Is Being a Lark Healthier for Patients with Type 1 Diabetes Mellitus?

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Abstract

Background Sleep quality and mood have been evaluated in type 1 diabetic (T1DM) patients, but chronotypes were not studied. Our objectives were to analyze chronotypes, sleep and mood variables and to describe their association with some metabolic variables in this population.

Methods An observational, cross-sectional study was performed. Adults with a diagnosis of T1DM were included. We evaluated chronotypes by the Morningness-Eveningness Questionnaires, sleep quality by Pittsburgh Sleep Quality Index (PSQI), excessive daytime sleepiness by Epworth Sleepiness Scale (ESS), symptoms of depression by Patient Health Questionnaire - 9 (PHQ-9) and emotional well-being by Emotional Well Being Index (IWHO-5). A few metabolic variables were included.

Results Ninety-five patients participated. The mean age was 38 years old (range 18–70). The average body mass index (BMI) was 24.4 Kg/m^2 (standard deviation [SD]: 4.6). Out of the total sample, 52.6% were males. The Intermediate chronotype was predominant: $n = 56$ (55%). We found poor quality of sleep in 67.4% of the sample, excessive daytime sleepiness in 14.7%, depressive symptoms in 6.3% by PHQ9 and low perception of well-being by IWHO-5 in 16.8%. Evening chronotype scored worse in sleep quality ($p = 0.05$) and had lower well-being ($p = 0.03$) compared with the other chronotypes. Higher MEQ values (morningness) correlated with lower height ($p = 0.043$), lower values in the PSQI ($p = 0.021$); and higher values in emotional well-being ($p = 0.040$).

Conclusions We found that the predominant chronotype in T1DM was the intermediate. Two-thirds reported poor quality of sleep and 14,7% excessive daytime sleepiness. Possible diagnosis of a depressive disorder in 6.3% and poor self-perception of emotional well-being in 16. 8% were observed. The morning chronotype had significant correlation with better sleep quality and higher scores in emotional well-being.

Keywords
- sleep
- depression
- type 1 diabetes mellitus
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Introduction

Type 1 Diabetes Mellitus (T1DM) represents < 10% of the universe of patients with DM.[1] T1DM is commonly diagnosed in childhood and adolescence, although it may occur at any age. Some forms of T1DM have no known etiology and are therefore considered idiopathic.[2]

Sleep parameters, sleep disorders, chronotypes, and mood variables have been largely studied in previous studies in patients with type 2 Diabetes Mellitus (T2DM).[3–5] Only one study approached social jetlag and glycemic control in DM1,[6] but none addressed the relation of chronotypes in T1DM.

All biological processes and functions oscillate rhythmically. Circadian rhythms are controlled by a master clock, located in the suprachiasmatic nucleus in the hypothalamus, with an oscillatory expression of genes with a period of ∼ 24 hours. Despite its endogenous rhythmicity, it is influenced by environmental cues, being the most important the light-dark cycle.[6]

The circadian temporal regulation system also includes the multiple peripheral cellular or tissue clocks, controlled by the master clock. The interruption or desynchronization of the circadian clocks are responsible for the pathogenesis of several diseases, including diabetes.[7]

A person's "preference" pattern of sleep hours relative to the 24-hour clock is called a chronotype. It is particular for each individual and can vary over the years. This preference can be assessed using the Hörne and Östberg Morningness-Eveningness Questionnaire (MEQ), categorizing five chronotypes: extreme evening, moderate evening, intermediate, moderate morning and extreme morning,[8] or simplified in three chronotypes, "larks" (early risers), "owls" (evening chronotype), and the group in between.[9]

Previous studies demonstrated that "Owls" have an increased risk of cardiometabolic diseases.[10–12]

The underlying causes that lead to these disorders have not been clearly defined, but appear to be related to a circadian misalignment, caused in some cases by chronic sleep deprivation for example, which leads to the dysregulation of metabolic, immune, and hormonal processes that govern energy regulation and glycemic control[13–16] especially in the "owl" chronotype.

Although several studies tend to point the harmful effect of the evening chronotype in several physiological and affective parameters, we hypothesize that the morning chronotype (M) would present better sleep quality, less daytime sleepiness, fewer mood disorders, and fewer altered metabolic parameters related to T1DM.

