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## The association of stress level with the central serous chorioretinopathy development

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### Abstract

**Background.** The impact of stress on the central serous chorioretinopathy development has been studied in a small number of studies, and the results are conflicting.

**Aim.** To assess the association of the level of individual stress with the central serous chorioretinopathy development.

**Material and methods.** A cross-sectional study based on a survey of 110 patients with central serous chorioretinopathy (the main group) and 110 individuals without central serous chorioretinopathy was conducted. The stress level was assessed on the Perceived Stress Scale. Quantitative and categorical data between the groups were compared. Comparison of groups by quantitative indicator was performed using the Mann–Whitney U-test, and by categorical indicator — using the odds ratio and its 95% confidence intervals.

**Results.** The groups of respondents were comparable according to the main demographic indicators. The median total score for the “Overstrain” subscale in the central serous chorioretinopathy group was 12 points ( $Q_{25\%}$ – $Q_{75\%}$  9.25–14 points), in the control group — 10 points ( $Q_{25\%}$ – $Q_{75\%}$  7–12 points;  $p=0.0002$ ). The median total score for the “Stress Response” subscale in the central serous chorioretinopathy group was 7 points ( $Q_{25\%}$ – $Q_{75\%}$  5–8 points), in the control group it was 4 points ( $Q_{25\%}$ – $Q_{75\%}$  3–7 points;  $p=0.000003$ ). In the group with central serous chorioretinopathy, compared with the control group, the proportion of people with moderate stress level was higher (74.5% vs. 53.6%; odds ratio 2.53, 95% confidence interval 1.43–4.48) and the proportion of people with low stress level was lower (19.1% vs. 45.5%; odds ratio 0.28, 95% confidence interval 0.15–0.52).

**Conclusion.** The study demonstrated the association of stress with the development of central serous chorioretinopathy.

**Keywords:** psychogenic risk factors, stress, central serous chorioretinopathy.

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### Background

Central serous chorioretinopathy (CSCR) is a serious eye disease that manifests as impaired visual perception; moreover, complete loss of vision in the event of the disease progression is also possible. This pathology leads to a limitation in the ability to perform daily tasks and, as a result, to a decrease in the quality of life [1]. However, there is still no consensus on the etiology of CSCR.

The numerous and often contradicting theories of the development of CSCR hinders the development of population-based and individual programs for the prevention of this disease. Various studies

have considered possible genetic, biological, and environmental risk factors for CSCR [2–6]. In addition, the possible impact of stress on the disease development was suggested. In 1927, Horniker suggested that spasm of retinal vessels underlies the disease pathogenesis [7]. Several studies have demonstrated an increase in the level of the “stress hormone,” cortisol, in patients with acute CSCR compared with healthy people [8–10].

The effect of stress on the development of CSCR has been analyzed in a small number of studies, and the results obtained are contradictory, which both confirm [11–14] and disprove [15, 16] this

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relationship. Accordingly, the question of the effect of stress on the development of CSCR remains to be clarified.

### Aim

This study aimed to evaluate the relationship between the level of individual stress and the development of CSCR.

### Materials and methods

A one-stage (cross-sectional) study was performed based on a questionnaire survey of patients with CSCR (main group) and those without CSCR (control group). To reduce the probability of false differences between the main and control groups, groups comparable in age and gender were formed. A total of 220 patients were included in the study.

The equation of Kelsey et al. was used to determine the required sample size [17]. The study included patients aged 18 years and older who gave informed consent to participate in the study. Two groups (main and control) of 110 patients each were formed. The group 1 included patients with diagnosed CSCR. In all patients, the diagnosis was confirmed by optical coherence tomography. The survey was conducted immediately after the diagnosis was made.

Enrollment of participants in the main group was performed in Kazan at Professor E.V. Adamyuk Republican Clinical Ophthalmological Hospital of the Ministry of Health, Republic of Tatarstan, and the ophthalmological clinic “Kuzlyar.”

