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REVIEW ARTICLE

Changes in the circadian cycle due to night work as a risk factor for cardiovascular diseases

Cambios en el ciclo circadiano por el trabajo nocturno como factor de riesgo de enfermedades cardiovasculares

Alterações no ciclo circadiano pelo trabalho noturno como fator de risco para doenças cardiovasculares

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Abstract

This study aimed to analyze and discuss how circadian changes interfere with night-shift health workers' lives. This is a descriptive literature review with bibliometric analysis that aims to describe and analyze the profile of publications worldwide on circadian changes related to night shift work and their correlation with cardiovascular comorbidities. Analyses were made of publications that correlated night work with cardiovascular risk from 2000 to 2023 and published in the LILACS, MEDLINE via PubMed and BVS databases. Using the JoinPoint program, a segmented regression analysis was performed, which did not show any inflection points, explaining the increasing constancy in the publications. The annual percentage variation was estimated at 13.9%, with 95% confidence intervals. It was found that the United States of America has the highest percentage of studies on the subject, approximately 27.5% more than Brazil. At the same time, there is a demonstrated lack of studies in the continents of Oceania, Africa, and Central America. It was concluded that to reduce the prevalence of cardiovascular diseases and better understand the underlying biological mechanisms of work activities, it was important to understand the working conditions and the correlation with the occupational health disease process.

Descriptors: Occupational Health; Systemic Arterial Hypertension; Worker's Health; Primary Health Care; Working Environment.

Resumén

El objetivo fue analizar y discutir cómo los cambios circadianos interfieren en la vida de los trabajadores sanitarios nocturnos. Se trata de una investigación descriptiva de revisión de literatura con análisis bibliométrico que tuvo como objetivo describir y analizar el perfil de las publicaciones a nivel mundial sobre cambios circadianos relacionados con el trabajo nocturno y la respectiva correlación con comorbilidades cardiovasculares. Se analizaron publicaciones que correlacionaron el trabajo nocturno con el riesgo cardiovascular en el período de 2000 a 2023 y que se encuentran publicadas en las bases de datos LILACS, MEDLINE vía PubMed y VHL. Con el programa JoinPoint se realizó un análisis de regresión segmentada, que careció de puntos de inflexión, explicando la creciente consistencia en las publicaciones. Se estimó una variación porcentual anual del 13,9%, con intervalos de confianza del 95%. Se encontró que Estados Unidos de América tiene el mayor porcentaje de estudios sobre el tema, aproximadamente un 27,5% más que Brasil, mientras que falta evidencia en los continentes de Oceanía, África y Centroamérica. Se concluye que para reducir la prevalencia de enfermedades cardiovasculares y comprender mejor los mecanismos biológicos que subyacen a las actividades laborales, era importante comprender las condiciones de trabajo y la correlación con el proceso salud-enfermedad ocupacional.

Descriptores: Salud Ocupacional; Hipertensión Arterial Sistémica; Salud del Trabajador; Atención Primaria de Salud; Ambiente de Trabajo.

Resumo

Objetivou-se analisar e discutir como as alterações circadianas interferem na vida dos trabalhadores da saúde do período noturno. Trata-se de pesquisa de revisão bibliográfica, do tipo descritivo, com análise bibliométrica que visou descrever e analisar o perfil das publicações no tocante mundial sobre alterações circadianas relacionadas ao trabalho do turno noturno e a respectiva correlação com comorbidades cardiovasculares. Foram feitas análises de publicações que correlacionaram o trabalho noturno com risco cardiovascular no período de 2000 a 2023 e que estão publicados nas bases de dados LILACS, MEDLINE via PubMed e BVS. Com o programa *JoinPoint*, foi realizada uma análise de regressão segmentada, a qual ausentou pontos de inflexão, explicitando a crescente constância nas publicações. Foi estimada a variação anual percentual de 13,9%, com intervalos de confiança de 95%. Constatou-se que os Estados Unidos da América possuem o maior percentual de estudos referentes ao tema, aproximadamente 27,5% a mais que o Brasil, enquanto há demonstração de carência nos continentes Oceania, África e América Central. Conclui-se que para a diminuição da prevalência de doenças cardiovasculares e melhor compreensão dos mecanismos biológicos subjacentes das atividades laborais foi importante compreender as condições de trabalho e a correlação com o processo saúde-doença de cunho ocupacional.

