

# The cross talk between chronotype, depression symptomatology, and glycaemic control among sudanese patients with diabetes mellitus: A case-control study

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## ABSTRACT

**Aim of the Study:** There is an increasing awareness about chronotype and depression among patients with diabetes mellitus as commonly ignored serious association. We aimed to investigate the same among patients with type 2 diabetes mellitus and their relation to glycaemic control. **Subjects' and Methods:** This case-control study conducted at two diabetes centers in Omdurman, Sudan during the period from April 2019 to September 2019. Ninety-two patient with type 2 diabetes and 94 controls signed a written informed consent then interviewed using a structured questionnaire based on the morningness-eveningness scale and the 12-item general health questionnaire; A blood sample was taken for the glycated haemoglobin to assess glycaemic control. The Statistical Package for Social Sciences was used for Data analysis. **Results:** They were 92 patients with diabetes (58.7% women) and 94 healthy control subjects (52.1% women); matched for ages ( $57.03 \pm 8.59$  for diabetic patients and  $58.46 \pm 10.58$  years for control subjects) and sex. Morning chronotype was reported in 95.3% vs. 47.5% and intermediate chronotype was evident in 52.4% vs. 4.3% in controls and patients respectively,  $P < 0.05$ . Depression symptomatology was found in 76.1% of patients with diabetes vs. 40.4% of control subjects,  $P < 0.05$ . No association was shown between depression symptomatology, chronotype, age, sex, and HbA<sub>1c</sub>,  $P > 0.05$ . **Conclusion:** Sudanese patients with diabetes were more likely intermediate, less morning chronotype, and more depressed compared to their counterparts. No association was found between depression symptomatology and other patient's characters. Larger studies investigating the risk behind depression, chrono-nutrition, and social jetlag among patients with diabetes are needed.

**Keywords:** Chronotype, depression, Sudan, type 2 diabetes

## Introduction

Diabetes mellitus (DM) is approaching an epidemic worldwide and due its vascular complications, DM is a leading cause of mortality and morbidity. According to the International Diabetes Federation, 10.9% of Sudanese adults are suffering from DM with 613.6 thousand undiagnosed.<sup>[1]</sup>

Circadian rhythm is inherited and varies across individuals (diurnal preferences), Morning chronotype (Larks), evening (night Owls), and intermediate. Although the wakefulness and sleep are mainly regulated by the suprachiasmatic nuclei and connections, but light, stress, hormones, and genes are major influences.<sup>[2]</sup> Therefore, working inappropriately against the inherited circadian rhythm (circadian misalignment) might end in serious diseases including coronary syndrome, diabetes mellitus, and the metabolic syndrome. The sharp upsurge of diabetes mellitus globally cannot be explained solely by traditional risk factors (unfriendly diet, job involving lack of physical activity, and genetic predisposition). Other factors including sleep and chronotype have emerged as

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Received: 07-04-2021

Revised: 07-07-2021

Accepted: 01-11-2021

Published: 31-01-2022

### Access this article online

#### Quick Response Code:



Website:  
www.jfmpc.com

DOI:  
10.4103/jfmpc.jfmpc\_656\_21

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**How to cite this article:** Mirghani HO. The cross talk between chronotype, depression symptomatology, and glycaemic control among Sudanese patients with diabetes mellitus: A case-control study. J Family Med Prim Care 2022;11:330-5.

possible causes of the dramatic increase in diabetes mellitus prevalence.<sup>[3]</sup>

The lifetime prevalence of major depressive disorders ranged from 2-21% worldwide with the highest prevalence reported in Europe, while lower rates were observed in Asia.<sup>[4]</sup> In Sudan, the situation is alarming, a study conducted among internally displaced camp population indicated that 92% were either depressed (31%) or had depressive symptomatology (61%) and the level is on the rise due to internal displacement and instability.<sup>[5,6]</sup>

Previous literature indicated that evening chronotype is associated with seasonal mood variation and global seasonality of mood, because of modernization that extends the night artificial exposure and resulting in circadian rhythm disruption. Moreover, the relationship of scoring low on the morningness/eveningness questionnaire and the seasonality of mood was robust even among populations who are not using electrical light network at home.<sup>[7]</sup> A study conducted in the USA observed the association of depressive symptomatology among patients with type 2 diabetes.<sup>[8]</sup>

