International Journal of Contemporary Issues in Social Sciences
Volume 3, Issue 1, 2024 ISSN(P):2959-3808 | 2959-2461

DISRUPTIVE CIRCADIAN RHYTHM, DIABETES MELLITUS TYPE 2 AND IMMUNE DYSREGULATION AMONG ADULT FEMALES HAVING PCOS

Dr Zarghuna Naseem*[1], Shireen Iftikhar[2]

*[1]Chairperson Psychology, Lahore Garrison University, [2]MS Scholar, Lahore Garrison University

*[1]drzarghunanaseem@lgu.edu.pk, [2]shireeniftikhar123@gmail.com

Corresponding Author:*

Received: 29 December, 2023 **Revised:** 18 January, 2024 **Accepted:** 24 January, 2024 **Published:** 9 February, 2024

ABSTRACT

This study investigated the relationship between Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation among adult females having PCOS**. A** Correlational design was used. The sample (n=121) was collected from the females having PCOS from different hospitals of Lahore. The age range was from 20 to 55 and the data was collected through purposive sampling. Tools of the study were, Circadian Rhythms and Mood (SCRAM) Questionnaire, with three subscales that are 1) Good Sleep, 2) Morningness, 3) Depressed Mood (Byrne, et al., 2017). For Polycystic Ovarian Syndrome a self-inventory questionnaire having six items by Bedrick (2020) was used. For diabetes, the PAID was a self-report questionnaire that contained 20 items, developed by Polonsky (1995) was used. Immune System Assessment Questionnaire (ISAQ) based on 17-items by Hartmut (2014) was to identify patients suffering from immunodeficiency or systemic autoimmunity. Result showed that Circadian Rhythm and its subscales, Good Sleep and Morningness, has inverse relationship and Depressed Mood has significant positive relationship with PCOS. Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation significantly predicted PCOS among adult females. Implications for clinicians, psychologists, and for society have been discussed to improve the life style to reduce PCOS.

Keywords: Disruptive Circadian Rhythm, Diabetes Mellitus Type 2, Immune Dysregulation

INTRODUCTION

The aim of this study was to explore circadian rhythm, diabetes mellitus type 2 and immune dysregulation among adult females having polycystic ovarian syndrome (PCOS). The Circadian Rhythm is the display of a sidereal day (sunrise-sunset) that gives allowance to adapt the external (Vitaterna, et al., 2001). Circadian Rhythm is a 24 hours natural clock of our body that is regulated by the exposure of day-night light. Circadian Rhythm, driven by superchiasmatic core inside the central system interconnected with the human immune system (Hastings, et al., 2018). It is also called a biological clock that balances our daily life routine such as eating, sleeping, mood, behaviors, biological and psychological health or immunity. This desynchronization of biological clock is called Disrupted Circadian Rhythm (Zee, et al., 2013). Circadian Rhythm disturbance can lead to many biological and psychological problems. In DSM-5 there are Circadian Rhythm Sleep-Wake Disorders (APA, 2005). It is the natural body cycle, also called a natural healer and plays an important role to maintain people's healthy life style (Ruan, et al., 2021).

Several factors can lead to circadian rhythm disruption (Baron, et al., 2014) such as People who work night shifts or rotating shifts often experience disrupted circadian rhythms because their work schedule conflicts with their body's natural sleep-wake cycle (Smith, et al., 2012). Shift work or irregular schedules can challenge their natural tendency to wake up early (Carrier, et al., 1997). Another factor is jet lag, where rapid travel across multiple time zones can lead to the body's internal

clock out of sync with the local time to the destination resulting in sleep disturbances, fatigue, and other symptoms (Baron, et al., 2014). Irregular sleep patterns, such as staying up late and waking up irregularly, can disrupt the body's natural rhythm (Potter, et al., 2016). Excessive screen time or exposure to artificial light during the night can interfere with the body's production of the sleep hormone melatonin, which can disrupt the sleep-wake cycle (Majumdar, et al., 2020). Certain medical conditions such as sleep disorders, neurological disorders, and hormonal imbalances can also lead to disrupted circadian rhythms (Turek, et al., 2001). Environmental factors, like irregular meal times, lack of natural light exposure during the day, and inconsistent daily routines, can contribute to circadian rhythm disruption (Gamble, et al., 2014). It can not only impact sleep quality but can also contribute to daytime fatigue, reduced cognitive performance, impaired mood (Brainard, et al., 2015), difficulty sleeping during the day and staying awake at night, leading to ongoing sleep deprivation and related health issues (Md, 2010). It is related with metabolic disorders such as obesity, type 2 diabetes, and metabolic syndrome. Irregular eating patterns and lack of synchronization between the body's internal clock and meal times can lead to altered metabolism (Potter, et al., 2016). It influences the release of various hormones, including cortisol and melatonin. Disruptions can lead to dysregulation of these hormones, affecting not only sleep but also stress responses and overall hormonal balance (Meléndez-Fernández, et al., 2023). Proper sleep and a stable circadian rhythm are crucial for maintaining emotional well-being (Bechtel, 2015).

If Circadian rhythm disturb, it disturbs our lifestyle that affects our health and cause different physiological and mental illness like cancer, depression (Farhud & Aryan, 208). Circadian rhythm itself is not the sole cause of the mental issues but if the predominant symptoms are present, then it can (Ahmad et.al, 2020). Recent studies show the relationship of mood disorder and Circadian Rhythm disruptions (Walker et al, 2020). Disruption in circadian rhythms also leads to cognitive deficits and decreased alertness, particularly during times that are typically aligned with sleep (Xu, et al., 2021). The disruption has been associated with an increased risk of heart disease, hypertension, and other cardiovascular issues (Chellappa, et al., 2019), also plays a role in an elevated risk of certain types of cancer, including breast cancer and colon cancer (Savvidis, & Koutsilieris, M, 2012). As people age, their circadian rhythms can become less robust and contribute to sleep difficulties and daytime sleepiness (Brown, et al., 2011).

