



HEALTH-RELATED QUALITY OF LIFE IN PRIMARY OPEN-ANGLE GLAUCOMA PATIENTS

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SUMMARY – The purpose of this research was to evaluate the relationship between general health-related quality of life (GHRQL) and sociodemographic factors in primary open-angle glaucoma (POAG) patients. A prospective cross-sectional study included 207 glaucoma patients. GHRQL was determined *via* two self-administered questionnaires: the 36-Item Short Form Survey (SF-36) and the EuroQol-5D (EQ-5D) questionnaire. Male and 50- to 69-year-old glaucoma patients, followed by patients who regularly used antiglaucoma therapy and those without progression of glaucoma reported a significantly higher quality of life as measured by the EQ-5D index and the EQ-5D visual analog scale (VAS) ($p < 0.05$ all). Similarly, the Physical Component Summary (PCS) and Mental Component Summary (MCS) of SF-36 had significantly higher values for these patients ($p < 0.05$ all). Furthermore, glaucoma patients with higher education and economic status, glaucoma patients who lived in rural areas, and those who were married achieved higher scores on EQ-5D and SF-36. In conclusion, progression of the disease, female sex, older age, lower education and economic status, urban area and unmarried status negatively affect quality of life in glaucoma patients.

Key words: *Glaucoma; Health-related quality of life; Sociodemographic factors*

Introduction

Glaucoma with a prevalence of around 2% in persons older than 40 years is the second most common cause of blindness worldwide. It has a significant impact on the economy and healthcare system due to the increased treatment expenses and incidence of disability¹⁻³. It is estimated that primary open-angle glaucoma (POAG) as the most common form of the disease will affect approximately 80 million individuals by 2020 and over 110 million people by 2040^{4,5}. Since glaucoma can influence general health-related quality of life (GHRQL) and vision-related quality of life (VRQL) *via* mode of treatment and as a result of visual impairment, determination of the general health

status and visual status of these patients can be of great significance^{6,7}. A combination of sociodemographic indicators, clinical examination and questionnaires that measure quality of life enables clinicians to better estimate the influence of glaucoma seriousness on the patient quality of life. This can help achieve better patient education and compliance, as well as helping select optimal treatment⁸. Loss of vision negatively affects the patient quality of life and psychosocial status, and *vice versa*, patients with lower psychosocial status and poorer quality of life show poorer outcomes of glaucoma treatment. Despite the significant progress achieved in recent years, insufficient compliance of patients with respect to their physicians or prescribed therapies is a significant limiting factor in the treatment of glaucoma⁹⁻¹². There are many difficulties regarding patient compliance, such as long-term treatment, environmental factors, difficulties in drug use, forgetfulness, lack of discipline, lack of understanding that glaucoma is a serious illness, poor communication

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Received October 22, 2020, accepted November 29, 2020

with the doctor, high prices and side effects of ocular medicines, etc.¹³⁻¹⁵. Thus, improvements in communication between patients and ophthalmologists and better understanding of the nature of POAG may considerably increase regularity of taking antiglaucoma medications^{16,17}.

Surveys conducted in India and Spain showed that poorer economic status, lower education level, female sex and older age contributed directly to poorer quality of life in glaucoma patients^{18,19}. Buys *et al.* and Jones *et al.* showed that socioeconomic deprivation and visual field (VF) worsening were associated with greater severity of glaucoma at presentation and a decline in VRQL^{20,21}. It has been shown that quality of life is negatively associated with the frequency of depression and anxiety, especially in female and unmarried patients with POAG²². Labiris *et al.* showed that urban residence was associated with a tendency towards beneficial effects on the 'Distant activities' and 'Social functioning' subscales of the vision-specific quality of life measure²³. To our knowledge, no published data are available regarding the impact of glaucoma on the quality of life of people living in Bosnia and Herzegovina.

Considering the above-mentioned issues, our research was conducted with the aim of determining the relationship between subjective estimation of the health condition of POAG patients and disease progression and sociodemographic factors.

