

PREVALENCE OF PSEUDOEXFOLIATION SYNDROME AND PSEUDOEXFOLIATION GLAUCOMA IN POPULATION OF NORTH-WEST CROATIA AGED 40 AND OVER

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SUMMARY – The purpose of this study was to assess the prevalence of pseudoexfoliation syndrome and pseudoexfoliation glaucoma and to evaluate its association with open-angle glaucoma in patients attending the Department of Ophthalmology, Dr Tomislav Bardek General Hospital in Koprivnica, northwestern Croatia. This prospective study was conducted at Dr Tomislav Bardek General Hospital between December 2012 and October 2013. A total of 5349 subjects aged 40 or above presenting for general ophthalmic examination were screened for pseudoexfoliation syndrome and pseudoexfoliation glaucoma. Each patient underwent complete ophthalmologic examination including ocular history, visual acuity testing, slit-lamp examination, applanation tonometry, optic disc evaluation, visual field analysis, and gonioscopy if glaucoma was suspected. Exclusion criteria were pseudophakic and/or aphakic patients of any age, patients with concomitant congenital eye disease, and patients with very dense ocular media opacities. Out of 5349 patients examined, there were 1994 (38.38%) males and 3201 (61.61%) females. The prevalence of pseudoexfoliation syndrome was 3.6% and primary open angle glaucoma 9.4%, out of which 23.6% with pseudoexfoliation glaucoma. The findings of this study improve our knowledge of pseudoexfoliation syndrome and pseudoexfoliation glaucoma in Croatia, particularly in the northwest region.

Key words: *Exfoliation syndrome – epidemiology; Prevalence; Elderly; Glaucoma*

Introduction

Pseudoexfoliation syndrome (PXS) is an aging-related systemic disease with cardiovascular and cerebrovascular morbidity¹⁻³ and hearing loss^{4,5} but only ocular manifestations. It is the single most important risk factor for glaucoma worldwide and a major factor predicting glaucoma progression⁶. The reported preva-

lence of PXS varies extensively in different population-based studies from 4.0% in England, 4.7% in Germany, 6.3% in Norway⁷, 23% in northern Sweden⁸, 1.81% in Pakistan⁹, 1.49% in India¹⁰, 10.7% in Iceland¹¹, 16.1% in Crete (Greece)¹², 26% in the Bantu of South Africa¹³, 7.10% in South Kashmir¹⁴, 12.2% in Anatolia (Turkey)¹⁵, 25.5% in Estonia¹⁶ and 6.5% in Spain¹⁷. Even within a country, the prevalence varies from one region to another because of different types of patient groups examined, therefore many results are incomparable.

The incidence of PXS roughly doubles each decade of life after the age of 50¹⁸. Since PXS has been linked

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to multiple pathological entities of the eye including glaucoma, cataract, perioperative complications during eye surgery¹⁹⁻²⁴ and postoperative complications after cataract surgery²⁵, it is of utmost importance to recognize ocular manifestations of PXS. Pseudoexfoliation (PEX) at baseline was identified as an independent risk factor for primary open-angle glaucoma (POAG) and relation between increased intraocular pressure (IOP) and PXS was established in different studies^{26,27}, suggesting obstruction of the aqueous humor outflow. Exposure to PXS and a mean IOP ≥ 25 mm Hg increases the risk of POAG 56-fold²⁸, indicating a high prevalence of POAG in a population with a high prevalence of PXS. POAG in PXS has been shown to have a more serious clinical course than POAG without PXS²⁹. Higher age, positive family history^{30,31}, high myopia, increased IOP together with PXS have been associated with a higher incidence of POAG. With the increasing number of elderly in the population, an increase of POAG and pseudoexfoliation glaucoma (PXG) is expected in the future.

The prevalence of POAG, PXS and PXG in north-west Croatia is unknown and has never been analyzed before. According to data of the Association of the Blind and Visually Impaired of Northwest Croatia, 25% of blindness cases are caused by glaucoma.

Patients and Methods

This hospital based prospective study was carried out at the Department of Ophthalmology, Dr Tomislav Bardek General Hospital in Koprivnica, north-west Croatia, from December 2012 to October 2013. The study was carried out in adherence to the tenets of the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of Dr Tomislav Bardek General Hospital.

