

Original Research Article

Prevalence of Erectile Dysfunction and Associated Factors among Adults Accessing Services at Ndola Teaching Hospital from 2017 to 2022

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Abstract: Erectile dysfunction is a prevalent urological problem affecting 3%-76.5% of men globally, yet its prevalence and associated factors in Zambia remain unknown. Therefore, this study aimed to investigate the prevalence of erectile dysfunction and associated factors among adults accessing services at Ndola Teaching Hospital from 2017 to 2022. This retrospective cross-sectional study involved 500 male patients from 2017 to 2022, both with and without erectile dysfunction. The study used Stata/SE version 17 for univariate and multiple logistic regression analyses, with a p-value of <0.05 indicating statistical significance. The prevalence of erectile dysfunction was found to be 34.7%. Formal employment (AOR 0.38; 95% CI: [0.15 – 0.94], $p = 0.037$), married (AOR 0.35; 95% CI: [0.13 – 0.95], $p = 0.039$), single (AOR 0.09; 95% CI: [0.02 – 0.35], $p = 0.001$), and widowed (AOR 0.03; 95% CI: [0.01 – 0.13], $p < 0.001$) were associated with a reduced risk of developing erectile dysfunction. Drinking alcohol (AOR 8.50; 95% CI: [3.98 – 18.16], $p < 0.001$), diabetes mellitus (AOR 34.3; 95% CI: [13.75 – 85.60], $p < 0.001$), hypertension (AOR 3.90; 95% CI: [1.77 – 8.59], $p = 0.001$), anti-depressants (AOR 17.2; 95% CI: [6.18 – 47.92], $p < 0.001$) and Obesity (AOR 28.8; 95% CI: [2.42 – 343.99], $p = 0.008$) were associated with increased risk of developing erectile dysfunction. The study revealed that erectile dysfunction is a prevalent problem among men, with several risk factors identified, emphasizing the need to address these to prevent and effectively treat the condition.

Keywords: Erectile dysfunction, Men, associated factors, prevalence, Ndola Teaching Hospital, Risk factors, Urological services.

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INTRODUCTION

Erectile dysfunction (ED) is a widespread medical condition experienced by men regardless of their age but is more common in older men. It is marked by the failure to reach or sustain the required erection for successful coitus, and has multiple causes, including both physical and psychological factors (Nguyen & Hellstrom, 2017). Global statistical estimates show that ED is one of the most common urological problems in men affecting about 3-76.5% worldwide (Kessler *et al.*, 2019). Studies that have been done on the prevalence of ED have reported varying results. In Europe and Asia, studies reported ED estimates ranging from 19.3% to 81.5 (Bin Nordin *et al.*, 2019; Paulsen *et al.*, 2020; Li *et al.*, 2022; Herkommer *et al.*, 2023; Rezali *et al.*, 2023). In sub-Saharan Africa, ED estimates of 29.7% were reported in Tanzania (Nyalile *et al.*, 2020) and an ED rate of 58.9% was reported in Nigeria (Oyelade *et al.*, 2016).

In Zambia, a previous study reported a prevalence of 58.6% (Chitambala & Bowa, 2020).

Erectile dysfunction has multiple causes, including both physical and psychological factors (Nguyen *et al.*, 2017). There are three types of causes: iatrogenic (connected to medical or surgical therapy), neurogenic (affecting innervation and nerve function), and nonendocrine (affecting blood supply) (Yafi *et al.*, 2016). Lower serum testosterone levels are one of the endocrine factors associated with erectile dysfunction, however the precise mechanism is however unclear. Psychological factors are frequently involved in organic erectile dysfunction, which has a detrimental effect on mood, relationships with others, and overall quality of life (Yafi *et al.*, 2016). Neurogenic erectile dysfunction is caused by an inadequate transmission of nerve signals to the corpora cavernosa. This can result from various conditions, such as traumatic brain injury, spinal cord

injury, Parkinson's disease, multiple sclerosis, lumbar disc disease, radical pelvic surgery (such as radical prostatectomy, radical cystectomy, abdominoperineal resection) and also diabetes (Yafi *et al.*, 2016). Organic erectile dysfunction is most commonly caused by vasculogenic factors. Reduced blood flow, arterial insufficiency or arterial stenosis resulting from vascular disease and endothelial dysfunction can lead to erectile dysfunction (Yafi *et al.*, 2016).