Sleep Regulation and Circadian Rhythms: A Two-Process Model

Circadian Rhythm and sleep are said to be important in the context of immune system. The sleep disturbance can cause inflammation and miserection (Jagannath, et al., 2017).

Two interrelated theories – recuperative and circadian – collaborate to expound on the reasons behind sleep. The ability to initiate sleep hinges on the synchronization of two bodily processes, the circadian rhythm, which governs the periodic release of various hormones, such as melatonin, which play a role in sleep regulation. The second process involves the recuperative function, demonstrated by the accumulation of sleep-inducing substances within your body over a span of 16 hours each day (Borbély, 1982).

While the exact purpose of sleep is not fully understood, it is known to play a vital role in various aspects of physical, mental, and emotional health (Ferrara, 2001; Chokroverty, 2010).

Lack of sleep can result in sleep deprivation, reduced sleep quality, and a variety of negative health outcomes, including mood disturbances, impaired cognitive performance, and increased risk of chronic diseases (Potter, et al., 2016). The two main categories of sleep are rapid eye movement sleep, essential for cognitive and emotional processing, as well as creative thinking (Blumberg, et al., 2020) and non-rapid eye movement sleep is crucial for physical restoration, immune function, and memory consolidation (Carskadon, et al., 2005). Each stage serving distinct purposes (Chokroverty, 2010).

Circadian Rhythm is affected by environmental factors like light, darkness and seasons (Czeisler, et al., 1998). Morningness, refers to an individual's natural tendency to feel more awake, alert, and productive during the early hours of the day (Taillard, et al.,1999). The body's internal circadian rhythm, which is regulated by the suprachiasmatic

nucleus (SCN) in the brain, plays a significant role in determining an individual's natural tendency toward morningness ((Basnet, et al., 2018; Hur, et al., 1998). Conversely, individuals who have an eveningness preference tend to be more productive and energetic later in the day). Morningness individuals alertness may vary throughout the day, affecting their overall productivity and well-being (Kudielka, et al., 2006; Watts, et al., 1983). Sleep disruptions can lead to irritability, fatigue, and reduced quality of life (Hasan, et al., 2022).

Addressing the disruptions to the circadian rhythm through strategies like light management, maintaining a consistent sleep schedule, and practicing good sleep hygiene can help mitigate the negative effects of a disrupted internal clock. Remedies to disrupted circadian rhythm is exposure to natural light during the morning and minimizing light exposure at night (Terman, et al., 2001). Maintaining a regular sleep-wake schedule, even on weekends, can support circadian alignment. (Lu, & Zee, 2006). Practicing good sleep hygiene, such as creating a comfortable sleep environment and avoiding stimulants before bedtime, can promote healthy sleep patterns (Schaefer, et al., 2012). Morningness individuals can prioritize activities requiring focus and productivity during their peak alertness hours (Gau, et al., 2007).

The Social Zeitgeber Theory refers to external environmental cues that synchronize human circadian rhythms. Mood episodes are triggered by life stress, which results in disturbances to people's social routines and subsequently affects their biological circadian rhythms (Grandin, et al., 2006).

Polycystic Ovarian Syndrome (PCOS)

Polycystic ovarian syndrome is a metabolic and a lifestyle disorder that manifests further Type 2 Diabetes Mellitus (T2DM), obesity and other many more hormonal imbalances (Kahn, et.,al,1999). In 2012, World Health Organization (WHO) described that almost 116 million women among all over the world have been affected by PCOS (Kabel et al., 2016). Polycystic Ovarian Syndrome (PCOS), is an endocrine or hormonal problem starts in puberty age in which females face irregular menstrual periods, may have heavy or prolonged periods, or might skip periods altogether. Females may have issues in giving birth in future because of high androgens levels and cysts in their ovaries. Its physical symptoms are having oily and acne face, obesity or underweight, irregular menstruation problems like menorrhagia, in which menstrual cycle get prolonged more than normal cycle and dysmenorrhea in which females face abdominal cramps and pains and loss of hair or excessive growth of hair (Aziz, 2004). It is called a lifestyle disorder.

There are many risk factors of PCOS. One is insulin resistance, women are at high risk of developing Diabetes Mellitus Type 2 in future because high sugar in blood causes increase in male androgen hormones that result in difficulty in ovulation process of females (Legro, 2001). Genetic factors are involved in PCOS, however most of them are the environmental factors. Disturbed circadian rhythm contribute in PCOS (Shan, et al., 2015), leads to diabetes type 2 and immune dysregulation in future (Wang, et al., 2023).

Other factors like hormonal imbalance particularly elevated levels of androgens such as testosterone can lead to various symptoms and complications (Diamanti-Kandarakis, et al., 2006). It also disrupts the normal process of ovulation, making it difficult for individuals with the condition to conceive. This is a leading cause of infertility in people with PCOS. It is a lifelong condition, but its symptoms can often be managed with a combination of lifestyle changes, medications, and sometimes surgical interventions. Treatment goals include regulating menstrual cycles, managing hormonal imbalances, improving insulin sensitivity, and addressing specific symptoms like acne or excess hair growth. Lifestyle changes such as maintaining a healthy weight, regular exercise, and a balanced diet are often recommended otherwise females can have diabetes and disrupted immune systems.

