Journal of Biology and Medicine: Open Access

Research Article | Vol 1 Iss 2

Gender Differences in Risk of Cardiovascular Diseases in Population With Sleep Disturbances in Russia/Siberia: WHO Program MONICA-Psychosocial

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Received: December 02, 2020; **Accepted:** December 18, 2020; **Published:** December 26, 2020

Abstract

Objective: ***To determine the gender differences in the effect of sleep disturbances (SD) on risk of myocardial infarction (MI) and stroke in an open population 25-64 years in Russia/Siberia over 16 years of follow-up.*** ***Methods:*** ***Within the framework of the III screening of WHO's MONICA-psychosocial program, a random representative sample of the population of both sexes of 25-64 years of Novosibirsk in 1994 (men n = 657, women: n = 689) was examined. The screening included: socio-demographic data, the definition of the SD. The SD studied by means of the Jenkins scale. The analysis included persons of both sexes without myocardial infarction, stroke. New-onset cases of MI and stroke in women - 15 and 35 cases and in men - 30 and 22 cases, respectively detected in the cohort over 16 years of follow-up. To assess the risk taking into account the different control times a single-factor and multivariate regression models of proportional Cox risks (Cox-regression) were used.*** ***Results:*** ***In the open population aged of 25-64 years 48,6% of men and 65,9% of women had SD (x2 = 24,427 df = 1 p = 0,0001). In a single-factor Cox regression analysis the risk of stroke was higher among men than among women with SD over 16-year period. Multivariate regression analysis revealed that risk of stroke in men and women is approximately the same among people with SD. Widowed men with SD had an increased risk of developing a stroke. The risk of stroke was higher in men with primary education than women. There was an increased risk of stroke in women with college degree and with sleep problems. Cox single-factor regression analysis showed an increased risk of MI in men with SD over 16-year period in 2.4 times. The influence of SD on the risk of MI in women has not been received. The risk of MI among men with SD who never married was 3-fold, in divorced was 4.3-fold and in widowed men risk MI was 7.5-fold higher than without SD.*** ***Conclusion:*** ***Sleep disorders are a significant risk factor of stroke in both men and women. The risk of myocardial infarction was only increased in men. A disadvantaged social gradient (single, divorced, widowed) in men was an additional risk factor of myocardial infarction, supplemented by an increased risk of stroke in widowed men. Moreover, primary education was an additional risk factor of stroke in both men and women.***

Keywords: ***Sleep; Gender differences; Sleep disturbance; Myocardial infarction; Stroke; and Relative risk.***

Citation: Gafarov VV, Gromova EA, Panov DO, et al. Gender differences in risk of cardiovascular diseases in population with sleep disturbances in Russia/Siberia: WHO Program MONICA-Psychosocial. J Bio Med Open Access. 2020;1(2):117.

1. Introduction

Sleep disturbance (SD) is a very common condition in industrialized developed countries. It has been calculated that the prevalence of at least one of the symptoms of SD may reach 33% in the general population [1]. All pathophysiological mechanisms leading to SD and its relationship with cardiovascular diseases are not fully understood. For example, the disorder is manifested by an imbalance of the autonomic nervous system in response to chronic stress, which is often accompanied by metabolic rate, heart rate, decreased heart rate variability and increased cortisol secretion [2]. Thus, a violation of autonomic nervous regulation and a violation of the hypothalamus-pituitary axis of the forming mechanism linking sleep disturbance and cardiovascular diseases [3-5]. A causal relationship between sleep disturbance and cardiovascular diseases is also confirmed experimentally. For example, sleep deprivation leads to an increase in blood pressure and the level of inflammatory mediators. The violations of carbohydrate metabolism as well as acceleration of atherogenesis are predisposing factors of cardiovascular diseases in those with SD [6-7]. In addition, fragmentation of sleep can impair blood circulation in the brain and associated with cerebrovascular accident [8-9].

In comparison to men women complain about the quality of their sleep more often, especially in an advanced age: 81% of women complain of insomnia, while sleep disturbances are less common among men - in 78% of cases. Women more often (50%) wake up early than men (41%) and fall asleep more difficult - 33% and 31%, respectively [10].

In this regard, the aim of this article is to establish a gender differences in the effect of sleep disturbance on the risk of myocardial infarction (MI) and stroke over a 16-year period in an open population aged 25–64 years in Russia / Siberia.

