

Suicide risk in juvenile open angle glaucoma patients

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Abstract

• **AIM:** To investigate the association between juvenile open angle glaucoma (JOAG) and mental health among Koreans.

• **METHODS:** This study used nationally representative data from the 8th Korea National Health and Nutrition Examination Survey (KNHANES) 2021. Glaucoma diagnosis followed the International Society of Geographical and Epidemiological Ophthalmology criteria based on glaucomatous structural defects, visual field defects, corrected vision, and intraocular pressure. As outcomes, suicidal behaviors, psychiatric counseling, and depression were evaluated through mental health questionnaires. Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated using logistic regression models, adjusting for covariates.

• **RESULTS:** Among 7090 participants, 3446 met the inclusion criteria for analysis, and 88 (2.6%) were diagnosed with open angle glaucoma (OAG). After adjusting for age, sex, and best-corrected visual acuity (VA), participants with OAG were revealed to have significantly higher odds of suicidal behaviors (*i.e.*, ideation, planning, or attempts) compared with those without OAG (OR: 2.70; 95%CI: 1.12-6.54; $P=0.028$). This association remained significant after further adjustments for socioeconomic status, lifestyle

factors, and presence of chronic conditions ($P=0.031$ and 0.035 , respectively). However, there was no significant difference for the other two outcomes, psychiatric counseling and depression. An age-stratified analysis revealed a stronger association between OAG and suicidal behaviors in younger JOAG participants (<40y) than in older OAG participants ($\geq 40y$; OR: 3.80 vs 2.22; 95%CI: 0.79-18.22 vs 0.56-8.80, respectively).

• **CONCLUSION:** OAG patients show a higher risk of suicidal behaviors than those without glaucoma particularly in JOAG patients.

• **KEYWORDS:** glaucoma; juvenile open angle glaucoma; suicide; suicidal behavior

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INTRODUCTION

Glaucoma is one of the leading causes of blindness^[1-2]. Although it is commonly found in elderly patients, adolescents and young adults may also be diagnosed with juvenile open angle glaucoma (JOAG). The estimated prevalence of JOAG varies in different populations, ranging from 0.002% to 3.4%^[3]. Being a disease of childhood and young adults, the management of JOAG is important for maintenance of quality of life and socially productive status.

Previous studies have reported negative impacts on quality of life for juveniles diagnosed with glaucoma^[4-5]. Diminished quality of life can be associated with various mental illnesses, such as depression, anxiety, or suicidal ideation. It is important to evaluate the mental health of glaucoma patients and initiate any necessary treatment, as it can affect treatment compliance and mortality. And since poor compliance results in glaucoma progression, especially in younger patients who have longer life expectancy, earlier psychological evaluation and intervention may be essential to their care.

In a previous study, older patients with open angle glaucoma (OAG) showed a higher prevalence of depression than those without glaucoma^[4]. Also, a recent study reported that a higher rate of suicide death among glaucoma patients aged 40 to 65 compared with those aged 65 years and older^[5]. However, the mental health of younger glaucoma patients remains to

be elucidated. A former study reported that young patients aged under 30 showed higher risk of depression among high myopia patients^[6]. This suggests a potential vulnerability to psychological health issues among younger patients with chronic ocular conditions. In this context, we investigated the associations between JOAG and mental health among Koreans, as well as whether such associations differ by age, using data from the Korea National Health and Nutrition Examination Survey (KNHANES) 2021.

SUBJECTS AND METHODS

Ethical Approval The study protocols of KNHANES 2021 were approved by the Institutional Review Board of the Korea Disease Control and Prevention Agency (2018-01-03-5C-A). Prior to participating in the KNHANES, all of the participants provided written informed consent, and all of the survey data were anonymized before being analyzed.

Study Population The KNHANES is an ongoing, cross-sectional, and nationally representative survey conducted by the Korea Disease Control and Prevention Agency to monitor the health and nutritional status of the non-institutionalized population in Korea. A complex and multistage probability sampling design is used to select a representative sample of the Korean population. KNHANES data collection includes a health interview, health examinations, and nutrition surveys. KNHANES details are available at <https://knhanes.kdca.go.kr/knhanes/main.do>.