The inclusion criterion was age ≥ 40 in all patients presenting to the Ophthalmology Polyclinic for various ocular problems. Exclusion criteria were pseudo-phakic and/or aphakic patients of any age, patients with dense ocular media opacities, and patients with concomitant congenital eye disease. A total of 5349 patients aged ≥ 40 were examined and screened for PXS and PXG. All patients underwent detailed ophthalmologic examination including ocular history, visual acuity testing, slit-lamp biomicroscopy for evidence of pseudoexfoliatory material on the edge of the pupil or

lens, applanation tonometry and indirect funduscopy. In patients suspected of glaucoma and/or diagnosed with PXS, an additional examination was carried out including gonioscopy and visual field testing. Functional glaucoma testing was used to diagnose PXG, considering that at the time of the study optical coherence tomography device was not available, although it is an inevitable structural diagnostic tool required for detecting early structural optic nerve head changes.

The criteria for glaucoma suspected group were IOP ≥ 23 mm Hg, focal glaucomatous disc change (disc hemorrhage, notch of the neuroretinal rim, marked sloping of the rim tissue, narrowest remaining rim of 0.1 disc diameter or less), cup to disc ratio asymmetry (≥ 0.3) and vertical cup to disc ratio (> 0.8). The criterion used to diagnose PXS was the presence of pseudoexfoliatory material on one or more anterior segment structures. The criterion for diagnosing PXG was the presence of pseudoexfoliatory material on one or more anterior segment structures with or without raised IOP in the presence of visual field defects compatible with glaucoma. The χ^2 -test was used to assess differences in the prevalence of different glaucoma related diagnoses according to age, gender and PXS groups. Furthermore, χ^2 -test was used in the analysis of PEX prevalence differences according to age and gender. All p values below 0.05 were considered statistically significant. MedCalc Statistical Software version 13.0 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2014) was used in all statistical procedures.

Results

Out of 5349 patients examined, there were 1994 (38.38%) males and 3201 (61.61%) females. Distribution of patients according to age groups is shown in Table 1. Study patients were classified into groups as follows: 1) healthy subjects without glaucoma (WG); 2) glaucoma suspected group (GSG); 3) primary open-angle glaucoma (POAG); 4) primary angle-closure glaucoma (PACG); and 5) secondary glaucoma (SG).

Differences in the prevalence of various glaucoma related diagnoses in study patients according to gender are shown in Table 2. Only one significant difference was noted, i.e. PACG was more prevalent in female gender as compared with male gender (4.81% *vs.*

Table 1. Distribution of patients according to age groups

	Age group (yrs)				Total
	40-49	50-59	60-69	≥70	
Number of patients	705	1370	1287	1987	5349

Table 2. Gender difference in the prevalence of different glaucoma related diagnoses (χ^2 -test)

		Gender				P
		Male		Female		
		N=1994		N=3201		
		n	%	n	%	
Group	WG	1689	84.7%	2680	83.7%	0.368
	GSG	80	4.0%	154	4.8%	0.199
	POAG	191	9.6%	297	9.3%	0.755
	PACG	7	0.4%	38	1.2%	0.003
	SG	27	1.4%	32	1.0%	0.306

WG = without glaucoma; GSG = glaucoma suspected group; POAG = primary open-angle glaucoma; PACG = primary angle-closure glaucoma; SG = secondary glaucoma

Table 3. Age difference in the prevalence of various glaucoma related diagnoses (χ^2 -test)

		Age group (yrs)								P
		45-49		50-59		60-69		≥70		
		N=705		N=1370		N=1287		N=1987		
		n	%	n	%	n	%	n	%	
Group	WG	674	95.6%	1260	92.0%	1091	84.8%	1473	74.1%	<0.001
	GSG	16	2.3%	49	3.6%	64	5.0%	111	5.6%	<0.001
	POAG	10	1.4%	46	3.4%	105	8.2%	340	17.1%	<0.001
	PACG	0	0.0%	2	0.1%	9	0.7%	37	1.9%	<0.001
	SG	5	0.7%	13	0.9%	18	1.4%	26	1.3%	0.422

