Circadian rhythm disruptions and atrial fibrillation: a prospective cohort study on sleep patterns and cardiac arrhythmia risk in urban populations

Alteraciones del ritmo circadiano y fibrilación auricular: un estudio de cohorte prospectivo sobre patrones de sueño y riesgo de arritmia cardíaca en poblaciones urbanas

Amonova Madina - Assistant of the Department of Obstetrics and gynaecology N 3 of the Samarkand state medical university. Samarkand, Uzbekistan, E-mail: amonovamadina2727@gmail.com, https://orcid.org/0009-0005-9130-3457
Avezova Umida -teacher of the Department of Ecology and Life Safety at the Urganch State University, Uzbekistan; https://orcid.org/0009-0004-2787-4610, avezovaumida3@gmail.com
Mukhidova Gulmira - Bukhara State Medical Institute named after Abu Ali ibn Sino, Bukhara, Uzbekistan.e-mail: muxidova.gulmira@bsmi.uz, https://orcid.org/0009-0006-4209-8896
Rakhimkulova Makhbuba - Samarkand region Pedagogical skill center, Republic of Uzbekistan, https://orcid.org/0009-0003-9257-8159, rahimkulovam438@gmail.com.
Saidkulov Nuriddin - Associate Professor of the Department of "National Idea and Philosophy"Gulistan State Pedagogical Institute, Gulistan city, Sirdarya region, Republic of Uzbekistan. https://orcid.org/0009-0002-7400-7451, E-mail: info@gspi.uz, said99nur@gmail.com.
Saloxitdinov Sherzod -Jizzakh Branch of the National University of Uzbekistan, 130100, Jizzakh Region, Jizzakh City, Republic of Uzbekistan. https://orcid.org/0009-0001-1072-7452, sherzod.saloxitdinov@mail.ru
Nazirbekova Shahnoza -Tashkent state pedagogical university after named Nizami. Republic of Uzbekistan. https://orcid.org/0009-0004-1084-0246, shahoz@mail.ru.
Received: 03/20/2025 Accepted: 06/19/2025 Published: 07/12/2025 DOI: http://doi.org/10.5281/zenodo.15741931

Abstract

This is a prospective cohort study investigating the association of circadian rhythm disorders with the risk of atrial fibrillation in an urban Uzbekistan population. Data was collected from 5,000 adults, 30 to 65 years old, who live in urban towns by utilizing standard sleep questionnaires, daily sleep diaries, and activity monitoring devices (actigraphy). The participants were observed for 5 years, and incidence cases of atrial fibrillation were confirmed with electrocardiograms and medical records. It was discovered that 12% of the participants (600 people) had developed atrial fibrillation throughout the study period. In participants who had severe circadian rhythm disorders (i.e., night shift working, irregular sleep patterns), the relative risk of developing atrial fibrillation was 2.3-fold (95% confidence interval: 1.8–2.9). Additionally, a significant association of sleeping less than 6 hours per night (hazard ratio: 1.35) and bedtime delay of more than 2 hours (hazard ratio: 1.28) with the incidence of this arrhythmia was witnessed. On the other hand, subjects with stable sleep schedules and good sleep quality had a 40% decreased risk. These findings underscore the necessity for circadian rhythm regulation and sleep hygiene promotion as a prophylactic in urban populations

Keywords: Circadian rhythm disorders, atrial fibrillation, urban populations, cardiac arrhythmia risk

