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# Chrononutrition And Metabolic Disease: A Review Of Circadian Influences On Metabolic Syndrome, Type 2 Diabetes, And Cardiometabolic Health

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## Abstract

Metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM) some of the most common metabolic disorders worldwide and the major causes of heart disease and deaths. In the conventional nutritional therapy, diet composition and calorie restriction remain the main tools; nevertheless, there are increasing pieces of evidence that the timing of eating has an important part in metabolic homeostasis. Chrononutrition is one of the new areas which deal with interaction of nutrients, circadian rhythm, and metabolic processes. The circadian system controls glucose metabolism, insulin secretion, lipids, hormones production, and energy expenditure. Misalignment of circadian rhythm because of irregular eating time, shifts at work, social jetlag, and nighttime eating increases risk for obesity, MetS, and T2DM development. Clinical research has revealed that synchronization of eating time with the internal clock through TRE, eTRF, and optimal eating time can have beneficial impact on insulin resistance, metabolic health, body weight, blood pressure, and cholesterol levels. Recently it has become known that there are several mechanisms involved in linking eating schedule with metabolism, including gut microbiota and hormonal pathways. This review provides an overview of the existing evidence related to chrononutrition and its relevance in metabolic syndrome and T2DM through circadian biology, clinical practice, and therapeutic perspectives. An appreciation of the importance of meal timing can help achieve an efficient complementary intervention for cardiometabolic disorders.

**Keywords;** Chrononutrition, Circadian Rhythm, Metabolic Syndrome, Type 2 Diabetes Mellitus, Time-Restricted Eating, Cardiometabolic Health.

## INTRODUCTION

Metabolic Syndrome (MetS) and Type 2 Diabetes Mellitus (T2DM) are some of the most important public health concerns worldwide. Both conditions have become highly prevalent in recent decades because of urbanization, physical inactivity, improper nutrition, and rising obesity rates. MetS involves a combination of related metabolic abnormalities such as visceral fat accumulation, insulin resistance, abnormal lipid levels, high blood pressure, and altered glucose metabolism, which significantly increases the likelihood of developing cardiovascular problems and earlier death [1,3]. Likewise, T2DM involves hyperglycemia caused by a reduction in insulin sensitivity and progressive  $\beta$ -cell dysfunction in the pancreas [3,4].

Classic diets aimed at preventing and controlling metabolic diseases have emphasized energy balance, nutritional composition, and food quality. Despite their significance, recent studies suggest that meal timing can be as essential in ensuring favourable metabolic responses. Chrononutrition refers to a relatively new scientific discipline devoted to the study of the effects of meal timing, food intake frequency, periods of fasting, and alignment of nutrition with circadian rhythm on health [1,2].

The chrononutrition concept stems from the fundamental assumption that humans possess an endogenous circadian rhythm that governs many physiological functions within a day cycle.

Circadian rhythms are driven by the internal body's timing mechanism, coordinating physiological activities with environmental factors, such as the availability of light, sleep, and eating [20].

The circadian clock is situated in the SCN of the hypothalamus and controls peripheral metabolic clocks found in metabolic tissues like the liver, pancreas, fat tissue, muscle tissue, and the digestive system [20,21]. Such clocks coordinate physiological metabolic processes that are relevant for glucose balance, lipid metabolism, hormonal regulation, and energy expenditure.

Research has found epidemiological, experimental, and clinical evidence indicating the contribution of circadian disruptions to the occurrence of obesity, metabolic syndrome, and type 2 diabetes mellitus [14–17]. Many aspects of modern lifestyle practices may contribute to disturbances of circadian rhythms through behaviors like long eating intervals, nighttime snacking, erratic eating times, sleep loss, and shift work. This kind of circadian misalignment may result in poor glucose tolerance, reduced insulin sensitivity, heightened inflammation levels, and cardiovascular complications.

One of the most widely investigated chrononutritional strategies includes time-restricted eating (TRE), wherein food intake is confined within a certain period during the day without changing the calorie content of meals. Scientific evidence indicates that TRE could be beneficial to health, as it increases insulin sensitivity, improves blood pressure levels, results in body weight loss, and enhances lipid profiles [7–10]. Likewise, studies conducted on the effect of meal timing and calorie distribution show that eating larger portions earlier in the day is more beneficial than late evening meals [11–13].