2. Materials and Methods

Within the framework of the III screening of the WHO MONICA-psychosocial program (Monitoring trends in morbidity and mortality from cardiovascular diseases and their determining factors) [11,12] a random representative sample of general population 25-64 years in the of the city district in Novosibirsk was examined in 1994. (men - n = 657, mean age - 44.3 ± 0.4 years, response - 82.1%; women n = 689, mean age - 45.4 + -0.4 years, response - 72.5%). The sample was formed according to the requirements of the WHO MONICA – psychosocial protocol [11,12].

2.1 The screening examination program included the following sections

Registration of socio-demographic data was carried out according to the standard epidemiological protocol of the WHO MONICA-psychosocial program: identification number, place of residence, full name, date of birth, date of registration. Gender: 1 - male, 2 - female. The distribution by age group is presented in Table 1.

Table 1: Sleep Disorders in General Population of 25-64 Years (III screening, 1994).

	25-34				35-44				45-54				55-64				25-64			
Sleep	M		F		M		F		M		F		M		F		M		F	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Good	93	61,2	49	48	65	48,1	42	31,8	59	42,8	12	30,8	80	52,3	7	14	297	51,4	110	34,1
Poor	59	38,8	53	52	70	51,9	90	68,2	79	57,2	27	69,2	73	47,7	43	86	281	48,6	213	65,9

Total	152	100	102	100	135	100	132	100	138	100	39	100	153	100	50	100	578	100	323	100
	χ2=3,762 df=1 p=0,05				χ2=6,747 df=2 p=0,009				χ2=1,353 df=1 p>0,05				χ2=21,021 df=1 p=0,0001				χ2=24,427 df=1 p=0,0001			

Marital status (Table 2), education level (Table 3), professional level (Table 4) were taken into account.

Table 2: Sleep Disorders and Marital Status in Population of 25-64 Years (III screening, 1994).

Sleep	Marital Status															
	Never married				Married				Divorced				Widowed			
	M		F		M		F		M		F		M		F	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Good	28	68,3	10	37	243	49,7	83	33,5	17	47,2	11	35,5	9	75	6	35,3
Poor	13	31,7	17	63	246	50,3	165	66,5	19	52,8	20	64,5	3	25	11	64,7
Total	41	100	27	100	489	100	248	100	36	100,	31	100	12	100	17	100
	χ^2= 5,245 df= 1 P<0,05				χ^2=16,91 df=1 P <0,001				χ^2=0,523 df= 1 P>0,05				χ^2=2,994 df=1 p>0,05			

Table 3: Sleep Disorders and Educational Degree in Population of 25-64 Years (III screening, 1994).

	Degree															
Sleep	University				College				High School				Primary School			
	M		F		M		F		M		F		M		F	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Good	81	50,6	39	41,1	92	57,9	34	28,1	67	49,3	31	43,7	57	46,3	6	16,7
Poor	79	49,4	56	58,9	67	42,1	87	71,9	69	50,7	40	56,3	66	53,7	30	83,3
Total	160	100	95	100	159	100	121	100	136	100	71	100	123	100	36	100
	χ^2=1,825 df=1P>0,05				χ^2= 23,404 df=1P <0,001				χ^2=0,384 df=1 P>0,05				χ^2=9,048 df=2 P<0,01			

2.2 Testing according to psychosocial methods

Sleep disorders were studied using the Jenkins scale [13]. The analyzed level of the risk factor was taken as its value in the original study and did not take into account the contribution of time dynamics. The methods were strictly standardized and corresponded to the requirements of the protocol of the WHO MONICA program - psychosocial [13]. Processing of the material under the WHO MONICA - psychosocial program was carried out at the MONICA Information Collection Center in Helsinki (Finland). Quality control was carried out in MONICA quality control centers: Dundee (Scotland), Prague (Czech Republic), Budapest (Hungary). The presented results were found to be satisfactory [14].

All women and men with identified cardiovascular pathology (ischemic heart disease, vascular diseases of the brain, arterial hypertension, myocardial infarction, diabetes mellitus) that occurred before or during the screening period were excluded from the study. The analysis included 384 women and 190 men age 25-64 years at baseline. The prospective follow-up period for participants was 16 years.

Table 4: Sleep Disorders and Occupational Status in Population of 25-64 Years (III screening, 1994).