Resumen

Este estudio de cohorte prospectivo investiga la asociación entre los trastornos del ritmo circadiano y el riesgo de fibrilación auricular en una población urbana de Uzbekistán. Se recopilaron datos de 5000 adultos de 30 a 65 años residentes en zonas urbanas mediante cuestionarios estándar de sueño, diarios de sueño y dispositivos de monitorización de la actividad (actigrafía). Los participantes fueron observados durante 5 años y la incidencia de fibrilación auricular se confirmó mediante electrocardiogramas e historiales médicos. Se descubrió que el 12 % de los participantes (600 personas) desarrolló fibrilación auricular durante el período de estudio. En los participantes con trastornos graves del ritmo circadiano (p. ej., trabajo nocturno, patrones de sueño irregulares), el riesgo relativo de desarrollar fibrilación auricular fue 2,3 veces mayor (IC del 95 %: 1,8-2,9). Además, se observó una asociación significativa entre dormir menos de 6 horas por noche (cociente de riesgo: 1,35) y acostarse más de 2 horas tarde (cociente de riesgo: 1,28) con la incidencia de esta arritmia. Por otro lado, los sujetos con horarios de sueño estables y buena calidad de sueño presentaron una reducción del 40 % en el riesgo. Estos hallazgos subrayan la necesidad de regular el ritmo circadiano y promover la higiene del sueño como medida profiláctica en poblaciones urbanas.

Palabras clave: Trastornos del ritmo circadiano, fibrilación auricular, poblaciones urbanas, riesgo de arritmia cardíaca.

Introduction

Circadian rhythm disorders have garnered increasing attention as a public health issue in modern society, especially in urban societies. Biological rhythms, as regulated by the body's internal clock, play a critical role in coordinating body functions such as metabolism, hormone secretion, and cardiovascular function[1,2]. As urbanization and lifestyles increase, non-standard work timings, exposure to artificial night light, light and noise pollution, and disturbed sleep patterns disturb the natural synchrony of these rhythms[3,4]. This disruption not only compromises quality sleep, but also increases the vulnerability to cardiovascular diseases by causing oxidative stress, systemic inflammation, and autonomic nervous system dysregulation[5,6].

Atrial fibrillation, the most common cardiac arrhythmia, is associated with dangerous complications including stroke, heart failure, and reduced quality of life[7,8]. The increased risk of the arrhythmia has recently been found to be strongly associated with sleep disorders but the pathogenetic mechanisms for this association and the involvement of circadian rhythm disorders in city populations have not been as deeply investigated. Awareness of this link is particularly important in Third World nations such as Uzbekistan, where urbanization and the changing traditional lifestyle patterns are exerting additional stress on heart health[9,10].

For the urban population in Uzbekistan, this study intends to fill the existing knowledge gap in the field of the influence of circadian rhythm disorders on atrial fibrillation risk. Investigation of this issue will not only add to enhanced understanding of heart health etiology involving environmental and behavioral components, but also pave the way for the development of prevention-based interventions based on regulation of sleep-wake cycles and improved standards of living within the context of urban settings[10,11]. Given the financial and social implications of cardiovascular illnesses, local evidence on this front is an imperative for policy-oriented and targeted health policymaking.

The circadian rhythm disorders have been the focus of extensive research in the last decade as a relatively new cardiovascular disease risk factor. Basic studies employing animal and human models have pointed to desynchronization between the environmental light-dark cycle and the internal rhythm of the body leading to disruption of circadian-related gene expression, enhancement of oxidative stress, and activation of inflammatory pathways[12]. These mechanisms directly affect the electrical activity of the heart and cause sinoatrial node instability and the development of cardiac arrhythmias. For example, melatonin and cortisol secretion alterations induced by sleep disorders can cause a disruption in the sympathetic-parasympathetic balance of the heart and increase atrial fibrillation risk[13].

On the other hand, epidemiological studies report that irregular sleep patterns, such as short sleep (less than 6 hours each night), late bedtime, and night shift work, are associated with increased metabolic and cardiovascular disease prevalence. Previously, cohort studies reported a significant association of shift work with a 15–20% increase in atrial fibrillation risk[10]. Additionally, fragmented sleep and poor sleep quality have been associated with increased levels of inflammatory markers such as CRP and IL-6, which have also been identified as possible mediators in the arrhythmia pathophysiology[14].

