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Prevalence of Hypogonadism Among Males with Type 2 Diabetes Mellitus in a Malaysian Tertiary Hospital: A Cross-Sectional Study

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Abstract

Objective. Previous studies have indicated that clinical hypogonadism is common among males with type 2 diabetes mellitus (T2DM). However, the reported prevalence varies due to the diverse diagnostic criteria used in these studies. This study aims to determine the prevalence of clinical hypogonadism among Malaysian T2DM males and their associated factors.

Methodology. A total of 360 participants who fulfilled the inclusion criteria were included in this study. Their socio-demographic and clinical parameters were documented and a total testosterone level was sampled from a morning fasting serum. Patients with serum total testosterone of 8-12 nmol/L had their serum total testosterone repeated and their symptoms assessed with the Aging Male Symptoms (AMS) scale. Clinical hypogonadism was diagnosed with total testosterone <12 nmol/L and cfT <0.255 nmol/L, in addition to an AMS score of >26.

Results. The prevalence of clinical hypogonadism among Malaysian T2DM males was 17.5% (n = 63), with 55.6% of them having hypogonadotropic hypogonadism. There is a significant association between clinical hypogonadism with waist circumference >94 cm (p <0.001), obesity (p <0.001), hypertension (p = 0.010), coronary artery disease (p = 0.014) and peripheral artery disease (p = 0.022). There is a significant difference in the weight (p = 0.001), BMI (p <0.001), waist circumference P <0.001), serum HDL-C levels (p <0.001), serum triglycerides levels (p = 0.001) and serum TyG index (p <0.001). Diabetic males with increasing age (adjusted OR = 1.070, 95% CI 1.004-1.146, p = 0.038), presence of coronary artery diseases (adjusted OR = 2.08, 95% CI 1.220-10.219, p = 0.020) and low total testosterone (adjusted OR = 2.451, 95% CI 1.908-3.155, p <0.001) are at higher risk of developing clinical hypogonadism.

Conclusion. This study is the first in the Asian region to use stricter criteria for diagnosing hypogonadism. Despite these stringent criteria, the prevalence of hypogonadism remains significantly high among Malaysian T2DM males. It is particularly common in diabetic males over 35 years old with coronary artery disease, regardless of A1c control and the duration of diabetes.

Key words: hypogonadism, type 2 diabetes mellitus, testosterone, prevalence

INTRODUCTION

Low serum testosterone (T) levels have been shown to be present in males with type 2 diabetes mellitus (T2DM), with a prevalence ranging from 11.6 to 52.0%. This wide variation in prevalence occurs due to the different diagnostic criteria used to define low T levels.[1–21]

Hypogonadism among T2DM males has been strongly linked to the dysglycaemic state, mainly contributed by insulin resistance and visceral adiposity. The dysglycaemic state further leads to a disruption of the hypothalamus-pituitary-gonadal axis characterised by increased pro-inflammatory cytokines that reduce sex hormone binding globulin (SHBG) levels and cause negative feedback on the axis, as well as elevated leptin levels that are inhibitory to Leydig cell function.[22]

It is pivotal to identify hypogonadal males with T2DM as both T2DM and low testosterone levels are independently associated with cardiovascular diseases.[23] T2DM is a known risk factor for coronary artery diseases (CAD) and the presence of hypogonadism further augments this risk. Low testosterone levels in men with diabetes have been shown to double the risk of cardiovascular events and deaths, whilst normalisation of testosterone in hypogonadal

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males reduces both outcomes.[24,25] The question of whether hypogonadism is an independent risk factor or a surrogate marker for CAD is still being debated.[11,12, 26,27]

Despite the high prevalence of T2DM in Malaysia, there has been only one study reporting the prevalence of hypogonadism among Malaysian males in the state of Sarawak, located on the Island of Borneo, which is limited by the utilisation of a single testosterone level.[16] The scarcity of local data, especially in the Peninsula of Malaysia, diminishes the magnitude of this problem. This study aims to determine the prevalence of hypogonadism among males with T2DM in a Malaysian tertiary hospital.