As objectives, we set ourselves to analyze the different chronotypes, other variables related to sleep and mood in patients with T1DM and to correlate the different chronotypes with some metabolic variables.

Material and Methods

An observational, cross-sectional study was done and previously approved by the Ethics Committee of Research Protocols (C.E.P.I.) of the Hospital Italiano de Buenos Aires.

The period of recruitment ranged from March 2016 to January 2020. The included patients were those who consulted consecutively in the outpatient Endocrinology Service of our hospital, during the period previously described.

The present report is based on a sample of 95 individuals > 18 years old. Gender was reduced to three main categories: female, male, and nonbinary.

Five patients were excluded because they did not fulfill the admission requirements.

The inclusion criteria were: the patient was willing to participate and gave their consent; the diagnosis of T1DM had to be made by health personnel, at least 6 months before and with an age between 18 and 75 years old.

Furthermore, we requested the possibility (not exclusive), to have complementary material laboratory results, made within 6 months prior to the medical consultation, as well as the glycosylated hemoglobin (HbA1) values, blood glucose values, basal cortisol values, cortisol 23 hours and vitamin D values if they had been performed previously.

The normal values considered[17,18] were:

- HbA1c: ≤ 7% (53 mmol/mol).
- Blood glucose: ≤ 126 mg/dl.
- Basal Cortisol: between 10 to 20 mcg/dl.
- Cortisol 23 hours: < 5 mcg/dl.
- Vitamin D: > 30 ng/ml.

The exclusion criteria were: patients who did not consent to participate; age < 18 years old and > 75 years old and those who had a terminal illness. Pregnancy and acute diabetes related disorder (acute hypoglycemia or diabetic ketoacidosis within the last 3 months).

Convenience sampling was used. Ninety-five patients agreed to participate. All participants gave their informed consent asserting to know their privacy would be protected by the Declaration of Helsinki and national laws.

Questionnaires

A survey was designed to evaluate different variables associated with the sleep and mood variables. The survey included standardized questionnaires:

a) To assess the chronotype of the subjects we used both the Horne and Ostberg version of the Morningness-Eveningness Questionnarie (MEQ)[8] adapted to Spanish (MEQ-SA) (Versión Castellana del Cuestionario de Matutinidad-Vespertinidad de Horne y Ostberg).[19] The scores range from 16 to 86 points. The 5 chronotypes categorized include: extreme evening (scores 16 to 30), moderate evening (31–41), intermediate (42–58), moderate morning (59–69) and extreme morning (70–86).[8] The categorization into 3 chronotypes includes: evening (scores ≤ 41), morning (scores ≥ 59), and intermediate chronotype (scores between 42 and 58).[19]

b) To assess sleep quality, we used the Spanish version of the Pittsburgh Sleep Quality Index (PSQI).[20,21] This is a 24-item self-administered scale, divided into 7 subcomponents (subjective sleep quality, sleep

latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medications, and daytime dysfunction). The score for each subcomponent ranges from 0 to 3 points. The global PSQI score ranges from 0 to 21. Scores ≤ 5 were considered good sleepers, while a score > 5 categorizes participants as poor sleepers.

c) To assess excessive daytime sleepiness, we used the Epworth Sleepiness Scale (ESS). It is a self-administered questionnaire that explores different daily life situations where subjects may be prone to fall asleep. The total score ranges from 0 to 24, with pathological values > 10.[22,23]

d) To assess depression symptoms, we used the Patient Health Questionnaire - 9 (PHQ-9).[24,25] The Spanish version of the PHQ-9 is a self-administered questionnaire designed to assess depression symptoms. The scores range from 0 to 27 points. The cutoff point for severity ranges were > 5 for mild cases, 10–14 for moderate cases, and ≥ 15 for severe depressive symptoms, respectively.

e) To assess the self-perception of emotional well-being and depression, we used the Spanish version of the Emotional Well Being Index (IWHO-5).[26] It consists of a 5-item self-administered scale, used to provide a measure of the feeling of emotional well-being. Higher scores are related to a greater sense of well-being and scores < 13 indicate low emotional well-being and have been related to symptoms of depression.[27,28]

The survey also included questions created ad hoc to evaluate variables related to demographic and some metabolic variables.

