DOI: 10.14744/eer.2023.72681
Eur Eye Res 2024;4(2):103–108

EUROPEAN EYE RESEARCH

ORIGINAL ARTICLE

Characteristics and frequency of pigmentary glaucoma in the Turkish population

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Abstract

Purpose: To analyze the prevalence and characteristics of pigmentary glaucoma (PG) and pigment dispersion syndrome (PDS) in patients diagnosed at a tertiary center eye clinic in Türkiye.

Methods: This retrospective, single-center study was conducted at the glaucoma clinic of Haydarpaşa Numune Training and Research Hospital. The files of patients with glaucoma diagnoses between 2015 and 2023 were retrospectively reviewed. The prevalence of PG and PDS, characteristics of the patients, surgical requirements, applied surgical procedures, and risk factors for PG were analyzed.

Results: Of the 7,800 files that were reviewed, 50 (0.64%) belonged to patients with PDS or PG. The mean follow-up time was 41.45±34.56 months, and the mean age of the patients was 48.9±12.86 years. Twenty-five (50%) patients were male. Of the 100 eyes reviewed initially, 56 had PDS, 44 had PG, and 17 (30.3%) with PDS progressed to PG during the follow-up period. The mean spherical equivalent (SE) was –1.03±1.62 diopter. In the comparison of eyes with PDS and PG, there were no significant differences with regard to age, sex, SE, central corneal thickness, or best-corrected visual acuity. A median intraocular pressure (IOP) of 17.5 mmHg was achieved on two median glaucoma medications at the last visit. Overall, 10 eyes with PG required surgical and laser interventions for IOP control. Laser peripheral iridotomy (LPI) was performed on nine of these eyes, trabeculectomy with antimetabolite augmentation on two (which had previously undergone LPI), and XEN® gel stent implantation on one.

Conclusion: Among the glaucoma patients, the detected frequency of PDS and PG was 0.64%. We did not detect male dominance. The median SE was –1.03±1.62 diopter, indicating mild myopia, which is consistent with the literature.

Keywords: Myopia; pigment dispersion syndrome; pigmentary glaucoma; Turkish population.

Pigment dispersion syndrome (PDS) is characterized by pigment dispersion from the posterior pigment epithelium of the iris and deposition of pigment granules on anterior chamber structures, such as the endothelium (Krukenberg's spindle), trabeculum, and anterior iris surface, as well as posterior chamber structures, including zonules and the lens capsule (Zentmayer sign).[1,2] The clinical manifestations of PDS include elevated intraocular pressure (IOP) and a type of glaucoma known as pigmentary glaucoma (PG).[2]

Cite this article as: Un Y, Alpogan O, Bolac R, Yildiz MB, Aslan CA, Turan Vural E. Characteristics and frequency of pigmentary glaucoma in the Turkish population. Eur Eye Res 2024;4(2):103–108.

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Submitted Date: 26.10.2023 **Revised Date:** 09.12.2023 **Accepted Date:** 18.12.2023 **Available Online Date:** 01.08.2024

The clinical features of PDS include heavy trabecular meshwork pigmentation, mild myopic refractive error, deep anterior chamber, midperipheral transillumination defects, and posterior iris bowing.[2,3] The mechanism underlying pigment dispersion is considered to be related to posterior iris bowing, resulting in friction between the posterior iris and anterior lens, which is called reverse pupil block.[1,4] Three clinical stages of PDS have been proposed.[1] The first includes pigment dispersion with or without an elevated IOP. The second presents an association between glaucomatous optic neuropathy and elevated IOP. The final stage is resorption, in which IOP decreases and pigment deposits resorb as a result of the healing process in the reverse pupil block. In some studies, the final clinical appearance of at least some cases has been considered normal tension glaucoma (NTG).[5]