Descritores: Saúde Ocupacional; Hipertensão Arterial Sistêmica; Saúde do Trabalhador; Atenção Primária à Saúde; Ambiente de Trabalho.

Introduction

Cardiovascular diseases (CVD), which encompass a range of illnesses related to the heart and blood vessels, are associated with the leading cause of death worldwide, with heart disease (coronary heart disease, rheumatic heart disease, congenital heart disease) being the leading cause of death over the last 20 years. In addition to pathologies that directly involve the heart, it is important to highlight peripheral arterial disease, deep vein thrombosis, pulmonary embolism, and cerebrovascular diseases among the set of CVDs that affect the world population and are also relevant when analyzing global death data[1].

Due to the huge number of people affected by CVDs, the scientific community is interested in understanding how such cardiovascular disorders present themselves and thus proposing measures that can alleviate human suffering, the private and public economic expenses involved (since CVDs can lead to partial or total work incapacity, in addition to the high number of hospital admissions) and also reduce social expenses (which are related to the emotional gap caused by the disease scenario)[1-5].

Since 2011, Systemic Arterial Hypertension (SAH) - a chronic multifactorial clinical condition that affects more than 30 million Brazilians - has been established in the presence of high and sustained pressure values with levels equal to or greater than 140 mmHg and/ or 90 mmHg[2,6].

This pathology was considered one of the main risk factors for the development of complications related to cardiovascular diseases. In this scenario, hypertension stands out as a disease of great importance for Primary Health Care (PHC) because it is an asymptomatic pathology that develops silently, since many patients neglect the correct treatment and this favors the onset of serious complications of metabolic disorders, which lead to CVDs that provide, in addition to cardiac problems such as Heart Failure, Acute Myocardial Infarction, acute and/ or chronic kidney disease, in addition to favoring strokes that can result in early death of a large portion of the economically active population (EAP), something that goes beyond just a public health problem, but also an economic one[3,7].

An unprecedented ecological study developed from 2018 to 2022 based on the Department of Information Technology of the Unified Health System (DataSUS), of the Brazilian Institute of Geography and Statistics (IBGE), and social security indicators collected from Social Security and the National Institute of Social Security (INSS) revealed that the average cost of hospitalization for Heart Failure in Brazil - a consequence/final pathway of many CVDs - exceeded R$2 billion reais, therefore configuring itself as an extremely costly condition for the Unified Health System (SUS) and also the main cause of cardiovascular hospitalization in Brazil[5].

In addition to public spending, this same study revealed that almost 80 thousand deaths were recorded, evenly distributed between the sexes, as a result of many CVDs, therefore representing a great loss of Economically Active Population (EAP)[8].

Currently, approximately 20 million individuals in Brazil's workforce work at night. Several recent studies have shown that night work has several negative effects on workers' health, including a greater predisposition to CVD[4,9,10].

Among the effects of this type of work, high rates of hypertension, lower cardiorespiratory capacity, increased propensity for ischemic stroke, onset of coronary diseases, increased abdominal fat, and obesity were recorded[11,12].

In this context, Human Chronobiology – a branch of science that studies the temporal organization of living beings, involving ultradian, infradian, circadian rhythms and the relationship with environmental events (recurrent and periodic) and physical-chemical events (luminosity, temperature) – reiterates that when there is temporal disorder, as a result of the inversion of the sleep and work periods, there are biochemical, physiological and behavioral changes that are related to the impairment of the individual's cardiovascular health[11].

This study aimed to identify global scientific production in the field of public health involving the highest risk of developing CVD in night workers due to changes in the circadian cycle, correlating the volume of publications, their temporal dynamics, and the countries of publication.

Methodology

This is a descriptive literature review study with bibliometric analysis of scientific production to determine the number of global publications on circadian rhythm changes in night workers and the presence of cardiovascular comorbidities. The development of the search strategy and evaluation of studies was based on the PICo strategy[13].

