ORIGINAL ARTICLE

Influence of glycemic control in sleep status in diabetes mellitus patients type 2 and its related with SNPs of SLC47A2: Intron variant

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ABSTRACT

Aim: The relationship between diabetes mellitus (DM) and lifestyle quality become important in diabetes research in last year. The present study aims to study the influence of metformin response in sleep in diabetes mellitus patients type 2.

Materials and Methods: A cross sectional study was designed to achieve study goal, glycemic parameters included fasting blood glucose (FBG), glycated protein (HbA1c%), insulin (IN), insulin resistance (HOMA-IR) and insulin sensitivity (IS). PCR sequencing was used to detect *SLC47A2* intronic variants and its related with glycemic control and sleep status.

Results: Among the study population, about 26.3% achieved well glycemic control, 30% were moderately controlled, and 43.8% were poorly controlled. Sleep quality assessment showed that the majority of participants in all glycemic groups experienced intermediate sleep. The prevalence of insomnia increased with worsening glycemic control, from 4.8% in the well-controlled group to 17.1% in poorly controlled participants, in non- statistically significant ($p = 0.722$). Biochemical parameters confirmed significant differences in fasting blood glucose and HbA1c across the three glycemic categories ($p < 0.001$), insulin, HOMA-IR, and insulin sensitivity did not differ significantly. Multiple regression analyses indicated that none of the biochemical predictors significantly explained sleep in any group ($p > 0.05$), in poorly controlled patients, non-significant opposing trends were observed for insulin and insulin resistance, sociodemographic factors included supplement use, education level, and employment were associated with better sleep among poorly controlled patients. Genetic analysis of two intronic variants in the SLC47A2 gene (g.19716681G>C and rs1597652185) revealed no significant associations with glycemic control or sleep, though both showed similar distribution patterns across groups. Statistical analysis didn't find significant association between either variant and glycemic or sleep status ($p > 0.05$).

Conclusions: Poor glycemic control was common and associated with higher insomnia prevalence. While demographic and clinical factors showed no clear links with glycemic control or sleep, supplement use emerged as a protective factor. FBG and HbA1c strongly differentiated control groups, but other biomarkers and SLC47A2 variants were not predictive. Findings suggest that combining metabolic management with supportive measures like supplementation may improve sleep and outcomes in type 2 diabetes..

KEY WORDS: glycemic control, sleep status, diabetes mellitus, type 2, glycemic control status

Wiad Lek. 2025;78(12):2707-2716. doi: 10.36740/WLek/213629 DOI

INTRODUCTION

A global health disorder in the world is Diabetes mellitus (DM) among population in last decades and this cause about 5 million deaths every year consequences by complications, diabetes mellitus type 2 (DM2) is a disease related to lifestyle and other factors like glycemic control by food intake and treatment, more than 422 million of adults are living with DM worldwide, projected to reach about 642 million by 2040 [1]. The diabetes burden is mostly impacted resource-limited countries where screening and access to medication and care are not readily available [2].

The major public health among DM patients is Poor and inadequate glycemic control and it is a significant risk factor of disease progression and development, that can markedly raise healthcare costs and life expectancy and quality reduction [3]. Glycemic control is considered the most effective means of preventing complications in DM [4]. However, a small percentage of DM cases maintain the level of blood sugar low than 7% glycated hemoglobin, while 53–70% of have uncontrolled [5].

Some reports found that good glycemic control might be implicated to access and availability to better knowledge level, primary care and best lifestyle [6, 7]. Furthermore, other investigations demonstrated that glycemic control is correlated with some factors like age, sex, disease duration, treatment type, body mass index (BMI), FBG, education, job type, comorbidities, self-care system, and psychosocial health [8-11].

Sleep duration and quality Optimizing is a way of glycemic control improving in DM2 [12]. Since sleep is related to some changes in hormone status which change glucose metabolism, it is important to assess the correlation between sleep duration with glycemic control [13].

AIM

The present article aims to study the influence of metformin response in sleep in diabetes mellitus patients type 2.

