

# Erectile Dysfunction and Associated Factors among Diabetes Mellitus Men at North East Amhara Comprehensive Specialized Hospitals

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## ABSTRACT

**Background:** Erectile dysfunction among diabetic patients ranges from 20%-90% and is the most neglected problem. It can affect all aspects of client life, including physical, emotional, social, sexual and relationships. Little has been studied in developing countries like Ethiopia; therefore, this study assesses the proportion of erectile dysfunction and associated factors among men with diabetes mellitus in north east Amhara comprehensive specialized hospitals.

**Methods:** A hospital-based cross-sectional study design was used from July to August 2023. A total of 361 participants were selected using the systematic random sampling method. The data were collected using pretested interviewer-administered questionnaires. The study tool for the outcome variable was checked for reliability using the Cronbach alpha test (0.7). The data were entered into Epi data version 4.2 and exported to Statistical Package for Social Science (SPSS) version 23 for further analysis. A binary logistic regression model was used to identify the association between dependent and independent variables. Finally, a p-value less than 0.05 was used as statistically significant.

**Result:** The proportion of erectile dysfunction among men with diabetes mellitus was 59% (95% CI 53.4%-64.4%). Being in the age group of 31-44 (AOR 4.46, 95% CI: 1.06-18.81); 45-59 (AOR 18.2, 95% CI: 2.9-34.5) and  $\geq 60$  years (AOR 19.7, 95% CI: 2.3-36.8). The presence of diabetic complications (AOR 5.5, 95% CI: 1.61-18.58) and the presence of co-morbidities (AOR 3.8, 95% CI: 1.3-10.6) were factors associated with erectile dysfunction. In addition, regular exercise (AOR 1.5, 95% CI: 0.07-0.33) and good glycemic control (AOR 1.5, 95% CI: 0.158-0.886) are inversely associated with erectile dysfunction.

**Conclusion:** The proportion of erectile dysfunction was high. So, there is a need for health care providers to incorporate screening for sexual dysfunction, like other complications of diabetes. This helps to prevent its early occurrence by reducing the occurrence of diabetic complications, treating co-morbidities, promoting good glycemic control and providing health information about engaging in regular exercise.

**Keywords:** Erectile dysfunction; Diabetes mellitus; Glycemic control

**Abbreviations:** AOR: Adjusted Odds Ratio; CI: Confidence Interval; COR: Crude Odds Ratio; DCSH: Dessie Comprehensive Specialized Hospital; DM: Diabetes Mellitus; ETB: Ethiopian Birr; IIEF-5: International Index Erectile Function; NIH: National Institute of Health; OPD: Out Patient Department; SD: Standard Deviation; SPSS: Statistical Package for Social Science; USA: United State of America; WCSH: Woldia Comprehensive Specialized Hospital; WHO: World Health Organization

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## INTRODUCTION

Medical treatment of erectile dysfunction and the National Institution of Health (NIH) consent conference panel define erectile dysfunction as the inability to attain or maintain penile erection to perform satisfactory sexual intercourse. It is a major problem in the world with a variety of severity and medical conditions like cardiovascular, endocrine and metabolic abnormalities, which are increasing from time to time due to sedentary lifestyles and changes in feeding styles from organic food to processed and trans food. The process of achieving penile erection involves complex processes. Result from the integration of psychological, neurological and vascular processes, which combine to initiate a physiologic response within the penile vasculature. The pathogenesis of erectile dysfunction results from vasculopathy, neuropathy, visceral adiposity, insulin resistance and hypogonadism. Diabetic vasculopathy concerns macroangiopathy, microangiopathy and endothelial dysfunction. Macrovascular disease in diabetes corresponds to atherosclerotic damage in the blood vessels, which limits blood flow to the penis [1].

The World Health Organization (WHO) reported that around 422 million adults lived with diabetes in 2014; diabetes increased the risk of erectile dysfunction threefold. A review of 145 studies states that the prevalence of erectile dysfunction among all types of diabetic patients was 52.5. The odds of having erectile dysfunction are three times higher as compared to the same age group of non-diabetic men. The magnitude of erectile dysfunction in all age groups without considering special medical causes is around 10%; this figure increases with age; the magnitude for age 50-80 was 35%-60% and the presence of other comorbidities increases its risk. Erectile dysfunction diabetic patients were 2-4 times and 10-15 years early within the same age as compared to non-diabetic patients.

