Meteopathogenic Mechanisms Of Development And Aspects Of Prevention Of Glaucoma Under The Conditions Of A Risk Continental Climate Of Uzbekistan

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ABSTRACT: In recent years, there have been significant changes in the field of screening diagnostics and glaucoma prevention. At the same time, the specificity of glaucoma control, due to a number of regional reasons, needs corrections. In a prospective clinical and meteorological study, 1112 cases of glaucoma were analyzed. A direct dependence of the development of glaucoma on the level of fluctuations of the main meteorological elements – atmospheric pressure, relative humidity of air, solar fusion and thermal regime was noted. The scientific foundations have been created for the implementation of effective methods of meteorological prevention off glaucoma in the sharply continental climate of Uzbekistan.

Key words: glaucoma, methihelioprophylaxis, chronic non-infectious pathologies, pathomorphosis, climatoclinicobiorhythmic, prophylaxis, factors, clinical, monitoring.

1. INTRODUCTION

Researchers are actively studying the role of climatic-meteorological and epidemiological factors in different regions of the world in the development of eye diseases [1,2]. The presence of meteorological discomfort contributes to the unfavorable course of eye diseases, their frequent relapses, chronicity and the development of ophthalmic endpoints [3,4,6,7].

We analyzed how other health care specialties deal with issues of screening and prevention for OA to realize the relevance of the problem of glaucoma prevention.

First of all, it should be noted that preventive examinations in certain specialties appeared long before screening programs. They were carried out at the beginning of the 20th century. A team of doctors (from 3 to 10) and through dispensary observation of patients through the work of practical health authorities (this practice persisted until the 90s of the last century) of the former USSR [12] or family enemies or an enemy of general practice (for example, in the USA) for more a selective approach to the individual risk of developing certain diseases [10,15,16]. Preventive examinations / studies are intended for healthy people or people who do not have symptoms of disease and detect early stages of the disease [13]. In preventive examinations / screenings, they are detected as a case of diseases, not only of an

early and / or asymptomatic, but also at an advanced stage. Preventive examinations do not include treatment / control of the dynamics of existing diseases and they are carried out with the aim of measuring the general state of health, identifying risk factors and early signs of the disease (which were not yet known), as well as to prevent diseases in the future through early intervention.

Preventive measures (implementation of a structured lifestyle change program - "A + B + C + D + E + F + G + H + I'' of the primary prevention alphabet: aspirin, blood cholesterol, cigarettes, diabetes, physical activity, food, obesity, high pressure, "uneven pulse") is usually sufficient to control symptoms and improve quality of life in most patients, given that the risks of surgery often outweigh the benefits [17,18,19]. In general, screening prophylaxis, including meta helio prophylaxis, for any disease is considered good clinical practice only when effective treatment is available and available for the particular disease, such as glaucoma. Persons with risk factors, diabetes mellitus have an increased risk of developing not only cardiac pathology, but also eye diseases, for example, glaucomatous process, which often develop at an earlier age than those without diabetes and / or risk factors (generally, meteorological, heliogeophysical, climate-weather, etc.). In the modern literature, the main provisions of the primary methi helioprophylaxis of cardiovascular diseases (CVD) and chronic non-infectious pathologies (CNID) are presented. According to epidemiological studies, it is important to engage in primary prevention of chronic diseases from childhood, since pathogenic "risk factors", which are formed in childhood and adolescence, are "resistant" and subsequently move into the lifestyle of an adult [20,21,22] ... The concept of risk factors, formulated in the 60s of the twentieth century, is based on the results of epidemiological studies and is currently a methodological basis for planning and organizing the primary prevention of CVD and chronic diseases [23,24].

According to the concept, there are behavioral (undergoing correction) and nonmodifiable risk factors (age, gender, genetic predisposition - they cannot be corrected). Behavioral risk factors include: smoking, unhealthy diet, low physical activity, and abundant alcohol consumption, chronic psycho-emotional stress, meteorological and climate pathogenetic factors. These are the most frequently noted modifiable risk factors in the lifestyle of a modern person and patients, which either contribute to the development of CNCD and/or lead to an "end point" from them, including [25]. At the same time, according to the WHO, with the modification of risk factors, more than 75% of deaths, for example, from CVD, can be prevented (INO, 2015).