MATERIALS AND METHODS

Study subjects and design of study: a cross sectional study was conducted in diabetes mellitus center in Al-Saader hospital city during (February to may/2024), about 80 DM type 2 cases were enrolled in this study, all patients under metformin drug (1000 mg/ day) only. Each patients was diagnosed as type 2 DM using clinical and biomarker which treated by metformin drug (1000 mg/ day) for at least 3 month.

ETHICAL APPROVAL

Ethical approval: this study was conducted according to ethical approval of environment and health ministry in Iraq on (20-9-2023), written consent was optioned from each case to contributed in this research.

SAMPLE COLLECTION

About 3 ml of blood was drained from Venus by disposable siring, about one ml put in EDTA tube and other quantity was using to serum extraction by gel tube, serum then transfer to store at -20 ^{0}C.

GENETIC STUDY

DNA was isolated from whole blood using extraction kit, the target SNPs of SLC47A2: Intron Variant sequence was amplified by specific primers and TM 58^{0}C, the products were sent to macrogene company (Korea) for sequencing, data were analyzed using MEGA11.

DATA COLLECTION:

Data was collected from patients by questionnaire which included (name, age, weight, length, sex, duration of disease, education, family history, job, sleep period and supplement uptake (including vitamins and minerals).

Exclusion criteria: the following criteria was excluded from this study included (obesity patients, cancer patients, viral infection patients, patients with other type of diabetic medications, diabetes complications and patients refused to contribute in this research).

Glycemic parameters test: Fasting blood glucose (FBG) and HbA1c% were estimated by routine lab work, insulin level was estimated using BT lab detection kit (E0010Hu), HOMA-IR and insulin sensitivity according to Minh et al., [14].

DATA ANALYSIS

The study subjects were classified to three categories of glycemic control included (<7 is good control, 7-8 is intermediate control and > 8 is poor control group) according to [15]. The sleep status also classified to three groups according to Seow et al., [16] included well sleep, intermediate sleep and insomnia. Results were represented as mean±SD for continuous data while percentage was used in categorical data. ANOVA one way and indpendant sample t test were used to compare among study groups, chi square, a linear regression to estimate the relationship between glycemic parameters and sleep in glycemic control groups, all analyses use $p < 0.05$.

RESULTS

The distribution of study subjects showed that only 26.3% of cases achieved well glycemic control, while 30% were in the moderately controlled group and the largest proportion, 43.8%, fell into the poor control group. This indicates that inadequate glycemic control was common among the study population.

When comparing sleep status across glycemic groups, the majority of cases in all categories were classified as having intermediate sleep quality. In the well-controlled group, 66.7% recorded intermediate sleep, whileist 28.6%

