International Journal of Advances in Medicine
Masum MD et al. Int J Adv Med. 2020 Dec;7(12):1767-1772
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20205038

Original Research Article

Evaluation of predictors of erectile dysfunction and hypogonadism in men with types 2 diabetes mellitus

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Received: 10 October 2020
Revised: 13 November 2020
Accepted: 17 November 2020

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ABSTRACT

Background: Now a day erectile dysfunction (ED) and hypogonadism of the patients with type 2 diabetes mellitus (T2DM) become two common complaints. The association among hypogonadism, erectile dysfunction and type 2 diabetes of man seem to be increased. The aim of this study was to evaluate the predictors of erectile dysfunction and hypogonadism in men with types 2 diabetes mellitus (T2DM).
Methods: This was a cross-sectional study which was conducted in the Department of Shaheed Monsur Ali Medical College Hospital, Dhaka, Bangladesh Hospital, Bangladesh during the period from January 2019 to December 2019. In total 352 newly detected T2DM male patients, with complete data were finalized as the study population. All data were processed by using SPSS program version 23.0.
Results: In this study, according to complement fixation test (cFT) and androgen deficiency in the aging male (ADAM) criteria, 119 (33.81%) participant had low cFT and ADAM positive under hypogonadal, 84 (23.86%) were with normal TT and ADAM negative (eugonadal), 37 (10.51%) were with low TT and ADAM negative (eugonadal), 112 (31.82%) were with normal TT and ADAM positive (eugonadal). On the other hand, according to the cFT and ADAM score in total 119 (33.81%) hypogonadal patients were with low cFT and ADAM positive. Besides this, 102 (43.78%) eugonadal patients were with normal cFT and ADAM negative and 131 (56.22%) eugonadal patients were with normal cFT and ADAM positive.
Conclusions: Hence, universal screening of testosterone level and androgen deficiency symptoms is recommended in newly detected T2DM patients.

Keywords: Erectile dysfunction, Hypogonadism, Sex hormone binding globulin, Types 2 diabetes

INTRODUCTION

Diabetes mellitus (DM) is one of the most frequent etiologies of erectile dysfunction. It is a state of impaired carbohydrate and other metabolisms caused by either lack of insulin secretion and or its action. Types 2 diabetes mellitus (T2DM) occurs due to progressive insulin deficiency in the background of insulin resistance. It is one of the commonest metabolic disorders that are characterized by hyperglycemia and other signs and its

incidence is rapidly increasing all over the world.[1] Diabetes mellitus affects an estimated 285 million people worldwide. This number is expected to reach 438 million by the year 2030.[2] Erectile dysfunction is the sexual activity, practice and behavior of human being characterized by the inability to develop an erection of the penis through sexual activity. Erectile dysfunction (ED) can have psychosomatic consequences as it can create relationship difficulties and self-image. On the other hand, male hypogonadism (MHG) denotes the diminished functional activity of the male gonads, which produces sperm from the testicle of the male reproductive gland. Testosterone levels and erectile function are known to decline as men age, leading to hypogonadism and ED. Men with T2DM have a particularly high prevalence of hypogonadism and ED. This population also has an increased risk for cardiovascular diseases, as well as exposure to other metabolic and cardiovascular risk factors, such as obesity. Many professional societies have recommended screening men with T2DM for testosterone deficiency. Hypogonadism is usually assumed when morning levels for total testosterone are 300 ng/dL and clinical symptoms are usually linked with androgen deficiency are present. MHG & ED emerge as predictors of cardiovascular disease (CVD) and may act in response to the lifestyle changes commonly recommended for patients with diabetes and metabolic syndrome.3Several studies found a high prevalence of ED in men with T2DM. But its prevalence is still debated.

Risk factors of ED in T2DM include patient age, disease duration, sedentary life, glycemic control. Subnormal testosterone concentrations contribute to ED as testosterone regulates nearly every component of erectile dysfunction.4ED occurs in up to 75% of men with T2DM and has complex pathogenesis owing to a combination of micro vascular, macro vascular, endocrine and neuropathic disease. ED is established as a self-determining marker for the development of coronary artery disease (CAD) occurring on average 3-5 years before the onset of CAD. Thus, timely detection of ED offers an opportunity for early intervention, thereby reducing morbidity associated with CAD.[5] MHG is a clinical syndrome that results from failure to produce physiological concentrations of testosterone.[6] It is significantly associated with various comorbidities reduced libido, erectile dysfunction, increased adiposity, low energy and fatigue.[7]