Chrononutritional research has been expanded recently, and the contribution of intestinal microbiota, hormonal processes, and molecular clocks to metabolic diseases has also been investigated [24–28].

Considering the escalating prevalence of metabolic syndrome and T2DM globally, it is imperative to appreciate the connection between circadian rhythms and nutrition. With this in mind, the purpose of this review is to compile knowledge concerning chrononutrition, especially with regard to its potential impact on metabolic syndrome and T2DM through modulation of circadian metabolism, time-based feeding studies, time-restricted feeding, and underlying mechanisms.

## CIRCADIAN RHYTHMS AND METABOLIC REGULATION

### *The Circadian System*

Circadian rhythm refers to a biological timing mechanism that controls physiology and behaviours on about a 24-hour period. Rhythms developed to allow animals to adjust their internal biological functions in response to predictable changes in the environment, especially those associated with the day/night cycle [20]. In humans, these rhythms affect our sleep/wake cycles, hormone release, body temperature, immune response, energy use, and feeding patterns.

The circadian clock resides in the suprachiasmatic nucleus (SCN), which lies in the anterior part of the hypothalamus. Light acts as the principal environmental signal (zeitgeber) which synchronizes the activity of the SCN and the environment via retinal input [20,21]. Upon synchronization, the SCN is capable of synchronizing peripheral clocks which can be found in almost all tissues and organs, such as the liver, pancreas, skeletal muscles, fat tissues, and gut.

Circadian rhythm denotes a biological timing system that regulates physiology and behaviour around a 24-hour interval. Biological rhythms have evolved to enable organisms to fine-tune their biological processes in response to environmental cues, particularly those related to the day/night pattern [20]. Human rhythms regulate our sleep and wakefulness patterns, hormonal secretion, body temperature, immune function, energy metabolism, and eating habits.

The circadian clock operates in the suprachiasmatic nuclei (SCN) located in the anterior portion of the hypothalamus. Environmental stimuli such as light are the main zeitgebers that enable synchronization between the SCN and its external environment via the input received from the retina [20,21]. After synchronization takes place, SCN can coordinate peripheral clocks present in nearly all tissues/organs, including liver, pancreas, muscle tissue, fat tissue, and the digestive tract.

### *Circadian Control of Glucose and Lipid Metabolism*

It has been shown that there is significant circadian variation in glucose metabolism. Insulin sensitivity, glucose tolerance, and  $\beta$ -cell function peak during the morning hours and tend to fall throughout the day [15,16]. As a result, ingestion of identical foods during the evening hours results in more postprandial hyperglycemia compared to meals taken during the earlier part of the day.

Several ways exist through which the circadian clock controls glucose homeostasis. Firstly, insulin secretion from pancreatic  $\beta$ -cells is rhythmic in nature and reflects the timing of nutrient intake to metabolic demands. Secondly, insulin sensitivity in muscles and adipose tissue is rhythmic and impacts glucose metabolism. Finally, glucose production in the liver is strictly regulated by circadian cues [15,27].

According to Morris et al., circadian timing and behavioural scheduling affect glucose tolerance independently, indicating that both biological rhythms and behaviour modulate metabolism [15]. In addition, Qian et al. showed that circadian misalignment affects the sensitivity and insulin secretion, thus leading to hyperglycemia and metabolic disorders [16].

The lipid metabolism system shows similar properties to glycolysis because its functioning relies on circadian clocks. Genes involved in cholesterol biosynthesis, fatty acid metabolism, storage of triglycerides, and lipoprotein metabolism show circadian variations coordinated with the feeding–fasting cycle. Lipid oxidation is increased when the organism is actively engaged in its activity, while lipogenesis occurs mainly in resting phases.

Circadian disorders disrupt metabolic rhythms and lead to dyslipidemia, ectopic fat deposition, and obesity, all of which are components of the metabolic syndrome [6]. Moreover, disruption of circadian clocks negatively impacts mitochondria, thus leading to poor metabolic flexibility and impaired carbohydrate and lipid oxidation switching [23].

