

A Review of Non-Syndromic Retinitis Pigmentosa, Ocular Associations in Jordanian Population Study

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Abstract

Aims: This study aims to explore the spectrum of ocular associations and their frequency among a sample of Jordanian patients with non-syndromic retinitis pigmentosa, and to analyze the association of these complications with age and gender.

Materials and methods: A total of fifty-nine patients with non-syndromic retinitis pigmentosa were selected from our data base at the Department of Ophthalmology, Jordan University Hospital, Amman from February 2017 to February 2018 to take part in this study. They underwent a comprehensive clinical evaluation in addition to corneal topography and retinal imaging with spectral domain optical coherence tomography.

Results: Upon analyzing the relation between retinitis pigmentosa complications and both age and gender, we found that the mean age of patients with posterior subcapsular cataract was significantly ($p < 0.001$) higher than those without posterior subcapsular cataract (36.5 ± 14.3 years and 24.7 ± 8.9 years, respectively). All patients with subclinical cystoid macular edema (CMO) were males (6 patients comprising 16.7% of males).

Conclusion: Posterior subcapsular cataract, CMO and posterior vitreous detachment (PVD) were the most common ocular association with non-syndromic retinitis pigmentosa. The older RP patients had a higher frequency of posterior subcapsular cataract, whereas male sex was associated with increased incidence of cystoid macular edema.

Keywords: Cystoid macular edema. Posterior subcapsular cataract, Retinal dystrophy, Retinitis pigmentosa

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Introduction

Retinitis pigmentosa is the name given to a group of progressive inherited retinal dystrophy (IRD), characterized by night blindness and progressive decrease of peripheral vision [1, 2]. At more advanced stages, the central vision is also reduced [3].

The worldwide prevalence of retinitis pigmentosa is about 1 in 4000 with a total of more than one million affected individuals [4], although reports vary from 1:9000 [5] to as high as 1:750 [6], depending on the geographic location. Typically, retinitis pigmentosa begins with degeneration of the rods followed by

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progressive and irreversible death of the cones, which leads to blindness [1, 2]. Almost 20-30% of RP patients have associated non-ocular diseases, where they are classified as “syndromic RP” [7].

Regular follow up of patients with retinitis pigmentosa reveals visual – threatening ocular associations, some of which may be amenable to treatment [8]. These associations may involve both anterior and posterior segments, such as, cataract [9], glaucoma [10] keratoconus, posterior vitreous detachment (PVD) [11], cystoid macular edema (CMO)(11), macular hole, epiretinal membrane [12, 13], optic nerve head drusen [14], and exudative retinal detachment [15, 16].

Posterior central subcapsular cataract with a clear nucleus is a common association, it occurs in approximately 45% of RP patients, which is usually present at mid stage in the evolution of the disease [9]. Although the cataract is not widespread, its central position blurs the remaining central visual field. Therefore, cataract provokes a sight restriction and generates photophobia. Cystoid macular edema (CMO) is another common association with RP, which may develop in up to 50% of patients [15].

Recently, FDA has approved first retinal implant Argus II retinal prosthesis system for patients with advanced RP [17].

The purpose of this study is to identify the associations between RP and different ophthalmological diseases in a sample of Jordanian patients.

Methods

We included 59 cases of RP that were selected from our data base at the Department of Ophthalmology, Jordan University Hospital, Amman from February 2017 to February 2018.

The details of history and clinical examination of the patients were recorded on specially-designed forms. Each patient underwent a complete ocular examination.

The diagnosis of retinitis pigmentosa was a clinical one, depending on the classical diagnostic triad of arterial attenuation, retinal bone spicule pigmentation, and waxy disc pallor.

All patients had typical isolated non-syndromic retinitis pigmentosa. Patients who had other causes of retinopathy and eyes that underwent previous ocular surgeries were excluded from the study. Ocular examination included the following:

- Both uncorrected and best corrected visual acuity using standard Snellen’s chart.
- Refraction using subjective refraction, Retinoscopy and auto refraction for patients with poor visual acuity.
- Slit lamp Biomicroscopy was performed to examine the anterior segment in detail.
- Intraocular Pressure was measured with Goldmann applanation tonometer.
- Detailed fundus examination was done using super-field lens.

Corneal topographic analysis was performed using a rotating Scheimpflug camera (Pentacam HR, OCULUS wetzlar, Germany). Images were reviewed by an experienced ophthalmologist (M.A, M.B) and the parameters selected were those related to the morphology of the cornea, including the mean curvature power (Km), keratometric power difference (KPD), corneal thinnest location, pachy apex, and average pachy progression. The results were classified accordingly into clinical and subclinical KC in which the cornea has no abnormal findings by both slit lamp examination and placido based corneal topography, with the fellow eye of clinical keratoconus [18].