Muscle weakness and low bone mass, depression, anxiety loss of libido, and erectile dysfunction and decreased quality, abnormal lipid profile, CVS path physiologic change.[8-11] Asian population tends to develop diabetes at younger ages and lower BMI levels than Caucasians. Several factors contribute to accelerated diabetes epidemic among Asians, including the “normal-weight metabolically obese” phenotype; high prevalence of smoking and unplanned urbanization; high intake of refined carbohydrates (e.g., white rice); and dramatically decreased physical activity levels.[12] One study found prevalence of diabetes mellitus and glucose intolerance to be high among the adult population of Bangladesh; around 10% and 23% of study participants had diabetes and pre-diabetes. On the other hand, hypogonadism or testosterone deficiency (TD) in adult men, as defined by low levels of serum testosterone accompanied by characteristic symptoms and/or signs which may adversely affect multiple organ functions and quality of life and can be found in long-recognized clinical entities such as Klinefelter syndrome, Kallmann syndrome, pituitary or testicular disorders, as well as in men with idiopathic, metabolic or iatrogenic conditions that result in testosterone deficiency.[13]

There are several mechanisms for the association of low serum testosterone level and T2DM with insulin resistance and obesity as central features. To date, mechanisms underlying association between T2DM and hypogonadism is unclear though various hypothesis involving abnormal regulation of hypothalamic pituitary gonadal axis at various level, impaired leading cell steroid genesis, dysglycemia, increased fatty acid, hyperinsulinemia and leptin have been proposed.[14,15] A large number of men with hypogonadism remain undiagnosed and untreated.[16,17] Hypogonadism is characterized by low serum testosterone levels together with clinical symptoms. The features of post pubertal hypogonadism include (1) sexual dysfunction, such as reduced libido, ED, diminished penile sensation, difficulty attaining orgasm, as well as reduced ejaculate with orgasm; (2) reduced energy, vitality, or stamina; (3) depressed mood or diminished sense of well-being; (4) increased irritability; (5) difficulty concentrating and other cognitive problems; and/or (6) hot flushes in some cases of acute onset. Signs of hypogonadism include (1) anemia; (2) muscle wasting (sarcopenia); (3) reduced bone mass or bone mineral density (BMD); (4) absence or regression of secondary sex characteristics; (5) abdominal adiposity (i.e. ‘pot belly’ obesity); and/or (6) oligospermia or azoospermia.[18] Despite high prevalence of diabetes there is paucity of literature regarding hypogonadism in newly detected diabetes in men in Bangladesh and hence clinical and biochemical assessment of hypogonadism in early stage of T2 DM is pertinent.

METHODS

This was a cross-sectional study which was conducted in the Department of Shaheed Monsur Ali Medical College Hospital, Dhaka, Bangladesh Hospital, Bangladesh during the period from January 2019 to December 2019. A total number of 352 newly detected type 2 DM male patients encompassing in the study. Demographic and anthropometric measures as well as other information of all participants were recorded in data collection sheet. Fasting morning at 8:10 am blood samples 5 ml were collected from each participant for hormonal assay in clot activator. Vacutainer tubes and kept in room temperature

in vertical position for 15-20 minutes. Serum was separated by centrifugation (around 8000 rpm) in room temperature and serum of each patient was transferred to two Eppendorf tubes after labeling and preserved at -200C until further analysis. Measurements of hormonal assay for serum TT, SHBG, LH, FSH, and albumin were performed. Normal values of semen parameters issued by the World health organization (WHO) in 2010 are generally used as reference values. Hormonal assay was performed in the department of laboratory medicine, BSMMU. Socio-demographic variables of the respondents were recorded by face to face interview using the semi structured questionnaire.

ADAM questionnaire was used to evaluate the clinical symptoms of androgen deficiency. Their anthropometric measures including height (HT), weight (Wt.), waist circumference (WC), and hip circumference (HC), blood pressure (BP) were recorded. This intervention was approved by the ethical committee of Shaheed Monsur Ali Medical College Hospital, Dhaka, Bangladesh Hospital.

Inclusion criteria

We included studies of adult humans with type 2 diabetes, non-insulin dependent diabetes mellitus, or adult-onset diabetes.

Exclusion criteria

We excluded studies where everyone was required to have at least one of the following comorbid conditions: ESLD, ESRD, cancer, new onset diabetes after organ transplant, or a recent cardiovascular event within the 3 months prior to study start.

After obtaining informed consent, fasting morning serum testosterone, LH, FSH, SHBG, lipid profile and HbA1c were measured. Collected data were entered and edited; error was identified and minimized. All data were processed by using SPSS program version 23.0.

RESULTS

In this study, among all the participants 36.08% were service holder, 17.05% were retired persons, 15.06% were businessmen, 11.93% were skilled laborer and the rest 19.89% were in several other profession (Table 1).

