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Original article

Biomarkers of burnout and their relationship with psychological characteristics in healthcare practitioners

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Abstract: *Background* — The goal of this study was to investigate how biomarkers can be indicators of burnout in healthcare workers and what is the relationship between these biomarkers and psychological characteristics.
Material and Methods — A total of 96 doctors and nurses from different clinics in Irkutsk were surveyed. The Maslach Burnout Inventory (MBI), Ware et al. 12-item Short-Form of the Medical Outcomes Study (SF-12), Beck Depression Inventory (BDI), Ways of Coping questionnaire, Mindful Attention Awareness Scale (MAAS) and Five Facet Mindfulness Questionnaire (FFMQ) were employed. Dehydroepiandrosterone sulfate (DHEA-S), thyroid-stimulating hormone (TSH), melatonin, serotonin, dopamine and cortisol were used as biomarkers.
Results — We established that doctors and nurses diagnosed with high-level burnout had higher concentrations of DHEA-S and cortisol in their saliva. Salivary cortisol and DHEA-S were associated with levels of depressive symptoms. Relationships were found between various biomarkers (melatonin, DHEA-S) and factors that prevent the development of stress. Such productive coping strategies as Planful Problem-Solving or components of mindfulness capable of reducing stress severity were negatively associated with the circadian rhythm regulator (melatonin) and DHEA-S. Presumably, psychological regulation can reduce objective stress rather than subjectively experienced stress alone.
Conclusion — Doctors and nurses with high burnout levels have high concentrations of DHEA-S and cortisol. Accordingly, these biomarkers can be considered as indicators of burnout. In addition, coping strategies and mindfulness components were identified that are associated with stress biomarkers and, presumably, can help reduce not only subjectively experienced stress, but also objective stress.

Keywords: burnout, stress, obstetrics and gynecology, biomarkers.

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Introduction

Burnout is a cognitive, emotional and behavioral state of emotional exhaustion, depersonalization and lack of personal achievement. Its prevalence can be judged from some publications [1] indicating that burnout is known at the level of 40.8% in healthcare workers in the fields of general surgery, anesthesiology, obstetrics and gynecology, and orthopedics; at the level of 30.0% in plastic surgery and pediatrics; and in 15.4% of otolaryngology and neurology professionals.

The prevalence of burnout among healthcare practitioners of various specialties [1, 2], the relationship of burnout with various social statuses [3, 4], and methods for reducing burnout [5, 6] are actively studied. Of interest is the relationship of burnout with various biomarkers. Biomarkers are often considered as indicators of various disorders, including psychoemotional (e.g., [7, 8]), and in connection with stress. Cortisol is conventionally considered a stress biomarker [9, 10, 11]. In addition, anabolic hormones that determine the regenerative and protective role are studied, primarily dehydroepiandrosterone (DHEA) and its sulfated metabolite (DHEA-S) [12, 13, 14]. Some studies showed that prolactin can be a stress marker as well [15, 16], while other studies demonstrated thyroid-stimulating hormone (TSH) [17] and neurotransmitters [18] as stress markers. In general [19], these different markers can contribute different weights to the allostatic load: some of them are primary (cortisol, DEHA-S, anti-inflammatory, etc.), while others are indirect. Therefore, in stressful situations, their dynamics can be different [13, 14].

The goal of this study was to determine which biomarkers can be indicators of burnout in healthcare workers and what is the relationship between these biomarkers and psychological characteristics.

Material and Methods

Participants

We invited 181 individuals to participate in the study. Inclusion criteria were as follows: employment at a healthcare institution as a doctor or nurse, signed informed consent, completed questionnaires, and submitted biomaterial. All participants were provided with a document on the objectives and procedures of the study. They gave written informed consent. The study was conducted in accordance with the principles of the 2013 Declaration of Helsinki amendment of the World Medical Association and was reviewed and approved by the Ethics Committee of the Federal State Budgetary Research Institution, *The Scientific Center for Family Health and Human Reproduction Issues* (Protocol No. 2 of 04 March 2021).

Some of potential participants were subsequently excluded from this study because they did not complete the questionnaires in full (n=37) or only completed the questionnaires but did not submit the biomaterial (n=48). A total of 96 doctors and nurses from various clinics were interviewed, both those specialized in obstetrics and gynecology (City Perinatal Center of Irkutsk, Scientific Center for Family Health and Human Reproduction Issues) and other fields (City Clinical Hospital No. 8 of Irkutsk, Medical Unit of the Irkutsk Academy of Postgraduate Education). They were selected by the researcher personally and sequentially after communicating with all specialists working in the departments.