Optical coherence tomography (OCT) images were done using OPTOVUE to measure central retinal thickness. CMO is defined as central subfield thickness more than 300 micron with loss of normal foveal contour. Subclinical CMO is seen only by retinal images.

Statistical Analysis

We used SPSS version 21.0 (Chicago, USA) for our descriptive analysis in this study. We reported our results in either mean (standard deviation; SD) or count (percentages).

We analyzed the demographic variables (age and gender) in relation with the number of patients, whereas we used the number of eyes to analyze the frequencies and associations. We used independent sample *t*-test to analyze the mean difference in age and other complications including both IOP and Km with gender, KC, lens opacity, PVD, CMO, and disc drusen. We used chi-square test followed by Z-test for proportions to analyze the difference in age, gender, KC, lens opacity, PVD, CMO, and disc drusen. A *p* value of 0.05 was our statistical threshold.

Results

A total of 59 patients were included in this study, with a mean age of 30.5 (± 13.2) years. They were 36 (61%) men with a mean age of 31.6 (± 14.8) years, and 23 (39%) women with a mean age of 28.7 (± 10.3) years (Table 1).

Table 1: This table shows the characteristic features of all patients included.

Condition	Count (frequency)
Clinical KC	2 (3.4%)
Subclinical KC	1 (1.7%)
Lens opacity	29 (49.2%)
Posterior vitreous detachment	13 (22%)
Clinical CMO	9 (15.3%)
Subclinical CMO	6 (10.2%)
Optic disc drusen	1 (1.7%)
Exudative RD	2 (3.4%)
On glaucoma medications	3 (5.1%)

Upon analyzing the relation between the age groups and RP complications, we found a significant mean difference in the posterior subcapsular cataract group ($p < 0.001$), as the mean age of patients with posterior subcapsular cataract was 36.5 years (± 14.3) compared to 24.7 years (± 8.9) for patients without posterior subcapsular cataract.

Upon analyzing gender differences and RP complications, we found a significant gender difference in prevalence of subclinical CMO ($p = 0.043$), as all patients with subclinical CMO

were males (6 patients comprising 16.7% of males).

A total of 115 eyes were included (3 eyes were prosthetic). The mean Km for the right eye was 43.1 (± 2.1), and for the left eye was 43.1 (± 1.9). The mean intraocular pressure for the right eye was 12.5 (± 2.7), and for the left eye 12.6 (± 2.6). Table 2 shows the characteristic features of all the eyes included.

Table 2: This table details the characteristic features of all eyes included.

	Right eye	Left eye
RP	57 (96.6%)	57 (96.6%)
Clinical KC	2 (3.4%)	2 (3.4%)
Subclinical KC	1 (1.7%)	0
Lens opacity	29 (49.2%)	26 (44.1%)
PVD	9 (15.3%)	13 (22%)
Clinical CMO	8 (13.6%)	8 (13.6%)
Subclinical CMO	5 (8.5%)	5 (8.5%)
Optic disc drusen	1 (1.7%)	1 (1.7%)
Exudative RD	1 (1.7%)	1 (1.7%)

Discussion

Non-syndromic retinitis pigmentosa is known to be associated with other ocular features that may include both the anterior and posterior segments of the eye; some of these ocular associations are treatable [8]. In this study that included a sample of non-syndromic

RP from Jordanian population (Middle-Eastern ethnicity), we found that posterior subcapsular cataract and CMO are among the most common associations in RP patients.

CMO and posterior central subcapsular cataract with a clear nucleus are the most commonly reported associations which may be found in up to 50% and 45% of patients respectively [9,19]. In the present study, we found that posterior subcapsular cataract is the most common ocular association, as it was found in almost half of RP patients (49.3%), followed by CMO both clinical and subclinical, as it was reported in 23.8%. Patients with RP, typically, develop combined posterior cortical and posterior subcapsular cataract with typically clear nucleolus. Taking into account the nature of the underlying retinal dysfunction, particularly the outer retinal atrophy at the macula, even relatively minor lens opacity may cause disproportionate functional symptoms. In addition, patients with RP become symptomatic at an early stage of cataract development as compared with normal individuals with age-related cataract.

The pathogenesis of cataract in retinitis pigmentosa is currently unknown, although a possible association with inflammation was recently suggested. That is [20]. Cataract surgery with intraocular lens implantation is beneficial and most patients reported subjective improvement of their visual symptoms after surgery although visual acuity may not improve [21].

