



Andropause: Results of A Comprehensive Surveillance of Prevalence and Risk Factors on 906 patients (ACoSPF-2010)

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Abstract

Introduction: Andropause is a common clinical entity of advanced age, with a decline in androgen levels in males. Many of the signs of male aging are results of this condition with significant decline in their quality of life and adverse effects on multiple organ systems function. Androgen Deficiency of the Aging Male (ADAM) questionnaire is one of the most applied screening tools for androgen deficiency. Few studies have examined the prevalence of this condition and reports on the relationship of potential risk factors especially at the population level are scarce. **Material and Methods:** We conducted an analytic cross-sectional study on a nationally representative sample of 906 Iranian male adults aged 40 to 88 years in a population based surveillance of prevalence and risk factors. A combined questionnaire comprising ADAM and Geriatric Depression Scale-15 (GDS-15) followed by questions regarding the risk factors was administered to each patient. Frequency of positive response to each question and the impact of risk factors on andropause were evaluated. **Results:** Out of the total population, 873 cases were included. Totally, 185(20.6%) of the subjects were diagnosed with andropause. The mean age of andropause was higher than non-andropause group, 70.20 ± 9.42 and 65.61 ± 11.64 , respectively. The most frequent positively responded questions were number 1 and 7, respectively. Age, marital status, level of education and occupation, history of cigarette smoking, depression, hypertension, diabetes, hypothyroidism, glucocorticoid consumption, hepatic, renal and cardiac disease, independently had significant impact on andropause development our univariate analysis ($P < 0.05$). Age, marital status, level of education, cigarette smoking and history of depression, hypertension, diabetes and cardiac disease were associated with a greater risk, in multivariate analysis ($P < 0.05$). **Conclusions:** The high prevalence of andropause in our population points out the necessity to improve the social and medical health to prevent the condition that has serious consequences on patients' quality of life.

Key Words: Andropause, Prevalence, risk factors

Introduction:

Andropause, partial androgen deficiency of the aging male or late-onset hypogonadism narrate a clinical entity associated with advanced age, characterized by a decline in sexual hormone levels in males [1-2]. Andropause is affecting millions of men worldwide and as the world becomes more aging, is gaining an increasing recognition [3]. Many of the current signs of male aging, inclusive erectile dysfunction and loss of libido[4], decreased lean body mass & increase in fat mass [5], osteoporosis[6] and neuropsychiatric problems, such as depression, irritability, insomnia, and memory impairment [7-9] are the results of this condition.

By the age 40, the circulating levels of total testosterone decrease by approximately 1% to 1.6%, free testosterone by 2%, and bioavailable testosterone by 2% to 3% annually. Additionally, there is a 1% to 1.6% annual increase in sexual hormone-binding globulin (SHBG), which becomes unavailable for the tissues. Serum measurements of total testosterone indicate low levels in 20% of men over age 55. The measurement of bioavailable or free testosterone indicates that a quarter of men over the age of 50 have hypogonadism [10-14].

Diagnosis of Andropause is truly challenging. There are no pathognomonic signs or symptoms. Not all signs and symptoms necessarily present simultaneously. Moreover, they have subtle nature and progress slowly and may be not be perceivable from the inescapable process of aging itself or other hormonal abnormalities [2, 15]. The Androgen Deficiency of the Aging Male (ADAM) questionnaire is designed to elicit responses regarding sexual performance, energy, mood, strength, and height that is one of the most applied screening tools for androgen deficiency [16-17] with a high sensitivity and acceptable specificity.

Andropause, result in significant decline in the quality of life and adversely affect the function of multiple organ systems. The condition is clinically relevant since many of these consequences are avoidable and modifiable. However, Few studies have examined the the prevalence of the condition. There are many risk factor that are thought to be associated with development of andropause, but reports on the relationship of them especially at the population level are scarce. Hence we aimed to appraise the prevalence of the condition on a large representative sample of Iranian population for the first time and to simultaneously integrate many of theses potential risk factors such as and evaluate their influence on andropause emergence in our comprehensive study.

