



CLINICAL STUDY ON THE FREQUENCY OF RISK FACTORS, MORPHOLOGICAL CHANGES AND FUNCTIONAL DISORDERS IN PATIENTS WITH DIAGNOSED GLAUCOMA

P. Todorova*, D. Dzhelebov, G. Zgureva, Z. Trifonov

Department of Ophthalmology, Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria

ABSTRACT

Aim: Determining the frequency of the risk factors: controllable and uncontrollable, frequency of morphological changes and functional defects and their interdependency. **Methods:** Clinical (statistical, snapshot) study of the database of glaucoma patients for half year (09.2011 – 02.2012). The patients have passed through the polyclinic and the ophthalmological clinic in the University Hospital in Stara Zagora, Bulgaria for diagnostic and therapeutic tests, follow-up or treatment of acute glaucoma crisis. The analysis does not include patients with intraocular hypertension – IOP over 21 mmHg with no changes in the optic nerve disk and in the field of view. **Results:** Included are 121 participants (242 eyes). Of them, 88 with primary open angle glaucoma (POAG), 31 with secondary open angle glaucoma, connected with pseudoexfoliation glaucoma (XFG), 2 with closed angle glaucoma. The patients are between 35 and 89 years of age, with a peak in the of 70-74 year range. POAG has an earlier age preference (after 40 – 45 years of age) than XFG. The first patients with XFG are after 55 years with a peak between 70 and 74 years of age. **Conclusions:** Glaucoma is a complex illness with multiple risk factors. Age is a leading factor in increasing IOP and developing POAG and XFG.

Key words: IOP (intraocular eye pressure), primary open angle glaucoma (POAG), angle closure glaucoma (ACG), pseudoexfoliation syndrome and glaucoma (XFS, XFG), tonometry, central corneal thickness (CCT), gonioscopy, perimetry.

INTRODUCTION

The term *glaucoma* has Greek origin (*glaukos* – *gray-blue*). Glaucoma is a chronically-progressive, ischemic, neuro-degenerative disease, which leads to characteristic changes in the optic nerve disk (papilla) and retina (1). They manifest in loss of nerve cells, leading to atrophy and excavation of the optic nerve, accompanied by progressive shortening of the peripheral sight and deterioration of the eye function up to blindness. Glaucoma is the second leading cause for blindness, after cataract, but cataract blindness is surgically curable. Therefore, glaucoma is the leading cause for permanent blindness. Frequency of glaucoma is 6 % in Caucasian Americans and 19% in Afro-Americans (due to smaller central corneal thickness, CCT).

Glaucoma is a complex disease with numerous risk factors. It has two aspects: morphological and functional. Morphologically (Greek *morphe* – from, *logos* – science, knowledge) it is shown in the pathology of the optic nerve disk – excavation. Functional changes are manifested in sight deterioration, which in the case of glaucoma are defects in the field of view (scotomas). In the early stages, there is a distortion of the color perception, sensitivity to contrast and adaptation to darkness. Later on, blinding from light appears.

Several factors influence the frequency of occurrence and the progression of glaucoma changes – *risk factors*. They are *controllable* (high IOP, vessels' dysregulation – vasospasm, hypertonia, social status, BMI, physically active lifestyle, smoking), which can be influenced, and *uncontrollable* (age, gender, race, genetic condition, refractive error - myopia), which cannot.

*Correspondence to: Petya Ivanova Todorova, 5-G Stara Planina str., apt. 89, box 6008, GSM +359 897 873 441, tel/fax: 042 623356, E-mail: petja_pik@abv.bg

Main risk factors:

1. Advanced age, above 40 years.
2. High IOP and fluctuations of the pressure
3. CCT < 550 μ m
4. High vertical excavation – horizontal/vertical ratio of the excavation to the optic disk size above 0,4
5. Diabetes mellitus, as a chronic complication
6. High PSD index

Additional risk factors

Race, genetic anamnesis for glaucoma, day/night fluctuations, XFS, post-cataract surgery with implanting IOL, myopia above 4D, cardio-vascular illnesses, vessel factors – systemic hypertension or hypotension, hyperlipidemia, Raynaud's Syndrome, atherosclerosis; endocrine disorders – hypo- and hyperthyroidism. POAG is more frequent among people with auto-immune disorders, neurological disorders, behavioral and social factors, social status – explains racial/ethnic differences, obesity (higher blood viscosity, episcleral pressure increase and lower flow of eye liquid).

Diet – intake of fats (cholesterol, saturated, poly-saturated) and antioxidants. POAG is influenced by free radicals, which damage the epithelium and trabecular apparatus.