Assessment of Open Angle Glaucoma

Ophthalmological examinations Participants aged 10 to 59y underwent ophthalmological examinations by trained ophthalmologists. The examinations included visual acuity (VA), autorefractometry, intraocular pressure (IOP) measurement, visual field (VF) testing, axial length measurement, non-mydratric fundus photography, and optical coherence tomography^[7].

VA was measured from a distance of 4 m using an international standard vision chart that follows the Snellen scale (Jin's vision chart; JV Institute, Seoul, Korea). For those who had a VA score lower than 0.8, the best-corrected VA was determined through full subjective refraction using autorefractometry (KR8800; Topcon, Tokyo, Japan). The best-corrected VA was classified into four categories: 0.8 to 1.0, 0.5 to 0.63, 0.25 to 0.4, and no light perception to 0.2. The IOP was measured in a sitting position using rebound tonometry (Icare PRO; Icare Finland Oy, Helsinki, Finland).

Participants who showed increased IOP (≥ 22 mm Hg) or a glaucomatous optic disc (e.g., a horizontal or vertical cup-to-disc ratio (CDR) ≥ 0.5 , the presence of retinal nerve fiber layer (RNFL) defect, the presence of optic disc hemorrhage, or a violation of the ISNT rule (neuroretinal rim width in order of inferior>superior>nasal>temporal) underwent frequency-

doubling technology (FDT, Humphrey Matrix; Carl Zeiss Meditec, Inc., Dublin, CA, USA).

Definition of Open Angle Glaucoma Glaucoma was categorized based on the International Society of Geographical and Epidemiological Ophthalmology criteria^[8]. Category 1 requires both a glaucomatous structural defect and a glaucomatous VF defect. For this category, glaucomatous structural defect is defined as at least one of the following: neuroretinal rim notching or thinning, vertical CDR ≥ 0.7 , asymmetrical CDR ≥ 0.2 , presence of RNFL defect, or presence of optic disc hemorrhage. For this same category, glaucomatous VF defect is defined as the presence of at least one location of reduced sensitivity (corresponding to optic disc or RNFL abnormality) with no fixation error and false-positive error ≤ 1 .

Category 2 applies in cases where there is a definite glaucomatous structural defect but no available reliable VF test. For this category, glaucomatous structural defect is defined as at least one of the following: vertical CDR ≥ 0.9 with neuroretinal rim notching or thinning, asymmetrical CDR ≥ 0.3 , or presence of RNFL defect with ISNT rule violation^[9].

Category 3 applies in cases where there is no optic disc data or available VF test results. For this category, glaucoma is defined as corrected VA < 0.05 and IOP ≥ 23 mm Hg (IOP ≥ 97.5 percentile).

Assessment of Mental Health Suicidal behaviors were defined as an affirmative answer to any questions on suicidal ideation, planning, or attempts occurring during the past year. These indicators are well-documented predictors of suicide risk used in previous surveys^[10]. Psychiatric counseling was defined as an affirmative answer to the question on an experience of any type of psychiatric counseling due to mental health issues. Depression was defined as one of the following conditions: 1) self-report of physician diagnosis and currently being depressed or 2) self-report of depressive symptoms lasting at least two weeks during the past year. All of the aforementioned mental health variables (i.e., suicidal ideation, planning, attempts, psychiatric counselling, and depression) were assessed in a yes/no format in the KNHANES survey, as demonstrated in detail in the associated previous KNHANES study^[11].

Assessment of Covariates

Sociodemographic factors Demographic covariates included age (y) and sex (male or female). Socioeconomic covariates included residential area (urban or rural), education level ($<$ high school graduate or \geq high school graduate), monthly household income (quartiles of equalized household income), and marital status (married or not).

Lifestyle, anthropometric, and disease-history factors We defined current smoking as current smoking of cigarettes every

day or some days; current drinking as drinking of alcoholic beverages at least once or more in the past 12mo; walking exercise as walking for at least 30min per session for more than 5d per week, and weight training as muscular exercise for more than 2d per week, respectively.

