

ANXIETY AND TREATMENT ADHERENCE AMONG GLAUCOMA PATIENTS DURING COVID-19 PANDEMIC AND EARTHQUAKES IN CROATIA

Dina Lešin Gaćina¹, Sonja Jandroković^{1,2}, Darko Marčinko^{2,3}, Ivan Škegro^{1,2}, Sania Vidas Pauk¹,
Martina Tomić⁴, Bernarda Škegro⁵, Marija Barišić Kutija¹ & Petra Kristina Ivkić¹

¹Department of Ophthalmology, Zagreb University Hospital Center, Zagreb, Croatia

²School of Medicine, University of Zagreb, Zagreb, Croatia

³Department of Psychiatry and Psychological Medicine, Zagreb University Hospital Center, Zagreb, Croatia

⁴Department of Ophthalmology, Vuk Vrhovac University Clinic for Diabetes, Endocrinology and Metabolic Diseases,
Merkur University Hospital, Zagreb, Croatia

⁵Srebrnjak Children's Hospital, Zagreb, Croatia

received: 20.12.2021;

revised: 30.1.2022;

accepted: 5.2.2022

SUMMARY

Background: The COVID-19 epidemic and earthquakes in Croatia during 2020 suddenly disrupted everyday life and caused psychological disturbances in population. The purpose of the present study was to assess the prevalence of anxiety symptoms and the level of treatment adherence in glaucoma patients during the pandemic. The paper also aimed to evaluate the correlation between anxiety symptoms, treatment adherence and treatment outcomes in the studied cohort.

Subjects and methods: This cross-sectional study was conducted among primary open-angle glaucoma (POAG) patients at the Department of Ophthalmology, Zagreb University Hospital Center, during one year. The Beck Anxiety Inventory (BAI) was used to measure the level of anxiety symptoms. Treatment adherence was estimated by the Culig adherence scale (CAS). Glaucoma damage was determined for each patient from the level of structural and functional impairment of the worse eye, by retinal nerve fiber layer (RNFL) thickness and mean defect (MD), respectively. Statistical analyses were performed, with a *P* value of less than 0.05 considered being statistically significant.

Results: This study included 113 POAG patients, with a mean age of 65.89 years. The median of the BAI total score in all patients was 10. According to the CAS, 60.2% of patients were non-adherent to glaucoma treatment during the COVID-19 outbreak. The BAI total score was significantly negatively related to adherence to local glaucoma treatment ($p < 0.001$). A significant negative association was also observed between adherence and MD ($p = 0.017$), while no correlation was found between adherence and RNFL thickness ($p = 0.228$).

Conclusion: Considerable proportion of patients with glaucoma have shown non-adherence to treatment during the COVID-19 pandemic. Anxiety severity was associated with lower adherence, thus indirectly influencing therapeutics outcomes. Special consideration should be given to the strategies promoting mental health and interventions focusing on treatment adherence in glaucoma patients in a time of emergencies.

Key words: glaucoma - treatment adherence – anxiety - visual impairment - COVID-19 pandemic

* * * * *

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) introduced the central quarantine in the contemporary world and created a global economic and public health crisis. Given the rate and extent of the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from Wuhuan, China, the World Health Organization (WHO) declared a global COVID-19 pandemic in March 2020 (WHO 2020). According to the recommendations of the international health organizations, the Croatian Government has adopted a variety of drastic public health measures in order to prevent further transmission and acquisition of the infection. Particular emphasis was placed on physical distancing, social restrictions, and (self)isolation, which highly impacted everyday living. This abrupt situation threatened the physical and mental health and social func-

tioning across the whole population (Jakovljevic et al. 2020a, Lauri Korajlija & Jokic-Begic 2020).

General concerns have been raised about the scientific facts related to the new virus and the completely unknown disease it causes (Jakovljevic et al. 2020b). The most distressing disturbances were the probability of getting infected, fear that the health care system could not cope with the pandemic, absence of specific treatment modalities, and doubts about vaccinations (Bogdan et al. 2020). Additionally, in the middle of the crisis caused by the COVID-19 pandemic, Croatia was hit by two most powerful earthquakes in the last 140 years. The first earthquake, being 5.5 on the Richter scale, affected Zagreb on 22nd March 2020. The region 60 km from the capital was an epicenter of the second earthquake of magnitude 6.4 on the Richter scale on 29th December 2020. The pandemics and devastating earthquakes caused high morbidity and mortality,

extensive property damage, and material loss. Besides health issues, people were also worried and insecure about the possibility of losing their jobs and existence (Bogdan et al. 2020, Curkovic et al. 2020).

