

Original article

Dynamics of Stress Biomarker Levels and Their Relationship with Psychological Characteristics of Healthcare Workers during the implementation of a Program for Reducing Occupational Burnout

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Abstract: *Objective* — The aim of this study was to examine the dynamics of stress biomarkers and their association with psychological characteristics in healthcare workers during a pilot implementation of a program for reducing occupational burnout.

Material and Methods — Physicians and nurses (n=20) from various clinics in Irkutsk, Russia, participated in the pilot program. Stress biomarkers included serum levels of thyroid-stimulating hormone (TSH) and dehydroepiandrosterone sulfate (DHEA-S), and salivary cortisol. Psychological indicators were measured using the Maslach Burnout Inventory (MBI), 12-Item Short Form Health Survey (SF-12), Beck Depression Inventory (BDI), the Ways of Coping Questionnaire (WCQ), Mindful Attention and Awareness Scale (MAAS), and the Five Facet Mindfulness Questionnaire (FFMQ).

Results — At follow-up, increased salivary cortisol levels were observed only in participants with low baseline burnout, while no significant changes in biomarkers were found in participants with high baseline burnout. In contrast, participants with high baseline burnout levels showed improvements in psychological measures, including reduced burnout symptoms and increased mindfulness.

Conclusion — The results indicate heterogeneous psychological and physiological changes depending on baseline burnout levels. Psychological improvements were observed predominantly in participants with high burnout levels, while changes in salivary cortisol levels were observed solely in participants with low burnout levels. Given the pilot nature of the study, the results should be interpreted as preliminary.

Keywords: burnout, stress, psychological characteristics and biomarkers, healthcare workers.

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Introduction

Burnout syndrome is defined as a state of physical and emotional exhaustion, depersonalization, and a diminished sense of personal worth. Its prevalence is illustrated, for example, by data [1], which report burnout rates of 40.8% among specialists in general surgery, anesthesiology, obstetrics and gynecology, and orthopedics; 30.0% in plastic surgery and pediatrics; and 15.4% in otolaryngology and neurology. Burnout affects the quality of diagnostic decision-making [2] and, more broadly, serves as a destructive factor for the development of the medical profession as a whole [3].

The prevalence of burnout among healthcare workers of various specialties has been extensively studied [4-6], along with strategies for its reduction [7, 8]. Of particular interest is the assessment of biomarker dynamics after the application of various interventions, as this provides an understanding of their effectiveness. Workplace stress among healthcare workers is generally understood as a specific manifestation of the cumulative effect of allostatic load initiated by chronic pathogenic occupational stressors [9]. Given the pathogenesis of chronic stress, a wide range of regulatory hormones and intermediates can serve as indicators of stress states, reflecting the balance and direction of reactions in the autonomic and central nervous

systems, the hypothalamic-pituitary-adrenal axis, and other immunological and biochemical markers associated with the effects of general adaptation syndrome.

Cortisol has traditionally been considered the primary biomarker of burnout [10, 11]. A comprehensive analysis of numerous studies by P. Eddy and colleagues found that burnout is correlated with elevated cortisol levels in most cases (regardless of gender, albeit more pronounced in men) [12]. However, other data [13] indicate significant inter- and intra-individual variability in cortisol levels. Cortisol levels may increase when a person experiences more negative emotions and decrease when emotions are less negative compared to baseline. As a result, studies have reported increases, decreases, or no change in morning cortisol levels, which may lead to premature conclusions about the absence of a relationship. Some studies suggest that high levels of burnout are associated with initially reduced cortisol levels, followed by a subsequent increase [14]. Another study [15, 16] found that salivary cortisol levels were differentially associated with different aspects of burnout: positively with emotional exhaustion and negatively with depersonalization. Similarly, the study by Traish AM et al. [17] identified salivary cortisol levels as a significant predictor of burnout in regression models among healthcare workers.

In addition to cortisol, anabolic hormones with regenerative and protective functions have been studied – primarily dehydroepiandrosterone (DHEA) and its sulfated metabolite (DHEA-S) [18, 19]. A short-term increase in DHEA-S levels during acute psychosocial stress may serve as a protective mechanism counteracting the effects of cortisol. However, other studies [19] reported decreased DHEA-S levels in young patients with burnout. Given that DHEA peaks in adulthood, individuals aged 25-35 years have significantly lower levels compared with the general population, which complicates its use as a stress biomarker [13].