METHODOLOGY

This cross-sectional study was approved by the hospital's institutional ethics and research committee. Employing a purposive sampling strategy, all male participants, aged 18-70 years with T2DM diagnosis, were screened during their scheduled diabetes clinic visits in a tertiary hospital between January 2018 and December 2021. Participants were screened using the inclusion criteria and excluded from the study if they had (1) established pituitary or testicular disorder; (2) acute or critical illness for the past 3 months; (3) liver cirrhosis, chronic kidney disease with estimated glomerular filtration rate (eGFR) <30 ml/min, severe heart failure, active malignancy; (4) receiving hormone replacement therapy; (5) current consumption of herbal or traditional medications where steroids or androgens as an ingredient cannot be excluded; and, (6) psychiatric illness.

Using the formula $n = [Z^2 P(1-P)]/d^2$, we calculated that the sample size of 360 participants was adequately powered for this study, with Z = 1.96 (corresponding to 95% confidence interval) and d = 0.05, for an estimated prevalence of 35.2% by Zheng et al.[7]

Clinical and socio-demographic characteristics were collected using a semi-structured questionnaire. The participants' national registration card determined their ethnicity. Anthropometric parameters, such as height, weight, and waist circumference, were measured by trained nurses under the supervision of the investigators. Waist circumference was obtained with a measuring tape midway between the inferior angle of the ribs and the supra-iliac crest. The body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters.

The T2DM diagnosis was based on the American Diabetes Association criteria of abnormal fasting blood glucose or modified oral glucose tolerate test (mOGTT) or HbA1c >6.3%.[28,29] Hypogonadism was defined as the presence of 1) low total testosterone (tT) level (<12 nmol/), 2) low repeated calculated free testosterone (cFT) levels (<0.255 nmol/L) and 3) Aging Male Symptoms (AMS) score of ≥27 (Figure 1). Hypergonadotropic hypogonadism was defined if the patients with hypogonadism had luteinising hormone (LH) levels >8.6 mIU/mL, while hypogonadotropic hypogonadism was defined if LH levels ≤8.6 mIU/mL.[30]

Insulin resistance was measured using the triglyceride and glucose index (TyG index) and calculated using the formula: ln [fasting TG (mg/dL) × fasting plasma glucose (mg/dL)/2]. TyG Index has been shown to be a useful surrogate marker for insulin resistance.[31,32]

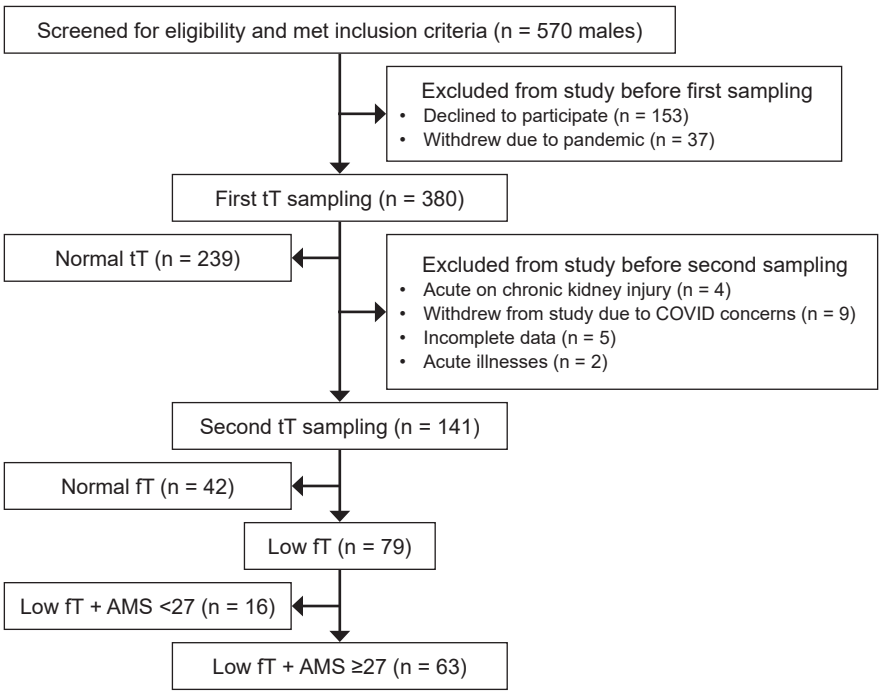

Figure 1. Flowchart of the patient recruitment process.