The mean age of the participants was 41.88±8.06. In total 40.34% participants were smokers whereas 59.66% were non-smokers. Family history of DM was positive in 50.85% whereas it was negative in 49.15% participants. The mean clinical characteristics, BMI, WC, HC, SBP and DBP were 26±5.72 kg/m^2, 85.18±7.56 cm, 84.03±7.83 cm, 128.79±10.54 mmHg and 81.16±6.27 mmHg respectively (Table 2).

In our study 30-39 years' group was highly of hypogonadal 51 (42.86%) and eugonadal 65 (27.90%). Then in 40-49 years' age group hypogonadal was 43 (36.13%) and eugonadal was 84 (36.05%), in >50 years' age group hypogonadal was 17 (14.29%) and eugonadal was 58 (24.89%) and in 20-29 years' age group hypogonadal was 8 (6.72%) and eugonadal was 26 (11.16%). In this study, according to cFT and ADAM criteria, 119 (33.81%) participant had low cFT and ADAM positive under hypogonadal, 84 (23.86%) were with normal TT and ADAM negative (Eugonadal), 37 (10.51%) were with low TT and ADAM negative (Eugonadal), 112 (31.82%) were with normal TT & ADAM positive (Eugonadal) (Table 3).

Table 1: Demographic characteristics of participants (n=352).

Variables	N	%
Occupation		
Service	127	36.08
Retired	60	17.05
Business	53	15.06
Skilled laborer	42	11.93
Others	70	19.89
Smocking status		
Smoker	142	40.34
Non- smoker	210	59.66
Family history of DM		
Present	179	50.85
Absent	173	49.15

Table 2: Laboratory findings of participants (n=352).

Variables	Mean ±SD
Age (years)	41.88±8.06
BMI (kg/m^2)	26±5.72
WC (cm)	85.18±7.56
HC (cm)	84.03±7.83
SBP (mmHg)	128.79±10.54
DBP (mmHg)	81.16±6.27

Table 3: Distribution of gonadal status according to age category using TT and ADAM criteria (n=352).

Age (in years)	Hypogonadal		Eugonadal		P value
	N	%	N	%	
20-29	8	6.72	26	11.16	0.1997
30-39	51	42.86	65	27.90	
40-49	43	36.13	84	36.05	
>50	17	14.29	58	24.89	
Total	119	100	233	100	

On the other hand, according to the cFT and ADAM score in total 119 (33.81%) hypogonadal patients were with low cFT and ADAM positive. Besides this, 102

(43.78%) eugonadal patients were with normal cFT and ADAM negative and 131 (56.22%) eugonadal patients were with normal cFT and ADAM positive (Table 4, 5).

Table 4: Frequency of gonadal status among participants according to TT and ADAM criteria (n=352).

Gonadal Status	N	%
Hypogonadal		
Low TT & ADAM positive	119	33.81
Eugonadal		
Normal TT & ADAM negative	84	23.86
Low TT & ADAM negative	37	10.51
Normal TT & ADAM positive	112	31.82
Total (N)	352	100

Table 5: Frequency of Gonadal status among participants according to cFT and ADAMS criteria (n=352).

Gonadal Status	N	%
Hypogonadal		
Low cFT & ADAM positive	119	33.81
Eugonadal		
Normal cFT & ADAM negative	102	43.78
Normal cFT & ADAM positive	131	56.22
Total (N)	352	100

Table 6: Biochemical parameters of the participants (n=352).

Biochemical parameters	Hypogonadal Mean±SD	Eugonodal Mean±SD	P value
TT (nmol/l)	9.8±1.56	15.3±4.1	<0.01
cFt (nmol/l)	0.254±0.1	0.351±0.1	<0.01
LH (mIU/l)	4.88±2.86	5.7±4.43	0.23
FSH (mIu/l)	5.61±4.43	7.47±6.24	0.08
SHBG (nmol/l)	21.7±11.6	30.71±22.6	0.05
HbA1c (%)	9.6±2.4	8.8±1.9	0.10
FBS (mmol)	12.48±6.7	10.39±3.6	0.07
2hrsA75gmG (mmol/l)	20.52±7.72	17.37±5.19	0.03
TG (mg/l)	260.85±148.58	221±101.03	0.20
TC (mg/l)	202±43.1	191.45±31.21	0.20
HDL (mg/dl)	37.82±7.32	36.98±6.54	0.57
LDL (mg/dl)	114.2±36.2	118.5±57.13	0.72

Independent t- test, FBS=fasting blood sugar, 2HrsA75gmG-2 hours after 75-gram glucose, OGTT=oral glucose tolerance test, TG=triglyceride.

In analyzing the biochemical parameters, we found significant correlation among hypogonadal and eugonadal patients in TT (nmol/l), cFt (nmol/l), SHBG (nmol/l) and 2 hrsA75gmG (mmol/l) findings where the p values were <0.01, <0.01, 0.05 and 0.03 respectively (Table 6).

