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ORIGINAL RESEARCH

The Impact of Early Morning Wakefulness on Circadian Hormonal Regulation: Implications for Chronobiology-Informed Nursing Practice

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ABSTRACT

Background: Circadian rhythms govern endocrine, metabolic, and immunological homeostasis. Early morning wakefulness, particularly between 04:00–05:00 AM, coincides with a transitional hormonal window that may influence systemic physiology and gene expression.
Objectives: This study aimed to evaluate the biochemical and molecular effects of early morning wakefulness on circadian hormone regulation, metabolic synchronization, and human systemic health.
Methodology: A randomized experimental study was conducted from August 2023 to September 2024 in five Indonesian regions with 210 healthy adults. Participants were randomized into an intervention group (early wakefulness at 04:00–05:00 AM for 4 weeks) and a control group (usual sleep patterns). Outcome measures included serum cortisol, melatonin, insulin, fasting glucose, β-hydroxybutyrate (BHB), and expression of core clock genes (BMAL1 (Brain and Muscle ARNT-Like 1) , PER2 (Period Circadian Regulator 2), CLOCK (Circadian Locomotor Output Cycles Kaput), CRY1 (Cryptochrome Circadian Regulator 1)) assessed via qRT-PCR (Quantitative Reverse Transcription Polymerase Chain Reaction).
Results: The early wakefulness group exhibited a 45% increase in morning cortisol levels and a 30% reduction in melatonin ($p < 0.001$). Fasting glucose and insulin decreased significantly, while BHB levels increased ($p < 0.05$), indicating a metabolic shift. Clock gene expression showed significant up regulation of BMAL1 and PER2 (1.5-fold, $p < 0.01$), correlating inversely with HOMA-IR scores.
Conclusion: Consistent early morning wakefulness positively modulates circadian hormonal dynamics, enhances metabolic flexibility, and up regulates key circadian genes, suggesting potential health benefits in metabolic and endocrine regulation. These findings provide molecular evidence supporting early wakefulness as a non-pharmacological intervention for circadian and metabolic alignment.

Keywords: circadian rhythm, early morning wakefulness, cortisol, melatonin, clock genes, metabolic regulation, qRT-PCR.

INTRODUCTION

A wide array of physiological activities in the human body—such as hormone regulation, metabolic processes, immune function, and the sleep–wake cycle—are governed by the circadian system. This internal biological timing is controlled by both central and peripheral clock genes, with the suprachiasmatic nucleus (SCN) in the hypothalamus serving as the central coordinator. The SCN aligns bodily rhythms with external environmental signals, predominantly light, through a mechanism known as entrainment,

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ensuring consistent 24-hour physiological balance [1, 2, and 3].

One critical and underexplored window in circadian physiology is the early morning phase between 04:00 – 05:00 AM, a period marked by abrupt hormonal transitions, particularly in cortisol and melatonin concentrations. This time corresponds to the onset of the cortisol awakening response (CAR), when circulating cortisol levels rise rapidly to prepare the body for physical and mental activity, while melatonin secretion diminishes in response to early light exposure [4, 5, and 6]. Disruptions or intentional interventions during this phase may have profound effects on metabolic pathways, autonomic regulation, and gene expression.

Emerging chronobiological studies suggest that early morning wakefulness, when consistently applied, may serve as a non-pharmacological strategy to modulate circadian alignment, impacting not only hormonal rhythms but also cellular metabolism, glucose-insulin dynamics, and transcriptional control of clock genes such as BMAL1 and PER2 [7, 8, and 9]. However, comprehensive human data—especially from healthy populations in tropical equatorial settings—remain limited.

The current study aimed to investigate the biochemical and molecular effects of early morning wakefulness (04:00–05:00 AM) on core circadian hormones (cortisol and melatonin), metabolic synchrony (insulin, glucose, and β-hydroxybutyrate), and the expression of peripheral clock genes (BMAL1, PER2, CLOCK, and CRY1). This intervention was implemented in real-life settings across five Indonesian regions and examined using a controlled experimental design.

The results revealed a 45% increase in morning cortisol levels and a 30% reduction in melatonin, with significant reductions in fasting glucose and insulin, alongside elevated β-hydroxybutyrate, indicating a shift in metabolic substrate utilization. At the molecular level, up regulation of BMAL1 and PER2 expression supported the hypothesis that early wakefulness resets peripheral clock gene expression, reinforcing systemic circadian alignment [10, 11, 12, 13, and 14].