Thyroid-stimulating hormone (TSH) has also been investigated as a potential biomarker [10]. Chronic stress stimulates TSH secretion and the release of thyroid hormones. However, prolonged stress leads to decreased activity of the hypothalamic-pituitary-thyroid axis and a significant decrease in hormone levels. This effect is more pronounced in women, who exhibit significantly lower TSH and T3 concentrations in response to high levels of perceived stress [13]. The limited research examining the link between burnout and thyroid dysfunction may be partly due to the overlapping symptomatology of these two conditions.

Various biomarkers have been used in evaluating the effectiveness of various programs for reducing occupational burnout, often yielding conflicting results. Overall, as established in [20], definitive conclusions cannot be drawn regarding the relationship between burnout and stress biomarkers due to heterogeneity in study design and methodology (including patient characteristics, biomarker assessment, and control for confounding factors), which complicates the interpretation of results.

In our earlier study, we also did not observe significant correlations between burnout measures and biomarkers. We found that adaptive coping strategies, such as problem-solving planning, were inversely correlated with melatonin levels, while mindfulness was associated with both DHEA-S and cortisol. Based on these results, we concluded that coping strategies and mindfulness could theoretically contribute to a reduction in the secretion of certain hormones [7].

The goal of this study was to examine the dynamics of stress biomarker levels and their association with psychological characteristics in healthcare workers during the implementation of a pilot program for reducing occupational burnout.

Material and Methods

Design

The study employed a non-randomized, longitudinal, quasi-experimental design with repeated measures. The study was conducted from January 2021 to June 2023 at the Federal State Budgetary Scientific Institution, *Research Center for Family Health and Human Reproduction* (SCFHHR). A detailed description of the study design is provided in [7] and [21].

Participants

Inclusion criteria: (1) complete questionnaire data and hormonal analysis results, and (2) age over 18 years. All participants received written information about the study's objectives and procedures and provided informed consent. The study complied with the principles of the Declaration of Helsinki (2013 edition) and was reviewed and approved by the Ethics Committee of SCFHHR (Protocol #2 of March 4, 2021).

Initially, 181 healthcare workers from various clinics in Irkutsk were invited to participate in the study. During the first stage of recruitment, 85 participants were excluded due to incomplete questionnaire data and/or missing hormonal tests, which were required for inclusion according to predetermined criteria.

Following this initial recruitment, the intervention group was formed following the development of the burnout reduction program. Due to the pilot nature of the study and logistical constraints associated with group training and biological sample collection, the number of participants who could be included in the program was limited. Priority was given to healthcare workers with higher levels of burnout during this stage, in line with the intervention goals.

A total of 29 participants were enrolled in the burnout reduction program. Of these, 20 participants had complete longitudinal biological material available for analysis at the required time points, constituting the final analytical sample. Thus, the final sample included participants with varying degrees of burnout who completed all required assessments.

Instruments

Biological samples included serum and saliva. Serum DHEA-S and TSH concentrations were determined using the Alcor Bio Group test systems (Russia). Reference ranges: TSH – 0.23-3.4 μ U/mL; DHEA-S – 1.0-4.2 μ g/mL (men), 0.8-3.9 μ g/mL (women). Salivary cortisol levels were measured using the Cortisol Saliva ELISA kit (Diagnostics Biochem Canada, Inc.); the reference value was \leq 21.6 ng/mL. Measurements were performed using an ELx808™ Absorbance Microplate Reader (BioTek Instruments, Inc., VT, USA).

Burnout was assessed using the Maslach Burnout Inventory (MBI) [22]. To identify protective factors against burnout, participants completed the Ways of Coping Questionnaire (WCQ) [23], the Beck Depression Inventory (BDI), the Perceived Stress Scale-10 (PSS-10) [24], and the short form of the 12-Item Short Form Health Survey (SF-12) [25]. Mindfulness was assessed using the Five Facet Mindfulness Questionnaire (FFMQ) and the Mindful Attention Awareness Scale (MAAS) [26]. A detailed description of these methods is provided in [7].