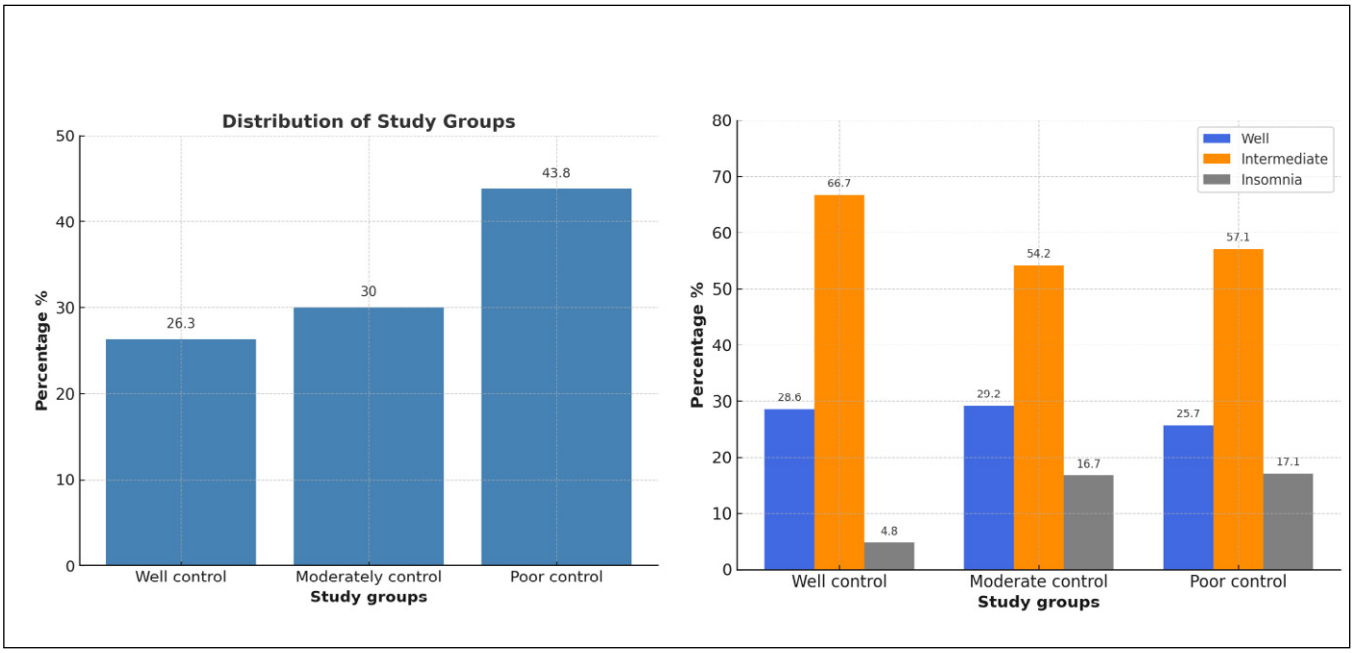

Fig. 1. Classification of Diabetes Mellitus (DM2) patients and sleep status based on glycemic control groups
Source: Own materials

had good sleep and low proportion 4.8% suffered from insomnia. In the moderately controlled group, 54.2% recorded intermediate sleep, 29.2% good sleep, and 16.7% insomnia. Among poorly controlled participants, 57.1% had intermediate sleep, 25.7% good sleep, and 17.1% insomnia, all changes were non-significant assocation (p=0.722) (Fig. 1).

These findings suggest that insomnia prevalence increased with worsening glycemic control (rising from 4.8% in well-controlled to 17.1% in poorly controlled participants). At the same time, the proportion of individuals with good sleep was lower in the poor control group compared with well and moderately controlled groups. Overall, the results indicate that poorer glycemic control is associated with greater sleep disturbance, although intermediate sleep problems were common across all glycemic categorie (Fig. 1).

The comparison of baseline characteristics among glycemic control groups demonstrate no statistically significant differences in age, BMI, or disease duration (p > 0.05). Similarly, educational level, family history of diabetes, sex distribution, and job status did not differ significantly between groups. Although not significant, a greater proportion of poorly controlled patients had only primary school education (80%) compared with well-controlled patients (61.9%).

Supplement use was only variable reporting a statistically significant difference was (p = 0.048). A higher proportion of patients in the well-controlled group reported supplement intake (23.8%) compared with those in the moderate (4.8%) and poor control groups (8.6%). This suggests a possible beneficial role of supplementation in maintaining better glycemic control.

Overall, the results indicate that demographic and socio-clinical factors such as age, sex, education, occupation, or family history were not strongly associated with glycemic control. However, supplement intake appeared to have a positive association with glycemic outcomes, and poor glycemic control tended to coincide with a higher prevalence of sleep disturbance.

The comparison of study variables across the three glycemic control groups is clarified in Table (1). As expected, FBG and HbA1c% showed highly significant differences among the groups (p = 0.000). Patients in the poor control group had markedly higher FBG (293.02 ± 87.69 mg/dL) compared with the moderate (209.9 ± 49.04 mg/dL) and well control groups (139.04 ± 45.11 mg/dL). In same manner, HbA1c% values elevate progressively from the well-controlled group to the moderate group and were highest in the poor control group in Table (2).