Patients and Methods

Patients

A prospective, cross-sectional study was conducted at the Department of Ophthalmology, Mostar University Hospital, Mostar, Bosnia and Herzegovina, between June 2018 and June 2020. A total of 207 patients with POAG were included in the study. The inclusion criteria were as follows: diagnosis of POAG (increased intraocular pressure (>21 mm Hg), typical glaucomatous defects in VF, optic disk lesions and open angle of anterior chamber), patients over 50 years of age, existence of glaucomatous defects in VF up to 12 dB (mean defect (MD) <12 dB) and cataract up to C2NC2P2 level, since higher opacity in the lens significantly decreased visual acuity and contributed to VF defects. Patients were excluded from the study if they presented any of the following: surgical and/or laser procedures

on an eye, all types of glaucoma except for POAG, cataract of higher level than C2NC2P2, corneal and retinal pathology that significantly reduced visual acuity, and advanced stage of glaucoma (MD >12 dB). Patients who met the inclusion criteria were interviewed and gave written informed consent prior to participation in the study. All procedures and examinations were approved by the Ethics Committee of the Mostar University Hospital. The study was conducted in compliance with the Declaration of Helsinki.

Clinical evaluation

All participants underwent a standard ophthalmologic examination that included uncorrected and best-corrected visual acuity, applanation tonometry, pachymetry, gonioscopy, slit lamp inspection, and dilated fundus examination. VF defects were detected by static perimetry with an Octopus 900 PRO device (Haag-Streit, Koeniz, Switzerland) using G TOP/White/White standard program. Images were analyzed using the MD and pattern standard deviation (PSD) parameters of VF defects. Measurements of cup-disk ratio and peripapillary retinal nerve fiber layer (RNFL) thickness were performed using a Cirrus spectral-domain, high-definition optical coherence tomography device (OCT, Carl Zeiss Meditec Inc., Dublin, CA, USA). The patients included in the research were invited for follow-up examinations at 6, 12 and 18 months after initial ophthalmologic examination. Every check-up included complete ophthalmologic examination, VF recording and OCT of the optic nerve, and peripapillary RNFL. After final follow-up examination at 18 months, patients were divided into two groups of patients with and without POAG progression according to the criteria for glaucoma progression established by Hodapp *et al.*²⁴.

Instruments used on data collection

All respondents filled out three questionnaires, i.e. general questionnaire on sociodemographic data (sex, age, educational level, personal income, place of residence and marital status) and two questionnaires measuring GHRQL: the 36-Item Short Form Survey (SF-36) and the EuroQol-5D (EQ-5D) questionnaire. SF-36 is a set of generic, coherent and easily administered quality of life measures which rely upon patient self-reporting and are now widely utilized for

routine monitoring and assessment of care outcomes in adult patients. It is a short form survey of the Medical Outcomes Study, consisting of 36 questions. After completing this questionnaire, an eight-domain profile of functional health and benefit scores, as well as summarized measures of physical and mental health and a usefulness index based on health priorities, were created. Each domain included between 2 and 10 questions and each question had between 2 and 6 possible answers. The domains of physical functioning, restrictions due to physical health, bodily pain and general health created a summary scale measuring the Physical Component Summary (PCS), while the domains of vitality, social functioning, restrictions due to emotional problems and mental health created a summary scale measuring the Mental Component Summary (MCS).

The EQ-5D is a generic multidimensional questionnaire composed of two parts: the EQ-5D descriptive system (index) and the EQ-5D visual analog scale (EQ-5D VAS). Five dimensions were considered: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and severe problems. Each answer was converted to a single-digit number and the digits for each dimension were combined into a five-digit number describing the patient health state. This five-digit number was then elaborated using a unified scoring algorithm. The EQ-VAS cards measured self-reported general health status using a vertical thermometer-analog scale where the endpoints are labeled 'best imaginable health state' and 'worst imaginable health state'.

