DOI: https://doi.org/10.2298/SARH211005078B
UDC: 617.7-007.681(497.113)

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Prevalence of glaucoma in the city of Novi Sad

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SUMMARY

Introduction/Objective Our study aimed to estimate the prevalence of glaucoma and its subtypes in the population of Novi Sad, Vojvodina, Serbia, and provide the demographic and clinical analysis of glaucoma patients involved.

Methods Our study was designed as an observational, retrospective, cross-sectional, monocentric, including all the patients with the address of residence within the city of Novi Sad, with clinically diagnosed glaucoma, at least in one eye, treated at the University Eye Clinic, Clinical Centre of Vojvodina, Novi Sad. We analyzed the five-year prevalence of different types of glaucoma, together with the characteristics of visual field and risk factors in the form of coexisting diabetes mellitus and arterial hypertension.

Results Almost half of 3254 included patients (48.28%) were diagnosed with primary open-angle glaucoma (POAG), and its prevalence in the total population of Novi Sad was estimated to be 0.46%. The prevalence of other glaucoma types was as follows: primary angle-closure glaucoma (PACG) 0.17%, secondary glaucoma 0.09%, pseudoexfoliation glaucoma 0.09%, normal-tension glaucoma 0.13%, pigmentary glaucoma 0.01%, and juvenile glaucoma 0.01%. In the population above 40 years of age, the prevalence of all glaucoma cases was 1.9%, while the prevalence of POAG was 0.93%, and the prevalence of PACG was 0.35%.

Conclusion Our study represents the first attempt to address the epidemiological problems of glaucoma in our region in a comprehensive, evidence-based way. The prevalence of various glaucoma types and observed age-specific prevalence trends were lower than those published by other authors involving comparable populations, and we offered several potential explanations for this in our paper.

Keywords: prevalence of glaucoma; type of glaucoma; glaucoma epidemiology

INTRODUCTION

Glaucoma is progressive optic neuropathy accompanied by characteristic morphological changes of the optic nerve head and the nerve fiber layer of the retina. It manifests in visual field loss, usually asymptomatic in the early stages of the disease, leading to irreversible blindness if untreated. It represents the second leading cause of preventable blindness in the world. It has been estimated that 60.5 million people were suffering from glaucoma globally in 2010, with 6.7 million bilaterally blind. This number is expected to rise in the future, and it is estimated that 111.8 million people will have glaucoma in 2040 [1]. The main reason for this is considered to be a worldwide increase in the average life expectancy.

Based on its etiopathogenesis, glaucoma can broadly be divided into open-angle (OAG) and angle-closure (ACG) glaucoma, with further classification into primary, secondary, congenital (present on birth), and juvenile form (appearing between the ages of three and 40) [2].

Analysis of global glaucoma prevalence proved to be a complex undertaking, often leading to inconclusive and results that are difficult to compare. The situation improved after the introduction of the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) classification of glaucoma for use in population-based surveys which more precisely defined diagnostic and classification criteria of different glaucoma types. However, many obstacles persist to this day [3].

Different subtypes of glaucoma have different racial and geographical prevalence. Africa and North America are found to have the highest prevalence of POAG (4% and 3.4%, respectively), while Oceania had the lowest (1.8%) [3]. The situation in China and India favors PACG, which accounts for 50–60% of all glaucoma cases [4].

According to the latest epidemiological studies and meta-analyses, the global prevalence of adult forms of glaucoma is estimated to be 4.79%, with POAG accounting for 3.05% and PACG for 0.5% of the cases, and these values seem to be increasing [5].

There are no available data regarding the number of people with glaucoma in Serbia. At the 2011 census, Serbia had 7,186,862 citizens and 3,849,267 people older than 40 years [6]. Extrapolating the prevalence data from the aforementioned studies, it has been estimated that around 100,000 people live with glaucoma in Serbia, with at least 75,000 POAG cases.

Our study aimed to estimate the prevalence of glaucoma and its subtypes in Novi Sad, Vojvodina, Serbia, with a population of 341,625 on the last census, and to provide with

Received • Примљено: October 5, 2021
Accepted • Прихваћено: July 22, 2022
Online first: August 4, 2022

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the demographic and clinical analysis of glaucoma patients involved.