Participants' standing height (cm), body weight (kg), and waist circumference (cm) were measured by trained examiners using standardized examination procedures and calibrated equipment, with participants in light clothing. Body mass index was computed as the ratio of measured weight to standing height squared (kg/m^2).

The presence of hypertension was defined as either of the following: 1) currently taking prescribed hypertension medicine; 2) systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg^[12]. The presence of diabetes was defined as at least one of the following: 1) physician diagnosis; 2) currently taking diabetes medication, including insulin; 3) fasting plasma glucose at or above 126 mg/dL^[13]. The presence of metabolic syndrome was defined as at least three of the following based on the criteria of the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III): 1) waist circumference of ≥ 90 cm for males or ≥ 85 cm for females^[14]; 2) systolic blood pressure of ≥ 130 mm Hg and diastolic blood pressure of ≥ 85 mm Hg; 3) fasting plasma glucose level of ≥ 100 mg/dL or current use of diabetes medication; 4) serum triglyceride level of ≥ 150 mg/dL or current treatment for this lipid abnormality; 5) serum high-density lipoprotein (HDL) cholesterol level of < 40 mg/dL for males or < 50 mg/dL for females or current treatment for this lipid abnormality.

Statistical Analysis All of the statistical analyses incorporated survey weights accounting for the complex sampling design of the KNHANES using the PROC SURVEY procedures in SAS 9.4 software (SAS Institute Inc., Cary, NC, USA). We presented the baseline characteristics of the total study population and between the glaucoma groups as the means and their standard errors (SEs) for continuous variables and as the prevalence and their SEs for categorical variables. The statistical significance of differences in glaucoma presence was determined using the student *t*-test for continuous variables and the Rao-Scott χ^2 test for categorical variables.

Multivariable logistic regression models were used to examine the association between glaucoma presence and mental health, with covariate-adjusted odds ratios (ORs) and 95% confidence intervals (CIs). We ran three different multivariable models: 1) age-, sex- and best-corrected VA-adjusted; 2) additionally adjusted for residential area, education, household income, marriage, smoking, drinking, and exercise; 3) additionally adjusted for disease history. We further performed stratified analyses for associations between glaucoma and mental health

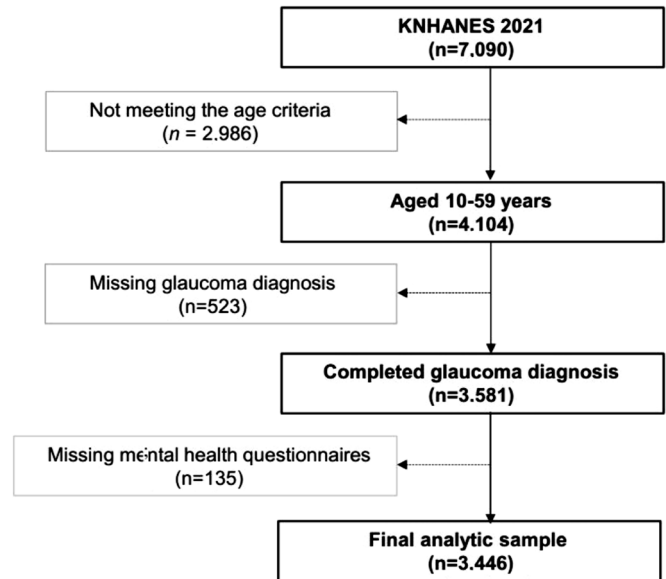


Figure 1 Study participant flow chart, Korea National Health and Nutrition Examination Survey (KNHANES), 2021.

outcomes by age (< 40 or ≥ 40 y). All of the tests were two-sided, with the level of significance set at 0.05.

RESULTS

Among the 7090 participants in the 8th KNHANES 2021, we excluded participants if they had any of the following conditions: 1) not meeting the age criteria for ophthalmological examinations (< 10 or ≥ 60 y; $n=2986$); 2) missing glaucoma diagnosis ($n=523$); 3) missing mental health questionnaires ($n=135$). Ultimately, 3446 participants (1550 males and 1896 females) were included in this study (Figure 1).

