IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 11 Ser.13 (November. 2020), PP 15-20
www.iosrjournals.org

"Predictors of Erectile Dysfunction and Hypogonadism in Men with Types 2 Diabetes Mellitus"

Dr. A.H.M. Aktaruzzaman[1], Dr. Afsar Ahammed[2], Dr. Mst. Sabina Yasmin[3], Dr. Md. Shafiqul Islam Dewan[4]

[1]*Associate Professor, Department of Endocrinology, National Institute of Traumatology and Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh.*
[2]*Assistant Professor, Department of Endocrinology, National Institute of Traumatology and Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh.*
[3] *Assistant Registrars, Department of Endocrinology, National Institute of Traumatology and Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh.*
4 Indoor Medical officer, Department of Endocrinology, National Institute of Traumatology and Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh.
Corresponding Author: Dr. A.H.M. Aktaruzzaman.

Abstract
Background: *Basically, erectile dysfunction is an inability to get or keep an erection firm enough to have sexual intercourse. On the other hand, hypogonadism of male or testosterone deficiency is a failure of the testes to produce the male sex hormone testosterone, sperm, or both. Now a day both the disorders are considered to be associated with Types 2 Diabetes Mellitus. But we have a very few data regarding this issue.* ***Aim of the study:*** *The aim of this study was to determine the frequency of erectile dysfunction & hypogonadism status of the male patients with T2DM.* ***Materials and Methods:*** *This was a cross-sectional study and it was conducted among 168 newly detected T2DM male patients, in the department of endocrinology, NITOR, Dhaka, Bangladesh. During the period from January 2018 to December 2019. This study was approved by the ethical committee of the mentioned hospital. Before starting the main part of this intervention proper written consents were taken from all the participants. A pre-designed questioner was used to collect the patient data. All data were collected, processed, analyzed and disseminated by MS-Office and SPSS version 16 programs.* ***Results:*** *We found, gonadal status among HBA1c category according to ADAM and TT criteria >10 category was with the highest of hypogonadal, 18 (45%) and eugonadal was the highest, 66 (51.56%) in 7-10 category. Here the p value was 0.798. Besides these, gonadal status among HBA1c category according to cFT and ADAM criteria 7-10 category was with the highest hypogonadal, 12 (48%) and eugonadal was also the highest, 70 (48.95%) in the same category. Here the p value was 0.495. According to TT and ADAM criteria of comparison of biochemical characteristics on the gonadal statuses of the participants, we found significant correlation regarding all the parameters (TT, cFT, LH, FSH, SHBG, HbA1c, FBS, 2HrsA75gmG, TG, TC and HDL) except LDL. On the other hand, in analyzing the logistic regression predictive association of clinical as well as biochemical variables with hypogonadism we found significant correlation in family history of ED only.* ***Conclusion:*** *This study demonstrated the significant relationship between ED, man hypogonadism and T2DM of newly detected male with T2DM on the basis of TT, cFT and ADAM score criteria. So TT, cFT and ADAM statuses may be considered as the potential predictors of erectile dysfunction and hypogonadism in men with types 2 diabetes mellitus.*

Key Words: *Erectile Dysfunction, Hypogonadism, T2DM, SHBG.*

Date of Submission: 18-11-2020 Date of Acceptance: 04-12-2020

I. Introduction

Basically, erectile dysfunction is an inability to get or keep an erection firm enough to have sexual intercourse. On the other hand, hypogonadism of male or testosterone deficiency is a failure of the testes to produce the male sex hormone testosterone, sperm, or both. Now a day both the disorders are considered to be associated with Types 2 Diabetes Mellitus. But we have a very few data regarding this issue. Diabetes Mellitus (DM) is one of the most frequent etiologies of erectile dysfunction. It is a state of impaired carbohydrate & other metabolisms caused by either lack of insulin secretion and or its action. In fact, 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] Yearly, diabetes mellitus (DM) affects an estimated 285 million people worldwide. This number is expected to

reach 438 million by the year 2030.[2] On the other hand, erectile dysfunction is the sexual activity, practice and behavior of human being characterized by the inability to develop an erection of the penis during sexual activity. ED can have psychosomatic consequences as it can create relationship difficulties and self-image. Besides this, 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 functions 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.[3]Several 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.[4]ED 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 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]All data were collected, processed, analyzed and disseminated by MS-Office and SPSS version 23 programs.