Different studies showed that in the in the USA, Boston, Japan and Turkey, the proportion of erectile dysfunction was 48.5%, 90% and 72%, respectively. Studies from Africa content: In Nigeria, Egypt and Tanzania, the proportion of erectile dysfunction was 58%, 42.9% and 55.5%, respectively. Factors associated with erectile dysfunction among diabetes patients were older age, increased duration of diabetes, poor glycemic control, alcohol drinking, smoking cigarettes, the presence of comorbidity, overweight, hypertension, other cardiovascular diseases and the presence of diabetes complications like diabetic nephropathy, retinopathy and neuropathy [2].

Though different guidelines and implementation manuals recommended that all adults with diabetes should be screened for erectile dysfunction using sexual function history, there is still a gap in implementing a screening program; only 10% of patients discussed their problem with their physician. Moreover, erectile dysfunction was an independent predictor of poor glycemic control, other co-morbidities like hypertension, cardiovascular abnormalities and late complications of diabetes like nephropathy, neuropathy and macro- and microvascular problems. Erectile dysfunction affects the quality of life; males feel depressed and loss of self-confidence may end with divorce. For female partners, the magnitude of reduced sexual interest is

relatively higher for those who live with impotent men than non-impotent men (60%, 29% respectively).

Though the problem is very high in developing countries like Ethiopia, little has been known about the issue. Many men with diabetes develop erectile dysfunction at a young age or in middle adulthood in the study area, but due to cultural and social barriers, the problem is not discussed with health care professionals. Therefore, this study aims to assess the proportion of erectile dysfunction and factors associated with men with diabetes mellitus in Ethiopia [3].

## MATERIALS AND METHODS

### Study area and period

This study was conducted at north east Amaha region compressive specialized hospitals from July to August 2023. There are two compressive specialized hospitals, which are Dessie Compressive Specialized Hospital (DCSH) and Woldia Compressive Specialized Hospital (WCSH). DCSH is located in the northeast part of Ethiopia in the South Wollo administrative zone of the Amara region, located 401 km away from the capital city, Addis Ababa and 425 km from Amara regional stat city, Bahir Dar. According to the central statistics agency report, Dessie has an estimated total population of 151,094 and DCSH has 300 beds providing health services to the people of Dessie and the adjacent regions. Diabetic care and follow-up is one of the many services delivered by the unit. A total of 1000 clients with diabetes are on follow-up at DCSH. WCSH is located 521 km from the capital city of the country and 388 km from Bahir Dar, the capital city of the Amhara region. The hospital serves 3.5 million people in the north Wollo zone and its neighbors' regions. The hospital has 240 beds and provides chronic care and follow-up services. Currently, the total number of adult patients attending the service is 800.

### Study design

An institutional-based cross-sectional study design was conducted using the quantitative data collection method.

### Source population

All men with diabetes mellitus who were on follow-up at north east Amhara compressive specialized hospitals.

### Study population

All men with diabetes mellitus who were on follow-up at north east Amhara compressive specialized hospitals during the study period.

### Inclusion criteria and exclusion criteria

**Inclusion criteria:** All men with diabetes mellitus who were on follow-up at north east Amhara compressive specialized hospitals aged above 18 years old and married or in a sexual relationship were included in the study.