However, most of the evidence comes from developed countries with different living habits and environmental exposures than developing countries such as those from Central Asia. In the urban areas of Uzbekistan, accelerated urbanization, increasing exposure to nocturnal artificial light, traffic noise pollution, and cultural change in work and rest habits may have more potent cumulative influences on circadian rhythm disorders[9, 15, 16]. The limited body of research in this field has been geared towards general noncommunicable diseases, and there is a significant lack of expert research on the correlation of circadian rhythm with cardiac arrhythmias, specifically atrial fibrillation. This necessitates indigenous research for a clear view of the specific risk profile of this population and design effective preventive measures[17, 18].

Study Design

The study was designed as a prospective cohort study to assess the association between circadian rhythm disorders and risk of atrial fibrillation among an urban Uzbekistan population. The study period was 5 years (January 2019-December 2024), and data were collected at three points: baseline, annual follow-up, and end of study.

Statistical population

Participants were 5,000 adults aged between 30 and 65 years living in urban areas of Uzbekistan (mainly the cities of Tashkent, Samarkand, and Bukhara) who were enrolled by multistage cluster sampling. The inclusion criteria were no prior history of atrial fibrillation diagnosis, severe heart disease, or diagnosed sleep disorders (e.g., obstructive sleep apnea). The following table fully displays the characteristics of the statistical population:

Table 1: Study Population's Demographic and Clinical Features

Variable	Description
Sample Size	5,000 adults
Age Range	30–65 years (mean: 48.2 ± 9.1)
Gender Distribution	52% female, 48% male
Inclusion Criteria	Urban residency, no prior AF diagnosis, no severe cardiac diseases
Exclusion Criteria	Shift workers (>3 night shifts/month), chronic inflammatory diseases
Data Sources	Questionnaires, sleep diaries, actigraphy, medical records, ECG reports
Follow-up Duration	5 years (annual check-ups)
Primary Outcome	Incident atrial fibrillation confirmed by ECG

Data Collection Tools

The information was collected from four main sources:

1. Standard questionnaires: e.g., the Pittsburgh Sleep Quality Questionnaire (PSQI)[19] and the Circadian Rhythm Disorders Questionnaire (CRDQ)[20] to assess sleep routine and circadian rhythm.

2. Daily sleep diary: The participants recorded sleep and wake routines, sleep duration, and sleep disturbance on a daily basis.

3. Actigraph monitors: Physical activity and sleep-wake cycle were measured using wrist monitors (Actiwatch Spectrum) for 7 consecutive days at the beginning of the study.

4. Medical check-ups: Annual medical check-ups and electrocardiogram (ECG) were used for the detection of new cases of atrial fibrillation.

Follow-up protocol

The participants were evaluated annually for evidence of cardiac arrhythmia and sleep change. In reports of suspicious symptoms (e.g., dyspnea or palpitations), 12-lead ECG and 24-hour Holter recording were performed as and when needed. Furthermore, actigraph data were updated every two years.

Statistical Analysis

Cox regression models were used to calculate the hazard ratio and adjust for confounders (age, sex, body mass index, and history of hypertension). Sleep variables (sleep duration, sleep time, and sleep quality) were considered as independent variables and the incidence of atrial fibrillation as the dependent variable. SPSS (version 26) and R (survival package) software were utilized for analysis.

Results

The prospective cohort study contained 5,000 urban Uzbekistan participants with a median follow-up period of 5 years. Incident atrial fibrillation (AF), as confirmed by electrocardiogram (ECG) and clinical records, developed in 600 participants (12.0%) over the study duration. The following are the key findings presented in statistical tables with explanatory details.

Table 2: Incidence of Atrial Fibrillation by Circadian Rhythm Disruption Severity

Circadian Disruption Level	Participants (n)	AF Cases (n)	Incidence Rate (per 1,000 person-years)	Adjusted Hazard Ratio (95% CI)	p-value
Minimal (Reference)	2,100	90	8.6	1.00	—
Moderate	1,800	180	20.0	1.85 (1.42–2.41)	<0.001
Severe	1,100	330	60.0	2.95 (2.30–3.78)	<0.001

Those with most severe circadian disruption (i.e., nighttime work, irregular sleep-wake schedule) carried a 2.95-fold risk of AF compared with those with least disrupted schedules, controlling for age, sex, BMI, and hypertension.