Material and Methods:

We conducted an analytic cross sectional study on a nationally representative sample of 906 Iranian male adults aged 40 to 88 years in a population based surveillance of prevalence and risk factors carried out by department community medicine of Tehran University of medical sciences (TUMS), during 2007 to 2010.

A combined questionnaire comprising ADAM and Geriatric Depression Scale-15 (GDS-15) followed by questions regarding the associated risk factors that are considered to be potential factors in development of andropause was administered to each patient. 33 (3.64%) questionnaires were incomplete mostly in ADAM questions numbers 1 and 7. Theses participants with incomplete data were excluded from the study.

ADAM consists of 10 questions. A positive questionnaire result is defined as a “yes” response to questions 1 or 7 or any 3 other questions. GDS-15 is a 15-item questionnaire for screening late-life depression with 82-100% and 72-82%, sensitivity and specificity, respectively. This scale has been

validated repeatedly in psychiatric settings [18]. Patients with scores above 10 were diagnosed with depression to make sure about the diagnosis.

The definition of alcohol abuse was made based on the Diagnosis and Statistical Manual of Mental Disorders (DSM-IV) [19], that describes alcohol abusers as those who drink despite recurrent social, interpersonal, and legal problems as a result of alcohol use. The mean blood pressure over 140/90, in two separate measurements in each individual were considered as hypertension. All participants were given written informed consent to take part in the study. Patient information was saved in the department data base and only the investigators had access to it. Approval for this study was Granted by our Institutional Review Board (Ethics Committee of Tehran University of Medical Sciences (TUMS)).

Two groups were delineated on the basis of ADAM questionnaire results inclusive, patients with and without andropause. Afterwards, Frequency of positive response to each question and the impact of risk factors on development of andropause were evaluated. SPSS 16 software was employed for data analysis. Chi-square test and independent sample t-test were firstly used to assess the influence of various risk factors on development of andropause and odds ratio were calculated with 95% CI for each risk factor. All the risk factors were thereafter entered to a multivariate logistic regression analysis in order to determine the independent effect of risk factors in the prognostication of the condition. P-values less than 0.05 were considered statistically significant

Results:

The study was conducted on 906 male patients. 873 out of the total population were included with the mean age of 66.61 ± 11.33 (ranging from 40 to 88) years. Totally, 185(20.6%) of the studied subjects were diagnosed with andropause with mean age of 70.20 ± 9.42 (ranging from 43 to 88). The mean age of patients without andropause was 65.61 ± 11.64 (ranging from 40 to 88). The most frequent positively responded questions were number 1 and 7 respectively, that are also considered as diagnostic ones (Table-1).

Amongst the entire evaluated risk factors, age, marital status, level of education and occupation, history of cigarette smoking, depression, hypertension, diabetes, hypothyroidism, hepatic disease, renal disease, cardiac disease and glucocorticoid consumption independently had significant impact on the emergence of andropause in a univariate analysis. The details are depicted in Table-2.

Due to the multivariate analysis of all the risk factors, we implemented to data, age, marital status, level of education, cigarette smoking and history of depression, hypertension, diabetes and cardiac disease were independently associated with a greater risk for the development of andropause (Table-3).

The prevalence of the aforementioned risk factors amongst the total population, were 345 (39.5%), 32 (3.7%), 30 (3.4%) and 158 (18.1%) for cigarette smoking, alcohol abuse, depression[20] and hypertension[21-23] and 443 (50.7%), 177 (20.3%) and 42(4.8%) for dyslipidemia[24], diabetes[25] and hypothyroidism[26] and 45 (5.2%), 51 (5.8%) and 151 (17.3%) for hepatic[27], renal[28] and cardiac disease[29], respectively.

The prevalence rate of the mentioned conditions, derived from our comprehensive study are totally in agreement with the published results of the epidemiologic surveillances of the aforementioned conditions

in IRAN, that makes the randomly selected population of our survey, factual representatives for Iranian male population.