Diabetes Mellitus Type 2

Diabetes is derived from Greek word means siphon: “to pass through” and the Latin word “mellitus” means honeyed or sweet. Over 425 million people around the world are currently living with diabetes. The sugar in urine and blood was found in 1776 in Great Britain. It has two types that is type 1 and 2 diabetes. In Diabetes Type 1, pancreas does not secrete insulin because of defect or inherited problem. In Diabetes Type 2, pancreas secretes insulin, but insulin resistance occurs because of beta

cells. Pancreas is the gland, helps in controlling sugar levels by secreting two hormones insulin and glucagon. When blood glucose decreases, pancreas starts releasing the glucagon (Spielman, et al. 2014). One of the main reasons is poor diet (DeFronzo, et al., 2015). It mostly happens in adulthood because of obesity and lack of exercise (Kaul, et al, 2013).

Misalignment in our circadian rhythms, such as sleep-awake cycle, eating habits, cause the resistance to produce insulin in the body, results in Diabetes Mellitus type 2. Excessive burn out or physical activities can also increase the risk of diabetes mellitus in adulthood beside the other genetic factors (Goyal & Jilal, 2018). Diabetes Mellitus can also lead to psychological problems such as depression, anxiety and more severe diseases such as heart attack or skin diseases (Pouwer, 2009. Inflammation causes higher risks of cardio vascular diseases, tooth diseases, osteoporosis and Diabetes problems (Haffner, 1998). People with gestational and Type 2 Diabetes are more in population than type 1 diabetes mellitus (Ben-Haroush, et al., 2004).

Immune Dysregulation:

The immune system is responsible for defending the body against infections, diseases, and other foreign invaders, while also distinguishing between the body's own cells and foreign substances. When the immune system doesn't function properly, it can lead to a variety of health issues (Barosi, 2014). Most functions of the immune system such as circulation of T-cells and production of pro inflammatory cytokines is at peak during nighttime. Cytotoxic leukocyte and anti-inflammatory production are at peak during daytime. The disruptions of sleep due to circadian rhythm can lead to dysfunction of immune system (Jerigova, et al., 2022). The brain function of sleep and circadian rhythm shares the neuro endocrinological effects to send the control of immune system (Davidson & Diamond, 2001). Moreover, growth hormone show peak at nighttime and more works properly by sleep (Ahmad et.al, 2020). In result, it is evidenced that the circadian rhythm and sleep both evoke the effects in the immune system and secretions of the anti/pro-inflammatory secretions and cause serious clinical distress (Ahmad et.al, 2020). The disruption in the circadian clock and immune function can cause inflammatory diseases and in compromise of immune function (Haspel, 2020).

To understand the relationship of sleep, Circadian Rhythm and immune functions, in this research, we will study how desynchronization of our biological clock causes Disruptive Circadian Rhythm, Diabetes Type 2, Immune Dysregulation in adult females having PCOS.

LITERATURE REVIEW

The interplay between psychological distress and sleep disturbances in the context of reproduction has received limited attention but could be a pivotal factor to take into account when addressing and treating infertility (Goldstein et.al.,2016). Shang et.al, (2020) did research on rats and showed that altered circadian clock caused change in reproductive and metabolic dysfunctions, which further led to PCOS. Recent findings suggest the circadian system plays a pivotal role in governing various systems implicated in the genesis of mood disorders (McClung, et al., 2016). A study by Wang, et al., (2021) revealed a significant correlation between PCOS and night shift work and genome-wide Chrono disruption in ovarian granulosa cells.

Conn, et.al. (2000)'s study was done to see the prevalence of PCOS with diabetes, among premenopausal women, showed that 82% of women with diabetes type 2 had PCOS, 52% had menstrual irregularity. Talbott, et. al., (2007) reported that 6% to 10% of prevalence of Diabetes Type 2 was found in women with PCOS. In all incident cases 15.0% to 35.6% of Diabetes Type 2 in white women. Sleeping late and less, coupled with constant metabolic excess change both internal and external environmental stimuli to the brain and due of these alterations, the circadian rhythm clock disrupts leading to the metabolic disorders and Diabetes Mellitus Type 2 (Kreier, et al., 2007). Zhu, et.al, (2020) did not find association of PCOS with risk of diabetes, stroke or coronary heart disease. However, other features of PCOS like obesity, high testosterone levels and low sex hormones etc. may explain the association between PCOS and cardio metabolic disorders.

Moulana (2019) checked the immune etiology of PCOS in female rats and found that potential immune system dysregulation suggests a link between excess androgen, chronic inflammation, and immune-mediated diseases in patients having PCOS.

Castanon-Cervantes, et. al., (2010) induced circadian disruption experimentally, that altered the immune responses. Endotoxin shock induced by LPS was given, that led to hypothermia and death after 4 continuous weeks of 6 hours of light and dark schedules. With 89% death rate compared with 21% mice in un-shifted control. This was due to the increase in the release of proinflammatory cytokines in response to LPS treatment in shifted animals. Stress and sleep deprivation altered the immune function and were the potential mediators of the effect.

Rationale:

The prevalence of PCOS has increased by 65% over the past decade worldwide (Yang, 2022) so there is a need to identify the factors which contribute this disease. As people are getting busy in daily life activities and their workloads is increasing so their life balance of internal bodies and outside environment becomes desynchronized. It causes Disruptive Circadian Rhythm which can further lead to diabetes and immune dysregulation, causing PCOS among young women. In this study researcher wanted to explore whether unhealthy lifestyle causes PCOS. This study focused on identifying relationship between Disruptive Circadian Rhythm, Polycystic Ovarian Syndrome, Diabetes Mellitus Type 2 and Immune Dysregulation among adult females having PCOS.

Hypothesis:

There would be a significant relationship between Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation among adult females having PCOS.

