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Poltava Medical State University, Poltava**

## **CORRELATION ANALYSIS OF CIRCADIAN RHYTHM WITH SEVERITY OF PSORIASIS AND OBESITY**

e-mail: yanaumsa@ukr.net

The recent increase in cases of comorbidity of psoriasis and obesity leads to severe, atypical, disabling, and therapy-resistant forms of dermatosis, significantly worsen the quality of life of patients, reduces work capacity and social activity of patients, which determines not only the medical but also the social significance of the problem. There is a theoretical rationale for the possible role of circadian rhythm disturbances, manifested by a change in eating behavior, a decrease in sleep duration, and the individual chronotype of patients in developing obesity and some autoimmune diseases. However, this issue remains insufficiently studied and proven. The purpose of our study was to identify the correlation between the circadian rhythm and indicators of changes in the chronotype of a person's working capacity and indicators of the severity of the course of psoriatic disease, the degree of obesity, and the degree of the negative impact of the disease on the quality of life of patients. The results of the correlation analysis showed a very high negative correlation between the chronotype of patients' working capacity and BMI indicators and a high negative correlation between the indicators of the PASI index, ACTIVITY, and the chronotype of patients' working capacity.

**Key words:** psoriasis, alimentary obesity, chronotype, quality of life.

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## **КОРЕЛЯЦІЙНИЙ АНАЛІЗ ЦИРКАДНОГО РИТМУ З ТЯЖКІСТЮ ПСОРІАЗУ ТА ОЖИРІННЯМ**

Збільшення випадків коморбідності псоріазу та ожиріння, що спостерігаються останнім часом, призводить до тяжких, атипових, інвалідизуючих та резистентних до терапії форм дерматозу, значно погіршує якість життя пацієнтів, знижує працездатність та соціальну активність хворих, що визначає не тільки медичну, але й соціальну значимість проблеми. Існує теоретичне обґрунтування можливої ролі порушень циркадного ритму, яке проявляється зміною харчової поведінки, зменшення тривалості сну та індивідуального хронотипу в хворих в розвитку ожиріння та деяких аутоімунних захворювань. Однак дане питання залишається недостатньо вивченим і доведеним. Метою нашого дослідження стало виявлення кореляційної залежності між циркадним ритмом за показниками змін хронотипу працездатності людини та показниками тяжкості перебігу псоріатичної хвороби, ступенем ожиріння, та ступенем негативного впливу захворювання на якість життя пацієнтів. Результати кореляційного аналізу показали дуже високу негативну кореляційну залежність між хронотипом працездатності хворих та показниками ІМТ та високу негативну кореляційну залежність між показниками індексу PASI, ДІЯЖ та хронотипом працездатності хворих.

**Ключові слова:** псоріаз, аліментарне ожиріння, хронотип, якість життя.

*The study is a fragment of the research project "Development of improved methods of diagnosis and complex treatment of chronic dermatoses and infections, which are mainly sexually transmitted, taking into account the determination of additional factors significant in the pathogenesis of these diseases", state registration No. 0117U000272.*

Psoriasis is one of the most common dermatoses, which, according to WHO world statistics, affects 2 % to 4 % of the world's population [13]. The recent increase in cases of comorbidity of psoriasis and obesity leads to severe, atypical, disabling, and treatment-resistant forms of dermatosis, significantly worsening the quality of life of patients and reduces the ability to work and social activity of patients, which determines not only the medical but also the social significance of the problem. At present, obesity is considered a multifactorial disease with the leading role of overeating and low physical activity against genetic predisposition [11]. In addition to these factors, possible causes of obesity include epigenetic changes, exposure to endocrine disruptors, intestinal microflora disorders, eating disorders, disruption of the body's circadian system, and reduced sleep duration. The lifestyle of a modern person has undergone significant changes over the past few decades: a decrease in physical activity, a change in the nature of nutrition, the emergence of new dishes, fashion for restaurants, coffee shops, bakeries, and snack bars, advertisements with colorful illustrations of food and drinks, fast food promotion, reduced sleep duration, shift work, long transatlantic flights. Also, the modern lifestyle is characterized by chronic stress and tension experienced by people in a big city while performing professional duties at work and home. All this contributes to the formation of the wrong type of eating behavior, circadian system disorders, and desynchronization development [8]. Disorders facilitate the formation of incorrect eating stereotypes in the synthesis and secretion of hormones that regulate appetite (serotonin, leptin, ghrelin, orexin, etc.), as well as disorders of the rhythmic functioning of the circadian system [4, 5, 8, 10]. The circadian system is a complex hierarchical structure that synchronizes all physiological processes in the body with each other