Statistical Analysis

The results of qualitative variables were expressed as frequencies and percentages. The quantitative variables were expressed as mean and standard deviation (SD). Measures of trend and distribution were used to describe the groups.

The stratification of the characteristics of the participants was made according to the three or five categories of morning-evening types based on their Morningness-Eveningness Questionnaire-Spanish Adaptation (MEQ-SA) (Versión Castellana del Cuestionario de Matutinidad-Vespertinidad de Horne y Ostberg).

We used the Kruskal-Wallis test to compare population means when they had a similar distribution.

Analysis of variance (ANOVA) was used for comparison of means among the analyzed groups. Bivariate correlations were performed among the final score of the MEQs and the other quantitative variables. All data were analyzed with PASW Statistics for Windows, version 18 (SPSS Inc., Chicago, IL, USA). P-values < 0.05 were considered statistically significant.

Results

Ninety-five patients were included. Five were excluded because they did not fulfill the admission requirements. The mean age was 38 ± 13.6 years old (range 18–70 years old). The mean body mass index (BMI) was 24.4 Kg/m^2 (SD: 4.6). Chronotypes were distributed in morning chronotype: $n = 10$ (10.5%), intermediate chronotype: $n = 28$ (29.5%), and evening chronotype: $n = 7$ (7.4%). We have not been able to calculate the mean/SD of T1DM diagnosis time, since this variable was not requested in the distributed surveys.

Demographic and other variables data are shown in ►**Table 1**. The intermediate chronotype was predominant in our sample (58.9%). We found a very high prevalence of poor sleep (PSQI > 5) in the whole T1DM population (67.4%). Excessive daytime sleepiness was found in 14.7% of the sample. Depressive symptoms by PHQ9 were seen in 6.3%, and 16.8% scored < 13 in the IWHO-5 (indicating low emotional well-being and depression).

►**Table 2** shows the analysis of the different components of PSQI by the chi-squared test. The components were more altered in the intermediate group, followed by the evening group. In the case of the analysis of component 1, we showed the number and percentage of those patients who reported poor or quite poor sleep quality. Component 2: we showed those who had a sleep onset latency > 30 minutes, once or twice a week. Component 3: we expressed those who reported sleeping < 6 hours. Component 4: we showed those in which sleep efficiency was $< 75\%$. Component 6: we

Table 1 Variables data outcomes.

Demographic Variables		
Age (years old)		38 ± 13.6
Male		50 (52.6%)
Female		45 (47.4%)
Questionnaires		
Epworth Sleepiness Scale		$6{,}7 \pm 3{,}9$
ESS > 10 = excessive daytime sleepiness		14 (14.7%)
Pittsburgh Quality of Sleep Index		$6{,}9 \pm 3{,}2$
PSQI > 5 (poor sleep quality)		64 (67.4%)
PHQ9		3.8 ± 3.8
PHQ9 ≥ 10 (depressive symptoms)		6 (6.3%)
IWHO5		$15{,}8 \pm 4{,}8$
IWHO5 < 13 (depression)		16 (16.8%)
Chronotypes (MEQ)	Extreme Morning	2 (2.1%)
	Moderate Morning	21 (22.1%)
	Intermediate	55 (57.9%)
	Moderate Evening	14 (14.7%)
	Extreme Evening	3 (3.2%)
Simplified Chronotypes (MEQs)	Morning	17 (17.9%)
	Intermediate	56 (58.9%)
	Evening	22 (23.2%)

Abbreviations: ESS, Epworth Sleepiness Scale; IWHO-5, Emotional Well-Being Index; MEQ, Horne and Östberg Questionnaire; PHQ-9, Patient Health Questionnaire; PSQI, Pittsburgh Sleep Quality Index.
Values expressed as mean $\pm$ SD or frequencies (percentages).

Table 2 Analysis of the different components of the PSQI using the chi- squared test.