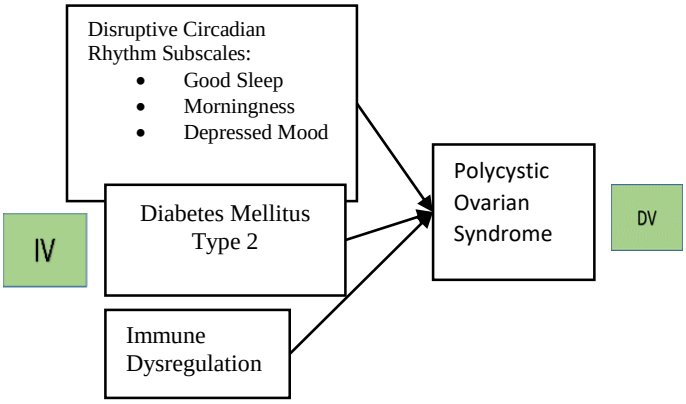
There is likely to be a negative relationship between good sleep and PCOS among adult females.

There is likely to be an inverse relationship between Disruptive Circadian Rhythm's subscale morningness and PCOS, and positive relationship between depressed mood and PCOS among adult females.

There is likely to be a positive relationship between diabetes and PCOS among adult females.

Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation will predict PCOS in adult females.

Hypothized Model



Method

In this study, correlational design was used. Sampling strategy was non-probability purposive sampling. The sample was consisted of 121 young and middle-aged (20 to 55 years) adult married and unmarried females, having PCOS. The data was collected from the females having PCOS from government and private hospitals of Lahore. Sample's demographic characteristics has been shown through descriptive statistics.

Majority of the participants were middle-aged (n= 73, 59.8%), 49 females (40.2%) were from young adult age group that was from 20 to 28 years. The married females were 87 (71.3%), while 35 were unmarried (28%). 72 of them (62.3%) did not have any child while 46 females that were married, had children (37.7%). 80 females (65.6%) had reported their family history of PCOS. Among them 88 females (72.1%) had diabetes while 34 (27.9) were free of this disease.

Assessment Measures

The Sleep, Circadian Rhythms and Mood (SCRAM) Questionnaire, 15-item with three subscales that are 1) Good Sleep, 2) Morningness, 3) Depressed Mood (Byrne, et al., 2017) was used in this study. For Polycystic Ovarian Syndrome a self-inventory questionnaire having six items by Bedrick (2020) was used. For diabetes, the Problem Areas in Diabetes (PAID) is a self-report questionnaire that contains 20 items, describe negative emotions related to diabetes, developed by Polonsky (1995) was used. Immune System Assessment Questionnaire (ISAQ) based on 17-items by Hartmut (2014) was to identify

patients suffering from immunodeficiency or systemic autoimmunity. For the present study, all the items were adapted and made binary, and for the scoring of binary items, a negative response got always the weight 0.5, whereas a positive response received the weight 4 or 2. The ISAQ score of an individual represents the sum of the weighted items (Peter, et al., 2014).

Results

The data was analyzed through the statistical package for social sciences (SPSS). For this purpose, descriptives, correlation and regression analysis were used.

Table 1

Psychometric Properties of the study measure of PCOS, Disruptive Circadian Rhythm (Good Sleep, Morningness & Depressed Mood), Diabetes Mellitus Type 2 & Immune Dysregulation.

Variables	Range								
	k	*M*	*SD*	*a*	*Potential*		*Actual*		*Skew*
					Min.	Max.	Min.	Max.	
PCOSQ	6	22.86	4.38	.70	1	5	10	32	-.15
SCRAM	15								
Subscales									
1-Good Sleep	5	13.71	3.47	.67	1	5	8	24	.92
2-Morningness	5	17.28	3.91	.65	1	5	10	28	.47
3-Dep. Mood	5	21.21	3.36	.66	1	5	12	26	-.83
PAID	20	48.55	20.47	.93	0	76	.8	3.3	-1.31
ISAQ	17	10.00	4.17	.61	0	.9	5	26	1.84

Note. M=Mean, SD= Standard Deviation and α=Cronbach's Alpha reliability

Table 1 illustrates the values of Cronbach alpha reliability which lies from 0.61 to .93. The highest is the reliability values of Problem Areas in Diabetes (PAID) scale and lowest for Immune System Assessment Questionnaire (ISAQ) that is also acceptable and reliable.

Table 2

Summary of Correlations, Mean and Standard Deviation for the scores on the PCOS, Disruptive Circadian Rhythm (Good Sleep, Morningness & Depressed Mood) and Immune Dysregulation (N=122)

Measure	M	SD	1	2	3	4	5	6
PCOS	22.8	4.38	-	-.36**	-.40**	.40**	.33**	.35**
Good Sleep	13.7	4.47	-.36**	-	.39**	-.56**	-.41**	-..28**
Morningness	17.2	3.91	-.40**	.39**	-	-.52**	-.47**	-.26**
Depressed Mood	21.2	3.36	.40**	-.56**	-.52**	-	.46**	.27**
Diabetes Type 2	48.5	20.4	.33**	-.41**	-.47**	.46**	-	.32**
Immune Dysregulation	10.0	4.17	.35**	-.28**	-.26**	.27**	.32**	-

Note: M= Mean, SD= Standard Deviation, * is significant at the 0.05 level ** is significant at the 0.01 level

Table 2 revealed that PCOS has highly significant positive relationship with Depressed Mood, Diabetes Mellitus Type 2 and Immune Dysregulation. PCOS has significant negative relationship with Good Sleep and Morningness. Good Sleep has highly significant positive relationship with Morningness and significant negative relationship with PCOS, Depressed Mood, Diabetes Mellitus Type 2 and Immune Dysregulation. Morningness has highly significant positive relationship with Good Sleep and significant negative relationship with PCOS, Depressed Mood, Diabetes Mellitus Type 2 and Immune Dysregulation. Depressed Mood also has highly positive significant relationship with PCOS, Diabetes Mellitus Type 2 and Immune Dysregulation and significant negative relationship with Good Sleep and Morningness. Diabetes Mellitus Type 2 has highly significant positive relationship with PCOS, Depressed mood and Immune Dysregulation

and significant negative relationship with Good Sleep and Morningness. Immune Dysregulation also has highly significant positive relationship with PCOS, Depressed Mood and Diabetes Mellitus Type 2 and highly significant negative relationship with Good Sleep and Morningness.

