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ORIGINAL RESEARCH

Visual acuity impairment in patients with retinitis pigmentosa

Hamideh Sabbaghi [1], Narsis Daftarian [2], Maryam Fakhri [3], Bahareh Kheiri [3], Hamid Ahmadieh*[3]

1. *Ophthalmic Epidemiology Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
2. *Ocular Tissue Engineering Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
3. *Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

*Corresponding Author:
Address: Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, 23 Paidar Fard, Bostan 9, Pasdaran Ave., 16666 Tehran, Iran.
Email: hahmadieh@hotmail.com
ORCID: 0000-0002-8139-2661

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Abstract

Purpose: To determine the visual acuity (VA) impairment in patients with retinitis pigmentosa (RP) in different age groups.

Materials and Methods: This descriptive study was extracted from the recorded data in the National Registry for Inherited Retinal Diseases (IRDs) in Iran (IRDReg®). The clinical records of 441 patients with a diagnosis of RP were investigated in the present study. The comprehensive visual and ocular examination with retinal imaging were conducted for all study subjects to ascertain the definite clinical diagnosis of RP. VA was classified based on the presenting VA (PGVA) of the better eye according to the International Classification of Diseases reported by the World Health Organization (WHO).

Results: In this study, a total of 441 RP patients with the mean age of 38.66 ± 14.24 years (range, 4 to 74) were included. Generally, the majority of RP patients in the age range of 20 to 40 years had visual impairment (80%; 95% CI, 74.3% to 84.9%). RP patients with younger ages had mild visual impairment (26.3%; 95% CI, 14.4% to 41.7%), while patients with no light perception was only found in older ages (3.4%; 95%CI, 1.4% to 6.8%), (P<0.001). The most frequency of RP patients suffering from visual impairment had disease onset at age ≤20 years (82.0%; 95% CI, 77% to 86.2%), and also severe visual impairment was observed in patients with earlier disease onset (2.6%; 95% CI, 1.2% to 5.1%), (P=0.001).

Conclusion: Based on our findings, more disease progression and subsequently visual acuity reduction was observed in RP patients who had older ages and disease onset in younger ages.

Keywords: Visual acuity, Visual impairment, Retinitis pigmento

Introduction

Retinitis pigmentosa (RP) is a type of inherited retinal dystrophy (IRD) resulted from the progressive degeneration of the photoreceptors and retinal pigment epithelial cells (RPE) [1]. As reported, RP is the most prevalent type of IRDs with an estimation of about 1.5 million individuals worldwide [2]. It is found that the mutations in more than 45 causative genes are responsible for presenting RP [1], which can be transmitted to the next generation by different Mendelian patterns of inheritance including autosomal dominant, autosomal recessive, or X- linked recessive [3, 4]. As a whole, it appears primarily by involvement of the outer retina and RPE cells resulted into death of these cells [5, 6], and in the end stages of disease, choriocapillaris may also be involved which manifests as chorioretinal atrophy in fundus examination [6, 7].

Patients with retinitis pigmentosa typically lose their night vision in adolescence, peripheral vision in young adulthood and central vision in old ages due to the natural progressive degeneration of the cone and rod photoreceptor cells [1, 8]. Additionally, these patients mostly complain of restricted field of vision named as tunnel vision, lack of fixation, and color vision deficiency [9]. Other clinical manifestations including cataract, retinal pigmentary change, depigmentation of RPE, waxy pallor of the optic disc, photoreceptors loss and attenuated retinal vasculature are presented which usually are associated with abnormal response to the electrophysiologic and visual acuity tests [9, 10]. Although no definite treatment has been discovered for RP, the results of clinical trials show that the nutritional agents such as vitamin A palmitate and omega- 3- rich fish can be influential in slow progression of RP disease [1, 11, 12]. The recent studies show that the new advancement has been occurred in the gene therapy of patients with RP, which is resulted from the study of the biochemical pathways, and development of animal models [1, 13].

According to the literature, different grades of visual impairment was reported in RP patients by several studies [8, 14, 15]. While, different frequencies of the legal blindness was also observed in a range of 20% to 25% among RP patients [14, 15]. Additionally, no light perception (NLP) was found in 0.46% of RP cases with visual acuity worse than 20/200 [8].