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 began. Participants were instructed on how to complete the questionnaires and informed that the survey would not have any impact on their work or personal lives. Second, the researcher collected sociodemographic information to determine whether they met the inclusion criteria. Third, participants signed written informed consent and completed all the aforementioned questionnaires. Fourth, participants provided saliva and blood samples. Before the start of any therapy, on an empty stomach, between 8 and 9 a.m., after a 15-minute rest, blood was collected from the median cubital vein into disposable vacuum blood collection tubes on days 3-9 of the menstrual cycle (if present) or in the presence of amenorrhea. Saliva (4-5 mL) was collected in a clean, dedicated tube (SaliCaps, IBL International GmbH, Hamburg, Germany) without coercion or stimulation, before eating, drinking, or brushing teeth. Before collecting samples, study participants simply rinsed their mouths with water. All samples were then

stored at 4°C until sent to the laboratory. A detailed description of these methods is provided in [27].

Data analysis

Data processing was performed using the REDcap system [28]. Statistical calculations were performed using IBM SPSS Statistics (v.23.0), with the significance level set at $p < 0.05$. Quantitative variables are presented as mean and standard deviation (SD), and for nonparametric data, as median and interquartile range (Q1; Q3). Mean values were compared using a two-tailed t-test, and for nonparametric data, the Mann-Whitney U test. Qualitative variables are presented as count (n) and percentage (%). Relationships between quantitative variables were tested using the Pearson correlation test, and for nonparametric data, the Spearman's rank correlation coefficient.

The study was approved by the local ethics committee. All procedures involving human participants were performed in accordance with the ethical standards of the institutional and national research ethics committee and with the principles of the 1964 Declaration of Helsinki and its later amendments.

Results

The sociodemographic characteristics of the sample are presented in [Table 1](#). A total of 20 physicians and nurses working in obstetrics and gynecology participated in the study; 95% were

women and 5% were men. They were predominantly Caucasian (95%), married (70%), and religious (70%). Their mean age was 37.81 (11.33) years, ranging from 22 to 69 years. The participants had 17.4 (11.2) years of professional experience.

During the first stage of the study, we analyzed the dynamics of the main biomarkers of occupational burnout: TSH, salivary cortisol, and DHEA-S ([Table 2](#)).

First, we found changes in salivary cortisol level: its concentration increased after completion of the training program. This effect was observed primarily among participants without pronounced symptoms of burnout. In contrast, participants with high levels of occupational burnout did not show significant changes in stress biomarkers immediately after program completion.

During the second stage, we analyzed the dynamics of burnout indicators, coping strategies, and mindfulness among healthcare workers who participated in the pilot implementation of the OsNOVA mindfulness training program [21]. The analysis focused on the results obtained immediately after program completion, as this was the stage at which biochemical data was available ([Table 3](#)).

We analyzed the dynamics of psychological indicators among healthcare workers who participated in the program, both with high and low levels of burnout.

Table 1. Sociodemographic information

Variable		Total sample (n=20)	High burnout (n=12)	Low burnout (n=8)
Age, years (mean±SD)		37.81 (11.33)	36.26 (11.6)	38.74 (10.28)
Gender; count (%)	Male	1 (5%)	1 (8.33%)	0 (0%)
	Female	19 (95%)	11 (91.66%)	8 (100%)
Ethnic group; count (%)	Caucasian	19 (95%)	11 (91.66%)	8 (100%)
	Asian	1 (5%)	1 (8.33%)	0 (0%)
Work experience; count (%)	<1 year	3 (15%)	2 (16.66%)	1 (12.5%)
	1-5 years	4 (20%)	4 (33.33%)	0 (0.00%)
	6-10 years	5 (25%)	3 (25%)	2 (25%)
	11-20 years	4 (20%)	1 (8.33%)	3 (37.5%)
	21-30 years	4 (20%)	2 (16.66%)	2 (25%)
	31-40 years	0 (0.00%)	0 (0.00%)	0 (0.00%)
Marital status; count (%)	>40 years	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Single	3 (15%)	2 (16.66%)	1 (12.5%)
	Common law marriage	1 (5%)	1 (8.33%)	0 (0.00%)
	Living apart together	1 (5%)	1 (8.33%)	0 (0.00%)
	Married	14 (70%)	7 (58.33%)	7 (87.5%)
	Divorced	1 (5%)	1 (8.33%)	0 (0.00%)
Religious status; count (%)	Not specified	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Not reported	0 (13.79%)	0 (0.00%)	0 (0.00%)
	Atheist	6 (30%)	5 (41.66%)	1 (12.5%)
Profession; count (%)	Religious	14 (70%)	7 (58.33%)	7 (87.5%)
	Physician	12 (60%)	6 (50%)	6 (75%)
	Nurse	8 (40%)	6 (50%)	2 (25%)