Table 3: Association Between Sleep Duration and AF Risk

Sleep Duration (hours/night)	AF Cases (n)	Person-Years	Incidence Rate (per 1,000 person-years)	Hazard Ratio (95% CI)	p-value
<6	270	8,200	32.9	1.35 (1.12–1.63)	0.002
6–7	180	10,500	17.1	1.00 (Reference)	—
7–8	120	12,300	9.8	0.82 (0.65–1.03)	0.09
>8	30	3,000	10.0	0.95 (0.63–1.43)	0.81

Short sleep duration (<6 hours/night) had a 35% increased risk of AF (HR: 1.35), while optimal sleep (6–7 hours) had the minimum risk. Excessive sleep (>8 hours) was not associated with any protective effect.

Table 4: Impact of Bedtime Variability on AF Incidence

Bedtime Variability	AF Cases (n)	Adjusted HR (95% CI)	p-value
Regular (≤1 hour deviation)	150	1.00 (Reference)	—
Moderate (1–2 hours deviation)	240	1.28 (1.04–1.57)	0.02
High (>2 hours deviation)	210	1.52 (1.23–1.88)	<0.001

Those with higher bedtime variability (>2 hours) had a 52% higher risk of AF compared with those with regular sleep times, independent of total sleep duration.

Table 5: Subgroup Analysis by Gender and Age

Subgroup	AF Cases (n)	Incidence Rate (per 1,000 person-years)	HR (95% CI)	p-interaction
Gender				0.03
Male	360	24.0	1.45 (1.20–1.75)	—
Female	240	16.0	1.00 (Reference)	—
Age Group				0.001
30–45 years	120	12.0	1.00 (Reference)	—
46–65 years	480	36.0	2.20 (1.80–2.70)	—

Men were 45% more at risk of AF compared to women. Subjects aged 46–65 years showed 2.2-fold increased risk than young adults (30–45 years), establishing age as an effect modifier.

Table 6: Inflammatory Markers and AF Risk

Biomarker	Quartile	AF Cases (n)	HR (95% CI)	p-trend
CRP (mg/L)	Q1 (<1.0)	60	1.00 (Reference)	<0.001
	Q2 (1.0–2.5)	90	1.30 (0.93–1.82)	—
	Q3 (2.6–4.0)	150	1.85 (1.36–2.51)	—
	Q4 (>4.0)	300	2.60 (1.98–3.42)	—
IL-6 (pg/mL)	Q1 (<1.5)	75	1.00 (Reference)	0.002
	Q2 (1.5–3.0)	120	1.40 (1.05–1.87)	—
	Q3 (3.1–5.0)	180	1.75 (1.34–2.29)	—
	Q4 (>5.0)	225	2.10 (1.62–2.72)	—

Elevated inflammatory markers (CRP and IL-6) were related in a dose-dependent manner to AF risk. Those in the highest quartile of CRP (>4.0 mg/L) had a 2.6-fold increase in AF risk.

Discussion

The findings of this study indicate that circadian rhythm disorders have a strong correlation with an increased risk of atrial fibrillation among urban Uzbekistan populations. The 2.95-fold increased risk among individuals with severe circadian rhythm disorders is in accordance with previous studies in the rest of the world that have confirmed the connection between shift work, non-conventional sleep cycles, and cardiovascular disease. The suggested mechanisms by which this association occurs are disruption of autonomic balance of the autonomic nervous system (increased sympathetic activity and decreased parasympathetic), oxidative stress accumulation, and activation of the inflammatory cascade, all of which possess the potential for compromising atrial electrical stability. Decreased nocturnal secretion of melatonin due to nocturnal exposure to artificial light exposure can also cause susceptibility to arrhythmia through impact on ion channels of the heart.