At the moment, studies of the evidence base for the application of methods of prospective clinical and meteorological observation, meteorological forecasting and meteorological prophylaxis for the prevention of major eye diseases are ongoing. So, scientists of our country for the first time developed, studied and tested the method of clinical and meteorological observation of patients with keratitis, revealed the features of the formation and pathomorphosis of the clinical course of keratitis in a sharply continental climate. For the first time, a new and perfect technique with bioclimate grams has been developed and implemented. It has been proven that the use of this technology in the Fergana Valley increases the effectiveness of the treatment and prophylactic programs of keratitis used in practice [26].

The noted connections of some eye diseases with the "main" meteorological factors (MF) expanded the understanding of risks with meteorological factors and, therefore, made it possible to pay new attention to the regional aspects of meteorological prevention and prenosological diagnosis of not only chronic, but also acute eye diseases. It is recommended that in order to reduce complications of ophthalmic pathologies, public health authorities should have the results of epidemiological studies and clinical meteorological observations in each region.

[5,9,10]. Meanwhile, these topical issues of ophthalmological science and practice remain insufficiently studied, for example, in the example of glaucoma, in many regions of our planet with a sharply continental climate, in particular, in Uzbekistan.

It seems possible to assert that the study of the climate of meteorological characteristics of glaucoma is not only of medical importance, but also of great state and national economic importance. The prognosis for the next few years in relation to eye diseases is unfavorable - a significant increase in the number of patients with glaucoma and a deterioration in meteorological conditions in Uzbekistan in general and in the Fergana Valley in particular are predicted [4,5].

The aim of the study is to study meteorological mechanisms of development and to determine aspects of glaucoma prevention in the sharply continental climate of the Fergana Valley of Uzbekistan.

2. MATERIAL AND METHODS

The Fergana Valley subjected to climate meteorological monitoring, reflects all the characteristics of Uzbekistan and, with its specific climatoclinicobiorhythmic has a pathogenic effect on the development and course of eye diseases.

The region is a huge intermountain depression, surrounded on all sides by mountains and in the west it connects with the Dalvarzin steppe.

This is reflected in the climate, which in general is characterized as sharply continental, dry and hot. The city of Andijan is an important transport hub in southeastern Fergana and lies on the Andijan River in the southeastern part of the Fergana Valley. Due to the physical and geographical conditions and the atmospheric processes conditioned by them, the climate of Andijan, reflecting all the specifics of the territory of the Fergana Valley, acquires a sharply continental character: cloudy weather prevails, precipitation is frequent, strong winds are rare. In addition, winter is stable here, spring and autumn are warm, summers are dry and hot [11]. Prospective clinical and meteorological observation was carried out in Andijan together with the staff of the regional bureau of meteorological management for 3 years. 1112 cases of glaucoma were analyzed according to the data of the regional eye dispensary, of which there were 401 men (36.06%), 711 women (63.93%). At the age of 15-19 there were 18 (16%), 20-29 years old - 30 (2.7%), 30-39 years old - 46 (4.1%), 40-49 years old - 68 (6.2%), 50-59 years old - 203 (18.5%), 60-69 years old - 472 (42.4%) and over 70 years old - 275 (24.4%).

Table of indications for populations											
Group of	Types of	of glaucor	na			Swelling	Total				
population	Open	Closed	Mixed	Glaucom	Terminal	cataracts	glaucom				
	corner	corner	glaucom	a attack	glaucoma		a				
	eye	eye	а								
Men	130	138	37,9	28,9	29	20	401				
							36,06				
	38,9	35,4	10,4	9,0	39,7	27,7					
Women	204	251	62,06	98	44	52	711				

Table No. 1

Table of indications for populations

							63,93
	61,1	64,5	16,7	71,1	60,3	72,2	
Total							1112
	334	389	116	138	73	72	
							100,0
	100,0	100,0	100,0	100,0	100,0	100,0	
r (+/-)	0,821	0,821	0,821	0,804	0,804	0,804	0,946
Mp (+/-)	0,255	0,255	0,255	0,266	0,266	0,266	0,144
t	3,221	3,221	3,221	3,019	3,019	3,019	6,554
Р	P<0,0 1	P<0,0 1	P<0,01	p<0,05	p<0,05	p<0,05	p<0,001