Since it is already known that a crisis causes significant physical and psychological stress, a negative impact on the nation's mental health was inevitable (Curkovic et al. 2020, Lauri Korajlija & Jokic-Begic 2020). Furthermore, some groups are more susceptible and vulnerable to psychosocial influences, such as the elderly, immunodeficient people, and people with acute and chronic diseases (Lancet 2020). Regarding that, there are reports about the impact of actual pandemics on the health care and treatment outcomes among ophthalmic patients during this era (Gupta et al. 2020, Pujari et al. 2021).

Glaucoma is one of the leading causes of permanent visual impairment in the world (European Glaucoma Society guidelines 5th ed. 2020). According to Hattenhauer et al., the 20-year cumulative probability of blindness was estimated to be 9% in both eyes and 26% in at least one eye for primary open-angle glaucoma (POAG) patients (Hattenhauer et al. 1998). The only modifiable risk factor, at the moment, that may prevent the disease progression, is high intraocular pressure (IOP) (Zimmerman & Zalta 1983, European Glaucoma Society guidelines 5th ed. 2020). The traditional treatment approach aims to reduce IOP via long-term local medications and thus prevent glaucomatous optic neuropathy and visual field loss (European Glaucoma Society guidelines 5th ed. 2020). The therapeutic success of the prescribed medication in chronic diseases, in general, depends on the patient's perseverance in applying the therapy (Dunbar-Jacob et al. 2000), and taking that into consideration, the significant correlation between adherence and treatment outcomes in various chronic diseases have been demonstrated (Osterberg & Blaschke 2005). Adherence is the extent to which a person's behavior in taking medication corresponds with agreed recommendations from a healthcare provider in terms of dosage, times, and frequency of drug administration (Sabaté 2003). Systematic reviews before the COVID-19 era estimate the medication nonadherence rate from 30% to even 80% among glaucoma patients (Olthoff et al. 2005, Nordstrom et al. 2005). In that line, it is already known that nonadherent behavior leads to a higher rate of glaucoma progression resulting in increase risk of blindness, which is emphasized as a significant health and economic problem (Robin & Muir 2019). Treatment adherence is a multidimensional measure influenced by various factors, and the patient's mental status when prescribing topical therapy is well-established (Sabaté 2003).

Numerous pre-epidemic studies have indicated a higher prevalence of mood and anxiety disorders in glaucoma than in general (Lim et al. 2016, Zhang et al. 2017). Glaucoma patients experience increased fear of blindness and consequent complications, fear of inabi-

lity to perform daily activities (including driving), fear of losing financial stability, and concern to be emotionally and socially isolated (Janz et al. 2007, Ramulu et al. 2012, Burmedi et al. 2002). Since anxiety is associated with reduced adherence to treatment and irregular application of topical therapy, disease deterioration in those patients is expected (Zhang et al. 2017). Due to its chronic course and effects on physical health and occupational functioning, anxiety is a significant health problem that notably compromises the quality of life (Bruce et al. 2005).

Therefore, the present study aimed to evaluate the prevalence of anxiety symptoms among glaucoma patients, level of treatment adherence, and its correlation with visual impairment and other factors during the COVID-19 pandemic and Croatia's earthquake crisis.

SUBJECTS AND METHODS

Setting and subjects

The cross-sectional study was conducted at the Department of Ophthalmology, University Hospital Centre Zagreb, in Zagreb, Croatia. The data collection period was from 1st April 2020 to 1st April 2021.

All subjects underwent comprehensive ophthalmologic examinations, including best-corrected visual acuity (BCVA) using the Snellen chart, slit-lamp biomicroscopy, gonioscopy, and dilated fundus examination. IOP was measured using a Goldmann applantation tonometer. Functional impairment, the visual field (VF), was estimated using automated static perimetry (Octopus 900/G program Visual Field Analyzer, Haag Streit). Optical coherence tomography (OCT), assessed by Optopol Copernicus HR, was used to quantify the structural defects.

POAG patients aged 18 years or older were randomly recruited. POAG was based on criteria for diagnosis setting: IOP values from medical history higher than 21 mmHg, presence of an open angle with a Shaffer grading of > 2 on gonioscopy, typical glaucomatous disc cupping, and compatible VF defects. All subjects had been prescribed topical hypotensive therapy for at least one year.

