Prevalence of primary angle-closure disease in retinitis pigmentosa

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Purpose: To determine the prevalence of primary angle-closure disease (PACD) in patients with retinitis pigmentosa (RP). Methods: This was a retrospective review of the electronic medical records of all RP patients over the age of 10 years attending the Genetics Eye Clinic of a tertiary-care hospital during a 7-year period. Information regarding age, gender, vision, refraction, lens, intraocular pressure (IOP), type of RP, and inheritance pattern using pedigree charts for all patients were obtained. Patients with a shallow anterior chamber, high IOP, or glaucomatous optic discs were referred to the glaucoma department where they underwent additional IOP measurements, a gonioscopy, and disc evaluation by a glaucoma specialist. The prevalence of PACD was determined. Results: A total of 6,186 RP patients were examined during the study period, of which 95.1% had typical RP. The prevalence of primary angle-closure suspects was 2.9%, primary angle closure was 0.65%, and primary angle-closure glaucoma (PACG) was 2.27%. In contrast, the prevalence of primary open-angle glaucoma was 1.29%. The prevalence of PACG in those older than 40 years was 3.8% (95% confidence interval: 1.6–6.0). Conclusion: The prevalence of PACG in RP patients over 40 years was higher than that found in the general population of a similar age (3.8% vs. 0.8%). In our cohort of RP patients, 5.9% had PACD. Hence, gonioscopy is warranted in all RP patients to identify this condition and treat it appropriately.

Key words: Glaucoma, primary angle-closure disease, retinitis pigmentosa

There is an established association between retinitis pigmentosa (RP) and primary open-angle glaucoma (POAG).[1-3] The prevalence of POAG in RP is reported to be between 2% and 12%,[1] There is also some literature on the association between primary angle-closure glaucoma (PACG) and RP.[4,5] A study performed in Canada on a predominantly Caucasian RP population over 40 years of age found the prevalence of PACG to be 1.03%.[4] Another case series from Nepal that included both primary and secondary (lens-induced) angle-closure disease found the prevalence of angle-closure disease to be 2.13%.[6] A population-based study from Taiwan that used the health insurance database from 1996 to 2010 found that RP patients had 3.64-fold greater odds of having acute angle closure.[7] Therefore, there does seem to be some predilection for angle-closure glaucoma (acute and chronic) in patients with RP. However, a systematic evaluation of the different stages of primary angle-closure disease (PACD), that is, primary angle-closure suspects (PACS), primary angle closure (PAC), and PACG, in RP is lacking.

The purpose of the present study was to determine the prevalence of PACD in patients with RP.

Methods

This was a retrospective review of the electronic medical records of all patients over the age of 10 years with RP attending the genetics eye clinic of a tertiary hospital between April 2012 and June 2019. The study was performed in compliance with the Declaration of Helsinki and was approved by the institutional review board and ethics committee.

All patients attending the genetics eye clinic of the hospital routinely undergo a thorough medical history, family history and pedigree charting, and complete ocular examination including vision, refraction, slit-lamp examination, intraocular pressure (IOP) measurement, and dilated fundus examination with a 90-D lens. They also undergo a macular Spectralis SD-OCT and autofluorescence imaging (Heidelberg Engineering) if media clarity allows. Visual fields examination (Humphrey Field Analyzer II, model 720i) is performed when possible. The demographic data (age, gender, presence of systemic illnesses such as diabetes mellitus and hypertension, lens status, IOP) of all RP patients were retrieved. RP was defined based on clinical fundus appearance (waxy disc pallor, bony spicules, attenuation of blood vessels, etc.) and confirmed on full-field electroretinogram (grossly reduced or unrecordable scotopic and photopic responses) in case of atypical fundus picture. The patients in whom the medical history was suggestive of RP but the abovementioned clinical criteria were not fulfilled were grouped as atypical RP. RP patients who presented with
characteristic systemic features known to be associated with this disease were classified as syndromic RP. All patients with a shallow anterior chamber, IOP greater than 21 mm Hg, or cup: disc ratio > 0.6 were referred to the glaucoma department for the opinion of a glaucoma specialist. Here, additional IOP measurements on Goldmann Applanation tonometry (GAT), gonioscopy using a 4 mirror goniolens, and a stereoscopic optic disc evaluation were performed. These supplementary data and the information regarding glaucoma treatment were also included for analysis. Other details collected were the type of RP and mode of inheritance. Patients with retinal dystrophy other than RP and patients under 10 years of age (as they may not cooperate for a complete eye examination) were excluded.

The following definitions were used to classify patients referred to the glaucoma clinic:

Primary angle-closure suspect (PACS): >180° of iridotrabecular contact (ITC), IOP <21 mm Hg, and cup: disc ratio ≤0.6 with no glaucomatous features (rim notching or thinning).

