



# Prevalence and determinants of erectile dysfunction among male type 2 diabetes mellitus patients with chronic kidney disease: a cross-sectional study

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**Background:** Erectile dysfunction (ED) is a common complication among patients with diabetes mellitus (DM) and chronic kidney disease (CKD). However, limited research has focused on the association between ED and CKD and, highlights a gap in addressing this issue. This study aimed to determine the prevalence of ED and identify the associated factors in patients with DM and CKD.

**Methods:** This cross-sectional study recruited 280 male patients, aged 18 years old and above, who had DM and CKD. Those with underlying psychiatry disorders, inability to understand Bahasa Malaysia, and on renal replacement therapy were excluded. The questionnaire contained demographic and clinical information and the Malay Version of the Hospital Anxiety and Depression Scale (HADS). Their sexual function was evaluated using the Malay Version of International Index of Erectile Function-5 (IIEF-5). The data was analyzed with simple and multiple logistic regressions.

**Results:** The prevalence of ED among DM patients with CKD was 95.0% (n=228). Metformin usage [adjusted odds ratio (adj. OR) =6.64; 95% confidence interval (CI): 1.54, 28.53; P=0.01], elevated urea levels (adj. OR =1.57; 95% CI: 1.10, 2.23; P=0.01), increased glycosylated hemoglobin (HbA1c) (adj. OR =1.75; 95% CI: 1.09, 2.82; P=0.02) and high educational attainment (adj. OR =0.21; 95% CI: 0.05, 0.88; P=0.03) were associated with ED among DM patients with CKD.

**Conclusions:** The prevalence of ED among patients with DM and CKD is high. Thus, clinicians should explore this matter during consultation to ensure early detection and appropriate management can be carried out.

**Keywords:** Erectile dysfunction (ED); diabetes mellitus (DM); chronic kidney disease (CKD)

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## Introduction

Erectile dysfunction (ED) is defined as a consistent or recurrent inability of a man to achieve or maintain penile erection sufficient for sexual activity (1). Numerous studies have established an association between ED and diabetes mellitus (DM), with metabolic abnormalities recognized as a risk factor for ED in individuals suffering from chronic kidney disease (CKD) (2). CKD frequently occurs in DM patients, affecting approximately 20–40% of the population (3). ED is significantly more common in patients with CKD than in the general population, particularly those with end-stage renal disease (ESRD) (4).

CKD is defined as persistently high urine albumin to creatinine ratio of  $\geq 30$  mg/g and/or a sustained reduction in estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m<sup>2</sup>, with stages categorized as 3A (45–59 mL/min/1.73 m<sup>2</sup>), 3B (30–44 mL/min/1.73 m<sup>2</sup>), 4 (15–29 mL/min/1.73 m<sup>2</sup>) and 5 (<15 mL/min/1.73 m<sup>2</sup>) (5). eGFR is the measure to calculate renal function based on the blood concentration of endogenous substances mainly creatinine (6). As CKD progresses, the hypothalamic-pituitary-gonadal axis is disrupted, resulting in abnormal secretions of gonadotrophin-releasing hormones that decrease testosterone levels, impairing libido and erections (7,8). A reduction in eGFR also increases luteinizing

hormone levels and follicle-stimulating hormone levels which invariably lead to reduced testosterone levels. Additionally, reduced renal clearance leads to hyperprolactinemia which causes testosterone reduction.

ED is a significant indicator of cardiovascular disease resulting from endothelial dysfunction. It may be the sole manifestation of cardiovascular disease in individuals with DM and CKD. Notably, 70% to 85% of patients reported a history of ED approximately 4 to 6 years before the angiographic confirmation of cardiovascular disease (9).

The prevalence of ED in individuals with kidney failure is estimated at 50% to 70% (10), with one study reporting that 64.7% of patients entering dialysis programs experienced ED (11). The prevalence rates of ED with CKD are similar to those in individuals with ESRD. For example, Costa *et al.* [2018] found an overall prevalence of ED at 72.7%, with rates of 62.0% in stage 3, 82.5% in stage 4, and 73.6% in stage 5 CKD patients (12). Sexual dysfunction was the most reported complaint among Chinese patients with diabetic kidney disease (DKD) (13) thus reinforcing the notion that this issue is dire and warrants review.