### ***Consequences of Circadian Disruption***

There is now an established link between the development of metabolic disorders and circadian disruption. Circadian misalignment refers to a mismatch between behavioural and physiological rhythms, where behavioural activities such as sleeping, waking, and eating become misaligned with internal biological rhythms. Examples include shift work, jet lag, social jet lag, lack of sleep, and irregular meal times.

Scheer et al. have offered one of the first experimental studies of the impact of circadian disruptions on metabolism in reporting an increase in blood pressure, insulin resistance, and inflammatory biomarkers associated with circadian misalignment in healthy humans [14]. This has raised the possibility of direct effects of circadian disruptions on cardiometabolic disease, separate from lifestyle influences.

Additional support has come from investigations of shift workers, which have shown rotating night-shift workers to be significantly more susceptible to obesity, metabolic syndrome, and type 2 diabetes than day workers [19]. Regular shift work has a disruptive effect on both sleep and eating patterns, leading to chronic circadian disruption.

Social jetlag, which refers to the difference between biological and social time, has also been linked to negative effects on metabolism. People who experience social jet lag at higher levels are more likely to suffer from obesity, insulin resistance, and poor glycemic control [18]. This is due, in part, to their irregular eating times and poor sleep quality as well as hormonal dysregulation.

It is widely acknowledged that circadian misalignment impacts several interrelated systems such as glucose metabolism, lipid metabolism, satiety regulation, inflammation, and energy balance [17]. Therefore, attempts to restore circadian alignment through optimized meal times and chrononutrition therapy would yield therapeutic gains in people at risk of metabolic syndrome and type 2 diabetes.

Advances in knowledge about the biology of circadian rhythms have had a profound impact on the way that nutrition and metabolism are viewed. In addition to considering only nutritional content, recent studies emphasize the role of matching food intake to our biological clock. The principles underlying chrononutrition theory can be applied to understand the link between eating and metabolic syndrome.

## **CHRONONUTRITION AND METABOLIC SYNDROME**

### ***Concept of Chrononutrition***

Chrononutrition is a new science that studies the connection between nutrition and meal timing and their effect on human circadian rhythms. Unlike traditional approaches to nutrition, which concentrate only on caloric and nutrient values of food products, chrononutrition is based on the fact that food timing is essential for efficient metabolic activity. This is because the human metabolism changes according to endogenous circadian rhythms, and it may be possible to optimize metabolism by adjusting nutrition time accordingly [1,2].

Meal time functions as one of the environmental factors that regulate the peripheral body clocks in different organs involved in metabolic processes. For instance, proper synchronization between meal times and biological rhythms leads to enhanced efficiency of metabolic processes such as

glucose regulation, lipid metabolism, and energy expenditure. In contrast, improper synchronization might interfere with the circadian regulation system [5,6].

Chrononutrition involves such factors as meal timing, eating frequency, daily feeding period duration, breakfast consumption, and timing of the main meal per day. These elements influence human metabolism and play an important part in developing metabolic syndrome [1].

### ***Meal Timing and Energy Balance***

Conventionally, the energy balance is regarded as the interaction between energy consumption and expenditure. Nevertheless, there are scientific data indicating that meal timing can affect both factors [6].

There are various physiological determinants accounting for this observation. Firstly, insulin sensitivity is maximally elevated in the morning hours. Secondly, diet-induced thermogenesis, or the increased expenditure of energy after a meal, is observed in the daytime rather than during the night-time hours [22]. Thus, food ingested in the morning will likely be used more effectively, while consuming calories in the evening leads to fat accumulation and insulin resistance.

According to research findings, extended daily food consumption intervals, usually longer than 14-16 hours, result in higher calorie consumption, increased body weight, and poor metabolism. It has been proven that reducing eating periods enhances metabolic efficiency and helps manage one's weight [2].

Thus, it can be concluded that meal timing needs to be taken into account when recommending dietary changes for avoiding metabolic syndrome and cardiometabolic diseases.

### ***Late-Night Eating and Metabolic Risk***

Consuming food during the nighttime period has been identified as one of the major chrononutrition-related factors leading to metabolic diseases. Due to modern lifestyles, eating becomes frequent in the evening and nighttime periods, which is a time characterized by inefficient metabolism regulation.