METHODS

This observational, retrospective, cross-sectional, monocentric study included all the patients with clinically diagnosed glaucoma, at least in one eye, treated at the University Eye Clinic, Clinical Centre of Vojvodina, Novi Sad in the period from August 2007 to December 2012. The patients' data were populated from the electronic health records database used in the clinic. The dataset included 3254 patients, with the residence address within the city of Novi Sad, who met strict inclusion criteria of confirmed glaucoma diagnosis, regardless of age, sex, and type of glaucoma, excluding glaucoma suspects and patients with ocular hypertension. The onset of the disease was not necessarily in the period between January of 2007 and January of 2012, but a patient's first examination at the clinic was within that period. All the patients were examined by several experienced ophthalmologists working at the Glaucoma Department of the Eye Clinic.

We analyzed the period prevalence of different types of glaucoma, including POAG, PACG, secondary, juvenile, and congenital glaucoma, and the age and sex distribution of the patients. In addition, assessment of the cup/disk ratio of the optic disc using the 90D non-contact lens at slit lamp was done in every patient. Visual field testing was performed with Humphrey visual field analyzer (HFA; Carl Zeiss Meditec AG, Jena, Germany), C24-2 testing protocol, equipped with STATPAC. Mean deviation (MD) visual field index calculation has been considered an indicator of the stage of perimetric glaucoma disease. Finally, we analyzed the presence of two of the established glaucoma risk factors: diabetes mellitus and arterial hypertension.

Subjects' written consent was obtained in accordance with the Declaration of Helsinki, and the ethics committees of the Eye Clinic, Clinical Centre of Vojvodina, approved the study.

Data were statistically analyzed using SPSS, Version 16.0 (SPSS Inc., Chicago, IL, USA) using the following descriptive statistical methods: arithmetic mean, standard deviation, median, quartiles, frequencies, and percentages, with confidence interval (CI) set at 95%. The results are presented in the form of tables and graphs with comments.

All procedures performed in this study were in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Written consent to analyze and publish all shown material was obtained from the patient, and the approval for the study was given by the Ethics Committee of Eye Clinic, Clinical Centre of Vojvodina.

RESULTS

There were 3254 patients enrolled in our study, the majority of them being females (1949 *vs.* 1305; 59.9% *vs.* 40.1%).

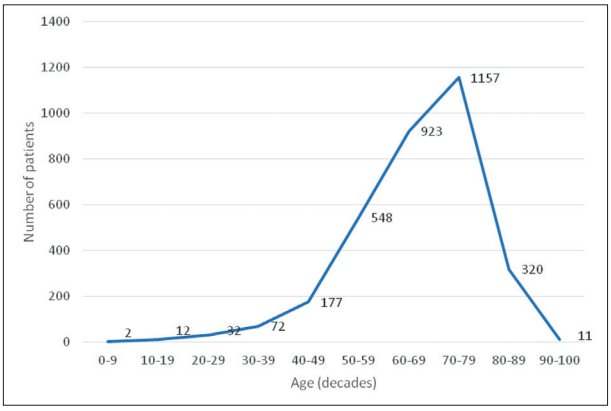


Figure 1. Age distribution of glaucoma patients

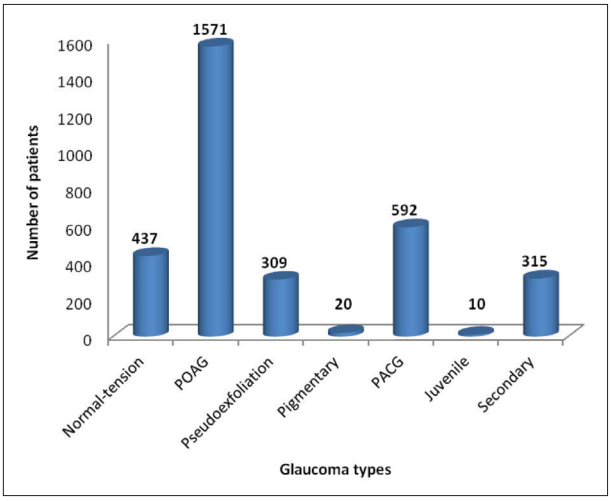


Figure 2. Distribution of glaucoma types;
POAG – primary angle-closure glaucoma; PACG – primary angle-closure glaucoma

The average age of the patients surveyed did not express normal distribution and was calculated using the median value (25th–75th percentile) at 68 (59–75) years. The youngest patient was eight years old, and the oldest was 100 years old. Age distribution of glaucoma patients shows a predominance of patients older than 40 years of age, with most cases during the eighth decade of life (Figure 1).