Patients who were not eligible to participate in this study were patients with other glaucoma types or other eye diseases that impaired central and peripheral vision and VF defects caused by other systemic diseases (i.e., neurological). Patients who had incisional eye surgeries or laser treatments within the previous three months before the enrollment were also not included in the study. In addition, patients with cognitive impairment, mental disorder, psychotherapeutic or psychopharmacological treatment in history were not included. From the study were excluded subjects who have any of the unanswered items in questionnaires. Subjects with VF and OCT findings unreliable and could not be accurately analyzed were not eligible for the study.

This study was conducted following the guidelines of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). All procedures performed in the study involving human subjects were under the ethical standards of the institutional research committee. The Ethics Committee of the University Hospital Centre Zagreb approved the study protocol. Informed consent was obtained from each respondent. Data collection was voluntary and anonymous.

Study instruments

Once they agreed to participate in the study, subjects were given a self-administered survey. The questionnaires were conducted anonymously.

Socio-demographic data were assessed, including age, gender, education level, living conditions, and marital status. Clinical information was recorded, including systemic comorbidities, family history of glaucoma, and duration of POAG (less than two years, 2 - 5 years, more than five years). Drug information, including the type and dosage of antiglaucoma medications and systemic therapy, were also collected.

Structural defects were quantified by the average retinal nerve fiber layer (RNFL) thickness values of the better eye and worse eye using OCT. The extent of functional impairment was assessed by mean defect (MD) values of the better eye and worse eye on VF findings.

The 21-item Beck Anxiety Inventory (BAI) was used for self-reported anxiety symptoms evaluation. The questionnaire was designed for the measurement of generalized anxiety and distinguishing between symptoms of anxiety and depression. It consists of 21 items and the total score is calculated by finding the sum of all items, with a higher score indicating higher self-reported anxiety regarding reliability, internal consistency for the BAI (Cronbach's alpha coefficient of the BAI = 0.95) (Beck et al. 1988).

Medication adherence was evaluated using the Culig Adherence Scale (CAS), the valid and reliable self-administered instrument which consists of several parts. Adherence is defined by detecting the frequency of missed application of the prescribed medications. The possible answers were: I never forget to take my medication, I forget to take my medication during the last week, last month, last 1 - 3 months, and more than the last three months. Depending on the answer to this item, subjects were divided into two groups. Those who answered this question with "never forget" were defined as adherent. All other respondents were considered nonadherent. The less time has passed of skipping medications, the more likely the patient is nonadherent and often forgets to take the medication. The psychometric properties of the questionnaires have been previously confirmed in Croatia population (Cronbach's alpha coefficient = 0.94) (Momirović et al. 2016).

Statistical analysis

Statistical analysis was performed by Statistica software package version 13.5 (TIBCO Software Inc. 2018. TIBCO Statistica™ Software, Version 13.5. USA, TIBCO Software Inc.). The normality of data distribution was tested by the Kolmogorov-Smirnov or Shapiro-Wilk test, and the homogeneity of variance by the Leven test. Results of descriptive analyses were expressed as means \pm SD or median (min, max) for continuous variables and percentages for categorical variables. Differences between continuous data were determined by a one-way ANOVA test or Kruskal-Wallis test. A nonparametric test was used when the assumption of homogeneity of variance for tested variables was not met. Scheffe post-hoc test and multiple comparisons of the Kruskal-Wallis test were used where needed. Differences among categorical data were evaluated by the Chi-square test. The Spearman's rank and Kendall's tau correlation tests were used to assessing the strength of associations. In all analyses, a P value of less than 0.05 was considered statistically significant.

RESULTS

This study included 113 primary open-angle glaucoma patients (48 males / 65 females), with a mean age of 65.89 ± 8.53 years. 4 (3.5%) patients had POAG less than two years, 27 (23.9%) between two and five years, and 82 (72.6%) patients had it more than five years. Only 31 (27.4%) patients had a positive family history of glaucoma. In glaucoma treatment, 84 (74.3%) patients used one antiglaucoma medication, 24 (21.2%) two, and 5 (4.4%) patients used three antiglaucoma medications. In addition, 86 (75.7%) patients also had some systemic comorbidities, while 27 (24.3%) had none.

