Association of Sleep Quality and Duration with Poor Glycemic Control among Type 2 Diabetes Mellitus Patients in Felege Hiwot Comprehensive Referral and Specialized Hospital, Northwest Ethiopia

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Abstract

Background: Poor glycemic control is currently the most serious tragedy in type 2 diabetic patients. Sleep disruption is associated with increased circulating cortisol levels, sympathetic activity, and epinephrine secretion. These physiological conditions are either directly or indirectly related to glucose metabolism in our body cells. However, sleep quality and duration of glycemic control levels have yet to be studied in Ethiopia. Therefore, this study aimed to assess the association of Sleep quality and duration with Glycemic control among type 2 diabetes mellitus patients in Felege Hiwot Comprehensive Referral and Specialized Hospital, Northwest Ethiopia.

Methods: An institutional-based cross-sectional study was conducted among 407 types 2 diabetes mellitus patients selected by systematic random sampling technique from July 1, 2020, to April 28, 2021. Five milliliters of blood were taken from each patient to determine their fasting blood sugar level. The Pitts Burg Sleep Quality Index was used to evaluate patients' sleep quality, and the STOP-BANG questionnaire was used to determine the presence or absence of Obstructive Sleep Apnea. Data were analyzed using STATA version 14.1. Variables with a P-value of <0.05 were considered statistically significant.

Results: The magnitude of poor glycemic control was 54.05% (95% CI: 49.20%, 58.90%). Being female (AOR = 2.7, 95% CI: 1.23, 6.15), type 2 diabetes mellitus patients who had poor sleep quality (AOR = 3.3, 95% CI: 1.16, 9.37), patients who were at low risk of Obstructive Sleep Apnea (AOR = 0.03, 95% CI: 0.01, 0.12), intermediate risk of Obstructive Sleep Apnea (AOR = 0.14, 95% CI: 0.05, 0.43), short sleep duration (< 6 hours) (AOR = 8.3, 95% CI: 2.66, 25.85) were associated with glycemic control.

Conclusion: The prevalence of poor glycemic control in type 2 diabetes mellitus patients was high. Poor sleep quality, both short and long sleep duration, and intermediate and low risk of obstructive sleep apnea were statistically associated with poor glycemic control. Thus hospitals that have diabetes mellitus follow-up clinics should assess and consult sleep quality, duration, and obstructive sleep apnea types 2 diabetes mellitus patients to maintain a glycemic level.

Keywords: glycemic control; sleep quality; sleep duration; napping; types 2 diabetes mellitus

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Introduction

Diabetes mellitus (DM) is a group of metabolic disorders that share hyperglycemia as a common characteristic (American Diabetes, 2010). Depending on the pathogenic process, DM can be grouped into Type1Diabetes mellitus (T1DM) which is characterized by absolute insulin deficiency due to autoimmune β-cell destruction, and Type 2 Diabetes mellitus (T2DM) which is characterized by insulin resistance, impaired insulin secretion, tissue insensitivity to insulin, and excessive hepatic glucose production (American Diabetes Association,2018; Longo *et al*, 2013).

According to the American Diabetes Association (ADA) standards of medical care in Diabetes, poor glycemic control is defined as an average fasting blood glucose (FBG) level ≥ 152 mg/dl, which is comparable with hemoglobin A1c (HbA1C) ≥7% (American Diabetes Association, 2018).

Despite patients being on treatment, glycemic control is not achieved at the desired target. This is either directly or indirectly associated with the development of macro and microvascular complications. This is common in T2DM, including extremity amputations, peripheral neuropathy, end-stage renal disease (nephropathy), cardiovascular disease, cerebrovascular disease, and retinopathy (Zhuo *et al*, 2013).

The prevalence of poor glycemic control in T2DM patients is increasing at an alarming rate worldwide. It is variably reported among studies from Malaysia, (72%) (Firouzi *et al*., 2015), America (12.9%) (Ali, *et*

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al, 2012), Venezuela (76%) (Moreira Jr *et al*., 2010), Jordan (65.1%) (Khattab *et al*., 2010), Hawaii (68.5%) (Juarez *et al.,* 2012) and Kenya, (60.5%) (Mwavua *et al.,* 2016).