Sleep	Occupational class																													
	Executives				Middle Managers				Managers				Engineers				Heavy Manual				Moderate Manual				Light Manual				Students				Retirees			
	M		F		M		F		M		F		M		F		M		F		M		F		M		F		M		F		M		F	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Good	9	36	1	25	24	51,1	5	21,7	25	48,1	17	45,9	44	57,9	21	36,8	66	50,4	2	22,2	78	52,7	21	38,9	9	45	18	28,1	7	77,8	1	100	35	50	7	15,6
Poor	16	64	3	75	23	48,9	18	78,3	27	51,9	20	54,1	32	42,1	36	63,2	65	49,6	7	77,8	70	47,3	33	61,1	11	55	46	71,9	2	22,2	0	0	35	50	38	84,4
Total	25	100	4	100	47	100	23	100	52	100	37	100	76	100	57	100	131	100	9	100	148	100	54	100	20	100	64	100	9	100,0	1	100	70	100	45	100
	χ^2=0,019 df=1 P>0,05				χ^2= 4,331 df=1 P<0,05				χ^2=0,001 df=1P>0,05				χ^2=4,966 df=1P<0,05				χ^2= 1,665df=1P>0,05				χ^2=2,494 df=1P>0,05				χ^2=1,291 df=1P>0,05				χ^2= 0 df=1P>0,05				χ^2=12,571 υ=1P<0,05			

This article identified the following "endpoints": new-onset cases of myocardial infarction (MI), stroke. Registration of all cases of MI was carried out on the basis of the WHO program "Registry of acute myocardial infarction". Sources used to identify cases of stroke: annual survey of individuals in the population cohort, medical records, inpatient discharge reports, district clinics, death certificates, interviews with relatives, autopsy and forensic reports. During the observation period, the cohort revealed 15 cases of new-onset myocardial infarction in women and 30 in men, and 35 cases of new-onset stroke in women and 22 in men.

Statistical analysis was performed using the SPSS software package version 11.5 [15]. To check the statistical significance of differences between groups, we used: Pearson's chi-square test x2 [16]. To assess the risk ratio - hazard ratio (HR) and its 95% CI (confidence interval) (minimum-maximum), taking into account different control times, we used the univariate single-factor Cox-regression and multivariate proportional-hazards regression model [17]. Reliability in all types of analysis was accepted at a significance level of $p \leq 0.05$.

3. Results

It was found that 48.6% males and 65.9% females aged 25-64 years in an open population had sleep disturbance (x2 = 24.427 df = 1 p = 0.0001); the prevalence of sleep disturbance increased with age in both sexes. Never married and married women are more common than men had sleep disorders (63% and 31.3% for unmarried, respectively; x2 = 5.245 df = 1 p <0.05; 66.5% and 50.3% for married, respectively; x2 = 16.91 df = 1 p <0.001).

The significantly highest level of sleep disorders was observed in the group with primary level of education. Moreover, less educated women (83.3%) had a higher level of sleep disorders than men (53.7%) (x2 = 9.048 df = 2 p<0.01). Also, a higher frequency of sleep disorders was observed in women (71.9%) in comparison with men (42.1%) in the group with college degree (x2 = 23.404 df = 1 p<0.001).

Occupational levels among women and men with sleep disorders were follows. There was a significant increase in sleep disorders in women compared with men in the categories of middle managers (78.3% and 48.9%, respectively), among engineering and technical workers (63.2% and 42.1%, respectively), as well as among pensioners (84.4% and 50%,

respectively). In other professional categories, there was also a tendency for women with sleep disorders to prevail over men.

Univariate Cox regression analysis showed an increase in the risk of MI in men with SD during a 16-year period by 2.4 times (95% CI 1.1-5.3; p <0.05) compared to those without SD. There was no effect of SD on the risk of MI in women. The multivariate Cox regression model also did not reveal the effect of SD on the risk of MI in women HR = 2.09 (95% CI 0.23-18.75; p> 0.05). Including in the model social parameters like marital status, education, professional level as well as age attenuates risk of MI in men and there was only a tendency to increase the risk by 1.08 times (95% CI 0.4-4.7; p < 0.05).

Marital status had a huge impact on the risk of MI in men with SD. The risk of MI in men who have never been married was 3-fold higher (95% CI 1.9-9; p <0.0001), in divorced persons HR = 4.3 (95% CI 2.1-8.9) and the highest risk was in widowed men HR = 7.5 (95% CI 2.5-22; p <0.0001). No such dependence was found in women. It was found that in the presence of SD the risk of MI in men aged 55-64 years is higher HR = 6.4 (95% CI 2-21; P <0.01) than in women in the same age group HR = 2, 6 (95% CI 1.06 - 6.5; P <0.05) in comparison with persons 25-54 years without SD. In univariate Cox regression analysis over 16-year period individuals with SD had a higher risk of stroke among men HR = 3 (95% CI 1.2-7.6; p <0.05) than among women HR = 1.9 (95% CI 1.03 -3.7; p <0.05).

Multivariate Cox regression analysis with the inclusion of marital status, educational level, professional status and age in the model revealed the similar risk of stroke in men HR = 2.8 (95% CI 1.1-7.1; p < 0.05) and women HR = 2.7 (95% CI 1.4-5.42; P <0.01).

