prevalence and Risk Factors of Testosterone Deficiency in Aging Thai Male Outpatients. J Med Assoc Thai 2021;104:921-6.

doi.org/10.35755/jmedassocthai.2021.06.11391

Table 1. ADAM questionnaire

ADAM questionaire	Hypogonadal participants (n=9); n (%)	Eugonadal participants (n=147); n (%)	p-value
Do you have a decrease in libido (sex drive)?	8 (88.9)	79 (53.7)	0.045
Do you have a lack of energy?	5 (55.6)	48 (32.7)	0.275
Do you have a decrease in strength and/or endurance?	8 (88.9)	92 (62.6)	0.158
Have you lost height?	4 (44.4)	49 (33.3)	0.49
Have you noticed a decreased "enjoyment of life"?	6 (66.7)	42 (28.6)	0.025
Are you sad and/or grumpy?	2 (22.2)	18 (12.2)	0.324
Are your erections less strong?	8 (88.9)	71 (48.3)	0.034
Have you noted a recent deterioration in your ability to play sports?	7 (77.8)	88 (59.9)	0.484
Are you falling asleep after dinner?	6 (66.7)	72 (49.0)	0.495
Has there been a recent deterioration in your work performance?	7 (77.8)	78 (53.1)	0.183
ADAM questionnaire positive	9 (100)	115 (78.2)	0.205

ADAM=androgen deficiency in the aging male

factors associated with testosterone deficiency in Phramongkutklao Hospital.

Materials and Methods

The Institutional Review Board Royal Thai Army Medical Department approved the present study cross-sectional study and acquisition of consent was waived (IRBRTA 1060/2561). Data from the present study were conducted from the urological male outpatients. To be eligible to participate in the study, men had to meet the following inclusion criteria, 1) age 40 years old or older, 2) ability to provide a blood sample, 3) willingness to answer a brief set of questions related to medical history, social history, concomitant medications, and testosterone deficiency signs and symptoms. The only specified exclusion was the participants with history of testicle injury, orchiectomy, testosterone replacement therapy, or androgen deprivation therapy.

All eligible participants underwent a serum testosterone assessment by a single morning blood draw (between 7 a.m. and 11 a.m.) to test for concentrations of total testosterone. All serum samples were sent to Phramonkutklao laboratory and analyzed by electrochemiluminescence immunoassay (ECLIA). For the present study, testosterone deficiency was defined as total testosterone of less than 300 ng/dL[9].

For all participants, demographic characteristics, medical history, comorbid conditions, concomitant medications were recorded by the researcher on case report forms.

The operational definition of testosterone deficiency in the present study followed the Clinical Practice Guideline by The American Urological Association[10]. To define testosterone deficiency, two combined criteria were needed, 1) having signs and symptoms of testosterone deficiency, 2) serum testosterone lower than 300 ng/dL for two times assessment[10-12].

Symptoms of testosterone deficiency were screened by the St. Louis University androgen deficiency in the aging male (ADAM) questionnaire that contained 10 questions covering areas on libido, energy, strength or endurance, height loss, and enjoyment of life, sadness in mood, erectile dysfunction, sports performance, sleepiness after dinner, and work performance. A positive Saint Louis ADAM questionnaire was defined as a positive answer to question 1 (loss of libido), question 7 (Erectile dysfunction), or any other three questions. Table 1 shows information of St. Louis University ADAM questionnaire[13]. The participants diagnosed as testosterone deficiency were sent to evaluated risk and benefit for treatment by urologist.

Data analysis was done using the IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). The primary statistical analyses focused on descriptive statistics and prevalence estimation. Demographic data, frequency counts were tabulated for categorical variables, and means, standard deviations (SDs), and ranges were tabulated for continuous variables. Prevalence of testosterone deficiency was computed as the number of men with testosterone deficiency divided by the total number of participants. Secondary, association between testosterone deficiency and potential covariates were analyzed by chi-square test, Fisher's exact test for categorical variables and Student's t-test

Table 2. Demographic variables (n=156)

Characteristics	Total; n (%)
Age (year); mean±SD	67±8.7
BMI (kg/m^2); mean±SD	23.9±3.3
Waist (cm); mean±SD	87±8.6
Maritual status	
Single, never married	19 (12.2)
Married or living in a married-like relationship	119 (76.3)
Divorced/separated/widowed	18 (11.5)
Educational status	
Secondary school or less	59 (37.8)
Graduated from university	72 (46.2)
Postgraduate	25 (16.0)
Smoking	
Never smoker	96 (61.5)
Former smoker	39 (25.0)
Current smoker of <20 cigarettes per day	21 (13.5)
Current smoker of >20 cigarettes per day	0 (0.0)
Drinking	
Never drinking	46 (29.5)
Had less than 12 drinks in the past 12 months	97 (62.2)
Current drinking	13 (8.3)

BMI=body mass index; SD=standard deviation

for continuous variables. Crude odds ratios and the corresponding 95% confidence intervals (CIs) were constructed for these purposes.