Although PDS and PG have been well defined since 1949, when they were first described by Okafor et al.,[6] epidemiologic studies on these conditions have mostly had inconclusive results, probably due to their silent course and underdiagnosis. Most studies have shown male predominance, mild myopia, young age (30–50 years), and Caucasian descendants as risk factors for PDS and PG.[3,7] However, other studies have reported that PG is much more prevalent in men,[8] with 78–93% of patients with PG being male,[3,9] whereas PDS has similar prevalence across men and women,[10] and myopia represents a risk factor for PDS development.[3] Moreover, myopia has a positive correlation with PDS severity, i.e., the more myopic the eye is, the more likely it will be affected.[11,12] In a recent report on patients seeking refractive surgery, the prevalence of PDS was found to be 25.9% (165/637 eyes); however, these data were probably affected by bias due to the high prevalence of myopic patients involved in the study.[13] Ritch et al.[10] reported that in a largely people of European descent, PDS accounted for only 2.45% of all glaucoma cases. Previous studies have indicated a 15% to 50% risk of PG development in patients with PDS.[12] PG and PDS have been thought to be rare in the Asian population,[7] despite the high prevalence of myopia.[5] In addition, the prevalence of NTG is high in Asians, even higher than in Caucasians.[14] It has been hypothesized that cases of NTG in Japan may include some with PG in the regression phase.[5]

In this study, we aimed to investigate the prevalence of PDS and PG in our glaucoma clinic and analyze the eye characteristics and demographics of patients with PDS and PG, which may be representative of the Turkish population. To our knowledge, this is the first study analyzing the frequency of PDS and PG in Turkish patients.

Materials and Methods

This study was approved by the local ethics committee (registration code: HNEAH-KAEK 2023/145) and adhered to the tenets of the Declaration of Helsinki. It is a retrospective, single-center study conducted in the ophthalmology clinic of Haydarpaşa Numune Training and Research Hospital. A total of 7,800 patient files obtained from all glaucoma clinics were reviewed, and the files of patients with a diagnosis of PDS or PG who had at least 6 months of follow-up data were included in the study.

The age, sex, and eye examination notes, including best-corrected visual acuity (BCVA), central corneal thickness (CCT) refractive status, glaucoma medication, cup-to-disc ratio (CDR), peripapillary nerve fiber layer (RNFL) thickness, and visual field (VF), were retrospectively analyzed. BCVA was measured in decimals using a Snellen chart. Refractive status was obtained as the sum of the sphere and half of the cylinder and expressed in spherical equivalent (SE). RNFL measurements were performed using the notes in patient files. These measurements were taken by two different optical coherence tomography devices: Optovue (Optovue Inc., Fremont, CA, USA) and Topcon DRI-OCT (Triton, Topcon, Tokyo, Japan). The mean RNFL values were noted. For VF examinations, the Goldman perimetry 30/2 full-threshold strategy (Humphrey Field Analyser; Carl Zeiss Meditec, Dublin, CA, USA) was used for all procedures. According to the findings, patients with false positives and negatives and those with fixation losses of <30% were accepted to have reliable data, and their mean deviation (MD) and pattern standard deviation (PSD) values were analyzed.

IOP measurements were undertaken from the first visit to the last visit using Goldman applanation tonometry. The number of active molecules in glaucoma medications was noted. CCT was measured optically using an air-puff tono-pachymeter (Topcon Corporation, Tokyo, Japan). The PDS diagnosis was made based on the detection of the following findings: Krukenberg's spindle in the endothelium, pigment clumps on the iris surface, gonioscopic open angle with dense uniform pigmentation without any glaucomatous optic neuropathy, and a VF or RNFL defect. In the presence of glaucomatous optic neuropathy findings and compatible VF defects with or without an IOP of over 21 mmHg, the PG diagnosis was made.

The follow-up times of the patients were obtained from the files. Surgical interventions performed for IOP control and any other intraocular procedures were also analyzed for both patients with PDS and those with PG.

The patients with PDS and PG were compared with respect to age, sex, refraction, CCT, MD, PSD, and RNFL measurements. We also conducted a regression analysis to detect the main effect of the investigated parameters on glaucoma development.

Statistical Analysis

We conducted statistical analyses using the Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 (SPSS Inc., Chicago, IL). We employed the t-test for parametric data, the Mann–Whitney U test for independent non-parametric data, and the Wilcoxon test for non-parametric paired data comparisons. Categorical values were compared using the Chi-square test. We also utilized multivariate and univariate logistic regression analyses to examine the relationship between the investigated variables and PG diagnosis. A significance threshold of $P < 0.05$ was applied.