According to research, eating a large proportion of calorie intake in the evening leads to higher body mass index, fasting glucose level, insulin resistance, and unfavourable lipid profile [1,6]. People eating late dinners and those who snack in the evening have poorer metabolic

outcomes than people who eat the largest part of their meals in the daytime.

Another possible mechanism explaining the association between late-night eating and metabolic diseases is the loss of insulin sensitivity and impaired glucose tolerance in the evening hours. As a result, equal meals in the evening cause significantly elevated glucose and insulin response compared to the same meal eaten during morning hours [15,16]. It seems that such metabolic disturbances contribute to obesity, metabolic syndrome, and type 2 diabetes.

In addition, late-night eating could disrupt synchronization between central and peripheral clocks, which leads to circadian misalignment. This factor is known to increase cardiometabolic risks because of its influence on hormonal secretion and energy metabolism [17].

### ***Social Jetlag and Shift Work***

Social jet lag occurs due to a difference between the biological clock of the person and socially enforced schedules. This problem is common for people who have different sleep and feeding habits in the course of weekdays and weekends. Despite not being very popular, social jet lag has recently been determined as one of the main causes of metabolism-related problems [18].

Roenneberg et al. found out that social jet lag sufferers were more prone to weight gain and obesity as well as having adverse metabolic traits [18]. The process of having meals at different times than they should be because of social jet lag can impair the biological control of glucose metabolism, appetite hormones, and energy consumption by the organism.

The shift work may be considered a more intense type of disruption of circadian rhythms. Employees who work nights are forced to stay awake and eat their meals at night, which is supposed to be the period of fasting and sleep. Many epidemiological studies have confirmed that shift workers are at a high risk of developing obesity, metabolic syndrome, cardiovascular disease, and T2DM [19]. Women performing shifts had a higher chance of developing T2DM in contrast to employees working late at night [19].

Several mechanisms mediate the negative impact of shift work on an individual's metabolism, such as insomnia, hormonal disruptions, inflammation, dietary changes, and glucose metabolism impairment [17].

### ***Epidemiological Evidence Linking Chrononutrition and Metabolic Syndrome***

Epidemiological data increasingly suggest that chronic changes in meal timing habits can lead to metabolic consequences. As highlighted by Pot, many epidemiological investigations found that irregular meal times, non-consumption of breakfast, extended food consumption window, and late dinner consumption were repeatedly associated with increased cardiometabolic risks [1]. Likewise, recent systematic reviews found that timed eating practices resulted in better weight management, reduced insulin resistance, and overall improved cardiovascular health [5,6]. Those people who follow habitual meal routines and consume greater proportions of calories during the early part of the day tend to show better metabolic health indicators.

Observational research does not allow to draw any conclusions on causation, but still, the consistent results in diverse groups of people support the idea of meal timing being one of the factors affecting metabolic condition. This assumption is also supported by experimental studies that reveal biological rationale for such observations.

Overall, scientific evidence shows that chrononutrition is an essential element in the management of metabolic health. By synchronizing eating with the body's biological clock, one can decrease the likelihood of developing metabolic complications such as obesity and insulin resistance. The implications are highly applicable to people suffering from type 2 diabetes mellitus since proper meal timing affects blood glucose levels.

## **CHRONONUTRITION IN TYPE 2 DIABETES MELLITUS**

### ***Circadian Influence on Glycemic Control***

Type 2 diabetes mellitus (T2DM) is a condition that entails hyperglycemia as a consequence of both insulin resistance and impairment of insulin production by  $\beta$ -cells. While proper dietary habits are essential for the treatment of T2DM, new research indicates that even meal timing can impact the development of the disease. Chrononutrition is a field of study that explores interactions between circadian rhythms and glucose metabolism [3,4].

Circadian rhythms play a major role in the regulation of glucose homeostasis. Daily changes in insulin sensitivity, responsiveness of the  $\beta$ -cells, and tolerance of glucose affect the effectiveness of carbohydrate processing, which increases sharply in the morning but gradually fades as the

day progresses [15,16]. This means that carbohydrates will be processed better in the morning compared to the evening.