Results

The 156 men who agreed to be interviewed were also invited for an early morning total testosterone test. The characteristics of the study population are shown in Table 2. The mean age for all participants was 67 years. The mean body mass index (BMI) and waist circumference for all participants was 23.9 kg/m^2 and 87 cm, respectively.

The prevalence of testosterone deficiency calculated by using the operational definition, the overall prevalence was 5.8% (Figure 1).

The mean age in testosterone deficiency group was 63.6 years and 67.2 years in no testosterone deficiency. Age had no association to testosterone deficiency in the present study. BMI and waist circumference were associated to testosterone deficiency (Table 3).

History of comorbid medical conditions in the present study participants included 25.6% with diabetes, 23.7% with dyslipidemia, and 34% with hypertension. Comorbid medical conditions in the

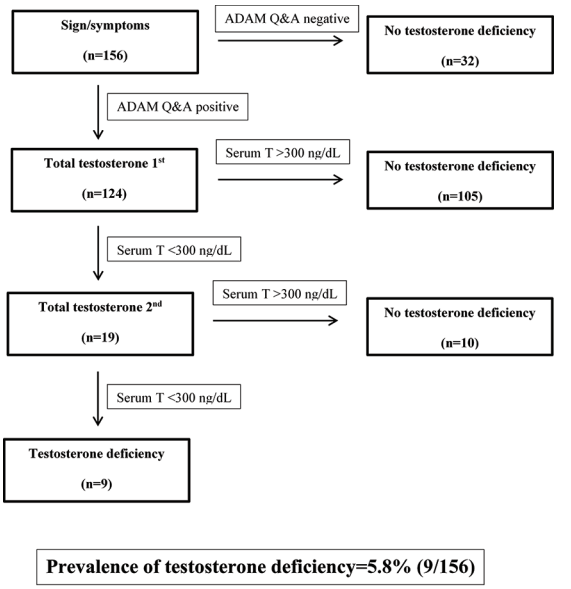

Figure 1. Operational definition of testosterone deficiency.

testosterone deficiency were 66.7% diabetes, 55.6% dyslipidemia, and 66.7% hypertension. For exploring risk factors for testosterone deficiency, central obesity with a waist circumference of 90 cm or larger, obesity with a BMI greater than 25 kg/m^2, diabetes, and dyslipidemia were associated with testosterone deficiency ($p<0.05$ for all of the conditions) and increased odd of having testosterone deficiency (waist circumference: OR 5.35, 95% CI 1.28 to 22.4, obesity: OR 7.48, 95% CI 1.77 to 31.6, diabetes: OR 6.65, 95% CI 1.58 to 28, dyslipidemia: OR 4.49, 95% CI 1.14 to 17.7) (Table 3, 4).

From the ADAM questionnaire, prevalence of symptomatic testosterone deficiency was 79.5%. Decrease libido, erectile dysfunction, and decrease enjoyment of life were associated with testosterone deficiency ($p<0.05$ for all the conditions) (Table 1).

Discussion

In the present random-sample population-based study of 156 men with complete symptom and testosterone data, the authors found 5.8% of men had symptomatic testosterone deficiency, using a definition that incorporates both clinical symptoms and testosterone levels of less than 300 ng/dL, which is quite similar to Araujo et al in Boston area[14] and Massachusetts male aging study[15]. Among the forty studies, the prevalence of testosterone deficiency ranged from 2% to 70%, due to the discrepant testosterone thresholds used to define low testosterone and definition of testosterone deficiency at different