Primary angle closure (PAC): >180° of ITC with peripheral anterior synechiae (PAS) or IOP >21 mm Hg, and cup: disc ratio ≤0.6 with no glaucomatous features.

Primary angle-closure glaucoma (PACG): >180° of ITC, IOP >21 mm Hg, and cup: disc ratio ≥0.7 with glaucomatous features.

Primary open-angle glaucoma (POAG): Open angles, IOP >21 mm Hg, and cup: disc ratio ≥0.7 with glaucomatous features.

Secondary glaucoma: IOP >21 mm Hg with an identifiable secondary cause such as phacomorphic glaucoma and subluxated lens.

Mean with standard deviation (SD) was calculated for continuous variables, and frequency with percentage (%) was tabulated for categorical variables. The prevalence of the above conditions in this cohort of RP patients was then determined. If the primary angle-closure disease (PACD) was asymmetric between the 2 eyes of a patient, the diagnosis given to the patient would be based on the eye with the more severe disease. ANOVA statistic was used to compare the clinical parameters between RP patients with and without glaucoma. Chi-square test was used to identify any association between the glaucoma diagnosis and RP features. Statistical analysis was performed using Stata version 14.2 (StataCorp, College Station, Tx). P <5% was considered statistically significant.

Results

The electronic medical records of 618 RP patients were analyzed, and the demographic data are shown in Table 1. The mean age was 41.4 ± 15.8 years. The visual impairment of all patients was determined based on the presenting distance visual acuity of the better eye and was classified based on the ICD-10 definitions (2006 revision). Mild or no visual impairment (visual acuity equal to or better than 6/18) was seen in 242 (39.16%) patients. Moderate visual impairment (visual acuity worse than 6/18 but equal to or better than 6/60) was seen in 208 (33.66%) patients. Severe visual impairment (visual acuity worse than 6/60 but equal to or better than 3/60) was seen in 23 (3.72%) patients. Blindness (visual acuity worse than 3/60) was seen in 145 (23.46%) patients. Typical RP was noted in 95.1% of the cohort. The clinical ocular data are shown in Table 2. The mean IOP was 14.0 ± 6.1 mm Hg, and the mean cup: disc ratio was 0.5 ± 0.2. Cataract extraction had been performed in 11% of the eyes. Eyes with the presence of PAS or IOP >21 mm Hg without glaucomatous disc features were classified as PAC, and eyes with glaucomatous features were classified as PACG.

Based on the examination in the glaucoma clinic, 18 (2.9%) RP patients were noted to be PACS and four (0.65%) had PAC. Based on the definitions of glaucoma, 14 patients (2.3%) had PACG and eight patients (1.3%) had POAG as shown in Table 1. There was no significant association between the type of RP (typical, atypical, or syndromic) and the glaucoma diagnosis (r = 3.91, P = 0.95). There was no significant association between the inheritance pattern of RP and the glaucoma diagnosis. (r = 24.25, P = 0.06). The mean age (standard error) of RP patients with glaucoma was found to be significantly higher than those without glaucoma (52.7 ± 2.4 vs. 41.0 ± 0.4, P < 0.001). In RP patients over 40 years of age, the prevalence of PACG was 3.8% (95% confidence intervals: 1.6–6.0).

The mean IOP (standard deviation) in RP eyes with glaucoma was higher than those without glaucoma (23.0 ± 11.8 vs. 13.6 ± 5.5,

### Table 1: Demographic and clinical features of 618 patients with retinitis pigmentosa (RP)

| Feature                        | 618 RP patients |
|--------------------------------|-----------------|
| Mean Age (years)               | 41.4±15.8       |
| Male gender (%)                | 381 (61.7%)     |
| Prevalence of hypertension (%) | 69 (11.2%)      |
| Prevalence of diabetes (%)     | 62 (10%)        |
| Type of RP (%)                 |                 |
| Typical RP                     | 588 (95.1%)     |
| Atypical RP                    | 21 (3.4%)       |
| Syndromic RP                   | 9 (1.5%)        |
| Inheritance of RP (%)          |                 |
| Sporadic RP                    | 236 (38.2%)     |
| Autosomal recessive RP         | 114 (18.5%)     |
| Autosomal dominant RP          | 28 (4.5%)       |
| Undetermined                   | 240 (38.8%)     |
| Glaucoma diagnosis (%)         |                 |
| No glaucoma                    | 572 (92.56%)    |
| Primary angle-closure suspect  | 18 (2.91%)      |
| Primary angle closure          | 4 (0.65%)       |
| Primary angle-closure glaucoma | 14 (2.27%)      |
| Primary open-angle glaucoma    | 8 (1.29%)       |
| Secondary glaucoma             | 2 (0.32%)       |