Instruments

Psychological questionnaires

Burnout symptoms were measured using the Russian version of the Maslach Burnout Inventory (MBI) [20]. This instrument is currently the most frequently used to assess burnout in healthcare workers. The MBI consists of 22 items. Three subscales of the MBI were analyzed separately: emotional exhaustion (EE), depersonalization (DP), and reduced personal accomplishment (PA). Means were calculated and the subscales were classified into low, moderate, and high burnout using the cutoff values proposed by the adaptation [16]: for the EE subscale, this translates into ≤15, 16-24, and ≥25 pts, respectively; for the DP subscale, ≤5, 6-10, and ≥11 pts, respectively; and for the PA subscale, ≤30, 37-31, and ≥37 points, respectively. Higher scores on the EE and DP subscales imply a higher level of burnout, while a higher score on the PA subscale indicates a lower degree of burnout. To assess quality of life and depression, we employed the Ware et al. 12-item Short-Form of the Medical Outcomes Study questionnaire (SF-12) and the Beck Depression Inventory (BDI) adapted for Russia [21]. To assess coping strategies, we used the Russian version of the Ways of Coping questionnaire [22]. The coping strategies for which the subject scored the highest were considered the main ones. We also used the Russian version of the Five Facet Mindfulness Questionnaire (FFMQ) and the Mindful Attention Awareness Scale (MAAS) [23] to assess mindfulness.

Biomarker diagnostics

Blood serum, blood plasma and saliva were used as biomaterials for the study. The concentration of various hormones in the blood serum was studied: for DHEA-S and TSH, we used the ELISA test system by Alkor Bio Ltd., Russia; for melatonin, we used the Melatonin ELISA test system (IBL, Canada); for serotonin, we using the test system by IBL International, Germany; and for diagnostic quantitative determination of dopamine in human plasma, we employed Dopamine ELISA Kit (IBL International, Germany). The cortisol level was assessed using the Cortisol Saliva ELISA Kit by Diagnostics Biochem Canada, Inc. Measurements were performed using a BioTek ELx808™ Absorbance Microplate Reader (BioTek Instruments, Inc., Virginia, USA). Among the parameters determined in the complete blood count (blood formula), the percentages of neutrophils, lymphocytes, monocytes, eosinophils and basophils were especially noted. The stress response index was calculated using the formulas from the publication by A. Shikhlyarova [24].

Table 1. Sociodemographic data

Variable		*Total sample*	*High burnout (n=42)*	*Low burnout (n=54)*	*p-value*
Age, years (mean ± SD)		40.87 (11.51)	39.81 (11.60)	42.15 (10.28)	0.74**
Gender, count (%)	Male	10 (10.41)	5 (11.90)	5 (9.30)	0.674*
	Female	86 (89.58)	37 (88.10)	49 (90.70)	0.674*
Ethnic group, count (%)	Caucasian	82 (85.50)	37 (88.10)	45 (83.30)	0.512*
	Asian	14 (14.50)	5 (11.90)	9 (16.70)	0.512*
	Multiracial	0 (0)	0 (0)	0 (0)	-
	Not specified	0 (0)	0 (0)	0 (0)	-
Professional affiliation, count (%)	Physician	61 (63.54)	30 (71.43)	31 (57.40)	0.157*
	Nurse	35 (36.46)	12 (28.57)	23 (42.60)	0.157*
Work experience, count (%)	Less than 1 year	0 (0)	0 (0)	0 (0)	-
	1-5 years	20 (20.83)	12 (28.60)	8 (14.80)	0.100*
	6-10 years	13 (13.54)	7 (16.70)	6 (11.10)	0.431*
	11-20 years old	25 (26.04)	10 (23.80)	15 (27.80)	0.661*
	21-30 years old	26 (27.08)	8 (19.00)	18 (33.30)	0.154*
	31-40 years old	9 (9.38)	4 (9.50)	5 (9.30)	0.965*
	More than 40 years	3 (3.13)	1 (2.40)	2 (3.70)	0.712*
	Not specified	0 (0)	0 (0)	0 (0)	-
Working hours per week (Median, Q1, Q3)		40 (39; 48.75)	40 (39; 51.50)	40 (39; 40.75)	0.84**
Number of night shifts per month (Median, Q1, Q3)		0 (0; 2)	0 (0; 0)	0 (0; 3.75)	0.71**
Marital status, count (%)	Unmarried	15 (15.63)	6 (14.30)	9 (16.70)	0.750*
	Common law marriage	13 (13.54)	5 (11.90)	8 (14.80)	0.680*
	Separate accommodation with a partner	1 (1.04)	1 (2.40)	0 (0)	0.255*
	Married	49 (51.04)	22 (52.40)	27 (50.00)	0.817*
	Divorced	18 (18.75)	8 (19.00)	10 (18.50)	0.948*
	Not specified	0 (0)	0(0)	0 (0)	-
Religiosity, count (%)	Preferred not to reply	13 (13.54)	3 (7.10)	10 (18.50)	0.107*
	Not religious	23 (23.96)	11 (26.20)	12 (22.20)	0.652*
	Religious	60 (62.50)	28 (66.70)	32 (59.30)	0.458*
	Not specified	0 (0.00)	0 (0)	0 (0)	-