These findings align with the growing emphasis in nursing science on non-pharmacological, lifestyle-based interventions for promoting metabolic and endocrine health. Nurses play a pivotal role in educating individuals and communities about circadian hygiene, sleep management, and behavioral rhythms. The integration of early wakefulness protocols into nursing practice could provide a cost-effective and biologically grounded approach to chronic disease prevention, particularly in populations at risk for insulin resistance, sleep disturbances, or hormonal imbalance.

This study offers foundational evidence linking early wakefulness to synchronized circadian physiology at both hormonal and gene expression levels, bridging basic chronobiology with practical nursing applications. The results contribute to a growing body of research advocating for chronotherapeutic strategies within evidence-based nursing interventions, aiming to enhance health outcomes through temporal optimization of behavior and physiology.

AIMS OF THE STUDY

This study aimed to evaluate the biochemical and molecular effects of early morning wakefulness on circadian hormone regulation, metabolic synchronization, and human systemic health.

METHODOLOGY

This experimental study was conducted between August 2023 and September 2024 across five locations in Indonesia: Palopo, Luwu, Luwu Timur, Kolaka, and Kolaka Utara. A total of 210 healthy adult participants, aged 20–45 years, were recruited through stratified random sampling. Eligibility criteria included self-reported good health, no history of chronic disease, and no current medication use that could influence endocrine or

metabolic regulation. Ethical clearance was obtained from the Sulawesi Selatan Institutional Review Board under protocol number EC/7830/07/2023.

Participants were randomly allocated into two equal groups. The intervention group (n = 105) was instructed to wake up consistently between 04:00–05:00 AM every day for four consecutive weeks, while the control group (n = 105) maintained their habitual waking schedule, typically between 06:30–07:00 AM, without enforced early rising. Compliance was verified through daily sleep logs and weekly actigraphy monitoring. Both groups were matched for age, sex, BMI, and baseline sleep patterns. The purpose of this intervention was to assess the short-term physiological impact of early morning wakefulness, particularly during a transitional circadian phase characterized by naturally rising cortisol and declining melatonin levels [1, 2, and 3].

Physiological and biochemical data were collected at baseline and at the end of the 4-week intervention period. Blood samples were drawn between 05:30 and 06:00 AM after an overnight fast to capture circadian-specific hormonal fluctuations. Serum cortisol and melatonin concentrations were measured using standardized enzyme-linked immunosorbent assay (ELISA) kits validated for circadian timing analysis [2, 4]. Fasting glucose, insulin, and beta-hydroxybutyrate (BHB) were assessed using spectrophotometric and electrochemical enzymatic methods, while insulin resistance was quantified with the HOMA-IR index, calculated as (fasting insulin × fasting glucose)/22.5 [5, 6].

Molecular analysis of circadian gene expression was performed on buccal epithelial cell samples collected at the same early morning time point. Total RNA was extracted using the Trizol method, followed by cDNA synthesis and amplification. Target genes included BMAL1, PER2, CLOCK, and CRY1—core regulators of circadian rhythm [4, 7]. Gene expression levels were normalized to GAPDH and analyzed using the ΔΔCt method to determine relative fold changes pre- and post-intervention. To minimize confounding, participants were advised to maintain consistent dietary intake, regular physical activity, avoid excessive nocturnal light exposure, and manage stress throughout the study.

To evaluate the synchrony between metabolic and molecular outcomes, correlations were examined between BMAL1 and PER2 expression and HOMA-IR scores, reflecting the link between circadian clock dynamics and metabolic regulation [7, 8]. Statistical analyses were conducted using SPSS v26.0. Within-group changes were analyzed using paired t-tests, between-group differences were assessed with ANOVA, and Pearson correlation tests were applied to determine associations between variables. A p-value < 0.05 was considered statistically significant.

It is important to note that the 4-week intervention period was designed to capture short-term adaptations in hormonal and molecular circadian dynamics. However, this timeframe may not fully reflect long-term metabolic changes such as stable insulin resistance reduction or persistent gene expression shifts, which often require longer observation periods of three to four months [5, 6, 7, and 8]. Thus, findings should be interpreted as preliminary evidence of early biological responses to consistent early wakefulness. Future studies with extended intervention durations are recommended to confirm the sustainability and clinical relevance of these outcomes.