Sleep apnea – repeating occurrences of 10 seconds to 1 minute, manifesting in total or partial collapse of the pharyngeal way in sleep. Risk factors are obesity, male gender, snoring. They influence the blood flow to posterior eye segment.

METHODS*Clinical study**Statistical snapshot study*

- Period – half year: 09.2011 to 02.2012, 121 patients (242 eyes)
- Place – a polyclinic and the ophthalmological clinic in the University Hospital in Stara Zagora, Bulgaria
- Sample – glaucoma patients for diagnostic or therapeutic tests, follow-up or treatment of acute glaucoma crisis.

The analysis did not include patients with intraocular hypertension – IOP above 21mmHg without changes in the optic nerve disk and in the field of view. Nevertheless, elevated intraocular pressure is an important risk factor and is also considered to be a causative factor in glaucoma currently (2), it is the only modifiable causative factor (3).

Diagnostic algorithm

1. Anamnesis for determining the risk factors
2. Tests
 - Visual acuity test
 - Slit lamp biomicroscopy
 - Goldman applanation tonometry – *gold standart – 1954z.*
 - Gonioscopy - indirect gonioscopy Goldman three mirror lens
 - Ultrasound pachymetry – Avg CCT = 550 μ m
 - Ophthalmoscopy – direct, indirect for finding structural (morphological) changes, which precede the functional
 - Indirect stereobiomicroscopy with 90D lens
 - Visual field test – static automated perimetry (SAP), program 30 – 2 of OCTOPUS 900

Statistical analysis of the data with STATISTICA 8.

RESULTS

Table 1. Regional distribution of the glaucoma patients.

Regional distribution	
Stara Zagora	81
Haskovo	15
Yambol	7
Sliven	4
Sofia	2
Burgas	2
Pleven	2
Kardjali	2
Vratza	2
Plovdiv	1
Dobrich	1
Kustendil	1
Pazardzhik	1

Table 1 shows that most patients included in the clinical study are from Stara Zagora region (81), followed by Haskovo (15) and Yambol (7) regions.

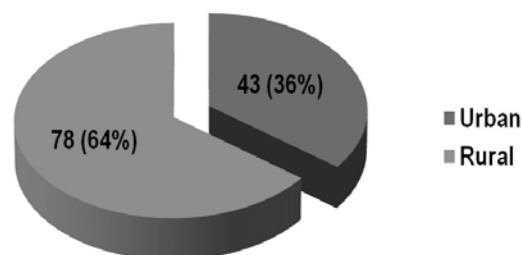


Figure 1. Distribution between urban and rural population

The rural population is a majority (64 %)

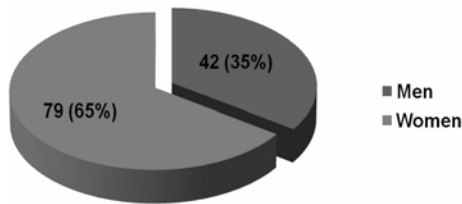


Figure 2. Gender distribution

The female patients are a majority (65%)

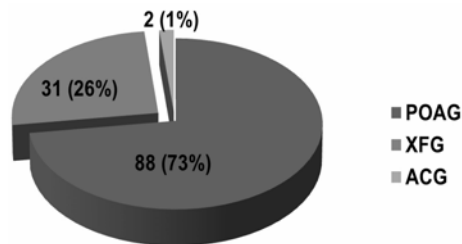


Figure 3. Types of glaucoma

Most patients are with Primary open angle glaucoma POAG (73%) The patients with pseudoexfoliation glaucoma (XFG) are second with 26 %. The smallest percentage is Angle closure glaucoma (ACG) 2%.

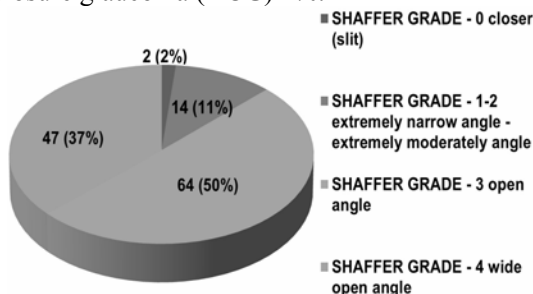


Figure 4. Shaffer grade

Half of the patients are with open angle grade - 3. 37 % are with wide open angle (grade 4),

followed by 11 % with extremely narrow angle - extremely moderately angle (grade 1 – 2). The patients with closer (slit) angle (grade 0) are only 2%.