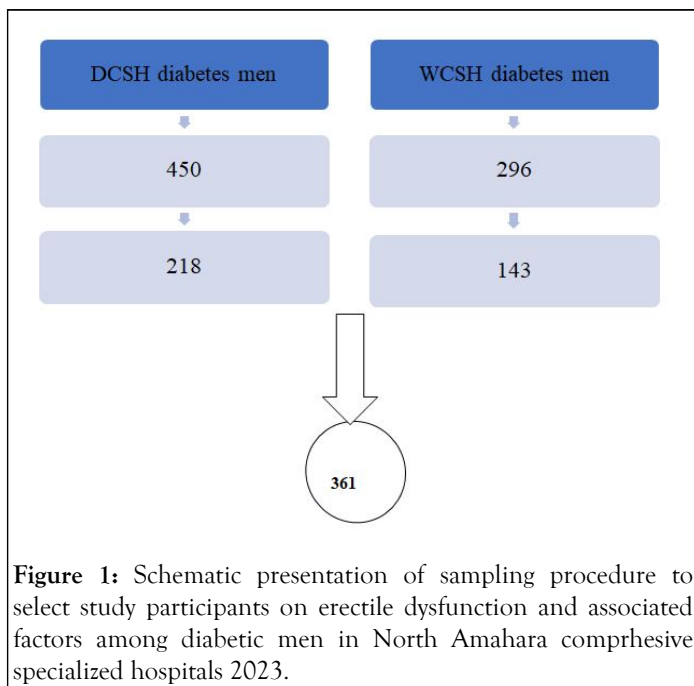
**Exclusion criteria:** Diabetic men who had a history of pelvic surgery, a history of pelvic and spinal cord trauma and were unable to communicate due to severe pain were excluded from the study.

### Sample size determination

The sample size was determined by using a single population proportion from a study conducted in central and northern Tigray with a proportion of erectile dysfunction of 69.9%. After considering the 10% non-response rate, the final sample size was 361.

### Sampling technique and sampling procedure

The list of all diabetic patients at Dessie comprehensive specialized hospital and Woldia comprehensive specialized hospital was recorded. A proportional allocation was made based on the case load. Then, from the given lists, 361 study participants were selected by using a simple random sampling technique (Figure 1) [4].



**Figure 1:** Schematic presentation of sampling procedure to select study participants on erectile dysfunction and associated factors among diabetic men in North Amahara comprehensive specialized hospitals 2023.

### Variables

**Dependent variable:** Erectile dysfunction.

**Independent variables:** Socio-demographic and economic factors include age, educational level and economic level. Personal and behavioral factors include smoking cigarettes, chat chewing, drinking alcohol, physical exercise and fruit and vegetable consumption. Diabetic-related factors include type of DM, duration of DM and the presence of other complications like neuropathy, nephropathy and retinopathy. Co-morbid conditions include obesity, overweight, hypertension and cardiovascular disease [5].

### Operational definition

**Erectile dysfunction:** International Index of Erectile Function (IIEF-5) score less than 22. Severe (1-7), moderate (8-12), mild-moderate (12-16), mild (17-21) and no erectile dysfunction (22-25).

**Good glycemic control:** HbA1C < 7 mg/dl

**Poor glycemic control:** HbA1C > 7 mg/dl

**Low monthly income:** < 1500 ETB

**Medill income:** 1500-2500 ETB

**High income:** > 2500 ETB

**Hypertension:** BP > 140/90 mmHg

**Overweight:** BMI of 25-30 kg/m<sup>2</sup>.

**Obesity:** BMI of > 30 kg/m<sup>2</sup>

**High physical activity:** A person reaching any of the following criteria: Vigorous intensity activity for at least 3 days per week, achieving a minimum of at least 1,500 minutes per week; or 7 or more days of any combination of walking and moderate vigorous intensity activities per week, achieving a minimum of at least 3,000 minutes per week.

**Moderate physical activity category:** Three or more days per week of vigorous intensity activity for at least 20 minutes per day, 5 or more days per week of moderate-intensity activity or walking for at least 30 minutes per day or 5 or more days per week of any combination of walking and moderate or vigorous intensity activities, achieving a minimum of at least 600 MET-minutes per week [6].

**Low physical activity:** Those who had low levels of physical activity; moderate and high levels of physical activity were collapsed in further analysis.

**Alcohol users:** Participants who have ever consumed a drink that contains alcohol (such as beer, wine, fermented cider like tella, tej, areqi, etc.) during their lifetime.

**Heavy drinkers:** Participants who consume seven drinks per week that contain alcohol.

A smoker is someone who, at the time of the survey, smokes any tobacco product either daily or occasionally. Smokers may be further divided into two categories.