Given its high prevalence and impact on quality of life, erectile dysfunction is a major burden on society and is also a significant risk factor for cardiovascular disease, dementia and mortality (Kessler *et al.*, 2019). A review of the studies found that the existing findings from longitudinal studies suggest that erectile dysfunction is an important predictor of the risk of CVD (Corona *et al.*, 2020). In addition, a meta-analysis found that the presence of erectile dysfunction increased the risk of depression (OR: 2.92, 95% CI: 2.37-3.60) than in those without erectile dysfunction (Liu *et al.*, 2018). Furthermore, the majority of erectile dysfunction complications are emotional for the patient as well as his spouse. It may negatively affect these individuals' quality of life and put a strain on relationships (Sooriyamoorthy & Leslie 2023). Men with erectile dysfunction experience relationship difficulties and reduced sexual satisfaction, while women experience less satisfaction and sexual activity when their partner develops erectile dysfunction. Erectile dysfunction also places a substantial economic burden on employers, as men who suffer from erectile dysfunction between the ages of 40 and 70 have higher rates of absenteeism and reduced productivity at work (Elterman *et al.*, 2021).

Furthermore, previous studies suggest that ED is associated with a multifactorial and complex interplay between socio-demographic, psychological and clinical factors (Yafi *et al.*, 2016; Montejo *et al.*, 2019; Rothmore 2020; Sooriyamoorthy & Leslie 2023). Various studies conducted in different parts of the world have reported a wide range of prevalence and associated factors. However, in Zambia, the prevalence of erectile dysfunction and its associated factors are still poorly understood due to limited studies. By determining the prevalence of erectile dysfunction and associated factors in a specific population, healthcare professionals can better understand the impact of this condition on individuals and develop targeted interventions. Hence, further studies are required for a better understanding. This study therefore, brings out findings on the prevalence of erectile dysfunction and associated factors among adults accessing services at Ndola Teaching Hospital, from 2017 to 2022.

MATERIALS AND METHODS

Study Design

The study used a retrospective cross-sectional design that involved the extraction of secondary data

from the patient records of Ndola Teaching Hospital from 2017 to 2022.

Study Setting

The study was conducted at the Ndola Teaching Hospital, Department of Urology, in the Copperbelt Province of Zambia. The selection of this hospital was due to its status as the main referral centre for urology cases in the province. In particular, the Department of Urology was chosen because it oversees the treatment of all urological problems in the male population, including erectile dysfunction.

Study Population and Sample size

This study focuses on male patients managed by the Department of Urology at Ndola Teaching Hospital from 2017 to 2022. The study included all male patients with various conditions and excluded those with missing diagnosis information or patient record files. The study reviewed all files of patients from 2017 to 2022 that met the selection criteria, aiming to include all patients seen over a five-year period. A total of 500 files were retrieved and included in the study.

Data Collection

At the outset of data collection, authors visited the Urology Department at Ndola Teaching Hospital, where they extracted patient medical files of all male patients treated under the department from 2017 to 2022. The medical files were screened for eligibility, and only those that met the study criteria were retained. Utilizing a data extraction checklist, information on ED and potential predictors was extracted from the patient medical files. Google forms was used to capture data. This process occurred daily over the data collection period, spanning from December 2023 to January 2024. The variables included in the study were determined through a review of relevant literature. The outcome variable of interest was erectile dysfunction, categorized as a binary variable ('yes' for confirmed diagnosis of ED and 'no' if not diagnosed with ED). Additionally, various explanatory variables were considered; including socio-demographic factors such as age, occupation, marital status, location, and education level. Lifestyle-related factors included the history of smoking, drug abuse, and alcohol consumption among participants. Clinical factors included the presence of co-morbidities such as diabetes, hypertension, chronic kidney disease, cancer, HIV, as well as the history of specific surgeries (penile/prostate/testicular).