Among our patients, the most common glaucoma type was primary open-angle glaucoma (POAG), diagnosed in 1571 patients (48.28%). There were 592 (18.19%) patients with primary angle-closure glaucoma (PACG), while the secondary glaucoma was found in 315 (9.68%), pseudoexfoliation glaucoma in 309 (9.5%), normal-tension glaucoma in 437 (13.43%), pigmentary glaucoma in 20 (0.61%) patients, and 10 patients (0.31%) had juvenile glaucoma. There were no cases of congenital glaucoma in our group of patients (Figure 2).

According to the 2011 census, the population of the city of Novi Sad had a total of 341,625 citizens. There were 3254 glaucoma patients registered in our study, giving the total glaucoma prevalence of 0.96%. POAG had the highest prevalence of all glaucoma types (0.46%), followed by PACG (0.17%), and normal-tension glaucoma (0.13%).

There were 164,789 persons older than 40 years in the city of Novi Sad, making the total glaucoma prevalence

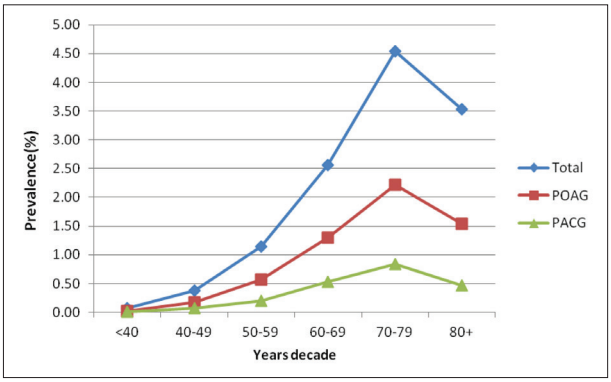


Figure 3. Age distribution of primary open-angle glaucoma (POAG), primary angle-closure glaucoma (PACG), and total glaucoma prevalence

for this age group 1.9%. The prevalence of patients in the group of 40–49 years was 0.38%, in the 50–59 years group the prevalence was 1.15%, for the group of 60–69 years the prevalence was 2.56%, for the age group of 70–79 years the prevalence was 4.54%, while the prevalence in the population above 80 years was 3.53% (Figure 3).

The prevalence of POAG among populations older than 40 years was 0.93%, while the prevalence of PACG in the same population was 0.35%. POAG showed a higher prevalence throughout all age groups, comparing to PACG. As with total glaucoma cases, the highest prevalence of both POAG and PACG is found among the population in the eighth decade of life (2.22% and 0.83%, respectively), with the decrease among the patients over the age of 80 (Table 2).

Table 1. Prevalence of glaucoma types

Glaucoma type	Prevalence % (95% CI)
Normal-tension	0.13 (0.1159–0.1399)
POAG	0.46 (0.4371–0.4825)
Pseudoexfoliation	0.09 (0.0803–0.1005)
Pigmentary	0.01 (0.0032–0.0084)
PACG	0.17 (0.1593–0.1872)
Juvenile	0.01 (0.0011–0.0047)
Secondary	0.09 (0.0821–0.1023)

POAG – primary open-angle glaucoma; PACG – primary angle-closure glaucoma

Table 2. Age distribution of open-angle glaucoma (POAG), primary angle-closure glaucoma (PACG), and total glaucoma prevalence

Years of life	POAG prevalence %	PACG prevalence %	Total glaucoma prevalence % (95% CI)
< 40	0.02	0.01	0.07 (0.0546–0.0787)
40–49	0.18	0.08	0.38 (0.3274–0.4403)
50–59	0.56	0.2	1.15 (1.0528–1.244)
60–69	1.3	0.53	2.56 (2.394–2.721)
70–79	2.22	0.83	4.54 (4.28–4.791)
80+	1.54	0.47	3.53 (3.158–3.9055)

Taking into consideration all types of open-angle glaucoma (POAG, normal-tension, and pigmentary glaucoma), there were 2028 cases recorded in our study. This makes the collective prevalence of these types of glaucoma at 0.59% in the general population and 1.23% if we calculate only for the population above the age of 40 years.

Automated perimetry using Humphrey visual field analyzer (HFA) (C24-2 testing protocol) showed a mean MD index value of -6.51dB (± 8.4 dB).