The strongest non-inherited circadian zeitgeber for human is light-dark alternation and due to the growing technology preference, a rapid transformation to eveningness chronotype emerged. The increasing use of technological devices during night hours was shown to negatively influence mental and physical health (including diabetes mellitus risk). Furthermore, eveningness chronotype increased risk-taking behaviour, smoking, drug abuse, and poor school performance.<sup>[9]</sup> Active cooperation between primary care physicians and psychiatrists for the earlier detection of at risk in the general population and management will decrease hospital admission and a positive impact on the mental health of the community.<sup>[10]</sup> Furthermore, primary care physicians may play an important role in screening and management of sleep disorders and the identification of those requiring specific treatment in sleep centers.<sup>[11]</sup>

The relationship between diabetes mellitus, depression, and chronotype is complex and may exacerbate one another when to co-exist.<sup>[12]</sup> To the best of our knowledge, this is the first research to study the chronotype and depression among patients with type 2 diabetes in Sudan, studies performed in the developed countries may not apply to Sudan. Thus, we conducted this research to assess chronotype and psychopathology among patients with type 2 diabetes and their relation to diabetes control.

## Methodology

### Study design

This case-control study was conducted among 92 patients with the diagnosis of type 2 diabetes mellitus and 94 control subjects at two diabetes centers (Elnour Complex and Almutakamel in Omdurman), Sudan during the period from April 2019 to

September 2019. The Fische formula for case-control studies was used to calculate the sample size.<sup>[13]</sup>

### Data collection

The participants were interviewed using a structured questionnaire based on the English versions of the morningness-eveningness questionnaire and the Arabic version of 12-item general health questionnaire. Experienced translators and the principal researcher translated the morningness-eveningness questionnaire into Arabic; the co-patients were present to explain any difficulties in understanding the questions. Patients with type 2 diabetes were approached in a ratio of 1:1 and those who reported comorbidities that might affect sleep including severe diabetes complications, active rheumatic disorders, psychosis, dementia, and shift workers were excluded.

The Morning Evening questionnaire has been previously validated.<sup>[14,15]</sup> The questionnaire consists of 19 multiple choice as follows:

- Eleven questions were allowed for choice and scored from one to four
- Five questions scored from one to five
- Two questions scored 0, 2, 4, and 6
- One question scored 0, 2,3, and 5

The total score define participants as morning (score 70-86), moderate morning (score 59-69), intermediate (score 42-58), moderate evening (score 31-41) and definite evening with a score of (16-30).<sup>[16]</sup>

The 12-item general health questionnaire was used for the diagnosis of psychopathology. It is a useful validated screening test for minor psychiatric morbidity and mental illness in diabetes with a primary focus on depressive symptomatology.<sup>[17,18]</sup> The questionnaire inquirers are being able to concentrate on what you are doing, losing much sleep over worries, feeling that you are playing useful part of things. Also, felt able about making decisions, feeling constantly under strain, and felt you could not overcome your difficulties. Besides been able to enjoy your normal day-to-day activities, able to face up your problems, feeling unhappy or depressed, been losing confidence in yourself, and feeling of yourself as a worthless person. Lastly, been feeling reasonably happy all thing considered, each question ranged from 0-3 with 0 = less than usual, 1 = no more than usual, 2 = rather more than usual, and 3 = much more than usual with a total score of 36. The Likert scale marking (0:0:1:1) was used in this research to eliminate the bias with a cut off (5,6) regarded as no psychopathology and 7 or more psychopathology. We used the questionnaire in unity to minimize the bias.<sup>[19,20]</sup> The questions no 2, 5, 6, 9, 10, and 11 of the scale are marked negatively.

The demographic data, duration of diabetes, diabetes medications were also collected.

A blood sample was taken for HbA1c measurement to assess glycaemic control using the glycol haemoglobin reagent set from HB1C Siemens Healthcare Diagnostics Newark, DE 19714, USA.

The ethical committee of Elnour Polyclinic approved the research (Ref. No. R. 19. 1).

### Data analysis

The Statistical Package for Social Sciences (SPSS version 20, New York) was used for data analysis; the binary logistic regression was used to assess the relationship of chronotype, psychopathology, age, sex, and glycaemic control. The data were presented as a mean ± SD or percentages unless otherwise specified with a *P* < 0.05 considered significant.