Data Analysis

Data was analyzed using Software STATA version 17.0 (StataCorp LLC, College Station, TX). Descriptive statistics were used to summarize and describe all participants' characteristics. Categorical variables were summarized as percentages and frequencies. Continuous variables were summarized using medians and interquartile ranges as the data did not meet the normality assumption. The prevalence of

erectile dysfunction was estimated by taking the number of patients that were diagnosed with erectile dysfunction and dividing it by the total number of study participants.

In order to determine the factors associated with erectile dysfunction, multi-variable logistic regression was used to determine factors associated with erectile dysfunction. This was performed both at unadjusted and adjusted levels. At adjusted logistic regression analysis, the machine led stepwise logistic regression and investigator lead stepwise regression were performed. The final model was based on investigator led backward logistic regression analysis and all explanatory variables with a p-value <0.05 were retained in the model. The Akaike Information Criteria (AIC) and the Bayesian Information Criteria (BIC) were used to determine the best-fit model. All forms of analysis in this study were performed at a 5% significance level and 95% confidence level.

Ethical Considerations

The study was approved by the University of Lusaka Research Ethics Committee (REF No: FWA00033228-03311/23). The study was approved by the Ministry of Health, Ndola Teaching Hospital's Senior Medical Superintendent, and the Head of Urology Department, and confidentiality was maintained by

extracting no patient personal information or identifiers from hospital record files.

RESULTS

Demographic Factors

Table 1 shows the demographic characteristics of the study participants. A total of 500 records for men between 2017 and 2022 were included in the study. The average age of men is 46 (37–60) years. Regarding their employment status, 184 (36.9%) were in formal employment, 141 (28.3%) were in informal employment/self-employment and 127 (25.4%) were unemployed. Most participants were married (274, 54.8%). More than three quarters were non-smokers (411, 82.7%), and more than two thirds of the participants did not consume alcohol (345, 69.4%). Regarding co-morbidities, most participants did not have diabetes (398, 80.1%), did not have hypertension (363, 72.9%), did not have chronic kidney disease (457, 91.9%), did not have cancer (490, 98.4%) and were HIV negative (343, 68.6%). In addition, most participants were not taking antidepressants (402, 80.9%), not taking cardiovascular medications (484, 97%), not taking antibacterial medications (489, 98%), and not taking anti-cholinergic medications (494, 98.8%). Furthermore, most participants were not obese (476, 97.7%).

Table 1: Demographic factors of study participants accessing urological services at Ndola Teaching Hospital from 2017 to 2022 (n=500)

Demographic factors	Median	Interquartile range
Age	46	37 – 60
Demographic factors	Frequency (n)	Percent (%)
Employment Status		
Student	47	9.4
Unemployed	127	25.5
Formal employment	184	36.9
Informal employment/self-employed	141	28.3
Total	499	100
Marital status		
Divorced	56	11.2
Married	274	54.8
Single	109	21.8
Widower	61	12.2
Total	500	100
Smoking		
No	411	82.7
Yes	86	17.3
Total	497	100
Alcohol Consumption		
No	345	69.4
Yes	152	30.6
Total	497	100
Diabetes		
No	398	80.1
Yes	99	19.9
Total	497	100
Hypertension		
No	363	72.9

Yes	135	27.1
Total	498	100
Chronic Kidney disease		
No	457	92
Yes	40	8.1
Total	497	100
Cancer		
No	490	98.4
Yes	8	1.6
Total	498	100
HIV Status		
Negative	343	68.6
Positive	95	19
Unknown	62	12.4
Total	500	100
Anti-depressants		
No	402	80.9
Yes	95	19.1
Total	497	100
Cardiovascular Medication		
No	484	97
Yes	15	3
Total	499	100
Antibiotics		
No	489	98
Yes	10	2
Total	499	100
Anti-cholinergic		
No	494	98.8
Yes	6	1.2
Total	500	100
Obese		
No	476	97.7
Yes	11	2.3
Total	487	100

Prevalence of erectile dysfunction among adults

The study determined the prevalence of erectile dysfunction among male patients accessing urological

services at Ndola Teaching Hospital from 2017 to 2022. The prevalence of erectile dysfunction was found to be 34.7% as shown in Figure 1.