In contrast, IN did not differ significantly across groups (6.32 ± 4.93, 10.32 ± 13.04, and 7.34 ± 8.43 mIU/L, p = 0.513). Likewise, HOMA-IR values were higher in the moderate (92.20 ± 110.71) and poor control groups (94.40 ± 116.80) compared to the well control group (39.58 ± 31.39), but the difference did not reach statistical significance (p = 0.185), likely due to large variability. IS also showed no significant variation between groups (p = 0.472).

When cases were compared according to sleep status groups (good, intermediate, insomnia), no statistically significant differences were found across biochemical parameters (p > 0.05). Age, BMI, and disease duration were comparable between groups, though cases with insomnia tended to have slightly longer disease duration (9.27 ± 4.83 years) than those with good (6.65 ± 4.84 years) or intermediate sleep (6.11 ± 5.19 years). FBG and

Table 1. Social-demographic distribution of study subjects according to glycemic control group

Study variables	Well control	Moderate control	Poor control	P
Age (year)	49.38±8.85	52.25±	53.02±9.233	0.590
BMI (kg/M2)	28.17±3.92	27.50±2.95	26.76±4.478	0.402
Duration	5.17±5.28	7.68±5.21	6.93±5.980	0.787
Education				
Primary school	13 (61.9)	17 (70.8)	28 (80.0)	0.5205
High school	5 (23.8)	5 (20.8)	6 (17.1)	
Undergraduate	3 (14.3)	2 (8.3)	1 (2.9)	
Family history				
Yes	13 (61.9)	16 (66.7)	26 (74.3)	0.604
No	8 (38.1)	8 (33.3)	9 (25.7)	
Sex				
Male	7 (33.3)	8 (33.3)	16 (45.7)	0.529
Female	14 (66.7)	16 (66.7)	19 (54.3)	
Sleep period				
Well	6 (28.6)	7 (29.2)	9 (25.7)	0.722
Intermediate	14 (66.7)	13 (54.2)	20 (57.1)	
Insomnia	1 (4.8)	4 (16.7)	6 (17.1)	
Supplement				
Yes	5 (23.8)	1(4.8)	2 (8.6)	0.048
No	16 (76.2)	23 (95.2)	33 (91.4)	
Job				
Yes	10 (47.6)	8 (33.3)	13 (37.1)	0.597
no	11 (52.4)	16 (66.7)	22 (62.9)	

Source: Own materials

Table 2. Glycemic parameters and sleep period mean differences in the study groups.

Study variables	Well control	Moderate control	Poor control	P
FBG mg/dL	139.04±45.11	209.9±49.04	293.02±87.69	0.000
HbA1c%	5.96±0.52	7.90±0.724	11.43±1.797	0.000
IN mIU/L	6.32±4.93	10.32±13.04	7.34±8.43	0.513
HOMA-IR	39.58±31.39	92.20±110.71	94.40±116.8	0.185
IS	1.12±0.413	1.20±0.46	1.06±0.46	0.472
Sleep period (hours)	6.09±1.37	6.00±1.44	5.80±1.47	0.741

Source: Own materials

HbA1c% were non-significant highest in the insomnia group (256.9 ± 87.74 mg/dL and 9.93 ± 2.56%), Insulin and HOMA-IR levels varied widely across groups; patients with insomnia showed lower insulin (3.67 ± 1.57 µIU/mL) and lower HOMA-IR (41.81 ± 20.92) compared to the other groups, though again without statistical significance. Insulin sensitivity (IS) was slightly decrease in the insomnia group (0.92 ± 0.27) compared to those with better sleep, but the trend was not significant.

In other words, the results suggest that while cases with insomnia showed a tendency toward poorer glycemic control (higher HbA1c and FBG, lower insulin sensitivity) and longer disease duration, these differences were non statistical significance (Table 3).

Multiple regression analysis was performed separately for the well, moderate, and poor glycemic control groups, with sleep as the dependent variable. Across all three groups, none of the biochemical predictors were statistically significant ($p > 0.05$). In the well-controlled group, IN showed the highest standardized coefficient (β = 1.154, $t = 0.988$, $p = 0.339$), suggesting a possible positive influence on sleep, although the effect was not significant. Other predictors, including FBG and HbA1c, demonstrated weak and non-significant effects.