Results

Of the 7,800 reviewed files, 50 (0.64%) belonged to patients diagnosed with PDS or PG. The median age of the patients was 48.9±12.86 years, with a median follow-up of 41.45±34.56 months. The sex distribution was equal, with the sample including 25 (50%) male and 25 (50%) female patients. The mean BCVA was 0.88±0.17 in decimal. The mean CCT was 551.04±35.2 microns, the mean CDR was 0.48±0.24, and the mean SE was −1.03±1.62 diopters (D).

At the initial visit, of the 100 eyes of 50 patients, 56 had PDS and 44 had PG. During the follow-up, 17 (30.3%) eyes with PDS progressed to PG, with an average progression time of 11±4.3 months. The final distribution of the eyes with a diagnosis of PDS and PG is shown in Figure 1. The comparison of ocular characteristics between the PG and PDS groups is presented in Table 1.

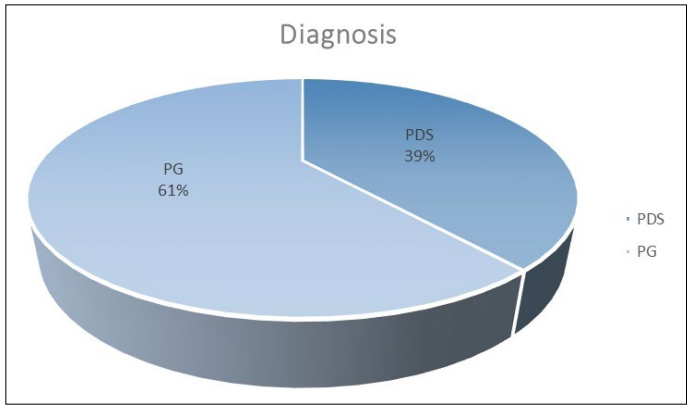

Fig. 1. Final distribution of the eyes diagnosed with PDS or PG. PDS: Pigment dispersion syndrome; PG: Pigmentary glaucoma.

There were no statistically significant differences between the PG and PDS groups in relation to BCVA, age, sex, SE, or CCT. However, significant differences were observed in CDR, MD, PSD, and the mean RNFL values between the two groups. The patients with PG had a mean initial IOP of 19.86±6.76 mmHg while on an average of 2.59±0.86 (median: 2) glaucoma medications. The patients with PDS, who were not using any glaucoma medication, had a mean IOP of 21.33±5.17 mmHg. The IOP measurements at both the initial and last visits were statistically significantly higher in patients with PDS (p=0.08 and 0.001, respectively). Table 2 presents the IOP values measured at the initial and last visits of the patients in both groups.

During the follow-up period, none of the patients with PDS underwent any ocular laser or surgical interventions. In contrast, 13 (21.3%) eyes with PG required such interventions, including phacoemulsification and intraocular lens implantation in 3 (4.9%) cases, laser peripheral iridotomy (LPI) in 9 (14.7%), trabeculectomies with antimetabolite augmentation in 2 (3.2%) (with a previous history of LPI), and XEN® gel stent implantation in 1 (1.6%). All surgical interventions performed for IOP control resulted in IOP values under 21 mmHg, with only two cases (one following LPI and another following LPI and trabeculectomy) achieving IOP control without any glaucoma medication at the last visit. Of the eyes with PG, 83.6% (n=51) were treated with glaucoma medication, while 16.3% (10 eyes) required surgical interventions for IOP control.

Multivariate and univariate logistic regression analyses, including sex, CCT, SE, and age, did not show a significant effect of these variables on PG development (Table 3).