Optimizing sleep duration and quality is a way of improving glycemic control in T2DM patients (Dallaire *et al.*, 2018). Since sleep is linked to several hormonal changes that alter glucose metabolism, it is crucial to assess the association between sleep duration and sleep quality with glycemic control. Glycemic control is the most challenging problem of the Ethiopian T2DM population. However, there is no research conducted on sleep duration and sleep quality among DM patients. Therefore, this study aimed to assess the association of Sleep quality and duration with Glycemic control among T2DM patients in Felege Hiwot Comprehensive Referral and Specialized Hospital, Northwest Ethiopia.

Materials and Methods

Study Setting, Design, and Period

An institutional-based cross-sectional study was conducted on known T2DM patients who had treatment follow-up at Felege Hiwot Comprehensive Referral and Specialized Hospital's Chronic Disease Clinic from July 1, 2020, to April 28, 2021. The hospital is found in Bahir Dar city, which is located 560 km northwest of the capital city of Ethiopia, Addis Ababa. It is the leading referral hospital in Northwest Ethiopia and provides a referral service to the region's over 10 million residents. It employed 1041 people, including 121 doctors, 370 nurses, 59 midwives, 51 pharmacists, 72 laboratory technicians, and the rest are administrative personnel. The hospital had more than 350 beds. This hospital provides diabetes follow-up services to over 6000 registered DM patients.

Population, Inclusion/ Exclusion Criteria

All type 2 DM patients with age >18 years who visited chronic illness follow-up clinics during the study period were included. While, pregnant women, patients with a known psychiatric illness, severely ill patients, and patients who had no consecutive month follow-up and recorded Fasting Blood Sugar (FBS) were excluded from this study.

Sample size Determination and Sampling Technique

The sample size was calculated using a single population proportion formula considering the proportion of poor glycemic control of 59.8% reported in a study conducted at the University of Gondar Comprehensive Referral and Specialized Hospital Gondar, Ethiopia (Fasil, A., *et al*, 2018), 95% confidence level, 5% margin of error and 10% nonresponse rate. The final sample size was 407. The chronic follow-up clinic of the Felege Hiwot Comprehensive Referral and Specialized Hospital gives follow-up services to an average of 100 diabetic patients 1 day per week. A systematic random sampling technique was used to select study participants.

Data Collection Procedure and Measurement

Data were collected by the following method:

Face to Face Interview; was conducted using a structured questionnaire. The questionnaire is used to collect information on socio-demographic data, such as sex, age, marital status, educational status, occupation, residence, and clinical, including obstructive sleep apnea (OSA), DM duration in years, family history of DM, as well as lifestyle and habits data, including physical activity, sleep duration, sleep quality, and napping and also record review on a drug regimen, DM complication, hypertension, body mass index, and drug adherence.

Fasting Blood Glucose: About 5 ml of blood was collected in the morning before breakfast and the FBG level was determined by glucose oxidase method using MINDRAY BS-200E (Shenzhen Mindray, Bio-Medical Electronics Co., Ltd., Shenzhen, China) (Gozashti *et al*., 2016).

Sleep Quality Assessment: Pittsburgh Sleep Quality Index (PSQI) was used to assess patients' sleep quality. The presence or absence of obstructive sleep apnea (OSA) in patients was checked by using the Brazilian version of the STOP-BANG questionnaire (Morisky, D. E., *et al.* 1986).

Operational Definitions

Napping: taking daytime sleep which is not more than 30 minutes.

Drug Adherence: The 8-item Morisky Medication Adherence Scale (MMAS) was used to assess drug adherence. Patients are required to answer the questions

with either a 'yes' or a 'no' to seven MMAS-8 and the final question takes the form of a typical five-point Likert item. Positive answers (i.e. yes) are scored a 1 and negative answers (i.e. no) are scored a 0. From these responses a final score was calculated with three possible outcomes; a score of >2 corresponded to low medication adherence, a score of 2 corresponded to medium medical adherence, and a score of 1 corresponded to high medication adherence (Morisky *et al*., 1986).

Sleep Quality; According to the Pittsburgh Sleep Quality Index (PSQI), clients with a global score of > 5 had poor sleeping quality, while those with a global score of ≤ 5 had good sleeping quality(Salahuddin *et al*., 2017).