The prevalence of ED among DM and CKD patients is exceedingly high, with those suffering from both diseases facing an equally high or greater risk. Although global literature has increasingly explored ED in CKD populations, particularly among end-stage renal failure patients such as hemodialysis, there remains a significant gap in studies focusing on CKD patients who have never undergone dialysis. Understanding the prevalence and associated characteristics of ED is crucial for improving management and enhancing overall health outcomes. While the high prevalence of ED in DM and CKD is well documented globally, unique cultural and socioeconomic factors in Malaysia remain underexplored. Malaysia's multiethnic society faces challenges such as cultural stigma, varying health-seeking behaviors, and healthcare access disparities, which may influence ED prevalence and management.

Thus, this study aimed to determine the prevalence of ED and the determinant of ED among men with DM and CKD. Identifying the risk factors could help the physician to focus and pay more attention to sexual issues among DM patients with CKD to improve care and quality of life. We present this article in accordance with the STROBE reporting checklist (available at <https://tau.amegroups.com/article/view/10.21037/tau-2024-751/rc>).

### Highlight box

#### Key findings

- The prevalence of erectile dysfunction (ED) among patients with diabetes mellitus (DM) and chronic kidney disease (CKD) was 95% with significant associations identified for metformin use, elevated urea levels, increased glycosylated hemoglobin (HbA1c), and education attainment.

#### What is known and what is new?

- ED is a common complication among patients with DM and CKD, but limited studies have explored its prevalence and associated factors in this population.
- This study highlights an alarmingly high prevalence of ED in DM patients with CKD and identifies metformin use, elevated urea levels, increased HbA1c, and educational attainment as significant associated factors.

#### What is the implication, and what should change now?

- Clinicians should routinely screen for ED in patients with DM and CKD to enable early detection and targeted management, particularly in those with identified risk factors.

## Methods

### *Study design and participants*

A cross-sectional study was conducted from July 2023 to November 2023. Participants were selected via non-proportionate systematic random sampling in a ratio of 1:2 based on the attendance list from the Family Medicine Clinic and the Nephrology Clinic at Hospital Pakar Universiti Sains Malaysia (HPUSM). Sexually active males aged 18 years old and above with underlying DM and CKD of an eGFR of less than 60 mL/min/1.73 m<sup>2</sup> were included in our study. Patients who had underlying psychiatric disorders, inability to understand Bahasa Malaysia, and on renal replacement therapy were excluded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Human Research Ethics Committee of Universiti Sains Malaysia (No. USM/JEPeM/22050284) and informed consent was obtained from all individual participants. As HPUSM operates under Universiti Sains Malaysia, ethical approval was obtained from the university's human research ethics committee, which oversees research within its affiliated institution.

The sample size was calculated based on the single proportion formula as follows:

$$n = \frac{(Z)^2 \times P(1-P)}{\Delta^2} \quad [1]$$

where n = minimum required sample size, Z = value of standard normal distribution for 95% confidence interval (CI) (1.96), Δ = precision (0.06), P = proportion of ED among CKD patients (71.02%) (2). The minimum required sample size was 220. However, after considering the non-response rate of 20%, the sample size calculated was 275.

### *Instruments*

Sociodemographic characteristics obtained from the sociodemographic questionnaire included age, race, educational level, employment, monthly family income, smoking, and frequency of sexual intercourse. The clinical profile included body mass index, medical comorbidities (hypertension, hyperlipidemia, cardiovascular disease, cancer, respiratory disease, stroke), medications (oral hypoglycemic agents, insulin, beta blocker, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, diuretics, calcium channel blockers, statins, aspirin) and clinical parameters (HbA1c, urea, creatinine, glomerular filtration rate, total cholesterol, low-density

lipoprotein, high-density lipoprotein and triglycerides level) which were obtained from the patient's medical profile.