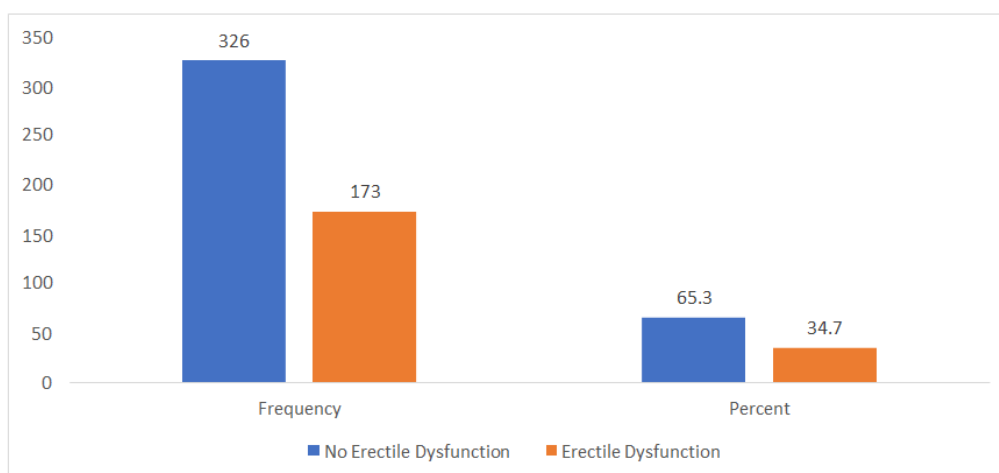


Figure 1: Prevalence of erectile dysfunction among male patients accessing urological services at Ndola Teaching Hospital from 2017 to 2022

Table 2 shows that the ED rate was higher in older men over 45 years of age than in younger men aged 45 years or younger (39.1% versus 29.5%, $p = 0.024$).

Table 2: The distribution of Erectile dysfunction by age groups among patients accessing urological services at Ndola Teaching Hospital from 2017 to 2022

Presence of Erectile Dysfunction				
Age Group	Yes	No	Total	P value
17 – 45 years	69 (29.5%)	165 (70.5%)	234 (100.0%)	0.024
46 – 91 years	104 (39.1%)	162 (60.9%)	266 (100.0%)	
Total	173 (34.6%)	326 (65.4%)	499 (100.0%)	

Risk factors associated with erectile dysfunction among adults at Ndola Teaching Hospital

Additionally, univariate and multi-variable logistic regression analysis was performed to identify significant factors associated with erectile dysfunction. The results of the univariate analysis in Table 3 show that age, employment status, marital status, smoking, alcohol consumption, diabetes, hypertension, chronic kidney disease, HIV status, anti-depressants, cardiovascular medication, and obesity were associated with erectile dysfunction among male patients ($p < 0.05$).

In the multi-variable regression analysis after accounting for the influence of other variables, formal employment, being married, single, and widowed were associated with a lower risk of developing erectile dysfunction, while alcohol consumption, diabetes, hypertension, antidepressants, and obesity were associated with an increased risk of developing erectile dysfunction. The multi-variable logistic regression analysis revealed that formal employment was associated with a lower risk of developing erectile dysfunction compared to unemployment (AOR 0.38; 95% CI: [0.15

– 0.94], $p = 0.037$). Compared to divorced, married (AOR 0.35; 95% CI: [0.13 – 0.95], $p = 0.039$), single (AOR 0.09; 95% CI: [0.02 – 0.35], $p = 0.001$), and widowed (AOR 0.03; 95% CI: [0.01 – 0.13], $p < 0.001$) were associated with a reduced risk of developing erectile dysfunction.