Scientific research shows that identical meals have different effects on the glucose level depending on the time of the day. For example, meals taken during the biological morning lead to lower glucose levels, and the body responds more effectively to insulin action. In contrast, eating during the evening leads to increased glucose concentration and longer periods of hyperglycemia [15,27].

In people with T2DM, however, the differences between daytime and nighttime are amplified. The negative impact that existing deficiencies in insulin sensitivity and  $\beta$ -cell function can suffer due to meals being taken during non-biologically appropriate time intervals can lead to poor glucose levels and diabetes complications [3].

Several recent review articles have brought the concept of chrononutrition into focus as an additional method of dealing with diabetes. Through the process of synchronizing meals with endogenous rhythms, better glucose control can be achieved without having to reduce calorie intake [3,4].

### ***Breakfast Consumption and Glucose Metabolism***

It is generally considered that the first meal of the day is the most important one in relation to chrononutrition since it happens during the time when people are insulin sensitive and metabolically efficient. Many studies have been conducted to explore the impact of breakfast on glucose metabolism in patients with T2DM.

For example, Jakubowicz et al. reported that individuals who skipped breakfast and delayed eating until midday had significantly higher postprandial blood glucose levels after lunch and dinner [12]. Participants who skipped breakfast showed poor insulin response and larger glucose excursion than those who ate their breakfast.

This process has been called the "second meal effect" because breakfast intake improves glucose tolerance and insulin sensitivity at subsequent meals. Lack of breakfast breaks the metabolic rhythms and thus leads to a higher risk of increased blood glucose level after other meals [12].

There are many possible explanations for the observed results. Breakfast promotes insulin secretion, reduces glucose production in the liver, and activates metabolic processes that help prepare the body for efficient nutrition. Meanwhile, long periods of fasting during the daytime can

disturb these processes and result in worse glycemic regulation [4].

In addition, people who forego breakfast often end up overeating later on in the day, thus making themselves more prone to developing metabolic complications. Researches have shown that skipping breakfast is strongly linked with obesity, insulin resistance, and increased prevalence of T2DM [1,3].

It therefore follows that eating breakfast regularly should form a significant part of chrononutrition diabetes therapy.

### ***Caloric Distribution Across the Day***

However, beyond breakfast consumption, it seems clear that energy intake distribution across the day plays an important role in metabolism regulation. The traditional methods of eating involve total intake of calories, whereas, according to recent chrononutrition studies, calorie consumption times might affect weight and glycemic management.

For example, Jakubowicz et al. investigated the impact of a high-calorie breakfast with a low-calorie dinner on body mass in comparison with a low-calorie breakfast and a high-calorie dinner in obese patients with metabolic disorders [13]. It was found that patients who ate most of their calories in the morning had more significant weight loss and decreased waist circumference than the group eating most of the calories at night.

In addition, a study conducted on patients with T2DM showed that the combination of a high-energy breakfast with low-energy dinner led to decreased daily hyperglycemia [11]. Patients had lower glucose spikes after meals and better insulin response to meals.

This study is in line with the front-loading approach to food consumption, where a greater share of calories is ingested during the early and middle parts of the day. The strategy is in tune with the physiological changes relating to glucose sensitivity and metabolism occurring throughout the day.

In fact, having large meals in the evening promotes fat storage, affects blood sugar levels, and raises cardiometabolic risk factors. Eating in the evenings happens in a low metabolic environment, which is less sensitive to insulin and diet-induced thermogenesis [22].

From all the presented findings, one can conclude that proper calorie distribution can be beneficial for metabolic outcomes in people suffering from T2DM.

### ***Clinical Implications for Diabetes Management***

Incorporating chrononutrition concepts into the care of diabetic patients has several clinical considerations. Traditional guidelines have focused on the importance of controlling calorie intake, carbohydrate content, and macronutrient composition. Nevertheless, recent data suggest that meal timing is equally crucial when designing personalized diabetic patient treatment plans [4].

Based on the latest research on chrononutrition, several recommendations can be made. First, patients should be advised to follow regular meal timings and avoid long stretches of irregular nutrition patterns. Adherence to fixed mealtimes helps synchronize periphery clocks and promote appropriate glucose levels.

Second, regular consumption of breakfast should be advocated, especially among those with poor glucose control or T2DM. Regular breakfast consumption is associated with improved glucose homeostasis and decreased metabolic stress during the day [12].