The psychological profile was assessed using the Hospital Anxiety and Depression Scale (HADS) questionnaire. This self-reported questionnaire consists of 14 items scale. The scores are then summed to produce two sub-scales corresponding to anxiety and depression. The Malay version of HADS is a validated instrument for use in the Malaysian population and showed 90% sensitivity and specificity of 86.2% for anxiety and a sensitivity of 93.2% and a specificity of 90.8% for depression. The translated scale was shown to have a Cronbach's alpha of 0.87. Each question has four options: (I) yes, definitely; (II) yes, sometimes; (III) no, not much; and (IV) no, not at all. The possible scores range from 0 to 21. Higher scores denote increased symptoms of anxiety and depression. The scores of ≥8 and ≥9 indicate anxiety and depression respectively (14).

The International Index of Erectile Function-5 (IIEF-5) is an abbreviated version of the IIEF-15, which was the original instrument developed as a diagnostic tool for ED. The IIEF-5 is a subset of IIEF-15 and comprises items 2, 4, 5, 7, and 15. The Malay version of the IIEF-5 was an acceptable measurement as the area under the receiver operating characteristic (ROC) curve was 0.86 and the sensitivity and specificity were 85% and 75%, respectively (15). IIEF-5 contains five questions and each of the questions has five to six different answer choices which carry marks of 0 to 5. The summation score of all questions ranged from 1 to 25. A score ≤21 indicates the presence of ED. ED was classified into four categories based on IIEF-5 scores: severe [1–7], moderate [8–11], mild to moderate [12–16], mild [17–21], and no ED [22–25] (16).

### *Procedure*

Eligible men with type 2 DM and CKD at the research locations were identified, and informed consent was obtained. They were escorted to a designated room to provide privacy while completing the self-administered questionnaire, with a researcher ready for assistance if required. The researcher then completed the clinical parameters according to the most recent medical records. Patients who were found to have ED would be offered a referral to the in-house men's health clinic.

### *Statistical analysis*

The study used SPSS version 28.0 for data entry and

analysis, evaluating sociodemographic and clinical data via descriptive statistics and expressing them as means and standard deviations for continuous variables, and as frequencies and percentages for categorical data, while also determining the prevalence of ED among male patients with type 2 DM and CKD. Categories with limited sample sizes were determined, and meaningful combinations of categories were performed as necessary.

The research utilised simple logistic regression to determine probable factors contributing to ED in males with DM and CKD, and multiple logistic regression to ascertain factors leading to sexual dysfunction, while correcting for confounding variables and included those with a P value below 0.25. The significance level was set at a P value <0.05, with a 95% CI.

## Results

The total number of respondents who participated in this study was 240, equalling a response rate of 87.3%. The mean age of the study participants was 62.73 years (SD =7.03 years). The mean duration of DM was 14.08 years (SD =9.10 years). Most of the patients were of Malay ethnicity, 225 (93.8%). One hundred and twenty-eight (53.3%) participants studied up to secondary school while 89 (37.1%) attained tertiary education. The employment status of the participants was 93 (38.8%), 57 (23.8%), and 90 (37.5%) for unemployed, self-employed, and government/private employee, respectively. 74.2% of the participants earned less than Ringgit Malaysia (RM) 5,000 per month. 49.2% of the participants never smoked. The frequency of sexual intercourse was 1–2 times per month for 45.7% of participants. The mean glycosylated hemoglobin (HbA1c) from this study was 8.47% (SD =2.06%) while the mean glomerular filtration rate was 43.43 mL/min/1.73 m<sup>2</sup> (SD =13.35 mL/min/1.73 m<sup>2</sup>). The mean urea and creatinine were 8.25 mmol/L (SD =5.56 mmol/L) and 176.4 µmol/L (SD =93.2 µmol/L), respectively. Most of the respondents had comorbidities with hypertension and dyslipidemia being the highest at 90% and 80%, respectively. Among the antihypertensive medications, the highest usage was of calcium channel blockers at 53.8% while beta-blockers were the second most at 41.7%. Based on the eGFR readings, CKD stage 3A was the largest participant group (55.4%). Our participants were assessed for depression and anxiety using the HADS questionnaire where 74 (30.8%) and 19 (7.9%) were positive for depression and anxiety, respectively (Table 1).

Our study revealed a prevalence of ED at 95.0% with 47 (19.6%) having severe ED, 24 (10.0%) having moderate ED, 100 (41.7%) having mild to moderate ED and 57 (23.8%) having mild ED. Only 5.0% of the respondents had normal erectile function (Table 2).

