IAA Journal of Applied Sciences 14(1):72-78, 2026. www.iaajournals.org
©IAAJOURNALS ISSN: 2636-7246
https://doi.org/10.59298/IAAJAS/2026/1417278 IAAJAS: 141000

Circadian Rhythm Disruption, Sleep Disorders, and Their Role in Obesity-Linked Diabetes

Abner Tom Kalukusu

Department of Clinical Medicine and Dentistry Kampala International University Uganda
Email: abnertomkalukusu@studwc.kiu.ac.ug

ABSTRACT

Circadian timekeeping aligns cellular metabolism with daily cycles of light, feeding, and activity. In obesity-linked type 2 diabetes (T2D), misalignment between endogenous clocks and behavior via shift work, social jetlag, evening eating, short/fragmented sleep, insomnia, or sleep-disordered breathing exacerbates insulin resistance (IR), impairs β-cell function, and worsens glycemic variability. Molecular clocks (CLOCK, BMAL1, PER, CRY) coordinate transcriptional oscillations in liver, skeletal muscle, adipose tissue, pancreas, and gut; disruption alters glucose production, lipid handling, adipokine release, mitochondrial quality control, and inflammatory tone. Acute sleep restriction reduces insulin sensitivity within days through sympathetic and HPA-axis activation, increased evening cortisol, GH, and catecholamine shifts, and elevated free fatty acids; chronic restriction sustains ectopic fat and endothelial dysfunction. Obstructive sleep apnea (OSA) adds intermittent hypoxia and arousal-driven surges in sympathetic activity, raising nocturnal glucose and blood pressure and aggravating NAFLD. Meal timing interacts with clocks: late eating increases postprandial glycemia and decreases diet-induced thermogenesis; early time-restricted eating improves fasting glucose and HOMA-IR independent of large weight loss. Interventions: sleep hygiene, cognitive behavioral therapy for insomnia (CBT-I), positive airway pressure for OSA, light management, melatonin timing in circadian disorders, exercise timing, and chrononutrition restore alignment and augment pharmacotherapy (GLP-1 receptor agonists, SGLT2 inhibitors, TZDs) and surgery when indicated. Precision strategies combine chronotype, actigraphy/polysomnography, continuous glucose monitoring (CGM), and metabolomics to tailor timing prescriptions and medication dosing. This review synthesizes mechanisms linking circadian/sleep disruption to diabesity, evaluates disease-specific sleep disorders, and outlines pragmatic, scalable, and equitable chronobiology-informed care.

Keywords: circadian rhythm; sleep disorders; insulin resistance; time-restricted eating; type 2 diabetes

INTRODUCTION

Type 2 diabetes (T2D) is a disorder of impaired metabolic flexibility across the liver, skeletal muscle, adipose tissue, pancreatic islets, and the vasculature[1–3]. While excess adiposity is the dominant modifiable risk factor, *when* we sleep, move, and eat importantly influence *how* we metabolize nutrients. Circadian clocks, hierarchically organized by the suprachiasmatic nucleus (SCN) in the hypothalamus and distributed to peripheral tissues, synchronize physiology to the 24-hour day. Light timing entrains the SCN; feeding, physical activity, and temperature help entrain peripheral clocks. At the cellular level, transcription-translation feedback loops (CLOCK and BMAL1 driving PER and CRY, which feedback to repress CLOCK: BMAL1) generate ~24-h rhythms in thousands of genes controlling glucose transport (GLUTs), insulin signaling, mitochondrial biogenesis, oxidative phosphorylation, lipolysis/lipogenesis, and inflammatory programs[4, 5].

In healthy alignment, metabolic processes are phased: insulin sensitivity and β-cell responsiveness peak in the biological morning/early day; hepatic gluconeogenesis and lipolysis ebb with feeding; diet-induced thermogenesis is higher earlier; and sleep supports overnight growth hormone pulses, glymphatic clearance, and immunologic resetting[5]. Modern environments strain this design. Artificial light at night, late meals, round-the-clock work, screen exposure, and social jetlag (weekday vs weekend schedule shifts) uncouple central and peripheral clocks. Behavioral misalignment compresses sleep duration and fragments architecture (less slow-wave sleep), elevating sympathetic outflow and HPA-axis activity. These changes reduce insulin-mediated glucose uptake in muscle, blunt insulin's antilipolytic effects in adipose tissue (raising free fatty acids), and

increase hepatic glucose output, hallmarks of insulin resistance[6, 7]. Elevated evening cortisol and catecholamines further oppose insulin; inflammatory cytokines (IL-6, TNF-α) rise, and endothelial function declines. Within days, sleep restriction impairs glucose tolerance; within weeks to months, weight gain and ectopic fat increase, particularly hepatic fat, compounding metabolic dysfunction[8, 9].