Table 3. Factors of enrolled participants with evaluable total testosterone

Factors	Hypogonadal participants (n=9); n (%)	Eugonadal paticipants (n=147); n (%)	p-value
Age; mean±SD	63.6±7.7	67.2±8.8	0.222
BMI (kg/m^2); mean±SD	26.3±2.6	23.7±3.3	0.021
Waist (cm); mean±SD	93.2±7	86.6±8.6	0.025
Central obesity (waist circumference ≥90 cm)	6 (66.7)	40 (27.2)	0.02
Obesity (BMI ≥25)	6 (66.7)	31 (21.1)	0.006
Hypertension	6 (66.7)	47 (32.0)	0.063
Diabetes mellitus	6 (66.7)	34 (23.1)	0.009
Dyslipidemia	5 (55.6)	32 (21.8)	0.035
Osteoporosis	0 (0.0)	8 (5.4)	1
Prostatic disease	1 (11.1)	31 (21.1)	0.687
Insomnia	1 (11.1)	9 (6.1)	0.458
COPD	0 (0.0)	1 (0.7)	1
Rheumatoid arthritis	0 (0.0)	1 (0.7)	1

BMI=body mass index; COPD=chronic obstructive pulmonary disease; SD=standard deviation

Table 4. Crude odd ratio of factors associated to testosterone deficiency

Factors	OR (95% CI)	p-value
Obesity (BMI ≥25)	7.48 (1.77 to 31.6)	0.006
Central obesity (waist circumference ≥90 cm)	5.35 (1.28 to 22.4)	0.02
Diabetes mellitus	6.65 (1.58 to 28)	0.009
Dyslipidemia	4.49 (1.14 to 17.7)	0.035

BMI=body mass index; OR=odds ratio; CI=confidence interval

times[16].

In the present study, the authors found that 19 participants had low testosterone deficiency in the first assessment, but only nine had low testosterone in the second assessment. The result may be affected by due to the health status of participants at the time of testing, circadian rhythms in testosterone production, intra-individual variability, and inconsistencies in the assays themselves. To ensure accuracy and precision, it is necessary to obtain at least two serum total testosterone measurements in an early morning fashion to diagnose patients with low testosterone. At this time, there is no definitive evidence indicating what the optimal time interval should be between the two separate tests[10,17,18].

Normal aging is associated with about 1% to 2% per year decrease in total testosterone levels in men older than 40 years[5]. In the previous study, advancing age was associated with the prevalence of testosterone deficiency[15,19,20], but in the present study, age had no association. This could be due to the small sample size in the present study, which limited the power to detect any significant results.

Similar to the other studies, increasing BMI and waist circumference were associated with greater prevalence rates of testosterone deficiency. In addition, among the metabolic conditions, obesity, diabetes, and dyslipidemia showed significant association with testosterone deficiency and the odds of testosterone deficiency were higher than other risk factors[21,22].

Some authors reported a significant lower testosterone levels in hypertensive than normotensive subjects[23]. This is not surprising since insulin resistance, which underlies hypertension, have been shown to be associated with low testosterone levels. However, the present study failed to show any relationship between hypertension and testosterone deficiency same as the other study[19-24]. At present, the association between testosterone deficiency and hypertension is still inconsistent[25].

Morley et al validated a 10-question screening questionnaire for ADAM[13]. In the present study, the loss of libido[26], erectile dysfunction[27], and decrease enjoyment of life[28] were the symptoms closely associated with testosterone deficiency. The symptoms as mentioned previously may be used for specific question to adapt and develop short and easy questionnaires to ask suspected patients.

However, the prevalence of testosterone deficiency symptoms in the present study was about 79.5% but when clinical symptoms and testosterone level were used together, the prevalence of testosterone deficiency was 5.8%. Therefore,

testosterone symptoms alone may not be a good indicator for diagnosis of testosterone deficiency.

Conclusion

In summary, the present study showed the prevalence of testosterone deficiency was similar to previous studies that used a similar operational definition of testosterone deficiency. Clarification of the comorbidity that affected testosterone level may provide the information for preventive testosterone deficiency. Specific symptoms of testosterone deficiency may be adapted and developed for questionnaires to ask the suspected patients in the future. The limitations of the current study include the small sample size that lack of statistical power to identify some risk factor. Furthermore, comorbid condition that affected the Sex Hormone Building Globulin (SHBG) level were not included. Future free testosterone usages in alteration of SHBG participant may be required to study.

What is already known on this topic?

Racial differences may exist in endogenous hormonal levels in pre and postmenopausal women. However, these differences exist in hormonal levels in men is unknown and the epidemiology of testosterone deficiency and risk factors in Thai men has never been described.

What this study adds?

This study shows the prevalence of testosterone deficiency and associated risk factors, diabetes, obesity, and dyslipidemia in Thai men similar to the previous study.

Conflicts of interest

The authors declare no conflict of interest.

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