11 (10.1%) patients graduated primary school, 55 (48.6%) high school, 19 (16.5%) collage, 23 (20.2%) faculty, and 5 (4.6%) had the educational level of Master of Science or PhD. 24 (21.5%) patients lived alone, and 89 (78.5%) lived in a family. Most of the patients (76%) were married, while 3.8% were divorced, 13.5% were widows or widowers, and 6.7% of patients were single never married.

The median of the BAI total score in all patients was 10 (min 0, max 53). According to the anxiety level, patients were divided into three groups. 92 (81.4%) patients had low level of anxiety (group 1 - BAI score: 0-21), 16 (14.1%) had moderate (group 2 - BAI score: 22-35), and 5 (4.5%) patients had high level of anxiety (group 3 - BAI score: \geq 36) (Table 1). The groups did not significantly differ in age ($p=0.429$), gender ($p=0.507$), duration of POAG ($p=0.242$), and the number of antiglaucoma medications ($p=0.601$). However, patients with a low anxiety level had less frequently a positive than a negative family history of glaucoma than patients with moderate and high anxiety

Table 1. BAI total score, family history of glaucoma, intraocular pressure, structural and functional impairment of the worse eye and adherence to the local glaucoma treatment of patients divided into three groups according to the level of anxiety

	Level of anxiety			H ^a Chi ^b F ^c	p
	Low (n=92)	Moderate (n=16)	High (n=5)		
BAI total score*	9 (0, 21)	23.5 (22, 34)	42 (39, 53)	51.352 ^a	<0.001
Family history of glaucoma (positive/negative)**	21.6/78.4	50/50	40/60	6.077 ^b	0.048
IOT (mmHg)***	16.04±2.44	17.50±3.44	16.20±1.30	2.176 ^c	0.118
RNFL (µm)*	97 (52, 122)	93 (69, 106)	103 (98, 115)	4.571 ^a	0.102
MD (dB)*	2.9 (-1.3, 23.9)	3.3 (0.2, 15.0)	0.7 (-0.5, 1.9)	8.256 ^a	0.016
Adherence to the local glaucoma treatment (yes/no)**	45.6/54.4	12.5/87.5	20/80	7.109 ^b	0.029

* median (min, max); ** percentages; *** mean±SD; ^a Kruskal-Wallis test; ^b Chi-square test df=2; ^c ANOVA; BAI - the 21-item Beck Anxiety Inventory; IOT - intraocular pressure; RNFL - retinal nerve fiber layer thickness; MD - mean defect

levels (p=0.048). No significant difference between the anxiety groups was observed in educational level (p=0.471), living conditions (p=0.310), marital status (p=0.796), and the prevalence of systemic comorbidities (p=0.215).

In all patients included in the study, the median of peripapillary RNFL thickness of the better eye was 101 (min 58, max 139) µm and of the worse eye 97 (min 52, max 122) µm, while the median of MD of the better eye was 1.3 (min -1.0, max 16.0) dB and of the worse eye 2.9 (min -1.3, max 23.9) dB. For each patient, the glaucoma damage was determined from the level of structural and functional impairment of the worse eye, so in the further statistical analysis, the median of peripapillary RNFL thickness and the median of MD of the worse eye was used. No significant difference was observed between the mean values of IOP associated with RNFL thickness of the worse eye and IOP associated with MD of the worse eye (16.23±2.63 mmHg vs. 16.22±2.60 mmHg, p=0.877); thus, the mean value of both IOPs of the worse eye was further analyzed. Table 1 shows the intraocular pressure, structural and functional impairment of the worse eye of patients divided into three groups according to the level of anxiety. The groups did not significantly differ in IOP (p=0.118) and RNFL thickness (p=0.102), but a significant difference was observed in MD between the studied groups (p=0.016). However, multiple comparisons show that only patients with a moderate anxiety level had significantly higher MD than those with a high anxiety level (3.3 dB vs. 0.7 dB, p=0.012).

According to the Culig Adherence Scale, only 45 (39.8%) patients were adherent to local glaucoma treatment and never skipped their medication. In the nonadherent group (60.2%), 7 (10.3%) patients did not take the medication last week, 35 (51.5%) last month, 19 (27.9%) last 1 - 3 months, and 7 (10.3%) patients did not take it more than last three months. Table 1 presents the adherence and nonadherence to local glaucoma treatment of patients divided into three

groups according to the level of anxiety. Patients with moderate and high anxiety levels were less frequently adherent than nonadherent to local glaucoma treatment than patients with a low anxiety level (p=0.029). However, no significant difference in the degree of nonadherence was observed between the studied groups (p=0.732).