and with environmental rhythms [8, 9]. Light impulses, meal times, planned physical activity, and social factors are powerful desynchronizers that affect the circadian system [12]. The concept of patients' chronotypes is closely related to the circadian system. A chronotype is a stable individual temporal periodization of the psychophysiological state of a person based on the genetically determined duration of the endogenous circadian rhythm, reflecting individual characteristics of the organization of daily rhythms. There are three variants of patients' chronotypes: morning type – “lark”, evening type – “owl”, intermediate type – “pigeon”. There is a theoretical basis for the possible role of eating disorders and individual chronotypes in the development of obesity. However, this issue remains insufficiently studied and proven [3].

Therefore, further, more in-depth study of the dependence of the severity of psoriasis, and the severity of obesity, on the circadian rhythm will help to find new ways to limit and prevent the harmful effects of abiotic factors on the course of the disease.

**The purpose** of the study was to determine the role of circadian rhythm, eating disorders, and chronotype in patients with psoriasis with concomitant alimentary obesity of I-II degree and the correlation between the chronotype of patients and the severity of psoriasis, obesity and the impact of the disease on the patient's quality of life.

**Materials and methods.** We examined 80 patients diagnosed with widespread vulgar psoriasis, progressive stage, moderate severity with concomitant obesity of I-II degree, 51 (64 %) men and 29 (36 %) women aged 35 to 65 years, the duration of the disease ranged from 3 to 36 years. All patients underwent inpatient treatment at the Poltava Regional Dermatologic and Venereological Dispensary during the examination. Psoriatic lesions were widespread in all patients. According to the history of the disease, 28 (35 %) patients had autumn-winter psoriasis, 2 (2.5 %) had spring-summer psoriasis, and 50 (62.5 %) had undifferentiated psoriasis. When determining the number of psoriasis relapses per year, it was found that the disease relapsed once a year in 2 (2.5 %) patients, two times a year in 11 (14 %) patients, three times a year in 46 (57.5 %) patients, and four times a year in 21 (26 %) patients. Psoriasis was diagnosed according to the protocol (Order No. 312 of May 8, 2009).

The PASI (Psoriatic Area and Severity Index) index was used to assess the severity of psoriasis [13].

To determine the impact of skin rashes on patients' quality of life, questionnaires were used to calculate the DLQI (Dermatology Life Quality Index) [3, 11].

Body mass index (BMI) was determined to assess the severity of alimentary obesity [14]. Individuals with a BMI of 30-40 kg/m<sup>2</sup> were included in the study.

To determine the chronotype of human performance, the international Horn-Ostberg test in the modification of S. I. Stepanova (1986) [5].

Statistical processing of the obtained results was done using Statistica 7.0. The difference was considered significant at  $p < 0.05$ . Paired factor correlation analysis was performed using Pearson's correlation coefficient (r) calculation.

