

# Evaluation and correlation of stress scores with blood pressure, endogenous cortisol levels, and homocysteine levels in patients with central serous chorioretinopathy and comparison with age-matched controls

Abhishek Agarwal, Monika Garg, Nikhil Dixit, Rohini Godara

**Context:** Stress had been associated with the development of central serous chorioretinopathy (CSC). The study was designed to evaluate the effect of stress on other risk factors of CSC such as serum cortisol levels, serum homocysteine levels, and blood pressure (BP) in CSC patients. **Aims:** To compare stress scores, serum cortisol and serum homocysteine levels, and BP of CSC patients with that of control population and to correlate stress scores of CSC patients with BP, serum cortisol levels, and serum homocysteine levels. **Materials and Methods:** Stress scores, serum morning and evening cortisol levels, serum homocysteine levels, systolic and diastolic BP of 54 CSC patients were measured and compared with that of 54 age- and sex-related controls using Student's *t*-test. Stress scores of CSC patients were correlated with systolic and diastolic BP, serum morning and evening cortisol levels and serum homocysteine levels and Pearson correlation coefficient (*r*) were calculated. **Results:** Stress scores, serum homocysteine levels, serum morning and evening cortisol levels, and systolic and diastolic BP were all elevated in CSC patients as compared with age- and sex-related controls ( $P < 0.05$ ). Stress scores of CSC patients were found to correlate strongly with serum homocysteine levels, serum morning and evening cortisol levels, and systolic and diastolic BP, with *r* values 0.82, 0.8, 0.8, 0.8, and 0.81, respectively ( $P < 0.0001$ ). **Conclusions:** Stress scores were elevated in CSC patients and were strongly correlated with serum homocysteine and cortisol levels and BP.

**Key words:** Central serous chorioretinopathy, cortisol, homocysteine and blood pressure, stress score

Central serous chorioretinopathy (CSC) is characterized by the accumulation of transparent fluid at the posterior pole leading to development of neurosensory retinal detachment or retinal pigment epithelial (RPE) detachment.<sup>[1]</sup> The pathophysiology of CSC is still not completely understood. It was originally thought to be a disorder of the RPE; however, it is now widely accepted that the disease originates from choroidal hyperperfusion.<sup>[2,3]</sup> The pathophysiology of choroidal hyperperfusion in CSC remains unknown. Choroidal vessels have been suggested to be under the control of the autonomic nervous system; therefore, systemic factors may influence choroidal hyperperfusion. Therefore, analysis of systemic findings in patients with CSC could help us to better understand the pathophysiology of choroidal hyperperfusion.

Clinically, CSC was more frequent among individuals with Type A personality who were more susceptible to psychological stress.<sup>[4,5]</sup> It was also found to be linked with pregnancy, Cushing's syndrome, hypertension, *Helicobacter pylori* infection, and sleeping disturbance.<sup>[6-9]</sup> Patients with CSC were found to be more likely to use psychopharmacologic medications and corticosteroids.<sup>[10]</sup>

Mental stress was shown to elevate heart rate, blood pressure (BP), and plasma homocysteine level in young

men.<sup>[11]</sup> Hyperhomocysteinemia was also associated with retinal vessel atherosclerosis and retinal vascular occlusive disease.<sup>[12,13]</sup> Furthermore, studies in a mouse model of hyperhomocysteinemia revealed abnormal RPE cell morphology and function.<sup>[14]</sup>

The purpose of this study was to compare stress scores, serum cortisol, serum homocysteine levels, and BP of CSC patients with that of age- and sex-related control population and to correlate stress scores of CSC patients with BP, serum cortisol levels, and serum homocysteine levels.

## Materials and Methods

Approval for this study was obtained from the Institutional Review Board. All research and data collection adhered to the tenets of the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants. This clinical study involved 108 subjects. Group A included 54 cases with CSC who presented to our hospital, and Group B included 54 age- and sex-matched controls who visited our hospital for routine eye examination or refraction. At the time of inclusion into our study, all subjects underwent a systemic

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Department of Vitreo-retinal Services, Sri Jagdamba Charitable Eye Hospital, Sri Ganganagar, Rajasthan, India