The control group included patients who applied for a medical examination at the Health Center of the Central City Clinical Hospital No. 18 in Kazan and underwent an examination by an ophthalmologist, which included history taking, identifying complaints, visual acuity test, biomicroscopy, ophthalmoscopy, and ocular tonometry.

Criteria for inclusion in the control group were the absence of acute complaints of visual impairment and the absence of retinal pathology according to the results of an ophthalmological examination. Criteria for exclusion from the control group were the presence of cataracts, glaucoma, and/or diabetic retinopathy.

The study was approved by the local ethics committee of Kazan State Medical University, protocol No. 10 dated 12/18/2018.

Stress levels were assessed using the Perceived Stress Scale [18]. Concurrently, a validated Russian-language version of the Perceived Stress Scale-10 questionnaire was used [19]. Points were calculated according to the following scheme:

– Answers to the questions of the subscale “Overstrain” (B1, B2, B3, B6, B9, B10) were as-

essed in the range of 0–4 points (O1 = 0; O2 = 1; O3 = 2; O4 = 3; O5 = 4), and the scores were summed.

– Responses to the questions of the subscale “Stress Response” (B4, B5, B7, B8) were assessed in the range of 0–4 points in inverted form (O1 = 4; O2 = 3; O3 = 2; O4 = 1; O5 = 0), and scores were summed.

– The scores for both subscales were summed.

After summing up the scores, a final assessment of the individual level of stress was performed for each study participant; the risk was assessed as low with a score of 0–13 points, moderate with a score of 14–26 points, and high with a score of 27–40 points.

*Statistical data analysis.* Quantitative data were presented as a median (Me) and interquartile range ( $Q_{25\%}$ ;  $Q_{75\%}$ ), the normality of the data distribution was evaluated using the Shapiro–Wilk test. The statistical significance of differences in the groups was assessed using the Mann–Whitney  $U$  test. Qualitative patient survey data were presented as a relative indicator (share, %). Statistical significance of differences was assessed using Yates-adjusted  $\chi^2$  test or odds ratio and its 95% confidence intervals. The results obtained were considered statistically significant at  $p < 0.05$ . Statistical data analysis was performed using Microsoft Office Excel 2010 programs, Jamovi programs, and OpenEpi online calculators (<http://www.openepi.com>).

### Results

The groups of respondents were comparable in terms of the main demographic indicators (age, gender). In both groups, the youngest patients were 18 years old; the oldest participant was 73 years in the main group and 72 years in the control group. The median age ( $Q_{25\%}$ ;  $Q_{75\%}$ ) of participants in the main group was 37 years (29–45.8), and that of the control group was 35.5 years (25–48.8).

The results of a survey of patients using a validated Russian version of the questionnaire Perceived Stress Scale-10 enabled to identify differences between the groups.

*Questions of the subscale “Overstrain”.* When answering the questions “In the last month, how often have you been upset because of something that happened unexpectedly?” (Q1) and “In the last month, how often have you felt that you were unable to control the important things in your life?” (B2), the answer “never” was statistically significantly more common in the control group than in the CSCR group—that is, 11 (10%) and 0, respectively ( $\chi^2 = 9.6$ ;  $p = 0.002$ ), for question B1 and 37 (33.6%) and 5 (4.5%), respectively ( $\chi^2 = 28.3$ ;  $p = 0.0000001$ ), for question B2. Conversely, the an-

**Table 1.** Distribution of patients according to the frequency of the detected level of stress in the main and control groups (according to the Perceived Stress Scale-10).