Hypertension and dyslipidaemia were considered present if the participants received medications for either of the above conditions or if there were abnormalities in the blood pressure levels or serum lipids. Coronary artery disease (CAD) was defined as a previous diagnosis of coronary vessel abnormalities by angiography or on current treatment for CAD. Echocardiography criteria confirmed heart failure, while proteinuria was defined as persistent microalbuminuria or proteinuria on more than one occasion. Chronic kidney disease was diagnosed based on the estimated glomerular filtration rate eGFR of <60 mL/min/1.73 m^2 for at least 3 months. Peripheral arterial disease (PAD) was defined as self-reported claudication pain, angiographically-confirmed PAD or the presence of erectile dysfunction (ED). Participants were classified as smokers (usual consumers in the last 3 months) or non-smokers.

All participants with low serum tT in the initial testing were assessed for hypogonadal symptoms and quality of life using the AMS questionnaire and sexual function using the International Index of Erectile Function (IIEF-5) questionnaire. The AMS questionnaire has been validated to assess the quality of life among hypogonadal males.[33] It includes three subcategories (somato-vegetative, psychological and sexual) of a defined set of items. Each question is rated on a scale of 1 to 5. Participants with an AMS score of <27 were classified as having few or no symptoms; 27-36 was as mild; 37-49 as moderate; and ≥50 as severe. The AMS scale has been translated and adapted into the Malay language.[34]

Sample collection, preparation and analysis

Five millilitres of venous blood sample was drawn from each participant between 8 AM and 10 AM after an overnight fast. The blood samples were transferred into plain tubes, left to clot for 30 minutes and centrifuged at 3000 g for 10 minutes. The serum was aliquoted and stored at -20°C. Serum tT was measured using chemiluminescent immunometric assays (Roche Cobas e411; Roche Diagnostics GmbH, Mannheim, Germany). The reference values for T were 8-28 nmol/L; for LH: 1.7-8.6 mIU/mL; for oestradiol (E2): 11.3-43.2 pg/mL; and for SHBG: 18.3-54.1 nmol/L. The laboratory technicians were blinded to the participants' information.

A tT level <12 nmol/L was considered as low. Participants with low tT levels were subjected to scoring of hypogonadal symptoms using the AMS scale and IIEF-5 questionnaires, as well as a repeated fasting morning tT, E2, LH, and SHBG. FT was calculated from SHBG, serum albumin and tT using the formula suggested by Vermeulen et al. with levels <0.255 nmol/L deemed low.[35]

Statistical analysis

Statistical analysis was performed using SPSS 23 software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) Continuous data were presented as mean ± SE while categorical data were presented as frequencies and proportions. Data analysis showed that the variables were normally distributed; hence, the chi-square test and Fischer's exact test were used as a test of significance for qualitative categorical data, whilst the t-test was used as a test of significance to identify the mean difference between two quantitative variables.

RESULTS

A total of 570 T2DM participants were screened, and 380 who fulfilled the study criteria were recruited for the initial screening. (Table 1). However, due to incomplete data, acute illnesses and COVID-related concerns, only 360 out of 380 participants were included in the final data analysis. Based on the low tT and fT levels and AMS result, 63 participants were diagnosed to have hypogonadism (Figure 1).