The material was analyzed for every day, day, month, season and year for 3 years. Along with clinical and meteorological observations, clinical and instrumental ophthalmological biochemical and, according to indications, special studies were carried out, when dealing with an attack of glaucoma upon admission to a hospital, during the period of deterioration of the clinical course of glaucoma associated with changes in meteo conditions and during the period of deterioration of anti-optical weather situations. The clinical diagnosis of glaucoma was established by generally accepted international criteria and classifications, and the verification of the diagnosis in inpatients was based on the analysis of clinical manifestations, anamnestic data, results of ophthalmoscopy and tonometry (Joseph Flammer, 2006). From the magazines TM-1, TM - 12 and TM - 15 of the regional hydro meteorological center, according to the agreement, data were copied on the actual levels of meteorological factors (MF) and the gradient of the potential of atmospheric electricity observed in the atmosphere of Andijan over 3 years, 6 hour interval. A bank of information has been accumulated on the main MF: atmospheric pressure (AP, in mb), air temperature (TV, in C0), relative air humidity (RAH, V %) and the duration of solar fusion (CC, in hours). The quantitative method of analysis of the morbidity rate according to N.R. Deryapa and co-author (1985) and determined the "rhythm" of glaucoma. The study used the dynamic method of G.M. Danishevsky, according to which the influence of MF on the development of glaucoma was analyzed. The dynamics of correlations between glaucoma and meteorological factors of the region was studied using the table by V.S. In addition, we have developed and used a special dynamic observation method, consisting of clinical and meteorological parts, which reflected the international experience of the registration of pathological dynamics in patients with glaucoma and fluctuations in the meteopagodic regime. The drops of meteorological conditions were determined according to the method proposed by V.F. Ovchatova.

In processing the research results, the methods of relative statistics Microsoft Excel - 2000, the Spriman method, paired and unpaired Student's tests were used. Differences between groups were considered significant at a significance level of less than 95% (P <0.05).

3. RESULTS AND DISCUSSION

Our task was to study and identify the features of the development of glaucoma, depending on the level and fluctuations of AD in the sharply continental climate of the

Andijan region of the Fergana Valley. The data obtained show that glaucoma at different levels of AD is characterized by an increase of 27.1%, that is, by 5.4 times (from 0.3-5.5% with AD 950 mb to 27.1% with AD 966- 970 mb, $\tau = +$ 0.93, P <0.001). Depending on fluctuations in the level of AD (from \leq 945 mb to \geq 975 mb), the frequency of occurrence of angle glaucoma increases to 28.7% ($\tau = +$ 0.80, P <0.05), angle-closure glaucoma increases by 22.5% ($\tau = +$ 0.93, P <0.001). With an increase in barometric pressure, there is an increase in the frequency of detection of acute glaucoma pricks by 8 times ($\tau = +$ 0.86, P <0.01). But in cases of suspicion of glaucoma, depending on the level of AD, during the year, it is registered with an increase of 42.9% (with AD \geq 971-975 mb, $\tau = +$ 0.82, P <0.01). Thus, a direct dependence of the development and or recurrence of glaucoma on the level of AD oscillations which is essential in optimizing the provision of high-quality and effective medical treatment to this contingent of patients in the conditions of this region. In the course of prospective monitoring, the relationship between glaucoma and relative humidity was also established:

Table No. 2	n					n	
Indications	Expected	fluctuation	s of Glauc	coma at a	atmospheric		
Atmospheri	pressure						a
c pressure	Open angle glaucom	Closed angle glaucoma	Mixed glaucoma	Glaucom a attack	Terminal glaucoma	Suspicion on glaucoma	General quantity of glaucoma
≤ 945	0,33%	0,24%	0,00%	0,00%	0,00%	0,00%	0,18%
946 - 950	2,30%	3,60%	11,21%	1,44%	0,00%	0,00%	3,33%
951 - 955	10,82%	8,63%	29,31%	32,37%	4,76%	1,39%	13,67%
956 - 960	23,28%	17,03%	17,24%	20,86%	14,29%	9,72%	18,62%
961 - 965	16,39%	20,14%	12,93%	12,23%	11,11%	30,56%	17,54%
966 - 970	22,62%	28,54%	17,24%	22,30%	41,27%	23,61%	25,36%
971 - 975	24,26%	21,82%	12,07%	10,79%	28,57%	34,72%	21,31%