### Results

They were 92 patients with type 2 diabetes and 94 healthy controls matched for age and sex (51.94 ± 10.84 versus 51.23 ± 13.39 years and 58.7% vs. 52.1% respectively, *P* = 0.690 and 0.368. The morningness-eveningness score was lower among patients with diabetes (58.02 ± 7.02) compared to their counterparts (72.04 ± 7.24), *P* = 0.000. While the psychopathology score was higher (20.10 ± 4.32 and 18.11 ± 3.35), *P* = 0.001. The above results imply that patients with diabetes more intermediate (50% vs. 0.0 in controls), while controls scored high in morning chronotype (96.8% and 44.6% respectively), *P* = 0.000. Depression symptomatology was reported in 76.1% of patients with diabetes and 40.4% of control subjects with a highly significant statistical difference, *P* = 0.000 [Table 1].

In this survey, the duration of diabetes was 9.93 ± 7.89 years, HbA1c, was 9.02 ± 2.56, and 82.6% were not targeting the recommended HbA1c. Table 2.

In the present study, no relationship was found between psychopathology, chronotype (*P* = 0.473, 95% CI, 0.951–1.115), age (*P* = 0.882, 95% CI, 0.939–1.051), sex (*P* = 0.259, 95% CI, 0.616–6.067), the duration since the diagnosis of diabetes (*P* = 0.415, 95% CI, 0.895–1.047), and the glycosylated haemoglobin (*P* = 0.093, 95% CI = 0.537–1.049). Table 3.

### Discussion

Evening chronotype is awake during the evening and consume meals, they also tend to skip breakfast and consume larger dinner. Importantly, they are prone to serious health problems including diabetes when working against their circadian preference. A previous study stated that certain genes and eveningness predispose to diabetes.<sup>[21]</sup> In the present study, more than half of patients with diabetes were intermediate chronotype and reported more depression compared to healthy controls. The current findings were in line with a study conducted in the USA and showed the association of eveningness and depression among patients with diabetes.<sup>[22]</sup>

**Table 1: Basic characters of the study group**

Character	Diabetes (n=92)	Controls (n=94)	P
Age	51.94±10.84	51.23±13.39	0.690
Sex			0.368
Women	54 (58.7%)	49 (52.1%)	
Men	38 (41.3%)	45 (47.9%)	
Chronotype score	58.02±7.02	72.04±7.24	<0.001
Depression symptomatology score	20.10±4.32	18.11±3.35	0.001
Chronotype%			<0.001
Morning	41 (44.6%)	91 (96.8%)	
Evening	1.0 (1.1%)	3.0 (3.2%)	
Intermediate	46 (50.0%)	0.0 (0.0%)	
Depression symptomatology	70 (76.1%)	38 (40.4%)	<0.001

**Table 2: Characters of patients with diabetes**

Character	Mean±SD
Duration since the diagnosis of diabetes	9.93±7.89
The glycosylated hemoglobin	9.02±2.56
Targeting a glycosylated hemoglobin of ≤7 (no %)	16 (17.4%)
Insulin use	14 (15.7%)

**\*Table 3: The relationship of depression, chronotype, age, diabetes duration, HbA1c, and sex among patients with type 2 diabetes**

Character	Wald	df	P	95% CI
Chronotype	0.514	1	0.473	0.951-1.115
Age	0.051	1	0.822	0.939-1.051
Duration since the diagnosis of diabetes	0.664	1	0.415	0.895-1.047
HbA1c	2.825	1	0.093	0.537-1.049
Sex	1.276	1	0.259	0.616-6.067
Constant	0.004	1	0.948	

\*Binary logistic regression analysis

The current data showed that 76.1% of the diabetic patients were depressed compared to 41.3% of healthy controls, similarly researchers from Egypt<sup>[23]</sup> conducted a study among patients with type 2 diabetes and found similar results, our findings were higher than Mushtaque *et al.*<sup>[24]</sup> who concluded depression in 38.7% of patients with diabetes. A great effort is needed to screen for depression and treat when appropriate in our country due to the high rates of depression among patients with diabetes. Importantly, the patients were not receiving any form of treatment for depression reflecting the lack of cross-care. Besides, the lack of resources for integrative diabetes holistic care adds to the patients suffering.