Table 2. Dynamics of biomarkers of occupational burnout in healthcare workers before the start of the study and after three months of observation

Sample		TSH			Cortisol			DHEA-S		
		Before	After	t	Before	After	t	Before	After	t
Total sample	M	1.88	2.10		65.75	80.36		3.80	4.13	
	SD	0.92	1.30	-1.481	29.25	25.15	-2.192*	2.30	2.12	-1.362
High burnout	M	1.55	1.32		70.45	71.33		4.43	4.19	
	SD	0.79	0.82	-0.420	23.71	18.28	-0.524	2.18	1.71	-0.314
Low burnout	M	2.17	2.70		61.57	87.39		3.24	4.07	
	SD	0.96	1.31	-0.421	34.32	28.44	-2.521**	2.38	2.50	-0.560

** significant at the 0.01 level (two-tailed); * significant at the 0.05 level (two-tailed).

Table 3. Dynamics of psychological indicators in the sample

Variable		Ascertaining stage M (SD)	Control stage M (SD)	t
Emotional exhaustion	High burnout	38.10 (7.77)	30.88 (7.47)	3.28**
	Low burnout	24.40 (4.28)	25.80 (8.2)	-0.63
	Total sample	34.52 (7.62)	28.92 (7.85)	3.24**
Depersonalization	High burnout	17.00 (1.86)	15.63 (2.1)	2.40
	Low burnout	7.60 (1.52)	8.20 (5.48)	-0.48
	Total sample	13.82 (1.59)	12.06 (3.98)	1.36
Reduced personal accomplishment	High burnout	32.80 (4.29)	39.00 (10.1)	-2.99*
	Low burnout	40.02 (6.01)	42.80 (6.61)	-1.25
	Total sample	35.86 (5.37)	40.46 (8.75)	-2.80*
Confrontation coping	High burnout	9.2 (3.2)	8.24 (1.67)	1.37
	Low burnout	8.2 (2.49)	8.06 (2.35)	0.16
	Total sample	8.92 (2.94)	8.16 (1.86)	1.42
Distancing	High burnout	10.8 (4.69)	8.38 (4.14)	1.90
	Low burnout	9.8 (3.42)	8.4 (5.41)	0.90
	Total sample	10.52 (3.98)	8.38 (4.68)	2.60*
Self-control	High burnout	15.5 (3.64)	13.45 (3.71)	2.65*
	Low burnout	13.10 (5.1)	11.6 (5.77)	0.78
	Total sample	14.66 (4.66)	12.54 (4.75)	2.02
Seeking social support	High burnout	13.54 (3.88)	11.4 (2.98)	2.16
	Low burnout	11.42 (1.89)	12.2 (2.28)	-1.06
	Total sample	12.82(2.57)	11.77 (2.65)	1.80
Accepting responsibility	High burnout	7.8 (2.3)	7.74 (1.75)	0.10
	Low burnout	6.32 (3.03)	6.56 (2.88)	-0.23
	Total sample	7.2 (2.6)	7.11 (2.67)	0.15
Escape and avoidance	High burnout	15.34 (2.1)	13.62 (2.44)	2.62*
	Low burnout	12.8 (4.21)	11.92 (4.03)	0.60
	Total sample	14.26 (3.15)	12.84 (3.3)	1.40
Planful problem solving	High burnout	12.1 (3.07)	12.24 (5.09)	-0.12
	Low burnout	13.04 (4.00)	12.00 (3.02)	0.84
	Total sample	12.46 (3.26)	12.15 (4.26)	0.37
Positive reappraisal	High burnout	12.8 (3.33)	13.38 (3.54)	-0.58
	Low burnout	13.78 (4.32)	13.1 (3.9)	0.47
	Total sample	13.12 (3.56)	13.26 (3.53)	-0.18
SF-12	High burnout	69.67% (9.98%)	77.53 % (6.84%)	-3.24**
	Low burnout	75.88% (5.98%)	82.17% (6.25%)	-2.91*
	Total sample	72.04% (8.61%)	79.41% (7.38%)	-4.12**
BDI	High burnout	14.6 (4.06)	8.5 (5.34)	4.50**
	Low burnout	5.54 (3.13)	3.8 (2.49)	1.75
	Total sample	11.28 (4.28)	5.59 (4.95)	5.51**
Describing	High burnout	30.10 (3.21)	32.6 (6.31)	1.18
	Low burnout	32.8 (6.29)	28.75 (4.71)	2.09*
	Total sample	31.00 (4.86)	30.85 (5.32)	0.13