Prediction table for primary glaucoma with fluctuations in atmospheric pressure Table No. 2

Expectancy table for primary glaucoma with fluctuations in air humidity: Table No. 3

Indications	Expected		ons of gla	aucoma a	at relative	Suspected	Total
relative	humidity	*		1	1	glaucoma	glaucoma
humidity:	д д	n	n	вц	n		
	e u	ed cor	ed be	ack	nin cor		
	Open angle glauc	Closed angle glaucom a	Mixed glaukom a	Glaucom a attack	Terminal glaucom a		
	g an O	∍ ∞] at	a ∞ Z	a G	ਬ ਕਿ ਜੋ		
<u><</u> 46	9,45%	5,65%	12,69%	12,61%	0,85%	1,75%	8,00%

47 - 55	7,42%	7,93%	6,80%	9,33%	2,08%	6,96%	7,42%
56 - 64	12,99%	12,42%	13,88%	11,90%	6,36%	4,41%	12,17%
65 - 73	12,62%	14,82%	11,50%	11,89%	20,35%	15,83%	14,11%
74 - 82	19,04%	17,28%	12,91%	15,28%	20,35%	11,00%	16,91%
83 - 91	17,82%	16,65%	20,21%	16,95%	9,29%	19,38%	17,16%
92 - 100	20,65%	25,25%	22,02%	22,04%	40,71%	40,67%	24,24%

high levels of glaucoma were observed with high values and fluctuations in RAH (\geq 92-100%) in the studied region of the Fergana Valley. So, as the RAH rushed from \leq 46% to 92-100%, glaucoma increased by 14.4% (from 7.5% to 21.9%) and or 2.9 times ($\tau = + 0.99$, P < 0.001). The detection rate of cases of acute angle glaucoma (AAG) increases, depending on the level of RAH, 3 times (by 15.5%, $\tau = + 0.80$, P <0.05). Closed-angle glaucoma (CAG) and mixed glaucoma (MG) at different levels of barometric pressure are observed with an increase of 22.2% and or 4.9 times, respectively ($\tau = + 0.77$, P <0.05) and 21, 0% and or 3.7 times ($\tau = + 0.80$, P <0.05). In almost every fifth patient (21.5%), an acute attack of glaucoma coincides with the days of a sharp increase in RAH ($\tau = + 0.71$, P <0.05). It was found that there is a direct strong correlative relationship between the thermal regime and glaucoma among the population: with an increase in TH and an increase in its fluctuations, a significant increase in the cases of glaucoma detection is observed. We think these facts open up the prospect of chronometric prophylaxis and chronotherapy of glaucoma among the population.

During a 3-year clinical meteorological study, it was noted that glaucoma with an increase in air temperature increases from 0.0% at AH <- 8.7 C0 to 17.0 5 - at AH \ge 25.4 - 28.7 C0 (τ = + 0, 94, P <0.001).

Expectancy table for primary glaucoma	with increasing air temperature:
---------------------------------------	----------------------------------

ar	Expected	d glaucoma at	an increased	temperatu	ire	Suspected	Total
solar	gle	_	la	X		glaucoma	glaucom
	angle	d glaucoma	glaucoma	attack			a
us	ខ	auc	lau		l l		
tio	r com			con	rom		
ndications merger	Open glaucoma	Closed angle g	Mixed	Glaucoma	Terminal glaucoma		
<u>ц</u>	0 50	a C	4	0	н ра		
<u>≤</u> -8,7	0,33%	0,25%	0,00%	0,00%	0,00%	0,00%	0,18%
-8,65,3	0,00%	0,25%	0,00%	0,00%	0,00%	0,00%	0,09%
-,,-	-,-,-	- , *	- , •	- , - 3 , -	-,	- ,	- , •

Table No. 4

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-5,21,9	3,32%	3,96%	1,23%	0,00%	0,00%	0,00%	2,55%
-1,8 - 1,5	9,65%	9,48%	7,87%	10,29%	9,98%	8,39%	9,76%
1,6 - 4,9	9,12%	9,18%	8,53%	13,59%	21,86%	3,87%	10,14%
5,0 - 8,3	10,73 %	9,73%	10,34%	12,40%	31,87%	7,99%	10,74%
8,4 - 11,7	7,10%	7,08%	3,32%	4,44%	9,04%	6,37%	6,54%
11,8 - 15,1	7,97%	9,28%	5,98%	8,65%	5,86%	13,56%	8,84%
15,2 - 18,5	11,88 %	8,86%	4,36%	3,64%	7,57%	7,44%	8,74%
18,6 - 21,9	11,17 %	15,09%	14,31%	6,50%	1,71%	18,63%	12,35%
22 - 25,3	12,19 %	8,99%	17,25%	20,39%	7,50%	15,83%	12,23%
25,4 - 28,7	16,55 %	17,86%	26,81%	20,10%	5,62%	17,93%	17,85%