Simple logistic regression identified education (OR =0.28; 95% CI: 0.08–0.95; P=0.04) and urea (OR =1.52; 95% CI: 1.06–2.19; P=0.02) were significantly associated with ED. Other variables, including hypertension (OR =3.29; 95% CI: 0.83–13.08; P=0.09), cardiovascular disease (OR =5.08; 95% CI: 0.64–40.08; P=0.12), metformin (OR =2.12; 95% CI: 0.66–6.81; P=0.21), and HbA1c (OR =1.39; 95% CI: 0.95–2.05; P=0.09) were not statistically significant but were included in the multiple logistic regression analysis (Table 3).

These parameters were then tested using multiple logistic regression. Participants taking metformin were 6.64 times more likely to get ED than those not (95% CI: 1.54–28.53; P=0.01). Patients with an increase in 1 mmol of serum urea were 1.57 times more likely to get ED than patients with a decrease in serum urea (95% CI: 1.10–2.23; P=0.01). Patients with a 1% increase in HbA1c are associated with 1.75 times the odds of developing ED (95% CI: 1.09–2.82; P=0.02). Patients with tertiary education are 0.21 times less likely to get ED as compared to patients with non-tertiary education (95% CI: 0.05–0.88; P=0.03) (Table 4). The presence of cardiovascular disease and hypertension were not statistically significant, with P value of 0.09 and 0.13, respectively.

## Discussion

The prevalence of ED among DM patients with CKD in our study is 95.0%. This finding aligns with a study conducted by Costa *et al.* [2017], which reported an ED prevalence of 72.5% among CKD patients on conservative treatment (2). Similarly, Pizzol *et al.* found that 76.0% of males with CKD experienced ED, based on a meta-analysis of 34 studies (4). However, a recent study in Greece revealed a lower prevalence of 46.5% for ED among DKD patients (3). The varying prevalence could be attributed to differences in the study population's cultural, socioeconomic, disease backgrounds, or stages of CKD.

A study in Greece that evaluated ED among DKD patients showed the prevalence of ED by severity was 23.2%, 32.5%, 11.6%, and 32.5% for mild, mild to moderate, moderate, and severe ED respectively (3). Our study's prevalence was comparable for the mild (23.8%)

**Table 1** Sociodemographic, clinical data and psychological profile (n=240)

Variables	Values
Sociodemographic characteristics	
Age (years)	62.73 (7.03)
Race	
Malay	225 (93.8)
Chinese	14 (5.8)
Indian	1 (0.4)
Educational level	
No formal education	1 (0.4)
Primary	22 (9.2)
Secondary	128 (53.3)
Tertiary	89 (37.1)
Employment	
Unemployed	93 (38.8)
Self-employed	57 (23.8)
Government/private employee	90 (37.5)
Family monthly income	
Less than RM 1,000	64 (26.7)
RM 1,000–5,000	114 (47.5)
RM 5,001–10,000	46 (19.2)
More than RM 10,000	16 (6.7)
Smoking	
Active smoker	24 (10.0)
Former smoker	98 (40.8)
Never smoked	118 (49.2)
Frequency of sexual intercourse <sup>†</sup>	
Less than 1 per month	58 (33.5)
1–2 per month	79 (45.7)
1–2 per week	32 (18.5)
3–4 per week	3 (1.7)
More than 4 per week	1 (0.6)
Clinical data	
HbA1c (%)	8.47 (2.06)
Urea (mmol/L)	8.25 (5.56)
Creatinine (μmol/L)	176.4 (93.2)
eGFR (mL/min/1.73 m <sup>2</sup> )	43.43 (13.35)
Total cholesterol (mmol/L)	4.62 (1.42)
LDL (mmol/L)	2.76 (1.17)
HDL (mmol/L)	1.09 (0.24)