	Chronotypes						
	Morning		Intermediate		Evening		*p-value*
	n	%	*n*	%	*n*	%	
PSQI > 5	13	13.7	37	38.9	14	14.7	0.292
PSQI - Latency > 30	4	4.3	15	15.8	7	7.4	0.276
PSQI - Duration < 6 hour	8	8.4	19	20	2	2.1	0.175
Component 1: Subjective Sleep Quality	7	7.4	25	26.3	11	11.6	0.122
Component 2: Sleep latency	6	6.3	23	24.2	11	11.6	0.062
Component 3: Sleep duration	8	8.4	19	20.0	2	2.1	0.175
Component 4: Usual Sleep Efficiency	0	0	7	7.4	1	1.1	0.185
Component 5: Sleep disturbances	11	11.6	19	20.0	6	6.3	0.408
Component 6: Use of sleep medication	0	0.0	4	4.2	1	1.1	0.442
Component 7: Dysfunction during the day	6	6.3	11	11.6	7	7.4	0.196

showed those who used sleep medication one or more times per week. Component 7: we showed those who reported dysfunction the next day at least once a week and that it caused them a moderate problem. We found no significant differences among the groups analyzed.

►**Table 3** shows that there were no significant differences using univariate ANOVA among the 5 chronotypes and poor sleep quality (PSQI > 5) and other variables related to sleep, daytime sleepiness (ESS >10) and variables related to mood (depression): PHQ9 ≥ 10 and IWHO-5 < 13.

►**Table 4** shows the relationship among the three simplified chronotypes, and variables related to sleep and mood questionnaires using univariate ANOVA. As expected, the E chronotype had a significative difference with respect to other chronotypes in the mean bedtime and wake up time. The evening Chronotype scored higher in the PSQI (worse sleep quality) and lower in emotional well-being by the IWHO-5.

►**Table 5** shows Pearson bivariate correlations made among the M chronotype and other questionnaires, such as the PSQI, the ESS, the PHQ9, and the IWHO5. We found that the M chronotype correlated with a lower score in the PSQI (good sleep); they go to bed earlier ($p = 0.038$; correlation coefficient R = - 0.2); and get up earlier ($p = 0.000$; correlation coefficient R = - 0.5) with a higher value of the R coefficient in the IWHO-5 (lower depression).

►**Table 6** shows the relationship among the 3 different chronotypes and metabolic variables by ANOVA. We found a lower baseline cortisol value in the M and E chronotypes compared with the I chronotype. The intermediate chronotype had higher basal cortisol values.

►**Table 7** shows Pearson bivariate correlations, among the M chronotype and other quantitative variables such as age, weight, height, BMI, and different metabolic variables as blood glucose, HbA1c, basal cortisol, and vitamin D values.

Table 3 Relationship between the chronotypes and different questionnaires evaluating sleep and mood in DM1.

	Chronotypes					*p-value*
	Extreme Morning	Moderate Morning	Intermediate	Moderate Evening	Extreme Evening	
Sex (Female)	2 (2.1%)	9 (9.6%)	26 (27.7%)	7 (7.4%)	3 (3.1%)	0.27
PSQI > 5	0	14 (14.9%)	35 (37.2%)	11 (11.7%)	3 (3.2%)	0.16
SSOL (> 30 minute)	0	5 (5.3%)	14 (14.9%)	4 (4.3%)	3 (3.2%)	0.06
TST (< 6hs)	0	9 (9.6%)	17 (18.1%)	2 (2.1%)	0	0.24
ESS > 10	0	3 (3.2%)	10 (10.6%)	1 (1.1%)	0	0.91
PHQ-9 ≥ 10	0	1 (1.1%)	4 (4.3%)	1 (1.1%)	0	0.98
IWHO-5 < 13	0	3 (3.2%)	8 (8.5%)	5 (5.3%)	0	0.62

Abbreviations: ESS, Epworth Sleepiness Scale; IWHO-5, Emotional Well-Being; PHQ-9, Patient's Health Questionnaire; PSQI, Pittsburgh Sleep Quality Index; SSOL, Subjective Sleep Onset Latency; TST, Total Sleep Time.
Values expressed as frequencies (percentages).

Table 4 Relationship among different chronotypes and different questionnaires using univariate ANOVA.