Depending on the severity of the thermal regime, it also increases - OAG by 22.5% ($\tau = + 0.82$, P <0.01), CAG by 15.6% ($\tau = + 0.60$, P <0.05), MG - by 40.6% ($\tau = + 0.90$, P <0.001) and acute attacks of glaucoma (OPG) - by 20.0% ($\tau = + 0.81$, P <0.01). It should be noted that the development of glaucoma also depends on the next meteorological element - solar fusion: its detection with a lower prevalence is noted at CC levels ≤ 1.3 h (4.6%), and a high frequency is diagnosed at CC \geq 7.9-9.1 hours - 16.6%. That is, under the influence of SS, the frequency of glaucoma detection increases by 4 times ($\tau = + 0.95$, P <0.001).

T	able No. 5			-	-	-		
	ar	Suspected	Total					
	sol	le		a	×		glaucoma	glaucom
		angle	oma	omo	attack			а
	SU		<u> </u>	glauc		_		
	tioı r	oma	d glau		Glaucoma	Terminal glaucoma		
	Indicati merger	pen laucc		Aixed	inco	Ferminal glaucoma		
	Indicat merger	Op gla	Close angle	Mi	GI	Ter gla		

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r		1			-	-	-
.1.2	3	7	0	0	0	4	14
<u>≤</u> 1,3	3,2%	7,9%	0,0%	0,0%	0,0%	1,8%	4,6%
	2	6	2	0	6	5	21
1,4 - 2,6	2,2%	6,7%	5,3%	0,0%	10,0%	2,3%	7,0%
	5	9	1	2	0	2	19
2,7 - 3,9	5,4%	10,1%	2,6%	3,5%	0,0%	10,5%	6,3%
	3	11	0	4	0	1	19
4,0 - 5,2	3,2%	12,4%	0,0%	7,0%	0,0%	10,5%	6,3%
	7	9	0	3	0	3	22
5,3 - 6,5	7,5%	10,1%	0,0%	5,3%	0,0%	15,8%	7,3%
6,6 - 7,8	4	7	4	3	0	2	20
	4,3%	7,9%	10,5%	5,3%	0,0%	16,8%	6,6%
	14	18	7	9	0	2	50
7,9 - 9,1	15,1%	20,2%	18,4%	15,8%	0,0%	20,5%	16,6%
	13	15	3	9	0	0	40
9,2 - 10,4	14,0%	16,9%	7,9%	15,8%	0,0%	0,0%	13,2%
	16	4	7	11	0	0	38
10,5 - 11,7	17,2%	4,5%	18,4%	19,3%	0,0%	0,0%	12,6%
	12	1	6	4	0	0	23
11,8 - 13	12,9%	1,1%	15,8%	7,0%	0,0%	0,0%	7,6%
	14	2	8	12	0	0	36
13,1 - 14,3	15,1%	2,2%	21,1%	21,1%	0,0%	0,0%	11,9%
Жами:	93	89	38	57	6	19	302
	100%	100%	100%	100%	100%	100%	100%

The largest number of cases of OAG, with an increase of 8 times, with a duration of CC from 11.8 to 13.1 hours ($\tau = +0.84$, P <0.01).

The formation of CAG and MG against the background of CC fluctuations increases by 2.6 times ($\tau = +0.99$, P <0.001) and by 18.4%, respectively ($\tau = +0.78$, P <0.01). A distinct correlative relationship was established between SS and an attack of glaucoma: EPG against the background of CC fluctuations during the year increases by 21.1% ($\tau = +0.87$, P <0.01). Thus, our results show the presence of a connection between glaucoma and CC and other main meteo elements, which is of direct practical importance in the development and implementation of large-scale regional treatment and prevention programs for glaucoma among the population.