*, χ^2 test; **, t-test.

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Table 2. Expression of biomarkers in medical workers with and without burnout

Hormones	*Burnout*	*M*	*SD*	*t*	*p*
TSH	High burnout (n=42)	1.63	1.05	1.164	0.247
	Low burnout (n=54)	1.43	0.65		
DHEA-S	High burnout (n=42)	191.05	110.66	2.687	0.009
	Low burnout (n=54)	137.55	83.36		
Dopamine	High burnout (n=42)	26.58	9.90	0.652	0.516
	Low burnout (n=54)	25.15	11.31		
Serotonin	High burnout (n=42)	63.91	55.30	0.082	0.935
	Low burnout (n=54)	63.09	37.71		
Cortisol	High burnout (n=42)	63.01	21.53	2.182	0.032
	Low burnout (n=54)	53.06	22.64		
Melatonin	High burnout (n=42)	19.91	3.69	-0.270	0.788
	Low burnout (n=54)	20.15	4.36		

TSH, thyroid-stimulating hormone; DHEA-S, dehydroepiandrosterone sulfate.

Table 3. Multiple logistic regression model

Factors	*B*	*SE*	*Wald*	*df*	*P*	*OR*
THS	0.652	0.304	4.602	1	0.032	1.920
DHEA-S	0.007	0.003	5.944	1	0.015	1.007
Cortisol	0.023	0.012	3.675	1	0.055	1.023
Marital status	0.463	0.212	4.760	1	0.029	1.589

TSH, thyroid-stimulating hormone; DHEA-S, dehydroepiandrosterone sulfate; * p<0.05.

Procedures

All participants were invited to participate in the study on a voluntary basis. First, the purpose of the study was explained before the survey. Participants were given instructions on how to fill out the questionnaires and they were informed that the survey would not have any impact on their work or personal life. Second, the researcher obtained sociodemographic information to determine whether they met the inclusion criteria. Third, participants signed a written informed consent form and all aforementioned questionnaires. Fourth, saliva and blood of the participants were sampled. Before the start of any therapy, blood was collected from the median cubital vein in disposable vacuum blood collection tubes from 8 to 9 am on an empty stomach after a 15-minute rest on days 3-9 of the menstrual cycle or in the presence of amenorrhea. Saliva samples (4-5 mL) were collected in a clean tube (SaliCaps®, IBL International GmbH, Hamburg, Germany) without coercion or inducement before eating, drinking or brushing teeth. Before saliva collection rinsed the mouth was rinsed with water. All samples were then stored at 4 °C until sent to the laboratory.

Data analysis

Data management was carried out using the REDCap web application [25]. Statistical calculations were performed using IBM SPSS Statistics (v.23.0), and statistical significance was assumed at p<0.05. Quantitative variables are presented as mean and standard deviation (SD) or median, Q1 and Q3 for nonparametric data. The Shapiro-Wilk test was used to check the normality of the data. Mean values were compared using a two-tailed t-test or χ^2 test for nonparametric data. Qualitative variables are presented as count (n) and percentage (%). Relationships between quantitative variables were tested using the Pearson correlation coefficient. A multiple logistic regression model was created to identify predictors (independent variables) of burnout (dependent variables). A p-value < 0.05 for the Wald test was considered an indicator of regression coefficients significantly different from zero. Results are shown as odds ratios (Exp.) with 95% confidence intervals (95% CI) for EXP (B). Model fit was assessed using the likelihood ratio statistic.