The research was carried out between August 2023 and April 2024, through consultation of the bibliographic databases: Latin American and Caribbean Literature in Health Sciences (LILACS), MEDLINE via PubMed, and Virtual Health Library (BVS). For the search, Descritores em Ciências da Saúde (DeCS) and Medical Subject Headings (MeSH) were used. In English: “Cardiovascular Diseases” (DeCS and Mesh), “Circadian Rhythm” (DeCS and MeSH), “Shift Work Schedule” (DeCS and Mesh), “Night Shift Work” (Mesh). In Portuguese: “Doenças Cardiovasculares’’ (DeCS), “Ritmo Circadiano” (DeCS) and “Trabalho Noturno” (DeCS).

The selection of articles was produced by two researchers independently and selection conflicts were resolved by a third researcher, using the Rayan software.

The Boolean expression “AND” was used, always crossing the first descriptor (Cardiovascular Diseases) with one of the following (Circadian Rhythm and Night Work). The search was conducted in English in all databases. Only in the LILACS and BVS databases was the search also conducted in Portuguese, since these databases present results of articles published in these languages.

Publications published in Portuguese and English between 2000 and 2023 with full-text availability online and addressing the research topic were analyzed. The following were excluded: incomplete articles with access only to the abstract, theses, dissertations, and letters to the editor. After the exclusion of duplicates, the abstracts were read by the reviewers separately. If they were considered

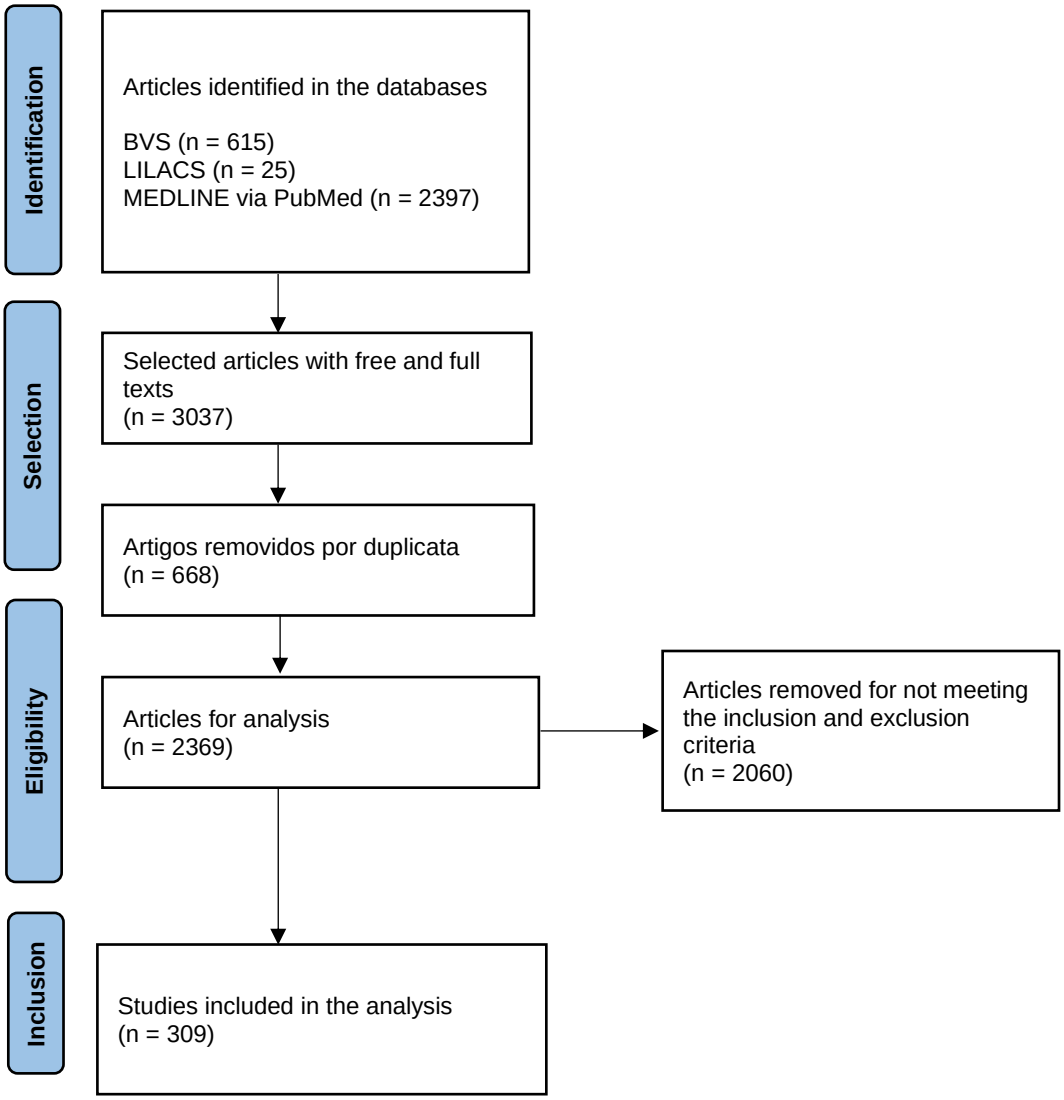
appropriate for the topic, the articles were included in the database for analysis.