Stress level	Main group (with CSCR)	Control group (without CSCR)	OR (95% CI)	p
Low	21 (19.1%)	50 (45.5%)	0.28 (0.15–0.52)	0.0001
Moderate	82 (74.5%)	59 (53.6%)	2.53 (1.43–4.48)	0.002
High	7 (6.4%)	1 (0.9%)	7.41 (0.89–61.25)	0.07

Note: OR—odds ratio; CI—confidence interval.

swer “quite often” was given in the CSCR group more often than in the control group—that is, 46 (41.8%) and 20 (18.2%), respectively ( $\chi^2 = 13.5$ ;  $p = 0.0002$ ), for question B1 and 26 (23.6%) and 6 (5.5%), respectively ( $\chi^2 = 13.2$ ;  $p = 0.0003$ ), for question B2.

In the CSCR group, there were 2.6 times more patients who noted that they experienced nervous tension or stress quite often (question B3) than in the control group (64 (58.2%) and 25 (22.7%), respectively;  $p = 0.0000002$ ). There were no differences between the groups in the distribution of responses to the questions “In the last month, how often have you found that you could not cope with all the things that you had to do?” and “In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?”

The answer to the question “In the last month, how often have you been angered because of things that were outside of your control?” (B9) was “never” significantly more often in the control group than in the group of CSCR patients, with 15 (13.6%) and 2 (1.8%), respectively ( $\chi^2 = 9.2$ ;  $p = 0.002$ ).

The median of the total indicator on the “Overstrain” subscale in the CSCR group was 12 points ( $Q_{25\%}$ – $Q_{75\%}$  9.25–14 points); and in the control group, it was 10 points ( $Q_{25\%}$ – $Q_{75\%}$  7–12 points; Mann–Whitney  $U$  test 4316,  $p = 0.0002$ ).

*Questions of the subscale “Stress Response”.* The answers to the questions of the subscale “Stress Response” were consistent with the results on the scale “Overstrain.” When answering the questions of the “Stress Response” subscale (Q4 “In the last month, how often have you felt confident about your ability to handle your personal problems?” and Q5 “In the last month, how often have you felt that things were going your way?”), the answer “never” was more common in the CSCR group than in the control group—that is, 29 (26.4%) and 4 (3.6%), respectively ( $\chi^2 = 20.5$ ;  $p = 0.000006$ ) for question B4 and 14 (12.7%) and 3 (2.7%), respectively ( $\chi^2 = 6.3$ ;  $p = 0.012$ ) for question B5.

When answering the questions “In the last month, how often have you been able to control irritations in your life?” (Q7) and “In the last month,

how often have you felt that you were on top of things?” (B8), the answer “never” was also more frequently registered in the main group compared to the control group—that is, 25 (22.7%) and 3 (2.7%), respectively ( $\chi^2 = 18.1$ ;  $p = 0.00002$ ), for question B7 and 23 (20.9%) and 2 (1.8%), respectively ( $\chi^2 = 18.1$ ;  $p = 0.0002$ ), for question B8. The answer “sometimes” was more common in the control group than in the CSCR group, with 69 (62.7%) and 26 (23.6%), respectively ( $\chi^2 = 32.7$ ;  $p = 0.0000001$ ) for question B7 and 46 (41.8%) and 19 (17.3%), respectively ( $\chi^2 = 14.7$ ;  $p = 0.0001$ ), for question B8.

The median of the total indicator on the subscale “Stress Response” in the CSCR group was 7 points ( $Q_{25\%}$ – $Q_{75\%}$  5–8 points), and it was 4 points ( $Q_{25\%}$ – $Q_{75\%}$  3–7 points) in the control group; differences were statistically significant (Mann–Whitney  $U$  test 3858,  $p = 0.000003$ ).

After adding all the points obtained, a stress level indicator was calculated for each patient. The distribution of patients with different levels of stress, based on belonging to one of the groups, is presented in Table 1. It was established that the proportion of patients with a moderate level of stress in the CSCR group was statistically significantly higher than that in the group without CSCR. Conversely, the proportion of patients with low levels of stress was higher in the control group compared with the main group.