Drinking alcohol was associated with an eight times greater risk of developing erectile dysfunction than abstaining from alcohol (AOR 8.50; 95% CI: [3.98 – 18.16], $p < 0.001$). Diabetes mellitus was associated with a higher risk of developing erectile dysfunction than without diabetes mellitus (AOR 34.3; 95% CI: [13.75 – 85.60], $p < 0.001$). Hypertension was associated with 3.90 times the risk of developing erectile dysfunction than not having hypertension (AOR 3.90; 95% CI: [1.77 – 8.59], $p = 0.001$). Anti-depressants were associated with the increased risk of developing erectile dysfunction (AOR 17.2; 95% CI: [6.18 – 47.92], $p < 0.001$). Obesity was associated with increased risk of developing erectile dysfunction (AOR 28.8; 95% CI: [2.42 – 343.99], $p = 0.008$).

Table 3: Risk factors associated with erectile dysfunction among adults at Ndola Teaching Hospital

Demographic factors	COR (95% CI)	P-value	AOR (95% CI)	P-value
Age	1.01 (1.00 - 1.03)	0.025		
Employment Status				
Unemployed	Ref		Ref	
Student	1.16 (0.58 - 2.29)	0.68	2.92 (0.82 - 10.38)	0.098
Formal employment	0.71 (0.44 - 1.14)	0.157	0.38 (0.15 - 0.94)	0.037
Informal employment/self-Employed	1.02 (0.62 - 1.68)	0.922	0.48 (0.19 - 1.22)	0.125
Marital status				
Divorced	Ref		Ref	
Married	0.45 (0.25 - 0.80)	0.007	0.35 (0.13 - 0.95)	0.039
Single	0.29 (0.15 - 0.58)	<0.001	0.09 (0.02 - 0.35)	0.001
Widower	0.26 (0.12 - 0.58)	0.001	0.03 (0.01 - 0.13)	<0.001
Smoking				
No	Ref			
Yes	4.14 (2.54 - 6.73)	<0.001		
Alcohol Consumption				
No	Ref		Ref	
Yes	10.78 (6.92 - 16.79)	<0.001	8.50 (3.98 - 18.16)	<0.001
Diabetes				
No	Ref		Ref	
Yes	30.36 (15.50 - 59.44)	<0.001	34.31 (13.75 - 85.60)	<0.001
Hypertension				
No	Ref		Ref	

Yes	10.17 (6.45 - 16.04)	<0.001	3.90 (1.77 - 8.59)	0.001
Chronic Kidney disease				
No	Ref			
Yes	2.50 (1.30 - 4.80)	0.006		
Cancer				
No	Ref			
Yes	3.19 (0.75 - 13.53)	0.115		
HIV Status				
Negative	Ref			
Positive	4.15 (2.58 - 6.68)	<0.001		
Unknown	1.36 (0.76 - 2.42)	0.3		
Anti-depressants				
No	Ref		Ref	
Yes	40.56 (18.92 - 86.95)	<0.001	17.20 (6.18 - 47.92)	<0.001
Cardiovascular Medication				
No	Ref			
Yes	3.97 (1.34 - 11.82)	0.013		
Antibiotics				
No	Ref			
Yes	1.26 (0.35 - 4.53)	0.721		
anti-cholinergic				
No	Ref			
Yes	1.91 (0.38 - 9.54)	0.433		
Obese				
No	Ref		Ref	
Yes	20.71 (2.63 - 163.22)	0.004	28.84 (2.42 - 343.99)	0.008

DISCUSSION

The study aimed to investigate the prevalence of erectile dysfunction and associated factors among adults accessing services at Ndola Teaching Hospital from 2017 to 2022. The prevalence of erectile dysfunction was 34.7%. Associated with erectile dysfunction were employment status, marital status, alcohol consumption, diabetes, hypertension, antidepressants and obesity.