After reading, any disagreements regarding inclusion or exclusion will be resolved by the principal investigator. The annual percentage change (APC) was estimated, which yielded results of positive or negative variations in publications during the proposed time series, through a segmented regression (SR) that verified important points of change and smoothed out the inflection points over the years. Successive segments of the line connected by these change points were adjusted.

The JoinPoint program performed a segmented linear regression to estimate the annual percentage variation and identify inflection points at which the trend changes. Models were successively adjusted, assuming a different number of "points" of change, from zero (in which case the trend is represented by a single straight-line segment) to the maximum number of possibilities indicated by the software, due to the number of observations. The model chosen was the one with the highest number of inflection points and that maintained statistical significance ($p < 0.05$). 95% confidence intervals were calculated for the APC.

The analysis of the studies considered the metrics according to the country of publication and main findings. The following software programs were used: Excel® from Microsoft Office, Joinpoint, version 5.0.1 (Statistical Research and Applications Branch, National Cancer Institute, Rockville, MD, USA), and EndNote Web.

Figure 1. Flowchart of selection of studies that comprised the bibliometric review on changes in the circadian cycle as a risk factor for cardiovascular diseases in night workers. Araras, SP, Brazil, 2000-2023



Results

A total of 3,037 articles associated with the descriptors that were delimited in this research were found, with 615 publications (20.26%) in BVS, 2,397 publications (78.92%) in MEDLINE and 25 publications (0.82%) in LILACS.

After checking for duplication via EndNote Web software and analysis by reading, 668 papers were excluded and, after applying the inclusion criteria, 2,060 articles were discarded from the final analyses. In the end, 309 articles comprised the sample for review, as shown in Figure 1.

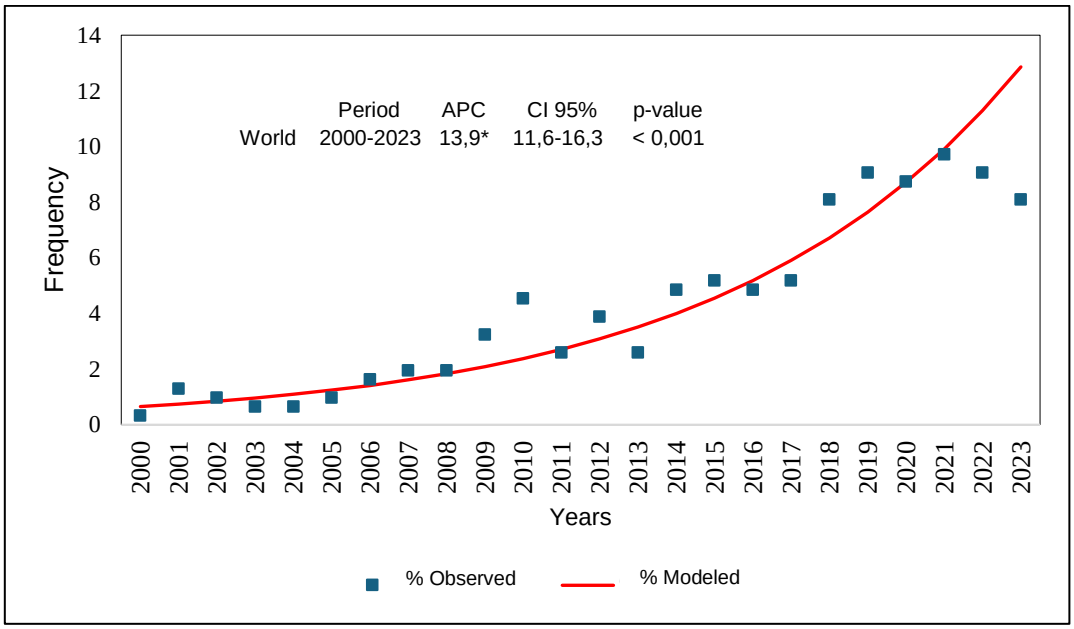
Of the 309 works analyzed according to their country of publication between the years 2000 and 2023, 31.71% (n=98) were published in journals in the United States of America, 17.47% (n=54) were published in journals in England, 10.67% (n=33) in Switzerland and only 4.20% (n=13) were authored by Brazil (Table 1).

