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## Epidemiological and clinical-functional aspects of the combined course of age-related macular degeneration and primary glaucoma

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*Age-related macular degeneration (AMD) and glaucoma are currently the main causes of irreversible vision loss in developed countries.*

**Purpose.** To study the epidemiological and clinical-functional aspects of the combined course of age-related macular degeneration and primary glaucoma and to assess the quality of life of these patients.

**Material and Methods.** The analysis of 5,000 outpatient records of patients over 40 years of age who were observed in the consultative polyclinic of the multidisciplinary clinic of the Tashkent Medical Academy in the period 2011-2022 was carried out. All patients were divided into three groups: group 1 – glaucoma, group 2 – AMD and group 3 – glaucoma + AMD.

**Results.** A retrospective analysis of 5,000 outpatient records of patients older than 50 years revealed the presence of glaucoma in 30.3% of cases, AMD – in 37.94% and their combination – in 20.3%. At the same time, in the structure of AMD, signs of the dry form of the disease were diagnosed in 74% of cases, geographical atrophy – in 12% and wet form – in 14%. However, it requires careful monitoring of the dynamics of visual-functional and structural changes in the retina and optic nerve, as well as timely correction of therapy.

**Conclusion.** The combined course of diseases having a neurodegenerative nature of the lesion leads to a decrease in not only visual, but also cognitive functions, significantly affecting the quality of life of patients of the older age group and their adaptation in society.

### Keywords:

age-related macular degeneration, primary glaucoma, geographic atrophy

**Introduction.** With an increase in life expectancy and the number of elderly people in the structure of the population, the prevalence of age-dependent diseases also sharply increases, of which diseases of the organ of vision are the most significantly affecting the quality of life. According to UN forecasts, in the next 40 years, the proportion of people over 60 will almost double: from 11.7% in 2013 to 21.1% of the world population by 2050. [1]. In Uzbekistan, in 2019 the proportion of people of retirement age was 10.2% of the total population, and in Tashkent, their number already reaches 15.7%. [2, 3, 4]. More than 246 million people worldwide are visually impaired, of which 45 million are blind, with an annual increase of 1-2 million per year. Glaucoma and age-related macular degeneration (AMD) are the main causes of severe vision loss, and in the case of glaucoma, even complete blindness. [5, 6].

A meta-analysis showed that 7-8% of the world population suffer from AMD, the approximate number of cases in the world by 2020 was 196 million people and will increase to 288 million in 2040. [7]. The diagnosis of glau-

coma was established in 67 million people, which is 12.3% of the world population, it is expected to increase the number of such patients to 76 million by 2020 and to 111,8 million by 2040. In Europe, glaucoma is diagnosed in 21,8% of the population, while in the structure of blindness, it is 20.8%, AMD - 26%. [8]. In the Russian Federation, glaucoma leads in the structure of causes of blindness and averages 27%, the share of AMD is 12.5%. [9, 10]. Epidemiological studies have revealed a common prevalence of AMD and glaucoma in the population aged 52–85 years of 0.1%, and among patients with AMD, the incidence of glaucoma averaged 5,4%. [11]. For the period from 2014 to 2019 in the Republic of Uzbekistan, the average period rates of primary and general incidence of glaucoma in Uzbekistan amounted to  $39,8 \pm 0,4$  and  $161,2 \pm 0,9$  cases per 100,000 adults, and for the first time recognized as disabled by glaucoma increased by 2,5 times, the number of

people with general disability increased by 1,3 times. [12-16].

As chronic progressive multifactorial diseases, AMD and glaucoma are becoming the main causes of suffering in older patients. [17]. The common features of these independent, seemingly independently occurring diseases are the relationship with age, common risk factors, asymptomatic onset, chronic progressive course, bilateral asymmetrical process, and the need for early diagnosis. [18, 19]. The combined course of diseases in the absence of adequate control of the level of intraocular pressure and the degree of functional and structural disorders leads to a pronounced decrease or loss of vision.

By affecting peripheral and central vision, both diseases significantly affect the quality of life and have a higher likelihood of suffering from problems with movement, the possibility of self-administration of medications and poor psychological health, which significantly affects the health of the nation and increases healthcare costs. Thus, in the advanced stage of glaucoma, a decrease in photosensitivity by 5 dB is associated with an increase in the likelihood of disturbances in daily activities, and a decrease in visual acuity in AMD in the better-seeing eye by one line is associated with a 35% increase in this probability [20].