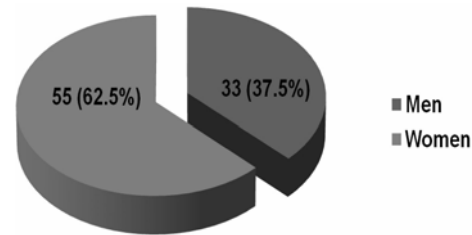


Figure 5. POAG gender distribution

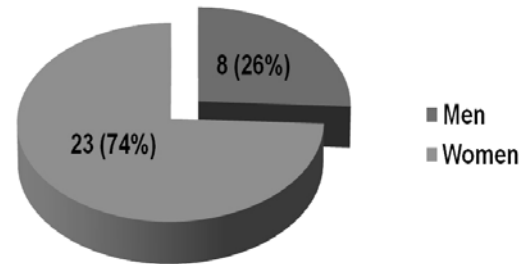
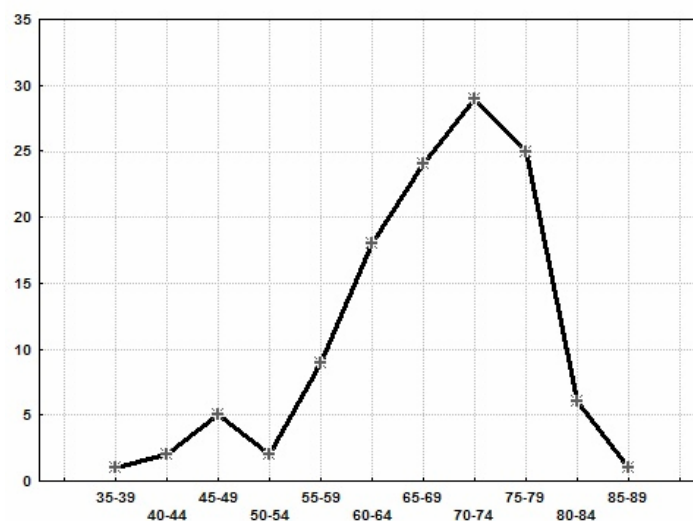


Figure 6. XFG gender distribution.

Table 2. XFS gender distribution (by number of eyes) $\chi^2=0.75, p=0.3864 > 0.05(df=1)$

	XFS	non XFS	Total
Male	15	67	82
Female	37	123	160
Total	52	190	242

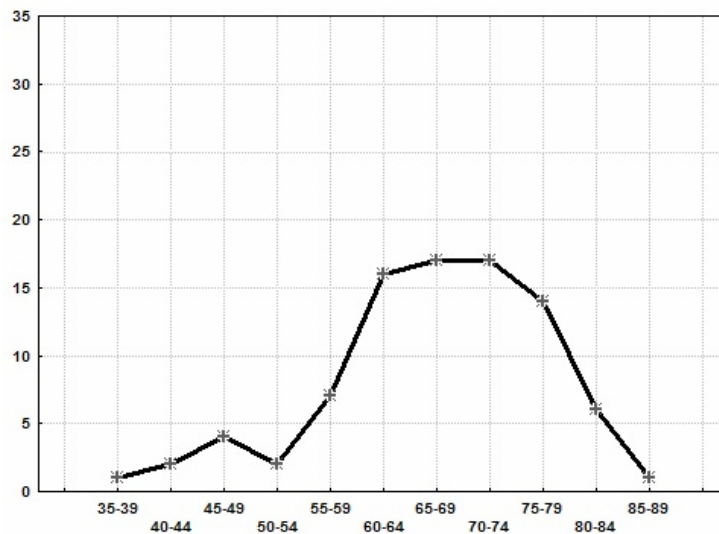
Conclusion: There is no statistically significant difference in the XFS frequency by gender Both eyes of patients are considered separately for XFS, because it can occur in one or both eyes.



Graph 1. Age distribution of glaucoma patients in 5-year clusters.

Note: Glaucoma patients are 35 to 89 years of age, with a peak in 70 – 74 years. The graph has a steep increase after the 50 years' mark.