There was a 13.9% increase per year in the worldwide frequency of publications. The most appropriate segmented regression to adjust the frequencies did not consider any change point in the historical series studied, with one segment in the regression being sufficient to explain the positive trend in publications (Figure 2).

Table 1. Countries with freely accessible scientific production on changes in the circadian cycle as a risk factor for cardiovascular diseases in night workers in the LILACS, MEDLINE via PubMed and BVS databases. Araras, SP, Brazil, 2000-2023

Countries	No. of publications	%	Countries	No. of publications	%
United States	98	31.7	Italy	2	0.6
England	54	17.5	Croatia	2	0.6
Switzerland	33	10.7	Poland	2	0.6
Finland	28	9.1	Iran	2	0.6
Netherlands	17	5.5	Oman	1	0.3
Brazil	13	4.2	Egypt	1	0.3
Spain	10	3.2	Hungary	1	0.3
Germany	7	2.3	United Arab Emirates	1	0.3
Japan	6	1.9	India	1	0.3
South Korea	6	1.9	Russia	1	0.3
France	4	1.3	Austria	1	0.3
China	4	1.3	South Africa	1	0.3
Australia	4	1.3	Cuba	1	0.3
Canada	3	1.0	New Zealand	1	0.3
Pakistan	3	1.0	Türkiye	1	0.3

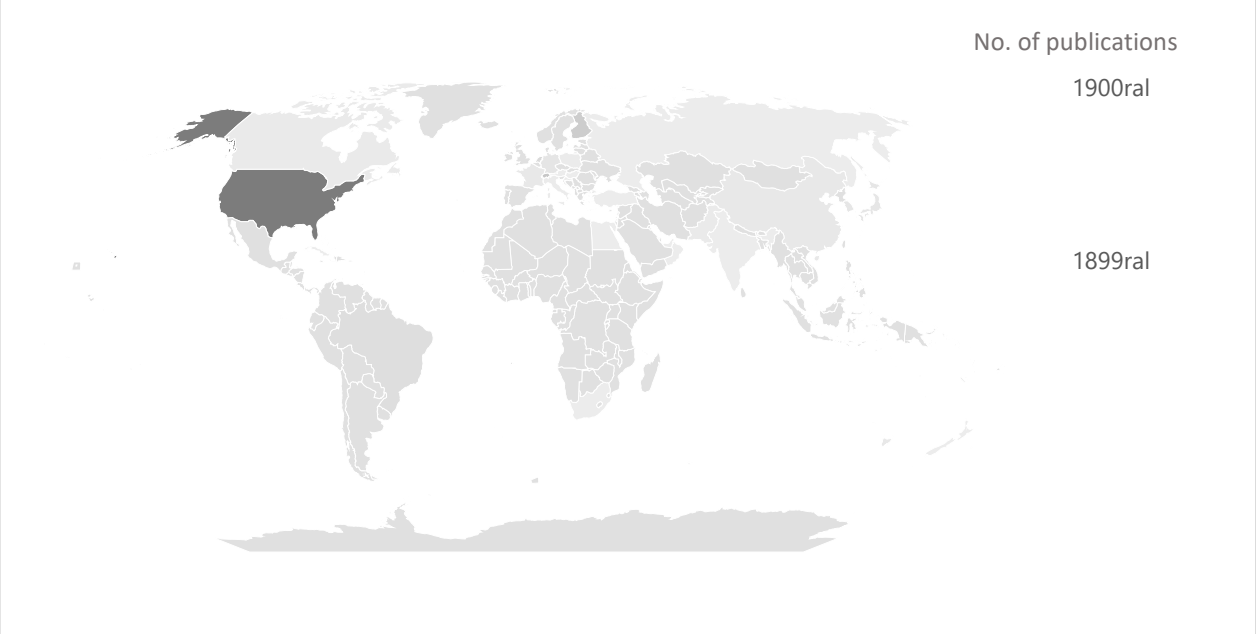
Figure 2. Segmented regression (Join Point Regression) and annual percentage change (APC) of the frequency of publications related to cardiovascular risks related to changes in the circadian cycle due to night work in the LILACS, MEDLINE via PubMed and BVS databases according to year of publication, worldwide publications. Araras, SP, Brazil, 2000-2023