Significant and marginal correlations between the BAI total score, socio-demographic and clinical data are presented in Table 2. The BAI total score was significantly positively associated with the female gender (p<0.001) and a positive family history of glaucoma (p<0.001), while negatively with the educational level (p=0.048). The marginal negative association of BAI total score was observed for living conditions (p=0.052), though positive for systemic comorbidities (p=0.058). No association was found between the BAI total score and age (p=0.257), duration of POAG (p=0.316), the number of antiglaucoma medications (p=0.602), marital status (p=0.241), IOP (p=0.799), RNFL thickness (p=0.253), and MD of the worse eye (p=0.398), nor even after dividing the patients into anxiety groups (p>0.05). Though, the BAI total score was significantly negatively related to the adherence to local glaucoma treatment (p<0.001) (Table 2). Other significant and marginal correlations of the adherence to local glaucoma treatment are presented in Table 3. The adherence to local glaucoma treatment was significantly positively correlated with the educational level (p=0.022), while marginally negatively with a positive family history of glaucoma (p=0.057) and the number of antiglaucoma medications (p=0.058). A significant negative association was also observed between the adherence to treatment and MD of the worse eye (p=0.017). No correlation was found between the adherence to treatment and age (p=0.252), gender (p=0.947), duration of POAG (p=0.688), living conditions (p=0.379), marital status (p=0.695), the prevalence of systemic comorbidities (p=0.473), IOP (p=0.165), and RNFL thickness of the worse eye (p=0.228), nor even after dividing the patients into anxiety groups (p>0.05).

Table 2. Correlations between the BAI total score, socio-demographic, clinical data and the adherence to local glaucoma treatment

	The 21-item Beck Anxiety Inventory total score		
	Kendall Tau	Z	p
Gender (female)	0.242	3.806	<0.001
Family history of glaucoma	0.243	3.741	<0.001
Educational level	-0.128	-1.974	0.048
Living conditions	-0.118	-1.798	0.052
Systemic comorbidities	0.112	1.765	0.058
Adherence to the local glaucoma treatment	-0.259	-4.076	<0.001

Table 3. Correlations between the adherence to local glaucoma treatment, educational level, and clinical data

	Adherence to the local glaucoma treatment		
	Kendall Tau	Z	p
Educational level	0.148	2.2844	0.022
Family history of glaucoma	-0.125	-1.8960	0.057
Number of antiglaucoma medications	-0.122	-1.8180	0.058
MD of the worse eye	-0.153	-2.3890	0.017

DISCUSSION

The presented study investigated the level of anxiety symptoms and adherence to glaucoma treatment in POAG patients during the COVID-19 pandemic.

The COVID-19 outbreak has burdened healthcare systems worldwide since the focus on coronavirus - infected population has prioritized medical, personnel, and material resources. Consequently, awareness of the negative impact of the pandemic on the clinical outcomes of various chronic patients has increased.

If not treated properly, patients with glaucoma may experience irreversible vision loss due to chronic-progressive course and initial asymptomatic nature of disease (European Glaucoma Society guidelines 5th ed. 2020). Given the importance of IOP control as a major etiological risk factor, adherence to local antihypertensive therapy is generally recognized as a key component in the treatment of the disease, especially considering that IOP is the only modifiable factor (European Glaucoma Society guidelines 5th ed. 2020, Zimmerman & Zalta 1983). Poor adherence to glaucoma treatment is globally recognized as a significant public health problem, that exacerbated during lockdown (Subathra et al. 2021, Mylona et al. 2021). Our results showed that only 39.8% of patients were adherent to local glaucoma treatment during the COVID-19 pandemic, which is in compliance with researches worldwide.

In this study, most subjects who did not adhere to the prescribed therapy reported forgetfulness as the main reason for non-compliance with the drug, which is consistent with previous investigations (Newman-Casey et al. 2015). No correlation was found between the adherence to treatment and the main socio-demographic factors of our subjects. However, educational level was positively associated with adherence to

medication, similar to Mylona et al., who demonstrated that the pandemic has disproportionately affected patients of lower educational levels in Greece population (Mylona et al. 2021).