A daily smoker is someone who smokes any tobacco product at least once a day (with the exception that people who smoke every day but not on days of religious fasting are still classified as daily smokers).

**Non-smoker:** Someone who, at the time of the survey, does not smoke at all.

Ex-smokers are people who were formerly daily smokers but currently do not smoke at all.

Never-smokers are those who either have never smoked at all or have never been daily smokers and have smoked less than 100 cigarettes (or the equivalent amount of tobacco) in their lifetime.

## Data collection method and tool

The data was collected using an interview-administered questionnaire for primary data from clients and a chart review for the presence of other co-morbidities and recent laboratory results. The questionnaire was comprised of socio-demographic characteristics, DM-related, co-morbidity and complication questions and the International Index of Erectile Function (IIEF-5) which contains five questions that account for 0-5 and are totally scored from 25. The questionnaires were developed from different texts. Three data collectors and one supervisor who is a health professional were recruited [7].

## Data quality control

To ensure the quality of the data, training was given to data collectors and supervisors. Questionnaires were pre-tested on 5% of the sample size before the actual data collection. Strict supervision was provided by the principal investigator and supervisors. The collected data were checked for completeness, accuracy and consistency by the principal investigator every day. Anything that was unclear was corrected and communicated to the data collectors the next day. The interview-administered questionnaire was prepared in English by adopting the pertinent variables and terminologies from various studies. Then it was translated into the local language of the study area, Amharic. Finally, it was translated back to English by another expert in order to ensure its consistency in meaning.

## Data processing and analysis

The data was entered into Epi data 4.2 and analyzed using SPSS version 23 after cleaning and assumption checking were

performed. Descriptive statistical analysis was done to describe the characteristics of the study participants. Cross-tabulation was used to assess the adequacy of each cell. A binary logistic regression model was fitted to identify the association between independent variables and erectile dysfunction. Both crude and adjusted odds ratios were computed with their 95% confidence intervals and independent variables that showed association with the dependent variable at a p-value less than 0.2 were included in the initial multivariable logistic regression. A P-value less than 0.05 was used to declare statistical significance in this study [8].

## RESULTS

### Socio-economic and demographic factors

From a total of 361 participants, 354 were involved, which gives a response rate of 98%. The mean ages of respondents were  $46.8 \pm 12.8$  SD and 81% were below the age of 60. One hundred eighty-four (52.4%) of the respondents were Muslims, followed by 133 (37.5%) Orthodox and 130 (36.7%) of the respondents had college and above as their level of education (Table 1).

**Table 1:** Socio-demographic variables among diabetic men attending North East Amhara comprehensive specialized hospitals, 2023.

Variable		Frequency	Percentage
Age	18-30	43	12.1
	31-44	109	30.8
	45-59	138	39
	$\geq 60$	64	18.1
Religion	Orthodox christianity	133	37.6
	Muslim	184	52
	Protestant	27	7.6
	Catholic	10	2.8
Residency	Urban	150	42.37
	Rural	204	57.63
Educational label	No formal education	58	16.4
	Primary school	71	20.1

Occupation	Secondary school	95	26.8
	College and above	130	36.7
	Farmer	61	12.7
	Government employee	90	25.4
	NGO employee	34	9.6
	Merchant	88	24.9
	Daily labour	49	13.8
Monthly income	Others	32	9
	<850 ETB	38	10.7
	850-1680 ETB	97	27.4
	>1680 ETB	219	61.9

**Note:** Others: Privet employee, broker, beggary and jobless

### Personal and behavioural factors of the respondents

Seventy-two (20.3%) and 33 (9.3%) of the respondents currently drink alcohol and smoke cigarettes, respectively. Two hundred eighteen (61.6%) of the study participants didn't engage in regular exercise (Table 2).

**Table 2:** Personal and behavioural factors erectile dysfunction among diabetic men attending North East Amhara comprehensive specialized hospitals, 2023.