Sleep disorders amplify these mechanisms. Insomnia heightens arousal and nocturnal cortisol; restless legs/periodic limb movements fragment sleep; circadian rhythm sleep-wake disorders (delayed sleep-wake phase, non-24-h, shift-work disorder) chronically misalign internal time with external demands; and obstructive sleep apnea (OSA) induces intermittent hypoxia and intrathoracic pressure swings that repeatedly trigger sympathetic surges and oxidative stress[10]. OSA severity correlates with impaired insulin sensitivity, dyslipidemia, hypertension, and NAFLD conditions tightly linked to diabesity. Importantly, meal timing interacts with sleep and circadian phase: late eating increases postprandial glucose and reduces fat oxidation; skipping breakfast and concentrating calories at night worsens 24-h glycemia. Conversely, early time-restricted eating (eTRE; e.g., 8 a.m.–4 p.m.) improves fasting glucose, HOMA-IR, and blood pressure even without large weight changes[10].

Mechanistically, clock disruption alters mitochondrial dynamics and autophagy, impairs brown/beige fat thermogenesis, shifts adipokine balance (decreases adiponectin, increases leptin resistance), and changes bile-acid and microbiome rhythms that regulate GLP-1 and FGF19 signaling. β-cell clocks govern stimulus–secretion coupling; their disruption reduces first-phase insulin. Inflammation follows circadian patterns; misalignment promotes a pro-inflammatory set point that sustains insulin resistance[11]. These insights motivate chronobiology-informed care: restore regular sleep timing/duration; reduce evening light; align meals with the biological day; use light, melatonin, and behavioral therapy to correct circadian disorders; treat OSA; and pair with pharmacotherapy targeting weight, insulin sensitivity, and organ protection. Precision phenotyping (chronotype, actigraphy, DLMO, CGM) individualizes prescriptions and sequencing with lifestyle, drugs, and, when indicated, metabolic surgery[12].

The sections that follow summarize circadian biology and metabolic homeostasis; delineate mechanisms by which sleep loss and misalignment drive insulin resistance and β-cell stress; review sleep disorders relevant to diabesity; examine organ-to-organ chronometabolic crosstalk, including the microbiome; outline measurement and phenotyping tools; and present intervention strategies, including chrononutrition and precision timing, integrated with pharmacologic and surgical care.

2. Circadian Timekeeping and Metabolic Homeostasis

The circadian system comprises a master pacemaker in the SCN and autonomous clocks in most cells. The SCN receives light via melanopsin-containing retinal ganglion cells; blue-enriched light in the evening delays circadian phase, whereas morning light advances it[4, 11–13]. Peripheral clocks in liver, muscle, adipose tissue, pancreas, heart, and gut are entrained by feeding–fasting cycles, temperature, autonomic input, and local hormones. Molecularly, CLOCK: BMAL1 drives rhythmic transcription of PER/CRY; PER/CRY complexes accumulate and inhibit CLOCK: BMAL1, closing the loop. Auxiliary loops (REV-ERBs, RORs) stabilize period and amplitude and couple to metabolic genes (gluconeogenic enzymes, lipogenic genes, fatty-acid transporters, mitochondrial regulators)[4, 14].

Metabolic processes are phased to anticipate behavior. In the biological morning, insulin sensitivity is higher: skeletal muscle exhibits enhanced GLUT4 translocation and PI3K–Akt signaling; adipose tissue is more antilipolytic; liver suppresses gluconeogenesis more effectively[15]. Diet-induced thermogenesis peaks earlier in the day, improving postprandial efficiency. During the biological night, fasting physiology dominates: hepatic glucose output maintains euglycemia; growth hormone pulses support lipolysis and substrate mobilization; melatonin rises, modulating pancreatic secretion and peripheral tissues. Brown/beige fat thermogenesis shows circadian patterns, assisting temperature regulation and lipid handling.

Clock outputs coordinate mitochondrial biogenesis and quality control via PGC-1α, SIRT1, and AMPK; VDAC/MCU-mediated Ca2+ rhythms tie to oxidative metabolism. Autophagy/mitophagy cycles support organelle renewal[16]. The immune system is rhythmic: leukocyte trafficking, cytokine release, and inflammasome activity oscillate, shaping insulin sensitivity. Endocrine rhythms, such as cortisol, melatonin, GH, and thyroid hormones, interact with clocks to set tissue responsiveness. The gut exhibits diurnal motility, permeability, and hormone secretion (GLP-1, PYY), with the microbiome oscillating in composition and function, feeding back via SCFAs, bile-acid modifications, and indoles. Together, these rhythms align supply and demand, preventing metabolic overload during rest and facilitating efficient processing during the active/feeding phase[17].

