

Epidemiological aspects of central serous chorioretinopathy

D.R. Agliullin^{1*}, G.R. Khasanova¹, E.A. Abdulaeva², S.T. Agliullina¹,
A.N. Amirov², A.N. Kuskov³, A.A. Kim⁴, A.Yu. Raschekov⁵, D.A. Lipinsky⁶

¹Kazan State Medical University, Kazan, Russia;

²Kazan State Medical Academy: Kazan, Russia;

³Republican Clinical Ophthalmological Hospital named
after Professor E.V. Adamuk, Kazan, Russia;

⁴Clinic “KORD”, Kazan, Russia;

⁵Clinic “Eye-surgery Raschekov”, Kazan, Russia;

⁶Clinic “Third eye”, Kazan, Russia

Abstract

Aim. To analyze the incidence of central serous chorioretinopathy among the Kazan’s population between 2009 and 2018.

Methods. A descriptive epidemiological study of the incidence of Central serous chorioretinopathy of the population of Kazan between 2009 and 2018 was conducted. It included an analysis of long-term changes in the incidence of male and female population and an assessment of the structure of morbidity by sex for the entire period and in dynamics. Testing for differences was performed using the nonparametric Mann–Whitney U test and Chi-square test with Yates correction.

Results. 831 new cases of central serous chorioretinopathy were registered in Kazan during 2009–2018, the ratio of men and women was approximately 1:1. In the dynamics of morbidity, the proportion of men increased from 24.2% in 2009 to 60.7% in 2018 ($p=0.000002$), while the proportion of women decreased from 75.8% in 2009 to 39.3% in 2018 ($p=0.000002$). The long-term dynamics for 2009–2018 is characterized by a statistically significant increase in the incidence rate of central serous chorioretinopathy in men ($p=0.004$) from 3.2 per 100 000 in 2009 to 14.8 per 100 000 in 2018. During the study period, the incidence rate in women remains at the same level, varying from 5.4 per 100 000 to 8 per 100 000 ($p=0.663$). Men are more likely to have central serous chorioretinopathy at a younger age ($p=0.0001$). The median age at the time of diagnosis in women was 55 years (Q_{25} – Q_{75} 45–65 years), in men — 45 years (Q_{25} – Q_{75} 37–56 years).

Conclusion. From 2009 to 2018, the incidence rate of central serous chorioretinopathy among men in Kazan significantly increased in both intensive ($p=0.004$) and extensive indicators ($p=0.000002$); central serous chorioretinopathy in men develops at an earlier age compared with women (median age of women at the time of diagnosis was 55 years, median age of men — 45 years, $p=0.0001$).

Keywords: central serous chorioretinopathy, epidemiology, retrospective analysis, incidence, structure by gender, age.

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Background. Central serous chorioretinopathy (CSCP) is a multifactorial disease characterized by localized sensorineural retinal detachment development caused by fluid leakage at the retinal pigment epithelium level [1]. CSCP is considered to be the fourth most frequent non-surgical retinopathy after age-related macular degeneration, diabetic retinopathy, and branch retinal occlusion [2]. The disease

is a serious medical and social problem due to its potential vision loss and disability.

The pathogenesis of CSCP remains poorly understood. Currently, some published results from studies regarding risk factors are conflicting. According to a systematic review and meta-analysis results, arterial hypertension, coronary heart disease, autoimmune diseases, and steroid drugs

usage can be the most likely risk factors for CSCP [3]. It is generally accepted that CSCP often affects male more than female [4–6].

The epidemiology of CSCP including age and sex structure of the incidence has not been studied both in the Russian Federation and in the Tatarstan Republic. In addition, the assessment of the incidence rate and its structure is important for disease prevention program development.

Aim. This study aimed to conduct an analysis of CSCP incidence among the Kazan population between 2009 and 2018.

Materials and methods. A descriptive epidemiological study of CSCP incidence in the Kazan population between 2009 and 2018 was conducted using data from newly diagnosed cases of CSCP selected from the Professor E.V. Adamyuk Republican Clinical Ophthalmological Hospital, Cord clinic, Ophthalmological Center Eye-Surgery Raschetskoff, ophthalmological clinic Kuzlyar, ophthalmological clinic Third Eye, and Federal State Statistics Service archives.