Current Smoker: Someone who smoked greater than 100 cigarettes in their lifetime and had smoked in the last 28 days (Sahile *et al*., 2020).

Body Mass Index (BMI): A person was classified as underweight (BMI < 18.5 kg/m2), normal body weight (BMI 18.5−24.9 kg/m2), overweight (BMI 25–29.9 kg/m^2), or obese (BMI ≥ 30 kg/m2 (Weir et al., 2019)

Hypertension was defined as systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg or the use of antihypertensive medication irrespective of the current BP (Fekadu *et al*., 2019).

Physical activity: Having physical exercise once preweek.

Sleep duration: sleep for six hours or less is considered poor, 6 to 9 hours is normal, and 9 hours or more is a long sleep duration (Najafi *et al*., 2022).

Poor glycemic control was defined in this study as FBG ≥152 mg/dl, which is comparable with >7% HbA1C according to ADA Standards of Medical Care in Diabetes (American Diabetes Association, 2018).

Obstructive sleep apnea (OSA): Low, intermediate, and high risk of OSA is defined as 'yes' to 0-2 3-4, and 5-8 questions respectively (Morisky., *et al.* 1986).

Data Quality Control

Data collectors were trained for one day regarding the technique and data collection process before the actual data collection. Pre-test was done on 5 % of the study sample size before the actual data and amendments were done based on the result. Frequent supervision of data collectors and completeness of data was checked.

Data Processing and Analysis

Data were cleaned, coded, and entered into Epi Data version 3.1 Software and exported to STATA version 14.1 for further analysis. Descriptive statistics, including tables, graphs, and charts were used. Bi-variable and multivariable logistic regression analyses were used to identify factors associated with poor glycemic control. Those variables with a p-value ≤0.2 in the bivariable analysis were considered for multivariable logistic regression analysis. Variables with a P-value of <0.05 at a 95% Confidence interval (CI) in multivariable analysis were considered statistically significant factors associated with Poor glycemic control.

Ethical Consideration

Ethical clearance was obtained from the Institutional Review Board of the School of Medicine, University of Gondar with protocol number 1958/2020. Before data collection, informed and signed consent was obtained from each participant. All ethical considerations, such as confidentiality and privacy were considered.

Results

Socio-Demographic Characteristics of Participants

A total of 407 T2DM patients were enrolled in this study with a 100% response rate. The age of the participants ranged from 20 to 50 years old. Majority of the study participants were male in sex 220(54.2%), urban dwellers 251(61.7%), orthodox religion follower 261(64.1%), and married 278(68.3%). About 117(28.8%) and 139(34.2%) of study participants were government employees and unable to read /write, respectively (Table 1).

Table 1: Socio-demographic characteristics of T2DM patients attending Felege Hiwot Comprehensive Referral and Specialized Hospital, Northwest Ethiopia, 2021 (n=407).

Variable		Number	Percent
Age in year	≤ 24	3	0.74
	25-44	140	34.4
	45-64	195	47.9
	≥ 65	69	17
Sex	Male	220	54.2
	Female	187	46
Residence	Urban	251	61.7
	Rural	156	38.3
Religion	Orthodox	261	64.1
	Muslim	100	24.6
	Protestant	37	9.19
	Catholic	9	2.2
Occupation	Farmers	70	17
	Merchant	39	9.6
	Government employ	117	28.8
	Self-employed	54	13.3
	Housewife	84	20.6
	Jobless	43	10.6
Marital status	Married	278	68.3
	Single	48	11.8
	Widowed	41	10.1
	Divorced	40	9.8
Educational status	Not read and write	139	34.2
	Primary	85	20.9
	Secondary	75	18.4
	College & above	108	26.5

Diabetic related characteristics

About 55.3% of the study participants had less than seven years after being diagnosed with DM. The majority of the study participants had no family history of diabetes (73.5%), were without DM complications (65.4%), non-hypertensive (62.9%), highly adherent to their medication (75.92%), did exercise 287(70.5%) and no smoking habit 342 (84%).

About 43.5% of study participants took metformin drugs. The majority of the study participants had a normal BMI (58%). The majority of the study participants were not taking napping 280 (68.8%), 76% had a high quality of sleep and more than half of the participants 214 (52.58%) had average or normal sleep duration (Table 2). About 53.1% of the study participants had a moderate risk of OSA (Fig 1).