	Chronotypes			
	Morning ($n = 22$)	Intermediate ($n = 56$)	Evening ($n = 17$)	*p-value*
MEQ	64.2 ± 4	49.6 ± 4.4	35.3 ± 5.4	0.00
PSQI	5.9 ± 2.7	6.8 ± 3.2	8.4 ± 3.1	0.05
PQSI #1 (Bedtime)	22:58 (0:55)	23:44 (1:04)	01:04 (1:04)	0.00
PQSI #3 (Time to wake up)	06:30 (1:11)	07:28 (1:12)	09:28 (0:58)	0.00
ESS	6.4 ± 3.7	6.7 ± 4	7.1 ± 3.8	0.85
PHQ-9	2.9 ± 3	4.1 ± 4	4.3 ± 4.4	0.42
IWHO-5	18 ± 6.1	15.4 ± 4	14.2 ± 4.5	0.03

Abbreviations: ESS, Epworth Sleepiness Scale; IWHO-5, Emotional Well-Being Index; MEQs, Horne and Östberg Questionnaire; PHQ-9, Patient Health Questionnaire; PSQI, Pittsburgh Sleep Quality Index.
Values expressed as mean ± SD.

Table 5 Pearson bivariate correlations between morningness and different questionnaires in DM1.

	MEQ ≥ 59	
	p-value	R
Total PSQI	0.02	−0.237
PQSI #1 (Bedtime)	0.04	−0.213
PQSI #3 (Time to wake up)	0.00	−0.540
ESS	0.47	−0.076
PHQ-9	0.36	−0.096
IWHO-5	0.04	0.214

Abbreviations: ESS, Epworth Sleepiness Scale; IWHO-5, Emotional Well-Being Index; MEQs, Horne and Östberg Questionnaire; PHQ-9, Patient's Health Questionnaire; PSQI, Pittsburgh Sleep Quality Index; R, Pearson correlation coefficient.

Table 7 Pearson bivariate correlations between morningness and metabolic variables in DM1.

	MEQ ≥ 59		
	n3	*p-value*	R
Age	95	0.07	0.188
Height (m)	89	0.04	−0.215
Weight (k)	88	0.61	−0.055
BMI (k/m2)	86	0.40	0.091
Blood glucose (mg/dL)	38	0.53	0.105
HbA1c (%)	78	0.25	0.133
Basal Cortisol (µg/dl)	65	0.76	0.038
Cortisol 23h (µg/dl)	43	0.29	−0.165
Vitamin D (ng/mL)	44	0.10	0.252

Abbreviations: BMI, Body Mass Index; HBA 1C, glycosylated hemoglobin; R, Pearson correlation coefficient.

Table 6 Relationship among different chronotypes and metabolic variables by ANOVA in DM1.

	Chronotypes			
	Morning ($n = 22$)	Intermediate ($n = 56$)	Evening ($n = 17$)	*p-value*
Age	41.6 ± 15.4 (22)	38.3 ± 13.5 (56)	32.7 ± 10 (17)	0.12
Height (m)	1.65 ± 0.1 (22)	1.67 ± 0.1 (53)	1.68 ± 0.1 (14)	0.61
Weight (k)	68.4.2 ± 13.7 (20)	68.4 ± 19.4 (53)	66.3 ± 11.8 (15)	0.91
BMI (k/m2)	25.1 ± 4.2 (20)	24.4 ± 5.2 (52)	23.1 ± 2.4 (14)	0.44
Blood glucose (mg/dL)	127 ± 32 (8)	135 ± 65 (25)	110.8 ± 32 (5)	0.83
HbA1c (%)	8.46 ± 1.7 (20)	8.54 ± 1.5 (44)	8.23 ± 1.9 (14)	0.42
Basal Cortisol (µg/dl)	9.9 ± 4.8 (14)	15 ± 8.1 (37)	9.9 ± 9.2 (14)	0.04
Cortisol 23h (µg/dl)	2.6 ± 1.5 (9)	3.7 ± 2.4 (26)	5.3 ± 6.1 (8)	0.17
Vitamin D (ng/mL)	32.9 ± 24.2 (10)	24.2 ± 8.7 (26)	27.8 ± 9.9 (8)	0.05

Abbreviations: BMI, Body Mass Index; HBA 1C, glycosylated hemoglobin.
Values expressed as mean ± SD (frequencies).

