# Association between Sleep Duration and Glycemic Control among Patients with Type 2 Diabetes in Tertiary Care Hospital

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### **ABSTRACT**

Introduction: Sleep problems are more common in people with diabetes than in people without the condition. Sleep issues are common medical conditions that have a detrimental effect on type 2 diabetes mellitus (T2DM). Common issues like nocturia caused by poor glucose control or peripheral neuropathy can seriously impair sleep quality. The purpose of the current study is to examine the relationship between diabetes mellitus and sleep habits. The results could help medical practitioners provide comprehensive lifestyle advice to diabetics.

Materials and Methods: The sample size for the study was 88 obtained by using open-epi software. A validated and pre-tested semi-structured questionnaire was used to gather study data. Subjective sleep quality, sleep latency, length, habitual sleep efficiency, sleep disruptions, usage of sleeping medication, and daytime dysfunction are the seven components of the 19-question PSQI questionnaire. Every component has a score between 0 and 3, which can be understood as follows: A score of zero indicates no sleep issues, a score of one indicates light sleep issues, a score of two indicates moderate sleep issues, and a score of three indicates severe sleep issues. The global PSQI score is obtained by adding up all the component scores, ranging from 0 to 21. A PSQI score of 5 or higher indicates poor sleep quality.

Results: Higher PSQI scores, which indicate poorer sleep quality, were substantially linked to higher HbA1c levels, underscoring the importance of both sleep duration and quality in glycemic control. Significant correlations were also found between sociodemographic characteristics such gender, location, employment, education, and kind of treatment. Regression and correlation studies supported the idea that sleep is important for managing diabetes. These results highlight how important it is to incorporate sleep evaluation into regular diabetes care. Improving sleep quality could be an easy and affordable addition to current treatment methods.

**Key words:** Sleep duration, glycemic control, lifestyle advice to diabetes

# INTRODUCTION

Around 150 million people globally are thought to have diabetes at the moment, and by 2025, that number is expected to increase to 300 million, with type 2 diabetes accounting for the bulk of cases.[1] Hyperglycemia, a sign of type 2 diabetes mellitus, is caused by varying degrees of insulin resistance and decreased insulin production. Food, exercise, alcohol consumption, and smoking have traditionally been the lifestyle factors of greatest interest in type 2 diabetes research. Another behavior that has received a lot of attention lately in health research is sleep.[2] There is mounting evidence that diabetes is more likely to develop in people who have sleep difficulties.[3] As a result, people with diabetes have more sleep problems than people without the condition.[4] Sleep disturbances and type 2 diabetes mellitus (T2DM) are common health conditions that have a detrimental effect on each other.[5] There are several ways in which sleep disorders can impact the pathways that predispose individuals to type 2 diabetes. An increase in sympathetic neural output is one important mechanism.[6] Sleep may also influence the risk of type 2 diabetes by altering cortisol levels, which have a strong circadian rhythm.[7] Additionally, inflammation acts as a link between diabetes and sleep.[8]

Diabetes can also impair sleep through different mechanisms. Common complications such as peripheral neuropathy or nocturia resulting from poor glycemic control can significantly disrupt sleep quality.[9,10] A periodic breathing pattern during sleep is more frequently observed in individuals with diabetes, though its role in causing sleep-related symptoms remains uncertain.[11] Restless legs syndrome (RLS) is frequently observed in individuals with type 2 diabetes, with a reported prevalence of 17–27%. While the exact mechanism linking type 2 diabetes to increased RLS risk remains unclear, peripheral neuropathy may play a contributing role.[12] Diabetes can be diagnosed by HbA1c level as it reflects average blood glucose levels over the past two to three months and is widely used as a marker for long-term glycemic

control.[13] Whereas The Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval.[14]

This clearly explains how improving sleep patterns can be a successful non-pharmacological diabetes control tactic. In order to enhance the body of current research, raise awareness, and highlight the significance of sleep-focused interventions, the current study is to investigate the relationship between sleep patterns and diabetes mellitus. The results could help medical practitioners provide comprehensive lifestyle advice for people with diabetes.