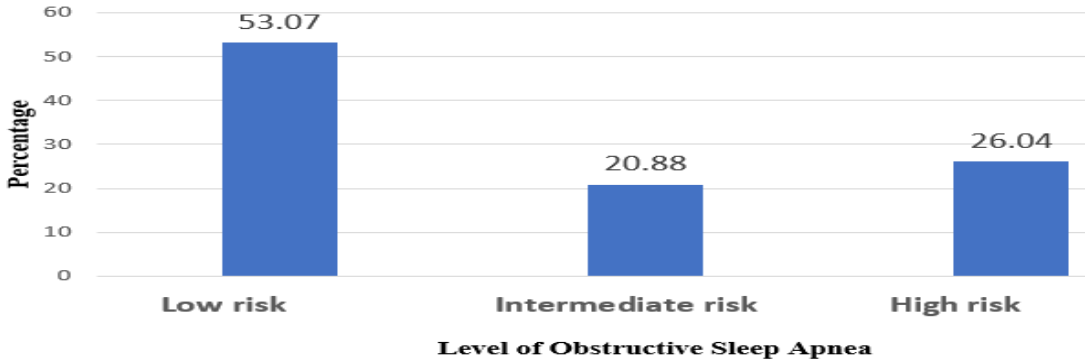

Figure 1: The level of Obstructive Sleep Apnea (OSA) in T2DM patients attending Felege Hiwot Comprehensive Referral and Specialized Hospital Northwest Ethiopia, 2021.

Table 2: Clinical, anthropometric, and behavioral characteristics of T2DM patients attending Felege Hiwot Comprehensive Referral and Specialized Hospital Northwest Ethiopia (n=407)**.**

Variable		Number	Percent
DM duration	< 7 year	225	55.3
	≥ 7year	182	44.7
Family history of DM	Yes	108	26.5
	No	299	73.5
Drug regimen	Insulin	159	39.1
	Metformin	177	43.5
	Mixed	71	17.4
Body mass index	Underweight	14	3.4
	Normal	236	58
	Overweight	128	31.7
	Obese	29	7.1
Hypertension	Yes	151	37.1
	No	256	62.9
DM complication	No	266	65.3
	Retinopathy	70	17.2
	Nephropathy	30	7.4
	Others	41	10.1
Drug adherence	Low	52	12.8
	Medium	46	11.3
	High	309	75.9
Sleep Quality	Good	269	66.1
	Poor	138	33.9
Sleep duration	Normal sleep duration	214	52.58
	Long sleep duration	70	17.2
	Short sleep duration	123	30.22
Napping	Yes	127	31.2
	No	280	68.8
Physical exercise	Yes	287	70.5
	No	120	29.5
Current smoking	Yes	65	16
	No	342	84.

Prevalence of Poor Glycemic Control

The median FBG level of the study participants was 189.67±105 mg/dl. The overall magnitude of poor glycemic control was 54.05% (95% CI: 49.20%, 58.90%). It was higher among females (60.43%), rural residents (60.3), participants who were unable to read and write (63.31%), and poor sleep quality (87.7%) (Table 3).

Factors Associated with Poor Glycemic Control

In multivariable analysis, females in sex, low risk of OSA, and intermediate risk of OSA were factors identified to be associated with poor glycemic control.

Being female increased the odds of poor glycemic control by 2.7 times (AOR = 2.7; 95% CI: 1.2, 6.2) compared to males. T2DM patients who had poor sleep quality had 3.3 times (AOR = 3.3; 95% CI: 1.2, 9.4) higher chance of poor glycemic control than patients who had good sleep quality. The odds of having poor glycemic control among T2DM patients who were at low risk of OSA and intermediate risk of OSA were decreased by 97% (AOR = 0.03; 95% CI: 0.01, 0.1) and 86% (AOR = 0.1; 95% CI: 0.1, 0.4), respectively, compared to T2DM patients who were at high

risk of OSA. T2DM patients who had short sleep duration had 8.3 times (AOR = 8.3; 95% CI: 2.7, 25.9) higher odds of poor glycemic control than patients who had average sleep duration.T2DM patients who had long sleep durations had 2.6 times higher odds of poor glycemic control (AOR = 2.6;95% CI:1.1,6.0) than those who had average sleep durations (Table 4).