Overall, the methodological framework of this study integrates hormonal, biochemical, and molecular assessments to comprehensively evaluate the systemic effects of early morning wakefulness. This approach contributes to growing evidence that behavioral alignment with circadian biology—without pharmacological intervention—may represent a promising preventive care and chronobiology-guided nursing strategy [1, 2, 3, 4, 5, 6, 7, and 8].

RESULTS

The study demonstrated clear and statistically significant modifications in hormone secretion patterns, metabolic activity, and the expression of molecular circadian genes among individuals who consistently woke between 4:00 and 5:00 AM. As detailed in Tables 1 through 3, these outcomes highlight a well-integrated physiological adjustment that corresponds closely with circadian rhythm mechanisms.

As shown in Table 1, early risers exhibited marked shifts in key circadian hormones and metabolic indicators. Morning cortisol levels increased by 45% in this group relative to controls ($p < 0.001$), reflecting a heightened cortisol awakening response (CAR). This elevation supports the notion of greater hypothalamic–pituitary–adrenal (HPA) axis responsiveness during the early hours, potentially driven by circadian light cues and other time-of-day factors (1–3). Alongside this, serum melatonin concentrations dropped by 30% ($p < 0.01$), in line with the expected suppression of melatonin due to early light exposure and awakening stimuli (4,5).

In terms of metabolic indicators, fasting insulin levels declined by 15%, and fasting glucose dropped by 10%, while beta-hydroxybutyrate (BHB), a ketone body reflecting fat metabolism, increased by 20% ($p < 0.05$). These shifts suggest a metabolic transition toward enhanced lipid utilization and improved insulin sensitivity during early-phase wakefulness (6–10). The combination of hormonal regulation and metabolic efficiency suggests that early waking aligns physiological energy demands with endogenous timing mechanisms.

Table 2 presents the expression patterns of core circadian clock genes. Molecular assays showed a 1.5-fold increase in BMAL1 and PER2 expression in the early wakefulness group ($p < 0.01$), while CLOCK and CRY1 levels remained unchanged. These results highlight a selective transcriptional response, suggesting that early waking acts as a zeitgeber (time cue) that reactivates or reinforces peripheral clock mechanisms through hormonal entrainment and behavioral cues (11–13). The upregulation of BMAL1 and PER2 is consistent with findings in animal and human studies where these genes mediate synchronization between the central suprachiasmatic nucleus (SCN) and peripheral metabolic tissues (14–16).

Table 3 demonstrates the functional metabolic consequences of circadian gene activation. Specifically, the HOMA-IR index (Homeostatic Model Assessment for Insulin Resistance) decreased by 12% in the early wakefulness group compared to controls ($p < 0.05$), reflecting improved insulin sensitivity. Furthermore, there was a statistically significant inverse correlation between BMAL1 expression and HOMA-IR values ($r = –0.42$), supporting the hypothesis that transcriptional activity of circadian genes may contribute to favorable metabolic outcomes (17–20).

The integrated data across Tables 1 to 3 demonstrate a coherent and biologically plausible sequence of physiological changes induced by early morning wakefulness (04:00–05:00 AM), with consistent trends observed in neuroendocrine hormone levels, metabolic markers, and gene expression.

Table 1 reflects significant changes in core circadian hormones and metabolic substrates. The 45% increase in morning cortisol confirms an augmented cortisol awakening response (CAR), which serves as a reliable marker of hypothalamic–pituitary–adrenal (HPA) axis activation during early-phase circadian stimulation (1–3). Simultaneously, the 30% decrease in melatonin indicates effective circadian phase advancement, reflecting photic suppression or behavioral desynchronization of pineal output (4–5). These hormonal shifts are accompanied by favorable metabolic adaptations: decreased fasting insulin and glucose levels, and increased beta-hydroxybutyrate (BHB), a marker of fat oxidation. Collectively, these metabolic responses suggest improved insulin sensitivity and energy

flexibility, likely mediated by circadian alignment (6–10).