### MATERIALS AND METHODS

The study was conducted in a tertiary care hospital at Puducherry after obtaining approval from Scientific Research Committee and Institutional Human Ethical Committee. All type 2 diabetes patients who satisfied the eligibility criteria were recruited for the study using Convenience sampling technique. The sample size for the study was 88 obtained by using open-epi software.

The data for the study was collected using a validated and pre-tested Semi-structured questionnaire. The questionnaire consisted of two parts. Age, gender, residence, marital status, level of education (no formal education, primary school, middle school, high school, higher secondary school, graduate and above), employment status (employed & unemployed), height, weight, BMI (based on WHO classification), duration of diabetes, and treatment of diabetes were among the demographic questions in the first section. In the second section, type 2 diabetes is determined using HbA1c, FBS, and PPBS, and sleeping difficulties are determined using the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The PSQI questionnaire comprises 19 questions that are classified into seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each component has a score ranging from 0 to 3 that is interpreted as follows: no sleep problem: score of 0, mild sleep problem: score of 1, moderate sleep problem: score of 2 and severe sleep problem: score of 3. The global PSQI score is obtained by adding up all the component scores, ranging from 0 to 21. A PSQI score of 5 or higher indicates poor sleep quality.[15]

The data collected were entered in Microsoft Excel 2019 and the results were analyzed using SPSS software version 23.0. Quantitative data was expressed in Mean, Range, Frequency and Distribution. Independent 't' test and analysis of variance were used to find association and p value <0.05 was considered as significant. Pie charts and bar diagrams were used to represent the data pictographically.

# RESULTS Figure 1: Frequency Distribution of Age among the Participants (n = 88)

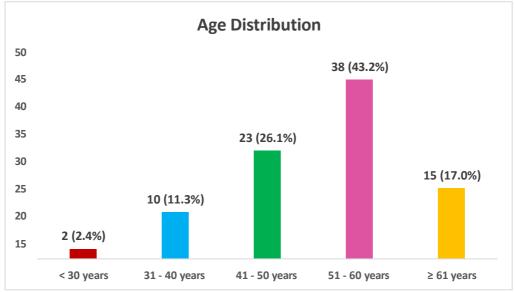


Figure 1 depicts the frequency distribution of age among the participants. It shows that highest proportion of participants 38 (43.2 %) were in the 51 to 60 years age group followed by 23 (26.1 %) aged 41 to 50 and 15 (17.0%) belonging to  $\geq$  61 years. About 10 (11.3 %) were between 31 - 40 years of age and 2 (2.4 %) were below 30 years.

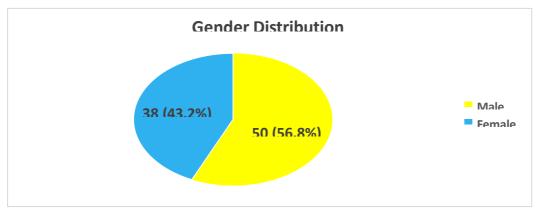


Figure 2: Frequency Distribution of Gender among the Participants (n = 88)

Figure 2 displays a pie chart representing the gender distribution of the participants. Males constituted the majority, with 50 individuals (56.8%), while females accounted for 38 participants (43.2%).

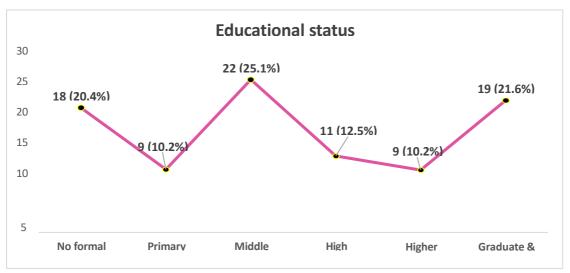


Figure 3: Frequency Distribution of Educational status among the Participants (n = 88)

Figure 3 illustrates the distribution of educational status among the participants. Twenty-two participants (25.1%) had completed middle school, while 19 participants (21.6%) had finished graduate school or above. Nine people each (10.2%) had finished basic and higher secondary education, while eleven participants (12.5%) claimed having a high school education. Interestingly, 18 participants (20.4%) did not have any formal schooling.