The purpose of the study was: to study the epidemiological and clinical and functional aspects of the combined course of age-related macular degeneration and primary glaucoma and to assess the quality of life of these patients.

**Material and methods**

We analyzed 5,000 outpatient records of patients over 40 years old, observed in the consultative polyclinic of the multidisciplinary clinic of the Tashkent Medical Academy in the period 2011-2022. All patients were divided into three groups: group 1 - glaucoma, group 2 - AMD and group 3 - glaucoma + AMD. Based on the data obtained, we analyzed: the incidence of glaucoma and AMD in different age groups, the distribution of AMD clinical forms depending on the stage of glaucoma, the distribution structure of concomitant diseases, demographic and clinical and functional parameters of patients in the compared groups. The use of

the NEI-VFQ-25 questionnaire allowed us to carry out a comparative analysis of the main characteristics that affect the quality of life of patients with glaucoma, AMD, AMD in combination with glaucoma, and control group patients.

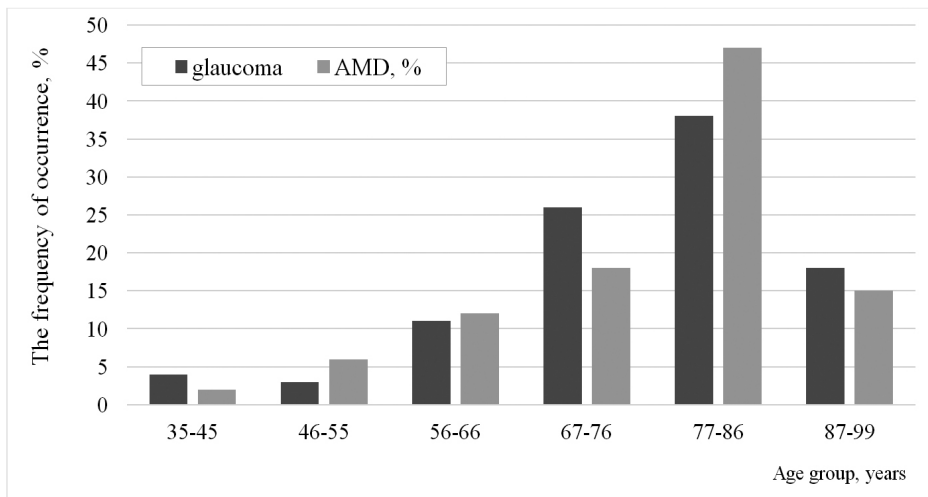
The obtained data were subjected to statistical processing using the statistical analysis software package using the Microsoft Excel 2010 software package, using the library of statistical functions with the calculation of the arithmetic mean (M), standard deviation function ( $\sigma$ ), standard error (m), relative values (frequency, %), when comparing quantitative and nominal data, Student's test (t) and Fisher's exact test were used, respectively, with the calculation of the error probability (P) of correlation analysis methods. The significance level for the respective criteria was  $P < 0.05$ .

**Results and discussion**

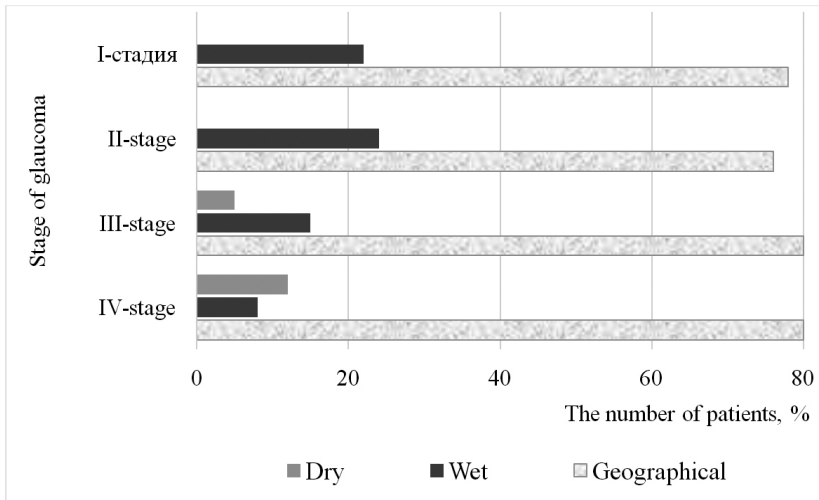
A retrospective analysis showed that 1651 (30,3%) people were diagnosed with glaucoma, 1897 (37.94%) with AMD, and 3245 (64,9%) with cataract. The combination of glaucoma with AMD was found in 1015 (20,3%) patients, glaucoma with cataract in 1289 (64.9%), AMD with cataract in 1579 (31,58%). Among patients with glaucoma, persons over the age of 60 account for 89.4% (including 25,97% over 80 years), among patients with AMD - 90% (including 54% over 80 years). The incidence rate in different age groups is shown in Fig.1.