In the present study, we aimed to determine the different grades of visual impairment in patients with RP.

Materials and Methods

This descriptive study was extracted from the recorded data in the National Registry for Inherited Retinal Diseases (IRDs) in Iran (IRDReg®) belong to RP patients referred to our clinic in the time period of February 2016 to September 2019. The clinical records of 441 patients with a diagnosis of RP were investigated in the present study.

The Ethics Committee of Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran approved this study and all study procedures were adhered to the tenets of the Declaration of Helsinki. After explaining the purpose of the study, written informed consent was obtained from all subjects for diagnostic procedure and visual acuity (VA) testing.

Inclusion and Exclusion Criteria

In The present study, cases with a definite clinical diagnosis of RP who were diagnosed based on the clinical examination and retinal imaging were included. Patients were excluded in cases with other ocular pathological conditions not directly related to RP, those with neurological problems and noncooperation to VA testing.

Visual and Ocular Examinations

The comprehensive clinical examinations and retinal imaging were conducted for all study subjects to identify the definite clinical diagnosis of RP. In this regards, firstly all subjects were interviewed by an optometrist to find the age of onset for disease manifestation and the common signs and symptoms including color vision deficiency, nyctalopia, restricted field of vision and previous general and ocular health status. Afterwards, the best corrected visual acuity (BCVA) was tested using a Snellen E-chart at a distance of 3 meters after refractive error correction. When a patient was not able to see the 0.1 LogMAR line of vision chart, BCVA measurement was continued by asking patient to count the examiner's fingers at different distances. In patients with the extreme decreased vision, BCVA was recorded by detection of hand motion. The ability of light perception was

recorded in the last step and patients with no perception of illumination was finally identified as no light perception (NLP). VA testing was conducted by an expert optometrist (H.S) for all study subjects.

Additional ophthalmic examination was also conducted including slit-lamp biomicroscopy, intraocular pressure (IOP) measurement using the Goldmann applanation tonometer and dilated fundus examination using a +78D lens. In addition, visual field testing was performed using Humphrey visual field (HVF; Carl. Zeiss Meditec Inc., Dublin, CA) using 30-2 Swedish Interactive Threshold Algorithm (SITA) standard method. Spectral domain optical coherence tomography (SD-OCT; SD-OCT-1000™; Topcon Corporation, Tokyo, Japan) scanning was also performed. Fundus photograph was provided by a digital stereoscopic camera (Visucam Pro NM; Carl Zeiss Meditec AG, Germany), as well. Infrared, fundus autofluorescence (FAF) and fluorescein angiography (FAG; Heidelberg Engineering GmbH, Germany) were also done. In addition, electrophysiological examinations including electroretinography (ERG) and/or electro-oculography (EOG; RETIport 21 system; version 7/03, Roland Consult, Osaka, Japan) were conducted in order to find the definitive clinical diagnosis.

Visual Acuity Classification

VA was classified based on the presenting VA (PGVA) of the better eye according to the International Classification of Diseases reported by the World Health Organization (WHO) [16]. Normal vision was defined in patients with PGVA better than 0.30 LogMAR. While low visual impairment was defined for patients with PGVA in the range of 0.30 to 0.48 LogMAR. Additionally, patients with PGVA worse than 0.48 LogMAR was considered as low vision which was classified in the two groups of 0.48 to 1.0 (G1) and 1.0 to 1.3 LogMAR (G2). Cases with PGVA worse than 1.30 LogMAR was considered as blind which was classified in the three severities of 1.30 to 1.78 (G3), 1.80 to 3.0 (G4) and 3.1 LogMAR (NLP, G5).

Statistical Analysis

To present data we used mean, standard deviation, median, range, frequency and percentage. All statistical analysis performed by SPSS software (IBM Corp. Released 2014. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). All tests were two-sided and P-value less than 0.05 considered statistically significant.

Results

In this descriptive study, a total of 441 patients with a clinical diagnosis of RP were included. Fifty-six percent of patients were male and the mean age of participants was 38.66 ± 14.24 (ranges from 4 to 74) years old.

Table 1. Basic characteristics of the study patients with retinitis pigmentosa.

