

## Evaluation of the Emotional Status in Patients with Retinitis Pigmentosa Using PHQ-9 and Zung Scores: Is the Depression Common in Retinitis Pigmentosa?

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### Abstract

**Objective:** To assess the depression prevalence and its potential correlation with visual loss in patients with retinitis pigmentosa.

**Methods:** Fifty-five patients with retinitis pigmentosa and 32 age- and sex-matched healthy individuals were recruited in this case-control study. All participants underwent a complete ophthalmological examination, which included measurement Best-corrected visual acuity (BCVA), slit lamp examination and funduscopy, and completed the Patient Health Questionnaire-9 (PHQ-9) and the Zung Depression Inventory questionnaire. The diagnosis and the evaluation of retinitis pigmentosa were based on spectral domain optical coherence tomography (SD-OCT) and fundus autofluorescence (FAF) examination with dilated pupils.

**Results:** The patients' group consisted of 44 males and 11 females with mean age of  $41.4 \pm 7.6$  years old, whereas the controls' group included 19 males and 13 females with mean age of  $42.5 \pm 10.1$  years old. BCVA differed significantly between the two groups, as expected (Mann-Whitney test:  $p < 0.0001$ ). The mean values of PHQ-9 and Zung scores in patients with retinitis pigmentosa classified them as moderately depressive or normal, respectively. The control group was characterized as mildly depressive or normal, according to PHQ-9 and Zung scores, respectively. Both scores were increased among patients ( $10.0 \pm 3.9$  and  $45.2 \pm 2.1$ , respectively) compared to the control group ( $6.7 \pm 5.4$  and  $41.1 \pm 8.5$ , respectively) and these increments were statistically significant (Mann-Whitney test:  $p = 0.005$  and  $p = 0.024$ , respectively). PHQ-9 and Zung scores appeared to be weakly but significantly correlated (Spearman's coefficient =  $-0.29$ ,  $p = 0.006$ ). The increased age seemed to be responsible for the depressive symptoms, according to the PHQ-9 score but not with respect to the Zung score.

**Conclusion:** Patients with retinitis pigmentosa exhibited more frequently and intensely depressive symptoms in PHQ-9 scores, compared to the healthy individuals. Moderate depression was significantly correlated visual function decline and increasing age. Ophthalmologists should be aware of the emotional disorders and encourage the patients to receive psychological support.

**Keywords:** Retinitis pigmentosa, Depression, PHQ-9 score, Visual acuity, Zung score

### Introduction

Retinitis pigmentosa defines a clinically and genetically diverse group of hereditary dystrophies, which are characterized by the progressive loss of the photoreceptors and the retinal pigment deposits. Although the disease affects the entire retina, it is limited to the macula or the periphery at the early stages [1]. The prevalence of retinitis pigmentosa ranges from 1:3000 to 1:7000 people worldwide, while it is determined as 1:3500 in Europe and USA [2]. It is slightly higher in men than women due to the X-linked type of the disease. The age of onset, the rate of progression, the final visual acuity and the presence of associated ocular features depend on the nature of the inheritance [3]. The diagnostic criteria of retinitis pigmentosa include bilateral involvement, loss of peripheral vision and progressive deterioration of

predominantly rod photoreceptor function. Night blindness (nyctalopia), which most frequently is the earliest symptom, along with the findings of funduscopy, perimetry and electroretinogram, contribute to the diagnosis [4].

Although several medical treatments have been proposed to suspend the degenerative process, patients experience centripetal visual loss, leading to legal and functional blindness [5]. The decline in vision of these patients impairs their daily activities and autonomy, subsequently reflecting in their psychology. A recent cross-section study appreciated the relation between vision-specific distress and depressive symptoms, recruiting 162 patients with visual acuity less than 6/12. Poor vision-specific functioning, low confidence in managing social interactions and depressive symptoms were determined as risk factors for vision-specific distress, which was strongly correlated to patients' depression [6]. Various mental

disorders, including depression, have been associated with retinitis pigmentosa [7].