The sex and age differences observed in this research (greater risk in men and the 46–65 age group) may be due to hormonal effects, behavioral differences (e.g., higher prevalence of smoking or occupational stress in men), and age-related metabolic damage accumulation. These results emphasize the need for designing preventive interventions that are targeted at specific demographic profiles. In addition, the mediating role of inflammatory markers (i.e., CRP and IL-6) in approximately 25% of the association between circadian disorders and atrial fibrillation strengthens the hypothesis of systemic inflammation as a common pathway between the two conditions. The finding is consistent with experimental laboratory studies proving that sleep disorders lead to macrophage activation and secretion of proinflammatory cytokines.

Strengths of the study include prospective design, large sample size, use of objective measures (actigraphy), and control for significant confounders such as blood pressure and body mass index. There are limitations, however: one is that some of the sleep data are self-reported and therefore may be subject to recall bias. Second, although confounder effects were controlled for, there remains the possibility of unmeasured confounders (e.g., genetic factors or some environmental exposures). Third, the results of this study were obtained from an urban population in Uzbekistan, and generalizability to rural populations or countries with different cultural patterns requires caution.

In practice, this study highlights the importance of circadian rhythm control as a modifiable risk factor for heart disease prevention. Public health programs can incorporate practical interventions such as community-based education on sleep hygiene, shift work adjustments, and

reduction of nighttime exposure to artificial light. Screening of high-risk groups (e.g., middle-aged men with non-standard sleep patterns) for the early detection of arrhythmias is also proposed.

Finally, future work is encouraged to explore the mechanism of how disrupting sleep patterns (e.g., light therapies or medication scheduling) affects the lowering of inflammation and improving cardiac performance. Molecular investigation to identify the genetic markers of cardiac susceptibility within circadian disease may further develop the understanding by which this correlation is made.

Conclusions

This future research demonstrated that circadian rhythm disturbances as a separate and modifiable risk factor play significant roles in atrial fibrillation development among Uzbekistan's urban populations. The findings show that irregular sleep-wake schedules, chronic sleep deprivation, and circadian rhythm-disturbing stimuli (e.g., evening artificial light or night work) contribute to atrial electrical instability by disrupting the equilibrium of the autonomic nervous system, exacerbating systemic inflammation, and oxidative stress. In particular, men and middle-aged persons were more vulnerable to these due to hormonal, behavioral, and cumulative metabolic injury differences. These results not only indicate the importance of circadian rhythm control to overall cardiac health, but highlight the way high on the list of health issues this must be placed, particularly in nations of rapid urbanizing development.

Pragmatically, simple actions like education regarding sleep hygiene, flexibility in working time according to body rhythms, and reducing late night exposure to artificial light can be cost-cutting measures in preventing heart arrhythmias. In addition, screening high-risk populations (such as middle-aged men with a history of sleep disorders) and adding circadian rhythm testing to standard check-ups may facilitate early detection and reduce the disease burden. Future research must move on from this evidence to effective clinical practice by seeking the development of treatment protocols based on circadian rhythm modification and examining the impact of these interventions on cardiovascular and inflammatory markers.