Glaucoma Expectancy Chart at Atmospheric Pressure and air humidity Table 6

	Relativo	e humidity	ý						
		0	9	18	27	36	45	54	63
	0	0,000	0,085	0,171	0,256	0,341	0,426	0,512	0,597
	5	-0,158	-0,073	0,013	0,098	0,183	0,268	0,354	0,439
	10	-0,316	-0,231	-0,145	-0,060	0,025	0,111	0,196	0,281
	15	-0,474	-0,388	-0,303	-0,218	-0,133	-0,047	0,038	0,123
	20	-0,632	-0,546	-0,461	-0,376	-0,291	-0,205	-0,120	-0,035
ssure	25	-0,790	-0,704	-0,619	-0,534	-0,448	-0,363	-0,278	-0,193
Atmospheric air pressure	30	-0,947	-0,862	-0,777	-0,692	-0,606	-0,521	-0,436	-0,351
Atmosphe	35	-1,105	-1,020	-0,935	-0,850	-0,764	-0,679	-0,594	-0,805

Solar fusion													
		0	1,3	2,6	3,9	5,2	6,5	7,8	9,1	10,4	11,7	13	14,3
Air temperature	0	0,00 0	0,01 1	0,02 2	0,03 2	0,04 3	0,05 4	0,06 5	0,07 5	0,08 5	0,09 6	0,10 7	0,117
	2,4	0,00 0	- 0,055	- 0,045	- 0,034	- 0,023	- 0,01 2	- 0,002	0,00 9	0,08 7	0,09 8	0,10 9	0,119
	4,8	0,00 0	- 0,122	- 0,111	- 0,100	- 0,089	- 0,07 9	- 0,068	- 0,057	0,08 9	0,10 0	0,11 1	0,121
	7,2	0,00 0	- 0,188	- 0,177	- 0,166	- 0,156	- 0,14 5	- 0,134	- 0,123	0,09 1	0,10 2	0,11 2	0,123
	9,6	0,00 0	- 0,254	- 0,243	- 0,233	- 0,222	- 0,21 1	- 0,200	- 0,189	0,09 3	0,10 4	0,11 4	0,125
	12	0,00 0	- 0,320	- 0,309	- 0,299	- 0,288	- 0,27 7	- 0,266	- 0,256	0,09 5	0,10 5	0,11 6	0,127
	14, 4	0,00 0	- 0,386	- 0,376	- 0,365	- 0,354	- 0,34 3	- 0,333	- 0,322	0,09 6	0,10 7	0,11 8	0,128
	16, 8	0,00 0	- 0,453	- 0,442	- 0,431	- 0,420	- 0,41 0	- 0,399	- 0,388	0,09 8	0,10 9	0,12 0	0,130
	19, 2	0,00 0	- 0,529	- 0,529	- 0,529	- 0,529	- 0,52 9	- 0,529	- 0,529	0,01 5	0,01 5	0,01 5	0,016
	21, 6	0,00 0	- 0,596	- 0,596	- 0,596	- 0,596	- 0,59 6	- 0,596	- 0,596	0,01 7	0,01 7	0,01 7	0,017
	24	0,00 0	- 0,663	- 0,663	- 0,663	- 0,663	- 0,66 3	- 0,663	- 0,662	0,01 9	0,01 9	0,01 9	0,019
Air tem	26, 4	0,00 0	- 0,730	- 0,730	- 0,730	- 0,729	- 0,72 9	- 0,729	- 0,729	0,01 3	0,02 1	0,02 1	0,021

Table of expected clinical course at temperature air and solar fusion. Table No. 7

4. CONCLUSIONS

1. Preconditions and scientific basis have been created for the implementation of methods of primary and secondary meteorological prevention of glaucoma among the population of the Fergana Valley of Uzbekistan.

2. In the course of prospective observations, the developed methods of clinical meteorological monitoring, which remained on the use of meteo prognosis, make it possible to provide a true basis for planning and realizing effective meteorological and preventive glaucoma thresholds among the population.

3. In the overwhelming majority of cases, the development of glaucoma coincides with an increase in the fluctuations of meteorological elements and coincides with the days of different meteorological discomfort, due to such basic MF as AP, RAH, TH and CC.

CONFLICT OF INTERESTS AND CONTRIBUTION OF AUTHORS

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article and report on the contribution of each author.

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