**Correspondence to:** Dr. Abhishek Agarwal, Department of Vitreo-retinal Services, Sri Jagdamba Charitable Eye Hospital, Annd Vidhalaya Campus, Sri Ganganagar - 335 001, Rajasthan, India. E-mail: abhishekretina@gmail.com

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evaluation, comprising a complete medical history and general physical examination. The ocular evaluation of cases comprised visual acuity testing, slit lamp biomicroscopy of the anterior and posterior segment (with a +78D lens). CSC was diagnosed first clinically on slit lamp biomicroscopy using 78D lens and then was confirmed on spectral domain optical coherence tomography examination (NIDEK RS-3000 OCT Retina Scan). Subjects with any other ocular or systemic disease, any surgery or trauma within 2 weeks of presentation and receiving any form of local or systemic medications were excluded from our study since all these conditions can independently alter the stress score, hypertension, serum homocysteine and serum cortisol levels. Patients with evidence of associated uveitis, polypoidal choroidal vasculopathy, or choroidal neovascularization were excluded from this study. Patients with CSC due to steroid use were also excluded from this study.

Stress scores of all subjects were then evaluated using National Stress Awareness Day Stress Questionnaire, published by international stress management association UK.<sup>[15]</sup> This questionnaire comprises 25 questions and the patient has to give a response in the form of "Yes" or "No." Stress score is then calculated by total number of "Yes" responses. If stress score is 14 points or more, then the patient is more likely to experience stress and stress-related illness.

All subjects were then called next morning at 6:30 a.m. Subjects were allowed to take rest for 10 min before testing BP. BP was tested in sitting position with sphygmomanometer. The subjects were seated comfortably with the back and arm supported and the upper arm bared without constrictive clothing. It was ensured that the legs should not be crossed and feet should be touching the ground. Middle of the cuff was placed at the level of right atrium (the mid-point of the sternum), and it was ensured that examiner should not talk to the subjects while measuring BP. Venous blood was drawn for serum homocysteine and serum cortisol (morning) level assessment at 7 a.m. Venous blood was again drawn at 11 p.m. for serum cortisol (night) level assessment. Serum homocysteine and serum cortisol levels were measured by chemiluminescent immunoassay.

Statistical analysis was done in two parts. In the first part, stress scores, systolic and diastolic BP, serum cortisol morning and evening levels and serum homocysteine levels of Group A and Group B were compared, using Student's *t*-test. Results were considered statistically significant if the  $P < 0.05$ .

For the second part of statistical analysis, stress scores of patients of CSC in Group A were correlated with serum homocysteine levels, serum cortisol morning and evening levels, and systolic and diastolic BP, and Pearson correlation coefficient (*r*) was calculated. The value of Pearson correlation coefficient (*r*) ranges between +1 and -1 inclusive, where 1 is total positive correlation, 0 is no correlation, and -1 is total negative correlation.

Statistical analysis was done with the help of InStat 3.10 software (GraphPad Software Inc., California, USA).

## Results

A total of 108 subjects were recruited for this study. Group A included 54 cases with CSC and Group B included 54 age- and sex-matched controls.

The first part of statistical analysis compared cases in Group A and controls in Group B. There was no significant difference in the age of subjects in Group A and Group B. The mean age (standard deviation and [range]) in Group A and Group B was 31.5 ([6.2] and [21-48]) years and 32.3 ([7.2] and [21-49]) years, respectively ( $P = 0.27$ ). Both cases and control groups consisted of 43 men and 11 women.

Stress scores were elevated in cases in Group A as compared to controls in Group B ( $P = 0.042$ ). Serum homocysteine levels were found to be increased in patients in Group A versus controls in Group B ( $P = 0.047$ ). Morning serum cortisol levels were raised in cases in Group A as compared to controls in Group B ( $P = 0.039$ ) and similarly evening serum cortisol levels were raised in cases in Group A as compared to controls in Group B ( $P = 0.047$ ). Both systolic BP and diastolic BP were increased in cases as compared to controls ( $P = 0.026$  and  $0.02$ , respectively) [Table 1].

In the second part of statistical analysis, stress scores of patients of CSC in Group A were correlated with serum homocysteine levels, serum cortisol morning and evening levels, and systolic and diastolic BP, and Pearson correlation coefficient (*r*) was calculated. Stress scores were found to be strongly correlated with serum homocysteine levels and serum cortisol morning and evening levels with *r* values 0.82, 0.8, and 0.8, respectively ( $P < 0.0001$ ). Correlation between stress scores and systolic and diastolic BP was also found to be strong with *r* values 0.8 and 0.81, respectively ( $P < 0.0001$ ) [Table 2].