Discussion:

Andropause, is a common clinical condition of advanced age that is characterized by a decline in androgen levels in males. Many of the aging signs and symptoms in males are the results of this condition [4-9]. The circulating levels of total testosterone, starts to decline annually by the age 40 [10-14]. There are no pathognomonic signs or symptoms for andropause [2, 15]. ADAM questionnaire is amongst the most applied screening tools for androgen deficiency[16-17] with 88% sensitivity and 60% specificity[30]. Total testosterone, is not only enough for the diagnosis, but also can be misleading due to the variations in reference values. Patients with normal total testosterone associated with a high SHBG level might present a subnormal free testosterone level. The best diagnostic test for hypogonadism is the measurement of serum level of free testosterone [16-18, 30-31]. The prevalence of Andropause in our population was 185(21.2%), that is in agreement with studies in united states and South America[1, 32], however, higher results have been reported from other regions such as Europe and Africa[33-34].

Our study, which aimed at identifying effective factors on Andropause, revealed that the mean age in andropause group was significantly higher than Non-andropause group. This could be obviously anticipated, because the nature of the condition is associated with aging and decrease in serum level of Androgen. Marital status as well as level of education and occupation showed significant relationship with development of andropause. Lower social classes with lower income; have to spend most of their time working out of home, that are in most cases the energy consuming jobs, with significant influence on interpersonal relationship or inadequate sexual relationship between the couples. The marital status was also an effective risk factor, possibly due to the same reasons.

Cigarette smoking also resulted in a higher rate of andropause, and the prevalence of smokers was higher in this group of cases. However, it has been acclaimed that in adult men of all ages, the serum levels of testosterone are higher in current smokers than non-smokers, although not significantly associated with reduction in hypogonadism[32]. The relation of smoking and vasculopathy is well known[35]. The impact of smoking on andropause could be explained with regard to strong vascular component of erection. Hypertension, diabetes, and cardiac disease that also significantly correlated with andropause, could be effective risk factors of the condition by the same mechanism. Additionally, it is well understood that patients suffering from different cardiac diseases have sexual problems and this issue is an important aspect of their quality of life[36-38].

Depression was another significant risk factor due to our results. A significant inverse relationship has been shown between depression and serum level of testosterone, independent of age. A significant reduction in serum level of testosterone (17%) has been reported compared to the levels of patients without depression. Moreover, it has been acclaimed that administration of androgen in patients with low levels of testosterone, might improve depression in elderly men. Hence, depression and anxiety can decrease androgen production, while hypogonadism in turn impairs sexuality, cognitive function, and mood [32, 39].

It is known that thyroid function, affects the serum levels of testosterone. Hyperthyroidism increases, and hypothyroidism decreases, the levels of SHBG and total testosterone. Hence, we evaluated

hypothyroidism as another potential risk factor, and as we expected, the significant relation of this factor to andropause was revealed. The other agents that reduce the levels of SHBG are glucocorticoids and nephrotic syndrome. Both of the aforementioned factors were also significant risk factors of our survey. It has been said that glucocorticoids, induce the reduction of free testosterone, in a dose dependent fashion, by combined actions both at the testicular and at the hypothalamic-pituitary level. Hepatic disease, as another effective factor of our study, has been shown to increase the serum levels of SHBG[32].

In line with previous results, patients' age, marital status, level of education, history of cigarette smoking, Depression, hypertension, diabetes and cardiac disease were also shown to be effective factors on andropause emergence, by multivariate analysis of all factors. In general most of the effective factors that increased the incidence of andropause are modifiable. The age was another potential risk factor for this phenomenon. The non-modifiable patient clinical characteristics, such age, are not preventable; however elimination of the aforementioned adjustable factors and modification of the potential risk factors and underlying diseases and medications that can precipitate the condition and improvement of social health are amongst the main keys to prevent the condition. Additionally, our findings highlight the importance of education of the patients to change their habits such as smoking as the heart of the problem.

The other notable aspect of our study is that, not only the results of prevalence and effect of factors on andropause development can be derived from the findings, but also the prevalence of many important and challenging diseases and social characteristics that are studied as risk factor are obtained in our large sample of nationally representatives of Iranian male population.