Since treatment adherence in glaucoma is a multi-dimensional concept which encompasses a complex relationship between patient's characteristics, healthcare system, society, and economy, today's global pandemic has affected all factors that have made treatment extremely challenging. Previously, multiple barriers with anti-glaucomatous therapy were identified (Newman-Casey et al. 2015). A recent study has shown that the COVID-19 pandemic negatively influences adherence in chronic diseases due to known factors that affect adherence and, in addition, due to other obstacles that are unique for a continuous period, like travel restrictions, limitation in availability of glaucoma medication in pharmacy, financial difficulties due to higher unemployment (Subathra et al. 2021). Moreover, the preventative measures implemented in the confrontation to novel coronavirus forced people to change their daily habits and routine, which are essential factor for appropriate adherence to glaucoma treatment (Newman-Casey et al. 2015). Loss of direct contact with family members and (self)isolation have resulted in reduced support and reminders, which are often necessary for proper adherence to glaucoma treatment. In addition, limited access to health facilities presented a significant problem for patients with chronic diseases who require regular visits and repeated medical prescriptions.

According to various reports, glaucoma patients are concerned and anxious about their eye health and risk of vision loss due to the limited provision of ophthalmic care during the pandemic (Pujari et al. 2021). Given this situation, most of our patients reported some degree of anxiety symptoms that

comply with numerous pre-epidemic studies showing a high prevalence of anxiety in glaucoma patients (Lim et al. 2016). Furthermore, there is a report about the progression of the disease due to negative emotions, suggesting that emotional stress itself may affect glaucoma (Shin et al. 2021). In addition, Zagreb, the Croatian capital, was hit by two devastating earthquakes, contributing to mental health disruptions (Curkovic et al. 2020). The current study of the general Croatian public revealed lower psychological well-being and higher scores of affective disorders compared to before COVID-19 (Lauri Korajlija & Jokic-Begic 2020).

In our study, the BAI total score was significantly positively associated with the female gender, which has already been reported as the risk factor for anxiety in glaucoma patients (Tastan et al. 2010). The relationships between age and anxiety showed inconsistency in previous literature (Wu 2019). However, our study revealed that age does not correlate with anxiety. Positive family history of glaucoma was another demographic factor that reached significant correlation with anxiety. This could be explained by the fact that some relatives have already experienced the consequences of disease progression, so a lot of patients felt an uncontrolled fear of vision loss. Furthermore, the evidence implied that more educated subjects felt less anxiety what was confirmed by the results of this study (Wu 2019).

Psychosocial disorders and psychological affection are already known barriers to maintaining the continuity of recommended glaucoma treatment (Zhang et al. 2017). Subathra et al. reported that stress due to the pandemic is a significant factor in non-adherence to treatment, which is consistent with our results (Subathra et al. 2021). In our study, the severity of anxiety symptoms was significantly correlated with poor medication adherence.

Moreover, investigators evaluated participants' functional and structural impairments as indicators of patients' current clinical status to assess the connection between anxiety, treatment adherence, and treatment outcomes.

This study showed a significant negative association between adherence to treatment and MD of the worse eye. At the same time, the results did not indicate an association between adherence, IOP, and RNFL thickness. These findings suggest that the lack of adherence to glaucoma treatment is associated with progressive visual field loss. It could implicate that the more severe visual field loss is, the more likely they were non-adherent, directly linking adherence to treatment and treatment outcome. Our findings are consistent with previous reports that showed that patients who did not adhere had 80% worse visual field impairment than those who adhered (Sleath et al. 2011). In non-adherent patients, additional medications are often

unnecessarily prescribed, or surgery must be performed, what could be avoided if they adhere properly.

Regarding anxiety and glaucoma damage, no association was found between our participants' anxiety symptoms and IOP, RNFL, and MD of the worse eye. On the contrary, according to Shin et al., anxiety was significantly associated with the rate of RNFL thinning in patients with glaucoma, as well as faster rates of RNFL decline (Shin et al. 2021). Additionally, disc hemorrhage and IOP fluctuation were other significant factors associated with anxiety. These results repeatedly suggest that anxiety increases the risk of glaucoma progression (Shin et al. 2021). On the other hand, Wu et al. demonstrated that the patients' self-reported quality of life, but not objective function components, like BCVA and MD, played the most crucial role in psychological distresses among glaucoma patients (Wu 2019).