Disruption by inadequate light cues, irregular sleep, shift work, or late eating uncouples clocks, blunting amplitude and altering phase relationships. The result is temporal "internal desynchrony," where liver, muscle, adipose, and islet clocks disagree about the time, degrading systemic homeostasis. Restoration requires *both* zeitgeber hygiene (light, meals, activity) and targeted therapies for disorders and comorbidities.

3. Mechanisms: How Misalignment and Sleep Loss Drive Insulin Resistance and β-Cell Stress

Neuroendocrine activation. Sleep restriction and circadian misalignment elevate evening cortisol and sympathetic tone, increasing hepatic glucose production, lipolysis, and glycogenolysis while reducing muscle

glucose uptake. Catecholamine and HPA-axis surges impair insulin signaling via serine phosphorylation of IRS proteins and activation of PKC/JNK pathways[18].

Adipose tissue and lipotoxicity. Reduced slow-wave sleep diminishes growth hormone's nocturnal actions and increases antilipolytic threshold, raising free fatty acids (FFAs). Elevated FFAs accumulate as DAGs and ceramides in the liver and muscle, activating novel PKCs that blunt insulin receptor signaling. Adipokine balance shifts (decrease adiponectin, increase leptin with resistance), sustaining systemic IR and endothelial dysfunction[19].

β-cell function. Circadian clocks gate insulin secretion; misalignment lowers first-phase insulin and increases proinsulin: insulin ratios. Melatonin-MTNR1B signaling interacts with insulin secretion, late melatonin peaks or exogenous dosing near the biological morning can transiently worsen glucose tolerance in susceptible genotypes. Glucolipotoxic stress and ER/mitochondrial dysfunction escalate under sleep loss, promoting β-cell fatigue and dedifferentiation[20].

Mitochondrial and oxidative stress. Clock disruption decreases PGC-1α/SIRT1 activity, reduces oxidative capacity, fragments mitochondrial networks, and impairs mitophagy; reactive oxygen species increase, activating stress kinases that impede insulin signaling and promote inflammation[21].

Inflammation and endothelial dysfunction. Short sleep and OSA increase IL-6, TNF-α, and CRP, activating NF-κB and JNK. Endothelial nitric-oxide bioavailability falls; adhesion molecules rise, impairing microvascular insulin delivery to muscle. Intermittent hypoxia from OSA triggers HIF-1α-mediated lipogenesis and oxidative stress, aggravating NAFLD[22].

Behavioral mediators. Sleep loss increases hedonic eating, snack frequency, and preference for high-glycemic foods; ghrelin rises, and leptin signaling blunts. Late eating reduces diet-induced thermogenesis and increases 24-h glycemic exposure. Physical activity declines with fatigue, further lowering insulin sensitivity[23].

Net effect. Within days of sleep restriction, insulin sensitivity drops; with chronic misalignment, ectopic fat accumulates, NAFLD progresses, and β-cell stress mounts, moving susceptible individuals from compensated IR to overt T2D[24].

4. Sleep Disorders in Diabesity: Insomnia, OSA, and Circadian Rhythm Disorders

Insomnia disorder (difficulty initiating/maintaining sleep with daytime impairment) is prevalent in T2D. Hyperarousal (cognitive/emotional/physiologic), conditioned wakefulness, and maladaptive behaviors sustain it[25]. Consequences include sympathetic activation, evening cortisol elevation, increased nocturnal eating, and reduced pain thresholds. Evidence-based management is CBT-I (stimulus control, sleep restriction therapy, cognitive restructuring, relaxation, circadian stabilization), often improving HbA1c modestly via better sleep and behavior. Hypnotic medications are adjuncts for selected patients; caution with residual sedation and OSA comorbidity[25].

Obstructive sleep apnea (OSA), driven by pharyngeal collapsibility and obesity, causes intermittent hypoxia and arousals. It increases IR independent of BMI, raises BP, worsens NAFLD, and elevates cardiovascular risk[26]. Positive airway pressure (PAP) is first-line; consistent use improves daytime sleepiness and BP and can improve glycemia, especially when baseline HbA1c is high, and adherence is robust. Adjuncts include weight loss, positional therapy, mandibular advancement devices, and upper-airway surgery in selected cases[27].