Note: *Indicates that the APC is significantly different from zero at the alpha = 0.05 level.

According to the concentration of publications in the continents and their subdivisions, it was observed that 52.75% (n=163) are in Europe, 32.68% (n=101) in North America, 8.09% (n=25) in Asia, 4.20% (n=13) in South America, 1.61% (n=5) in Oceania, 0.64% (n=2) in Africa and 0.32% (n=1) in Central America.

Figure 3. Countries that published the frequency of publications related to cardiovascular risks related to changes in the circadian cycle due to night work in the LILACS, MEDLINE via PubMed and BVS databases, worldwide publications. Araras, SP, Brazil, 2000-2023



Discussion

According to study[14], it was found that less than six hours of sleep was associated with a 29% higher risk of major coronary events compared with those who slept more ($p < 0.001$). Furthermore, individuals who worked night shifts ≥ 3 night shifts per week for ≥ 1 year had a 15% higher risk of major coronary events ($p = 0.01$) after a 2-year follow-up. This study concluded that night work can be considered an independent risk factor for adverse cardiovascular outcomes.

Epidemiological studies convincingly show an increased prevalence of cardiovascular disease in night shift workers versus day shift workers, and field studies in shift workers have demonstrated increased blood pressure and inflammatory markers during or after night shift work compared with day shift work or days off[15,16].

Globally, it is worth noting that this study revealed that the annual growth rate was 13.9%, indicating that there was a growing interest in the scientific community in understanding and demonstrating the correlation between night work, changes in the circadian cycle, and cardiovascular risks. The use of Segmented Regression was a useful tool strategy for modeling the temporal frequency of publications and, in the current study, the presence of a single straight-line segment was adequate to explain the positive trend in publications and the results were consistent. Notably, the absence of significant inflection points demonstrated that there were no drastic changes in the interest in understanding the topic addressed.

Compared to Brazil, the North American country has approximately 27.5% of additional publications. The explanations for this are related to the fact that the country has an extreme research infrastructure and financial resources that allow for the performance of comprehensive and quality studies in a context of millions of dollars in the scientific field, with renowned universities and research centers that have highly qualified specialists to conduct studies that address the cardiovascular area in depth, in addition to funding from government agencies, such as the National Institutes of Health (NIH), which significantly promote research involving cardiovascular health and the area of chronobiology, among other areas[17-19].

In this context, this analysis is based on the premise that increasing the rates of articles published globally contributes to the advancement of knowledge on the subject in question. Increased knowledge can have significant impacts on Public Health, reducing the prevalence of cardiovascular diseases, as well as a better understanding of the underlying biological mechanisms and the well-being of workers affected by these working conditions. In addition, this study offers an opportunity to identify existing gaps regarding the topic involved in several countries, mainly those present in the continents of Oceania, Africa, and Central America, showing that they require additional research to better understand the work dynamics and the impacts on the occupational health of individuals[20-22].

Final Considerations

The impacts of night shift work on circadian rhythms and, consequently, cardiovascular risks, is a significant area of study due to the implications that such occupational dynamics can have on the overall health of individuals. Such changes can lead to metabolic disorders, cardiovascular disease, obesity, diabetes, and a variety of other health conditions. Studies such as this highlight the importance of fully understanding the underlying mechanisms and developing effective interventions to mitigate the risks associated with night shift work.

The limitations of this research were the availability of full-text articles, and the time window used for data collection.

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