**Results of the study and their discussion.** Based on the clinical picture of the psoriatic lesion, the PASI index was calculated, which reflects the area, color intensity, infiltration, and scaling of psoriatic rashes. Analyzing the results, it was found that the mean group value of the PASI index in the studied patients was  $21.7 \pm 1.54$ , which corresponds to the mean severity of psoriasis. It is known from the anamnesis of the disease that all patients repeatedly received conventional treatment for psoriasis in outpatient and inpatient settings without considering comorbid conditions. Patients noted dissatisfaction with the therapy due to the duration of treatment and short-term periods of remission of up to 3 months with episodes of exacerbation 3 - 4 times a year, and some of them did not note a complete regression of psoriatic rashes at all and indicated the presence of permanent (so-called “regular”) plaques. In addition, all patients complained of sleep disturbances and feelings of uneasiness and anxiety, which led to a deterioration in the quality of life of patients, changes in chronotype, and an increase in the amount of food consumed in the evening and at night, which led to the rise in body weight.

Anthropometric parameters were determined, and BMI was calculated to assess the degree of obesity. According to the results obtained, following the classification of obesity by BMI, it was found that 29 (36.25 %) patients had grade I obesity (mean group BMI-34.04 kg/m<sup>2</sup>), grade II obesity – 51 (63.75 %) patients (mean group BMI-38.15 kg/m<sup>2</sup>).

The dermatological quality of life index (QOLI) was calculated to study the impact of the disease on the patient's life. Analyzing the study results, it was found that the average group QOL score was  $20.3 \pm 0.5$  points, indicating a pronounced impact of the disease on the quality of life of patients.

In determining the circadian rhythm, the data of the Horn-Ostberg human performance chronotype questionnaire in the modification of S.I. Stepanova were analyzed. According to the results of the study, it was found that 27 patients had a mildly expressed evening chronotype of performance, 50 patients had a clearly defined evening chronotype of performance, and three patients had an arrhythmic chronotype of

performance. Furthermore, the average group index of the patients' performance chronotype was  $40.6 \pm 10.2$  points. In turn, people with a mildly expressed evening chronotype of performance and a clearly expressed evening chronotype of performance are referred to as "owls" and people with an arrhythmic chronotype of performance are referred to as "pigeons".

To identify the relationships between the chronotype of patients' performance and indices of the disease's impact on the quality of life (QOL), the severity of clinical manifestations of psoriasis (PASI) and obesity (BMI), a paired correlation analysis was performed between the studied indices.

Investigating the dependence of BMI and circadian rhythm in patients with psoriasis with concomitant alimentary obesity, we conducted a correlation analysis between BMI and the chronotype of patients' performance (Table 1).

Table 1

**Correlation between the chronotype of patients' work capacity and clinical, anamnestic, and anthropometric parameters in patients with psoriasis with concomitant alimentary obesity of I-II degree**

Index	BMI	QOL	PASI
Chronotype of patients'	R = - 0.96399	R = - 0.87632	R = - 0.77374

The results of the study showed a very high negative correlation between these indicators (R = - 0.96399).

Investigating the dependence of the circadian rhythm on the quality of life in patients with psoriasis with concomitant alimentary obesity, we conducted a correlation analysis between the indicators of the DIAQ and the chronotype of patients' work capacity. The results of the study showed a high negative correlation between these indicators (R = - 0.87632).

Investigating the dependence of the circadian rhythm on the severity of psoriasis in patients with concomitant alimentary obesity, we conducted a correlation analysis between the PASI index and the chronotype of patients' performance. The results of the study showed a high negative correlation between these indicators (R = - 0.77374).

Analyzing the results of the correlation analysis, it was noted that the severity of psoriasis, the degree of alimentary obesity, and the impact of the disease on the patient's quality of life are associated with changes in the circadian rhythm of the studied patients. The results of the correlation analysis showed a very high negative correlation between the chronotype of patients' performance and BMI. Thus, the higher the BMI of the studied patients, the lower the index of the chronotype of the patient's work capacity, which corresponds to more pronounced changes in the circadian rhythm of the "owl" type. Thus, higher BMI values are observed in patients with a clearly expressed evening type of work capacity chronotype. Furthermore, a high negative correlation was observed between the PASI index, VAS, and patients' work capacity chronotype. Thus, in patients with lower values of the human performance chronotype, corresponding to a clearly expressed evening type ("owls"), a more severe course of the clinical picture of psoriasis and a negative impact of the disease on the quality of life of patients according to the PASI and VAS index were noted. The results of our studies are consistent with the results of large-scale observational studies that have revealed an inverse relationship between sleep duration and obesity [12]. In recent years, sleep disturbances have been considered the cause of the development of many chronic and autoimmune diseases, including obesity [3, 11].