Non-judging	High burnout	28.3 (6.06)	31.5 (6.37)	-1.78
	Low burnout	31.2 (7.73)	35.8 (9.56)	-1.51
	Total sample	30.02 (6.26)	34.13 (8.19)	-2.54*
Non-reacting	High burnout	21.8 (3.77)	22.13 (3.94)	-0.30
	Low burnout	21.4 (5.32)	22.00 (6.89)	-0.28
	Total sample	21.67 (4.15)	22.08 (4.99)	-0.40
Acting with awareness	High burnout	22.75 (5.95)	24.5 (5.58)	-1.05
	Low burnout	26.4 (6.19)	29 (6.04)	-1.20
	Total sample	24.15(6.07)	26.15 (5.94)	-1.49
Observing	High burnout	27.8 (4.83)	24.25 (6.71)	2.13
	Low burnout	28.6(5.13)	29.6 (5.77)	-0.52
	Total sample	28.07 (4.76)	26.31 (6.69)	1.37
MAAS	High burnout	52.93 (7.77)	57.61 (7.04)	-2.19*
	Low burnout	65.86 (7.76)	67.48 (10.11)	-0.51
	Total sample	56.59 (7.77)	63.57 (8.17)	-3.67**
Overvoltage	High burnout	24.92 (4.74)	20.64 (6.77)	2.58*
	Low burnout	14.10 (2.19)	11.86 (3.04)	2.42*
	Total sample	21.41 (3.88)	16.93 (4.30)	4.90**
Counteracting stress	High burnout	12.68 (3.21)	10.10 (3.61)	2.62*
	Low burnout	7.67 (1.59)	7.62 (1.12)	0.10
	Total sample	11.23 (2.66)	8.72 (2.68)	4.20**
Perceived stress	High burnout	37.60 (7.28)	30.74 (9.94)	2.76*
	Low burnout	21.76 (3.28)	19.48 (3.57)	1.88
	Total sample	32.74 (5.88)	25.64 (5.62)	5.52**

SF-12, 12-Item Short Form Health Survey; BDI, Beck Depression Inventory; MAAS, Mindful Attention and Awareness Scale; ** significant at the 0.01 level (two-tailed); * significant at the 0.05 level (two-tailed).

We observed a significant reduction in burnout symptoms among participants with high levels of burnout: decreased scores on the *Emotional exhaustion* scale and increased scores on the *Reduced personal accomplishment* scale (the latter is an inverted scale of the Maslach Burnout Inventory). This group also experienced a decrease in depressive symptoms and perceived stress, and an improvement in quality of life.

Among physicians and nurses with low baseline burnout, no significant changes were observed in burnout indicators; however, their quality of life also improved.

During the training, participants with high burnout reported decreased effectiveness of some coping strategies, viz., *Self-control* and *Escape and Avoidance*. In contrast, the coping strategies of participants without burnout remained unchanged.

The most significant changes were observed in mindfulness: healthcare workers with high burnout demonstrated an increase in mindfulness scores (MAAS).

During the third stage of the study, we examined the relationships between key biomarkers and sociodemographic and psychological characteristics. Before the program, *Depersonalization* was inversely correlated with cortisol and DHEA-S levels ($r=-0.674$ and $r=-0.526$, $p=0.001$ and $p=0.032$, respectively). Cortisol levels at baseline were unrelated to work experience, but exhibited an inverse correlation immediately after program completion ($r=-0.516$, $p=0.031$).