In the moderately controlled group, all predictors had small standardized coefficients with no significant differences to sleep. HbA1c (β = -0.119, $p = 0.659$) and IN (β = -0.126, $p = 0.968$) indicated weak negative associations, while insulin resistance (β = 0.207, $p = 0.948$) showed a negligible positive association.

In the poor-control group, only the model constant was statistically significant ($t = 2.315$, $p = 0.028$). While none of the biochemical variables independently pre-

Table 3. Glycemic parameters mean differences according to sleep status in the study groups

Study variables	Good sleep	Intermediate sleep	Insomnia	P
Age (year)	49.36±8.12137	52.76±10.05682	52.81±8.400	0.351
BMI (Kg/m2)	26.47±3.70	27.87±3.89	26.94±4.49	0.366
Duration (year)	6.65±4.84	6.11±5.19	9.27±4.83	0.182
FBG	206.00±88.214	231.00±95.416	256.90±87.74	0.312
HbA1c%	8.857±2.795	8.746±2.61	9.933±2.56	0.410
IN	8.92±8.923	8.53±10.51	3.67±1.57	0.266
HOMA-IR	79.29±80.770	88.17±118.92	41.81±20.92	0.398
IS	1.17±0.48	1.14±0.46	0.92±0.27	0.295

Source: Own materials

Table 4. Multiple regression analysis of predictors of sleep across glycemic control groups

Variable	Well Control β	t	Sig.	Moderate Control β	t	Sig.	Poor Control β	t	Sig.
Constant	–	1.260	0.227	–	1.574	0.133	–	2.315	**0.028**
FBG	-0.216	-0.437	0.668	0.021	0.059	0.953	-0.087	-0.356	0.724
HbA1c	0.166	0.603	0.555	-0.119	-0.448	0.659	0.115	0.632	0.532
IN	1.154	0.988	0.339	-0.126	-0.041	0.968	0.909	1.002	0.325
IS	-0.690	-1.387	0.186	-0.075	-0.149	0.883	0.228	0.758	0.454
IR	-0.411	-0.383	0.707	0.207	0.066	0.948	-0.901		

Source: Own materials

dicted sleep, IN (β = 0.909, $p = 0.325$) and IR (β = -0.901, $p = 0.284$) showed relatively stronger but opposing trends, suggesting potential metabolic imbalance in this subgroup (Table 4).

Comparison across groups found that the well-controlled group display slightly stronger insulin-related effects, the moderate group displayed the weakest associations overall, and the poor-control group demonstrate more pronounced but non-significant trends for IN and HOMA-IR

These outputs indicate that glycemic biomarkers alone do not significantly predict sleep in any control category. Sleep quality in DM2 may instead be influenced by a combination factors including disease duration, psychological stress and lifestyle. Although IN and HOMA-IR trends in the poor-control group may point to underlying biological relationships, further studies with others factors are needed to clarify these associations.

In the well and moderate glycemic control groups, no significant changes were found in sleep across supplement use, education level, job status, family history, and sex. This suggest that in patients with better glycemic regulation, sociodemographic variables did not appear to have a measurable impact on sleep quality.

By contrast, in the poor control group, some sociodemographic factors effect significantly in the sleep. Supplement use was associated with higher sleep, indicating a potential benefit of supplementation in cases with poor glycemic control. Education level also influenced sleep quality, with high school graduates reporting better sleep compared with those with primary or undergraduate education. Job status was another significant factor, as employed individuals had higher sleep compared to unemployed individuals. Sex differences were not significant but showed a trend toward higher sleep in males compared to females. Family history did not show any significant relationship with sleep in any of the groups (Table 5).

Taken together, these findings suggest that sociodemographic factors exert a stronger influence on sleep quality among DM2 with poor glycemic control, while their impact is negligible in those with well or moderately controlled diabetes. This finding highlights the complex interaction between metabolic control and sociodemographic determinants in shaping sleep outcomes.