Discussion

PG and PDS are typically observed in young, myopic, Caucasian males.[9] Genetic factors have been suggested as a potential cause, with a key finding indicating that zonules inserted into the anterior capsule in bundles are more likely to cause pigment to rub off the posterior iris compared to single strands.[2,15] This supports Campbell's theory of the reverse pupil block mechanism,[15] which leads to friction between the posterior iris epithelium and the anterior lens surface. Genetic differences can explain the varying prevalence across different ethnic populations. The prevalence of PDS in the USA has been reported to be 2.5%, and it accounts for 1–1.5% of glaucoma cases in Western countries.[8] However, non-Caucasians exhibit a lower prevalence, potentially due to differences in iris and lens anatomy or iris behavior.[2,7] For instance, atypi-

Table 1. Characteristics of patients and eyes with PG or PDS

Variables	PDS	PG	Total	P-value
Age	47.92±9.4 (M: 48)	49.52±14.72 (M: 49)	48.9±12.86 (M: 48)	0.507[1]
Sex (male/female)	8/12	16/14	24/26	0.202[3]
BCVA	0.92±0.14 (M: 1)	087±0.19 (M: 1)	0.88±0.17 (M: 1)	0.335[1]
SE	−0.91±1.77 (M: −0.75)	−1.1±1.53 (M: −0.75)	−1.03±1.62 (M: −0.75)	0.615[2]
CCT	558.84±36.57 (M: 560)	546.29±33.82 (M: 550)	551.04±35.2 (M: 551.5)	0.118[1]
CDR	0.32±0.15 (M: 0.3)	0.58±0.22 (M: 0.5)	0.48±0.24 (M: 0.4)	0.000[1]
MD	−2.00±1.89 (M: −1.65)	−4.7±6.77 (M: −2.89)	−3.79±5.74 (M: −2.54)	0.012[1]
PSD	1.88±0.59 (M: 1.79)	296±2.51 (M: 2)	2.59±2.12 (M:1.91)	0.029[2]
RNFL	100.41±9.68 (M: 100)	88.58±18.79 (M: 92)	93.22±16.81 (M: 96)	0.001[1]

[1]t-test; [2]Mann-Whitney U test; [3]Chi-square test; M: Median; PDS: Pigment dispersion syndrome; PG: Pigmentary glaucoma; BCVA: Best-corrected visual acuity; SE: Spherical equivalent; CCT: Central corneal thickness; CDR: Cup-to-disc ratio; MD: Mean deviation; PSD: Pattern standard deviation; RNFL: Retinal nerve fiber layer.

Table 2. IOP values of the groups measured at the first and last visits

IOP (mmHg)	PDS	PG	Total	p[1]
First visit	21.33±5.17 (M: 20) (n=56)	19.85±6.76 (M:19) (n=44)	20.43±6.21 (M: 19)	0.08
Last visit	17.94±3.04 (M: 17.5) (n=39)	15.34±3.28 (M: 15) (n=61)	16.28±3.42 (M: 16)	0.001*

[1]Mann-Whitney U test; *statistically significant; PDS: pigment dispersion syndrome; PG: pigmentary glaucoma; IOP: intraocular pressure.

Table 3. Logistic regression analyses of the correlation between PG diagnosis and investigated variables

Variables	Multivariate					Univariate				
	B	Sig.	Exp (B)	95% CI for Exp (B)		B	Sig.	Exp(B)	95% CI for Exp(B)	
				Lower	Upper				Lower	Upper
SE	0.009	0.958	1.009	0.721	1.412	−0.073	0.611	0.930	0.703	1.231
Sex (male)	−0.781	0.144	0.458	0.161	1.305	0.527	0.204	1.694	0.752	3.819
CCT	−0.007	0.347	0.993	0.978	1.008	−0.011	0.120	0.989	0.976	1.003
Age	0.006	0.759	1.006	0.966	1.048	0.010	0.542	1.010	0.978	1.042

CI: Confidence interval; PG: Pigmentary glaucoma; SE: Spherical equivalent; CCT: Central corneal thickness.

cal features are reported in the people of African descent, such as an association with older age, hyperopia, and female sex preponderance.[16]

In our analysis, we found a prevalence of 0.64% for PDS and PG among the patients diagnosed in our glaucoma clinic. During the follow-up, 30.3% of the PDS cases progressed to PG. The mean age was 48.9±12.86 years, with an equal sex distribution. While some studies have reported male predominance in PG cases, our analysis, representing the Turkish population, showed a similar frequency of PDS and PG in both males and females. The mean SE was −1.03±1.62 D, indicating mild myopia. We observed mild myopic refraction but not high myopia.