The structure of CSCP incidence by sex in total and in dynamics was analyzed for the period 2009–2018. Extensive values of CSCP incidence (percentage, %) were calculated. A comparative analysis of the values of morbidity structure by sex was performed between 2009 and 2018. The statistical significance of differences in the morbidity structure was assessed using the χ^2 test with Yates correction.

Intensive values of CSCP incidence (per 100 thousand of male and female population, respectively) were calculated to analyze the long-term changes in male and female incidence. The trend of long-term changes in CSCP incidence in male and female groups for 2009–2018 was studied: the incidence dynamics was assessed using a polynomial trend line. Theoretical values of incidence (I theor., per 100 thousand) were calculated. The growth rate and accession rate were calculated to characterize the long-term dynamics of morbidity [7]. The statistical significance of the trend of long-term changes in the incidence was determined by the transgression of 95% confidence intervals (95% CI) of the theoretical values of the first and last years of the trend line. The incidence prediction is provided separately for the male and the female population by continuing the polynomial incidence trend line. The mean predictive incidence rate in 2019 and its probable maximum and minimum values (per 100 thousand) were calculated.

The quantitative parameters of the age of patients with CSCP were analyzed, and data were compared in male and female patients. The normality of distribution for quantitative data was

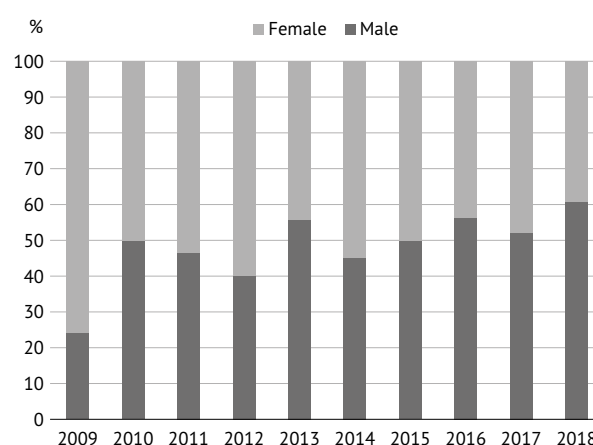


Fig. 1. Sex structure of central serous chorioretinopathy incidence in the Kazan population during 2009–2018

assessed using the Shapiro–Wilk test. Due to the fact that the quantitative data were out of the normal distribution law, they are presented as a median (Me) and an interquartile range (Q25; Q75). The statistical significance of differences in groups was assessed using the Mann–Whitney U test. Statistical processing of the obtained data was performed using Microsoft Office Excel 2010 and statistical software Jamovi. Results were considered statistically significant at $p < 0.05$.

Results. *Analysis of the CSCP incidence structure by sex.* During the study period, 831 new cases of CSCP were registered in Kazan. In general, male to female ratio was 1:1 (50.4 and 49.6%, respectively). In addition, statistically significant changes were noted in long-term dynamics of CSCP incidence structure by sex (Fig. 1): an increase in the proportion of men from 24.2% in 2009 to 60.7% in 2018 ($p = 0.000002$) and a decrease in the proportion of women from 75.8% in 2009 to 39.3% in 2018 ($p = 0.000002$; when comparing values of 2009 and 2018, χ^2 with Yates correction is 22.2).

Analysis of long-term changes of CSCP incidence in male and female. An increase in CSCP incidence in male from 3.2 per 100 thousand in 2009 to 14.8 per 100 thousand in 2018 is specific for long-term changes during 2009–2018 (Fig. 2). When comparing 95% confidence limits of theoretical levels of male incidence I theor. for 2009 ($3.1 \div 7.0$ per 100 thousand) and I theor. for 2018 ($9.8 \div 15.7$ per 100 thousand), no transgression was revealed, that is, a statistically significant upward trend ($p = 0.004$) with a growth rate of 110.7% and accession rate of +10.7% is specific for dynamics of the CSCP incidence annual values among the Kazan male population in 2009–2018.

