Retinitis pigmentosa in Puerto Rico

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Introduction: **Previous studies have reported that the prevalence of retinitis pigmentosa (RP) varies between one per 3,000 to one in per 5,000 in the general population.**

Purpose: **To study the incidence and ocular findings of RP in a sub-urban community in Puerto Rico.**

Methods: **We conducted a non-concurrent prospective study of 10,100 patients in a sub-urban San Juan community.**

Results: **44 out of the 10,100 patients had RP (0.44 %). Eight out of the 44 patients (18%) had nystagmus, twenty-eight (31.8%) had microcornea, 3 patients (6.8%) had sluggish papillary reaction. Six patients (13.6%) had mild cataracts, 27 (65.9%) had attenuated retinal vessels and thirty five patients (81.4%) had bony spicules. Fifteen patients (34.1%) out of the 44 had retinitis pigmentosa as part of the Bardet-Biedl syndrome.**

Conclusion: **Incidence of RP in Puerto Rico is higher when compared to Maine and Spain ($p < 0.001$). Autosomal recessive pattern of inheritance is the most common in Puerto Rico. These findings could be due to the island's geographic isolation, and inbreeding.**

Key words: Retinitis pigmentosa, Retinal degenerations, Photoreceptors, Incidence of retinitis pigmentosa in Puerto Rico, Bardet-Biedl syndrome

Retinitis pigmentosa (RP) is a group of progressive retinal degenerations associated to an abnormal production of photoreceptor proteins (1). Retinitis pigmentosa may be sporadic (in 40 to 50% of affected patients) or inherited as an autosomal dominant, autosomal recessive, or X-linked trait (2). Further, RP may occur associated with various genetic disorders such as: Usher syndrome (3); Leber congenital amaurosis (4); Bardet-Biedl syndrome (5); Alstrom disease (6); and Phytanic acid storage disease (7) to name a few.

Previous studies (1) have reported that the prevalence of RP is between one per 3,000 to one in every 5,000 making it one of the most common causes of visual impairment in all age groups. To our knowledge, the incidence and prevalence of RP have not been determined in Puerto Rico. We report on the incidence and ocular findings of patients with RP in a sub-urban population of the San Juan metropolitan area of Puerto Rico.

Patients and Methods

We conducted a non-concurrent prospective study of 10,100 patients from a sub-urban community in the San Juan metropolitan area of Puerto Rico. These patients underwent a comprehensive ophthalmic evaluation by one of the authors from June 1993 to July 2005. Descriptive statistics and statistical analysis was done using Fisher's exact test to compare this study results with prior historical controls.

Results

Forty-four out of the 10,100 patients had RP (0.44 %). There were 19 female (43.2%) and 25 male (56.8%) patients out of the 44 patients with RP. Age ranged from 5 to 72 years of age (average = 29.8 years of age).

Best corrected visual acuity (BCVA) ranged from 20/20 to LP (mode = 20/60) and from 20/20 to LP (mode = 20/400) in the right and left eye respectively. There were 29 (65.9%) patients with BCVA of 20/200 in at least one eye. Refractive errors (in spherical equivalents) ranged from +14.25 sph to –9.25 sph (mean = +0.57 sph) and from +14.25 sph to -9.0 sph (mean = +0.68 sph) in the right and left eye respectively.

Thirty-three out of the 44 (75%) patients were orthophoric; three out of the 44 patients (7%) had exotropia; and eight out of the 44 patients (18%) had nystagmus.

Twenty-eight out of the 88 eyes (31.8%) had microcornea. These were sub-divided by horizontal corneal diameters into categories. Nine patients (32.1%) had a 10mm corneal diameter; six patients (21.4%) had a

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10.5mm diameter; and 13 patients (46.5%) had a corneal diameter of 11mm.

Forty patients 90.9% had round, reactive to light pupils, without Marcus Gunn; 3 patients (6.8%) had sluggish pupillary reaction; and a patient (2.3%) had corectopia.

There were 32 (72.7%) patients with clear lenses. Six patients (13.6%) had mild cataracts. Five patients (11.4%) were pseudophakic; and one patient (2.3%) was aphakic.