Prevalence of hypogonadism

The prevalence of hypogonadism among T2DM participants was 17.5% (95% CI 0.139-0.218). Based on data from Table 2, the incidence of hypogonadism seems to start occurring by the age of 35 to 44 years, was highest among male participants 65-70 years old (21/101) (20.8%), and most common among participants of Chinese ethnicity (22/109)

Table 1. Clinical and biochemical characteristics of patients according to gonadal status (n = 360)

Variables	Total (n=360)	Hypogonadism (n=63)	Eugonadal (n=297)	*p*-value (t-test)
Age, year	56.8 ± 10.80	58.8 ± 9.92	56.4 ± 10.95	0.113
Duration of diabetes, year	14.3 ± 9.29	14.8 ± 10.51	14.2 ± 9.03	0.649
Weight, kg	83.2 ± 16.12	89.3 ± 18.00	81.9 ± 15.42	<0.001*
Waist circumference, cm	100.9 ± 12.46	106.6 ± 15.05	99.69 ± 11.51	<0.001*
BMI[a], kg/m²	29.1 ± 5.15	31.4 ± 6.50	28.7 ± 4.69	<0.001*
eGFR[b], ml/min/1.73 m²	74.6 ± 21.23	71.6 ± 21.89	75.3 ± 21.07	0.106
HbA1c, %	8.4 ± 1.97	8.5 ± 2.08	8.4 ± 1.95	0.365
HDL-C[c], mmol/L	1.13 ± 0.259	1.03 ± 0.206	1.16 ± 0.264	<0.001*
Non-HDL-C[c], mmol/L	3.40 ± 1.214	3.21 ± 0.984	3.44 ± 1.256	0.164
Tg[d], mmol/L	1.68 ± 1.217	2.07 ± 1.802	1.59 ± 1.038	0.005*
ALT[e], IU/L	32.4 ± 18.70	33.9 ± 19.1	32.1 ± 18.61	0.469
TyG[f] Index, mg²/dL²	4.87 ± 0.373	4.95 ± 0.417	4.85 ± 0.361	0.024*
tT[g], nmol/L	14.90 ± 5.130	8.45 ± 2.783	16.26 ± 4.426	<0.001*

[a] body mass index; [b] estimated glomerular filtration rate; [c] high-density lipoprotein-cholesterol; [d] triglyceride; [e] alanine transaminase; [f] triglyceride-glucose index; [g] total testosterone

(20.2%). Furthermore, the proportion of hypogonadism was significantly higher in males with abdominal obesity (21.1%), hypertension (19.5%) and coronary artery disease (26.7%). (Table 2)

Symptoms and sexual function in diabetic males with clinical hypogonadism

Almost all of the hypogonadal respondents had sexual symptoms, with 76.2% (48/63) complaining of severe symptoms such as reduced sexual performance, reduced erections and poor libido[39] (Figure 2). Most respondents (55.6%, 35/63) had moderate somato-vegetative symptoms like reduced facial hair growth or feeling burnt out. The respondents mainly had mild to moderate psychological symptoms such as irritability and severe anxiety. Only 29 (46%) of the 63 hypogonadal males were sexually active (had sexual intercourse in the past 4 weeks). Based on the IIEF-5 score, almost one-third of these sexually active respondents had moderate to severe ED (Figure 3).

DISCUSSION

By far, this study is one of the few studies in the world evaluating the prevalence of hypogonadism in T2DM males using two persistent low total and free T levels, as well as the first in the Asian region to use stricter criteria to diagnose hypogonadism. With only one morning sample of tT <12

Table 2. Clinical and biochemical characteristics of patients according to hypogonadal status (n = 360)