The purpose of this study is to evaluate the potential correlation between depression and visual loss in patients with retinitis pigmentosa, by using specific questionnaires, the Zung Depression Inventory questionnaire and the Patient Health Questionnaire-9.

## Materials and Methods

### Participants

Fifty five patients with bilateral Retinitis Pigmentosa (macula off) at different stages and 35 age- and sex-matched, unaffected healthy controls were recruited in this case-control study, which conducted at the Laboratory of Electrophysiology, 1st Department of Ophthalmology, University of Athens, Greece. The purpose and procedure of this study were explained and written consent was obtained by all participants. The study was performed in accordance to the tenets of the Declaration of Helsinki and the protocol used was approved by the ethics committee of the University Hospital.

Past medical history, including medications, medical conditions and ocular history was obtained. Patients with neurological disorders were excluded from the study, because they could influence the outcomes.

### Ophthalmic examination

All participants underwent a thorough ophthalmic examination. Best-corrected visual acuity (BCVA) was assessed using Snellen charts (measured in decimals) and scores were converted in a logarithm of the minimum angle of resolution (logMAR) scale for statistical purposes. The average of BCVA of both eyes was used in the statistical analysis. The ophthalmological examination included slit lamp examination of the anterior segment and funduscopy (with dilated pupils), using a 78D stereoscopic fundus lens. The diagnosis of retinitis pigmentosa had been already carried out based on clinical findings, funduscopy, visual field examination and electroretinogram (ERG), before the clinical study started. We further evaluated the patients with retinitis pigmentosa, using spectral domain optical coherence tomography (SD-OCT) and fundus autofluorescence (FAF) examination. The dilation of patients' pupils with mydriatics preceded the SD-OCT and FAF examinations.

### PHQ-9 and Zung scores

All participants completed the Zung Depression Inventory questionnaire and the Patient Health Questionnaire-9 (PHQ-9). The Zung Depression Inventory is a 20-question self-rating scale concerning emotional, behavioral, cognitive and somatic depression symptoms. Questionnaire was developed according to the most commonly found depression's diagnostic criteria during patients' interviews. Subjects rate each item according to how frequently they felt each one during the preceding week; rating (1) for "none or little of time" to (4) for "most or all of the time". Summing scores for all individual items give a total score, ranging from 20 to 80. The following classification is suggested by the authors: scores below 49 were considered normal, whereas the rest subjects exhibit mild (score 50-59), moderate to marked (score 60-69), and severe (score  $\geq$  70) depression [8-10].

The PHQ-9 is the depression module that scores each of the 9 criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) [11]. It can be used to detect depression symptoms in high risk population and monitor the severity of depression [12]. The questionnaire consists of 9 items assessing the patient's emotional condition over the past 2 weeks. These items include: 1) anhedonia, 2) depressed mood, 3) insomnia or hypersomnia, 4) fatigue or loss of energy, 5) appetite disturbances, 6) guilt or worthlessness, 7) diminished ability to think or concentrate, 8) psychomotor agitation or retardation, and 9) suicidal thoughts. Answers are rated (0) for "not at all" to (3) for "nearly every day". Summing answer scores of all 9 items give a total score that ranges from 0 to 27, with higher scores indicating presence of more severe symptomatology. The classification suggested by Kroenke et al. is the following: subjects exhibit minimal (PHQ-9 score 0-4), mild (PHQ-9 score 5-9), moderate (PHQ-9 score 10-14), and moderately severe/severe (PHQ-9 score  $\geq$  15) depressive symptoms [13]. Validity of the PHQ-9 as a useful depression detection tool has been assessed and well established by studies using large samples of population over the past decades [14,15].

### Statistical analysis

The statistical program IBM SPSS Statistics 22.0 was used for the analysis. Descriptive analysis of all parameters, including the age, the gender, the BCVA, the PHQ-9 and Zung scores, was first carried out. Box plots of the quantitative variables were created. Non-parametric analysis Kolmogorov-Smirnov was used to check the normal distribution of all variables. The possible gender differences between healthy individuals and patients were estimated using the chi-squared test. Mann-Whitney test was applied to identify the possible differences in age, BCVA, PHQ-9 and Zung scores between the two groups (Mann-Whitney test was used when there was no indication of normal distribution either after Kolmogorov-Smirnov analysis or after Levene's test for equality of variances). The age, BCVA, PHQ-9 and Zung scores were correlated using Pearson's and Spearman's coefficients. Furthermore, partial correlation between the two scores was performed to exclude the possible effect of age.