Upon ophthalmoscopic examination: 27 patients (62.8%) patients had a healthy optic nerve; 9 patients (20.9%) had nerve pallor; 6 patients (14%) had optic nerve cups; and one patient (2.3%) had optic nerve atrophy. Twenty-seven out of the 44 patients (65.9%) had attenuated retinal vessels. There were 33 patients (80.5%) with an intact macula; six patients (14.6%) had macular pigment changes; a patient (2.5%) had a macular scar; and a patient (2.5%) had foveal hypolasia. Thirty-five patients (81.4%) had bony spicules and eight patients (18.6%) had mid-peripheral pigmentary changes.

As depicted in fig. 1, fifteen patients (34.1%) out of the 44 had retinitis pigmentosa as part of the Bardet-Biedl syndrome, two patients (4.5%) had RP as part of the Usher syndrome, two patients (4.5%) had RP associated to Leber congenital amaurosis, two patients (4.5%) had RP as part of the Refsum syndrome; and 19 patients had no known systemic association. Four patients (9%) out of the 19 patients with isolated RP had an X-linked inheritance pattern. None of them had an autosomal dominant pattern of inheritance.

Discussion

Retinitis pigmentosa (RP) is a group of progressive retinal degenerations that lead to blindness, due to loss of photoreceptor and retinal pigment epithelium cells diffusely across the fundus (8).

Carr and Heckenlively (4) reported that the incidence of retinitis pigmentosa varies with country and race. Bunker and co-workers (9) estimated that the prevalence of RP in Maine was one per 4,756 or 21 per 100,000. In our study, the incidence of RP was 1:230. This difference is statistically significant ($p < 0.0001$). The higher incidence in the studied population may be due to inbreeding worsened by geographic isolation.

Kaiser and co-workers (10) reported that RP may be sporadic (in 38% of the patients); have inheritance patterns such as autosomal dominant (20% of the patients); autosomal recessive (in 25% of the cases), X-linked recessive (9% of the patients); and undetermined in 8% of patients. In our study, we found that 47.7% of patients had RP with autosomal recessive inheritance pattern. Therefore the autosomal recessive pattern of inheritance is most common in Puerto Rico. Retinitis pigmentosa inherited as an autosomal recessive trait is more common in our study than in the Spanish population, with a statistically significant difference ($p<0.0001$). Autosomal recessive diseases tend to be more common with consanguineous marriages in isolated populations, such as Puerto Rico. On the other hand, there were 43.2% of patients with sporadic RP; and 9% of patients with an X-linked inheritance pattern. These findings are similar to previous studies reported by Kaiser and co-workers (10).

Ayuso and co-workers (11) reported that the relative frequencies of the different genetic types in 592 RP families of Spanish origin was 503 (85%) non-syndromic and 89 (15%) syndromic. In our study we found that 52.3% of the cases where non-syndromic and 47.7% where syndromic. This variation between the syndromic and non-syndromic patients with RP in Spain and Puerto Rico is statistically significant ($p < 0.0001$). This variation could be due to consanguineous marriages occurring in Puerto Rico as part of the geographic isolation. Ayuso and co-workers (11) reported in their study, that 79% of patients had the Usher syndrome. However, in our study, RP occurred most commonly associated with the Bardet-Biedl syndrome, in up to 34.1% of patients.