The participants diagnosed with glaucoma accounted for 2.6% (88 of 3446 participants). Their mean \pm SE age was 45.5 \pm 1.2y, which was older than that of those without glaucoma (37.6y; Table 1). They were more likely to be older, male, married, to smoke, drink alcohol, and have higher body mass index, waist circumference, hypertension, diabetes, and metabolic syndrome than were those without glaucoma (all $P<0.05$).

Table 2 presents the associations between glaucoma and mental health outcomes. After adjusting for age, sex, and best-corrected VA, participants with glaucoma had 2.7-times-greater odds of having any suicidal behaviors relative to those without glaucoma (OR, 2.70; 95%CI, 1.12–6.54; $P=0.028$). These associations remained significant after further adjustment for socioeconomic factors, lifestyle, and presence of chronic conditions ($P=0.031$ in model 2; $P=0.035$ in model 3). The participants with glaucoma had greater odds of having any type of depression or psychiatric counseling relative to those without glaucoma; however, the difference did not reach statistical significance in any of the multivariable-adjusted models. Table 3 shows the age-stratified associations between glaucoma and mental health outcomes (age groups: < 40 and ≥ 40). Although significance was marginal due to the limited

Table 1 Demographic and lifestyle characteristics of study participants (n=3446)

Parameters	Overall (n=3446)	No glaucoma (n=3358)	Glaucoma (n=88)	P ^a
Demographic				
Age, y	37.8 (0.3)	37.6 (0.3)	45.5 (1.2)	<0.0001
Female	1896 (48.7)	1861 (49.2)	35 (29.3)	0.001
Urban resident	2873 (87.2)	2798 (87.1)	75 (91.1)	0.258
Socioeconomic				
Education, high school graduate and higher	2840 (86.2)	2764 (86.1)	76 (89.1)	0.497
Household income, quartile 3+	978 (27.7)	948 (27.6)	30 (32.1)	0.407
Married	2116 (58.4)	2046 (57.9)	70 (77.0)	0.003
Lifestyle				
Current smoking	592 (20.9)	563 (20.5)	29 (36.6)	0.002
Current drinking	2487 (74.8)	2412 (74.5)	75 (85.2)	0.039
Walking exercise ^b	1161 (38.4)	1124 (38.2)	37 (44.7)	0.297
Weight training ^c	816 (25.6)	800 (25.7)	16 (19.7)	0.276
Comorbid conditions				
Body mass index, kg/m ²	23.9 (0.1)	23.9 (0.1)	24.9 (0.3)	0.004
Waist circumference, cm	82.0 (0.3)	81.9 (0.3)	86.9 (1.0)	<0.0001
Hypertension	524 (16.7)	495 (16.3)	29 (31.5)	<0.0001
Diabetes	250 (7.4)	232 (7.1)	18 (20.7)	<0.0001
Metabolic syndrome	673 (20.7)	639 (20.2)	34 (42.7)	<0.0001
Best-corrected visual acuity				
0.8–1.0	2705 (79.8)	2639 (79.9)	66 (76.3)	0.696
0.5–0.63	331 (9.4)	321 (9.4)	10 (10.0)	
0.25–0.4	256 (7.7)	248 (7.6)	8 (11.2)	
No light perception to 0.2	100 (3.1)	98 (3.1)	2 (2.4)	

All results are weighted and presented as mean (standard error) for continuous variables and as sample size (percentage) for categorical variables. ^aP values for differences by glaucoma group were obtained using t-tests for continuous variables and Rao-Scott Chi-square tests for categorical variables; ^bWalking exercise was defined as walking more than five days per week for at least 30min per session; ^cWeight training was defined as weight training more than two days per week.