**Table 1** (continued)**Table 1** (continued)

Variables	Values
TG (mmol/L)	1.64 (0.89)
BMI (kg/m <sup>2</sup> )	28.73 (6.53)
Duration of DM (years)	14.08 (9.10)
Stages of CKD	
Stage 3A	133 (55.4)
Stage 3B	64 (26.7)
Stage 4	33 (13.8)
Stage 5	10 (4.2)
Hypertension	
Yes	216 (90.0)
No	24 (10.0)
Dyslipidemia	
Yes	192 (80.0)
No	48 (20.0)
Cardiovascular disease	
Yes	73 (30.4)
No	167 (69.6)
Benign prostatic hyperplasia	
Yes	34 (14.2)
No	206 (85.8)
Cancer	
Yes	7 (2.9)
No	233 (97.1)
Respiratory disease	
Yes	17 (7.1)
No	223 (92.9)
Stroke	
Yes	16 (6.7)
No	224 (93.3)
Metformin	
Yes	161 (67.1)
No	79 (32.9)
SGLT-2 I	
Yes	33 (13.8)
No	207 (86.3)
Sulfonylureas	
Yes	75 (31.3)
No	165 (68.8)

**Table 1** (continued)



Table 1 (continued)

Variables	Values
Insulin	
Yes	153 (63.8)
No	87 (36.3)
Beta-blocker	
Yes	100 (41.7)
No	140 (58.3)
ACE inhibitor	
Yes	92 (38.3)
No	148 (61.7)
Angiotensin receptor blocker	
Yes	90 (37.5)
No	150 (62.5)
CCB	
Yes	129 (53.8)
No	111 (46.3)
Diuretic	
Yes	97 (40.4)
No	143 (59.6)
Statin	
Yes	222 (92.5)
No	18 (7.5)
Aspirin	
Yes	42 (17.5)
No	198 (82.5)
Psychological profile	
Depression	
Yes	74 (30.8)
No	166 (69.2)
Anxiety	
Yes	19 (7.9)
No	221 (92.1)

<sup>†</sup>, data on the frequency of sexual intercourse was available for 173 participants (missing: 67). Percentages are based on available data. Values are presented as n (%) or mean (SD). ACE, angiotensin-converting enzyme; BMI, body mass index; CCB, calcium channel blocker; CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RM, Ringgit Malaysia; SD, standard deviation; SGLT-2 I, sodium-glucose cotransport-2 inhibitors; TG, triglycerides.

Table 2 Severity of ED (n=240)

Severity of ED	Values
Severe	47 (19.6)
Moderate	24 (10.0)
Mild to moderate	100 (41.7)
Mild	57 (23.8)
Normal	12 (5.0)

Values are presented as n (%). ED, erectile dysfunction.

and moderate (10.0%) categories. However, the mild to moderate category constituted the majority at 41.6%, with severe ED at 19.6%. By contrast, Costa *et al.* [2017] found that the majority of CKD patients fell into the severe ED category (2), which may be attributed to differences in assessment tools used in the study. These differences could be due to smaller sample sizes in some studies, such as the Greek study which assessed only 50 participants.

Our study shows that a higher education level is a protective factor against ED. This finding is observed by another study where lower educational status was associated with ED (17). People with a higher education level would most likely be at a higher socio-economic status which would provide them with better avenues for ED prevention and treatment. People with lower levels of education would know less about ED, which would delay early detection and treatment (18).

Metformin use is the most significant predictor for ED based on our results. A similar association has been established in several studies. Metformin has been shown to reduce the serum total testosterone (TT) level through the inhibition of the cytochrome P450-C17a (19-21). Low serum TT levels have been proven to be related to the increasing severity of ED (22). Other than that, metformin reduces luteinizing hormone secretion and alters leptin secretion which leads to a considerable decrease in TT (21). While this study found a significant association between metformin use and ED, various potential confounders may have influenced the result. Additionally, metformin's impact on testosterone levels was not directly measured, leaving room for reverse causality. Expanding future research to control for these potential confounders, assess testosterone levels, and include a more diverse population would strengthen the validity of these findings.