Circadian rhythm sleep-wake disorders include shift-work disorder (SWD), delayed sleep-wake phase disorder (DSWPD), and irregular sleep–wake rhythm. SWD features insomnia/excessive sleepiness with shift schedules; chronic misalignment raises T2D risk. DSWPD delays sleep timing, causing insufficient sleep on required schedules; it often overlaps with evening light exposure and late meals[28]. Management targets phase and amplitude: timed morning bright light, evening blue-light reduction, melatonin at circadian-appropriate times (hours before DLMO for phase advance), and fixed wake times. For shift workers, anchor sleep in a consistent window, cluster night shifts, schedule strategic naps, and avoid large meals near biological night[28].

Restless legs syndrome/periodic limb movement disorder fragments sleep and increases arousal; iron deficiency is common and correctable. Chronic insufficient sleep (<6–7 h) without formal disorder still increases T2D risk; population strategies (start-time policies, light hygiene campaigns) are relevant[28].

Comorbidity intersections**.** Depression, chronic pain, and menopausal transition alter sleep and weight trajectories; integrated behavioral and medical care improves outcomes. Clinicians should screen systematically (Insomnia Severity Index, STOP-Bang for OSA, work schedule, chronotype) as part of diabesity management[29].

5. Organ Crosstalk and the Chronometabolic Network: Adipose, Liver, Muscle, Islets, Vasculature, and Microbiome

Adipose tissue: Clocks regulate lipolysis, adipogenesis, and thermogenesis. Misalignment increases nocturnal lipolysis and reduces adiponectin secretion; macrophage infiltration and inflammatory cytokines rise, producing a pro-inflammatory adipose niche. Catecholamine resistance in adipocytes and macrophages blunts lipolytic control and beiging[30].

Liver: Hepatic clocks gate gluconeogenesis, glycogen storage, and bile-acid synthesis. Late eating and circadian disruption increase FOXO-mediated gluconeogenesis and de novo lipogenesis, elevating hepatic triglycerides and VLDL secretion. FGF19 rhythms dampen; bile-acid pools and FXR signaling shift[31–33].

Skeletal muscle: Muscle clocks modulate mitochondrial biogenesis and substrate switching. Sleep loss and late eating reduce insulin-stimulated glucose uptake, capillary recruitment, and oxidative capacity; mitochondrial fragmentation and reduced PGC-1α ensue. Evening exercise can acutely improve next-day fasting glucose, but chronic misalignment blunts training adaptations[34].

Pancreatic islets: β-cell clocks time insulin granule trafficking and exocytosis; clock gene disruption reduces first-phase insulin and increases susceptibility to glucolipotoxic stress. α-cell glucagon rhythms alter hepatic glucose output overnight.

Vasculature: Endothelial NO and vascular tone are circadian; misalignment raises nighttime BP, reduces NO bioavailability, and increases adhesion molecules, impairing insulin delivery to muscle and raising CV risk.

Gut and microbiome: Microbial composition and metabolite production (SCFAs, secondary bile acids, indoles) oscillate with feeding/fasting. Nighttime eating and circadian disruption dampen microbial rhythms, increase intestinal permeability, and elevate endotoxemia, promoting hepatic and adipose inflammation. GLP-1/PYY secretion rhythms are blunted with irregular meals[35–37].

Integrative view: These organ-specific effects synchronize to either enhance or erode metabolic flexibility. Restoring alignment requires multi-level interventions—timed light, meals, activity, and sleep, plus treatment of sleep disorders and metabolic comorbidities.

6. Measurement and Phenotyping: From Chronotype to CGM

History and screening: Assess sleep duration/regularity, bed/wake times, naps, shift schedules, insomnia symptoms, snoring/apneas, RLS symptoms, stimulant and alcohol timing, and evening light exposure. Use validated tools: Munich ChronoType Questionnaire (MCTQ) or Morningness–Eveningness Questionnaire; Insomnia Severity Index; STOP-Bang for OSA[38].

Wearables and actigraphy: Wrist actigraphy estimates sleep timing/regularity and social jetlag; heart-rate and temperature proxies help identify circadian phase drift. Consumer wearables can aid coaching when interpreted with caution[39].

Polysomnography (PSG): Gold standard for OSA and limb movement disorders; home sleep apnea testing is scalable for high-probability cases. PAP adherence data inform ongoing care[40].

Circadian phase markers: Dim-light melatonin onset (DLMO) and core body temperature minima define biological night for precise phase-shifting (light/melatonin) protocols. Salivary melatonin or urinary aMT6s provides practical options in research or specialized care[40].