GENETIC STUDY OF SLC47A2: INTRON VARIANT

In this study, intronic variants of SLC47A2 gene were analyzed to investigate their potential association with glycemic control and sleep status in DM cases, two SNPs were identified: a novel variation g19716681G>C and rs1597652185, statistical analysis revealed non-significant association between either variants and glycemic or sleep quality (Tables 5 and 6), interestingly, both variants exhibited similar frequency across the study variables (Fig. 2), suggesting shared distribution pattern within the population samples.

Table 5 Mean ± SD sleep scores by sociodemographic variables across glycemic control groups

Variable	Well (Mean ± SD)	Moderate (Mean ± SD)	Poor (Mean ± SD)
Supplement (No)	6.13 ± 1.41	6.00 ± 1.48	5.59 ± 1.36
Supplement (Yes)	6.00 ± 1.41	6.00 ± 0.09	8.00 ± 0.00
P	0.864	0.950	0.005*
Education (Primary)	6.31 ± 1.25	6.24 ± 1.52	5.50 ± 1.43
Education (High school)	6.00 ± 1.73	5.40 ± 0.89	7.17 ± 0.98
Education (Undergrad.)	5.33 ± 1.53	5.50 ± 2.12	6.00 ± .
P	0.558	0.480	0.036*
Job (No)	6.18 ± 1.25	5.75 ± 1.39	5.32 ± 1.29
Job (Yes)	6.00 ± 1.56	6.50 ± 1.51	6.62 ± 1.45
P	0.771	0.239	0.010*
Family history (No)	6.13 ± 1.46	5.88 ± 1.13	5.33 ± 1.22
Family history (Yes)	6.08 ± 1.38	6.06 ± 1.61	5.96 ± 1.54
P	0.940	0.772	0.276
Sex (Male)	6.29 ± 1.80	6.13 ± 1.46	6.25 ± 1.53
Sex (Female)	6.00 ± 1.18	5.94 ± 1.48	5.42 ± 1.35
P	0.665	0.772	0.097

Source: Own materials

Table 6. The genotype distribution of g19716681G>C and rs1597652185 according to glycemic control

	Well control		Moderate control		Poor control		p
SNPs	GG	GC	GG	GC	GG	GC	
g19716681G>C	7	6	3	2	4	7	0.588051^{NS}
rs1597652185	7	6	3	3	4	7	0.588051^{NS}

Source: Own materials

Table 7. The genotype distribution of g19716681G>C and rs1597652185 according to sleep status.

	Good sleep		Intermediate sleep		Insomnia		p
SNPs	GG	GC	GG	GC	GG	GC	
g19716681G>C	4	2	9	9	1	2	0.3261^{NS}
rs1597652185	4	2	9	9	1	2	0.3261^{NS}

Source: Own materials

Table 6 shows the distribution of genotype of the two SLC47A2 intronic variants -g.19716681G>C and rs1597652185 - based on glycemic control status in DM cases. For the g.19716681G>C variant, the GG genotype was found in 7, 3, and 4 cases across the well-controlled, moderately controlled, and poorly controlled groups, respectively, while the GC genotype found in 6, 2, and 7 cases in the same respective groups. A similar distribution pattern was observed for rs1597652185, with the GG genotype recorded in 7, 3, and 4 individuals, and the GC genotype in 6, 3, and 7 individuals across the glycemic control groups, the statistical analysis showed non-significant association, these findings referred that the intronic SNPs g.19716681G>C and rs1597652185 do not significantly influence glycemic control in the studied DM cases

Table 7 clarified the genotypes distribution of SLC47A2 intronic variants - g.19716681G>C and rs1597652185—according to sleep status. For the g.19716681G>C variant, the GG genotype was observed in 4 cases with good sleep, 9 with intermediate sleep, and 1 with insomnia. The GC genotype was detected in 2, 9, and 2 cases, respectively, across the same sleep categories. A nearly identical distribution was observed for rs1597652185. Statistical analysis found a p-value of 0.3261 for both variants, indicating no significant association between genotype and sleep status. These findings suggest that the g.19716681G>C and rs1597652185 variants of the SLC47A2 gene are not significantly related to sleep quality among the cases.