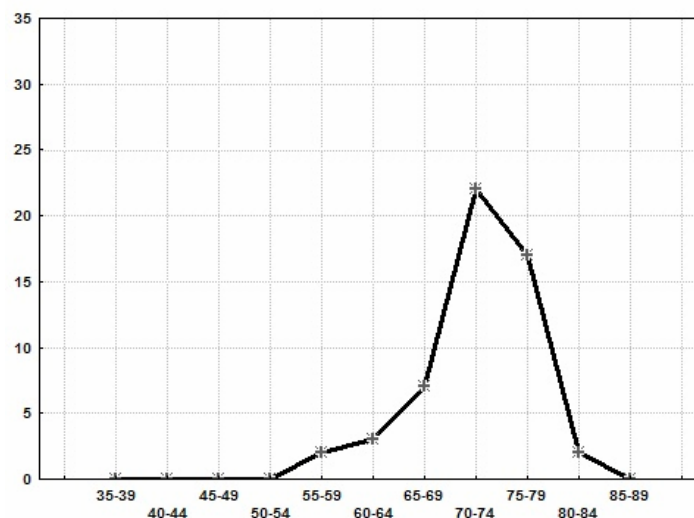
This factor is connected with the increased life expectancy.



Graph 2. POAG age distribution in 5-year clusters

Note: The graph has a similar shape regarding age distribution. It is less pronounced than graph 3 because of the fewer patients with XFG. The peak has a wider basis (59 to 80

years) than graph 3, because POAG manifests earlier in time (after 40 – 45 years age), which is demonstrated by another peak missing in XFG.



Graph 3. XFG age distribution in 5-year clusters

Note: The first patients are above 55 years of age with a peak between 70 and 74 years.

Table 3. Genetically predisposed (GP), not genetically predisposed (NGP) patients by gender; $\chi^2 = 1.76$; $p = 0.1848 > 0.05$ ($df=1$)

	GP	NGP	Total
Male	9	33	42
Female	26	53	79
Total	35	86	121

Conclusion: Nonparametrical analysis shows that there is no statistically significant gender difference.

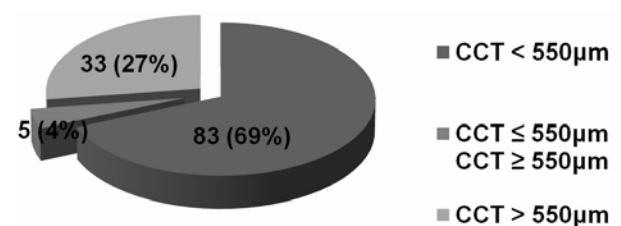
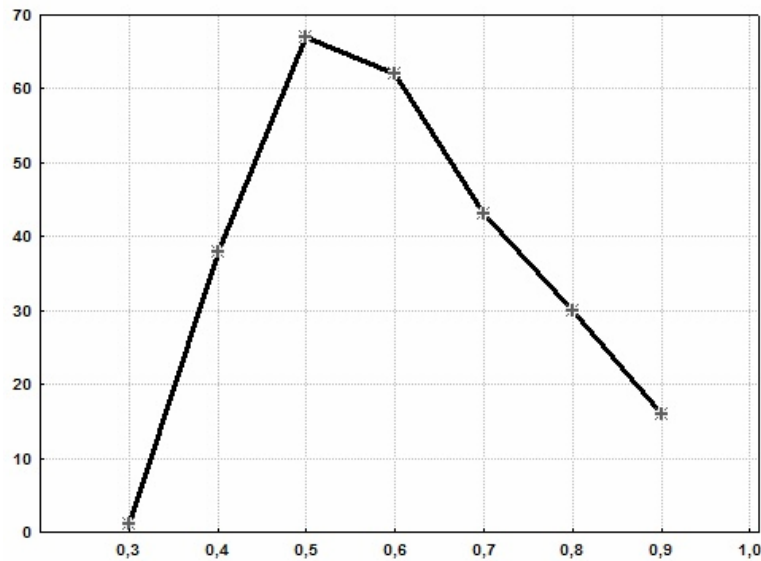


Figure 7. Pachymetry

The biggest share is thin cornea. Patients with cornea thickness of Avg CCT = 550 μm in one eye, and Avg CCT < 550 μm or Avg CCT > 550 μm in the other eye, are included in the group CCT $\leq$ 550 μm , CCT $\geq$ 550 μm .

Graph 4. The biggest percentage of patients is with a horizontal/vertical ratio of the excavation to the optic disk size 0.5



Graph 4. Distribution of number of eyes by excavation of the papilla of the optic nerve

The biggest number of patients has arterial hypertonia as a concurrent illness (78). Next in number are patients with diabetes mellitus (17).