Table 3

Regression Coefficient for PCOS on Disruptive Circadian Rhythm its Subscales, Diabetes Mellitus Type 2 and Immune Dysregulation

	PCOS				
Variables	***B***	***β***	***SE***	***p***	***R^2***
Step 1					.23
Constant	25.18		4.79	.00	
Good Sleep	-.199	.158	.124	.11	
Morningness	-.276	-.246	.107	.01	
Dep. Mood	.245	.188	.138	.08	
Step 2					.240
Constant	23.78		4.98	.00	
Good Sleep	-.175	-.139	.126	.16	
Morningness	.242	-.216	.112	.03	
Dep. Mood	.218	.168	.141	.12	
Diabetes 2	.022	.100	.021	.30	
Step 3					.277
Constant	21.52		4.96	.00	
Good Sleep	-.141	-.111	.124	.26	
Morningness	-.221	-.198	.110	.04	
Dep. Mood	.202	.155	.138	.14	
Diabetes 2	.013	.059	.021	.54	
Immune Dys	.219	.209	.090	.01	

N = 121 p < .00

Table 3 show the impact of Disruptive Circadian Rhythm that is Good Sleep, Morningness and Depressed Mood on females having PCOS. The R^2 value .23 revealed that the predictor variables explained 23% variance in outcome variable with F (3, 118) = 11.94, p< .00). The finding revealed that Good Sleep (*β=-.15, p<.11)* and Morningness *(β=-.24, p<.01)* negatively predicted PCOS. However, as Depressed Mood increases it causes .18 standard deviation increase in PCOS (*β=.18, p<.08).* The finding revealed that Diabetes Mellitus Type 2 (*β=.10,* p *<.30)* positively predicted PCOS among females. The impact of Immune Dysregulation on PCOS is large as 28% variance in outcome variable is due to disrupted immunity and other factors, with F (1, 116) = 6.00, *p*<.01. It means that as Immune Dysregulation increases, it also increases the PCOS.

DISCUSSION

The purpose of the study was to find out the relationship between Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation among females having PCOS.

The first hypothesis was based on the "relationship between Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation among females having PCOS**".** The results indicated a significant relationship among these variables. Females having PCOS had Disrupted Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation problems. Similar results were given by Shang li et al., (2020) that the altered circadian rhythm clock caused PCOS in the participants.

The second hypothesis was that "there is likely to be a negative relationship between Disruptive Circadian Rhythm's subscale, that is Good Sleep and PCOS among adult females." Correlation analysis indicted the presence of significant negative relationship between these two variables, supporting our hypothesis. When a person gets good sleep, his health improves and he becomes more alert and productive in daily life. When Circadian Rhythm gets disturbed, may lead to different diseases like PCOS. Similar results were given by Goldstein.et.al, (2016) that reproductive hormones can impact sleep patterns, and this relationship works both ways: sleep disruptions can also influence the secretion of reproductive hormones.

The third hypothesis was that "there is likely to be an inverse relationship between Disruptive Circadian Rhythm's subscale Morningness, and PCOS and positive relationship between Disruptive Circadian Rhythm's subscale that is Depressed Mood and PCOS among adult females." Correlation analysis indicted the presence of significant negative relationship between Morningness and PCOS. Wang, et al, (2021) showed that there was a significant association of night shift work with PCOS. Correlation analysis indicted the presence of significant positive relationship between Depressed Mood and PCOS, supporting the hypothesis. Similar results were given by McClung, et al., (2016), that all individuals grappling with mood disorders experience substantial disruptions in their circadian rhythms and the sleep/wake cycle. Disturbance in circadian rhythms induced by environmental factors such as shift work, transcontinental travel, and irregular social schedules tend to trigger or worsen episodes related to mood. Depressed mood is one of the primary symptoms of depression, a mental health disorder that can have a profound impact on a person's daily life and functioning (Kashani, et al., 1987). It means when the depressed mood increases, the PCOS problems also increases in adult females.

The fourth hypothesis was that 'there is likely to be a positive relationship between Diabetes Mellitus Type 2 and PCOS among adult females." Correlation analysis indicated the presence of significant positive relationship between these two variables. Similar results were given by Conn, et al, (2000) that women with Diabetes Mellitus Type 2 had higher prevalence of PCOS. 82% of women with diabetes type 2 had PCOS on ultrasound. Among these women, 52% had menstrual irregularity and cutaneous hyperandrogenism. And results of Talbott, et al., (2007) study showed that 6% to 10% of prevalence of Diabetes Type 2 was found in women with PCOS. In all incident cases 15.0% to 35.6% of Diabetes Type 2 in white women, it was estimated that it is attributable to Polycystic Ovarian Syndrome. The peripheral clock in the pancreas helps in the regulation of insulin secretion. Misalignment in our biological clock such as sleep-awake cycle, eating habits, cause the resistance to produce insulin in the body. This results in increased sugar levels in blood and cause Diabetes Mellitus type 2 (Goyal, & Jialal, 2018). In the present study, majority females having PCOS were diagnosed with Diabetes Mellitus Type 2. It was observed in both young and middle age groups of females.