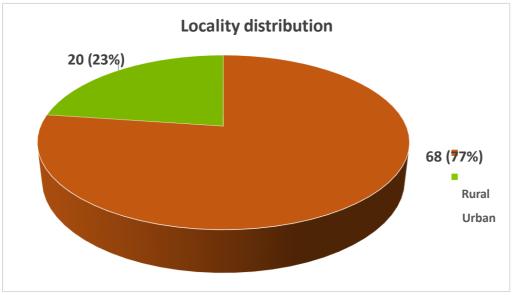


Figure 4: Frequency Distribution of Locality among the Participants (n = 88)

88)

Figure 4 presents the locality distribution of participants in the form of a pie chart. Majority of participants 68 (77%) were from rural area and 20 (23%) were from urban area.

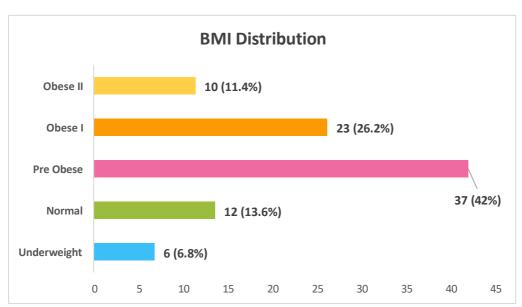


Figure 5: Frequency Distribution of Body Mass Index (BMI) among the Participants (n = 88)

Figure 5 presents the frequency distribution of BMI among the participants. The majority, 37 individuals (42%), fell into the pre-obese category, followed by 23 participants (26.2%) classified as Obese I. Additionally, 12 participants (13.6%) had a Normal BMI, 10 (11.4%) were categorized as Obese II, and 6 participants (6.8%) were underweight.

Table 1: Frequency Distribution of Employment and Marital status among the Participants (n= 88)

Variables	Status	Frequency	Percentage (%)
Employment status	ployment status Employed 43		48.8%
	Unemployed	45	51.2%
	Married	61	69.3%
	Unmarried	15	17.1%
Marital status	Seperated	5	5.6%
	Widow / Widower	7	7.9%

Table 1 highlights the distribution of employment and marital status among the participants. In terms of employment, 45 individuals (51.2%) were unemployed, while 43 (48.8%) were employed. Regarding marital status, out of 88 participants, 61 (69.3%) were married, 15 (17.1%) were unmarried, 5 (5.6%) were separated, and 7 (7.9%) were widowed.

Table 2: Frequency Distribution of HbA1C and Type of Treatment among the Participants (n=

Variables	Status	Frequency	Percentage (%)
HbA1C	Good	37	42%
	Poor	51	58%
	ОНА	62	70.4%
Type of Treatment	Insulin	18	20.4%
	Mixed	8	9.2%

Table 2 exhibits the frequency distribution of HbA1C and type of treatment received among the participants. With regard to glycemic control, 37 participants (42%) had good HbA1c levels, while 51 participants (58%) had poor control. In terms of treatment, the majority were on oral hypoglycemic agents (OHA) with 62 individuals (70.4%), followed by 18 participants (20.4%) on insulin therapy, and 8 participants (9.2%) receiving a combination of both.

Table 3: Frequency Distribution of PSQI and Sleep duration among the Participants (n= 88)

Variables	Status	Frequency	Percentage (%)
PSQI	Good (< 5)	38	43.1%
	Poor (> 5)	50	56.9%
	< 6 hrs	40	45.4%
Sleep duration	6 - 8 hrs	18	20.4%
	> 8 hrs	30	34.2%

Table 3 reveals the frequency distribution of PSQI and Sleep duration among the participants. According to PSQI scores, 38 participants (43.1%) had good sleep quality (score < 5), while 50 participants (56.9%) had poor sleep quality (score > 5). In terms of sleep duration, 40 participants (45.4%) reported sleeping less than 6 hours per night, 18 participants (20.4%) slept between 6 to 8 hours, and 30 participants (34.2%) reported sleeping more than 8 hours.