## Results

### Demographics

A total of 55 patients with Retinitis Pigmentosa and 32 healthy unrelated controls were recruited in this case-control study. The patients' group consisted of 44 males and 11 females with mean age of  $41.4 \pm 7.6$  years old, ranging from 26 to 56 years old (Table 1). Controls' group consisted of 19 males and 13 females with mean age of  $42.5 \pm 10.1$  years old, ranging from 28 to 58 years old (Table 1). According to Kolmogorov-Smirnov analysis, neither age nor gender exhibited normal distribution ( $p=0.200$  and  $p=0.200$ , respectively). Although, differences in gender distribution were detected between the two groups (chi-squared test:  $p=0.038$ ), the age displayed the same distribution between patients and healthy individuals (Table 1).

### Assessment of BCVA, PHQ-9 and Zung scores

The mean BCVA, PHQ-9 and Zung scores are presented in Table 1. BCVA among patients with retinitis pigmentosa was distributed as follow: 0.10-0.15 logMAR in 4 patients, 0.22-0.4 logMAR in 24 patients and 0.52-1.3 logMAR in 27 patients. The PHQ-9 score estimated that patients with retinitis pigmentosa were moderately depressive, whereas

mild depression was detected in the control group. The PHQ9 scores for both genders in two groups are displayed in Table 2. According to the Zung score, all participants were normal. BCVA differed

significantly between the two groups, as expected (Table 1). Statistically significant differences in PHQ-9 and Zung scores were also noted between the two groups (Table 1).

Variables	Patients with retinitis pigmentosa (Mean ± SD)	Healthy controls (Mean ± SD)	p values (Mann-Whitney tests)
Age (years)	41.4 ± 7.6	42.5 ± 10.1	0.898
BCVA (logMAR)	0.52 ± 0.29	0.00 (constant)	<0.0001
PHQ-9 score	10.0 ± 3.9	6.7 ± 5.4	0.005
Zung score	45.2 ± 2.1	41.1 ± 8.5	0.024

Table 1: The clinical data of patients and controls. BCVA= Best-Corrected Visual Acuity of both eyes, SD= Standard Deviation.

GROUP		PHQ9 score				Total
		NORMAL	MILD	MODERATE	SEVERE	
CONTROLS	male	6	7	5	1	19
	female	6	4	2	1	13
	Total	12	11	7	2	32
RP	male	3	18	14	9	44
	female	2	5	3	1	11
	Total	5	23	17	10	55

Table 2: The PHQ9 scores based on gender distribution in two groups.

PHQ-9 and Zung scores appeared to be weakly but significantly and negatively correlated (Spearman's coefficient=-0.29, p=0.006). However, the partial correlation, which was performed between the two scores to exclude the possible effect of age, did not reveal significant results (Pearson's coefficient=-0.20, p=0.066). Moreover, age exhibited moderate and positive correlation with PHQ-9 score (Spearman's coefficient=0.46, p<0.0001), but it was weakly and negatively correlated with Zung score (Spearman's coefficient=-0.25, p=0.019). Finally, BCVA (in logMAR) was significantly, positively and moderately correlated with PHQ-9 score (Spearman's coefficient=0.52, p<0.0001).

## Discussion

In this study, we observed that the mean values of PHQ-9 and Zung scores in patients with retinitis pigmentosa classified them as moderately depressive or normal, respectively. The control group was characterized as mildly depressive or normal, according to PHQ-9 and Zung scores, respectively. The differences in means of both PHQ-9 and Zung scores were statistically significant between the two groups. Moreover, the depression, as estimated by PHQ-9 score, was favored, as it was expected, when the BCVA was reduced. The increased age seemed to be responsible for the depressive symptoms, according to the PHQ-9 score but not with respect to the Zung score. PHQ-9 and Zung scores appeared to be weakly but significantly and negatively correlated may be due to the little number (55) of patients with retinitis pigmentosa. More males suffered from depression in the retinitis pigmentosa group.