The primary function of sleep, as a restorative process, allows the body to maximize adaptation to changing conditions of the external and internal environment. However, many people create an artificial lighting environment at night and change their chronotypes, thereby reducing the time of natural sleep and its protective properties, leading to various pathological conditions. As noted earlier, working a night shift leads to circadian rhythm disruptions and severe health consequences. Thus, according to a meta-analysis that included a review of 28 studies, it was shown that shift workers had a higher incidence of abdominal obesity. At the same time, permanent night workers demonstrated a 29 % higher risk than people working in shifts. Another severe problem contributing to weight gain is the nighttime eating syndrome, manifested by a violation of the timing of meals during the day. In this case, food consumption occurs in the evening and at night. Such people usually have altered secretions of physiological markers involved in appetite regulation, such as ghrelin, leptin, and insulin [6]. According to Salgado-Delgado and co-authors, it has been shown that eating during the time intended for sleep causes a more significant increase in body weight than consuming the same amount of calories during a natural period of activity. There is evidence in the literature that obesity, both as an isolated pathology and in combination with sleep disorders, is often associated with oxidative stress [13], activation of proinflammatory cytokines, and decreased nocturnal melatonin secretion [10]. Melatonin is a hormone produced in the pineal gland in response to darkness. It regulates several critical central and peripheral processes associated with cyclic secretion in the

reproductive, cardiovascular, immune, and endocrine systems. For example, in their studies, Alonso-Vale and co-authors [4] demonstrated that insulin-induced synthesis and release of leptin in isolated adipocytes are enhanced by melatonin. In addition, scientists have confirmed that melatonin also regulates such aspects of adipocyte biology that affect energy metabolism, hyperlipidemia, and body weight as lipolysis, lipogenesis, adipocyte differentiation, and fatty acid uptake [2].

Currently, a growing number of chronobiological studies emphasize the importance of timing meals and, therefore, the need to develop special diets in which the consumption of essential nutrients is linked to circadian activity. Scientists have shown that skipping the first meal (breakfast) increases the risk of developing obesity and its complications. In 2013, Garaulet and co-authors established a correlation between breakfast availability and the rate of weight loss in obese individuals with similar total caloric intake, physical activity, and sleep duration [10].

Taking into account the fact that obesity is both a consequence and a cause of circadian rhythm disorders, the relationship between obesity and sleep deprivation, chronodestruction, and circadian rhythm disorders of melatonin secretion is the basis for the development of scientifically based preventive and therapeutic concepts in this category of patients, to prevent the development of concomitant diseases and complications caused by the above disorders.

Recently, in the foreign literature, one can find works devoted to applying the time-restricted feeding method in experiments and clinical trials in obese patients as a type of fasting. For example, Melkani and co-authors and Villanueva and co-authors showed in their reviews that this method could treat obesity by normalizing the circadian rhythm system and eliminating metabolic disorders.

Another critical point in the fight against obesity is physical activity. Epidemiological studies show that regular exercise (at least 5 hours before the expected bedtime) positively affects sleep quality and daytime well-being. In addition, it has been suggested that physical activity can synchronize the circadian rhythm system with the actual time of day and regulate behavioral activity [7]. Insufficient duration and inadequacy of sleep are closely associated with excessive accumulation of adipose tissue in the body, so adequate sleep hygiene, both in childhood and adolescence and among the adult population, is an essential non-drug method of rehabilitation of obese patients.

Thus, according to the authors, disruption of time interval processes in the body may be one of the possible links between the qualitative characteristics of the diet and the development of autoimmune diseases.