Parameters	Level	Number	Percent
Gender	Female	196	44.4%
	Male	245	55.6%
Age (years)	1 - 20	40	9.1%
	20 - 40	220	50.2%
	40 - 60	147	33.6%
	>60	31	7.1%
Familial	No	150	35.4%
	Yes	274	64.6%
Ethnicity	Fars	191	50.5%
	Turk	96	25.4%
	Kurd	12	3.2%
	Lor	22	5.8%
	Gilak	8	2.1%
	Mazani	7	1.9%
	Baluch	33	8.7%
	Tat	1	0.3%
	Arab	7	1.9%
	Foreign	1	0.3%

Table 1 presents the basic characteristics of study participants. As shown the majority of our patients (n= 220, 50.2%) were in the age range of 20 to 40 years old and the less number of patients (n= 31, 7.1%) were in the oldest group (≥60 years old). A positive family history of RP was identified in 64.6% of patients, while 35.4% of cases were single affected.

Table 2. Visual acuity classification in different age categories in patients with retinitis pigmentosa.

Parameters	Level	1 - 20		20 - 40		40 - 60		> 60	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Normal		12 (31.6%)	18.6 to 47.3	44 (20.0%)	15.1 to 25.7	37 (25.2%)	18.7 to 32.6	7 (22.6%)	10.7 to 39.3
Visual Impairment		26 (68.4%)	52.7 to 81.4	176 (80.0%)	74.3 to 84.9	110 (74.8%)	67.4 to 81.3	24 (77.4%)	60.7 to 89.3
	Mild VI	10 (26.3%)	14.4 to 41.7	27 (12.3%)	8.4 to 17.1	18 (12.2%)	7.7 to 18.3	0 (0.0%)	-
	Low Vision (G1)	6 (15.8%)	6.9 to 29.7	60 (27.3%)	21.7 to 33.4	21 (14.3%)	9.3 to 20.6	5 (16.1%)	6.4 to 31.8
	Low Vision (G2)	3 (7.9%)	2.3 to 19.6	10 (4.5%)	2.4 to 7.9	3 (2.0%)	0.6 to 5.3	1 (3.2%)	0.4 to 14.1
	Blindness (G3)	6 (15.8%)	6.9 to 29.7	16 (7.3%)	4.4 to 11.3	2 (1.4%)	0.3 to 4.3	1 (3.2%)	0.4 to 14.1
	Blindness (G4)	1 (2.6%)	0.3 to 11.6	60 (27.3%)	21.7 to 33.4	61 (41.5%)	33.8 to 49.6	16 (51.6%)	34.5 to 68.4
	Blindness (G5)	0 (0.0%)	-	3 (1.4%)	0.4 to 3.6	5 (3.4%)	1.3 to 7.3	1 (3.2%)	0.4 to 14.1

VI, visual impairment; G, group; CI, confidence interval; n, number

The frequency of visual impairment severity in regard to age group is summarized in Table 2. Generally, the majority of RP patients in the age range of 20 to 40 years had visual loss (80%; 95% CI, 74.3% to 84.9%) and less

frequency of visual impairment was observed in the youngest age group (68.4%; 95% CI, 52.7% to 81.4%), (P<0.001).
RP patients with younger ages had mild visual impairment (26.3%; 95% CI, 14.4% to 41.7%), while patients with no light perception was only found in older ages (3.4%; 95%CI, 1.4% to 6.8%), (P<0.001).

Table 3. Visual acuity classification in different disease durations in patients with retinitis pigmentosa.

Parameters	Level	1 - 20		20 - 40		40 - 60	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Normal		48 (18.0%)	13.8 to 23	31 (24.2%)	17.4 to 32.2	16 (53.3%)	35.9 to 70.2
Visual Impairment		218 (82.0%)	77 to 86.2	97 (75.8%)	67.8 to 82.6	14 (46.7%)	29.8 to 64.1
	Mild VI	33 (12.4%)	8.9 to 16.8	15 (11.7%)	7 to 18.1	6 (20.0%)	8.8 to 36.7
	Low Vision (G1)	58 (21.8%)	17.2 to 27.1	30 (23.4%)	16.7 to 31.3	2 (6.7%)	1.4 to 19.7
	Low Vision (G2)	8 (3.0%)	1.4 to 5.6	9 (7.0%)	3.5 to 12.4	0 (0.0%)	-
	Blindness (G3)	20 (7.5%)	4.8 to 11.2	5 (3.9%)	1.5 to 8.3	0 (0.0%)	-
	Blindness (G4)	92 (34.6%)	29.1 to 40.4	36 (28.1%)	20.9 to 36.3	6 (20.0%)	8.8 to 36.7
	Blindness (G5)	7 (2.6%)	1.2 to 5.1	2 (1.6%)	0.3 to 4.9	0 (0.0%)	-