Variable		Frequency	Percentage
History of drinking alcohol	Never drink alcohol	197	55.60%
	Ex-drink alcohol	85	24.10%
	Currently drink alcohol	72	20.30%
History of smoking cigarette	Never smoker	273	77.10%
	Ex-smoker	48	13.60%
	Current smoker	33	9.30%
Sticks smoked per day	<10 sticks smokes/day	67	82.70%
	>10 sticks smokes/day	14	17.30%
History of chat chewing	Never chewer	223	63%
	Sometimes chewer	49	13.80%
	Daily chewer	42	11.90%
	Ex-chewer	40	11.30%
Engaged in regular exercise	Yes	136	38.40%

No	218	61.60%
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### Clinical history of the respondent

Two hundred forty-three (68%) of the study subjects had type 2 diabetes mellitus and the mean duration of diagnosis was  $9.35 \pm 5.8$ , ranging from 1-34 years. The mean glucose level was  $178 \pm 81$  mg/dl, ranging from 75 to 300 mg/dl. One hundred twenty-

six (36%) and ninety-seven (27%) of the diabetes men in this study live with co-morbid disease and have developed diabetes complications, respectively (Table 3) [9].

**Table 3:** Clinical history of diabetic men attending North East Amhara comprehensive specialized hospitals, 2023.

Variable		Frequency	Percentage
Type of DM	Type 1	111	31.40%
	Type 2	243	68.60%
Duration of Dx	<6	113	32.00%
	6-10	101	28.50%
	>10	140	39.50%
Rx for DM	Injection	131	37%
	Oral	223	63%
Label of glucose/FBS	Good	220	62.10%
	Poor	134	37.90%
Co-morbidity	Yes	129	36.40%
	No	225	63.60%
Types of co morbidity	Hypertension	59	16.70%
	Cardiovascular disease	33	9.30%
	Over weight	27	7.60%
	Obesity	10	2.80%
Complication	Yes	97	27.40%
	No	257	72.60%
Types of complication	Nephropathy	11	3.00%
	Neuropathy	37	10.40%
	Retinopathy	21	5.90%
	Foot ulcer	20	5.60%
	Others	9	2.50%

### Treatment seeking behaviour of the respondent

Only 17 (4.8%) of the respondents talked about sexual issues with their physician ever and 14 (4%) received treatment for erectile dysfunction, but more than 76.6% of the subjects, with

or without the problem, expressed interest in discussing the issue with their career.



Proportion of erectile dysfunction

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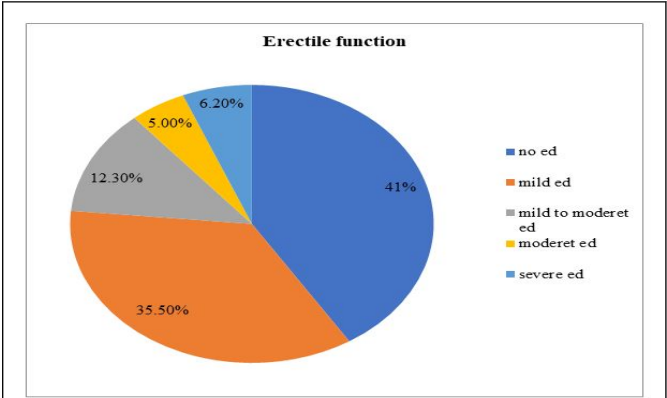


Figure 2: Proportion of erectile dysfunction among diabetic men attending North East Amhara comprehensive specialized hospitals, 2023.

Factors associated to erectile dysfunction

In bi-variable logistic regression analysis, older age, chat chewing, drinking alcohol, presence of diabetes complications and co-morbid disease, duration of diabetes, types of diabetes smoking cigarettes, engaging in regular exercise, poor glycemc control, income label <850 ETB, conception of fruit and vegetables were candidates for multivariable logistic regression analysis (p ≤ 0.2).

Multivariable logistic regression analysis found that older age, the presence of co-morbidity and developing any diabetes complications were positive predictors of erectile dysfunction in diabetic men. In addition, good glycemc control and engaging in regular exercise were negative predicators of erectile dysfunction at p-value ≤ 0.05 (Table 4) [10].