Our study aligns with the findings of Kusumawardhani *et al.* [2021], who linked elevated serum urea levels to sexual

**Table 3** Simple logistic regression analysis of factors associated with ED

Variables	Crude OR	95% CI	P value
Sociodemographic characteristics			
Age (years)	1.05	0.97–1.12	0.23
Education (tertiary)	0.28	0.08–0.95	0.04
Employment			
Self-employed	1.24	0.30–5.17	0.77
Government/private employee	2.00	0.49–8.25	0.34
Family monthly income			
RM 5,001–10,000	0.24	0.07–0.86	0.29
> RM 10,000	0.20	0.04–1.15	0.71
Smoking			
Smoker	0.73	0.23–2.38	0.61
Clinical profile			
Hypertension	3.29	0.83–13.08	0.09
Cardiovascular disease	5.08	0.64–40.08	0.12
Stroke	0.78	0.09–6.41	0.81
Metformin	2.12	0.66–6.81	0.21
SGLT-2 I	0.79	0.17–3.76	0.76
Sulfonylureas	0.90	0.26–3.10	0.87
Insulin	1.82	0.57–5.81	0.32
Beta-blocker	1.46	0.43–4.97	0.55
ACE inhibitor	0.61	0.19–1.94	0.40
Angiotensin receptor blocker	1.21	0.35–4.14	0.76
CCB	1.17	0.37–3.74	0.79
Diuretic	1.38	0.40–4.71	0.61
Statin	1.13	0.14–9.27	0.91
Aspirin	1.06	0.22–5.04	0.94
HbA1c (%)	1.39	0.95–2.05	0.09
Urea (mmol/L)	1.52	1.06–2.19	0.02
Creatinine (μmol/L)	1.01	0.99–1.03	0.27
eGFR (mL/min/1.73 m <sup>2</sup> )	0.95	0.90–1.01	0.11
Total cholesterol (mmol/L)	1.01	0.67–1.53	0.95
LDL (mmol/L)	1.07	0.64–1.79	0.79
HDL (mmol/L)	0.92	0.08–10.23	0.95
Triglyceride (mmol/L)	0.82	0.48–1.41	0.48
BMI (kg/m <sup>2</sup> )	0.96	0.90–1.03	0.25
Duration of DM (years)	1.04	0.97–1.12	0.32

ACE, angiotensin-converting enzyme; BMI, body mass index; CCB, calcium channel blocker; CI, confidence interval; DM, diabetes mellitus; ED, erectile dysfunction; eGFR, estimated glomerular filtration rate; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OR, odds ratio; RM, Ringgit Malaysia; SGLT-2 I, sodium-glucose cotransporter-2 inhibitors.

**Table 4** Multiple logistic regression analysis of factors associated with ED

Variables	Adjusted OR	95% CI	P value
Metformin	6.64	1.54–28.53	0.01
Urea (mmol/L)	1.57	1.10–2.23	0.01
HbA1c (%)	1.75	1.09–2.82	0.02
Education (tertiary)	0.21	0.05–0.88	0.03

Model fitness was tested by Hosmer-Lemeshow goodness-of-fit test, classification table and area under the ROC curve. The overall accuracy of the model was 96.7%, indicating satisfactory performance since it exceeded 80%. The area beneath the curve was 0.867, indicating its efficacy for discrimination. The Hosmer-Lemeshow test yielded a P value of 0.818 (P value >0.05), implying that the model was valid. CI, confidence interval; ED, erectile dysfunction; HbA1c, glycosylated hemoglobin; OR, odds ratio; ROC, receiver operating characteristic.

dysfunction. Uremia induces histological changes in the testis which decreases spermatogenic activity and leads to low testosterone levels (23). These lowered testosterone levels lead to a negative feedback state which increases the follicle-stimulating hormones and luteinizing hormones, subsequently elevating the serum prolactin levels. Elevated serum prolactin levels can exacerbate testosterone deficiency by damaging the testis, leading to reduced sexual drive and impaired erectile function (7,23).

Our investigation revealed that elevated HbA1c levels were significantly associated with ED, consistent with findings from previous studies (19,24). Chronic hyperglycemia causes endothelial injury, reducing nitric oxide production and impairing smooth muscle relaxation in the corpus cavernosum, which are critical mechanisms for achieving erections. Secondly, the autonomic nervous system is more susceptible to damage from hyperglycemia, leading to impaired transmission essential for initiating and maintaining erections (25). Furthermore, elevated HbA1c levels are linked to reduced testosterone levels, worsening ED. Insulin resistance in poorly controlled diabetes leads to increased leptin synthesis, which impairs Leydig cell activity and suppresses testosterone production. Additionally, insulin resistance results in a decrease in hepatic sex hormone-binding globulins further lowering testosterone levels (26).