Therefore, further, more in-depth study of the relationship and pathogenesis of the comorbidity of psoriatic disease, obesity, and circadian rhythm changes is promising and essential for developing scientifically based principles of early prevention and timely correction of these comorbidities.

## Conclusion

Thus, changes in a person's circadian rhythm and chronotype lead to changes in eating behavior, increase the stress sensitivity of patients and contribute to the onset or worsening of the course of diseases. Most of the patients we studied had an evening chronotype of human performance, the intensity of which depended on the severity of psoriatic disease, the degree of obesity, and the severity of the negative impact of the disease on the quality of life of patients.

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R.I. Isakov, L.O. Herasymenko, P.V. Kydon,  
Yu.O. Fysun, O.O. Belov<sup>1</sup>, N.G. Pshuk<sup>1</sup>, A.M. Skrypnikov  
Poltava State Medical University, Poltava  
<sup>1</sup>National Pirogov Memorial Medical University, Vinnytsya

## PREDICTORS OF THE FORMATION AND FEATURES OF THE CLINICAL PICTURE OF ADJUSTMENT DISORDERS

e-mail: larysaherasymenko@gmail.com

The war in Ukraine influenced the emergence of a significant number of people who have suffered severe psychological trauma and need forehanded, modern and effective medical care. The purpose of the study was to investigate the predictors of the formation of adjustment disorders and the features of the course and differences in the clinical picture of adjustment disorders during the war in Ukraine. The following methods were used to achieve the purpose and implementation of the tasks of this study: information-analytical, clinical-anamnestic, clinical-psychopathological, psychodiagnostic, psychometric and statistical methods of mathematical processing of the obtained results. According to the results of the conducted research, it was found that the main predictors of the formation of adaptation disorders are forced relocation, both within the country and abroad, and especially during which a person feels the influence of a stress factor, in particular, and experiencing negative emotions for a long time.

**Key words:** adjustment disorders, internally displaced persons, stress, depression, anxiety.

Р.І. Ісаков, Л.О. Герасименко, П.В. Кидонь, Ю.О. Фисун, О.О. Белов,  
Н.Г. Пшук, А.М. Скрипніков

## ПРЕДИКТОРИ ФОРМУВАННЯ ТА ОСОБЛИВОСТІ КЛІНІЧНОЇ КАРТИНИ РОЗЛАДІВ АДАПТАЦІЇ

Війна в Україні вплинула на появу значної кількості осіб, що перенесли важку психотравму та потребують своєчасної, сучасної та ефективної медичної допомоги. Метою роботи було дослідити предиктори формування, особливостей перебігу та відмінностей клінічної картини розладів адаптації під час війни в Україні. Для досягнення мети і реалізації завдань даного дослідження були використані наступні методи: інформаційно-аналітичний, клініко-анамнестичний, клініко-психопатологічний, психодіагностичний, психометричний та статистичні методи математичної обробки отриманих результатів. За результатами проведеного дослідження встановлено, що основними предикторами формування розладів адаптації є вимушене переселення, як в межах країни, так і за її межами та особливо під час якого людина відчуває вплив стресового фактору, зокрема, і переживання тривалий час негативних емоцій.

**Ключові слова:** розлади адаптації, внутрішньо переміщені особи, стрес, депресія, тривога.

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Interest in various aspects of mental disorders of a stressogenic nature is periodically fueled by social cataclysms that cause an increase in the number of patients of the corresponding profile [9]. Unfortunately, the war in Ukraine influenced the emergence of a significant number of people who have suffered severe psychological trauma and need forehanded, modern and effective medical care [1, 5]. Predictors of the emergence and formation of traumatic stress disorders are not only direct participation in hostilities, but also social perturbations in persons who were forced to leave their homes and became refugees or internally displaced persons (IDP). The causes of distress that lead to the development of adaptation disorders are change in the usual environment: unusual living conditions, moving both within the country and relocation to another country, change in the language environment and, as a result, a barrier during communication, change in cultural and religious traditions [10, 13]. During the COVID-19