With regard to the level of education, the respondents were divided into two groups by applying the International Standard Classification of Education (ISCED) 2011, the standard framework used to categorize and report cross-nationally comparable education statistics. Patients categorized as 'lower education' were those who had ISCED level 0 – early childhood education, ISCED level 1 – primary education and ISCED level 2 – lower secondary education. Patients categorized as 'higher education' were those who had ISCED level 3 – upper secondary education, ISCED level 4 – post-secondary non-tertiary education and ISCED levels 5-8, which describe various levels of tertiary (academic) education. The average personal annual income in Bosnia and Herzegovina for the years

2018 and 2019 was approximately 8,860.00 BAM (~5,000.00 USD).

Statistical analysis

Descriptive statistical methods were used for description of the frequency distribution for all variables analyzed. Continuous variables were expressed as mean \pm standard deviation, while the values of categorical variables were expressed as N (%). Student's t-test was used to compare continuous variables between groups. Logistic regression analysis was used to determine predictors of glaucoma progression. The odds ratios, confidence intervals and levels of significance were examined to evaluate the individual predictor variables. The level of statistical significance was set at $p < 0.05$. Analyses were carried out using SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 207 respondents met the criteria for inclusion in the study, of which 80 (38.6%) were men and 127 (61.4%) were women. The mean age of patients with POAG was 68.52 ± 9.10 years, ranging from 50 to 89 years. The SF-36 and EQ-5D instruments were used, where a higher score indicated higher quality of life for all described domains/scales of SF-36 and EQ-5D questionnaires.

Table 1 shows the EQ-5D-determined quality of life for patients with POAG with respect to sex, age, regularity of using antiglaucoma eyedrops, progression of disease, education level, economic status, area of living and marital status. From these results, it is clear that male and patients aged 50-69 years had a significantly higher quality of life, followed by patients who regularly used antiglaucoma therapy and those without progression of glaucoma, as measured by the EQ-5D index and EQ-5D VAS ($p < 0.05$ all). Furthermore, glaucoma patients with a higher educational level and economic status, patients who lived in rural areas and those who were married achieved higher scores on EQ-5D. The difference was statistically significant for 'Personal income' as measured by the EQ-5D index ($p = 0.003$) and EQ-5D VAS ($p = 0.001$).

Table 2 shows the SF-36-determined quality of life for patients with POAG with respect to sex, age, regularity of using antiglaucoma eyedrops, progression of

Table 1. Quality of life in patients with POAG measured with EQ-5D

Variable	n	EQ-5D index	t-test	p	EQ-5D VAS	t-test	p
Sex							
Male	80	0.57±0.28	2.237	0.026	60.88±17.27	2.750	0.006
Female	127	0.50±0.27			56.04±16.60		
Age (yrs)							
50-69	104	0.57±0.27	3.357	0.001	61.44±16.87	4.711	0.001
≥70	103	0.47±0.26			53.78±16.17		
Topical AG therapy							
Regular	141	0.54±0.27	2.797	0.005	58.91±16.54	3.405	0.001
Non-regular	66	0.44±0.26			51.52±17.65		
Progression of disease							
Yes	63	0.45±0.15	3.625	<0.001	53.56±18.16	2.989	0.002
No	144	0.60±0.28			60.47±13.68		
Education							
Lower qualification	135	0.52±0.22	1.220	0.223	57.36±16.48	0.796	0.130
Higher qualification	72	0.57±0.27			60.00±20.71		
Personal income							
<5,000 USD	107	0.48±0.26	2.966	0.003	54.67±16.23	3.772	0.001
≥5,000 USD	100	0.56±0.25			60.80±17.17		
Area							
Urban	130	0.51±0.25	1.390	0.165	57.00±17.00	1.631	0.104
Rural	77	0.56±0.26			60.54±16.54		
Marital status							
Married	124	0.54±0.27	1.349	0.178	59.51±17.90	1.582	0.112
Unmarried	83	0.50±0.27			56.81±15.04		