We found that the M chronotype correlated with lower height ($p = 0.043$; correlation coefficient R = - 0.2). We did not find differences in the analyses of other metabolic variabilities.

Discussion

The present study analyzed, in addition to the various chronotypes, variables associated with sleep and mood in the T1DM population.

Regarding the first objective, we used the MEQ-SA to categorize the different chronotypes in T1DM, finding that, in our population, the intermediate chronotype was predominant. As you know, the MEQ has been used in research of biological rhythms in different types of populations, but not in T1DM patients.

In our study, the mean age was 38 years old. In the adult age, according to the literature, the M chronotype is predominant, perhaps due to lower temperature amplitude and an advance phase of the peak of body temperature.[29] The adult population also tends to wake up earlier due to work, social, and family duties.

Besides, we evaluated various subjective sleep-related parameters through the PSQI and we found that 67% of the population studied, more than a half, reported having poor quality of sleep. In the I chronotype, all the components of PSQI were altered. The M chronotype showed less altered components than the rest.

The literature reported that adult subjects with T1DM with poor sleep quality (mean PSQI > 5) had significantly greater nocturnal glycemic variability and fear of hypoglycemia. Nocturnal glycemic variability and fear of hypoglycemia were significantly associated with poor sleep quality.[30]

A relationship between glycemic control and sleep has been reported in people with T1DM. Subjects with higher mean glucose and higher glycemic variability had shorter duration of sleep in the same study.[31]

It is known that the deprivation of hours of sleep, even partial, induced behavioral changes in the general population.[32] The deprivation of hours of sleep can affect glycemic control causing insulin resistance and glucose intolerance, as well as learning, memory, and attention disorders, causing alterations in immune response, cardiovascular function and neurohumoral regulation. We found that 18.9% of I chronotype reported sleeping < 6 hours (fewer hours than those considered normal for adult patients), although the difference was not significant in relation to the other chronotypes.

When analyzing the delay in terms of bedtime and getting up, a positive correlation was observed with the E chronotypes which is consistent with observations made in other chronotype studies in the nondiabetic population. In our sample, the mean bedtime in the M chronotype was at 11:00 PM and in chronotype E at 1:00 AM It has been suggested that a prolonged sleep onset latency (insomnia) in T1DM could be due to greater glycemic variability.[32]

To analyze the chronotypes with prolonged sleep onset latency, we found that the M and I chronotypes manifested mild insomnia but the E chronotypes reported moderate insomnia. Good sleep quality is considered a key feature in metabolic health, since it was shown that poor quality in T2DM is negatively correlated with HbA1controls. It is known that having a good night's sleep, with an adequate duration and of good quality, can help regulate the metabolism and the activity of the sympathetic-adrenal system, improving glycemic control.[32]

When considering the daytime sleepiness assessed by the ESS, already studied in several T1DM populations,[32] but not in the population of our country, we found that 14% of the respondents presented pathological sleepiness. Barone et al. found that the scores of ESS in the DM1 patients were higher than those of the control group, without becoming pathological. We have not found a significant difference among the different chronotypes, but those of the I chronotype had a higher score in the ESS.

When analyzing variables related to mood, using the PHQ9, 6.3% reported symptoms of depression. Previous studies reported doubled prevalence of depression in patients with any type of diabetes.[33]

When evaluating the different chronotypes with respect to the PHQ9, we did not find significant differences. When using the IWHO-5, the M chronotype reported greater well-being compared with the E chronotype, which had scores near the cutoff point for depression. Gaspar-Barba et al.[34] suggested that the depressive symptoms are influenced by chronotypes, where the E chronotype has more suicidal thoughts, more problems at work, more paranoid symptoms, higher scores of anxieties, while the M chronotype shows a lower proportion of melancholic symptoms. Therefore, the M chronotype may have a protective factor for depression.