WG = without glaucoma; GSG = glaucoma suspected group; POAG = primary open-angle glaucoma; PACG = primary angle-closure glaucoma; SG = secondary glaucoma

Table 4. Differences in primary open-angle glaucoma (POAG) prevalence according to age groups (χ^2 -test)

		POAG	
		n	%
Age group (yrs)	40-49	10	2.0%
	50-59	46	9.2%
	60-69	105	21.0%
	≥70	340	67.9%
p<0.001			

4.01%, p=0.003). All other glaucoma diagnoses were equally distributed in both genders. Age difference in the prevalence of various glaucoma related diagnoses showed that glaucoma suspected diagnosis, POAG and PACG were significantly more prevalent among older patients (p<0.001). Patients without glaucoma disease were significantly more prevalent in younger age groups (Table 3). Differences in the prevalence of POAG according to age groups are shown in Table 4. Age-specific prevalence distribution in POAG group showed an increase from 2% in the 40-49 age group to 67.9% in the ≥70 age group.

A total of 5349 patients were examined for PXS and PXG. The prevalence of PXS was 3.6% and of POAG 9.4%, of which 23.6% of cases had PXG. Age and gender differences in the prevalence of PXS are shown in Table 5. PXS was significantly more prevalent in older age groups; more than 80% of patients with PXS were over 70 years of age (p<0.001). There was no significant gender difference (p=0.121).

Table 6 shows differences in the prevalence of PXS according to particular diagnoses. The most prominent

differences were recorded in the GSG and POAG groups (p<0.001). The prevalence of PXG in the PXS population was 63.3%. The GSG patients also showed a high prevalence of PXS (31.4%).

Discussion

Our study investigated the prevalence of PXS and PXG in northwest Croatia and their association with POAG. All our patients were Caucasians, which cor-

Table 5. Age and gender differences in the prevalence of pseudoexfoliation syndrome (PXS) (χ^2 -test)

		PXS				p
		No		Yes		
		n	%	n	%	
Age group (years)	45-49	704	13.60%	1	0.50%	<0.001
	50-59	1363	26.40%	7	3.70%	
	60-69	1259	24.40%	28	14.90%	
	≥70	1835	35.60%	152	80.90%	
Gender	Male	1932	38.60%	62	33.00%	0.121
	Female	3075	61.40%	126	67.00%	

Table 6. Differences in PXS prevalence according to various diagnoses (χ^2 -test)

		PXS				p
		No		Yes		
		N=5161		N=188		
		n	%	n	%	
Group	WG	4491	87.0%	7	3.7%	<0.001
	GSG	181	3.5%	59	31.4%	<0.001
	POAG	382	7.4%	119	63.3%	<0.001
	PACG	46	0.9%	2	1.1%	0.88
	SG	61	1.2%	1	0.5%	0.637

PXS = pseudoexfoliation syndrome; WG = without glaucoma; GSG = glaucoma suspected group; POAG = primary open-angle glaucoma; PACG = primary angle-closure glaucoma; SG = secondary glaucoma

responds to the demographic profile of the country. In our study, the overall prevalence of POAG was 9.4%. Considering the studies of racial distribution and the highest prevalence of POAG in the black populations of all ages^{32,33}, this region may be considered to be at low risk. Our results are comparable with data of previous studies^{34,35} concerning age differences in the prevalence of POAG. In our study, the age-specific prevalence distribution increased from 1.4% in the 40-49 age group to 17.1% in the ≥70 age group. In the study by Rudnicka *et al.*, the proven age proportional increase in the prevalence of POAG with age was highest in white populations³⁶. The odds ratio *per* decade increase in age was 2.3 in our population, which is comparable with the mentioned study. We found no gender differences in patients with POAG but in those with angle-closure glaucoma it was 3 times more prevalent in female gender. Similar data have also been reported from previous studies^{37,38}. The study by Bojić *et al.* investigated the incidence of acute angle-closure

glaucoma among residents of Dalmatia, the southern part of Croatia, and found the relative risk of developing acute angle-closure glaucoma to be 2.1 times higher in women as compared with men^{39,40}. We found the prevalence of PACG to be 0.9%. Such a low prevalence of PACG has been reported among Caucasians⁴¹.