The fifth hypothesis was "Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation will predict PCOS in adult females." Regression analysis was used for this purpose. In the first step all three subscales of disrupted circadian rhythm were included in the model and it explained 23% variance in outcome variable with $F(3, 118) = 11.94$, $p < .00$). The finding revealed that Good Sleep ($\beta = -.15$, $p < .01$) and Morningness ($\beta = -.24$, $p < .01$) negatively predicted PCOS. However, as Depressed Mood was the positive predictor of PCOS. In second step, the Diabetes was entered, but its impact on PCOS was low although Diabetes Mellitus Type 2 positively predicted PCOS among females. In the third step, the impact of Immune Dysregulation on PCOS was large. Overall, the predictors accounted 28% variation in the PCOS. Similar results were given by Shang li et al., (2020), when the rats were exposed with constant darkness had altered circadian rhythm clock, caused reproductive and metabolic hallmarks of PCOS in them.

CONCLUSION

The major aim of the present research was to increase the understanding of the relationship between Disruptive Circadian Rhythm, Diabetes Mellitus Type 2 and Immune Dysregulation among females having PCOS. The empirical data revealed a strong association between Disruptive Circadian Rhythm and its subscale with PCOS. Furthermore, diabetes and immune dysregulation were significantly related with PCOS among young adult females.

The study identified the predictors of PCOS through regression analysis, which revealed that the circadian disruption, leads to diabetes, and both disturb our immune system leading to the PCOS among adult women in Pakistan. The study stressed upon the need to change the life style such as sleep patterns and eating habits, which are altering due to the social media usage and technological advances. Our sleep patterns and eating habits have been changed, which is affecting our health and well beings. Parents, psychologists and clinicians and metrician's can help the females to restore their circadian rhythm to maintain healthy life, free of PCOS.

Limitations and Recommendations

The sample size was small and only adult females were included so the results cannot be generalized to the other populations such as adolescents. Many participants were reluctant while addressing about their disease. Psychotherapist can use this study for giving tips to their clients for the management of circadian rhythm. Doctors can make intervention plans to reduce PCOS among females.

Implications

Present study will play an important role in raising awareness about the PCOS and its determinants. This study will help people to maintain their life styles according to the nature and psycho-educate them that if they go against the nature then nature will go against them. Present research will help people not to rely only on long-term medications for these diseases. Medical professionals like doctors and nutritionists can make diet plan and charts to alter the bad eating habits of the females having PCOS. They can psycho-educate females about the importance of exercise and proper sleep. This study will also help clinical psychologists in diagnosing and treating circadian rhythm disorders in patients.

REFERENCES

Ahmad, M., Md. Din, N. S. B., Tharumalay, R. D., Che Din, N., Ibrahim, N., Amit, N., ... & Ahmad, S. A. (2020). The effects of circadian rhythm disruption on mental health and physiological responses among shift workers and general population. International journal of environmental research and public health, 17(19), 7156.

Aziz, R. (2004). PCOS: a diagnostic challenge. Reproductive biomedicine online, 8(6), 644-648.

Basnet, S., Merikanto, I., Lahti, T., Männistö, S., Laatikainen, T., Vartiainen, E., & Partonen, T. (2018). Seasonality, morningness-eveningness, and sleep in common non-communicable medical conditions and chronic diseases in a population. Sleep Science, 11(2), 85.

Barosi, G. (2014). An immune dysregulation in MPN. Current hematologic malignancy reports, 9, 331-339.

Baron, K. G., & Reid, K. J. (2014). Circadian misalignment and health. International review of psychiatry, 26(2), 139-154.

Bechtel, W. (2015). Circadian rhythms and mood disorders: are the phenomena and mechanisms causally related? Frontiers in psychiatry, 6, 118.

Bedrick, B. S., Eskew, A. M., Chavarro, J. E., & Jungheim, E. S. (2020). Self-administered questionnaire to screen for polycystic ovarian syndrome. Women's Health Reports, 1(1), 566-573.

Ben-Haroush, A., Yogev, Y., & Hod, M. (2004). Epidemiology of gestational diabetes mellitus and its association with Type 2 diabetes. Diabetic Medicine, 21(2), 103- 13.

Blumberg, M. S., Lesku, J. A., Libourel, P. A., Schmidt, M. H., & Rattenborg, N. C. (2020). What is REM sleep?. Current biology, 30(1), R38-R49.

Brainard, J., Gobel, M., Scott, B., Koeppen, M., & Eckle, T. (2015). Health implications of disrupted circadian rhythms and the potential for daylight as therapy. Anesthesiology, 122(5), 1170-1175.

Brown, S. A., Schmitt, K., & Eckert, A. (2011). Aging and circadian disruption: causes and effects. Aging (Albany NY), 3(8), 813.

Byrne, J. E., Bullock, B., & Murray, G. (2017). Development of a measure of sleep, circadian rhythms, and mood: the SCRAM questionnaire. Frontiers in Psychology, 8, 2105.

Borbély, A. A. (1982). A two process model of sleep regulation. Hum neurobiology, 1(3), 195 204.

Carrier, J., Monk, T. H., Buysse, D. J., & Kupfer, D. J. (1997). Sleep and morningness-eveningness in the 'middle'years of life (20–59y). Journal of sleep research, 6(4), 230-237.

Carskadon, M. A., & Dement, W. C. (2005). Normal human sleep: an overview. Principles and practice of sleep medicine, 4(1), 13-23.

Castanon-Cervantes, O., Wu, M., Ehlen, J. C., Paul, K., Gamble, K. L., Johnson, R. L., & Davidson, A. J. (2010). Dysregulation of inflammatory responses by chronic circadian disruption. The Journal of Immunology, 185(10), 5796-5805.

Chellappa, S. L., Vujovic, N., Williams, J. S., & Scheer, F. A. (2019). Impact of circadian disruption on cardiovascular function and disease. Trends in Endocrinology & Metabolism, 30(10), 767-779.

Chatterjee, S., Khunti, K., & Davies, M. J. (2017).Type 2 diabetes. The lancet, 389(10085), 2239-2251.