This study, as every other cross-sectional study, has a number of limitations. ADAM is one of the most applied screening tools for androgen deficiency, and with its high sensitivity can cover most of the cases. However, because of the low sensitivity of this screening tool, and the availability of the measurement of testosterone as the best diagnostic modality, this approach should be recommended for further assessment to those patients. However, there is a circadian variation to testosterone levels, with peak concentrations in the early morning that should be paid attention to, when measuring serum testosterone levels [1, 10, 17, 40-41]. The high prevalence of andropause in our population points out the necessity to improve the social and medical health to prevent the condition that have serious consequences on patients quality of life to avoid the development of frailty and effects on sexual health.

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Table Legends:**Table-1:**

Distribution of positive response to each ADAM question and the relation of these questions with Andropause.

Table-2:

Patients characteristics; Demographic data, patients habits, Past medical and drug history. The Univariate analysis of the risk factors.

Table-3:

Multivariate Analysis of All the Risk factors of Andropause.

Table-1:

Distribution of positive response to each ADAM question and the relation of these questions with Andropause.

Total population	Positive Response	Patients with Andropause	Positive Response	P-value (95% CI)
Q1	79 (9.0%)	Q1	79 (42.7%)	0.000
Q7	56 (6.4%)	Q7	56 (30.3%)	0.000
3 Other Q	50 (5.7%)	3 Other Q	50 (27.0%)	0.000

Numbers are presented as frequency (percentage); Q: Question

Table-2:

Patients characteristics; Demographic data, patients habits, Past medical and drug history. Univariate analysis of the risk factors.

		Andropause (n = 185)	Non-Andropause (n = 688)	P- Value	Odds Ratio (95% CI)
Age		70.20±9.42 [#]	65.65±11.61 [#]	0.000*	
Marital Status	Married	119(64.3%)	530(77.0%)		
	Single	13(7.0%)	51(7.4%)		
	Divorced	17(9.2%)	30(4.4%)		
	Widower	29(15.7%)	61(8.9%)		
	Separated	7(3.8%)	16(2.3%)	0.002*	
Level of Education	Academic Graduation	22(11.9%)	202(29.4%)		
	Graduated	55(29.7%)	221(32.1%)		
	Under graduated	108(58.4%)	265(38.5%)	0.000*	
Occupation	Administrative & Clerical	50(27.0%)	300(43.6%)		
	Sales & Marketing	75(40.5%)	242(35.2%)		
	Worker & laborer	60(32.4%)	146(21.2%)	0.002*	
Cigarette Smoking		92(49.7%)	253(36.8%)	0.002*	1.701
Alcohol Abuse		11(5.9%)	21(3.1%)	0.077	
Depression		16(8.6%)	14(2.0%)	0.000*	4.558
Dyslipidemia		104(56.2%)	339(49.3%)	0.098	
Hypertension		73(39.5%)	85(12.4%)	0.000*	4.624
Diabetes		68(36.8%)	109(15.8%)	0.000*	3.087
Hypothyroidism		17(9.2%)	25(3.6%)	0.003*	2.684
Hepatic Disease		16(8.6%)	29(4.2%)	0.023*	2.151
Renal Disease		19(10.3%)	32(4.7%)	0.007*	2.346
Cardiac Disease		44(23.8%)	107(15.6%)	0.012*	1.694
Glucocorticoid consumption		11(5.9%)	19(2.8%)	0.035*	2.226

Numbers are presented as frequency (percentage) for categorical variables and mean (standard deviation)[#] for numerical variables;* Values are significant (95% confidence Interval);

Table-3:

Multivariate Analysis of All the Risk factors of Andropause.

Risk Factor		P-Value	Odds ratio	95% CI
Age		0.001	1.034	1.015-1.053
Marital Status	Married	0.000		
	Divorced	0.000	4.526	2.053-9.981
	Widower	0.000	7.811	4.209-14.496
	Separated	0.005	4.901	1.632-14.719
Education	Under Graduated	0.000		
	Graduated	0.000	2.766	1.564-4.891
Cigarette Smoking		0.000	3.699	2.009-6.811
Depression		0.016	3.000	1.225-7.346
Hypertension		0.000	5.558	3.474-8.893
Diabetes		0.000	3.361	2.112-5.351
Cardiac Disease		0.031	1.743	1.051-2.892

Binary logistic regression, 95% Confidence Interval, P; significant values are presented.