Variable	Total (%) (n = 360)	Hypogonadism (%) (n = 63)	Eugonadal (%) (n = 297)	*p*-value
Age group				#0.606
18-24	4 (1.1)	0 (0)	4 (1.3)	
25-34	7 (1.9)	0 (0)	7 (2.4)	
35-44	48 (13.3)	9 (14.3)	39 (13.1)	
45-54	57 (15.8)	8 (12.7)	49 (16.5)	
55-64	143 (39.7)	25 (39.7)	118 (39.7)	
65-70	101 (28.1)	21 (33.3)	80 (26.9)	
Race				#0.318
Malay	196	36 (57.1)	160 (53.9)	
Chinese	109	22 (34.9)	87 (29.3)	
Indian	52	5 (7.9)	47 (15.8)	
Others	3	0 (0)	3 (1.0)	
Duration of diabetes				0.402
≤10 years	160 (44.4)	31 (49.2)	129 (43.4)	
>10 years	200 (55.6)	32 (50.8)	168 (56.6)	
Waist circumference				0.006*
≤94 cm	109 (30.3)	10 (15.9)	99 (33.3)	
>94 cm	251 (69.7)	53 (84.1)	198 (66.7)	
BMI [a] group				#0.036*
<25	61 (16.9)	5 (7.9)	56 (18.9)	
≥25	299 (83.1)	58 (92.1)	241 (81.1)	
Hypertensive				#0.01*
Yes	313 (86.9)	61 (96.8)	252 (84.8)	
No	47 (13.1)	2 (3.2)	45 (15.2)	
Dyslipidaemia				#0.149
Yes	341 (94.7)	62 (98.4)	279 (93.9)	
No	19 (5.3)	1 (1.6)	18 (6.1)	
Smoking				##0.351
Yes	91 (25.3)	13 (20.6)	78 (26.3)	
No	269 (74.7)	50 (79.4)	219 (73.7)	
Heart failure				#0.882
Yes	5 (1.4)	1 (3.6)	4 (1.3)	
No	355 (98.6)	62 (98.4)	293 (98.7)	
CAD [b]				##0.01*
Yes	86 (23.9)	23 (36.5)	63 (21.2)	
No	274 (76.1)	40 (63.5)	234 (78.8)	
CKD [c]				##0.879
Stage 1	96 (26.7)	7 (25.0	82 (27.6)	
Stage 2	169 (46.9)	13 (46.4)	139 (46.8)	
Stage 3	95 (26.4)	8 (28.6)	76 (25.6)	
Proteinuria				##0.190
Yes	173 (48.1)	35 (55.6)	138 (46.5)	
No	187 (51.9)	28 (44.4)	159 (53.5)	
PAD [d]				##0.022*
Yes	170 (47.2)	38 (60.3)	132 (44.4)	
No	190 (52.8)	25 (39.7)	165 (55.6)	
HbA1c group				##0.849
≤7%	105 (29.2)	19 (30.2)	86 (29.0)	
>7%	255 (70.8)	44 (69.8)	211 (71.0)	
TyG [e]				##0.491
>4.68 mg^2/dL^2	238 (66.1)	19 (30.2)	194 (65.3)	
≤4.68 mg^2/dL^2	122 (33.9)	44 (69l8)	103 (34.7)	

[a] body mass index; [b] coronary artery disease; [c] chronic kidney disease; [d] peripheral arterial disease; [e] triglyceride-glucose index; # Fischer's exact test; ## chi-square test

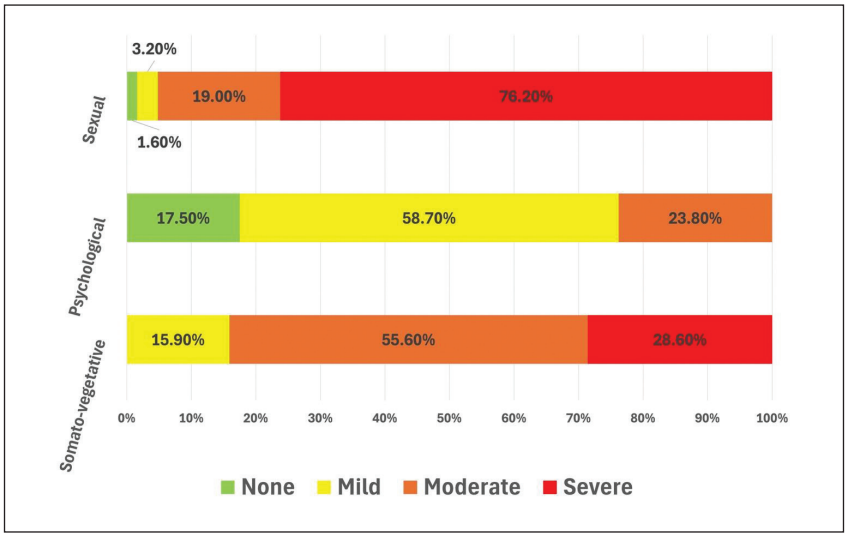

Figure 2. Hypogonadal symptoms among hypogonadal T2DM males (n = 63).