Of all the risk factors for the development of glaucoma, this study included two: diabetes mellitus and arterial hypertension. Diabetes was found in 76 (2.32%) patients, while the arterial hypertension was present in 86 (2.62%) patients.

DISCUSSION

Our study aimed at estimating the prevalence of glaucoma for the population of the city of Novi Sad for the 2007–2012 period. We have analyzed the records of 3254 patients, of the median age of 68 (59–75) years, with confirmed glaucoma diagnosis, treated at the Glaucoma Department of the Eye Clinic of the Clinical Centre of Vojvodina. Our clinic is the only tertiary ophthalmological center in our region, and most glaucoma patients are diagnosed and treated within its Glaucoma Department.

Sex predilection for glaucoma is still a debated topic in the literature. It was considered that women are more prone to suffer from glaucoma during their lifetime, as several population-based studies indicated in the past [7, 8]. This was especially true with PACG in people of Asian descent [3]. However, available data seem to show that males have a higher chance of being POAG patients. In the final multivariable model, Khachatryan et al [9] found male sex to be more associated with POAG risk (OR, 1.64; 95% CI, 1.44–1.87; $p < 0.001$), after adjusting for age, systemic hypertension, diabetes, and BMI.

There was a higher number of female patients (59.9%) in our group. This might reflect sex distribution among the general population of Novi Sad, with 52.54% of the population being women and due to the women's longer average life expectancy at birth (78.4 *vs*. 72.9 years) [6, 10]. Another potential explanation might be the phenomenon of sex-related differences in health behavior and the fact that women generally tend to visit physicians earlier and more often than men, that might lead to the larger pool of undetected male glaucoma patients in the general population [11].

The prevalence of glaucoma and its types shows significant regional variations, determined by the racial characteristics of the population. The latest pooled prevalence data, for the people over the age of 40, estimate it to be between 2.4% (95% CI 2 ~ 2.8%) globally, and between 2.23% and 2.93% for the people of European ancestry [5].

The population of the city of Novi Sad and Serbia is mainly Caucasian, of European origin [12]. The prevalence data found in our study was considerably lower than the ones in other sources. It was found to be 0.96%, including patients of all age groups, and 1.9% involving patients older than 40.

POAG is the most common type of glaucoma globally. Its overall prevalence is estimated 2.2–3.05%, being most prevalent in the people of the black, African ancestry, reaching 5.4%, and least common in the people of Asian

ancestry [13]. The prevalence for the white population is estimated to be within the 1.29–2.93% range [5, 14]. The results of our study show a prevalence of 0.46% for the general population and 0.93% in the population older than 40 years, which is lower than published data found by other researchers.

The situation with PACG regarding its geographical distribution is quite the opposite. Its prevalence is the lowest among the people of white and black race ranging 0.03–0.85% [5, 15]. On the other hand, Asian people have higher values reaching up to 1.2%, while the prevalence among the people of European ancestry is 0.42–0.69% [5, 13, 16]. The prevalence of this type of glaucoma in our survey was 0.17% for all age groups and 0.35% for patients above 40 years of age and was more similar to the results of earlier studies.

Numerous studies have shown that age-specific prevalence for both POAG and PACG increases with age [15, 17, 18]. Our research findings agree with most of the other studies, although with lover prevalence across all age groups. In addition, we found the maximum prevalence for both POAG and PACG among patients in the eighth decade of life, declining in later life. Similar results are present in the study by Kreft et al. [17], who conclude that the reason for this might be in the increased risk of additional health care risks in the form of more severe comorbidities or because of the mortality selection process, a tendency that fitter persons with a generally lower risk of morbidities, among them POAG and its risk factors, reach the highest ages.

Other glaucoma types have also shown the tendency of racial/geographical distribution, with variable prevalence globally. Normal-tension glaucoma is defined as open-angle glaucoma with IOP values within the physiological range for the given population (mean value of IOP +/- 2SD). It has been found in up to 30% of all POAG cases, depending on the selected cut-off IOP value [1, 19]. Our research found its prevalence to be 0.13%, which makes 22% of OAG prevalence (59%), the result comparable with the available data from the literature.

Pseudoexfoliation glaucoma also exhibits regional variations comprising 20% to more than 50% of open-angle glaucoma cases [20, 21]. We analyzed pseudoexfoliation glaucoma as a separate clinical entity and found its prevalence to be 0.09% in all age groups. We are not aware of any other study presenting these results in a similar, comparable fashion.