Table 4: Association between various factors and Glycemic control among participants (n = 88)

X7 + 1.1		Glycemic Co	ntrol	P – Value	
Variables	Categories	Good	Poor	(Chi square value)	
	< 30 years	2 (100%)	0 (0.0%)		
	31 - 40 years	5 (50%)	5 (50%)		
Age group	41 - 50 years	13 (56.5%)	10 (43.5%)	0.126 (7.170)	
	51 - 60 years	12 (31.5%)	26 (68.5%)	^	
	≥ 61 years	5 (33.3%)	10 (66.7%)		
Gender	Male	13 (26%)	37 (74%)	0.001 (12.234)	
Gender	Female	24 (63.1%)	14 (36.8%)		
Locality	Rural	22 (32.3%)	46 (67.7%)	0.001 (11.525)	
Locality	Urban	15 (75%)	5 (25%)	0.001 (11.535)	
	Married	21 (34.4%)	40 (65.6%)		
V6 - 1 - 1	Unmarried	10 (66.6%)	5 (33.4%)	0.031 (8.662)*	
Marital status	Seperated	1 (20%)	4 (80%)		
	Widow / Widower	5 (71.4%)	2 (28.6%)		
	No formal education	3 (16.6%)	15 (83.4%)		
	Primary	1 (11.1%)	8 (88.9%)		
Education	Middle	11 (50%)	11 (50%)	0.013 (14.362)	
	High	5 (45.4%)	6 (54.6%)		
	Higher Secondary	4 (44.4%)	5 (55.6%)		
	Graduate & above	13 (68.4%)	6 (31.6%)		
Employment stat	us Employed	28 (65.1%)	15 (34.9%)		

	Unemployed	9 (20%)	36 (80%)	0.001 (18.368)
	Underweight	3 (50%)	3 (50%)	
	Normal	2 (16.6%)	10 (83.4%)	
BMI	Preobese	19 (51.3%)	18 (48.7%)	0.315 (4.740)
	Obese I	9 (39.1%)	14 (60.9%)	
	Obese II	4 (40%)	6 (60%)	
	ОНА	21 (33.8%)	41 (66.2%)	
Treatment	Insulin	13 (72.2%) 5 (27.8%)		0.014 (8.495)
	Mixed	3 (37.5%)	5 (62.5%)	
PSQI	Good	29 (76.3%)	9 (23.7%)	2 224 (22 227)
(Sleep quality)	Poor	8 (16%)	42 (84%)	0.001 (32.235)
	< 6 hours	7 (17.5%)	33 (82.5%)	
Sleep Duration	6 - 8 hours	10 (55.5%)	8 (44.5%)	0.001 (18.702)
	> 8 hours	20 (66.6%)	10 (33.4%)	

<sup>\*</sup>fischer's exact test done

Table 4 provides the distribution of glycemic control across different participant characteristics and evaluates their associations using the chi-square test. Glycemic control among participants showed statistically significant associations with gender, locality, marital status, education, employment, treatment type, sleep quality, and sleep duration (p value  $\leq$  0.05). No significant association was found with age group or BMI.

Table 5: Association between various factors and Sleep quality based on PSQI score among participants (n = 88)

		Sleep Quality	P – Value		
Variables	Categories	Good	Poor	(Chi square value)	
		(<5)	(>5)		
	< 30 years	1 (50%)	1 (50%)		
	31 - 40 years	5 (50%)	5 (50%)		
<b>A</b>	41 - 50 years	12 (52.2%)	11 (47.8%)	0.266 (4.200)*	
Age group	51 - 60 years	17 (44.7%)	21 (55.3%)	0.366 (4.308)*	
	≥ 61 years	3 (20%)	12 (80%)		
0 1	Male	6 (12%)	44 (88%)	0.001 (45.886)	
Gender	Female	32 (84.2%)	6 (15.8%)		
T 1.	Rural	21 (30.9%)	47 (69.1%)	2.22.4 (1.2.4.1.2).t.	
Locality	Urban	17 (85%)	3 (15%)	0.001 (18.448)*	
	Married	22 (36.1%)	39 (63.9%)		
	Unmarried	10 (66.7%)	5 (33.3%)		