Results

The sociodemographic characteristics of the sample are presented in *Table 1*. A total of 96 doctors and nurses working in the field of obstetrics and gynecology participated in the study. Of these, 89.58% were women and 10.41% were men, mostly Caucasian (85.5%), married (51.04%) and religious (62.5%). The mean age was 40.87±11.51 years ranging from 22 to 69 years, and the length of service in the specialty was 17.4±11.2 years. Night shifts were characteristic of 30.2% (n=29) of the physicians and nurses.

First, we found that the mean score on the EE subscale for the entire sample was 25.33±11.22 pts, which implies quite high attrition rate. The mean score on the DP subscale was 11.09±7.28 pts, which was also rather high. Finally, the mean score on the reduced PA subscale was 38.69±6.69 pts, which indicates a high level of self-expression. Thus, the subjects exhibited primarily high levels of EE and DP rather than reduction in PA.

There are various criteria for diagnosing emotional burnout. As noted above, we used the criteria from T. Deneva et al. [16]. A diagnosis of burnout (yes/no) was made if respondents demonstrated high levels on at least two subscales (EE and/or DP, associated or not with low PA) or on three subscales based on the following assessments: EE>24 pts, DP>10 pts and PA<30 pts. According to this, 43.75% of doctors and nurses (n=42) demonstrated a higher level of burnout vs. 56.25% (n=54) with a lower burnout.

The distribution of doctors and nurses by the severity of emotional burnout is presented in *Table 1*. We did not reveal statistically significant differences in the sociodemographic characteristics between doctors and nurses with high burnout and without it. For doctors and nurses working night shifts/not working night shifts, and with different marital statuses and work experiences, no significant differences were established, albeit these parameters are considered the factors of professional burnout (e.g., by T. Deneva et al. [16]).

At the next stage, we examined the differences in the expression of some hormones between doctors and nurses with and without burnout (*Table 2*). Using the Shapiro-Wilk criterion, we discovered that the data for the scales of psychological questionnaires and biomarker indicators were normally distributed. Consequently, we employed parametric analysis methods and confirmed that healthcare workers (doctors and nurses) diagnosed with high burnout had higher concentrations of both DHEA-S and cortisol. At the same time, we did not reveal statistically significant differences between the stress response index scores between healthcare workers with and without severe burnout.

Multivariate logistic regression analysis (*Table 3*) was performed to identify predictors (independent variables) of burnout (dependent variable). We focused on demographic factors (gender, age, religiosity, marital status, work experience, working hours and night shifts) and biomarkers (salivary cortisol, TSH, DHEA-S, dopamine, serotonin, and melatonin). The logistic regression model was statistically significant (χ^2=15.726, P=0.003). The model explained 17.1% of the variance (Nagelkerke's R^2) in exhaustion and correctly classified 23.1% of cases. We concluded that this model did not adequately describe the influence of hormones on professional burnout. As a result, we analyzed how biomarkers were associated with psychological factors (*Table 4*).

Table 4. Correlation between biomarkers and psychological factors (n=96)

Variable	*TSH*	*DHEA-S*	*Dopamine*	*Serotonin*	*Salivary cortisol*	*Melatonin*
Confrontive Coping	0.046	-0.007	0.046	0.015	0.170	0.099
Distancing	0.106	-0.039	0.006	0.200	0.090	-0.005
Self-Controlling	0.103	0.114	0.015	0.038	0.079	-0.140
Seeking Social Support	0.198	0.054	0.058	-0.004	0.028	0.100
Accepting Responsibility	0.136	-0.200	-0.019	0.118	-0.053	-0.059
Escape-Avoidance	0.136	0.140	0.062	0.094	0.116	0.048
Planful Problem-Solving	0.123	-0.072	-0.019	0.190	0.050	-0.232*
Positive Reappraisal	0.060	-0.096	-0.049	0.166	-0.035	-0.204
SF-12	-0.086	-0.200	-0.114	0.030	-0.158	-0.116
BDI	0.119	0.400**	0.125	0.103	0.237*	0.036
Observing	-0.027	0.024	0.040	-0.032	-0.018	-0.121
Describing	0.063	-,304*	-0.137	-0.119	-0.092	-0.206
Acting with Awareness	-0.101	-,238*	0.043	-0.001	-0.207*	-0.247*
Non-Judging facet	-0.008	-0.012	-0.196	-0.134	0.037	0.083
Non-Reactivity facet	0.099	-0.128	0.020	0.069	0.001	-0.161
MAAS	-0.094	-0.184	-0.091	-0.160	0.001	-0.148

TSH, thyroid-stimulating hormone; DHEA-S, dehydroepiandrosterone sulfate; SF-12, Ware et al. 12-item Short-Form of the Medical Outcomes Study; BDI, Beck Depression Inventory; MAAS, Mindful Attention Awareness Scale.