The relationship between depression, chronotype, and glycaemic control is complex and multi-directional. Previous studies<sup>[25]</sup> showed the relationship between the evening chronotype and poor diabetes control. The deterioration observed in the HbA1c was attributed to the short duration of sleep but not to composite score of morningness that reflects the individual subjective preference of activities in the evening or the morning. Another plausible explanation is that evening chronotype people skip

breakfast and consume large dinner leading to poor glycaemic control. Further explanation might be that late chronotype is associated with poor glycaemic control only in the presence of social jetlag.<sup>[26]</sup> In addition, evening chronotype usually live a sedentary lifestyle.<sup>[27]</sup> It is interesting to note that not only the meal content but also the timing, for example a lower glycaemic index in breakfast and a high protein and fat content of the evening meal lead to a lesser postprandial blood glucose.<sup>[28]</sup>

In the current study, no relationship was found between chronotype, depression, and the glycated haemoglobin level. Regarding the association of depression and HbA<sub>1c</sub>, the evidence is conflicting, Chiu & Du., 2019<sup>[29]</sup> who conducted a longitudinal study among 398 in Tiwan showed higher glycated haemoglobin among those with depression. Similar results were reported by Hasanovic *et al.*<sup>[30]</sup> However, Mansori *et al.*<sup>[31]</sup> found no association of depression and the glycated haemoglobin, while others found the contrary (more hypoglycaemic attacks) attributed to lack of self-care and non-compliance to diet.<sup>[32]</sup> The use of continuous glucose monitoring (CGM) will resolve the issue of the conflicting above results regarding the association of depression and glycaemia. Continuous glucose monitoring will add more in terms of trends arrows, hypoglycaemia, and time in the range. The association of depression and the duration of diabetes is J-shaped; in the present data, we did not find a relationship between depression and the duration since the diagnosis of diabetes.<sup>[33]</sup> The current results indicated that the association of evening chronotype and glycated haemoglobin is not direct and might be socially (neighbourhood disadvantages, social jetlag, green space, noise/light exposure) or personality determined.<sup>[34]</sup> In addition, fragility and age are important mediators of poor glycaemic control among patients with depression.<sup>[31]</sup>

The relationship between age and chronotype is controversial. Some studies reported a change towards morning chronotype from 65-94 years but these studies were cross-sectional and not confirmed by longitudinal data, while others<sup>[35]</sup> reported a late shift during adolescence peaking at 19 years then shifting earlier thereafter. In the present study, we found no difference between intermediate and morning chronotype regarding age. The association of depression and sex is conflicting, the present findings showed no association. The relationship of sociodemographic factors depression, diabetes, and chronotype is complex and multidirectional, some are going in the same direction and other in opposite. The matter is complicated further by that fact that most of the patients with diabetes are not diagnosed,<sup>[36]</sup> one big limitation of the current project is that we did not investigate the control subjects for diabetes mellitus which may increase the bias.

## Limitations

The current study is limited by the absence of follow-up data that may change the rate of depression by discovering new cases in addition to recovery of some with time. Other limitations were the small size of the survey sample, the reliance of self-administered

questionnaire which is more prone to subjectivity, and we could not control for confounders like body mass index, physical activity, and diet. An important limitation of the current survey is the fact that it was conducted at two diabetes centers (tertiary care centers) that might increase the rate of depression. However, this is the first study to assess chronotype and depressive symptomatology and exclude those with chronic comorbidities and diabetes complications. Further, larger multi-center studies assessing the chrononutrition, personality, and social factors are highly needed.

## Conclusion and Recommendations

Depression symptomatology was prevalent among Sudanese patients with type 2 diabetes; the morning chronotype was commoner among the control subjects, while more than half of the patients with type 2 diabetes were intermediate chronotype. No association was found between the glycated haemoglobin, psychopathology and chronotype. Screening for psychopathology and chronotype preference could be part of the holistic care of diabetic patients. Raising the awareness about good sleep hygiene, depression, and chronotype might reduce the incidence of diabetes mellitus. Further studies investigating the risk behind depression and eveningness chronotype in particular social jetlag and meal interplay among patients with diabetes are needed. Screening the control subjects for undiagnosed diabetes mellitus is important.

## Key points

- Depression symptomatology was prevalent among Sudanese patients with type 2 diabetes.
- The morning chronotype was commoner among the control subjects, while more than half of the patients with type 2 diabetes were intermediate chronotype.

## Ethical approval

This study was conducted according to the Declaration of Helsinki. The ethical committees of Omdurman Teaching Hospital and Elnour Poly Clinic, Omdurman, Sudan approved the research (Ref. No. R. 19. 1, dated 14/3/2019). All the participants signed a written informed consent.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

## Financial support and sponsorship

Self-funded.

## Conflicts of interest

There are no conflicts of interest.

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