Metabolic profiling: Pair CGM with meal/sleep logs to reveal glycemic responses to timing (late meals, night shifts) and to guide chrononutrition. Morning vs evening oral glucose tolerance differences can expose misalignment. Lipid panels, ALT, and MRI-PDFF assess NAFLD. Inflammation (hs-CRP, IL-6) and autonomic tone (HRV) reflect stress burden.

Endotyping: Combine chronotype, social jetlag, OSA status, insomnia phenotype (sleep-onset vs maintenance), NAFLD presence, and activity patterns to guide interventions: eTRE for late eaters; CBT-I for insomnia; PAP for OSA; morning light/melatonin for delayed phase; evening blue-light reduction for all.

7. Interventions: Chronotherapy, Chrononutrition, and Integrated Care

Sleep duration/regularity: Target 7–9 h/night with ≤60-min variability across the week. Establish consistent anchors (fixed wake time), wind-down routines, and device curfews. Address caffeine (avoid after early afternoon) and alcohol (avoid near bedtime) timing[41].

CBT-I: First-line for insomnia: stimulus control, sleep-restriction therapy (with CGM awareness in insulin-treated patients), cognitive restructuring, relaxation, and circadian stabilization. Digital CBT-I expands access[41].

OSA treatment: PAP is the cornerstone; enhance adherence via mask fitting, humidification, desensitization, and behavioral support. Add weight loss, positional therapy, mandibular devices, or surgery when indicated. Monitor glucose and BP improvements[42].

Light and melatonin: Morning bright light (outdoor light or devices) advances phase; evening blue-light reduction (filters, dimming) prevents delay. Melatonin (0.3–3 mg) timed 4–6 h before DLMO advances circadian phase in delayed phase/SWD; avoid dosing near biological morning due to transient glucose tolerance worsening[42].

Chrononutrition: Prefer early time-restricted eating (eTRE) or earlier caloric distribution (larger breakfast/lunch, lighter dinner). Sequence meals (vegetables/protein before starch) to blunt glycemic peaks; plan post-meal walks (10–20 min) or short exercise bouts. Align carbohydrate intake to daylight and activity; reserve evenings for protein, vegetables, and healthy fats[42].

Exercise timing: Consistent timing stabilizes circadian phase; afternoon/evening resistance training can improve next-day fasting glucose; morning outdoor exercise adds light exposure. Avoid intense workouts late at night if it impairs sleep.

Medication timing: Coordinate insulin and secretagogues with earlier meals to minimize nocturnal hypoglycemia; consider morning dosing for agents with GI effects to align with meals. GLP-1 RAs and SGLT2 inhibitors pair well with eTRE; TZDs may benefit NAFLD phenotypes irrespective of timing, but monitor edema.

Shift-work mitigation: Cluster night shifts, anchor sleep after nights in a fixed window, use strategic naps, time caffeine early in the shift, employ bright light at work and sunglasses on commute home, and maintain eTRE on off-days when possible. Employers can rotate shifts forward (morning→evening→night), reduce quick turnarounds, and provide healthy meal options on nights.

Integration with weight-loss pharmacotherapy/surgery: Incretin-based agents and SGLT2 inhibitors synergize with sleep/meal timing to reduce appetite and glycemic excursions; CPAP enhances daytime energy for exercise. After bariatric surgery, reinforce regular sleep and early eating windows to protect remission.

Equity and scalability: Use low-cost approaches (morning sunlight, simple evening light curfews, consistent wake times, planned walks, culturally familiar early dinners). Leverage group programs, SMS prompts, and workplace policies to support alignment.

CONCLUSION

Circadian disruption and sleep disorders are not peripheral to diabesity; they are active drivers that can be measured and modified. Misalignment and sleep loss rapidly impair insulin sensitivity and β-cell function via neuroendocrine activation, lipotoxicity, mitochondrial and inflammatory stress, endothelial dysfunction, and disordered organ crosstalk. OSA adds intermittent hypoxia that amplifies cardiometabolic risk. The good news: alignment is treatable. Regular sleep, timed light, earlier eating windows, targeted treatment of insomnia and OSA, and synchronized activity meaningfully improve glycemia and cardiometabolic health, often independent of large weight loss, and potentiate the benefits of modern pharmacotherapy and surgery. Clinicians should screen for sleep and circadian issues as routinely as they measure HbA1c, pair CGM with sleep/meal logs to reveal timing effects, and deliver pragmatic, culturally attuned timing prescriptions. Research priorities include defining responder endotypes, refining melatonin/light protocols in T2D, integrating microbiome and metabolomic rhythms into care, and testing chronotherapy of antidiabetic agents. Embedding chronobiology into diabesity pathways shifts care from glucose chasing to time-aware disease modification, improving outcomes that matter: energy, sleep quality, productivity, and long-term vascular health.