Marital status	Seperated	0 (0.0%)	5 (100%)	0.004 (13.592)*	
	Widow / Widower	6 (85.7%)	1 (14.3%)		
	No formal education	4 (22.2%)	14 (77.8%)		
Education	Primary	4 (44.4%)	5 (55.6%)	0.198 (7.321)*	
	Middle	8 (36.4%)	14 (63.6%)		
	High	6 (54.5%)	5 (45.5%)		
	Higher Secondary	4 (44.4%)	5 (55.6%)		
	Graduate & above	12 (63.2%)	7 (36.8%)		
Employment status	Employed	20 (46.5%)	23 (53.5%)		
	Unemployed	18 (40%)	27 (60%)	0.538 (0.380)	
	Underweight	5 (83.3%)	1 (16.7%)		
	Normal	6 (50%)	6 (50%)		
BMI	Preobese	12 (32.4%)	25 (67.6%)		
DIVII	Obese I	10 (43.5%)	13 (56.5%)	0.192 (0.103)	
	Obese II	5 (50%)	5 (50%)		
	ОНА	26 (41.9%)	36 (58.1%)		
Treatment	Insulin	10 (55.6%)	8 (44.4%)	0.326 (2.240)	
	Mixed	2 (25%)	6 (75%)		
Sleep Duration	< 6 hours	12 (30%)	28 (70%)		
	6 - 8 hours	8 (44.4%)	10 (55.6%)	0.043 (6.303)	
-	> 8 hours	18 (60%)	12 (40%)		

<sup>\*</sup>fischer's exact test done

Table 5, this table presents the relationship between various participant characteristics and sleep quality, categorized as Good (PSQI  $\leq$  5) and Poor (PSQI  $\geq$  5). Sleep quality (as measured by PSQI) was found to be significantly associated with gender, locality, marital status, and sleep duration. Females, urban residents, widowed/unmarried individuals, and those with longer sleep duration reported better sleep quality (p value  $\leq$  0.05). No significant associations were observed with age, education, employment, BMI, or treatment type.

Table 6: Binary logistic regression between HbA1c and Sleep duration among participants (n = 88)

Correlates	В	Std. Error	Wald	Sig.	Exp(B)	95% C.I.	for Exp(B)
(Sleep duration)						Lower Bound	Upper Bound
Sleep duration	Sleep duration < 6 hrs is Reference						
6 - 8 hrs	-1.774	0.631	7.902	0.005	0.170	0.049	0.584
> 8 hrs	-2.244	0.568	15.579	0.000	0.106	0.035	0.323
Constant	1.551	0.416	13.885	0.000	4.714	-	-

<sup>\*</sup>p value less than 0.05 is statistically significant

Table 6 shows the binary logistic regression which was conducted to assess the association between Sleep duration and Glycemic control, as measured by HbA1c status. Sleep duration "< 6 hours" is used as the reference category. The model was statistically significant ( $\chi^2$  = 16.648, p < 0.001), indicating that sleep duration is a significant predictor of HbA1c control.

Compared to individuals who slept less than 6 hours per night, those who reported sleeping 6 to 8 hours had significantly lower odds of poor glycemic control (AOR = 0.170, 95% CI: 0.049-0.584, p = 0.005). Similarly, individuals who slept more than 8 hours also showed significantly reduced odds of poor glycemic control (AOR = 0.106, 95% CI: 0.035-0.323, p < 0.001).