POAG = primary open-angle glaucoma; EQ-5D = EuroQol-5D; n = number of patients; VAS = visual analog scale; AG = antiglaucoma

disease, education level, economic status, area of living and marital status. The PCS and MCS scales of SF-36 showed significantly higher scores in male and patients aged 50-69 years than in patients who regularly used antiglaucoma therapy and those without progression of glaucoma ($p < 0.05$ all). Furthermore, glaucoma patients with a higher educational level and economic status, patients who lived in rural areas and those who were married achieved higher scores on the PCS and MCS scales of SF-36. Statistical significance was achieved for 'Area' on the MCS scale ($p = 0.004$) and for 'Marital status' on the MCS scale ($p = 0.003$).

Predictive factors for glaucoma progression are shown in Table 3. Considering all domains/scales of EQ-5D and SF-36, as well as all sociodemographic factors, the 'Social functioning' domain of SF-36 was

found to be the only significant predictive factor for progression of POAG (OR=0.953; $p < 0.001$).

Discussion

Glaucoma influences daily living both through visual impairment and as a result of the glaucoma treatment itself. Quality of life is a measure that is hard for medical experts to quantify but is very important for patients. In glaucoma patients, it is necessary to be familiar with perceptions of personal health and disabilities in everyday activities^{6,12}. Since glaucoma does not only affect vision-related daily functions, we used the SF-36 and EQ-5D questionnaires in our research, as these are the most commonly used instruments for the assessment of GHRQL^{6,7}.

Table 2. Quality of life in patients with POAG measured with SF-36

Variable	n	SF-36 PCS	t-test	p	SF-36 MCS	t-test	p
Sex							
Male	80	40.96±9.65	2.968	0.003	42.79±10.69	2.979	0.003
Female	127	38.04±8.81			39.59±9.49		
Age (yrs)							
50-69	104	39.97±8.11	3.243	0.002	41.74±9.13	3.586	<0.001
≥70	103	35.75±8.43			36.12±8.72		
Topical AG therapy							
Regular	141	39.62±9.20	3.142	0.002	41.43±9.90	3.658	<0.001
Non-regular	66	35.79±8.37			36.61±9.47		
Progression of disease							
Yes	63	36.59±9.29	3.415	0.001	38.22±10.12	3.146	0.002
No	144	39.99±8.95			41.64±9.77		
Education							
Lower qualification	135	38.77±9.00	1.103	0.276	39.86±12.17	0.406	0.287
Higher qualification	72	40.74±10.60			40.68±9.73		
Personal income							
<5,000 USD	107	38.05±8.40	1.127	0.225	40.09±9.46	1.043	0.298
≥5,000 USD	100	39.91±9.84			41.14±10.50		
Area							
Urban	130	38.90±9.25	0.263	0.293	39.98±10.15	2.908	0.004
Rural	77	39.22±8.87			43.39±8.71		
Marital status							
Married	124	39.38±9.93	1.119	0.264	41.86±9.74	2.993	0.003
Unmarried	83	38.37±7.96			38.82±10.08		

POAG = primary open-angle glaucoma; SF-36 = 36-Item Short Form Survey; n = number of patients; PCS = Physical Component Summary; MCS = Mental Component Summary; AG = antiglaucoma

The results of our study showed that male patients with POAG had a significantly higher quality of life than female patients with POAG. These results mostly correlate with the results of numerous studies undertaken worldwide^{19,23}. The data can be interpreted as indicating that females in the general population have a slightly poorer quality of life than males in all age groups. In addition, respondents aged 50-69 years had a significantly higher quality of life than patients older than 70 years. This finding was confirmed by other studies, as well as by the fact that age has been negatively correlated with quality of life in the general population^{25,26}.