Table 2 Weighted odds ratios (95% confidence intervals) for mental health outcomes by glaucoma status, KNHANES 2021 (n=3446)

Parameters	No glaucoma	Glaucoma	P
Suicidal ideation, planning, or attempt			
Multivariable-adjusted model 1 ^a	1.00 (reference)	2.70 (1.12–6.54)	0.028
Multivariable-adjusted model 2 ^b	1.00 (reference)	2.48 (1.09–5.65)	0.031
Multivariable-adjusted model 3 ^c	1.00 (reference)	2.44 (1.06–5.57)	0.035
Psychiatric counseling			
Multivariable-adjusted model 1 ^a	1.00 (reference)	1.74 (0.59–5.15)	0.318
Multivariable-adjusted model 2 ^b	1.00 (reference)	1.53 (0.54–4.35)	0.420
Multivariable-adjusted model 3 ^c	1.00 (reference)	1.55 (0.55–4.42)	0.406
Depression			
Multivariable-adjusted model 1 ^a	1.00 (reference)	1.13 (0.53–2.41)	0.750
Multivariable-adjusted model 2 ^b	1.00 (reference)	1.07 (0.52–2.22)	0.850
Multivariable-adjusted model 3 ^c	1.00 (reference)	1.07 (0.52–2.23)	0.851

^aMultivariable-adjusted model 1 was adjusted for age, sex, and best-corrected visual acuity; ^bMultivariable-adjusted model 2 was additionally adjusted for residential area, education, income, marital status, smoking, drinking, and exercise; ^cMultivariable-adjusted model 3 was additionally adjusted for the presence of hypertension, diabetes, or metabolic syndrome.

prevalence of glaucoma, after adjusting for age, sex, and best-corrected VA, the suggestive positive association between glaucoma and suicidal behaviors was stronger in younger participants aged under 40y than in those aged 40y and older (OR, 3.80; 95%CI, 0.79–18.22 in participants <40y; OR, 2.22; 95%CI, 0.56–8.80 in participants ≥40y). However, the

presence of depression or psychiatric counseling was not associated with glaucoma in either age group (all P>0.05). The results were similar after further adjustment for the other confounders (models 2 and 3).

DISCUSSION

In this study, the rate of suicidal behavior was significantly

Table 3 Weighted odds ratios (95% confidence intervals) for mental health outcomes by glaucoma status, stratified by age

Parameters	<40y (n=1606)			≥40y (n=1840)		
	No glaucoma	Glaucoma	P	No glaucoma	Glaucoma	P
Suicidal ideation, planning, or attempt						
Multivariable-adjusted model 1 ^a	1.00 (reference)	3.80 (0.79–18.22)	0.095	1.00 (reference)	2.22 (0.56–8.80)	0.256
Multivariable-adjusted model 2 ^b	1.00 (reference)	3.50 (0.76–16.20)	0.108	1.00 (reference)	1.88 (0.53–6.72)	0.331
Multivariable-adjusted model 3 ^c	1.00 (reference)	3.36 (0.74–15.26)	0.117	1.00 (reference)	1.89 (0.53–6.77)	0.329
Psychiatric counseling						
Multivariable-adjusted model 1 ^a	1.00 (reference)	1.32 (0.30–5.94)	0.713	1.00 (reference)	1.95 (0.49–7.76)	0.343
Multivariable-adjusted model 2 ^b	1.00 (reference)	1.60 (0.35–7.38)	0.547	1.00 (reference)	1.36 (0.35–5.27)	0.654
Multivariable-adjusted model 3 ^c	1.00 (reference)	1.61 (0.35–7.54)	0.541	1.00 (reference)	1.33 (0.35–5.06)	0.671
Depression						
Multivariable-adjusted model 1 ^a	1.00 (reference)	0.99 (0.17–5.72)	0.987	1.00 (reference)	1.22 (0.48–3.10)	0.668
Multivariable-adjusted model 2 ^b	1.00 (reference)	1.03 (0.19–5.65)	0.976	1.00 (reference)	1.08 (0.44–2.62)	0.867
Multivariable-adjusted model 3 ^c	1.00 (reference)	0.97 (0.18–5.31)	0.976	1.00 (reference)	1.08 (0.45–2.62)	0.858