REFERENCES

1. AbdlWhab, H.M., Al-Saffar, A., Mahdi, O.A., Alameri, R.B.: The impact of insulin resistance and glycaemic control on insulin-like growth factor-1 in patients with type 2 diabetes: a cross-sectional study. Clin. Diabetes Endocrinol. 10, 36 (2024). https://doi.org/10.1186/s40842-024-00202-8
2. Alzaid, F., Fagherazzi, G., Riveline, J.-P., Bahman, F., Al-Rashed, F., Al-Mulla, F., Ahmad, R.: Immune cell–adipose tissue crosstalk in metabolic diseases with a focus on type 1 diabetes. Diabetologia. 68, 1616–1631 (2025). https://doi.org/10.1007/s00125-025-06437-z
3. Alum, E.U.: Optimizing patient education for sustainable self-management in type 2 diabetes. Discov. Public Health. 22, 44 (2025). https://doi.org/10.1186/s12982-025-00445-5
4. Engin, A.: Circadian Rhythms in Diet-Induced Obesity. Adv. Exp. Med. Biol. 960, 19–52 (2017). https://doi.org/10.1007/978-3-319-48382-5_2
5. Potter, G.D.M., Cade, J.E., Grant, P.J., Hardie, L.J.: Nutrition and the Circadian System. Br. J. Nutr. 116, 434–442 (2016). https://doi.org/10.1017/S0007114516002117
6. Meléndez-Fernández, O.H., Liu, J.A., Nelson, R.J.: Circadian Rhythms Disrupted by Light at Night and Mistimed Food Intake Alter Hormonal Rhythms and Metabolism. Int. J. Mol. Sci. 24, 3392 (2023). https://doi.org/10.3390/ijms24043392
7. Putilov, A.A., Poluektov, M.G., Dorokhov, V.B.: Evening chronotype, late weekend sleep times and social jetlag as possible causes of sleep curtailment after maintaining perennial DST: ain't they as black as they are painted? Chronobiol. Int. 37, 82–100 (2020). https://doi.org/10.1080/07420528.2019.1684937
8. Kent, B.D., McNicholas, W.T., Ryan, S.: Insulin resistance, glucose intolerance and diabetes mellitus in obstructive sleep apnoea. J. Thorac. Dis. 7, 1343–1357 (2015). https://doi.org/10.3978/j.issn.2072-1439.2015.08.11
9. Al-Sharif, F.M., El-Kader, S.M.A.: Inflammatory cytokines and sleep parameters response to life style intervention in subjects with obese chronic insomnia syndrome. Afr. Health Sci. 21, 1223–1229 (2021). https://doi.org/10.4314/ahs.v21i3.31
10. Karna, B., Sankari, A., Tatikonda, G.: Sleep Disorder. In: StatPearls. StatPearls Publishing, Treasure Island (FL) (2025)
11. Wada, T., Yamamoto, Y., Takasugi, Y., Ishii, H., Uchiyama, T., Saitoh, K., Suzuki, M., Uchiyama, M., Yoshitane, H., Fukada, Y., Shimba, S.: Adiponectin regulates the circadian rhythm of glucose and lipid metabolism. J. Endocrinol. 254, 121–133 (2022). https://doi.org/10.1530/JOE-22-0006
12. Sun, S.-Y., Chen, G.-H.: Treatment of Circadian Rhythm Sleep–Wake Disorders. Curr. Neuropharmacol. 20, 1022–1034 (2022). https://doi.org/10.2174/1570159X19666210907122933
13. BaHammam, A.S., Pirzada, A.: Timing Matters: The Interplay between Early Mealtime, Circadian Rhythms, Gene Expression, Circadian Hormones, and Metabolism—A Narrative Review. Clocks Sleep. 5, 507–535 (2023). https://doi.org/10.3390/clockssleep5030034
14. García-García, A., Méndez-Ferrer, S.: The Autonomic Nervous System Pulls the Strings to Coordinate Circadian HSC Functions. Front. Immunol. 11, 956 (2020). https://doi.org/10.3389/fimmu.2020.00956