CMO is a common finding among RP patients and is prevalent in all age groups [22]. Strong *et al.* recently suggested the followings mechanisms that may lead to development of CMO, including: breakdown of the blood-retina barrier, impaired function of the RPE pumping mechanism, Müller cell edema and dysfunction, anti-retinal antibodies, and vitreomacular

traction [19]. Unlike previous studies that showed higher frequency of CMO among females [23], we found that a significantly higher frequency of CMO is found in males, especially subclinical CMO. Acute episodes of macular edema may be successfully treated with carbonic anhydrase inhibitors, such as acetazolamide sodium at a daily dose of 500 mg or less. However, the macular edema in RP patients is most often chronic and does not improve with this treatment [24]. Refractory CMO can be treated with intravitreal injections, including steroids [25] and anti-vascular endothelial growth factors (anti-VEGFs) although studies do not agree with respect to the beneficial effects of anti-VEGF. Moreover, Salom *et al.* quantified the VEGF-A levels in aqueous humor of 16 eyes of 16 patients with RP, they found that aqueous VEGF-A levels were markedly lower in eyes with RP than in control patients [26].

Posterior vitreous detachment (PVD) was a frequent association among our patients as 13 out of our 59 patients (22%) had PVD, and was the third most common association. Patients with RP are prone for early onset PVD, which was reported in 47% of patients in a hospital-based study by Tayyaba *et al.* [27]. Previous studies pointed that RP patients are at greater risk of developing keratoconus, with an emphasis on the rarity of keratoconus even in RP patients [28]. We reported a low frequency of both clinical (3.4%) and subclinical keratoconus (1.7%) as well as primary open angle glaucoma (5.1%). Our data also demonstrated rare occurrence of both exudative retinal detachment (3.4%) and optic disc drusen (2%).

In this study, we only found two RP ocular associations related to demographic variables (age and gender). Patients with increased age have higher risk of posterior subcapsular cataract, and males have a higher risk of

developing subclinical CMO as detected by OCT. Regarding the relation of posterior subcapsular cataract and age, a previous report showed that this relation is dependent on genetic background, since only X-linked patients generally develop lens opacity at younger ages [29]. In our study, we found that posterior subcapsular cataract develops at older ages among RP patients. In another study investigating the prevalence of visually significant cataract among patients older than 75, it was 45.9% [30].

We believe that future studies should consider analyzing the genetic background of all RP patients, as genetic background is one of the main determinants of the eventual outcome and the ocular associations [31]. Multicenter studies should be conducted as well in order to include a larger sample size.

Conclusion

This study was conducted on a sample from Jordanian population and it showed that posterior subcapsular cataract, CMO and posterior vitreous detachment (PVD) were the most common ocular associations with non-syndromic retinitis pigmentosa. Advanced age RP patients have higher frequency of posterior subcapsular cataract, whereas male sex was associated with increased incidence of cystoid macular edema.

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أمراض العين المصاحبة لمرض العشى الليلي غير المتلازم

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الملخص

الأهداف الرئيسية : البحث في طيف أمراض العيون المصاحبة لمرض العشى الليلي غير المتلازم لدى عينه من المرضى الاردنيين، ومقارنتها مع البيانات المنشورة في الأبحاث السابقة .

منهجية البحث : مراجعة ملفات 59 مريضاً مصاباً بالعشى الليلي من مراجعي مستشفى الجامعة الاردنية في الفترة من شباط 2017 الى شباط 2018 ، حيث تم اجراء فحص سريري شامل لكلتا العينين بالإضافة إلى تصوير طبوغرافية القرنية و الشبكية .

النتائج : عند تحليل العلاقة بين مضاعفات العشى الليلي و السن و نوع الجنس وجدنا أن متوسط العمر لمريض الساد كان إلى حد كبير ($p < 0.001$) اعلى من المرضى غير المصابين بالساد (36.5 ± 14.3 سنه و 24.7 ± 8.9 سنه ، على التوالي) . كما وجدنا ان جميع المرضى المصابين بوذمة اللطخة الصفراء هم من الذكور (6 مرضى يشكل ما نسبته 16.7% من الذكور).

خلاصة البحث : كانت الساد و وذمة اللطخة الصفراء و انفصال السائل الزجاجي من امراض العيون الاكثر ارتباطا بمرض العشى الليلي غير المتلازم . و لوحظ ان المرضى الاكبر عمرا هم الاكثر عرضة للإصابة بمرض الساد بينما المرضى الذكور هم الأكثر عرضة للإصابة بوذمة اللطخة الصفراء.

الكلمات الدالة : العشى الليلي ، ضمور الشبكية ، الساد ، وذمة اللطخة الصفراء .