Considering the young median ages of our patients diagnosed with PDS or PG, we may have overlooked older PG cases, possibly misdiagnosing them as NTG. In addition, the high incidence of pseudoexfoliation in our clinic may have masked some PG and PDS cases. As PDS progresses naturally, posterior iris bowing leads to pigment dispersion, pigment deposition in anterior segment structures, and trabeculum-related IOP elevation. With aging, lens thickening reduces the reverse pupil block and pigment shedding. Over time, this may lead to the resorption of pigmentary deposits, potentially explaining NTG presentations.

In the comparison of patients with PDS and PG, we found no significant differences in BCVA, age, sex, SE, or CCT. However, the CDR, MD, PSD, and RNFL values differed significantly between the two groups. In terms of IOP, the patients with PG had an initial IOP of 19.86±6.76 mmHg while on an average of 2.59±0.86 glaucoma medications. The patients with PDS, who were not taking any glaucoma medications, had a mean IOP of 21.33±5.17 mmHg. The IOP value was significantly higher in the PDS group (p=0.08).

There were no significant factors effective in glaucoma development among the parameters included in multivariate and univariate analyses, namely, SE, CCT, and sex. We did not include IOP in the regression analysis due to the potential bias related to glaucoma medication use in only one group.

Gomez Goyeneche et al.[12] analyzed the progression of PDS to PG in a Latin American population. In their report, the rate of progression of PDS to PG was determined to be 37.5% after an average follow-up of 50.7 months. The authors also noted that an IOP greater than 21 mmHg was the only statistically significant risk factor for progression.

During the follow-up, none of the patients with PDS underwent ocular laser or surgical interventions, while 13 (21.3%) eyes with PG required such interventions, including phacoemulsification (n=3, 4.9%), laser LPIs (n=9, 14.7%), trabeculectomy with antimetabolite augmentation (accompanied by a history of LPI) (n=2, 3.2%), and XEN® gel stent implantation (n=1, 1.6%). All surgical interventions resulted in IOP values under 21 mmHg, with only two eyes achieving IOP control without any glaucoma medication. Of the eyes with PG, 83.6% were managed with glaucoma medication, whereas 16.3% required surgical interventions for IOP control.

There is not enough data on the prevalence and incidence of PG among the Turkish population. In 2005, Elgin et al.[17] reported 18 cases of PDS and PG in the Turkish population. They reported the median age to be 35.7±3.6 (31–45) years, and their sample included 15 (83.3%) male patients. The mean IOP, SE, and axial length values were determined to be 24.8±1.3 mmHg (22–28 mmHg), −4.9±1.2 D (−3–8) D, and 24.9±0.7 mm (24.2–26.1 mm), respectively. To our knowledge, our study represents the largest analysis of the frequency of PG in glaucoma cases in the Turkish population. However, our report differs from the study of Elgin et al.[17] in that our cases were less myopic and older and had an equal distribution in terms of sex.

The current analysis has some limitations, such as its retrospective and single-center design. Moreover, some asymptomatic cases of PDS and PG may have been overlooked. Although we screened all glaucoma files and included all eligible cases in the analysis, there is a need for multicenter studies to reach more conclusive results on the frequency and characteristics of PDS and PG among Turkish patients. The age distribution of our patients also suggests that we may have overlooked older PDS cases, possibly misdiagnosing them as NTG.

Conclusion

The prevalence of PG and PDS among glaucoma patients was 0.64%. Sex or high-degree myopia was not associated with PDS or PG. While 83.6% (n=51) of the eyes with PG were controlled with glaucoma medication, 16.3% (n=10) required surgical interventions for IOP control.

Ethics Committee Approval: Ethics Committee of Haydarpasa Numune Training and Research Hospital (date: 14/08/2023; registration code: HNEAH-KAEK 2023/145-4270).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: Y.U.; Design: Y.U.; Supervision: Y.U., E.T.V.; Resource: Y.U.; Materials: Y.U., O.A., R.B., M.B.Y., C.A.A., E.T.V.; Data Collection and/or processing: Y.U., O.A., R.B., M.B.Y., C.A.A., E.T.V.; Analysis and/or interpretation: Y.U.; Literature search: Y.U.; Writing: Y.U.; Critical reviews: Y.U., E.T.V.

Conflict of Interest: None declared.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study received no financial support.

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