Table 3: The magnitude of poor glycemic control across characteristics of study participants (n=407).

Variables	Categories	Glycemic control	
		Good (%)	Poor (%)
Sex	Male	113 (51.4)	107 (48.6)
	Female	74 (39.6)	113 (60.4)
Residence	Rural	62 (39.7)	94 (60.3)
	Urban	125 (49.8)	126 (50.2)
Education status	Not read and write	51 (36.7)	88 (63.3)
	Primary	36 (42.4)	49 (57.7)
	Secondary	42 (56.0)	33 (44.0)
	College and above	58 (53.7)	50 (46.3)
	Farmer	23 (32.9)	47 (67.1)
Occupational status	Merchant	18 (46.2)	21(53.9)
	Government employ	64 (54.7)	53 (45.3)
	Self-employed	29 (53.7)	25 (46.3)
	Housewife	35 (41.7)	49 (58.3)
	Jobless	18 (41.9)	25 (58.1)
Sleep Quality	Good	170 (63.2)	99 (36.8)
	Poor	17 (12.3)	121 (87.7)
OSA	Low risk	144 (66.7)	72 (33.3)
	Intermediate risk	30 (35.3)	55 (64.7)
	High risk	13 (12.3)	93 (87.7)
Sleep duration	<6 hrs.	11 (8.9)	112 (91.1)
	6-8 hrs.	151 (70.6)	63 (29.4)

Table 4: Factors associated with poor glycemic control among T2DM patients attending Felege Hiwot Comprehensive Referral and Specialized Hospital, Northwest Ethiopia, 2021(n=407).

Variable		Glycemic control		COR(95% CI)	AOR(95% CI)
		Good (%) N=(187)	Poor (%) N= 220		
Sex	Male	113 (51.4)	107 (48.6)	1	1
	Female	74 (39.6)	113 (60.4)	1.6(1.1,2.4)	2.8(1.2,6.2)
Sleep Quality	Good	170 (63.2)	99 (36.8)	1	1
	Poor	17 (12.3)	121 (87.7)	12.2(6.9,21.5)	3.3(1.2,9.4)
Obstructive sleep apnea	Low risk	144 (66.7)	72 (33.3)	0.1(0.04,0.13)	0.04(0.01,0.1)
	Intermediate risk	30 (35.3)	55 (64.7)	0.3(0.1,0.5)	0.1(0.1,0.4)
	High risk	13 (12.3)	93 (87.7)	1	1
Sleep duration (hour)	6-9	151 (70.6)	63 (29.4)	1	1
	<6	11 (8.9)	112 (91.1)	24.4(12.3,48.4	8.3(2.7,25.9)
	>9	25 (35.7)	45 (64.3)	4.3(2.4,7.6)	2.6(1.1,6.0)

CI; confidence interval, COR; crude odds ratio, AOR; adjusted odds ratio, hr.; hour

Discussion

The findings revealed that poor glycemic control was common in T2DM patients (54.5%) and female gender, poor sleep quality, both short and long sleep duration, and intermediate and low risk of obstructive sleep apnea were statistically associated with Poor glycemic control.

In the present study, the magnitude of poor glycemic control was 54.5%. This finding is consistent with a study conducted in Nigeria (55%) (Camara *et al.*, 2015). On the other hand, the results of the present study are lower than those studies conducted in India (74%) (Harrabi *et al.,* 2014), Malaysia (72%) (Firouzi *et al.*, 2015), Cameron (78.6%) (Ashur *et al*, 2016) and Kenya (83%) (Mwavua *et al*., 2016). On the other hand, the finding of the current study is higher than that of a study conducted in the United States of America (12.9%) (Zhuo *et al*., 2013). This discrepancy could be due to differences in DM treatment counseling, mentoring, and management criteria.

Poor glycemic control was significantly associated with the female sex in the study, which is supported by a study conducted in Tanzania (Kamuhabwa, & Charles, 2014). However, this contradicts the findings from China, Malaysia, and Jordan (Zhuo *et al*., 2013; Almutairi *et al*, 2013). The possible difference might be due to the difference in the metabolism of glucose by sex. For instance, testosterone stimulates lipolysis in adipose tissues, and low testosterone levels are associated with abdominal obesity and insulin resistance in females (Navarro *et al*., 2015). Another study also reported that metformin has a better effect on glucose metabolism in type 2 diabetic males than in females (Lyons *et al*., 2013). One study also indicates diabetic women are more likely to lose glucose homeostasis after menopause (Duarte *et al*., 2019).