Correlation analysis (biomarkers vs. personality variables) demonstrated the following associations: direct correlations of depressive symptoms (BDI scale) with salivary cortisol (r=0.237, p=0.05) and DHEA-S (r=0.4, p=0.01); an inverse correlation of a coping strategy of Planful Problem-Solving with melatonin level (r=-0.232, p=0.05); an inverse correlation of FFMQ subscales with DHEA-S level (Describing: r=-0.304, p=0.05; Acting with Awareness: r=-0.238, p=0.05); and an inverse correlation of Acting with Awareness with salivary cortisol (r=-0.207, p=0.05) and melatonin (r=-0.247, p=0.05).

We also analyzed the stress response measured by the complete blood count. However, no statistically significant correlations were revealed for any of the stress parameters (lymphocyte count, white blood cell count, etc.) with other burnout biomarkers (primarily hormones) or with psychological characteristics. This is likely due to the fact that the stress response is influenced by many factors including those not examined in this study.

Discussion

Thus, according to the obtained data, we discovered that healthcare workers (doctors and nurses) diagnosed with a high level of burnout had higher concentrations of DHEA-S and cortisol in their saliva. These findings are consistent with the results of P. Eddy et al. who found that in most cases, workplace stress correlated with the activation of the cortisol awakening response and its increased concentration in salivary samples in the afternoon and evening [11]. Also, according to A.M. Traish et al. [12, 13], an increase in DHEA-S during periods of acute psychosocial stress is a protective mechanism aimed at leveling the effects of cortisol. However, we did not receive results similar to those in the study by P.M. Mommersteeg et al. [14] who showed that young patients with professional burnout had a reduction in DHEA-S levels. This may be due to the mean age of the subjects in our study (40.87 years).

It is natural that salivary cortisol and DHEA-S are associated with the level of severity of depressive symptoms. More interesting is the connection of various biomarkers (melatonin, DHEA-S) with factors that prevent the development of stress. Such a productive coping strategy as Planful Problem-Solving [26] or components of mindfulness, which also reduce the severity of stress [27], are negatively associated with the regulator of circadian rhythms, melatonin, and DHEA-S. As we have already noted earlier, through lifestyle and psychological regulation, it is possible to reduce subjectively experienced stress [28]. Presumably, due to psychological regulation, its objective indicators can also be reduced.

As noted above, no statistically significant relationships were found for any of the stress response indicators measured by the complete blood count or hormones and depression, coping characteristics. We believe this is because stress is influenced by a significant number of factors, which we plan to take into account when refining our burnout model.

In general, we established that doctors and nurses with a high level of burnout had high concentrations of DHEA-S and cortisol. Accordingly, these biomarkers can be considered indicators of burnout. Besides that, in our study, we identified coping strategies and components of mindfulness that are associated with stress biomarkers and, presumably, can help reduce objective stress rather than subjectively experienced stress alone.

Conclusion

According to the results of this study, high concentrations of DHEA-S and cortisol are observed in doctors and nurses with high levels of burnout. Thus, these biomarkers can be considered as indicators of burnout. In addition, we identified psychological indicators that are associated with stress biomarkers (e.g., Planful Problem-Solving/Act with Awareness vs. melatonin, Acting with Awareness vs. DHEA-S/salivary cortisol). In our opinion, they can contribute to reducing stress in general, including both physiological and psychological components.

Limitation

Our study has some limitations. Although we ensured that the study sample, including subjects with high and low burnout, did not differ in demographics, there were few men in the overall sample. Gender may be a factor in burnout, although there is no consensus on this issue in science [29], [30], [31]. We also did not consider how burnout dynamics is related to biomarker dynamics. We plan to focus on this issue in a future study.

Conflict of interest

The authors declare that they have no competing interests.

Ethical approval

All procedures performed in our study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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