Significant associations were also found between several coping strategies and biomarkers at baseline: higher scores on *Painful problem solving* correlated with higher DHEA-S level ($r=0.523$, $p=0.03$), while higher scores on *Positive reappraisal* correlated with higher TSH levels ($r=0.508$, $p=0.040$). Some facets of mindfulness were associated directly with TSH: *Observing* and *Non-reacting* ($r=0.536$ and $r=0.690$, $p=0.028$ and $p=0.001$, respectively), while *Describing* was associated directly with cortisol ($r=0.620$, $p=0.009$).

Immediately after training, additional associations emerged: TSH was directly correlated with the coping strategies *Confrontation* and *Avoidance* ($r=0.552$ and $r=0.609$, $p=0.030$ and $p=0.019$, respectively). The mindfulness facet *Describing* correlated inversely with both TSH ($r=-0.624$, $p=0.009$) and DHEA-S ($r=-0.508$, $p=0.040$), while *Non-judging* facet correlated inversely with TSH ($r=-0.501$, $p=0.045$). Finally, perceived stress correlated directly with TSH ($r=0.604$, $p=0.020$).

Discussion

The goal of this study was to describe the dynamics of stress-related biomarkers (salivary cortisol, TSH, and DHEA-S) and their association with psychological characteristics in healthcare workers during a pilot implementation of the OsNOVA program for reducing occupational burnout. The study was designed as a pilot and exploratory study; therefore, the results obtained should be considered preliminary and primarily aimed at describing longitudinal patterns and generating hypotheses, rather than confirming the effectiveness of the intervention. This approach is consistent with the practice of pilot studies of mindfulness- and relaxation-based interventions, which often use small samples and single-group or quasi-experimental designs [29, 30]. At the same time, the obtained data allow us to evaluate the feasibility of the program and its potential psychological benefits for the most vulnerable group of healthcare workers.

One of the key observations of this study was that changes in salivary cortisol levels were detected solely in participants with low baseline burnout, while no significant changes in stress-related biomarkers were observed in participants with high baseline burnout. Thus, the differences between subgroups reflected the presence or absence of changes in cortisol levels, rather than the emergence of two symmetrical and statistically significant physiological trajectories. This observation highlights the heterogeneity of physiological responses depending on baseline burnout but cannot be interpreted as evidence of stable or different biomarker dynamics in subgroups.

At first glance, the increase in salivary cortisol levels in participants with low baseline burnout may seem paradoxical, given the traditional notion of cortisol as a stress marker. However, as noted in previous studies [1, 13, 31], the relationship between cortisol and burnout is inconsistent. The literature reports elevated, decreased, or unchanged cortisol levels, which is explained by significant inter- and intra-individual variability and possible phase-dependent changes under chronic stress. In this context, the present results should be interpreted as descriptive and preliminary.

It is important to emphasize that the observed increase in cortisol levels should not be interpreted as an unambiguous effect of the intervention. The lack of a parallel control group and the small sample size preclude a causal relationship, and the observed changes may reflect the influence of external or contextual factors during the observation period, as well as individual physiological variability. Similar caution in interpreting cortisol dynamics has been emphasized in previous pilot studies reporting heterogeneous and sometimes paradoxical hormonal responses following stress reduction or rehabilitation interventions [30]. A critical aspect of interpreting the present results is distinguishing between psychological and physiological changes. While the physiological change in the form of increased salivary cortisol levels was observed only among participants with low baseline burnout, participants with high baseline burnout demonstrated stable and clinically significant psychological improvements after the program. These included reductions in burnout symptoms, depressive symptoms, and perceived stress, as well as increases in mindfulness. This assemblage of psychological changes represents the primary practical value of the program for individuals with the highest levels of burnout. This discrepancy highlights that *the most pronounced changes* cannot be considered a single effect and should be analyzed separately for psychological and physiological outcomes.

We also hypothesized a possible role of mindfulness in the observed changes in cortisol levels. Specifically, participants without severe burnout initially demonstrated lower levels of mindfulness and associations with the *Description* facet. However, the present study did not examine longitudinal associations between changes in mindfulness and changes in cortisol levels, nor did it employ mediation or moderation analyses. Therefore, mindfulness cannot be considered a definitive mechanism underlying the observed physiological changes and should only be considered as a potential avenue for future research.