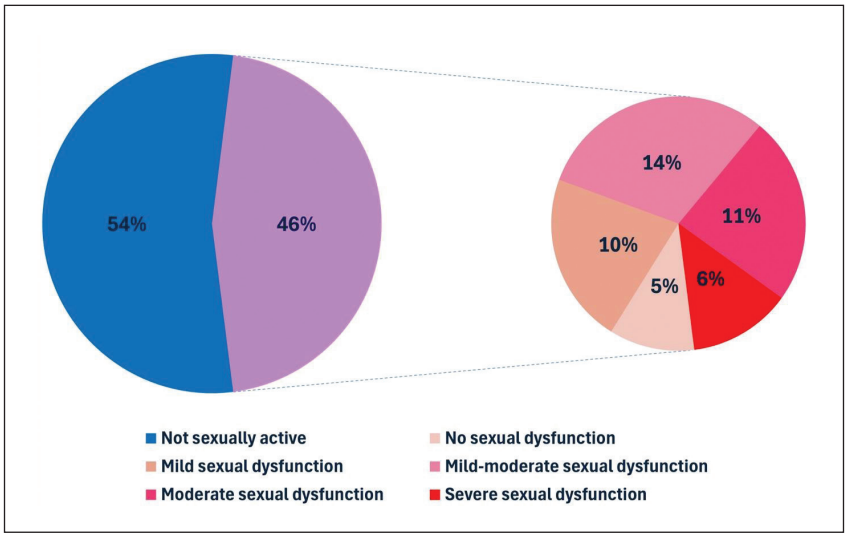

Figure 3. Sexual dysfunction among hypogonadal T2DM males (n = 63).

nmol/L, the prevalence of low tT was 37.1%, comparable to the other studies.[1,7] Using a lower tT threshold of <8 nmol/L, the prevalence of hypogonadism further dropped to 8.1%, comparable with the 11.6% reported by Herrero et al.[37]

From our 360 participants, 22.8% of T2DM males had hypogonadism if the criteria of an AMS score of ≥27 and a single tT of <12 nmol/L were applied. This result is consistent with the prevalence of 23.5% reported by an Ethiopian study which had used the similar criteria to diagnose hypogonadism among T2DM males.[38] Finally, using positive symptoms with one low tT and one repeated low cfT, the prevalence of hypogonadism that we derived from our sample population was 17.5%, comparable to the prevalence of 20.7% by Agarwal et al., who had used positive symptoms and two consistent low T results as diagnostic criteria.[13] Hence, we propose that hypogonadism among T2DM males should be diagnosed in the presence of hypogonadal symptoms and two consistently low T levels. In conjunction with this, fT should also be tested at least once, given the high prevalence of obesity among T2DM males, which has falsely lowered tT levels due to low serum SHBG concentration.[30]

To date, there has only been one prevalence study in Southeast Asia (Ahmad et al.) that reported a prevalence of 19.7% of hypogonadism among T2DM males attending a primary healthcare centre in the capital city of Sarawak. However, the diagnosis of hypogonadism utilised only a single reading of low total T levels with positive symptoms suggestive of hypogonadism.[16] Comparing our study with that of Ahmad et al., the mean age in both study populations were almost similar (56.8 years vs 57.7 years), with similar proportions of obesity (83.1% vs 86.4%), visceral adiposity (69.7% vs 73.9%), hypertension (86.9% vs 88.1%) and dyslipidaemia (94.7% vs 95.8%). There are some differences in the study population's ethnicity, namely Malays (54.4% vs 44.7%), Chinese (30.3% vs 30.8%) and others (15.2% vs 24.4%), as there are more Ibans and indigenous ethnic groups in the state of Sarawak.