Table 4: Logistic regression analysis of erectile dysfunction among diabetic men attending North East Amhara comprehensive specialized hospitals, 2023.

Variable	Erectile dysfunction		COR (95% CI)	AOR (95% CI)
	Yes	No		
Age	18-30	5	38	1
	31-44	55	54	7.741 (2.8, 21)
	45-59	95	43	16.79 (6, 45.6)
	≥ 60	54	10	41 (12.9, 129)
History of drinking alcohol	Never drink	101	96	0.63 (0.36, 1.097)
	Ex drinker	63	22	1.718 (0.87, 3.37)
	Current drinker	45	27	1
History of smoking cigarette	Never smoke	141	132	0.288 (0.12, 0.68)
	Ex-smoker	42	6	1.88 (0.57, 6.2)
	Current smoker	26	7	1
History of chat chewing	Never	115	108	0.26 (0.117, 0.603)
	Sometimes	26	23	0.28 (0.109, 0.73)
	Daily chew	36	6	1.5 (0.47, 4.78)
	Ex-chewer	32	8	1

Regular exercise	Yes	38	98	0.107 (0.06, 0.17)	0.151 (0.07, 0.327)**
	No	171	47	1	1
Blood pressure	Normal	129	132	0.159 (0.084, 0.29)	
	Hypertension	80	13	1	
Type of DM	Type 1	36	75	0.19 (0.12, 0.315)	
	Type 2	173	70	1	
Complication	Yes	92	5	22 (8.6, 55.9)	5.49 (1.625, 18.584)**
	No	117	140	1	1
Treatment for DM	Injection	53	78	0.29 (0.186, 0.458)	
	Oral	156	67	1	
Co-morbidity	Yes	116	13	12.6 (6.7, 23.8)	3.76 (1.331, 10.632)**
	No	93	132	1	1
Nocturia	Yes	1	18	2.9 (1.6, 5.17)	
	No	148	127	1	
Duration of diagnosis in year	<5	31	82	1	
	5-10	62	39	4.2 (2.36, 7.47)	
	>10	116	24	12.7 (6.99, 23.37)	
FBS	>126	102	118	0.218 (0.13, 0.359)	0.36 (0.158, 0.807)**
	<126	107	27	1	1
BMI category	Normal	147	132	0.49 (0.149, 1.64)	
	Overweight	52	10	2.83 (0.703, 11.4)	
	Underweight	4	4	1	
Income level	<850 ETB	29	8	2.83 (0.77, 0.33)	
	850-1680 ETB	51	45	1.41 (0.63, 3.16)	
	>1680 ETB	125	91	1	

## DISCUSSION

In this study, the overall proportion of erectile dysfunction among diabetic patients was 59% (95% CI 54.3%-63.4%). This study was much lower than the findings of the studies done in Tigray (69%) and Bahir Dar (85.5%). The possible justification for this discrepancy might be due to differences in personal and behavioural factors of the respondent, different inclusion and exclusion criteria; we exclude those who were not living with spouses or not in sexual relationships) and also because IIEF-5 was measured through a self-reported scale, there may be

variation. But the proportion of severe erectile dysfunction was consistent with the findings of the study in northern Tigray, which was 5.2%. In addition, the findings of this study were in line with the findings of the studies done in Tanzania, which was 55%, Nigeria, which was 56.4% and northern sir, which was 62.9%. This may be due to the similar age category of the study subject. The current study is lower than the findings of studies from Asian countries like Japan (9%) and China (Hong Kong) (63.6%). The possible reason might be socio-economic and cultural differences between the study population. Conversely, the findings of the current study were higher than the findings



of studies done in Italy (35.8%) and the USA (49%), which might be attributed to ethnic differences. In addition, Italy and the USA are high-income countries where technological advancement and other wealth-related factors may decrease the proportion of erectile dysfunction as compared to Ethiopia, which is a low-income country.