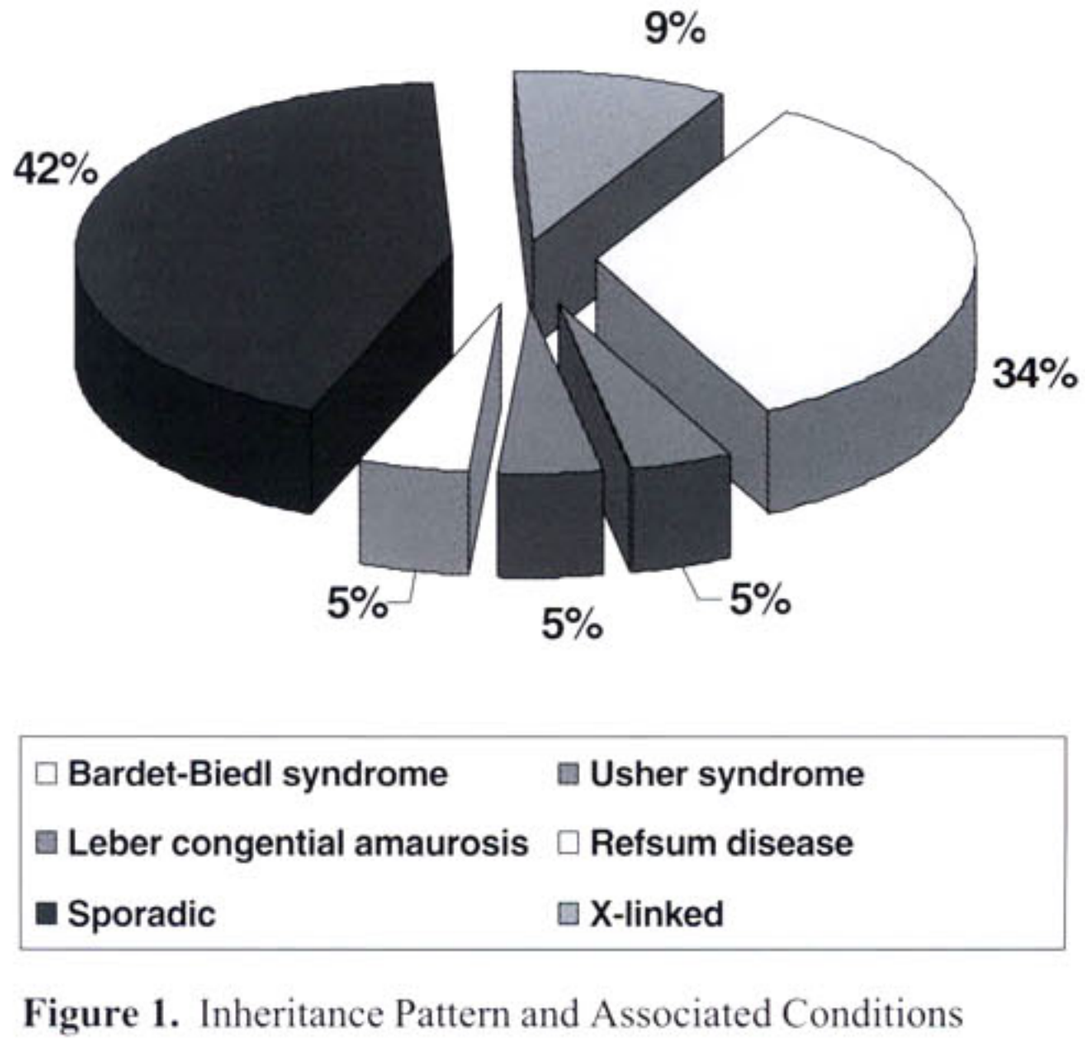

Figure 1. Inheritance Pattern and Associated Conditions

Previous studies (12) have reported that legal blindness from visual acuity loss occurred in a relative small percentage of patients with RP. Grover and co-workers (12) reported that approximately 80% of patients had BCVA of at least 20/200. In our study, analysis of BCVA showed that 67.4% of patients had a visual acuity of 20/200 or better in at least one eye. Grover and co-workers (12)

showed that 20% of patients with RP were legally blind. In the present study, we found that 32.6% of patients with RP had a visual acuity worst than 20/200 in at least one of the eyes. This association is statistically significant ($p < 0.0001$). The difference in visual loss could be due to more severe disease process such as occurs in Bardet-Biedl syndrome.

Sieving and Fishman (13) reported that up to 75% of patients with RP have myopia. In our study 56% of patients had myopia. This difference was statistically significant ($p<0.0001$). Gutiérrez and Fernández (14) describe that the myopic changes found in a high percentage of patients with RP could be associated with the atrophic changes of the uveal tract (14).

Previous studies by Weiss and Biersdorf (15) showed that 91% of the patients with congenital nystagmus were eventually found to have early onset RP. In our study, only 18% of patients with RP (all types included) had nystagmus. Early onset nystagmus has been associated in patients with RP as part of Leber congenital amaurosis (16). In our study all of the patients with Leber congenital amaurosis had nystagmus. These findings are compatible with Heher and co-workers findings (16).

Microcornea has been described in patients with the Bardet-Biedl syndrome (unpublished data). In our study, 31.8% of the patients had microcornea, compared to 53.3% of the patients of BBS.