Some limitations in this study should be addressed. The participants are collected from a single tertiary institution which may cause selection bias. The study's cross-sectional design made it unable to establish causality, and prospective studies will be needed to confirm the conclusions. Moreover, the BAI questionnaire cannot set a formal psychological diagnosis of anxiety, although it is a standard tool, regularly used for clinical and research purposes. The form of the questionnaire was self-administered, so the validity of the responses was challenging to control. Thus, further studies should utilize some of the objective methods for measurement of treatment adherence. Finally, the evidence of the impact of the COVID-19 pandemic is based on convenience samples, without comparable pre-pandemic data of our cohort.

CONCLUSION

Herein presented population study evaluates the adherence to medication and anxiety in glaucoma patients and provides critical and timely data about the impact of the COVID-19 pandemic on the management of glaucoma. The paper revealed a high prevalence of poor treatment adherence, which could be explained, on the one hand, by already known barriers to medication maintenance, and on the other hand, by impediments specific for the era of the pandemic. Anxiety is showed to be an independent risk factor for such neglectful behavior. Our findings showed that in terms of both, anxiety and adherence, especially risk group are patients of lower educational level. These implicate the importance of providing psychological assistance to ensure stable treatment and thus reducing the risk of disease progression. An interdisciplinary approach should manage mental health sequelae of the COVID-19 crisis and future emergencies, especially in vulnerable patients with chronic conditions, like glaucoma. In addition, treatment adherence strategies

and educational interventions need to be adapted to current technological advantages, such as telemedicine, mobile applications, etc., to prevent the risk of treatment discontinuation in time, and thus the risk of adverse clinical outcomes.

Acknowledgements: None.

Conflict of interest: None to declare.

Contribution of individual authors:

Dina Lešin Gačina: conceptualization, writing – original draft preparation, funding acquisition.

Sonja Jandroković: conceptualization, writing - review and editing, supervision.

Darko Marčinko: conceptualization, supervision.

Ivan Škegro: literature searches, writing - review and editing.

Sania Vidas Pauk: literature searches, writing – original draft preparation.

Martina Tomić & Bernarda Škegro: methodology, statistical analysis and interpretation of data.

Marija Barišić Kutija: literature searches, writing - review and editing.

Petra Kristina Ivkić: literature searches.