In this study, T2DM patients who have poor sleep quality have poor glycemic control levels. This is also supported by another study (Lou *et al*., 2012). It also showed that the majority of study participants 268 (66.09%) were good sleepers whereas 138 (33.91%) were poor sleepers. Those DM patients who sleep well had better glycemic control. This is congruent with the study conducted at Jimma Ethiopia (Jemere *et al.*, 2019)

Another factor that was significantly associated with poor glycemic control in our study was short sleep duration (< 6 hours). This is supported by research conducted in Brazil (Martorina *et al*., 2019). Long sleep duration (>8 hours) was also associated with poor glycemic control in this study. These findings are similar to studies conducted in Japan (Ohkuma, *et a*l., 2013) and China (Lee *et al*., 2017). The best sleep duration which helps to have good glycemic control is 6-8 hours (Grandner *et al.,* 2016).

In general, sleep pattern has a major modulatory effect on glucose metabolism and energy uptake that have a direct or indirect effect on the maintenance of good glycemic control level in T2DM patients., The increased prevalence of poor glycemic control levels with sleep deprivation and/or poor sleep quality could be due to upregulation of appetite, increased time for eating as well as reduced energy expenditure. Indeed, nocturnal awakening and arousal have been associated with altered leptin levels and leptin resistance leading to dysregulation of the hypothalamic-pituitary-adrenal axis, resulting in glucose metabolism impairment (Lee et al., 2017).

The other plausible mechanism related to sleep deprivation is the disturbance of melatonin hormone secretion under the control of the hypothalamic suprachiasmatic nucleus (SCN). This hormone or its receptor agonist's administration improved glucose homeostasis through, enhanced glucose uptake, increased glucose-induced insulin secretion, improved insulin sensitivity, decreased liver gluconeogenesis, and increase glycogen synthesis in the liver. In the normal sleep-wake-up cycle this hormone is secreted in the pineal gland under the control of the hypothalamic suprachiasmatic nucleus and detected in liver, fat, muscle, and pancreas cells to aid glucose homeostasis (Arendt *et al.,* 2022).

The other independent variable that was significantly associated with poor glycemic control in this study was obstructive sleep apnea. This is in line with a study conducted in India (Malik *et al*., 2017). Studies have demonstrated that intermittent hypoxia or OSA syndromes can induce liver damage and increase serum levels and activity of key liver enzymes such as serum aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase in both mice and humans (Savransky *et al*., 2007). Repeated attacks of OSA resulted in liver steatosis, necrosis, and inflammation with neutrophil accumulation and collagen deposits. This causes glucose homeostasis abnormalities even in T2DM patients. Obstructive sleep apnea syndrome can also cause oxidative stress and inflammation that results in the secretion of inflammation mediators (Li *et al*., 2005).

Conclusion

The prevalence of poor glycemic control in T2DM patients was high. Female gender, poor sleep quality, and

sleeping for short or long periods were statistically significant predictors of poor glycemic control. Healthy sleep habits are thus recommended in T2DM patients to improve glycemic control and prevent complications. Thus hospitals that have DM follow-up clinics should assess sleep quality, duration, and obstructive sleep apnea and counseling

T2DM patients to maintain a glycemic level. In addition, this study recommends further research on measuring glycemic control levels by using HbA1C and sleep quality by using actigraphy (polysomnography).

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Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

All authors made a substantial contribution to the conception, design, acquisition, and interpretation of data. All authors have revised the article critically for important intellectual content. All authors read and approved the final version of the manuscript.

List of Abbreviations

AOR; Adjusted Odds Ratio, BMI: Body Mass Index CI: Confidence Interval, COR; Crude Odds Ratio, DM; Diabetic Mellitus EDHS; Ethiopian Demographic and Health Survey, FBS; Fasting Blood Sugar, OSA; Obstructive sleep apnea, T2DM; Type 2 Diabetic Mellitus.

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