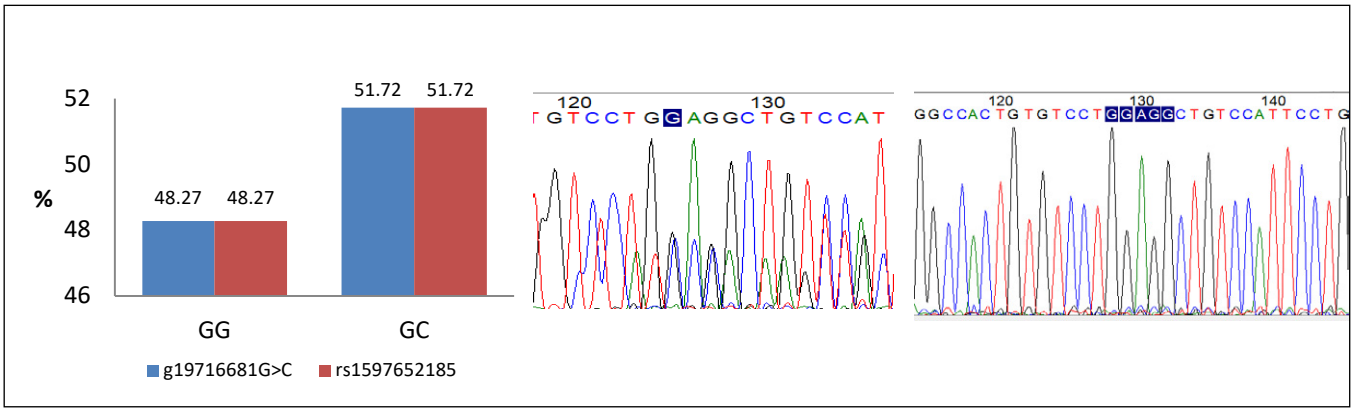

Fig. 2. The genotypes distribution of g19716681G>C and rs1597652185 with histogram in study cases
Source: Own materials

DISCUSSION

This study as suggested to investigate the problem of insomnia accompanying most of DM 2 patients, the results showed that HbA1c% which depended in study group classification has significant effect in sleep, evidences explored that good glycemic control achievement among DM2 cases is a paramount essential in delaying and/or early onset of complications preventing that related to morbidity and mortality elevation, high percentage of study subjects enrolled in poor glycemic control and this dis agree with general coverage in worldwide that found about 50% achieved good glycemic control [17], in sub-Saharan Africa region reports have demonstrated that majority (74%) of DM2 have poor glycemic control [18]. Other investigations agree with this results, [19] indicated that the prevalence of poor glycemic control observed was significantly high. The explanation in the poor glycemic control prevalence among DM2 have been reported in many countries and this perhaps belong to different factors, like health systems improvement including DM2 care and knowledge among patients and population about diseases like DM2 and how to improvement blood sugar levels control, also the Fragile health systems most common factors which effect in the diabetes care [20, 21]. The irregular follow up of patients, bad lifestyle, low exercise activity and genetic factors are implicated in glycemic control [22-23].

Sleep status is a factor that was significantly associated with poor glycemic control which based on the HbA1c% level in present work, results showed significant association with insomnia (<4 h). this result agree with report of [24, 25], in Brazil and Japan, in contrast, long sleep period significant association with poor glycemic control have been reported in Japan, and China who clarified that good sleep helps to have good glycemic control during 6-8 h [26, 27].

Generally, the pattern of sleep has a major modulatory impact on metabolism of glucose and energy uptake that have effects on the good glycemic control maintenance in DM2 cases, moreover, the high poor glycemic control prevalence with sleep deprivation and/or poor sleep quality can be belong to appetite up-regulation, and impairment of glucose metabolism [27], in addition to cortisol that causes elevation in plasma glucose and high insulin resistance and disturbance in melatonin hormone level which may affected by insulin [28, 29].