Besides these the correlations between calculated free testosterone and total testosterone with various clinical and biochemical parameters has been shown in (Table 7).

Table 7: The correlations between calculated free testosterone and total testosterone with various clinical and biochemical parameters.

Variables	r	P value
TT vs cFT	0.46	<0.01
TT vs Age	-0.15	0.8
cFT vs Age	-0.350	0.01
TT vs HbA1c	-0.12	0.25
cFT vs HbA1c	-0.07	0.6
TT vs SHBG	0.58	0.01
cFT vs SHBG	-0.37	<0.01
TT vs BMI	-0.11	0.3
cFt vs BMI	0.10	0.3

DISCUSSION

In this study, hypogonadism was evaluated in newly detected T2DM male subjects on the basis of TT, cFT and ADAM criteria in a tertiary level hospital. The present study demonstrated that in light of TT and ADAM criteria, about one-third of the newly detected T2DM male subjects were hypogonadal whereas about one fifth was found to be hypogonadal according to cFT and ADAM criteria. Among the study subjects, 63.7% were positive for ADAM questionnaire and were symptomatic for androgen deficiency symptoms. In the present study, The ADAM questionnaire was positive in 63.7% of the study subjects with the highest number of patients complaining of fatigue (71.3%) and erectile dysfunction (56.3%) and mood changes (55%).

Erectile dysfunction was seen in significantly higher frequency in hypogonadal subjects (>80%) defined by cFT/TT and ADAM criteria. In other studies, erectile dysfunction was the most common presentation occurring in T2DM subjects with low testosterone.[19] High frequency of fatigue and mood changes in the present study could be associated with classical symptoms and the psychological impact of the newly detected disease. Among hypogonadal subjects, according to cFT and ADAM criteria, the frequency of hypogonadotropic-hypogonadism was 80% which on the basis of TT and ADAM criteria was 92.5%.

There was no significant difference for hypogonadism among either the HbA1C categories (p=0.2) or age groups (p=0.6). Hypogonadal and eugonadal groups significantly differed both according to TT and ADAM (81.5% vs 43.4%; p=0.01) and cFT and ADAM (93.3% vs 47.7%, p≤0.001) criteria for erectile dysfunction.

There was a significant difference between the groups for SHBG (21.7±11.6 vs 30.71±22; p=0.05) by TT and ADAM criteria. Similarly, cFT and ADAM criteria also revealed statistically significant difference for SHBG (38.04±19.90 vs 25.28±19.37 nmol/l; p=0.03) and total cholesterol (211.40±44.7 vs 191.3±32.64 mg/dl p=0.04). However, in both groups, LH, FSH, HbA1c, fasting blood sugar, 2hrs after 75gm glucose, triglyceride, HDL, LDL did not differ significantly. cFT significantly correlated with age (r=-0.3503, p=001) and SHBG (r=-0.37, p≤0.01) while TT with SHBG (r=0.58, p=0.01). According to the multiple regression, erectile dysfunction and SHBG were significant predictors for hypogonadism (p=0.01, 0.03 respectively).

The present study demonstrates SHBG to be significantly low in the hypogonadal groups defined by the criterion of TT and ADAM but not with cFT. SHBG was also found to have a significant correlation with total and calculated free testosterone but positively with the previous one and the negatively with the latter. Hence implies that level SHBG needs to be taken into account before interpreting gonada status. Multiple logistic regression analysis revealed SHBG and erectile dysfunction to be an independent predictor of hypogonadism in the male population with T2DM and which could have significant clinical implications and warrants further study on the backyard of a high prevalence of hypogonadism in T2DM.

A significant number of newly detected male T2DM patients have symptoms of hypogonadism judged on the basis of TT, cFT and ADAM score. This aspect should be considered while diagnosing male subjects as T2DM.

Limitations

This was a single centered study with a small sized sample. So, the findings of this study may not reflect the exact scenario of the whole country.

CONCLUSION

Symptomatic hypogonadism is frequent in males with newly detected type 2 diabetes mellitus and mostly are hypogonadotropic hypogonadal. Androgen deficiency symptoms are common in the study population and erectile dysfunction is present in a significant proportion of hypogonadal patients. Hence, universal screening of testosterone level and androgen deficiency symptoms is recommended in newly detected T2DM patients. Large scale prospective study is required to assess the association and interventional studies may be essential for the effective management of the condition.

Recommendations

We would like to recommend for conducting similar more studies on the same issue for getting more specific information.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Masum MD, Talukder RM, Maksud SI, Haque E, Khanam J, Hossain S, Talukder SM. Evaluation of predictors of erectile dysfunction and hypogonadism in men with types 2 diabetes mellitus. Int J Adv Med 2020;7:1767-72.