Associations between stress-related biomarkers and psychological characteristics were also exploratory. In particular, the negative association between depersonalization and baseline cortisol and DHEA-S levels is consistent with previous reports of differential relationships between cortisol and different

components of burnout [15]. However, given the multiple correlation analyses used and limited statistical power, these results should be interpreted with caution and considered hypothesis-generating. No significant changes in mean TSH or DHEA-S values were observed. However, the nature of their relationships with psychological variables changed over time, which may reflect a reorganization of the relationships between psychological characteristics and physiological measures, rather than a direct hormonal effect of the intervention.

Overall, the main contribution of the present study is not the demonstration of statistically significant differences between subgroups, but the provision of an integrated longitudinal assessment of psychological characteristics and multiple stress-related biomarkers within a single pilot protocol. The results indicate that the program is associated with significant psychological improvements among healthcare workers with high levels of occupational burnout and can be considered a promising supportive approach for this group. They also highlight the heterogeneity of psychophysiological responses in the context of professional burnout and the need for further research with larger samples, pre-specified hypotheses, and controlled designs [29].

Conclusion

This pilot study provides a comprehensive longitudinal analysis of psychological characteristics and stress-related biomarkers among healthcare workers participating in a burnout reduction program. Results indicate heterogeneous patterns of change depending on baseline burnout, with psychological improvements (such as reductions in burnout symptoms, perceived stress, and depressive symptoms, as well as increased mindfulness) observed predominantly among participants with higher baseline burnout.

In contrast, a significant increase in a salivary cortisol level at follow-up were observed only among participants with lower baseline burnout, while no statistically significant changes in biomarker levels were found among participants with higher burnout scores. Given the exploratory nature of the study, the small sample size, and the lack of a parallel control group, these results should be interpreted with caution and considered hypothesis-generating, emphasizing the need for future studies with larger samples and controlled designs to clarify the psychophysiological dynamics of occupational burnout.

Limitations

A number of limitations of the present study should be noted. First, the sample size was relatively small (n=20), and further subdivision of participants based on burnout levels resulted in even smaller group sizes. This significantly reduced statistical power and increased the risk of random and systematic errors, although such limitations are typical and acceptable in the context of pilot and exploratory studies. Accordingly, the results obtained should be interpreted as preliminary rather than confirmatory.

Second, a significant limitation of the study is the lack of a parallel control group that did not participate in the burnout reduction program. As a result, the observed changes in psychological measures and stress-related biomarkers cannot be definitively attributed to the intervention per se; hence, the influence of external or contextual factors during the observation period cannot be ruled out. This design choice reflects the pilot and exploratory nature of the study. Similar preliminary studies of

mindfulness-, relaxation-, or rehabilitation-based interventions have often used single-group or quasi-experimental longitudinal designs without fully matched control groups, particularly when the primary objectives were feasibility assessment, descriptive characterization of biomarker dynamics, and hypothesis generation rather than confirmatory testing [29, 30]. In such studies, within-subject changes are cautiously interpreted as temporally related to program participation rather than as definitive evidence of intervention effectiveness.

Third, the issue of multiple statistical testing represents an additional limitation. A large number of correlation analyses were conducted between stress-related biomarkers and psychological measures, increasing the risk of Type I error. Formal corrections for multiple comparisons (such as the Bonferroni correction) were not applied because the study was designed as a pilot study aimed at exploratory analysis rather than hypothesis confirmation. Therefore, the reported associations should be considered hypothesis-generating and interpreted with caution.

Finally, the use of parametric statistical tests in a small sample presents another limitation. Despite the use of standardized psychological instruments and the absence of significant deviations from a normal data distribution, the limited sample size reduces the reliability of the parametric assumptions. Therefore, all statistical results should be interpreted with caution and considered exploratory in nature.

Conflict of interest

The authors declare no conflicts of interests.

Ethical approval

The study complied with the principles of the Declaration of Helsinki (2013 edition) and was reviewed and approved by the Ethics Committee of SCFHR (Protocol #2 of March 4, 2021). All participants received written information about the study's objectives and procedures and provided informed consent.

AI use statement

The authors did not use any artificial intelligence tools or technologies in preparing this manuscript.

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