In our study, the prevalence of GSG patients was 4.5%. The GSG patients also showed a high prevalence of PXS. Such prevalence has previously been reported in the Reykjavik Eye Study⁴². The prevalence of PXS was 3.6%. Analyzing the results from other European countries on the prevalence of PXS^{7,8,12,17}, our results place the northwest Croatia population in the low risk group for PXS. We found no significant gender difference but only age related difference among patients with PXS. Other studies showed a higher prevalence of PXS in women^{8,11,43}, but the study by Susić and Brajković conducted in the population of the southern part of Croatia revealed no significant gender difference in the prevalence of PXS either¹⁹.

Pseudoexfoliation syndrome was significantly more prevalent in older age groups and more than 80% of PXS patients were over 70 years of age. Similar data have been reported before^{8,11,17,43}. The increase in PXS was 66 times greater as compared with the 60-69 age group. A total of 119 (63.3%) patients in the PXS group exhibited glaucoma, while in the non PXS group only 7.4% of patients suffered from glaucoma. These data confirmed the high prevalence of glaucoma in the population with PXS.

Given the aging of the population in Croatia⁴⁴, further increase in PXS, PXG and POAG is expected in the future. Determination of the prevalence of glaucoma disease is important for each country in terms of healthcare planning and prevention of blindness, with particular reference to glaucoma disease and the elderly⁴⁵. The data on the prevalence of PXS and PXG recorded in this study are the first referring to the area of northwest Croatia. The benefit of this study is that it was the first such study performed in Croatia, especially considering the number of participants. Since we were unable to detect patients with preperimetric glaucoma because we could not use optical coherence tomography, we consider it a limitation of the study. Education of the population at large should be implemented, focusing on the importance of family history in all types of glaucoma³⁰. To our knowledge, this was the first study conducted in the northwest Croatia population to determine the prevalence of PXS, PXG, POAG and PACG. This study provided data for future studies and monitoring of the prevalence of different types of glaucoma.

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Sažetak

UČESTALOST PSEUDOEKSFOLIJATIVNOG SINDROMA I PSEUDOEKSFOLIJATIVNOG GLAUKOMA U POPULACIJI SJEVEROZAPADNE HRVATSKE U DOBI OD 40 GODINA I VIŠE

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Svrha ovoga istraživanja bila je procijeniti učestalost pseudoeksfolijativnog sindroma i pseudoeksfolijativnog glaukoma te njihovu povezanost s glaukomom otvorenog kuta kod bolesnika Očne poliklinike Opće bolnice "Dr. Tomislav Bardek" u Koprivnici, sjeverozapadna Hrvatska. Ovo prospektivno istraživanje provedeno je od prosinca 2012. do listopada 2013. godine. Ukupno je pregledano 5349 ispitanika u dobi od 40 godina i više. Kod svakog je učinjen kompletan oftalmološki pregled uključujući anamnezu, ispitivanje vidne oštine, pregled na biomikroskopu, aplanacijsku tonometriju, pregled ocnoga živca i pozadine oka te vidno polje i gonioskopiju kod onih sa sumnjom na glaukom. Kriteriji za isključenje bili su bolesnici s pseudofakijom/afakijom, bolesnici s prirođenim očnim bolestima te oni s vrlo gustim zamućenjem očnih medija. Od 5349 bolesnika bilo je 1994 (38,38%) muškaraca i 3201 (61,61%) žena. Učestalost pseudoeksfolijativnog sindroma bila je 3,6%, a primarnog glaukoma otvorenog kuta 9,4%, od čega 23,6% spada u skupinu pseudoeksfolijativnog glaukoma. Rezultati ove studije proširuju naše spoznaje o pseudoeksfolijativnom sindromu i pseudoeksfolijativnom glaukomu u Hrvatskoj, osobito u sjeverozapadnoj regiji.

Ključne riječi: *Eksfolijacijski sindrom – epidemiologija; Učestalost; Starija osoba; Glaukom*