The CSCP incidence in the Kazan male population has increased by 2.5 times over 9 years (I theor. for 2009: 5.1 per 100 thousand, and for 2018: 12.7

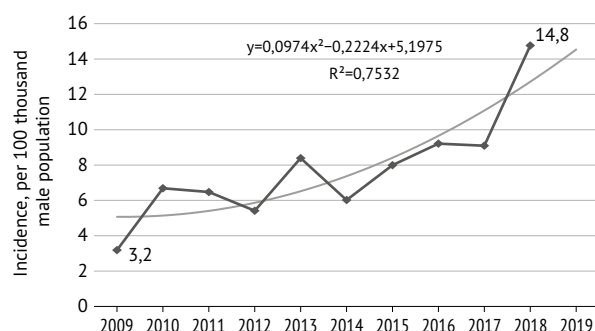


Fig. 2. Long-term dynamics of the central serous chorioretinopathy incidence among the Kazan male population in 2009–2018

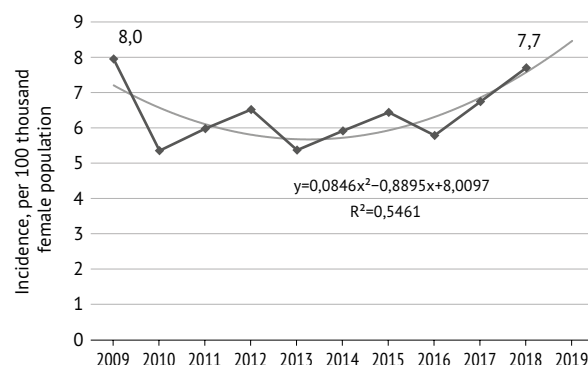


Fig. 3. Long-term dynamics of central serous chorioretinopathy incidence among the Kazan female population in 2009–2018

Table 1. Results of the central serous chorioretinopathy incidence trend assessment in the Kazan male and female population in 2009–2018.

Group	Value	Trend formula ($x = 1-10$)	First year of the trend	Last year of the trend	The difference in values of trend in the last years	Contribution to the general trend. %
Male	I	$I_{\text{theor.}} = 0.0974x^2 - 0.2224x + 5.1975$	5.1	12.7	7.6	86.5
	Abs.		25	70	45	
Female	I	$I_{\text{theor.}} = 0.0846x^2 - 0.8895x + 8.0097$	7.2	7.6	0.4	13.5
	Abs.		45	52	7	
Whole population	I	$I_{\text{theor.}} = 0.0906x^2 - 0.5957x + 6.7648$	6.3	9.9	3.6	100
	Abs.		70	122	52	

Note: I: incidence; I theor.: theoretical values of incidence.

per 100 thousand; see Fig. 2). The mean predictive male CSCP incidence rate in 2019 was 14.5 per 100 thousand, and the maximum and minimum predictive incidence rates were 16.2 and 13.4 per 100 thousand, respectively.

Moreover, female CSCP incidence over a similar period of time remains at the same level, varying from 5.4 to 8 cases per 100 thousand female population (Fig. 3). When comparing 95% CI of theoretical values of male incidence $I_{\text{theor.}}$ for 2009 (7.2 per 100 thousand; 95% CI 5.1 ÷ 9.3) and $I_{\text{theor.}}$ for 2018 (7.6 per 100 thousand; 95% CI 5.5 ÷ 9.6), a transgression of confidence limits was revealed; therefore, the trend of CSCP incidence dynamics among the Kazan female population in 2009–2018 is considered as statistically insignificant ($p = 0.663$). The mean predictive female CSCP incidence rate in 2019 was 8.5 per 100 thousand, and the maximum and minimum predictive incidence rates were 8.9 and 8.0 per 100 thousand, respectively.

The contribution of the incidence trends of each group to the trend of total values was also calculated. Males have the greatest influence on the general trend in the CSCP incidence in the Kazan

population in 2009–2018, with contribution of 86.5% (Table 1).

Analysis of age characteristics depending on sex. When analyzing the distribution of all CSCP cases by sex and age for 2009–2018 ($n = 831$), the female median age at the time of diagnosis was 55 years old (Q25–Q75: 45–65 years old) and the male median age was 45 years old (Q25–Q75: 37–56 years old; Mann–Whitney U test: 60,403; $p = 0.0001$). Therefore, CSCP develops in males at a younger age.