### Table 2: Clinical features of 1218 eyes of 618 patients with retinitis pigmentosa

| Feature                        | 1218 RP eyes |
|--------------------------------|--------------|
| Mean visual acuity (LogMAR)    | 0.95±0.88    |
| Mean intraocular pressure (mm Hg) | 13.96±6.13 |
| Mean cup: disc ratio           | 0.49±0.23    |
| Lens status (%)                |              |
| Clear phakic lens              | 656 (53.86%) |
| Pseudophakic lens              | 428 (35.14%) |
| Cataractous lens               | 127 (10.43%) |
| Aphakia                        | 7 (0.57%)    |
in the ocular genetics clinic and only those with a shallow anterior chamber on slit-lamp examination, increased IOP, or glaucomatous optic discs underwent a gonioscopy. This was done primarily for logistical reasons to ensure smooth patient flow in a busy ophthalmic clinic. However, based on the findings of the current study, we intend to perform a prospective study where every RP patient will undergo a complete examination by a glaucoma specialist. Second, in our study, prevalence indices were determined from hospital-based data, and a similar population-based study may be preferable in this regard. However, our clinic is one of the largest RP clinics in the country and one of the few that offers genetic counseling and testing. It is a tertiary center with a large referral base and hence well-represents the RP population of our country.

**Discussion**

This is the first study that has determined the prevalence of the entire PACD spectrum in patients with RP. It was conducted because there are several reports on angle-closure glaucoma diagnosed in patients with RP; some of these are case reports of acute angle closure in patients with RP.[6,48] A large population-based study from Taiwan determined the association between RP and acute angle-closure glaucoma during a 15-year follow-up period.[8] They excluded patients younger than 20 years and those who had already undergone cataract surgery. They included 382 RP patients and 3820 controls. Acute angle closure occurred in 1.3% of RP patients compared with 0.4% of controls. Their results showed that RP patients had 3.6-fold greater odds of having acute angle closure. It is in this context that we decided to investigate the prevalence of PACS, PAC, and PACG in RP patients attending our ocular genetics clinic.

The present study found that 2.9% of RP patients had PACS, 0.7% had PAC, and 2.3% had PACG. In contrast, most population-based studies have found that the prevalence of PACS is higher than PAC, which in turn is higher than PACG.[11,12] One possible reason for our RP population having a greater proportion of PACG eyes when compared to PAC could be the difficulty in differentiating glaucomatous optic nerve damage (on disc examination and visual fields) from damage secondary to RP. Hence, some eyes with PAC may have been misclassified as PACG. However, it is important to note that 5.9% of RP patients had some form of concomitant PACD that would likely require a YAG peripheral iridotomy. This is a clinically significant finding because RP patients often undergo an annual dilated fundus examination and because almost 6% of these patients are at risk of angle-closure glaucoma, a gonioscopy done for all RP patients may help to identify those at risk and prevent acute angle-closure episodes.

The present study found that in Asian-Indian RP patients over 40 years of age, the prevalence of PACG was 3.8%. Other studies have determined the prevalence of PACG in their cohort of RP patients over the age of 40 years. A study of 234 RP patients from Nepal found the prevalence of angle-closure disease to be 2.13%.[9] This is similar to that seen in our study. However, they included both primary and secondary angle-closure disease in their study. A Canadian study on 538 RP patients (predominantly white) found the prevalence of PACG to be 1.03%.[9] One of the most likely reasons for their prevalence being lower than ours is race, because angle-closure disease is known to be less common among Caucasians. However, in the present study, the prevalence of PACG in RP patients over the age of 40 years was 3.8%, which is higher than the prevalence of PACG found in population-based studies in India (0.8%).[1,10] Therefore, the association of RP and PACG is unlikely to be just a coincidence.

The main limitation of our study is that all the RP patients did not undergo gonioscopy. RP patients were screened for glaucoma for a variety of reasons at our clinic, and only those with a shallow anterior chamber on slit-lamp examination, increased IOP, or glaucomatous optic discs underwent a gonioscopy. This was done primarily for logistical reasons to ensure smooth patient flow in a busy ophthalmic clinic. However, based on the findings of the current study, we intend to perform a prospective study where every RP patient will undergo a complete examination by a glaucoma specialist. Second, in our study, prevalence indices were determined from hospital-based data, and a similar population-based study may be preferable in this regard. However, our clinic is one of the largest RP clinics in the country and one of the few that offers genetic counseling and testing. It is a tertiary center with a large referral base and hence well-represents the RP population of our country.

**Conclusion**

To conclude, almost 6% of RP patients in our cohort had PACD. Hence, gonioscopy is warranted in all RP patients to identify this condition and treat it appropriately.

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**Conflicts of interest**

There are no conflicts of interest.

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