Table 7: Correlation among HbA1c and Sleep duration, PSQI, Treatment among participants (n = 88)

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Variables	r value	P value
Sleep duration	-0.448	0.000
PSQI	0.605	0.000
Treatment	0.167	0.119

Table 7 shows the Pearson correlation analysis which revealed a moderate, statistically significant negative correlation between HbA1c and sleep duration (r = -0.448, p < 0.001), indicating that longer sleep duration is associated with lower HbA1c levels, suggesting better glycemic control. A moderate, statistically significant positive correlation was found between HbA1c and PSQI score (r = 0.605, p < 0.001), suggesting that poorer sleep quality (higher PSQI scores) is associated with higher HbA1c levels, reflecting poorer glycemic control. There was a weak negative correlation between HbA1c and treatment status (r = -0.167, p = 0.119), which was not statistically significant, suggesting no meaningful association between treatment type and HbA1c levels in this sample.

### **DISCUSSION**

Sleeping less than 7 hours regularly is associated with health risks like obesity, diabetes, heart disease, and increased mortality. Some people may benefit from sleeping more than nine hours, but its effects on the general population are unclear. [16] In our study, the majority of participants were between the ages of 51 and 60 (43.2%) and 41 and 50 (26.1%), which is similar to findings by Shibabaw YY et al. [17]. The mean age was 52.20 ± 12.02 years, which is in line with studies by Raut et al., Dijk MV et al., and Nuyujukian DS et al., while Ohkuma T et al. reported a higher mean age of 66 ± 10 years.[4,13,18,19] Males comprised 56.8% of participants, similar to the gender distribution reported by Shibabaw YY et al, Dijk mv et al, Ohkuma T et al, Jain et al and Hashimoto Y et al while Lou P et al et al. and Gore M et al. observed a female predominance.[4,9,17,19–22]

Regarding education, 25.1% of participants had completed middle school and 21.6% were graduates or above. In contrast, studies by Lou P et al et al, Nuyujukian DS et al and Hashimoto Y et al found a higher proportion of participants with education at the high school level or above.[18,21,22] Most participants in our study (77%) were from rural areas, whereas Shibabaw YY et al. reported greater urban representation.[17]

The mean BMI in our study was  $28.45 \pm 5.15$ , which aligns with findings from Resnick et al and Albers JD et al., while lower mean BMIs were reported in studies by Jain A et al., Ohkuma T et al., Lee DY et al., and Dijk MV et al.[2,4,11,19,20,23] Additionally, 51.2% of participants were unemployed, a finding similar to Nasir NFM et al., but contrasting with the observations of Nuyujukian DS et al., and Hashimoto Y et al. and Gore M et al.[9,18,21,24] In this study, 69.3% of the participants were married which was similar to Nuyujukian DS et al and Hashimoto Y et al.[18,21]

Among the 88 participants, 58% had poor glycemic control (HbA1c ≥ 7), similar to the findings reported by Keskin A et al., Jain A et al., and Martinez-Ceron E et al.[20,25,26] In contrast, Dijk MV et al. reported better glycemic control, with 51% of participants achieving target HbA1c levels.[4] With regards to treatment 70.4% of our study participants were on oral hypoglycemic agents (OHA), followed by 20.4% on insulin, aligning with the results of Jain A et al, Bironneau V et al and Martinez- Ceron E et al.[20,26,27] However, Zhu BQ et al reported a higher proportion (60%) of participants receiving insulin therapy, and a similar finding was also observed in the study by Shibabaw YY et al.[17,28] In the present study 56.9% of participants had a PSQ score >5, indicating poor sleep quality, which is comparable to the findings of Mehrdad M et al (69.5%) and Telford O et al (53%) who also reported a high proportion of poor sleepers.[29,30] In contrast, lower proportions of poor sleep quality were observed in studies by Shibabaw YY et al (33.9%), Asghari A (37%), Zhu B (47.1%) and Dijk MV et al (35.4%).[4,17,28,31] In

our study, 45.4% of participants reported sleeping less than 6 hours, followed by 34.2% who slept more than 8 hours, and 20.4% who slept between 6 to 8 hours. Similar findings was observed in the study by Nuyujukian DS et al.[18] In contrast, studies by Shibabaw YY et al, Lou P et al et al, Lee DY et al, and Dijk MV et al. reported a higher proportion of participants sleeping 6 to 8 hours, followed by those sleeping less than 6 hours.[4,17,22,23]