15. Huang, X., Liu, G., Guo, J., Su, Z.: The PI3K/AKT pathway in obesity and type 2 diabetes. Int. J. Biol. Sci. 14, 1483–1496 (2018). https://doi.org/10.7150/ijbs.27173
16. Vargas, E., Podder, V., Carrillo Sepulveda, M.A.: Physiology, Glucose Transporter Type 4. In: StatPearls. StatPearls Publishing, Treasure Island (FL) (2025)
17. Yavropoulou, M.P., Sfikakis, P.P., Chrousos, G.P.: Immune System Effects on the Endocrine System. In: Feingold, K.R., Ahmed, S.F., Anawalt, B., Blackman, M.R., Boyce, A., Chrousos, G., Corpas, E., de Herder, W.W., Dhatariya, K., Dungan, K., Hofland, J., Kalra, S., Kaltsas, G., Kapoor, N., Koch, C., Kopp, P., Korbonits, M., Kovacs, C.S., Kuohung, W., Laferrère, B., Levy, M., McGee, E.A., McLachlan, R., Muzumdar, R., Purnell, J., Rey, R., Sahay, R., Shah, A.S., Singer, F., Sperling, M.A., Stratakis, C.A., Trence, D.L., and Wilson, D.P. (eds.) Endotext. MDText.com, Inc., South Dartmouth (MA) (2000)
18. Młynarska, E., Bojdo, K., Bulicz, A., Frankenstein, H., Gąsior, M., Kustosik, N., Rysz, J., Franczyk, B.: Obesity as a Multifactorial Chronic Disease: Molecular Mechanisms, Systemic Impact, and Emerging Digital Interventions. Curr. Issues Mol. Biol. 47, 787 (2025). https://doi.org/10.3390/cimb47100787
19. Broussard, J.L., Chapotot, F., Abraham, V., Day, A., Delebecque, F., Whitmore, H.R., Tasali, E.: Sleep restriction increases free fatty acids in healthy men. Diabetologia. 58, 791–798 (2015). https://doi.org/10.1007/s00125-015-3500-4
20. Lee, J., Liu, R., de Jesus, D., Kim, B., Ma, K., Moulik, M., Yechoor, V.: Circadian control of β-cell function and stress responses. Diabetes Obes. Metab. 17, 123–133 (2015). https://doi.org/10.1111/dom.12524
21. Jurcău, M.C., Andronie-Cioara, F.L., Jurcău, A., Marcu, F., Țiț, D.M., Pașcalău, N., Nistor-Cseppentö, D.C.: The Link between Oxidative Stress, Mitochondrial Dysfunction and Neuroinflammation in the Pathophysiology of Alzheimer's Disease: Therapeutic Implications and Future Perspectives. Antioxidants. 11, 2167 (2022). https://doi.org/10.3390/antiox11112167
22. Lavie, L.: Oxidative stress inflammation and endothelial dysfunction in obstructive sleep apnea. Front. Biosci. Elite Ed. 4, 1391–1403 (2012). https://doi.org/10.2741/469
23. van Egmond, L.T., Meth, E.M.S., Engström, J., Ilemosoglou, M., Keller, J.A., Vogel, H., Benedict, C.: Effects of acute sleep loss on leptin, ghrelin, and adiponectin in adults with healthy weight and obesity: A laboratory study. Obes. Silver Spring Md. 31, 635–641 (2023). https://doi.org/10.1002/oby.23616
24. Zhang, F., Xue, Y., Li, W.: Exploring the impact of sleep duration and sleep disorders on metabolic dysfunction-associated steatotic liver disease in older adults. BMC Geriatr. 25, 444 (2025). https://doi.org/10.1186/s12877-025-06115-0
25. Nyhuis, C.C., Fernandez-Mendoza, J.: Insomnia nosology: a systematic review and critical appraisal of historical diagnostic categories and current phenotypes. J. Sleep Res. 32, e13910 (2023). https://doi.org/10.1111/jsr.13910
26. Mesarwi, O.A., Loomba, R., Malhotra, A.: Obstructive Sleep Apnea, Hypoxia, and Nonalcoholic Fatty Liver Disease. Am. J. Respir. Crit. Care Med. 199, 830–841 (2019). https://doi.org/10.1164/rccm.201806-1109TR
27. Bouloukaki, I., Stathakis, G., Moniaki, V., Mavroudi, E., Tsiligianni, I., Schiza, S.: Association of Positive Airway Pressure Adherence with Clinical Outcomes in Patients with Type 2 Diabetes and Obstructive Sleep Apnea. Diagnostics. 14, 2781 (2024). https://doi.org/10.3390/diagnostics14242781
28. Nobre, B., Rocha, I., Morin, C.M., Cruz, M.M. e: Insomnia and circadian misalignment: an underexplored interaction towards cardiometabolic risk. Sleep Sci. 14, 55–63 (2021). https://doi.org/10.5935/1984-0063.20200025
29. Ntikoudi, A., Owens, D.A., Spyrou, A., Evangelou, E., Vlachou, E.: The Effectiveness of Cognitive Behavioral Therapy on Insomnia Severity Among Menopausal Women: A Scoping Review. Life. 14, 1405 (2024). https://doi.org/10.3390/life14111405
30. Yao, J., Wu, D., Qiu, Y.: Adipose tissue macrophage in obesity-associated metabolic diseases. Front. Immunol. 13, (2022). https://doi.org/10.3389/fimmu.2022.977485
31. Basil, B., Myke-Mbata, B.K., Eze, O.E., Akubue, A.U.: From adiposity to steatosis: metabolic dysfunction-associated steatotic liver disease, a hepatic expression of metabolic syndrome – current insights and future directions. Clin. Diabetes Endocrinol. 10, 39 (2024). https://doi.org/10.1186/s40842-024-00187-4
32. Diehl, K.L., Vorac, J., Hofmann, K., Meiser, P., Unterweger, I., Kuerschner, L., Weighardt, H., Förster, I., Thiele, C.: Kupffer Cells Sense Free Fatty Acids and Regulate Hepatic Lipid Metabolism in High-Fat Diet and Inflammation. Cells. 9, 2258 (2020). https://doi.org/10.3390/cells9102258
33. Gastaldelli, A., Stefan, N., Häring, H.-U.: Liver-targeting drugs and their effect on blood glucose and hepatic lipids. Diabetologia. 64, 1461 (2021). https://doi.org/10.1007/s00125-021-05442-2
34. Gutierrez-Monreal, M.A., Harmsen, J.-F., Schrauwen, P., Esser, K.A.: Ticking for metabolic health: the skeletal muscle clocks. Obes. Silver Spring Md. 28, S46–S54 (2020). https://doi.org/10.1002/oby.22826
35. Ahn, J., Hayes, R.B.: Environmental Influences on the Human Microbiome and Implications for Noncommunicable Disease. Annu. Rev. Public Health. 42, 277–292 (2021). https://doi.org/10.1146/annurev-publhealth-012420-105020