Third, doctors can recommend early consumption of calories with increased breakfast and lunch sizes and reduced portions during dinner. This type of food intake pattern promotes insulin sensitivity and decreases the occurrence of postprandial hyperglycemia [11,13].

Last but not least, patients should be discouraged from eating late at night and encouraged to adhere to daytime food consumption habits. This recommendation seems to be particularly useful for overweight and obese patients and those with metabolic syndrome or diabetes [3,4].

However, based on current findings, chrononutrition appears to be a useful supplement to traditional nutritional therapy in this regard. The integration of meal timing practices into treatment may help optimize glycemic levels while limiting the incidence of complications from diabetes.

In addition, the increasing importance being placed on meal timing as a target for intervention has led to an increased focus on structured dietary therapies like time-restricted eating. Such diets aim at integrating feeding routines with the body's circadian rhythms and have been shown to yield positive outcomes in metabolic syndrome and T2DM patients alike. Thus, the following chapter discusses the scientific evidence for time-restricted eating as a chrononutrition intervention.

## TIME-RESTRICTED EATING AS A THERAPEUTIC STRATEGY

Time-restricted eating (TRE) has emerged as one of the most promising chrononutrition-based interventions for improving metabolic health. TRE involves restricting daily food intake to a specific time window, typically ranging from 6 to 12 hours, while fasting during the remaining hours of the day. Unlike conventional dietary interventions that focus primarily on calorie restriction or nutrient composition, TRE emphasizes the timing of food consumption and its alignment with the body's circadian rhythms [2].

The physiological basis of TRE lies in the interaction between feeding-fasting cycles and the circadian system. Under normal conditions, metabolic processes such as insulin secretion, glucose uptake, and lipid metabolism are optimized during daylight hours when humans are biologically programmed to eat and remain active. However, modern lifestyles often extend eating periods into the late evening and night, resulting in prolonged daily eating windows and disruption of circadian regulation [1]. Such misalignment has been associated with obesity, insulin resistance, dyslipidemia, and an increased risk of metabolic syndrome and T2DM [14–17].

TRE works on the principle of resynchronization of food intake and endogenous circadian rhythms. Timing meals to occur consistently during the day could boost metabolism efficiency by increasing insulin sensitivity, enhancing fat oxidation, and alleviating metabolic strain. Furthermore, TRE involves fasting phases where insulin can drop, allowing for better use of stored energy resources [6].

There have been several studies assessing the influence of TRE on cardiometabolic risks. One of the pioneering studies of this type was performed by Sutton et al., who studied the effect of early time-restricted feeding (eTRF) in prediabetic men. In their study, subjects were instructed to eat all their calories during the six-hour window during the day. TRE proved to be beneficial for improving insulin sensitivity,  $\beta$ -cell function, lowering blood pressure, and decreasing oxidative stress, without causing weight loss [10].

Likewise, in another study carried out by Wilkinson et al., the impact of 10 hours of intermittent fasting protocol on adults with metabolic syndrome was assessed. In their report, body weight, waist circumference, blood pressure, fasting glucose, and atherogenic lipid levels all declined after the intervention period. Better quality of sleep and

overall well-being were reported in participants, implying positive results for metabolic health in general [7].

Further support was offered in the study carried out by Cienfuegos et al., which involved a comparison between a 4-hour TRE protocol and a 6-hour TRE protocol in adults with obesity. In both groups, there were improvements in weight and insulin resistance when compared to control groups. Importantly, the benefits occurred without rigorous calorie monitoring by subjects, showing that reduced eating time is associated with lower calories [9].

In the more recent study carried out by Lowe et al., randomized controlled trials of TRE protocol in individuals with metabolic syndrome were performed. This research revealed several beneficial outcomes related to metabolism, albeit varying from person to person, implying the significance of individual factors in relation to metabolic health [8].

Taken together, the outcomes of these studies show that there could be multiple health benefits associated with the practice of TRE, such as an improvement in glucose metabolism, insulin sensitivity, reduction in body weight and waist circumference, decreased blood pressure levels, and a change in blood lipid profile for the better. Besides, compared with other dietary interventions, the practice of TRE appears to be more feasible because its effectiveness does not depend on numerous dietary restrictions.