Kecid and co-workers (17) evaluated the pupillary reaction to a standard light flash, and showed that the reaction diminished with visual field loss. In our study, 90.9% of the patients had rounded, reactive to light pupils. However, 6.8% of patients had a sluggish pupillary reaction, which correlated with a poor visual acuity. Patients with RP have peripheral visual field loss. This may lead to poor pupillary responses in patients with RP.

Fishman and co-workers (18) found that 53% of the patients with RP have posterior subscapsular lens opacities (PSC) or were bilaterally aphakic. In our study, 14% of patients had lens opacities and 11% had already had cataract surgery. Jackson and co-workers (19) believe that lens opacities occur at a younger age in patients with RP. In our study the mean age of patients who had lens opacities was 57 years of age. This discrepancy could be explained by the fact that the population that we studied was very young, with a mean age of 29.8 years of age.

Carr and Heckenlively (4) found that patients with RP have either pale or waxy appearing optic nerves, but in less-advanced cases they retain a normal color (4). In our study we found that 20.9% had pale optic nerves and 62.8% of patients had healthy optic nerves. These findings could be due to a younger patient population in our study.

Carr and Heckenlively (4) describe several characteristic ophthalmoscopic findings in patients with retinitis pigmentosa including: narrowing of the retinal arterioles; and pigment changes such as bony spicules, clumps or spots of pigment. Berson and co-workers (20) reported that 54% of the patients studied, presented with an increase in pigmentary changes over a period of three years. In our study, we found that 65.9% had attenuated retinal vessels and all of our patients had retinal pigment changes. The latter were sub-divided into 81.4% of patients with bone spicules; and 18.6% of patients with mid-peripheral pigment changes. Fishman and co-workers (21) reported that a 58% of the patients with retinitis pigmentosa studied, had lesions of the retinal pigmentary epithelium within the maculae of both eyes. In our study we found that only 14.6% of the patients had pigmentary changes on the macula. According to Sieving (8), the severity of the pigmentary changes increases with age. This may possibly explain our findings since we had a relative young population, and these changes have not yet being expressed noticeably. Ophthalmoscopic findings in our patients are similar to other reports of patients with RP.

In conclusion, there is an unusually high incidence of RP in Puerto Rico. Autosomal recessive inheritance of RP is common in PR. Further, systemic associations of RP need to be considered during the evaluation of patients with RP in Puerto Rico. These findings could be due to the island's geographic isolation, and inbreeding.

Limitations of this study include that we compared our population to historical controls. Further, these results do not represent the real prevalence of RP in Puerto Rico, since the study included a limited number of patients.

Further studies, ascertaining more of the population should be conducted to determine the real prevalence of retinitis pigmentosa in Puerto Rico. Both the patient population and health providers may benefit from these studies. Awareness of these diseases may lead to better management in patients with retinitis pigmentosa.

Resumen

Introducción: Estudios previos han reportado la prevalencia de retinitis pigmentosa (RP) en uno de cada 3,000 hasta uno de cada 5,000 personas en la población general.

Propósito: Estudiar la incidencia y hallazgos oculares de RP en una comunidad sub-urbana de Puerto Rico.

Métodos: Se llevó acabo un estudio prospectivo no-concurrente de 10,100 pacientes de una comunidad sub-urbana del área de San Juan, P.R.

Resultados: 44 de los 10,100 pacientes presentaron RP (0.44%). Ocho de los 44 pacientes (18%) tenían nistagmus, veintiocho (31.8%) tenían micro córnea, 3 pacientes (6.8%)

presentaron una reacción pupilar lenta. Seis pacientes (13.6%) tenían cataratas leves, 27 (65.9%) presentaron vasos de la retina atenuados y 35 (81.4%) con cambios de pigmentación en la retina. Quince (34.1%) de los 44 pacientes tenían retinitis pigmentosa como parte del síndrome de Bardet-Biedl.

Conclusión: La incidencia de RP en Puerto Rico es mayor cuando es comparada con la de Maine y España ($p < 0.001$). El patrón de herencia autosómico recesivo es el más común en Puerto Rico. Estos hallazgos podrían deberse al aislamiento geográfico de la isla y a la endogamia.

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