The study found that 34.7% of male patients treated in the urology department suffered from erectile dysfunction. The reported prevalence of 34.7% highlights the significant burden of erectile dysfunction in male patients treated in the urology department. It highlights the importance of addressing sexual health issues in clinical practice and public health interventions to improve the overall well-being and quality of life of people with erectile dysfunction. Similar prevalence rates of ED were reported in studies from Malaysia (31.6%) (Rezali *et al.*, 2023) and Tanzania (29.7%) (Nyalile *et al.*, 2020). In contrast, lower prevalence rates of ED (21%) were reported in studies from Germany (Herkommer *et al.*, 2023) and Pakistan (Saeed *et al.*, 2021). In a Danish study, the prevalence of erectile dysfunction among the general population was 19.3% (Paulsen *et al.*, 2020). On the other hand, higher prevalence rates of ED were reported in studies from United Kingdom (41.5%) (Li *et al.*, 2022) and Nigeria (58%) (Oyelade *et al.*, 2016). Differences in prevalence rates between studies may be due to methodological

differences. These include differences in study design, sampling methods, diagnostic criteria for ED and population characteristics. Due to differences in study populations and settings, hospital-based studies such as this one may report different prevalence rates than population-based studies. Due to differences in study participants and the specific hospital department used for the study, the results of hospital-based studies may vary.

The study identified factors associated with ED. Formal employment, being married, single or widowed were associated with a lower risk of ED. On the other hand, risk factors such as alcohol consumption, diabetes, high blood pressure, antidepressants and obesity were associated with an increased risk of ED. Formal employment was associated with a lower risk of developing erectile dysfunction compared to unemployment. Consistent with this finding, a study from Malaysia also found a significant association between employment status and erectile dysfunction (Rezali *et al.*, 2023). The possible reason for observing such a finding is unknown, but it could be speculated that the stability and financial security provided by formal employment may reduce stress levels, which is known to be a contributing factor to erectile dysfunction.

Compared to being divorced, being married, single or widowed were associated with a lower risk of erectile dysfunction. Consistent with the findings of this study, previous studies from Malaysia also found that relationship/marital status was associated with erectile dysfunction (Bin Nordin *et al.*, 2019; Rezali *et al.*, 2023).

The possible explanation for observing such results could be that the lower risk of dysfunction among married, single, or widowed individuals could be due to factors such as companionship, intimacy, and overall relationship satisfaction. However, it is important to recognize that the results may be influenced by reverse causality, as erectile dysfunction can strain relationships and potentially lead to divorce. Therefore, more research is needed to establish a definitive cause-and-effect relationship between marital status and the development of erectile dysfunction.

Drinking alcohol was associated with an eight times greater risk of developing erectile dysfunction than abstaining from alcohol. These findings are supported by findings from a study from Pakistan that found that males that used alcohol were at increased risk of erectile dysfunction (Saeed *et al.*, 2021). The results of this study also confirm previous findings suggesting that alcohol is associated with a higher risk of erectile dysfunction (Irfan *et al.*, 2020; Byemero *et al.*, 2023). Diabetes mellitus was another factor that was associated with a higher risk of developing erectile dysfunction than without diabetes mellitus. These findings are in line with studies from United States of America, Pakistan, Indonesia and Germany which reported that male patients with diabetes were at increased risk of erectile dysfunction (Hallanzy *et al.*, 2019; Kloping *et al.*, 2019; Saeed *et al.*, 2021; Pellegrino *et al.*, 2023). This increased risk is primarily due to the damage that diabetes can cause to blood vessels and nerves, which are essential for normal erectile function (Yafi *et al.*, 2016). It is therefore important for individuals with diabetes to closely monitor and manage their blood sugar levels in order to reduce the risk of developing erectile dysfunction.