36. Belančić, A.: Gut microbiome dysbiosis and endotoxemia - Additional pathophysiological explanation for increased COVID-19 severity in obesity. Obes. Med. 20, 100302 (2020). https://doi.org/10.1016/j.obmed.2020.100302
37. Izah, S.C., Betiang, P.A., Paul-Chima Ugwu, O., Ainebyoona, C., Uti, D.E., Echegu, D.A.: The Ketogenic Diet in Obesity Management: Friend or Foe? Cell Biochem. Biophys. (2025). https://doi.org/10.1007/s12013-025-01878-0
38. Fárková, E., Novák, J.M., Manková, D., Kopřivová, J.: Comparison of Munich Chronotype Questionnaire (MCTQ) and Morningness-Eveningness Questionnaire (MEQ) Czech version. Chronobiol. Int. 37, 1591–1598 (2020). https://doi.org/10.1080/07420528.2020.1787426
39. Shandhi, M.M.H., Wang, W.K., Dunn, J.: Taking the time for our bodies: How wearables can be used to assess circadian physiology. Cell Rep. Methods. 1, 100067 (2021). https://doi.org/10.1016/j.crmeth.2021.100067
40. Caples, S.M., Anderson, W.M., Calero, K., Howell, M., Hashmi, S.D.: Use of polysomnography and home sleep apnea tests for the longitudinal management of obstructive sleep apnea in adults: an American Academy of Sleep Medicine clinical guidance statement. J. Clin. Sleep Med. JCSM Off. Publ. Am. Acad. Sleep Med. 17, 1287–1293 (2021). https://doi.org/10.5664/jcsm.9240
41. Paterson, J.L., Reynolds, A.C., Dawson, D.: Sleep Schedule Regularity Is Associated with Sleep Duration in Older Australian Adults: Implications for Improving the Sleep Health and Wellbeing of Our Aging Population. Clin. Gerontol. 41, 113–122 (2018). https://doi.org/10.1080/07317115.2017.1358790
42. Patil, S.P., Ayappa, I.A., Caples, S.M., Kimoff, R.J., Patel, S.R., Harrod, C.G.: Treatment of Adult Obstructive Sleep Apnea With Positive Airway Pressure: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. J. Clin. Sleep Med. JCSM Off. Publ. Am. Acad. Sleep Med. 15, 301–334 (2019). https://doi.org/10.5664/jcsm.7638

CITE AS: Abner Tom Kalukusu (2026). Circadian Rhythm Disruption, Sleep Disorders, and Their Role in Obesity Linked Diabetes. IAA Journal of Applied Sciences 14(1):72-78. https://doi.org/10.59298/IAAJAS/2026/1417278