II. Materials And Method

This was a cross-sectional study and it was conducted among 168 newly detected T2DM male patients, in the department of endocrinology, NITOR, Dhaka, Bangladesh. The age of the participants was 20 years and above. During the period from January 2018 to December 2019. This study was approved by the ethical committee of the mentioned hospital. Before starting the main part of this intervention proper written consents were taken from all the participants. A pre-designed questioner was used to collect the patient data. 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 -20^0C 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 a reputed diagnostic center. 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. 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 SPSS version 16 and disseminated by several tables and charts.

III. Results

In this study the mean age, BMI (kg/m2),WC (cm),HC (cm), SBP and DBP were 44.28 ± 6.25 years, 26±4.12 kg/m2, 85.17 ±7.34 cm, 84.36±7.48 cm, 130.19±10.54 mmHg and 82.36±6.37 mmHg respectively. The highest numbers of participants were service holder which was 47%. Then 18%, 16%, 10% and 9% participants were retired persons, businessmen, skilled laborer and people with other professions. In This study we found, 68% non-smoker and 32% smoker among total participants. We found 52% participants had family history of DM whereas 48% had not. In this study we found most of the participants were with eugonadal status which was 73% and the rest 27% was with hypogonadal status. According to the logistic regression predictive association (Using TT and ADAM criteria) of clinical and biochemical variables with hypogonadism it was found that, 30-39 years' group was the using TT and ADAM criteria highest with hypogondal which was 18 (40%) and ugonadal was 45 (36.59%). On the other hand, following immediate age group was 40-49 years where hypogonadal were found 15 (33.33%) and eugonadal were 41 (33.33%) using TT and ADAM criteria. Here the P value was 0.008 which indicated a significant correlation. Moreover, gonadal status among HBA1c category according to ADAM and TT criteria >10 category was with the highest of hypogonadal, 18 (45%) and eugonadal was the highest, 66 (51.56%) in 7-10 category. Here the p value was 0.798. So there was not any significant correlation between the groups. Besides these, gonadal status among HBA1c category according to cFT and ADAM criteria 7-10 category was with the highest hypogonadal, 12 (48%) and eugonadal was also the highest, 70 (48.95%) in the same category. Here the p value was 0.495. So there was not any significant correlation between the groups. On the other hand, according to TT and ADAM criteria of comparison of biochemical characteristics on the gonadal statuses of the participants, we found significant correlation regarding all the parameters (TT, cFT, LH, FSH, SHBG, HbA1c, FBS, 2HrsA75gmG, TG, TC and HDL) except LDL. On the other hand, in analyzing the logistic regression predictive association of clinical as well as biochemical variables with hypogonadism we found significant correlation in family history of ED only.

Variables	Mean ±SD
Age (years)	44.28 ± 6.25
BMI (kg/m^2)	26±4.12
Waist circumference: WC (cm)	85.17 ±7.34
Hip circumference: HC (cm)	84.36±7.48
Systolic BP (mmHg)	130.19±10.54
Diastolic BP (mmHg)	82.36±6.37

Table I: Clinical status of participants (n=168)

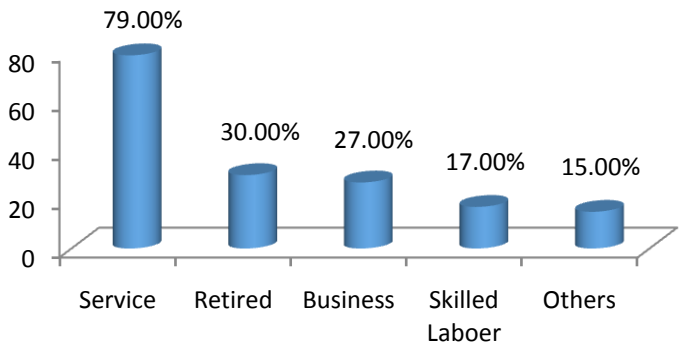

Figure I: Distribution of occupation among participants (n=168)

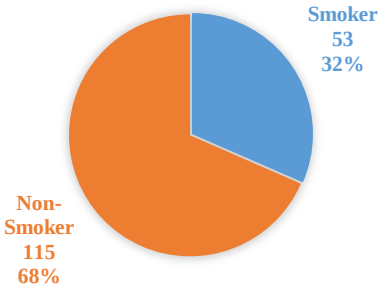

Figure II: Distribution participants on smoking habit (n=168)