Table 2 provides the molecular counterpart to these physiological outcomes. The upregulation of BMAL1 and PER2 by 1.5-fold indicates peripheral clock gene activation, possibly driven by neurohormonal cues such as increased cortisol and reduced melatonin (11–13). The stability of CLOCK and CRY1 expression implies a targeted transcriptional response, rather than generalized gene induction. These selective changes reflect entrainment of peripheral clocks, which are known to coordinate tissue-specific metabolic functions, particularly under fasting and feeding cycles (14–16).

Table 3 supports these observations with functional indicators of metabolic synchronization. The 12% reduction in HOMA-IR confirms a systemic improvement in glucose-insulin homeostasis, and the significant negative correlation between BMAL1 expression and HOMA-IR ($r = –0.42$) strengthens the mechanistic link between molecular clock activation and enhanced metabolic control (17–20). This finding underscores the importance of circadian gene expression not only as a biomarker, but as a functional mediator of metabolic health.

Taken together, these findings suggest that early morning wakefulness promotes systemic synchronization involving neuroendocrine signals, metabolic transitions, and gene-level entrainment. The observed CAR (cortisol increase), melatonin suppression, and insulin-glucose-BHB shifts are biochemically coherent with enhanced clock gene expression and functional metabolic improvements (21–25). This integrative effect supports the conceptual model of early wakefulness as a physiological synchronizer that modulates multisystem homeostasis through both endocrine and genetic pathways. Such findings hold clinical relevance in nursing, especially in the development of chronobiology-based interventions for patients with metabolic syndrome, circadian rhythm disorders, or shift work-related dysregulation.

DISCUSSION:

This research explored how waking up during the early morning hours (04:00–05:00 AM) affects hormonal cycles, metabolic flexibility, and the expression of genes related to circadian rhythms in healthy adults. The outcomes demonstrate a coordinated set of physiological responses, suggesting that this early wakefulness window may positively influence endocrine balance, energy regulation, and molecular clock mechanisms. These findings carry practical relevance for nursing practice, particularly in efforts to address or prevent disruptions in circadian and metabolic health.

A notable rise in cortisol levels (+45%) and a concurrent drop in melatonin levels (−30%) were observed among individuals who woke early, indicating a stronger alignment with the body's natural cortisol awakening response (CAR), which typically peaks in the early daylight period [1, 2, and 3]. This hormonal pattern supports heightened alertness and physiological readiness for daytime activity, potentially enhancing overall functioning when timed with morning light exposure. From a clinical nursing perspective, such insights highlight the significance of incorporating circadian principles into care planning, especially for patients dealing with sleep disturbances, depressive symptoms, or maladjustment to shift work [1, 4].

Moreover, participants exhibited improved metabolic indicators, including lowered fasting insulin and glucose levels, alongside increased beta-hydroxybutyrate (BHB) concentrations. These shifts point to a preference for fat-based energy utilization and suggest better metabolic adaptability—a sign of improved insulin responsiveness and mitochondrial efficiency [5, 6]. These findings are especially pertinent for nurses managing patients with conditions such as obesity, prediabetes, or metabolic syndrome. In such cases, aligning behavior with natural circadian rhythms could serve as an effective, non-pharmacological strategy to enhance metabolic outcomes [7, 10].

On a molecular level, an upsurge in the expression of circadian genes BMAL1 and PER2 (approximately 1.5-fold) confirms that peripheral clocks, such as those in epithelial tissues, are responsive to changes in behavioral timing like wake-up patterns. This reinforces existing models suggesting that external cues—including light and feeding schedules—can modulate peripheral gene expression via central regulation by the suprachiasmatic nucleus (SCN) [11, 12, and 13]. For nursing, this underlines the growing relevance of chronotherapy: designing treatment schedules and care delivery in sync with the patient's biological clock to maximize therapeutic benefit [13, 14].

Furthermore, the observed inverse correlation between BMAL1 expression and HOMA-IR scores suggests a genetic underpinning of improved insulin sensitivity in the early wakefulness group. These findings echo previous molecular chronobiology studies and support the hypothesis that early morning activity may enhance endocrine-metabolic alignment, reducing the risk for insulin resistance and type 2 diabetes [11, 15].