Table 3. Comparison of Asian studies on the prevalence of hypogonadism among type 2 diabetic males

Author (year of study)	Country and sample size	Sample population characteristic	Prevalence of hypogonadism using different criteria				
			1 tT + 1 cfT + symptoms	2 cfT + symptoms	1 tT or cfT + symptoms	2 cfT	1 tT or cfT
This study	Malaysia 360	T2DM males, age 18-70 years	17.5%		22.8%		37.1%
Waddankeri et al. (2024)[21]	India 250	T2DM males, age range unspecified			27.6% (tT)		
Singh et al. (2023)[20]	India 353	T2DM males, age 20-70			17.0% (cfT)		
Zhou et al. (2022)[19]	China 637	T2DM males, age 20-70					26.5% (tT or cfT)
Cai et al. (2021)[56]	China 294	T2DM males, age range unspecified			21.7 (cfT)		
Kumari et al. (2021)[18]	India 200	T2DM males, age 30-69					45.5%
Ahmad et al. (2020)[16]	Malaysia 360	T2DM males, 40-70 years			19.7% (tT)		
Anupam et al. (2020)[15]	India 150	T2DM males, 25-70 years			17.3% (cfT)		
Cao et al. (2018)[57]	China 205	T2DM males, age unspecified					34.1% (tT)
Agarwal et al. (2017)[13]	India 900	T2DM males, 30-59 years		20.7%			
Al Hayek et al. (2017)[58]	Saudi Arabia 157	T2DM males, 30-70 years			22.9% (tT)		
Li et al. (2017)[3]	China 122	T2DM males, age range unspecified					26.7-48% (tT)
Madhu et al. (2017)[12]	India 150	T2DM males, age 30-70					32-40% (tT)
Charan et al. (2017)[11]	India 100	T2DM males, age >18 years					34% (tT)
Zheng et al. (2016)[7]	China 2013	T2DM males, age unspecified					35.2% (tT)
Cheung et al. (2016)[6,10]	Hong Kong 1239	T2DM males, age 18-90					12.3% (tT)
Mattack et al. (2015)[6]	India 80	T2DM males, age 31-71					31% (tT) 38% (cfT)
Liu et al. (2013)[4]	Taiwan 766	T2DM males, age unspecified					32.5 (tT)
Mirzaei et al. (2012)[59]	Iran 247	T2DM males, age >30 years			17.3% (tT)		
Ganesh et al. (2009)[9]	India 100	T2DM males, age 25-50 years				15%	

In our study, we also noted a significant increase in the prevalence of hypogonadism as the patient reaches 35 years of age. The increase from 0% for those below the age of 35 to nearly 18.7% for those between the ages of 35 and 44 years demands further investigation. Interestingly, due to the high prevalence of T2DM in the country, anyone above the age of 35 has been recommended to have an annual screening of DM regardless of their risk factors. This recommendation is vital as the prevalence of T2DM approaches 5% in that age group, making screening cost-effective.

There has been a wide range of prevalence rates reported by previous authors, from 15-66%. However, most of these studies use different diagnostic criteria. Most guidelines recommend using two consistent low total or free T for a diagnosis of hypogonadism, as almost 30% of males with a low serum T level may be falsely diagnosed as hypogonadism, given that their repeated serum T will be normal.[39-43] Furthermore, T levels are significantly affected by diurnal and day-to-day variations and food intake. Hence, guidelines have recommended using two different morning fasting T levels, measured with an accurate and reliable method as suggested by the Center for Disease Control and Prevention (CDC) Hormone Standardization Program for Testosterone.[39,44] The gold standard fT measurement should be from equilibrium dialysis assays or cfT instead of direct analogue-based fT immunoassays, which are highly inaccurate.[39,44] In males with DM and obesity, the SHBG is often low, leading to a high rate of falsely lowered tT levels.[45] However, in ageing males, SHBG will be elevated, resulting in a higher range of tT levels. Hence, males with borderline tT and a high likelihood of SHBG alterations are recommended to be assessed using fT.