Out of 1650 patients with glaucoma (we take into account one worst eye), the majority (1421, 86.12%) have primary open-angle glaucoma, while 963 (58,34%) patients have been followed up for more than 5 years.

When analyzing the frequency of clinical forms, it is noteworthy that the structure of AMD (1897 eyes) is dominated by the dry form – 74%, patients with geographic atrophy accounted for 12% and the wet form was diagnosed in 14% of patients. With a combined course of the disease (1021 eyes), more than 79% is dry AMD, the number of eyes with geographic atrophy increases to 14%, and the number of diagnosed wet form decreases – 7% (compared to 14% without association with glaucoma).



**Fig.1.** The frequency of glaucoma and AMD in different age groups



**Fig. 2.** Distribution according to clinical forms of AMD depending on the stage of glaucoma

The obtained data on the dependence of the distribution of AMD forms depending on the stage of glaucoma also deserve attention (Fig. 2).

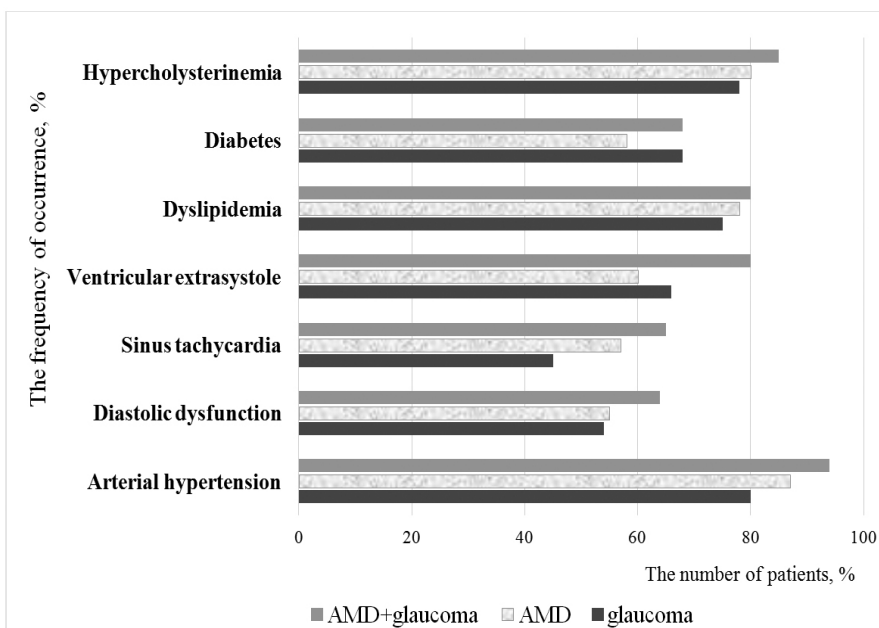
Thus, at the initial stage of glaucoma, 78% is dry form and 22% wet, while there is not a single case of diagnosed geographic atrophy. As the glaucoma process progresses, there is a redistribution towards an increase in the dry stage and geographic atrophy and a decrease in the occurrence of the wet form by almost 3 times towards the terminal stage of glaucoma.

Thus far, only a few studies have addressed the problem of the relationship between glaucoma and retinal diseases. Noteworthy is a large study in the USA (5174 patients), which showed that glaucoma often occurs against the background of other eye diseases or in parallel with them. At the same time, comorbid retinal pathology occurs more often in primary open-angle glaucoma (15,7%) than in its other forms (including normotensive, pseudoexfoliative and pigmentary). [21]. In our study, patients with primary open-angle glaucoma (49%) prevailed, but among

them, there were 42% of patients with angle-closure glaucoma and 9% with normotensive.