^aMultivariable-adjusted model 1 was adjusted for age, sex, and best-corrected visual acuity; ^bMultivariable-adjusted model 2 was additionally adjusted for residential area, education, income, marital status, smoking, drinking, and exercise; ^cMultivariable-adjusted model 3 was additionally adjusted for the presence of hypertension, diabetes, or metabolic syndrome.

higher in glaucoma patients aged 10-59y, while there was no significant intergroup difference in psychiatric counseling. As stratified by age, a stronger positive association between glaucoma and suicidal behaviors was observed in younger patients aged 10-39y than in older patients aged 40-59y. This suggests that glaucoma is associated with higher risk of suicide, especially in JOAG patients, compared with relatively older OAG patients.

This is the first study to provide a targeted analysis of comprehensive suicidal behaviors (*i.e.*, ideation, planning, and attempts) possibly leading to treatment discontinuation or mortality in JOAG patients. According to national statistics for the year 2021, the suicide rate in the general population under the age of 40 in Republic of Korea was 20.4 per 100 000 people, while for those aged between 40 and 60, it was 29.2 per 100 000 people in 2021. Rim *et al*^[15] also reported an increasing rate of suicidal ideation and attempts in relation to age. Interestingly, in our study, age-stratified analyses showed that suicidal ideation, planning, and attempts appeared to be higher among glaucoma patients under 40 years of age than among those over 40 years old. This result suggests that JOAG patients might be more vulnerable to experiencing suicidal behaviors than are relatively older OAG adults. Considering the fact that there was no significant difference in psychiatric counseling experience between the young and the old groups, it seems clear that JOAG patients need to be given more attention in terms of mental health.

Previous reports had shown that glaucoma patients had a higher incidence of depression than in the general population^[16-17]. Although several studies had attempted to

elucidate the association between depression and glaucoma, their results were mixed. Studies conducted in China and Singapore found that the risk of depression was significantly increased among glaucoma patients^[17-18], whereas a study conducted in California did not find any statistically significant differences^[19]. Our present study uncovered no significant association of depression with glaucoma in either age group. Note, however, that since it is based on self-reported data on mental health, depression prevalence may have been underestimated. This point should be examined further with additional clinical examination data on depression and glaucoma.

With regard to depression severity, a number of previous studies have shown a correlation with visual impairment^[5,20]. A study conducted in Mexico found that glaucoma severity was associated with increased depression severity as well as medication adherence^[21]. Ha *et al*^[5] previously reported that patients with visual impairment including glaucoma have a higher suicide rate than others among those aged 40y or older in Republic of Korea. However, this study included all causes of visual impairment (*i.e.*, glaucoma, diabetic retinopathy, age-related macular degeneration). Although the present study found no association between depression itself and glaucoma, we can assume, taking into consideration the direct relationship of severe forms of depression with suicidal behaviors, that our results are in line with former studies.

Our study has several limitations. First, although it is based on a nationally representative sample of Koreans, only a small number of participants were included in the final analysis, due to the low incidence of glaucoma, especially in relatively

younger adults. Second, the database lacks clinical information such as disease duration, disease severity, or treatment regimen. This restricts determining whether glaucoma itself is associated with suicidal ideation, planning and attempt, or if it results from visual dysfunction caused by glaucoma progression, or from stressful conditions encountered during the treatment process. A further study with detailed clinical data will be necessary. Third, due to the cross-sectional study design, the causal relationship between suicidal behaviors and glaucoma could not be determined; thus, caution in interpreting the present results is called for. Fourth, unmeasured or unknown factors may have impacted the given associations. For example, studies have shown that anxiety can affect glaucoma progression, as can the use of antidepressants. Therefore, further research is needed^[22-23]. Fifth and finally, this study targeted the Korean population, limiting its generalizability to other study settings.

In conclusion, individuals with OAG had a higher risk of suicidal behaviors than did those without OAG, especially among younger OAG patients. We believe that this study provides important insights into the association between glaucoma and suicide risk. JOAG patients, therefore, should be monitored for their mental health with regard to suicidal behavior, thereby allowing for timely mental health interventions to support JOAG patients at risk.

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