Hypertension was associated with 3.90 times the risk of developing erectile dysfunction than not having hypertension. These findings are very similar to what has been found in a previous study from United States of America where hypertension has been found to be associated with erectile dysfunction (Pellegrino *et al.*, 2023). Another study from Tanzania also reported an association between hypertension and erectile dysfunction (Nyalile *et al.*, 2020). Similarly, study from Indonesia found that hypertension was associated with an increased risk of erectile dysfunction (Kloping *et al.*, 2019). This significant increase in risk highlights the strong correlation between hypertension and erectile dysfunction. It is crucial for individuals with hypertension to closely monitor their blood pressure and seek appropriate medical treatment to mitigate the potential impact on their sexual health.

Anti-depressants were associated with the increased risk of developing erectile dysfunction. According to recent studies, it has been noted that patients using anti-depressants are more likely to experience erectile dysfunction compared to those who

are not on medication (Montejo *et al.*, 2019; Rothmore, 2020). The exact mechanism behind this correlation is still unclear, but it is believed that certain chemicals present in the medication may interfere with the normal functioning of the male reproductive system (Rothmore, 2020). As a result, patients may experience difficulties in achieving and maintaining an erection. It is important for healthcare providers to closely monitor patients on these medications and explore alternative treatment options or adjustments in dosage to minimize the risk of developing erectile dysfunction.

The study revealed that obesity was associated with an increased risk of developing ED. This finding is in line with studies from the United States of America and China, which reported that obesity was associated with erectile dysfunction (Liu *et al.*, 2023; Pellegrino *et al.*, 2023). Obesity is reported to lead to hormonal imbalances, decreased testosterone levels, and reduced blood flow, all of which contribute to difficulties in achieving and maintaining an erection (Skrypnik *et al.*, 2014; Moon, Park & Kim, 2019). Moreover, obesity is often accompanied by underlying health conditions such as high blood pressure and diabetes, which further heighten the risk of erectile dysfunction (Zatońska *et al.*, 2021; Ejigu & Tiruneh, 2023). Therefore, adopting a healthy lifestyle and losing weight can significantly improve sexual health and prevent the onset of erectile dysfunction.

Even though the study showed higher ED rate in older men aged over 45 years than in younger men aged 45 years or younger, the regression analysis did not show any association between age and erectile dysfunction. These findings are in contrast with the previous studies from United States of America and Tanzania, which reported that increasing age was associated with erectile dysfunction (Nyalile *et al.*, 2020; Pellegrino *et al.*, 2023). In this study, smoking was not associated with erectile dysfunction, which is inconsistent with the results of the previous studies from Pakistani, Democratic Republic of Congo and Cameroon, which revealed that active smokers were at a higher risk of erectile dysfunction when compared with participants with no smoking history (Saeed *et al.*, 2021; Byemero *et al.*, 2023; Nkafu *et al.*, 2023).

Limitations of the study include its cross-sectional nature, which makes it impossible to draw any conclusions about causality. In addition, the prevalence of erectile dysfunction may not be generalizable to the general population as this was a hospital-based study.

CONCLUSION

The study found that erectile dysfunction is common in men, with a rate of 34.7%. Several risk factors, including unemployment, divorce, alcohol consumption, diabetes, hypertension, antidepressant use and obesity, were identified as being associated with an increased likelihood of erectile dysfunction. The study

emphasises the importance of addressing these risk factors to prevent and effectively manage erectile dysfunction, and highlights the need for comprehensive assessment and management of underlying health conditions to improve sexual health outcomes.

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Availability of data and materials

The data used in the current study is available from the corresponding author [C.K] upon reasonable request.

Competing Interests: The authors declare that there is no conflict of interest.

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Author Contribution

C.K contributed to the conception, design of the study, data collection, analysis, interpretation of data and drafting of the manuscript. E.K contributed to the design of the study, interpretation of data, drafting of the manuscript and critical revision of the manuscript for intellectual content. J.L participated in the analysis of the data, interpretation of the data, and drafting of the manuscript. All authors approved the final manuscript for publication.

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