## Discussion

The pathophysiology of CSC is not completely understood. Various studies had associated CSC with Type A personality,

**Table 1: Comparison of central serous chorioretinopathy risk factors between Group A (cases) and Group B (controls)**

	Mean (SD)		P
	Group A	Group B	
Stress score	13.31 (4.56)	11.74 (3.26)	0.042
Serum homocysteine ( $\mu\text{mol/L}$ )	15.46 (9.68)	12.34 (5.98)	0.047
Serum cortisol (morning) ( $\mu\text{g/dL}$ )	14.03 (6.6)	11.73 (4.62)	0.039
Serum cortisol (evening) ( $\mu\text{g/dL}$ )	13.1 (6.49)	10.96 (4.29)	0.047
Systolic BP (mmHg)	134.74 (14.44)	129.15 (10.94)	0.026
Diastolic BP (mmHg)	84.3 (8.71)	81.1 (5.2)	0.02

BP: Blood pressure, SD: Standard deviation

**Table 2: Correlation of stress scores with other risk factors of central serous chorioretinopathy**

	<i>r</i>	<i>r</i> <sup>2</sup>	P
Serum homocysteine	0.82	0.68	<0.0001
Serum cortisol (morning)	0.8	0.65	<0.0001
Serum cortisol (evening)	0.8	0.63	<0.0001
Systolic BP	0.8	0.64	<0.0001
Diastolic BP	0.81	0.66	<0.0001

BP: Blood pressure

stress, Cushing's syndrome, hypertension, pregnancy, *H. pylori* infection, sleeping disturbance and trauma.<sup>[4-9,16]</sup>

Gelber and Schatz had found that a very disturbing psychological event had preceded the loss of vision due to CSC in 91% of the cases.<sup>[4]</sup> Yannuzzi had documented that Type A behavior pattern was significantly more frequent in patients with CSC than in control group.<sup>[5]</sup> Our study had shown that patients of CSC had elevated stress scores, as compared with age-matched controls ( $P = 0.042$ ). Ajith and Ranimenon *et al.* had documented association of hyperhomocysteinemia with eye diseases such as retinopathy, optic atrophy, and retinal vessel atherosclerosis<sup>[12]</sup> and Rosenbaum *et al.* had documented association of hyperhomocysteinemia with branch retinal artery occlusion and nonischemic central retinal vein occlusion.<sup>[13]</sup> Furthermore, Ibrahim *et al.* used studies in a mouse model of hyperhomocysteinemia and revealed abnormal RPE cell morphology and function.<sup>[14]</sup> Our study had shown that serum homocysteine levels were elevated in patients of CSC as compared with age-matched controls ( $P = 0.047$ ). Garg *et al.* had documented that endogenous cortisol levels were elevated in patients with CSC.<sup>[8]</sup> Eom *et al.* had documented that hypertension was more frequent in patients with CSC than in the control group.<sup>[17]</sup> In accordance with the previous studies, our study had shown that patients of CSC had elevated endogenous morning and evening cortisol levels and increased systolic and diastolic BP as compared to age-matched controls ( $P < 0.05$ ).

Sawai *et al.* had shown that mental stress elevates BP and plasma homocysteine level in young men.<sup>[11]</sup> Baig *et al.* had shown that evening serum cortisol concentration was significantly associated with Perceived Stress Scale stress score.<sup>[18]</sup> Similarly, our study had demonstrated strong correlation between stress scores and serum homocysteine levels, serum morning and evening cortisol levels and systolic and diastolic BP in CSC patients ( $P < 0.0001$ ).

Based on the results of our study, we believe that stress score evaluation should be included in routine workup of CSC patients along with measurement of BP, serum homocysteine levels, and serum cortisol levels. However, our study had not evaluated the role of other factors such as *H. pylori*, pregnancy, or sleep disorders in CSC or their effect on stress scores, which will be interesting to evaluate in future studies. It will also be interesting to study the effect of lowering stress levels by psychotherapy or behavioral therapy and treatment of other risk factors on the course of CSC.

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#### Conflicts of interest

There are no conflicts of interest.

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