Chokroverty, S. (2010). Overview of sleep & sleep disorders. Indian Journal of Medical Research, 131(2), 126-140.

Conrad, N., Misra, S., Verbakel, J. Y., Verbeke, G., Molenberghs, G., Taylor, P. N., & Cambridge, G. (2023). Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. The Lancet, 401(10391), 1878-1890.

Conn, J. J., Jacobs, H. S., & Conway, G. S. (2000). The prevalence of polycystic ovaries in women with type 2 diabetes mellitus. Clinical endocrinology, 52(1), 81-86.

Czeisler, C. A., Richardson, G. S., Zimmerman, J. C., Moore-Ede, M. C., & Weitzman, E. D. (1981). Entrainment of human circadian rhythms by light-dark cycles: a reassessment. Photochemistry and photobiology, 34(2), 239-247.

DeFronzo, R. A., Ferrannini, E., Groop, L., Henry, R. R., Herman, W. H., Holst, J. J., ... & Weiss, R. (2015). Type 2 diabetes mellitus. Nature reviews Disease primers, 1(1), 1-22.

Diamanti-Kandarakis, E., Kandarakis, H., & Legro, R. S. (2006). The role of genes and environment in the etiology of PCOS. Endocrine, 30, 19-26.

Farhud, D., & Aryan, Z. (2018). Circadian rhythm, lifestyle and health: a narrative review. Iranian journal of public health, 47(8), 1068. Medicine, 345(5), 340-350.

Ferrara, M., & De Gennaro, L. (2001). How much sleep do we need?. Sleep medicine reviews, 5(2), 155-179.

Gamble, K. L., Berry, R., Frank, S. J., & Young, M. E. (2014). Circadian clock control of endocrine factors. Nature Reviews Endocrinology, 10(8), 466-475.

Gau, S. S. F., Shang, C. Y., Merikangas, K. R., Chiu, Y. N., Soong, W. T., & Cheng, A. T. (2007). Association between morningness-eveningness and behavioral/emotional problems among adolescents. Journal of biological rhythms, 22(3), 268-274.

Goldstein, C. A., & Smith, Y. R. (2016). Sleep, circadian rhythms, and fertility. Current Sleep Medicine Reports, 2, 206-217.

Grandin, Louisa D., Lauren B. Alloy, and Lyn Y. Abramson. "The social zeitgeber theory, circadian rhythms, and mood disorders: review and evaluation." Clinical psychology review 26.6 (2006): 679-694.

Hasan, M. M., Jankowski, K. S., & Khan, M. H. (2022). Morningness-eveningness preference and shift in chronotype during COVID-19 as predictors of mood and well-being in university students. Personality and Individual Differences, 191, 111581.

Hastings, M. H., Maywood, E. S., & Brancaccio, M. (2018). Generation of circadian rhythms in the suprachiasmatic nucleus. Nature Reviews Neuroscience, 19(8), 453-

Haspel, J. A., Anafi, R., Brown, M. K., Cermakian, N., Depner, C., Desplats, P., Gelman, A. E., Haffner, S. M. (1998). Epidemiology of type 2 diabetes: risk factors. Diabetes care, 21(Supplement_3), C3-C6.

Harmat, H. (2014). Construction and Clinical Validation of a Questionnaire-based Risk Score to Identify Patients Suffering from Immunodeficiency or Systemic Autoimmunity. British Journal of Medicine & Medical Research 4(29): 4751-4769.

Hur, Y. M., Bouchard Jr, T. J., & Lykken, D. T. (1998). Genetic and environmental influence on morningness–eveningness. Personality and Individual differences, 25(5), 917-925.

Jagannath, A., Taylor, L., Wakaf, Z., Vasudevan, S. R., & Foster, R. G. (2017). The genetics of circadian rhythms, sleep and health. Human molecular genetics, 26(R2), R128-R138.

Jerigova, V., Zeman, M., & Okuliarova, M. (2022). Circadian Disruption and Consequences on Innate Immunity and Inflammatory Response. International Journal of Molecular Sciences, 23(22), 13722.

Kashani, J. H., Carlson, G. A., Beck, N. C., Hoeper, E. W., Corcoran, C. M., McAllister, J. A., ... & Reid, J. C. (1987). Depression, depressive symptoms, and depressed mood among a community sample of adolescents. The American Journal of Psychiatry.

Kreier, F., Kalsbeek, A., Sauerwein, H. P., Fliers, E., Romijn, J. A., & Buijs, R. M. (2007). "Diabetes of the elderly" and type 2 diabetes in younger patients: possible role of the biological clock. Experimental gerontology, 42(1-2), 22-27.

Kudielka, B. M., Federenko, I. S., Hellhammer, D. H., & Wüst, S. (2006). Morningness and eveningness: the free cortisol rise after awakening in "early birds" and "night owls". Biological psychology, 72(2), 141-146.

Legro, R. S. (2001). Diabetes prevalence and risk factors in polycystic ovary syndrome. Obstetrics and gynecology clinics of North America, 28(1), 99-109.

Lu, B. S., & Zee, P. C. (2006). Circadian rhythm sleep disorders. Chest, 130(6), 1915-1923.

Majumdar, P., Biswas, A., & Sahu, S. (2020). COVID-19 pandemic and lockdown: cause of sleep disruption, depression, somatic pain, and increased screen exposure of office workers and students of India. Chronobiology international, 37(8), 1191-1200.

McIntyre, H. D., Thomae, M. K., Wong, S. F., Idris, N., & Callaway, L. K. (2009). Pregnancy in type 2 diabetes mellitus-problems & promises. Current diabetes reviews, 5(3), 190-200.

McClung, C. A. (2013). How might circadian rhythms control mood? Let me count the ways... Biological psychiatry, 74(4), 242-249.