Regarding to others factors which depended in this study, the supplement uptake by DM2 cases showed that in the well and moderate glycemic control groups, sleep quality did not differ between supplement users and non-users ($p > 0.8$). However, in the poor control group, supplement users showed significantly better sleep ($p = 0.005$). This align with study that certain supplements - particularly magnesium - improve sleep duration and reduce insomnia severity in type 2 diabetes patients [30, 31]. Magnesium promotes melatonin production and regulates cortisol and GABA activity, thereby enhancing relaxation and sleep stability [32].

Regarding to Education Level no significant differences were observed in the well and moderate groups while significantly among poorly controlled patients, with high school graduates reporting better sleep. Lower education has been linked to reduced diabetes self-management capacity and increased sleep disturbance [33].

Job status did not affect sleep in well or moderate groups, but in the poor-control group, employed individuals had significantly better sleep ($p = 0.010$). Employment provides structure, social stability, and financial security, which are known to support healthier sleep patterns and diabetes outcomes. Family history had no significant impact on sleep in any group ($p > 0.27$), suggesting that hereditary predisposition alone does not directly influence sleep quality. Sex differences in sleep were non-significant in all group which partially dis agree with [34].

This study detected the association between two intronic variants of the *SLC47A2* gene g.19716681G>C and

rs1597652185 with glycemic control and sleep quality in DM2 cases, The finding revealed no significant results between either variant and glycemic markers or sleep quality. Both SNPs found similar genotype frequencies in study groups in non-significant p-values for both glycemic control ($p = 0.588$) and sleep status ($p = 0.326$), these suggesting that these intronic variants may not have a functional impact in the studied groups.

The *SLC47A2* gene encodes Multidrug And Toxin Extrusion Protein 2-K (MATE2-K), a renal transporter that has important role in endogenous metabolites and drugs excretion, like metformin (first-line antidiabetic agent). some reports have explored the pharmacogenetic role of *SLC47A2* variations, in the context of metformin pharmacokinetics and therapeutic efficacy. As well as, Becker et al. [35] found that common variants in *SLC47A2* can influence renal clearance of metformin, potentially affecting glycemic response. Moreover, [36] demonstrated that certain *SLC47A2* polymorphisms were correlated with variations in metformin efficacy among Chinese patients with T2DM.

However, most studies have highlighted on exonic or regulatory variants with known functional consequences, while the clinical significance of intronic variants remains less understood. Intronic SNPs may influence gene expression by impact on splicing or regulatory elements, but not all intronic changes exert measurable phenotypic effects. The absence of association in the current study may indicate that the investigated variants do not affect *SLC47A2* expression or function, or that their effect is too subtle to be detected in this sample size.

In addition, the disturbances in sleep are commonly recorded in DM2 cases and have been linked to poor glycemic control, insulin resistance, and cardiovascular complications [37, 38]. Despite of some genetic reports have studied clock genes or neurotransmitter-related pathways in relation to sleep regulation and DM, there is limited studies linking drug transporter genes such as *SLC47A2* to sleep status. Therefore, this findings of no significant association between these variants and sleep patterns are consistent with the current lack of mechanistic or clinical evidence supporting such a relationship.

CONCLUSIONS

This study demonstrated that poor glycemic control was common among the study population, with nearly half of the patients falling into the poorly controlled group. While sleep disturbances, particularly intermediate sleep quality, were prevalent across all glycemic categories, the prevalence of insomnia increased with worsening glycemic status. Although most demographic and clinical factors such as age, sex, BMI, education, occupation, and family history were not significantly associated with glycemic control or sleep, supplement intake emerged as a significant factor, being more frequent among well-controlled patients and associated with better sleep quality in poorly controlled individuals.

Regression analyses suggested that glycemic biomarkers alone were not sufficient to predict sleep quality. Finally, genetic analysis of SLC47A2 intronic variants revealed no association with glycemic status or sleep.

Overall, these findings highlight the interplay between glycemic regulation, sleep quality, and lifestyle factors, suggesting that interventions targeting metabolic control alongside supportive measures such as supplementation may improve sleep and health outcomes in patients with type 2 diabetes.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 16.08.2025
ACCEPTED: 26.10.2025