VI, visual impairment; G, group; CI, confidence interval; n, number

Different grades of visual impairment were also analyzed based on the onset age of disease as presented on Table 3. As shown, the most frequency of visual impairment is seen in RP patients with disease onset age of less than 20 years old (82.0%; 95% CI, 77% to 86.2%). Moreover, these patients show more severe visual impairment (2.6%; 95% CI, 1.2% to 5.1%), (P=0.001).

Discussion

Retinitis pigmentosa is the most common type of IRDs leading to untreatable visual impairment worldwide [17]. This type of retinal dystrophy is defined by night blindness, restricted field of vision and severe visual impairment, which is mostly associated with difficulty in daily activities [18, 19]. Additionally, depressive symptoms [20], lower quality of life [21] and poor mental health [22] have been reported as other subsequent complications of RP disease which is correlated with decreasing vision. Generally, we found that the most RP cases with visual impairment was in the age range of 20 to 40 years, and the least frequency of visual impairment was observed in the youngest ages (≤20 years old). Furthermore, more severe visual impairment was observed in patients with older administration age and those with younger age of disease manifestation. Total visual impairment was found in 76.1% of our study subjects, while it was reported to be 65.7% and 57.5% in the studies conducted by Onakpoya et al [23] and Eballe et al [24], respectively. The mean age of 38.66 years in the present study is in line with 36.7 years and 39 years reported by the two studies conducted in Nigeria [23, 25], and 35.1 years in Japanese patients with RP [26]. However, the mean age of RP patients was reported higher in some other studies as reported 43.3 years by Eballe et al [24] and 41 years by Grover et al [15]. These differences can be attributed to the delayed referral to the ophthalmic clinic. Patients with RP may postpone ophthalmologist visit in early stages and younger ages, hence most visits may perform in older ages, which leads to higher mean age of administration.
The majority of our patients with visual impairment was in the age of 20 to 40 years old which can be resulted from this fact that older patients usually do not intend to refer for ophthalmic examination due to the severe visual decreasing and inability to refer independently. Additionally, lack of disease symptom manifestation in early ages can be considered as the probable cause of less referral in patients with younger ages. Moreover, severe visual impairment categorized as different blindness subgroups was more frequent beyond age of 40 years. Similar findings were also presented by other studies reporting the significant increasing percentage of blindness associated with older age groups [23, 24]. Furthermore, we evaluated visual impairment severity based on different onset ages of disease manifestation. Disease age of onset has been mentioned as a prognostic factor for RP patients [27]. Based on our findings, more severity of visual impairment was observed among patients who experienced the initial visual symptoms at early ages.
The general incidence of blindness (G3, G4 and G5) was observed in 39% of our study patients, while it was 25% and 30% among RP patients in other studies [15, 24]. In addition, a retrospective cross sectional study conducted by Vezinaw et al [8] on a large cohort of RP patients shows that patients with visual acuities of hand motion, counting figure or light perception were observed in 6.8% of cases. These severe levels of visual impairment were classified in G4 and G5 with PGVA limitation of 1.8 to 3.1 LogMAR in the present study, which included 33.4% of our participants. The difference of results could be explained by different visual impairment definitions, considered by mentioned reports.
One of the limitations of the present study is that the disease onset age was identified based on patient's self-report. Therefore, cross-validation of patients' response with clinical

records was performed to increase the data validity. Additionally, lack of accessibility to the genetic analysis to evaluate the visual impairment based on different inheritance pattern can be considered as another limitation of the present study.

In conclusion, we found that more disease progression and subsequently visual acuity reduction was observed in RP patients who had older ages and disease onset in younger ages.

Conflict of interest

Authors declare no conflict of interest.

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