Md, M. (2010). The social and economic burden of shift-work disorder. Supplement to The Journal of Family Practice n Vol 59, No 1 / January 2010 S31

Meléndez-Fernández, O. H., Liu, J. A., & Nelson, R. J. (2023). Circadian Rhythms Disrupted by Light at Night and Mistimed Food Intake Alter Hormonal Rhythms and Metabolism. International Journal of Molecular Sciences, 24(4), 3392.

Moulana, M. (2019). Immunophenotypic profile of leukocytes in hyperandrogenemic female rat an animal model of polycystic ovary syndrome. Life sciences, 220, 44-49.

Peter, H. H., Goldacker, S., Haraldseide, J., Großmann, K., Gross, W., Warnatz, K., ... & Vach, W. (2014). Construction and clinical validation of a questionnaire-based risk score to identify patients suffering from immunodeficiency or systemic autoimmunity. British Journal of Medicine and Medical Research, 29, 4751-4761.

Potter, G. D., Skene, D. J., Arendt, J., Cade, J. E., Grant, P. J., & Hardie, L. J. (2016). Circadian rhythm and sleep disruption: causes, metabolic consequences, and countermeasures. Endocrine reviews, 37(6), 584-608.

Pouwer, F. (2009). Should we screen for emotional distress in type 2 diabetes mellitus?. Nature Reviews Endocrinology, 5(12), 665-671.

Rawshani, A., Rawshani, A., Franzén, S., Eliasson, B., Svensson, A. M., Miftaraj, M., ...& Gudbjörnsdottir, S. (2017). Mortality and cardiovascular disease in type 1 and type 2 diabetes. New England journal of medicine, 376(15), 1407-1418.

Reimer, R. A., Maurer, A. D., Eller, L. K., Hallam, M. C., Shaykhutdinov, R., Vogel, H. J., & Weljie, A. M. (2012). Satiety hormone and metabolomic response to an intermittent high energy diet differs in rats consuming long-term diets high in protein or prebiotic fiber. Journal of proteome research, 11(8), 4065-4074.

Ruan, W., Yuan, X., & Eltzschig, H. K. (2021). Circadian rhythm as a therapeutic target. Nature Reviews Drug Discovery, 20(4), 287-307.

Savvidis, C., & Koutsilieris, M. (2012). Circadian rhythm disruption in cancer biology. Molecular medicine, 18, 1249-1260.

Schaefer, E. W., Williams, M. V., & Zee, P. C. (2012). Sleep and circadian misalignment for the hospitalist: a review. Journal of hospital medicine, 7(6), 489-496.

Shan, B., Cai, J. H., Yang, S. Y., & Li, Z. R. (2015). Risk factors of polycystic ovarian syndrome among Li People. Asian Pacific journal of tropical medicine, 8(7), 590-593.

Smith, M. R., & Eastman, C. I. (2012). Shift work: health, performance and safety problems, traditional countermeasures, and innovative management strategies to reduce circadian misalignment. Nature and science of sleep, 111-132.

Spielman, R. M., et al. (2014). "Hunger and Eating." Psychology.

Talbott, E. O., Zborowski, J. V., Rager, J. R., Kip, K. E., Xu, X., & Orchard, T. J. (2007). Polycystic ovarian syndrome (PCOS): a significant contributor to the overall burden of type 2 diabetes in women. Journal of Women's Health, 16(2), 191-197.

Taillard, J., Philip, P., & Bioulac, B. (1999). Morningness/eveningness and the need for sleep. Journal of sleep research, 8(4), 291-295.

Terman, J. S., Terman, M., Lo, E. S., & Cooper, T. B. (2001). Circadian time of morning light administration and therapeutic response in winter depression. Archives of general psychiatry, 58(1), 69-75.

Turek, F. W., Dugovic, C., & Zee, P. C. (2001). Current understanding of the circadian clock and the clinical implications for neurological disorders. Archives of neurology,58(11), 1781-1787.

Vitaterna, M. H., Takahashi, J. S., & Turek, F. W. (2001). Overview of circadian rhythms. research & health, 25(2), 85.

Walker, W. H., Walton, J. C., DeVries, A. C., & Nelson, R. J. (2020). Circadian rhythm disruption and mental health. Translational Psychiatry, 10(1), 1-13.

Wang, F., Xie, N., Wu, Y., Zhang, Q., Zhu, Y., Dai, M., ... & Qu, F. (2021). Association between circadian rhythm disruption and polycystic ovary syndrome. Fertility and sterility, 115(3), 771-781.

Wang, J., Yin, T., & Liu, S. (2023). Dysregulation of immune response in PCOS organ system. Frontiers in Immunology, 14, 1169232.

Watts, C., Cox, T., & Robson, J. (1983). Morningness-eveningness and diurnal variations in self-reported mood. The Journal of Psychology, 113(2), 251-256.

Polonsky, W. H. Welch, G. W., Jacobson, A. M. (1997). The Problem Areas in Diabetes Scale: an evaluation of its clinical utility. Diabetes care, 20(5), 760-766.

Xu, S., Akioma, M., & Yuan, Z. (2021). Relationship between circadian rhythm and brain cognitive functions. Frontiers of Optoelectronics, 14(3), 278-287.

Zee, P. C., Attarian, H., & Videnovic, A. (2013). Circadian rhythm abnormalities. Continuum: Lifelong Learning in Neurology, 19(1 Sleep Disorders), 132.

American Psychiatric Association. (2015). Sleep-wake disorders: DSM-5® selections. American Psychiatric Pub.

Zhu, T., Cui, J., & Goodarzi, M. O. (2021). Polycystic ovary syndrome and risk of type 2 diabetes, coronary heart disease, and stroke. Diabetes, 70(2), 627-637.

Zhu, Y., & Zhang, C. (2016). Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective. Current diabetes reports, 16, 1-11.