ED is a microvascular issue commonly associated with inadequate glycemic control (24). A systematic review of 58 studies comprising 66,925 diabetic males revealed the association between HbA1c, ED, and nephropathy (27). Diabetic nephropathy, a microvascular complication of diabetes, is closely linked to elevated HbA1c levels and the development of ED. The progression of nephropathy often correlates with the decline of erectile function, highlighting the interconnectedness of both conditions (28). The average

HbA1c level in our study was 8.47%, which is a suboptimal level and places at high risk for ED. HbA1c levels should ideally be targeted below 7.0%, as this has been shown to decrease the incidence of ED and in some cases, lead to partial or complete recovery in patients experiencing ED (24).

The study's small sample size limited its ability to comprehensively evaluate the relationship between different stages of CKD in DM patients and ED. Notably, a meta-analysis highlighted that CKD stages III and IV had the highest prevalence of ED, as identified in only two out of 34 studies. This underscores the need for further research to validate these findings. Additionally, the small sample size reduces the generalizability of the study's results (29).

Our study did not demonstrate the same level of significance as previous research regarding the relationship between diabetes duration and ED (3,29). It is well-established that a longer duration of type 2 DM increases the risk of diabetes-related complications in patients (24). This notion is supported by the systematic study conducted by Dilixiati *et al.* [2024], which suggests that comorbidities associated with DM pose a greater risk for ED than diabetes duration alone (27). Additionally, DM-related comorbidities such as non-alcoholic fatty liver disease, obstructive sleep apnoea, and others are found to be significantly associated with ED (30,31). Future research should consider the broader spectrum of comorbidities and their potential synergistic effects on ED.

Depression is often associated with ED. This result is also postulated in our study with 32.5% of our respondents with ED fulfilling the criteria for depression, however, we were unable to show its correlation due to sample size limitations. The burden of CKD complications, along with unemployment and financial constraints, likely contributes to depression, which in turn reduces sexual frequency (7).



Elevated cortisol levels during psychological stress disrupt the balance of sex hormones leading to decreased libido and erectile function. Simultaneously the release of adrenaline is released as part of the stress reaction, causing vasoconstriction leading to decreased penile blood flow (8). Depression further negatively impacts mood and mental health which further decreases libido.

As with all research, there are several limitations to our study. The first is the study design where a cross-sectional study which limits causal inference. Longitudinal studies are needed to better establish temporal relationships between risk factors and ED. Another limitation of our study is that the cohort was primarily composed of individuals of Malay ethnicity, which limits the generalizability of our findings. Future research should include more diverse cohorts to enhance the applicability of the results. Our study lacks data on ED treatment and patient's willingness to seek treatment, which may have influenced the reported prevalence. Future research should systematically explore these aspects for a comprehensive understanding of treatment-seeking behavior in this population.

The prevalence of the ED in this study was based on IIEF-5, which is a self-administered questionnaire. Cavernosometry is the gold standard for evaluating erectile capability, but it is not practical for a population-based study like ours. The responses gathered from the IIEF-5 cater to the condition in the preceding 4 weeks thus acute conditions or events may influence the outcomes.

## Conclusions

This study highlights a high prevalence of ED among patients with DM and CKD. Significant factors associated with ED included educational level, metformin use, and elevated serum urea and HbA1c levels. Given the high prevalence of ED in CKD patients, it is crucial for physicians to address sexual health during consultation. Larger, population-based studies are needed to accurately determine the burden of disease in local populations. Such research is essential to guide the implementation of effective preventive and treatment strategies, ultimately improving patients' health outcome.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://tau.amegroups.com/article/view/10.21037/tau-2024-751/rc>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://tau.amegroups.com/article/view/10.21037/tau-2024-751/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Human Research Ethics Committee of Universiti Sains Malaysia (No. USM/JEPeM/22050284) and informed consent was obtained from all individual participants.

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