The study indicated that the age of the participant was found to be a significant associated factor, in which the probability of developing erectile dysfunction is higher among older men. As the age of the participant increases, the probability of developing erectile dysfunction will increase. Being in the age category of 31-44 was four times more likely to develop erectile dysfunction when compared to being in the age category of 18-30. Similarly, the probability of getting erectile dysfunction in the age range of 45-59 was 18 times higher in the age range of 18-30. In addition, the odds of developing erectile dysfunction among people aged  $\geq 60$  were 19 times higher when compared to the age category of 18-30. This finding is supported by studies done in Bahir Dar, Tigray, Tanzania, Darussalam, Jordan, Egypt, Nigeria, China and the USA. This may be due to the fact that as age increases, the blood vessels shrink and their elasticity decreases, which leads to poor filling of the penile cavernous during erection.

Additionally, as age increases, the occurrence of cardiovascular and other diseases will increase, which will influence penile erection. In the presence of diabetic complications, the probability of getting erectile dysfunction in diabetic men was five times higher than in the absence of diabetic complications. The findings of the studies were in agreement with this study, for instance: Studies done in Jordan, China and Japan. This factor may be attributed to endothelial cell dysfunction. In the presence of co-morbidity, the likelihood of developing diabetes and erectile dysfunction was almost four times higher than if there were no co-morbidity. This is supported by a study done in Jordan. The possible justification for this might be that the presence of co-morbidity increases the stress on the client, which has a negative effect on the client's erectile function.

However, engaging in regular exercise reduces the probability of developing erectile dysfunction by 85%. AOR=0.15 (0.077-0.327). The possible justification for this might be that doing physical exercise may strengthen pelvic muscles and the heart and penile blood vessels may become more resistant, which is very important during erection. Good glycemic control also reduces erectile dysfunction by 64% when compared to poor glycemic control, AOR 0.36 (0.158-0.807). Some of the studies in agreement with the current study were done in Italy and Iran.

## CONCLUSION

As the findings of this study revealed, the proportion of erectile dysfunction was high in the study area. Being older, the presence of diabetes complications and co-morbid disease were positive predictors of erectile dysfunction among men with diabetes. Whereas engaging in physical exercise and good glycemic control reduced the occurrence of erectile dysfunction. Therefore, screening for erectile dysfunction should be part of

the follow-up care service, especially for those who are in the advanced age group, have diabetic complications and live with other co-morbid. Furthermore, health care providers should incorporate screening for sexual dysfunction, like other complications of diabetes.

## STRENGTH AND LIMITATIONS OF THE STUDY

This study may be considered the first to assess erectile dysfunction and associated factors among diabetic men at north east Ethiopia. Multiple logistic regression was used to control the possible confounding factors to assess the relative effect of independent variables. We have used IIED-5 score to assess erectile dysfunction some respondents may have hidden their problem because in our culture it was related to male hood/masculinity.

## ETHICAL CONSIDERATION

Ethical clearance was obtained from the ethical review committee of Woldia university. For any of the eligible study participants, the purpose, benefits, confidential nature, discomforts and right to withdraw or stop filling out the questionnaire were described and discussed. For the confidentiality and privacy of participants, their name and identification number were not recorded on the questionnaire and data collection procedures were done in diabetic OPD by covering a privacy screen. Informed verbal consent was obtained. The questionnaires were kept in locked cupboards accessible only to principal investigators.

## ETHICAL APPROVAL AND CONSENT FORM

Ethical clearance was obtained from the Institutional Review Board of Woldia University. An official letter was written to DCSH and WCSH. Permission was obtained from the administrative staff of the hospital. Verbal informed consent was approved by the Institutional Review Board and the data were collected after taking informed oral consent from study participants. The study participants were also informed of the attainment of confidentiality and anonymity or any identifiers.

## CONSENT FOR PUBLICATION

Not applicable.

## AVAILABILITY OF DATA AND MATERIALS

The datasets used for analysis are available from the corresponding author on reasonable request.

## COMPETING INTERESTS

The authors declare that they have no competing interests.

## FUNDING

Not applicable.

## AUTHORS' CONTRIBUTIONS

AG wrote the main manuscript text, wrote the methodology and the discussion section, prepared tables and figures. AG contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

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