Viewed from a holistic standpoint, the findings of this research indicate that adopting a simple and inexpensive practice—waking between 04:00 and 05:00 AM—can significantly impact systemic physiological functions. Nurses hold a crucial position in encouraging this behavioral shift through targeted health education, continuous counseling, and structured interventions for sleep and wake cycles. This approach may be particularly beneficial for individuals recuperating from metabolic disorders, those participating in weight control programs, or patients in long-term care, where sleep–wake routines informed by chronobiological principles can be implemented and supervised by nursing professionals.

In addition, these results carry practical relevance for managing shift work among nurses. A clearer understanding of how early wake times affect hormonal rhythms may assist nurse administrators in designing shift patterns and recovery protocols that reduce the health risks associated with circadian misalignment, especially in night-duty personnel [2, 4].

Furthermore, this study reinforces the role of early waking as a non-pharmacological chronobiological strategy that supports the synchronization of hormonal outputs, boosts metabolic indicators, and stimulates the activity of clock-related genes. Applying this insight within nursing care strategies may introduce a new, evidence-supported pathway to maintain or restore physiological balance, especially in individuals affected by metabolic or circadian rhythm disorders.

CONCLUSIONS:

This study demonstrates that consistent early morning wakefulness between 04:00 and 05:00 AM induces significant changes in endocrine, metabolic, and molecular circadian rhythms. The biochemical outcomes—particularly the 45% increase in cortisol and 30% decrease in melatonin—indicate that early wakefulness acts as a strong regulator of hormonal balance and circadian adaptation. These findings conclude that waking up during this critical window enhances metabolic readiness and physiological alertness. The implications suggest that structured early wakefulness may be applied as a chronobiology-based strategy to optimize health, improve daily performance, and potentially support long-term well-being [6, 9, and 10].

On the metabolic level, the observed reductions in fasting insulin and glucose, along with elevated beta-hydroxybutyrate (BHB), indicate a shift toward enhanced fat utilization and improved metabolic flexibility [11, 14].

These effects were further substantiated by molecular data showing the upregulation of core circadian genes BMAL1 and PER2, which are key regulators of peripheral clock alignment and metabolic homeostasis [4, 5, 12, and 13]. The inverse correlation between BMAL1 expression and HOMA-IR scores supports a mechanistic link between early

wakefulness and improved insulin sensitivity, reinforcing the concept of circadian entrainment as a modifiable behavior with systemic health benefits [12, 15, and 20].

However, a conclusion of this kind relies on numerous other factors that warrant further consideration. Humans are heliophilic creatures, and light exposure remains the primary zeitgeber for circadian entrainment. Variables such as intensity, duration, and spectral composition of morning light, as well as individual chronotypes, sleep debt, and lifestyle behaviors, likely modulate the hormonal and metabolic outcomes observed in this study. Future research should therefore integrate light measurement, broader endocrine markers, and long-term clinical outcomes to validate the generalizability of these findings.

In the context of nursing, these findings have profound implications. Nurses, as frontline health professionals, play a pivotal role in educating patients on sleep hygiene, circadian alignment, and non-pharmacological interventions that promote metabolic health. The integration of early wakefulness protocols into nursing-led wellness programs may offer a low-cost and effective strategy to support patients with metabolic syndrome, type 2 diabetes, or disrupted circadian rhythms, such as shift workers or hospitalized individuals [17, 21]. Moreover, this research provides molecular and hormonal evidence that can inform chronobiology-based nursing care, emphasizing timing as a critical dimension of assessment and intervention planning.

The application of these findings in community health, preventive nursing, and personalized care models could represent a transformative approach in modern nursing practice.

By addressing the interplay between early wakefulness, light exposure, behavioral rhythms, and inter-individual variability, nursing science can advance toward chronobiology-based interventions that are both biologically grounded and clinically meaningful. Early morning wakefulness emerges as a viable, evidence-based behavioral intervention that enhances hormonal regulation, metabolic alignment, and gene expression consistency—offering a promising addition to the toolkit of health promotion strategies within nursing science [1 – 25].

Study Limitations:

This research presents certain limitations that warrant attention when drawing conclusions from the results. To begin with, the study population was restricted to healthy adults aged between 20 and 45 years. As a result, the findings may not be broadly applicable to other groups, such as elderly individuals, adolescents, or those experiencing metabolic or endocrine imbalances.

Secondly, the intervention period was relatively brief—limited to four weeks. Such a timeframe might be insufficient to reflect the prolonged biochemical and gene expression changes that could arise from early morning wakefulness. Future investigations incorporating longer observation periods may be better suited to explore sustained physiological responses.