Patients who regularly used antiglaucoma therapy achieved significantly higher scores on the EQ-5D and SF-36 questionnaires. The results of studies in

France, China, USA and Brazil showed that the main factors influencing poor compliance between doctors and patients and irregular use of antiglaucoma drugs were insufficient information given to patients about the nature of glaucoma disease, problems in understanding and in communication with a doctor, problems with application of the eyedrops, and high prices and side effects of ocular medicines^{13-15,27}. All these factors essentially disrupt the quality of life in glaucoma patients, and therefore improvement in communication between physicians and patients, as well as improved patient knowledge about the course of the disease may significantly increase the regularity of taking antiglaucoma medicines^{16,17}. Furthermore, development of new antiglaucoma eyedrops (such as analogs of prostaglandins and fixed combinations) that de-

Table 3. Predictive factors for glaucoma progression

Variable	Odds ratio	df	p
Mobility	3.670	1	0.055
Self-care	0.147	1	0.702
Usual activities	0.389	1	0.533
Pain/discomfort	0.211	1	0.646
Anxiety/depression	1.337	1	0.248
EQ-5D index	3.276	1	0.070
EQ-5D visual analog scale	1.120	1	0.290
Physical functioning	0.201	1	0.654
Restrictions due to physical health	0.029	1	0.865
Bodily pain	0.789	1	0.374
General health	0.065	1	0.799
Vitality	0.228	1	0.633
Social functioning	0.953	1	<0.001
Restrictions due to emotional problems	0.118	1	0.731
Mental health	0.029	1	0.864
Physical Component Summary	0.352	1	0.553
Mental Component Summary	0.001	1	0.975
Sex	3.162	1	0.075
Age	3.235	1	0.072
Education level	0.604	1	0.437
Personal income	0.044	1	0.834
Area	0.889	1	0.346
Marital status	1.172	1	0.279
Overall statistics	16.198	23	0.843

EQ-5D = EuroQol-5D

crease the number of drippings *per day* could certainly contribute to better patient compliance with the advice of ophthalmologists. However, the problem of the high price of new medicines still remains²⁸.

Our results revealed that patients with glaucoma progression had a significantly lower level of physical and mental health than patients without disease deterioration. In 2005, Lin and Yang conducted a cross-sectional research among 280 glaucoma patients using SF-36 and the National Eye Institute Visual Functioning Questionnaire-25 (NEIVFQ-25). The scores obtained by these questionnaires showed that progression of glaucoma negatively correlated with quality of

life⁸. Wilson *et al.* also report that worsening of glaucoma is a strong predictor of lower SF-36 scores²⁹. According to literature data, the association between VF loss and deterioration of VRQL is largely linear. This means that VRQL declines at a constant rate as the VF worsens^{30,31}. In fact, Jones *et al.* report that the association between VRQL decline and VF worsening is more likely to be described as monotonic. In other words, the relationship could have both slow and rapid stages, or even remain relatively constant for a time²¹. Some studies showed better correlation between VF worsening and VRQL decline obtained by using vision-specific questionnaires such as NEIVFQ-25, Glaucoma Quality of Life-15 (GQL-15) and Visual Function Index (VF-14). This can be explained by the assumption that specific questionnaires for eye diseases correlate more strongly with early VF changes in comparison to instruments that measure GHRQL^{7,32,33}.

The results of this research showed that glaucoma patients with a higher educational level and economic status achieved higher scores as measured by the EQ-5D index and EQ-5D VAS, as well as by the PSC and MCS scales of the SF-36 instrument. The results of other studies confirm that educational level is an important factor that significantly influences and positively correlates with quality of life^{23,25,34,35}. Kharicha *et al.* report that lower educational status and aging significantly contribute to poorer patient compliance with physicians' advice, and therefore negatively influence quality of life³⁶. Most studies have shown positive correlation between socioeconomic status and quality of life in glaucoma patients^{16,23,25,34}. Low socioeconomic status is associated with late diagnosis and more severe POAG at presentation. Indeed, socioeconomically deprived groups have demonstrated a higher need for information on the practical aspects of POAG, such as ocular medication usage, social support for visually-impaired individuals, irreversibility of optic nerve damage, and seriousness of glaucoma existence within the family³⁷. Patients with higher levels of education and higher incomes are in better position to use modern and more expensive antiglaucoma medications, and show a tendency to do so³⁴.