Age (years)	Hypogonadal (n=45)		Eugonadal (n=123)		P value
	n	**%**	**n**	**%**	
20 years to 29 years	4	8.89	12	9.76	0.008
30 years to 39 years	18	40.00	45	36.59	
40 years to 49 years	15	33.33	41	33.33	
≥50 years	8	17.78	25	20.33	
Total	45	100	123	100	

Table II: Distribution of gonadal status according to age category using TT and ADAM criteria (n=168)

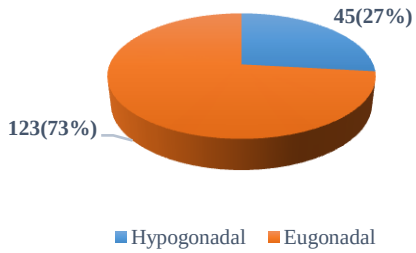

Figure II: Distribution participants on hypogonadal and eugonadal (n=168)

HBA1c category	Hypogonadal		Eugonadal		P value
	n	%	n	%	
<7	6	15.00	32	25.00	0.798
7-10	16	40.00	66	51.56	
>10	18	45.00	30	23.44	
Total	40	100	128	100	

Table III: Distribution of gonadal status among HBA1c category according to ADAM and TT criteria (n=168)

HBA1c category	Hypogonadal		Eugonadal		P value
	n	%	n	%	
<7	2	8.00	33	23.08	0.495
7-10	12	48.00	70	48.95	
>10	11	44.00	40	27.97	
Total	25	100	143	100	

Table IV: Distribution of gonadal status among HBA1c category according to cFT and ADAM criteria (n=168)

Biochemical parameters	Hypogonadal	Eugonodal	P-Value
	Mean ± SD	**Mean ± SD**	
TT (nmol/l)	9.76±1.42	15.53±4.18	<0.0001
cFt (nmol/l)	0.259±0.12	0.36±0.13	<0.0001
LH (mIU/l)	4.78±2.75	5.67±4.53	0.03
FSH (mIu/l)	5.72±4.39	7.56±6.34	0.002
SHBG	21.66±10.37	30.67±22.46	< 0.0001

(nmol/l)			
HbA1c (%)	9.46±2.34	8.78±1.69	0.002
FBS (mmol)	12.51±6.52	10.41±3.57	0.0003
2HrsA75gmG (mmol/l)	19.54±8.32	16.97±5.28	0.001
TG (mg/l)	259.65±146.62	220.18±101.14	0.004
TC (mg/L)	201±44.31	190.75±30.33	0.014
HDL(mg/dl)	38.27±6.42	37.11±6.49	0.101
LDL(mg/dl)	114.32±35.72	117.95±56.82	0.484

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

Table V: Comparison of biochemical characteristics among the gonadal status according to TT and ADAM criteria (n=168)

(n=168)

Variables	OR	SE	95% CI	p-Value
History of ED	12.21	0.75	2.75 - 0.04	0.024
History (loss of libido)	0.69	0.66	0.81 - 2.64	0.726
SHBG	1.13	0.03	1.04 - 1.09	0.045
HbA1c	0.84	0.14	0.64 - 1.01	0.273
Age	1.12	0.04	0.95 -1.1	0.262
TC	0.89	0.008	0.98 -1.01	0.681
Constant	0.41	0.78		

OR= Odds Ratio, SE= Standard Error, CI=Confidence Interval, TC= Total Cholesterol

Table VI: Logistic regression predictive association of clinical and biochemical variables with hypogonadism

IV. Discussion

In the present 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.[19,20] 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 hypogonado tropic-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. In conclusion, 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.

V. Conclusion& Recommendations

This study demonstrated the significant relationship between ED, man hypogonadism and T2DM of newly detected male with T2DM on the basis of TT, cFT and ADAM score criteria. So TT, cFT and ADAM statuses may be considered as the potential predictors of erectile dysfunction and hypogonadism in men with types 2 diabetes mellitus. These findings may be helpful in the treatment arena of erectile dysfunction and hypogonadism in men with types 2 diabetes mellitus and in further similar studies. But as it was a single center study with a small sized sample so the findings of this study may not reflect the exact scenario of the whole country. For getting more specific information we would like to conduct similar more studies in several places with larger sized samples.