There is also a bidirectional relationship between poor sleep and depression.[35]

Moreover, literature reports that depressed mood is worse in the morning but improves throughout the day.[36]

Both the diurnal variation of the mood and the alteration of the sleep-wake cycle indicate a possible alteration of the circadian rhythm.[37,38]

The explanation would be due to a decrease in the amplitude of the temperature rhythm throughout the day, which has been related to the pathophysiology of both sleep disorders and mood disorders, specifically depression.[39]

Also, the alteration of the rhythm of secretion of some hormones has been related to the pathophysiology of depression. For example, several attempts have been made to associate different chronotypes in perimenopausal women with depressive mood changes, but no differences were found among them.[40]

Besides, we must consider that the neurotransmitters that regulate mood also regulate sleep, and the vast majority of patients with depressive disorders have sleep disturbances. In the literature, it is recommended to reinforce the action of external zeitgebers, such as promoting physical activity,[41,42] promoting exposure to light, maintaining

regular times for sleeping and eating[43]; all would help improve mood swings in these patients. In our study, the M chronotype had better mood and sleep quality compared with the E chronotype, perhaps because waking up earlier, they had more time of exposure of external zeitgebers.

On the other hand, as a second objective, we proposed to correlate the different chronotypes with some metabolic variables. In our T1DM population, we did not find differences in HbA1c values in the different chronotypes, but the mean values were altered in all chronotypes.

We found a lower baseline cortisol value in the M and E chronotypes compared with the I chronotype. Cortisol is an adrenocorticoid hormone that presents a typical circadian profile with values that rise hours before waking up and values that are much lower throughout the day, reaching its minimum 2 hours after we begin to sleep.[44]

Cortisol increase consists in the preparation of the body to start the day, increases the blood pressure, the concentration of glucose and the cardiac output. It is considered a good marker of the circadian system. It can be affected by external factors such as stress situations, light exposure at certain times of the day, hyperprotein meals, aging, deprivation of sleep, a predominance of light sleep, nocturnal awakenings, which lead to increased cortisol levels. Interestingly in nocturnal experimental animals, it is corticosterone and not cortisol, and the profile of this hormone is inverse to that of daytime species, so the maximum value occurs at the beginning of the night, coinciding with the onset of nocturnal activity.[45]

Another interesting finding was that the I and E chronotypes presented low vitamin D values. The difference was nonsignificant among chronotypes. Vitamin D is the "vitamin of the sun," with light being one of the most important external zeitgebers for the circadian rhythm.[46]

We did not find that hypovitaminosis D in T1DM has been analyzed in relation to circadian rhythm and sleep in other studies.

We found that the M chronotype had a significant correlation regarding height (shorter height) when correlating with the rest of the chronotypes, but no other correlation was found regarding other evaluated parameters related to metabolic variables in the present study, as it was the only parameter (within the metabolic variables) found, we cannot issue conclusions about it.

Limitations and Strength

As biases, we must say that we have used subjective measures to assess circadian rhythm, sleep quality/disorders, and mood disturbances, but we were unable to make objective assessments of chronotypes or sleep disorders. However, the costs of these studies, the required technology and logistics, would be impossible to cover in our country for the required sample size. In addition, it is known that the subjective perception of chronotypes, and especially the subjective appreciation of sleep disorders and mood swings does not always correlate with objective evaluations.

As this was a cross-sectional study and we had a small sample of laboratory parameters, we were unable to carry out an exhaustive analysis of the metabolic aspects of T1DM that could be pathophysiologically associated with poor quality of sleep.

However, as a strength of the present study, we must say that according to our review of the literature, it was the first to examine the distribution of chronotypes in a sample of patients with T1DM

In conclusion, we found that the I chronotype was predominant in our population with T1DM; more than half of the patients reported being poor sleepers, and the I chronotype had a greater tendency to present all the components of the PSQI altered. The M chronotype showed the least altered components.

We also found that $< 15\%$ in this population of T1DM reported excessive daytime sleepiness.

Depressive symptoms were found in a small percentage, but $> 16\%$ reported a decreased well-being score.

Although it is necessary to increase the sample, we found that the morning chronotype (M), had a significant correlation with a better sleep quality and a lower risk of depression (higher scores in emotional well-being), partly corroborating our study hypothesis.

Ethical Responsibilities

Protection of people: the authors declare that no experiments were performed on humans for the present research.

Confidentiality of the Data

The authors declare that no patient data appear in this article. The survey used was anonymous.

Right to Privacy and Informed Consent

The authors declare that no patient data appear in this article.

Financing

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Conflict of Interests

The authors have no conflict of interests to declare.

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