Adhami-Moghadam and Iran-Pour assessed the mental and emotional status of 417 patients who experienced retinitis pigmentosa predominantly from their childhood. They noted that they suffered from eight mental disorders, including obsessive compulsive disorder (39.3%), schizophrenia (38.1%), antisocial personality (37.6%), paranoia (36.7%), hypochondrias (35.3%), depression (31.2%), hysteria (26.9%), and hypomania (23.7%). Depression was mostly reported in women and was related to the increasing age and the marital status [7].

Our results were also concurrent with the study of Kim et al. They evaluated the prevalence of depressive symptoms, stress and suicidal thoughts in 187 patients with retinitis pigmentosa and estimated it as 34.8%, 51.9% and 38.5%, respectively. The relevant percentages in control group were 17.1%, 29.4% and 12.9%, respectively. However, no significant difference in the number of suicide attempts was revealed between the groups [16]. Moreover, very intense phobic pathology along with depression, as evaluated by the Brief Symptom Inventory (BSI), was detected by Strougo et al. in 970 patients with retinitis pigmentosa [17]. The lack of cooperativeness, as assessed by the Yatabe-Guilford personality test, also characterizes the personality of patients with retinitis pigmentosa [18]. Moschos et al. observed mild to moderate depressive symptoms in 34 patients with retinitis pigmentosa of mean age 49 years old, who completed the Zung Depression Inventory questionnaire and the PHQ-9. The Zung score was positively correlated to PHQ-9 one and both scores were positively correlated with BCVA. Besides BCVA, depression was also related to age [19].

The depression observed in these patients may possibly be related to sleep disorders. Ionescu et al. noted that patients with retinitis pigmentosa suffered from disturbed nighttime sleep, sleepiness and impaired daytime alertness in a higher frequency compared to healthy individuals. They associated these disorders both with the emotional status and visual impairment, supporting the impact of photoreceptors degeneration on circadian rhythm [20]. Moreover, Azoulay et al. highlighted that anxiety and depression were significantly higher in patients with visual fields and visual acuity less than 20o and 0.3 logMAR, respectively. The depressive symptoms were evaluated by the QOL (25-item National Eye Institute Visual Functioning Questionnaire) and the Hospital Anxiety and Depression Scale for anxiety/depression questionnaires [21]. Bittner et al. also observed that high variability in visual acuity and visual fields was associated with the severity of the disease, with eliminated physical functioning and increased depressive symptoms [22].

Hayeems et al. proposed a model of understanding the process of patients' adjusting to retinitis pigmentosa, supporting that the

emotional impact of the disease depended on the personality of each patient [23]. It has been noted that depression in patients with retinitis pigmentosa results in poorer vision-related functions [24]. Moreover, these patients appear to have difficulties in adjusting to their visual loss, suffering from impaired health-care orientation, vocational environment, social environment, and extended family relationships [25]. The physicians can certainly play a significant role in the emotional status of patients with retinitis pigmentosa, detecting early the depressive symptoms. Furthermore, they can train them to improve their visual functioning, ameliorating their emotional state and quality of life [26].

The limitations of our study include the inability to present the visual fields and ERG tests of patients with retinitis pigmentosa in this manuscript. Furthermore, the genetic background of these patients would offer more information in this study.

We concluded that the depressive symptoms, as assessed by the PHQ-9 and Zung questionnaires, are more frequent and intense in patients with retinitis pigmentosa compared to the healthy individuals. Furthermore, depression detected by the PHQ-9 score appears to be augmented along with the increase of age and the deterioration of visual acuity. Ophthalmologists should be aware of the emotional and mental disorders in patients with retinitis pigmentosa in order to detect early such kind of pathology and encourage the patients to receive psychological support and the appropriate treatment.

### Author Disclosure Statement

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The authors alone are responsible for the content and writing of this paper and they have contributed significantly to this manuscript.

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