Table 4. Frequency of illnesses suffered by glaucoma patients

Diseases and glaucoma	
Arterial hypertension	78
Diabetes mellitus	17
Raunauld's syndrome	2
Thyrototoxicosis	2
Rheumatoid arthritis	2
Osteoporosis	2
Burger's Disease	2
Hashimoto's disease	1

Table 5. Distribution of the arterial hypertonia patients (AH) by type of galucoma, $X^2 = 2.83$ $p = 0.0923 > 0.05$ ($df=1$)

	with AX	without AX	Total
POAG	54	35	89
XFG	24	7	31
Total	78	42	120

Conclusion: There is no statistically significant difference in the frequency of AH patients by glaucoma type

Gathering of information for arterial hypertonia is done by anamnesis, not by physical measurement. Therefore the association is to be treated cautiously.

The biggest group of patients has a period of AH of 10 years.

Discussion:

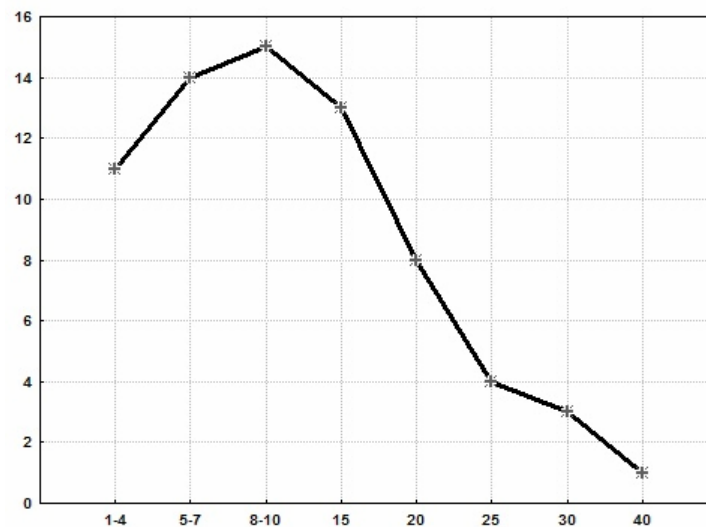
About age and family history

The risk of developing glaucoma increases with age. Everyone over age 60 is at risk of developing glaucoma. People in certain racial or ethnic groups are at higher risk of developing glaucoma at younger ages (3). XFS connected glaucoma appears after 60 to 65 years of age. About 5% of XFS patients develop XFG in 5 years, and about 15% in 10 years. XFG is more common in Scandinavian countries.

Glaucoma tends to run in families. Brothers and sisters of patients with open angle glaucoma are 5 times more likely to develop glaucoma by the time they are 70 years old than people whose siblings do not have the disease. Previous studies have also found that people with family histories of glaucoma are

more likely to already have some vision loss when they are first diagnosed with glaucoma (3). A prophylactic glaucoma test is recommended between 35 and 45 years of age

for individuals without genetic predisposition and between 25 and 30 years for predisposed ones.



Graph 5. Distribution of patients by duration of arterial hypertension

The **figure 8** shows no significant difference in glaucoma patients by the period of diabetes, in years.

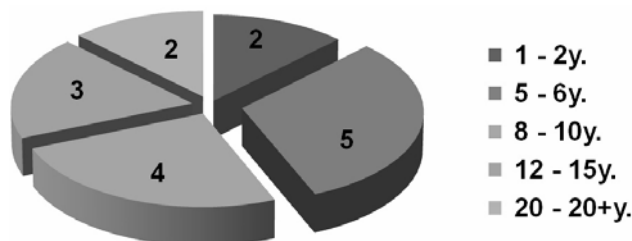


Figure 8. Distribution of patients by duration of diabetes mellitus in years.

About Medical conditions

People with certain medical or physical conditions, including diabetes, migraine, nearsightedness, and sleep apnea, appear to have a higher risk for glaucoma. High blood pressure may be a risk factor. Conditions that require the use of any oral or inhaled steroid, particularly high doses for prolonged periods of time, can cause glaucoma. Previous eye surgery also puts people at risk, as is nearsightedness (3). In this clinical study the biggest number of patients has arterial hypertension as a concurrent illness – 78. Next in number are patients with diabetes mellitus – 17.

CONCLUSION

Glaucoma is a complex illness with multiple risk factors. In glaucoma, a major cause of blindness, the ganglion-cell axons that make up the optic

nerve are damaged by a variety of factors, only some of which are understood (1).

Age is a leading factor in increasing IOP and developing POAG and XFG. The patients are between 35 and 89 years of age, with a peak in the of 70 – 74 years range. POAG has an earlier age preference (after 40 – 45 years of age) than XFG. The first patients with XFG are after 55 years with a peak between 70 and 74 years of age. Due to the small number of patients with myopia over 4D (under 1%), and patients with less acute myopia in this study, we did not investigate the relationship of these factors and glaucoma.

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