Glycemic control was found to be significantly correlated with gender, location, marital status, education, employment, treatment type, sleep length, and sleep quality (p < 0.05) in our study. However, the Dijk MV et al. study [4] found no meaningful correlations between sociodemographic characteristics and glycemic control. Males, those living in rural areas, those without jobs, and those with poor sleep quality or shorter sleep durations were more likely to have poor glycemic control. Similar results were found by Shibabaw YY et al., except that female sex was also substantially linked to poor glycemic control.[17] However, both studies agreed that higher education and insulin therapy were linked to better glycemic control, which contrasts with the findings of Camara et al. There was no significant association between BMI and glycemic control; a finding consistent with the results reported by Lee DY et al.[23]

In the present study, poor sleep quality was significantly associated with male gender, rural residence, marital status, and shorter sleep duration (p  $\leq$  0.05). It was found similar to the study of Maimaitituerxun R et al.[33] Significant association of poor sleep quality with marital status was noted in Gowthaman R et al., and Das S et al. [34,35] No significant associations were observed with age, education, employment status, BMI, or type of diabetes treatment. Age and BMI was not found to be significant with sleep quality in the study by Stefan L et al.[36] Using <6 hours as the reference, the study employed binary logistic regression to evaluate the relationship between sleep duration and glycemic management. Statistical significance was achieved by the model ( $\chi^2 = 16.648$ , p < 0.001). The odds of having poor glycemic control were considerably lower for participants who slept 6-8 hours (AOR = 0.170, p = 0.005) and >8 hours (AOR = 0.106, p < 0.001) than for those who slept for shorter periods of time. This result was comparable to the research done by Gozashti MH et al., Martorina W et al., Shibabaw YY et al., Ohkuma T et al., Tang Y et al., and Reutrakul S et al.[17,19,37-40]. Additionally, our research shows that enhanced glycemic management is substantially correlated with both longer sleep duration and higher-quality sleep. However, no significant association was found between treatment status and HbA1c levels in this study. This finding was supported by Zhuo X et al and Lou P et al. [22,41] Previous studies found that selfreported short sleep duration is associated with diabetes.[42-45] In contrast some studies have reported that long sleep duration is also associated with diabetes.[22,46,47]

**Limitations of the study:** The primary limitation of the study is that it was carried out in a single tertiary care hospital, which may restrict the applicability of the results to larger population. Self-reported methods (such as questionnaires) were used to measure sleep duration and quality, which could be prone to subjective interpretation and recall bias. Confounding factors that may affect both sleep and glycemic management, such as stress levels, eating patterns, physical activity, and comorbidities, may not have been completely controlled for.

**Recommendations:** The results of this study suggest that regular clinical care for patients with Type 2 Diabetes should include sleep examination. Patients should be informed by healthcare professionals on the significance of getting enough restful sleep as a vital part of managing diabetes. Glycemic management may be enhanced by sleep hygiene- focused interventions such behavioral counseling and lifestyle changes. To fully treat sleep-related disorders, a multidisciplinary strategy comprising diabetologists, psychologists, and sleep specialists should be promoted.

## CONCLUSION

Poor sleep quality, as indicated by higher PSQI scores, was significantly associated with elevated HbA1c levels, highlighting the role of both sleep duration and quality in glycemic control. Sociodemographic factors such as gender, locality, employment, education, and treatment type also showed significant associations. Correlation and regression analyses reinforced the impact of sleep on diabetes management. These findings emphasize the need to consider sleep assessment as part of routine diabetes care. Promoting better sleep may serve as a simple, cost-effective adjunct to existing treatment strategies.

**Acknowledgements:** We would like to thank the College Management for their logistic support and the Faculty of Department of General Medicine for their guidance throughout the study. We also thank all the participants of the study for their valuable time in carrying out the study.

Funding: Nil

Conflict of Interest: None

Ethical Approval: Approved by the Institutional Ethics Committee of Pondicherry University.

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