References

1. Beck AT, Epstein N, Brown G, Steer RA: An inventory for measuring clinical anxiety: Psychometric properties. *J Consult Clin Psychol* 1988; 56:893-897
2. Bogdan A, Ajduković D, Ajduković M, Apostolovski D, Bacinger Klobučarić B, Bandić I et al.: Koronavirus i mentalno zdravlje: Psihološki aspekt, savjet i preporuke. Hrvatska psihološka komora, Zagreb, 2020
3. Bruce SE, Yonkers KA, Otto MW, Eisen JL, Weisberg RB, Pagano M et al.: Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: a 12-year prospective study. *Am J Psychiatry* 2005; 162:1179
4. Burmedi D, Becker S, Heyl V, Wahl HW, Himmelsbach I: Emotional and social consequences of age-related low vision. *Vis Impair Res* 2002; 4:47-71
5. Curkovic M, Kosec A, Brečić P. Stay home while going out - Possible impacts of earthquake co-occurring with COVID-19 pandemic on mental health and vice versa. *Brain Behav Immun* 2020; 87:82-83
6. Dunbar-Jacob J, Erlen JA, Schlenk EA, Ryan CM, Sereika SM, Doswell WM: Adherence in chronic disease. *Annu Rev Nurs Res* 2000;18:48-90
7. European Glaucoma Society. Terminology and Guidelines for glaucoma, 5th ed. Savona: Publicomm srl, 2020. <https://www.eugs.org/eng/guidelines.asp>
8. Gupta PC, Kumar MP, Ram J: COVID-19 pandemic from an ophthalmology point of view. *Indian J Med Res* 2020; 151:411-418
9. Hattenhauer MG, Johnson DH, Ing HH, Herman DC, Hodge DO, Yawn BP et al. The probability of blindness from open-angle glaucoma. *Ophthalmology* 1998; 105:2099-2104
10. Jakovljevic M, Bjedov S, Jaksic N, Jakovljevic I: COVID-19 Pandemia and Public and Global Mental Health from the Perspective of Global Health Secur. *Psychiatr Danub* 2020a; 32:6-14
11. Jakovljevic M, Bjedov S, Mustac F, Jakovljevic I: COVID-19 Infodemic and Public Trust from the Perspective of Public and Global Mental Health. *Psychiatr Danub* 2020b; 32:449-457
12. Janz NK, Wren PA, Guire KE, Musch DC, Gillespie BW, Lichten PR: Fear of blindness in the Collaborative Initial Glaucoma Treatment Study: patterns and correlates over time. *Ophthalmology* 2007; 114:2213-2220
13. Lauri Korajlija A & Jokic-Begic N: COVID-19: Concerns and behaviors in Croatia. *Br J Health Psychol* 2020; 25:849-855
14. Lim NC, Fan CH, Yong MK, Wong EP, Yip LW: Assessment of depression, anxiety, and quality of life in singaporean patients with glaucoma. *J Glaucoma* 2016; 25:605-612
15. Momirovic A, Ganza M, Culig B, Leppee M, Prga I: Psychometric properties of the Culig's questionnaire. *Psychiatr Danub* 2016; 28(Suppl 2):234-241
16. Mylona I, Dermenoudi M, Glynatsis NM, Glynatsis MN: Patient Adherence to Glaucoma Treatment During the COVID-19 Pandemic. *Cureus* 2021; 13:e15545
17. Newman-Casey PA, Robin AL, Blachley T, Farris K, Heisler M, Resnicow K et al.: The most common barriers to glaucoma medication adherence: a cross-sectional survey. *Ophthalmology* 2015; 122:1308-16
18. Nordstrom BL, Friedman DS, Mozaffari E, Quigley HA, Walker AM: Persistence and adherence with topical glaucoma therapy. *Am J Ophthalmol* 2005; 140:598-606
19. Olthoff CM, Schouten JS, van de Borne BW, Webers CA: Noncompliance with ocular hypotensive treatment in patients with glaucoma or ocular hypertension: an evidence-based review. *Ophthalmology* 2005;112:953-61
20. Osterberg L, Blaschke T: Adherence to medication. *N Engl J Med* 2005; 353:487-497
21. Pujari R, Chan G, Tapply I; Addenbrookes Glaucoma COVID response consortium, Bourne RR; The impacts of COVID-19 on glaucoma patient outcomes as assessed by POEM. *Eye (Lond)* 2021; 9:1-3
22. Ramulu PY, van Landingham SW, Massof RW, Chan ES, Ferrucci L, Friedman DS: Fear of falling and visual field loss from glaucoma. *Ophthalmology* 2012; 119:1352-1358
23. Robin AL & Muir KW: Medication adherence in patients with ocular hypertension or glaucoma. *Expert Rev Ophthalmol* 2019; 14:4-5, 199-210
24. Sabaté E. Adherence to long-term therapies: Evidence for action. 1st Edition. Geneva: World Health Organisation, 2003
25. Shin DY, Jung KI, Park HYL, Park CK: The effect of anxiety and depression on progression of glaucoma. *Sci Rep* 2021; 11:1769
26. Sleath B, Blalock S, Covert D, Stone JL, Skinner AC, Muir K et al.: The relationship between glaucoma medication adherence, eye drop technique, and visual field defect severity. *Ophthalmology* 2011; 118:2398-402
27. Subathra GN, Rajendrababu SR, Senthilkumar VA, Mani I, Udayakumar B. Impact of COVID-19 on follow-up and medication adherence in patients with glaucoma in a tertiary eye care centre in south India. *Indian J Ophthalmol* 2021; 69:1264-1270

28. Tastan S, Iyigun E, Bayer A, Acikel C: Anxiety, Depression, and Quality of Life in Turkish Patients with Glaucoma. *Psychological Reports* 2010; 106:343-357
29. The Lancet: Redefining vulnerability in the era of COVID-19. *Lancet* 2020; 395:1089
30. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. World Health Organization: Geneva; 2020. Available from: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>
31. Wu N, Kong X, Gao J, Sun X. Vision-related Quality of Life in Glaucoma Patients and its Correlations With Psychological Disturbances and Visual Function Indices. *J Glaucoma* 2019; 28:207-215
32. Zhang X, Olson DJ, Le P, Lin FC, Fleischman D, Davis RM: The association between glaucoma, anxiety, and depression in a large population. *Am J Ophthalmol* 2017; 183:37-41
33. Zimmerman TJ, Zalta AH: Facilitating patient compliance in glaucoma therapy. *Surv Ophthalmol* 1983; 28(Suppl):252-8

Correspondence:

Dina Lešin Gačina, MD
Department of Ophthalmology, Zagreb University Hospital Center
Kišpatićeva 12, 10 000 Zagreb, Croatia
E-mail: dina.lesin@yahoo.com