Discussion. Kazan is one of the largest industrial centers in Russia. At the beginning of 2020, 1,257,391 people lived in Kazan. Males make up 44.6% and females 55.4% of the urban population of the Republic.

Our study revealed the individual trends of the CSCP epidemic process manifestation in Kazan. At the beginning of the studied period, females predominated in the incidence structure, with incidence rate of >2 times higher than that of the male (8.0 versus 3.2 per 100 thousand in 2009); however, males began to prevail in the last 4 years according to incidence rates. Reasons for the identified trends require further study.

Globally, only two descriptive studies of the CSCP was reported, which showed a male to female ratio of 5.7:1 in Olmsted County, Minnesota, USA, in 1980–2002 [5] and 1.74:1 in Taiwan in 2001–2006 [6]. Our results showed that the total male to female ratio was 1:1 in Kazan in 2009–2018, whereas dynamics of the incidence structure has changed with a predominance of the male proportion in recent years (60.7% versus 39.3% in 2018, male to female ratio in 2018 was 1.5:1).

CSCP more often affects males of working age [4]. Assuming that sex differences in the CSCP frequency is reasonable due to differences in the male and female hormonal background. Testosterone is a vasoactive hormone that increases vasodilation which in turn becomes a presumed step in CSCP development [8]. The link between CSCP occurrence and testosterone levels was first noted by M.A.Ahad et al., who reported a case of CSCP in a patient receiving long-term systemic testosterone therapy [9]. In 2018, a small study revealed a statistically significant excess of testosterone levels in patients with CSCP compared to that of the control group [10].

In females, CSCP develops less frequently [5,6]. Moreover, the risk of disease is also largely associated with hormonal changes. Researchers associate CSCP development with an increase of endogenous corticosteroid levels in females during pregnancy [2,11–15] or with the intake of endogenous testosterone by postmenopausal women to relieve certain symptoms of menopause, in particular, loss of libido [16].

A retrospective epidemiological analysis of CSCP incidence in 1980–2002 conducted using the data from Olmsted County, Minnesota, USA, revealed that the mean long-term incidence rate was 9.9 per 100 thousand (95% CI 7.4–12.4) in males and 1.7 per 100 thousand (95% CI 0.7–2.7) in females [5]. The second study conducted in Taiwan revealed an increase in CSCP incidence among the total population with mean annual incidence rate of 27 per 100 thousand in males and 15 per 100 thousand in females [6]. An increase in the incidence is also specific for long-term changes in Kazan during 2009–2018 [17]. In addition, males have the greatest influence on the general trend in CSCP incidence rate in the Kazan population in 2009–2018. The male incidence during the study period shows a statistically significant increase, whereas the female CSCP incidence remains.

In a retrospective epidemiological study conducted in Taiwan, the mean age of patients at the time of CSCP diagnosis was 40.5 ± 9.5 years in males and 37.2 ± 11.8 years in females [6], which is less than the age of patients in our study: female

median age was 55 years and male median age was 45 years. Our earlier study [17] revealed a change in the age incidence structure in dynamics with a tendency toward “rejuvenation”: Me of 56.5 years (Q25–Q75: 41–67) in 2009 versus 46 years (Q25–Q75: 37–61) in 2018. These changes are probable to be associated with an increase in intensive and extensive values of male CSCP incidence, which are characterized by a relatively early development of the disease ($\approx$ by 10 years earlier than females).

Patterns of CSCP epidemic process vary in different regions which in part can be related to differences in the distribution of risk factors. Consequently, it is important to monitor the epidemiological situation for a timely response to changes in the epidemic process manifestations, as well as to conduct studies to identify relevant risk factors for CSCP both in general and individual regions, which in the future can contribute to the development of an effective prevention strategy for this disease.

CONCLUSIONS

1. In 2009–2018 in Kazan, the male incidence of CSCP significantly increased in both intensive ($p = 0.004$) and extensive ($p = 0.000002$) values.
2. CSCP develops in males at an earlier age than in females (female Me age at the time of diagnosis is 55 years and male is 45 years, $p = 0.0001$).
3. Further trials are required to study the causes of the revealed trends in the CSCP incidence manifestations.

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