However, there are several limitations in the field that need to be mentioned. First of all, most of the existing studies in the literature are quite short-term in their nature, so the issue of the long-term sustainability of the effect produced by TRE still requires more evidence. In addition, due to multiple factors, comparisons between the outcomes of different studies could prove to be difficult.

Overall, recent scientific data suggest that TRE is a feasible and efficient method of chronic nutrition which can significantly improve cardiometabolic health. Through coordination of nutritional habits with internal clocks, TRE helps solve a significant, but at the same time neglected problem in metabolism and may be used as a useful addition to traditional diets in preventing and treating metabolic syndrome and T2DM.

## EMERGING MECHANISMS: GUT MICROBIOTA AND HORMONAL REGULATION

Recent findings indicate that the effect of meal timing on metabolism is not limited to glucose homeostasis and insulin

resistance. Gut microbiota and numerous hormones regulated by circadian rhythm are emerging key factors in chrononutrition and may play an important role in the development and progression of metabolic syndrome and T2DM.

There is an obvious daily fluctuation in gut bacteria composition that is affected by the circadian cycle of feeding and fasting states in the organism. On the one hand, during physiological processes, microbial communities exhibit their rhythm, which is necessary for optimal functioning in the processes of nutrient utilization, energy balance, and immunity [24]. On the other hand, disrupted circadian rhythm resulting from altered diet habits, shift working, or sleep disorders can disrupt the rhythm in gut bacteria composition and function, leading to microbial imbalance and metabolic dysfunctions.

In addition to microbial influences, hormonal regulation plays a critical role in chrononutrition. Melatonin, a hormone secreted primarily during darkness, influences glucose metabolism and insulin secretion. Elevated melatonin concentrations during the biological night are associated with reduced glucose tolerance, which may partly explain the adverse metabolic consequences of late-night eating [27]. Similarly, cortisol follows a circadian rhythm and contributes to the regulation of glucose homeostasis, lipid metabolism, and energy utilization. Disturbances in cortisol rhythms have been associated with insulin resistance, central obesity, and other components of metabolic syndrome [17,27].

Emerging research suggests that interactions among circadian clocks, gut microbiota, and hormonal pathways collectively influence metabolic health. Understanding these mechanisms may facilitate the development of personalized chrononutrition strategies and novel therapeutic approaches for metabolic disorders [28].

## **FUTURE PERSPECTIVES AND CLINICAL IMPLICATIONS**

Advancing knowledge in the field of chrononutrition has significant clinical implications. Even though previous nutritional recommendations focused mostly on macronutrient content and caloric intake, the timing of meals has now become a factor influencing the health benefits associated with particular diets.

Based on available data, chrononutritional interventions could be effective in patients with metabolic syndrome and T2DM. Some specific dietary suggestions would be

adhering to a routine eating schedule, having breakfast daily, avoiding nighttime meals, and matching food consumption with physical activity [4].

Long-term RCTs assessing the feasibility and efficacy of chrononutrition interventions over a prolonged period should be conducted in the future. In addition, personalized chrononutritional recommendations can be considered, as the chronotypes, age, gender, occupation, metabolic profile, and other parameters of individual patients can be used for tailoring dietary habits [1,6].

## **CONCLUSION**

Chrononutrition can be described as a novel paradigm in nutritional science which stresses the impact of the timing of meals on metabolic regulation. It has become clear that metabolic processes are regulated by the body clock and that their disruptions caused by irregularity in eating habits, shift work, social jet lag, and night eating lead to the development of metabolic syndrome and type 2 diabetes mellitus [14-19].

Investigations of meal timing interventions have revealed that intake of food following biological circadian clocks can improve various parameters. Meal regularity, early caloric distribution, eating breakfast, and meal restriction have been linked to improved results of glycemia, body mass, insulin sensitivity, blood pressure, and lipids [7-13]. Also, there are indications that gut microbiota and hormones controlled by circadian rhythms affect the metabolism in chrononutrition [24-28].

Despite the need for further long-term research to develop clinical recommendations, the above information provides a basis for using chrononutrition in the prevention and treatment of metabolic syndrome and type 2 diabetes mellitus.

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