Thirdly, although essential hormonal and molecular markers were analyzed, the study did not extend to practical health-related metrics, including sleep efficiency, cognitive outcomes, or long-term cardiovascular status. Evaluating such parameters could yield a more integrative picture of potential clinical benefits or drawbacks.

A fourth limitation involves participant adherence to the early wakefulness regimen. Data on compliance were primarily derived from self-reports and supervised timekeeping, which introduces the possibility of variation in protocol fidelity. Finally, while circadian gene expression was evaluated using qRT-PCR on keratinized epithelial cells, this peripheral measurement may not fully reflect the dynamics of central circadian regulation occurring in the suprachiasmatic nucleus (SCN). Given the SCN's pivotal role in orchestrating systemic rhythms, future work should aim to include more representative

assessments. Expanding sample diversity, extending intervention length, and integrating functional health indicators will be essential for substantiating and enhancing these preliminary findings.

Conflict of Interest Statement

The author declares no conflict of interest related to the design, conduct, or publication of this study.

Ethical Approval

This study was approved by the Health Research Ethics Committee of the South Sulawesi Provincial Health Office, Indonesia, under protocol number EC/7830/07/2023. All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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TABLES:

Table (1): Changes in Circadian Hormones and Metabolic Biomarkers Following Early Morning Wakefulness (04:00–05:00 AM).

Parameter	Early Wakefulness Group	Control Group	% Change	p-value	Interpretation
Cortisol (ng/dL)	↑ 45% from baseline	Stable	+45%	< 0.001	Significant cortisol awakening response (CAR) [1–3]
Melatonin (pg/mL)	↓ 30% from baseline	Mild decline	–30%	< 0.01	Early suppression of melatonin secretion [4–5]
Fasting Insulin (µIU/mL)	↓ 15% from baseline	No change	–15%	< 0.05	Improved insulin sensitivity [6–9]
Fasting Glucose (mg/dL)	↓ 10% from baseline	Slight decline	–10%	< 0.05	Enhanced glucose regulation [6–9]
Beta-Hydroxybutyrate (mmol/L)	↑ 20% from baseline	No change	+20%	< 0.05	Increased fat oxidation and metabolic flexibility [10]

Notes:

- Values represent percentage change from baseline after 4 weeks of intervention.
- All differences were statistically significant as shown.
- Data are interpreted based on established circadian and metabolic pathways [1–10].

Table (2): Differential Expression of Core Circadian Clock Genes in Early Wakefulness Group Compared to Controls

Gene	Function	Fold Change (Early Wakefulness vs Control)	p-value	Interpretation
BMAL1	Core transcription activator in circadian loop	↑ 1.5×	< 0.01	Significant upregulation; suggests peripheral clock activation [11–13]
PER2	Feedback repressor in clock gene loop	↑ 1.5×	< 0.01	Enhanced circadian regulation and metabolic alignment [14–16]
CLOCK	Heterodimer partner of BMAL1	No significant change	> 0.05	Expression stable; indicates selective gene response to early wake stimulus
CRY1	Negative feedback regulator of BMAL1:CLOCK	No significant change	> 0.05	Consistent with stable core repression loop under mild behavioral entrainment

Notes:

- Gene expression measured via quantitative RT-PCR in peripheral epithelial cells.
- Fold change values indicate relative mRNA expression compared to baseline/control.
- Only BMAL1 and PER2 were significantly altered following 4-week early wakefulness protocol [11–16].

Table (3): Metabolic Synchronization Indicators Following Early Morning Wakefulness

Parameter	Early Wakefulness Group	Control Group	% Change	p-value	Interpretation
HOMA-IR Index	↓ 12% from baseline	No change	–12%	< 0.05	Improved insulin sensitivity and glucose utilization [17–19]
BMAL1–HOMA-IR Correlation	r = –0.42	—	—	p < 0.05	Significant negative correlation: Higher BMAL1 linked to lower insulin resistance [20]

Notes:

- HOMA-IR: Homeostatic Model Assessment for Insulin Resistance.
- Negative correlation indicates favorable interaction between circadian gene activation and metabolic outcome.
- These findings reinforce the hypothesis that early wakefulness promotes molecular-metabolic alignment [17–20].