Common pathophysiological mechanisms of AMD and glaucoma development are discussed in the literature. [22, 23, 24]. Thus, when studying the structure of concomitant diseases in patients with glaucoma and AMD, it is noteworthy that 79% of patients had lipid metabolism disorders and 81% had an increase in serum cholesterol levels. In all groups of patients, the presence of concomitant pathology was found, while among persons comorbid for glaucoma and AMD, the incidence of nosological forms with similar vascular mechanisms of pathogenesis in their development significantly increases. The structure of concomitant vascular diseases is shown in Fig. 3.

The vascular theory of the development of these diseases is indisputable. Studies by H. Remsch et al. showed that choroidal and retinal blood flow is reduced in patients with neovascular AMD. [25]. Ischemia and hypoxia due to insufficient choroidal perfusion activate the development of neovascularization. [17, 26]. The formation of pathologi-



**Fig. 3.** The structure of the distribution of concomitant diseases

cal vessels serves as a trigger for the development of choroidal neovascularization, leading to a significant loss of central vision. For glaucoma, there are two main theories of pathogenesis: mechanical and vascular. An increase in IOP causes the development of glaucomatous optic neuropathy due to compression of the lamina cribrosa, circulatory disorders in the retinal blood vessels, and blockage of the axoplasmic current in nerve fibers, which aggravates the process and leads to its further progression. [27]. Recent studies have highlighted the importance of the vascular theory of pathogenesis, which explains the relationship between glaucoma and many other diseases that have similar mechanisms in their development, including impaired perfusion of the optic nerve head, retina, and choroid. [28]. Accordingly, glaucoma and AMD are two diseases that share similar pathophysiological mechanisms of development. Thus, in AMD, it was traditionally believed that all changes occur at the level of the outer layers of the retina, in particular, the pigment epithelium and photoreceptors with the outer limiting membrane. [29]. The main changes associated with the glaucoma process are determined mainly in the inner layers of the retina, in the ganglion cell complex: the layer of nerve fibers, the layer of ganglion cells, and the inner plexiform layer. [30].

A connection between defects in vision fields and a decrease in gray substance in the occipital cortex (mainly left hemisphere), as well as the reduction of white matter in the visual radiation and visual cortex, was found. [31]. Thus, glaucoma and AMD are neurodegenerative diseases with a chronic, progressive course, like Alzheimer's disease. [32]. In the outcome of the long-term course of these diseases lies the dystrophy of the cortex and retinotopic neuronal dystrophy. The development mechanism is identical and

treatment should be aimed not only at eye, but also at neurological disorders. [33]. As a result, a decrease in the cognitive functions of patients with a combined course of AMD and glaucoma becomes obvious.

H. Harrabi studies showed that patients with AMD and glaucoma not only had a lower speed of reading, mental processes and the process of recognizing even well-known objects, but also a slow speed and low quality of memorization, a slow reaction rate, which was inevitably accompanied by depressive disorders, a reduced ability to independent movement and limitation of motor activity. [34]. In accordance with the data of a meta-analysis, the average frequency of depression in eye diseases is 25%: in dry eye syndrome – 29%, in glaucoma – 25%, in AMD – 24%. [35]. A comprehensive assessment of the patient's physical, psychological and emotional state, based on his subjective perception, determines the patient's quality of life [36]. It is the decline in the quality of life that is another significant characteristic of these concurrent diseases.

The use of the NEI-VFQ-25 questionnaire allowed us to conduct a comparative analysis of the main characteristics that affect the quality of life of patients with glaucoma, AMD, AMD in combination with glaucoma, and the control group. Demographic and clinical and functional characteristics are presented in Tables 1 and 2.

An analysis of the most corrected visual acuity is reliably reduced in patients with the VMD and in the combined pathology group.