Studies using only biochemical criteria of low tT or fT/cfT reported a prevalence of 12.3%-40% and 19-50%, respectively.[1,3-6,8,10,17,46-52] While studies that utilise two low fT/cfT results to diagnose hypogonadism reported prevalence ranging from 15-20.7%[9,13,53] (Table 3). Authors using the presence of hypogonadal symptoms in the

diagnosis, either positive Androgen Deficiency in the Aging Male (ADAM) or AMS scores with one reading of low fT/cfT, reported a prevalence of 17.3%. Meanwhile, the prevalence of hypogonadism using positive symptoms with one reading of low tT reported a prevalence of 17-32%. Studies utilising two T levels with symptomatology have a narrower prevalence range than those using biochemical criteria alone.[1-16,21,38,54,55]

Sexual dysfunction is common among T2DM males.[60] Previous studies have reported that such symptoms may not be entirely due to low testosterone levels and can also be present among eugonadal T2DM males, especially when there are other comorbidities.[17,52] Nonetheless, hypogonadal T2DM males have a higher prevalence of sexual dysfunction compared to eugonadal T2DM males.[20,61] There have been many validated questionnaires used for screening of male hypogonadism. The most common screening tools used in T2DM research are the AMS and ADAM questionnaires, both showing a sensitivity of 83-97%.[62]

Our study demonstrated a high prevalence of hypogonadism among Malaysian T2DM males. The latest Malaysian clinical practice guidelines have recommended that all diabetic males with sexual dysfunction should be screened for hypogonadism.[63] In tandem with other guidelines, hypogonadism should only be diagnosed if there are at least two low serum total testosterone levels (use fT level if the patient is obese or elderly). Subsequently, the cause of hypogonadism should be investigated to exclude other causes of hyper- or hypogonadotropic hypogonadism.

Limitations and strengths

Our study was not powered enough to individually analyse predictors for hypergonadotropic or hypogonadotropic hypogonadism among T2DM males. Given the long-standing duration of DM in our study population, the findings may not apply to those with diabetes of shorter duration. Several patients withdrew from the study or were unable to give repeated blood samples due to the movement restriction order imposed by the government during the COVID-19 pandemic. This curtailed the number of subjects who could complete both blood samplings.

The strength of our study is that this is the first study in the country and region that utilised stricter diagnostic criteria for hypogonadism, where both low tT and fT with the presence of hypogonadal symptoms were necessary for the diagnosis. In addition, the multi-racial configuration of the study population closely resembles the country's major ethnic distribution.

CONCLUSION

As the prevalence of T2DM in Malaysia increased to 18.3% (according to the 2019 National Health and Morbidity Survey), the number of T2DM males complicated with clinical hypogonadism is expected to increase as well.[63] Our study confirmed that the prevalence of hypogonadism in T2DM males in Malaysia is 17.5% using a stricter criterion of two persistent low T levels (serum tT and serum fT level) and the presence of hypogonadal symptoms. Given that low testosterone levels are associated with various health outcomes, testing for clinical hypogonadism should be performed in diabetic males above the age of 35 years, regardless of the duration of diabetes and, especially in those with CAD. To date, there is no proven safe and effective treatment for clinical hypogonadism that exists other than weight loss.

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Statement of Authorship
All authors certified fulfilment of ICMJE authorship criteria.

CRedit Author Statement
KWH: Formal analysis, Investigation, Visualization; Supervision; **NAK:** Conceptualization, Methodology, Writing – review and editing; **NS:** Methodology, Investigation, Writing – original draft preparation, Writing – review and editing, Supervision.

Data Availability Statement
Datasets are not publicly available because participants in the study did not give written consent to share their data.

Conflict of Interest
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