References

[1]. Kahn SE, Hull RL, Utzschneider KM (2006). Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature; Vol 444:840.
[2]. International Diabetes Federation. IDF Diabetes Atlas. Epidemiology and Morbidity. International Diabetes Federation. Available from: http://www.idf.org/. Accessed on 2016 March 1.
[3]. Professor geoffreyhackett, erectile dysfunction, diabetes and cardiovascular risk, volume 16 issue 2 l april/May/june 2016. P- 53-57
[4]. Mohamed AbdelraoufKorani& Ahmed Sonbol(2018)Study of risk factors for erectile dysfunction in patients with type 2 diabetes mellitus: Correlation to serum testosterone level,Alexandria Journal of Medicine,54:4,319-321
[5]. Professor geoffreyhackett, erectile dysfunction, diabetes and cardiovascular risk, volume 16 issue 2 lapril/May/june 2016. P- 53-57
[6]. Basaria S. Male hypogonadism. The Lancet. 2014; 383(9924):1250-63. 3
[7]. Dandona P, Rosenberg MT. A practical guide to male hypogonadism in the primary care setting. Int J ClinPract. 2010; 64:682-96.
[8]. Aydogan U, Aydogdu A, Akbulut H, Sonmez A, Yuksel S, Basaran Y, et al. Evaluation of the isokinetic muscle strength, balance and anaerobic performance in patients with young male hypogonadism. Endocrine Journal. 2012; 59(4):3217.
[9]. Aydogan U, Aydogdu A, Akbulut H, Sonmez A, Yuksel S, Basaran Y, et al. Increased frequency of anxiety, depression, quality of life and sexual life in young hypogonadotropichypogonadal males and impacts of testosterone replacement therapy on these conditions. EndocrineJournal.2012;59(12):1099-105
[10]. Kupelian V, Page ST, Araujo AB, Travison TG, Bremner WJ, McKinlay JB. Low sex hormonebinding globulin, total testosterone, and symptomatic androgen deficiency are associated with development of the metabolic syndrome in nonobese men. J ClinEndocrinolMetab. 2006; 91:843-50
[11]. Sorisky A. Late-onset hypogonadism in middle-aged and elderly men. The New England Journal of Medicine. 2010; 363(19):1867-8.
[12]. Akter S, Rahman M, Abe S, Sultana P (2014). Prevalence of diabetes and prediabetes and their risk factors among Bangladeshi adults: a nationwide survey. Bulletin of the World Health Organization; Vol 92:204-213 3
[13]. Lunenfeld B, Mskhalaya G, Zitzmann M, Arver S, Kalinchenko S, Tishova Y, Morgentaler A (2015). Recommendations on the diagnosis, treatment and monitoring of hypogonadism in men. Aging Male; Vol 18:5–15
[14]. Ahima RS, Prabakaran D, Mantzoros C, Qu D, Lowell B, Maratos E, Flier JS (1996). Nature; Vol 382:250-252
[15]. Schneider JE, Wade GN (1989). Availability of metabolic fuels controls estrous cyclicity of Syrian hamsters. Science; Vol 244:1326-1328
[16]. Maejima Y, Kohno D, Iwasaki Y, Yada T. Insulin suppresses ghrelin-induced calcium signaling in neuropeptide Y neurons of the hypothalamic arcuate nucleus (2011). Aging; Vol 310:92-97.
[17]. Trinick TR, Feneley MR, Welford H, Carruthers M. International web survey shows high prevalence of symptomatic testosterone deficiency in men (2011). Aging Male; Vol 14:10–15
[18]. Seftel AD (2006). Male hypogonadism. Part I: Epidemiology of hypogonadism. International Journal of Impotence Research; Vol 18:115–120
[19]. Hu FB (2011). Globalization of Diabetes. Diabetes Care; Vol 34:1249-1257
[20]. Muraleedharan V, Marsh H, Kapoor D (2013). Testosterone deficiency is associated with increased risk of mortality and testosterone replacement improves survival in men with type 2 diabetes. European Journal of Endocrinology; Vol 169:725– 733

Dr. A.H.M. Aktaruzzaman., et. al. "Predictors of Erectile Dysfunction and Hypogonadism in Men with Types 2 Diabetes Mellitus". *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(11), 2020, pp. 15-20.