The study of the central visual field according to program 24-2 reveals a greater lesion in groups of patients with glaucoma, both as a single pathology and in combination with AMD, and according to program 10-2, a greater lesion was found in the group with AMD (single and in

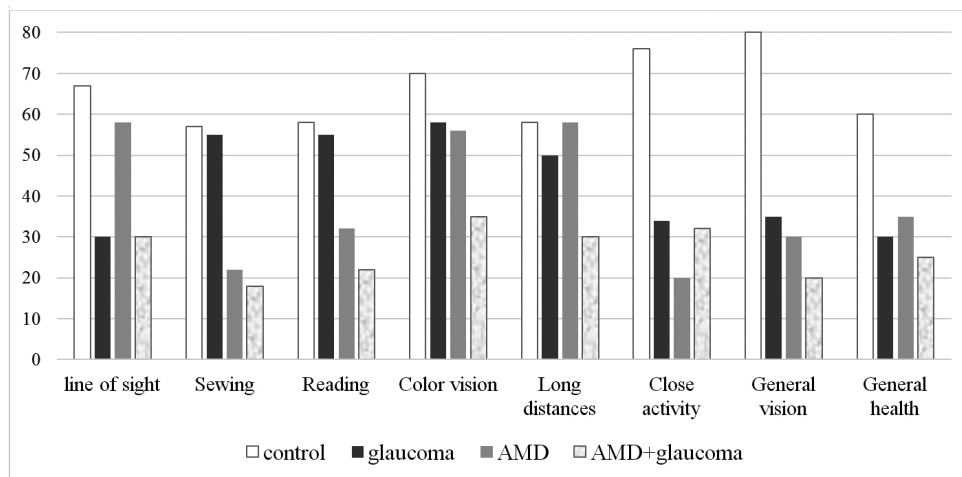
**Table 1.** Demographic characteristics of patients in compared groups

Characteristic	Glaucoma, n = 50	AMD, n = 50	Glaucoma + AMD, n = 50	Control, n = 50
Age, years	62,22 ± 5,66	64,88 ± 10,52	69,34 ± 8,66	66,63 ± 5,92
Number of men/ women	22/28	29/21*	28/21*	23/27

**Table 2.** Functional indicators of patients in compared groups

Characteristic	Glaucoma, n = 50	AMD, n = 50	Glaucoma + AMD, n = 50	Control, n = 50
The most corrected visual acuity	0,40 ± 0,1	0,35 ± 0,11*	0,35 ± 0,02*	0,39 ± 0,13
Fields of vision, dB	24 -2 Md	-4,90 ± 2,34*	-2,12 ± 1,44	-6,60 ± 1,35*
	24 -2 PSD	4,94 ± 3,45*	1,74 ± 1,11	5,77 ± 2,15*
	10 -2 Md	-2,34 ± 1,55*	-2,74 ± 1,55*	-7,34 ± 1,12*
	10 -2 PSD	4,23 ± 0,72*	2,12 ± 0,50*	5,13 ± 2,71*
Central Scotoma (number of patients)	3*	19*	18*	0

Note. Here and in table. 1 data are presented in the form of the arithmetic mean ± standard deviation; When comparing quantitative and nominal data, the criterion of Stuenkel and the exact criterion of Fisher were applied respectively; \* - the difference from the value of the corresponding indicator of the control group is statistically significant at p < 0.05.



**Fig. 4.** The degree of subjective assessment of the quality of life according to various characteristics

combination with glaucoma). The number of patients who consider their abilities to be satisfactory according to the given characteristics is shown in Fig. 4.

As follows from the survey, a decrease in the quality of life in patients with glaucoma and AMD is presented for all analyzed parameters. At the same time, in patients suffering from both glaucoma and AMD, activity at a close distance is significantly reduced, and the feeling of the field of vision, the ability to move over long distances and general health are satisfied by no more than 35% of the respondents. A correlation was found between visual acuity, the presence of central cataract and work at close range, which seems logical and natural.

### Conclusion

1. AMD and glaucoma, being chronic progressive multifactorial diseases, are becoming the main causes of suffering in older patients.

2. Both diseases have similar pathogenetic mechanisms of development, are often combined with cardiovascular and neurodegenerative diseases, and significantly affect the quality of life of patients.

3. In clinical practice, there has been a decrease in cases of the wet form of AMD against the background of the incidence of primary glaucoma with an increase in the tendency of early formation of geographic atrophy.

4. The combined course of AMD and glaucoma determines the need for careful monitoring of the dynamics of structural - clinical and functional indicators for timely and adequate treatment in order to preserve visual functions and ensure an acceptable quality of life in patients of the older age group.

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#### Disclosures

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