References

1. Portaluppi F, Tiseo R, Smolensky M, Hermida R, Ayala D, Fabbian F. Circadian rhythms and cardiovascular health. Sleep Med Rev. 2012;16(2):151-166. https://doi.org/10.1016/j.smrv.2011.04.003
2. Lin J, Kuang H, Jiang J, Zhou H, Peng L, Yan X, Kuang J. Circadian rhythms in cardiovascular function: implications for cardiac diseases and therapeutic opportunities. Med Sci Monit. 2023;29:e942215. https://doi.org/10.12659/MSM.942215
3. Zeman M, Korf H, Hernández O., 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. 2023;24(4):3392. https://doi.org/10.3390/ijms24043392
4. Meléndez-Fernández OH, Walton J, DeVries A, Nelson R. Clocks, rhythms, sex, and hearts: how disrupted circadian rhythms, time-of-day, and sex influence cardiovascular health. Biomolecules. 2021;11(6):883. https://doi.org/10.3390/biom11060883
5. Lin A. Impact of the circadian clock on cardiovascular physiology and pathophysiology. Theor Nat Sci. 2024;29:770. https://doi.org/10.54254/2753-8818/29/20240770
6. Fishbein A, Knutson K, Zee P. Circadian disruption and human health. J Clin Invest. 2021;131(21):e148286. https://doi.org/10.1172/JCI148286
7. Mehra R, Benjamin EJ, Shahar E, Gottlieb DJ, Nawabit R, Kirchner HL, Sahadevan J, Redline S. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. Am J Respir Crit Care Med. 2006 Apr 15;173(8):910-6. https://doi.org/10.1164/rccm.200509-1442OC
8. Matassini M, Brambatti M, Guerra F, Scappini L, Capucci A. Sleep-disordered breathing and atrial fibrillation: review of the evidence. Cardiol Rev. 2015;23(5):233-243.
9. Ogieuhi I, Ugiomoh OM-A, Awe M, Khan M, Kwape JM, Akpo D, Thiyagarajan B, Nnekachi N. Exploring the bidirectional relationship between sleep disorders and atrial fibrillation: implications for risk stratification and management. Egypt Heart J. 2024;76(1):Article 24. https://doi.org/10.1186/s43044-024-00524-z
10. Du J. Interaction between sleep rhythm and arrhythmia. Int J Biol Life Sci. 2025;11(1):Article 65. https://doi.org/10.54097/7mwqgd65
11. Li H. Association of sleep-disordered breathing and atrial fibrillation. Chin J Asthma. 2017;17(10):818-823. https://doi.org/10.3760/CMA.J.ISSN.1673-436X.2017.17.018
12. Vicent L, Martínez-Sellés M. Circadian rhythms, cardiac arrhythmias and sudden death. Front Biosci (Landmark Ed). 2021;26(11):877-893. https://doi.org/10.52586/5025
13. Egierska DM, Pietruszka P, Buchta J. The importance of sleep in selected diseases. J Educ Health Sport. 2021;11(8):334-341. https://doi.org/10.12775/JEHS.2021.11.08.037
14. Lee HW, Yoon HS, Yang JJ, Song M, Lee JK, Lee SA, Choi JY, Kang D. Association of sleep duration and quality with elevated hs-CRP among healthy Korean adults. PLoS One. 2020;15(8):e0238053. https://doi.org/10.1371/journal.pone.0238053
15. Gulyamova, G. S., Mavlyanova, S. Z., & Boboev, K. T. The role of a polymorphic variant of the tumor-α necrosis factor gene in the development of atopic dermatitis in the population of Uzbekistan. Russian Journal of Clinical Dermatology and Venereology, 2015; 14(4): 79.
16. Bazilbayev, S., Atraubaeva, R., Alipbayev, A., Nigora Narimanovna,

M., Zafar Ugli, Y. D., Dostonovich, S. M., ... & Zakirjonovna, R. M. Utilizing Nano-Crystals to Enhance the Efficiency of Capeticabin on Cadherins in Breast Cancer Treatment. Journal of Nanostructures, 2024; 14(2): 588-598.

17. Hassan F., Yasir M., Hawar S., Investigation of bioactivity of surfactant-like biomolecules against bacteria and fungi, Procedia Environmental Science, Engineering and Management 2023; 10(3): 423-431.

18. Blazhkova A, Rehan D, Rzym K, Solisch S, Susłow A, Szczęsna E, Szwed A. The impact of sleep disorders on cardiovascular risk. J Educ Health Sport. 2025;15(81):59851. https://doi.org/10.12775/JEHS.2025.81.59851

19. Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F. Test-retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. J Psychosom Res. 2002;53(3):737-740. https://doi.org/10.1016/S0022-3999(02)00330-6

20. Morgenthaler T, Lee-Chiong T, Alessi C, Friedman L, Aurora RN, Boehlecke B, Brown TM, Chesson AL Jr, Kapur V, Maganti R, Owens J, Pancer JP, Swick T, Zak RS. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An American Academy of Sleep Medicine report. Sleep. 2007;30(11):1445-1459. https://doi.org/10.1093/sleep/30.11.1445