Our results showed that patients with POAG who lived in rural areas achieved higher scores in EQ-5D and SF-36. A significant difference was observed only for the MCS scale. Vijaya *et al.* report a higher prevalence of POAG in urban population compared to rural

population, which could be caused by the possible influence of lifestyle differences and a higher prevalence of systemic diseases such as hypertension and diabetes in the urban population³⁸. This could explain the relatively higher quality of life of people living in rural areas. Contrary to our results, Labiris *et al.* report higher values for some aspects of VRQL in urban populations²³. We showed that glaucoma patients who were married scored higher on the EQ-5D and SF-36 instruments in comparison to unmarried patients with POAG. It was shown that older people living alone were more likely to report poor health, poor vision, difficulties with instrumental and basic activities of daily living, worse memory and mood, lower physical activity, risk of social isolation, etc.³⁶. All these factors may contribute significantly to poorer GHRQL. In 2005, a study conducted in Japan on 600 men and 2,587 women aged >65 showed that health status positively correlated with visual function, physical mobility, lack of depression and social integration³⁹. Studies have shown that bilateral VF defects and depressive symptoms were more prevalent in glaucoma patients with impaired VRQL^{40,41}. It was found that visual function and ganglion cell-inner plexiform layer thickness were decreased in depressive patients⁴². Furthermore, Jayawant *et al.* found the presence of depressive symptoms to negatively affect the regularity of taking antiglaucoma therapy and to increase the cost of glaucoma treatment⁴³.

In conclusion, progression of the disease and predisposing sociodemographic factors such as female sex, older age, lower education and economic status, urban area and unmarried status negatively affect quality of life in glaucoma patients.

Acknowledgments

Permission to use the EQ-5D questionnaire in our survey was obtained from the Executive Office of the EuroQol Organization (EuroQol Group, Rotterdam, The Netherlands), by courtesy of Mrs. Mandy Oemar and Mrs. Rosalind Rabin. Free use and translation of the SF-36 questionnaire into the Croatian language was enabled by the RAND Health Corporation (Santa Monica, California, USA).

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Sažetak

KVALITETA ŽIVOTA POVEZANA SA ZDRAVLJEM U BOLESNIKA S PRIMARNIM GLAUKOMOM OTVORENOG KUTA

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Svrha ovoga istraživanja bila je utvrditi odnos između kvalitete života povezane s općim zdravljem (GHRQL) i sociodemografskih čimbenika u bolesnika s primarnim glaukomom otvorenog kuta (POAG). Riječ je o presječnoj studiji u kojoj je sudjelovalo 207 bolesnika s POAG. GHRQL mjerena je pomoću dva upitnika: kratkog upitnika zdravstvenog statusa s 36 pitanja (SF-36) i upitnika EuroQol-5D (EQ-5D). Muškarci i bolesnici s glaukomom u dobi od 50-69 godina, zatim bolesnici koji su redovito koristili antiglaukomsku terapiju i oni bez progresije glaukoma izvijestili su o znatno višoj kvaliteti života mjerenoj indeksom EQ-5D i vizualnom analognom ljestvicom EQ-5D (VAS) ($p < 0,05$ za sve usporedbe). Slično tome, Sažetak fizičkih komponenata (PCS) i Sažetak mentalnih komponenata (MCS) upitnika SF-36 imali su značajno veće vrijednosti za ove bolesnike ($p < 0,05$ za sve usporedbe). Nadalje, ispitanici s visokim stupnjem obrazovanja i ekonomskim statusom, ispitanici koji žive u ruralnim područjima i oni koji su u braku postigli su veće rezultate na EQ-5D i SF-36. Zaključno, napredovanje bolesti, ženski spol, starija životna dob, niži stupanj obrazovanja i ekonomski status, urbano područje življenja i samoća negativno utječu na kvalitetu života bolesnika s glaukomom.

Ključne riječi: *Glaukom; Kvaliteta života povezana sa zdravljem; Sociodemografski čimbenici*