A secondary glaucoma is a diverse group of glaucoma diseases, occurring together with another underlying eye disease (lens-related, aphakic, pseudophakic, neovascular, traumatic, uveitic). According to published studies, it has been known to represent 1–11% of all glaucoma cases [4, 22]. Our data establish its prevalence at 0.09%, with 315 patients suffering from it.

The reason for the prevalence values obtained in our study to be at the lower end of the reported range might be in the fact that although most glaucoma patients in our region are treated at our clinic, some of them are registered at secondary levels of ophthalmology health care in community health care centers or several privately run clinics. Incorporating the data from these centers in our analysis should be the goal of future studies.

ISGEO defined diagnostic and classification criteria for glaucoma in population-based surveys. Among other criteria, it specified the "gold standard" of glaucomatous visual field loss using the threshold test strategy with the 24-2 test pattern of the Zeiss-Humphrey field analyzer II as a referent device [23]. We followed these recommendations in our survey and found the mean MD index value of -6.51dB (± 8.40dB) for all the glaucoma patients.

Multiple risk factors were associated with glaucoma and its subtypes. POAG link with diabetes mellitus was established by numerous authors [17, 24]. In the latest meta-analysis of seven prospective studies, Zhao and Chen [25] found diabetes mellitus to be associated with a significantly increased risk of glaucoma. The prevalence of secondary (neovascular) glaucoma was also linked with diabetes, although there has been a marked decrease in it in recent years, after the introduction of anti-VEGF therapy[26]. In our study, we report diabetes comorbidity in 2.32% of all glaucoma patients. Arterial hypertension is another risk factor associated with an increased risk of POAG development [27]. Our survey found it to be present in 2.62% of all the included patients.

CONCLUSION

Our monocentric, cross-sectional, retrospective, observational study represents the first attempt to address the epidemiological problems of glaucoma in our region in a comprehensive, evidence-based way. Its results demonstrated the sex and age distribution of glaucoma patients treated at our clinic for the follow-up period of five years. We estimated the period prevalence of various glaucoma types and observed age-specific prevalence trends in our population. The prevalence values found were compared with the ones published by other authors, involving an equivalent population. It is evident that our total and individual glaucoma type prevalence rates are lower than previously published, and we tried to give a credible explanation for that. Apart from that, we have also analyzed the average level of visual field defect and the presence of two glaucoma risk factors (diabetes mellitus and arterial hypertension) in our patients.

Conflict of interest: None declared.

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Преваленца глаукома на територији града Новог Сада

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САЖЕТАК

Увод/Циљ Циљ нашег истраживања био је да се процени преваленца глаукома, као и његових типова у популацији града Новог Сада и да се изврши анализа демографских и клиничких карактеристика болесника који болују од глаукома.

Методе Наша студија је осмишљена као опсервациона, ретроспективна, моноцентрична студија пресека, која је обухватила све болеснике са пребивалиштем на територији града Новог Сада, са клинички постављеном дијагнозом глаукома бар на једном оку, а који су лечени на Клиници за очне болести Клиничког центра Војводине. Испитивали смо петогодишњу преваленцу различитих типова глаукома, заједно са особеностима налаза видног поља и присуством шећерне болести и артеријске хипертензије као факторима ризика.

Резултати Код скоро половине од 3254 укључена болесника (48,28%) постављена је дијагноза глаукома отвореног угла и процењена преваленца овог обољења у становништву Новог Сада износи 0,46%. Преваленца осталих типова глаукома била је следећа: примарни глауком затвореног угла 0,17%, секундарни глауком 0,09%, псеудоексфолијативни глауком 0,09%, нормотензивни глауком 0,13%, пигментни глауком 0,01% и јувенилни глауком 0,01%. Код становништва старијег од 40 година преваленца свих глаукома износила је 1,9%, док је преваленца глаукома отвореног угла била 0,93%, а преваленца глаукома затвореног угла 0,35%.

Закључак Наша студија представља први покушај епидемиолошке анализе питања глаукома у нашем региону на свеобухватан, на доказима засновани начин. Процењена је преваленца различитих типова глаукома и уочени су њени трендови у зависности од узраста становништва. Добијене вредности преваленце ниже су од оних објављених од стране других аутора у популацијама сличним нашој и у нашем раду смо пружили неколико могућих објашњења за ту чињеницу.

Кључне речи: преваленца глаукома; тип глаукома; епидемиологија глаукома