We found that only widowed men with SD have an increased risk of stroke HR = 1.9 (95% CI 1.2-3; P <0.01) compared with married men without SD. No significant results were found in women. When comparing the risk of stroke among patients with SD and the different levels of education, it was found that the risk of stroke is higher in men with primary education HR = 5,3 (95% CI 1,4- 19,1; p <0,01), than in women HR = 4.2 (95% CI 1.25-14; p <0.05). There was also an increase in the risk of stroke in women with college degree and sleep problems HR = 3.7 (95% CI 1.1 - 11.9; P <0.05). We did not find differences in the risk of stroke in persons with SD in the older age group 55-64 years between men HR = 2.1 (95% CI 1.09-5.6; p <0.05) and women HR = 2 (95% CI 1.05-4.8; P <0.001).

4. Discussion

In all age groups without exception, women were more likely to have sleep problems in comparison to men. Moreover, the greatest problems with sleep were in women aged 55-64 years - 86%. Our results are consistent with the findings of other authors, who also indicate that women are more likely to complain of sleep disturbances [10], [18-20].

The structure of marital status between men and women in the studied population did not differ significantly. Nevertheless, the risk of new-onset myocardial infarction and stroke was higher in men with disadvantaged marital status and sleep disturbances, while we did not find such patterns in women. It is worth noting that the greatest risk of myocardial infarction and stroke was in widowed men with sleep disorders. One of the most stressful life events is the

loss of a close relative that often leads to severe emotional disturbances, a decrease in financial security, a change in lifestyle, and all this contributes to a deterioration in the quality of sleep [21]. We also found that individuals with a low level of education and sleep disturbance, both men and women, had the highest risk of stroke.

Considering the professional level, we present that in all professional groups there were more women with sleep disorders than men. However, no statistically significant differences in the effect of SD in various occupational groups among men and women on the risk of MI and stroke have been established.

Therefore, sleep disturbance increased the risk of myocardial infarction in an open population of men aged 25-64 years by 2.4 times. We found that the risk of myocardial infarction incidence was 2.6 times higher only at the age of 55-64 years in women with sleep disorders. In men in this age group, the risk of myocardial infarction was the highest - 6.4 times. The results obtained are confirmed by other researchers. For example, F. Gianfagna et al. found that serious sleep disturbance increases the risk of new-onset CVD by 1.8 times, and in persons over 48 years old by 1.97 times [22]. Men who slept no more than 5 hours per night had a 2.3 times higher risk of MI than those who had 6-8 hours of sleep [23]. In the MONICA / KORA study in Augsburg over a 10-year follow-up period the risk of MI was 2.98 times higher in women who slept 5 hours or less per day and the risk was 1.13 times higher in men [24]. The risk of stroke in persons with sleep disturbances was higher among men (HR = 3) than among women (HR = 1.9). However, taking into account the social gradient and age, the risk of stroke in men (HR = 2.8) and women (HR = 2.7) was equal. It is known from the literature that various sleep disorders such as insomnia, fatigue, increased sleepiness and parasomnia may precede stroke [25]. One of the important risk factors for stroke is breathing problems during sleep such as snoring. Sleep disturbance and breathing disturbance during sleep affect the general and cerebral blood circulation, which leads to hypoxemia at night. This theory confirms the high prevalence of stroke in the morning. During REM sleep there is a higher demand for oxygen and most apnea occurs during this stage [26]. K. Eguchi et al conducted a study on the effect of sleep duration on the risk of stroke. In hypertensive patients with a nighttime sleep of less than 7.5 hours the risk of stroke was more than 2 times higher than in normotensive patients [27].

5. Conclusions

- 48.6% of men and 65.9% of women suffer of sleep disorders in general population of 25-64 years. The prevalence of sleep disturbances increases with age.
- In men with sleep disorders the risk of myocardial infarction was increased 2.4-times. No differences were found in women with the exception of the older age group.
- In both men and women with sleep disorders the risk of stroke was significantly increased, however the risk was higher in the male group (HR = 3) in comparison to the female group (HR = 1.9).
- A disadvantaged social gradient (single, divorced, widowed) in men was an additional risk factor of myocardial infarction, supplemented by an increased risk of stroke in widowed men. Moreover, primary education was an additional risk factor of stroke in both men and women.

6. Conflict of Interest

The Authors declare no conflict of interest

7. Funding

The work was performed within the framework of the budgetary theme NIITPM - branch of the ICG SB RAS Reg. № AAAA-A17-117112850280-2, Gov.Task № 0324-2018-0001

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