## Discussion

Few studies have been conducted on the epidemiology of CSCR in Russia as well as in other countries, making it difficult to determine its incidence. According to our data, an increase in the incidence of CSCR was registered in recent years in Kazan [20]. The disease has an undoubted medical and socio-economic significance, since it is characterized by severe visual impairment and the risk of chronicity, with the possibility of complete loss of vision. Concurrently, CSCR mainly affects people of working age, thereby complicating their daily and work functions. Risk factors for the disease are underinvestigated, which makes the prevention difficult.

Our earlier systematic review with meta-analysis [21] demonstrated the role of the risk factors in the development of CSCR, namely arterial hypertension, coronary heart disease, autoimmune diseases, the use of steroid drugs, and infection with *Helicobacter pylori*. However, the study of stress as a potential risk factor was not included in the meta-analysis. This was because different authors used different methods and approaches to study stress, which made it difficult to combine and analyze the data published previously [21].

The results of studies on the influence of stress on the development of CSCR were ambiguous. For example, in their work, Bousquet et al. convincingly demonstrated that stress is a significant risk factor for CSCR [odds ratio (OR) 14.5; 95% confidence interval (CI) 4.8–44.1] [14]. Chatziralli et al. also demonstrated that stress and personality type A increased the risk of CSCR (OR 2.65; 95% CI 1.72–4.08) [11]. Similar data were obtained by Mansour regarding prolonged stress (OR 4.73; 95% CI 1.84–12.14) [13]. Concurrently, Matet et al. revealed no relationship between the level of stress and the development of CSCR (OR 1.70; 95% CI 0.66–4.34) [16]. Additionally, Kaye et al. drew attention to the fact that to date, there are no studies demonstrating an association between a decrease in stress levels and the resolution of CSCR [22].

According to the results of this cross-sectional study, the proportion of people with moderate levels of stress was higher in the group of patients with CSCR compared to the control group. Additionally, the proportion of individuals with low levels of stress was significantly higher in the control group (without CSCR) than in the main group.

Our study confirms the existence of an association between the level of individual stress and the development of CSCR.

The limitation of the work was the nature of the study; it was a one-stage (cross-sectional) study, which does not enable to determine the direction of the relationship between the studied phenomena; that is, it is not completely clear whether stress is a risk factor in the development of the pathology studied or a consequence of eye damage. CSCR is a rather serious disease that can presumably provoke the occurrence of stress on the resulting restrictions and a decrease in the quality of life. Nevertheless, available data from fundamental and clinical studies on the role of stress hormones, increased vascular tone, and arterial hypertension in the development of this pathology of the retina suggest the primacy of the influence of stress, although to answer the question of the causal relationship of these two phenomena, studies such as cohort or case-control trials are required.

A limitation of any study using questionnaires is the subjective nature of the responses, as well as the possibility of bias due to differences in the completeness of patients' memories.

Continuation of research on this issue in the future can be implemented, as well as the development of recommendations for the prevention of both the first episode of CSCR and its relapses. If the impact of stress and type A personality characteristics are considered as risk factors for the development of CSCR, then psychosocial support and stress management training for CSCR patients may improve their condition. Therefore, it is also logical to assume that pharmacological regulators of sympathetic agents and methods of increasing the body's resistance to stress can also be effective for the treatment and prevention of CSCR.

## Conclusion

The present study demonstrated the relationship between the level of stress and the development of CSR. There was a higher proportion of patients with a moderate level of stress and a lower proportion of people with low level of stress in the group with CSR compared with the control group.

**Author contributions.** G.R.H. developed the study concept and design, wrote and edited the manuscript, and approved the final version for publication; D.R.A. collected and cleaned the data, performed statistical analysis, and wrote the manuscript; E.A.A. and N.D.K. collected and processed the data, and wrote the manuscript; A.U.K. developed the study concept and design, and wrote the manuscript; S.T.A. performed statistical analysis and wrote the manuscript.

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