



Profiles and Clinical Characteristics of Newly Diagnosed Glaucoma in Urban Korea: A Multicenter Study

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Purpose: To explore the clinical characteristics and profiles of newly diagnosed glaucoma subtypes in urban Korea.

Methods: All newly diagnosed glaucoma patients enrolled in the participating ophthalmology outpatient clinics were included. A review of medical history including family history of glaucoma was conducted. The patients underwent complete ophthalmologic examinations including visual field test. The diagnosis of glaucoma was based on the International Society of Geographical and Epidemiological Ophthalmology criteria developed by glaucoma specialists.

Results: A total of 198,671 patients visited the participating ophthalmology outpatient clinics during the study period (from January 1, 2001 to June 30, 2016), of which 5,530 (2.8%) were diagnosed with glaucoma. The mean age of the newly diagnosed glaucoma patients was 52.0 ± 17.3 years (range, 6 to 89) and 2,830 patients were male (51.2%). The mean untreated intraocular pressure and vertical cup-to-disc ratio of the optic nerve head of newly diagnosed glaucoma eyes were 22.1 ± 10.6 mmHg and 0.66 ± 0.22 , respectively. The most frequently observed subtypes of glaucoma were: normal tension glaucoma (33.0%) primary open-angle glaucoma (28.4%), ocular hypertension (11.1%), chronic angle-closure glaucoma (6.8%), neovascular glaucoma (5.2%), glaucoma associated with inflammation (3.8%), acute angle-closure glaucoma (3.3%), and glaucoma associated with aphakia or pseudophakia (2.2%).

Conclusions: Normal tension glaucoma was the most frequently observed glaucoma subtype in urban ophthalmology outpatient clinics in Korea.

Key Words: Epidemiology, Glaucoma, Low tension glaucoma, Open-angle glaucoma

Glaucoma is one of the leading causes of blindness worldwide [1-3]. Among the subtypes of glaucoma, primary

open-angle glaucoma (POAG) was the most common type in many population-based studies [4-11]. However, the prevalence of glaucoma and its proportion of subtypes vary by nationality [12-15]. Also, in some studies, the prevalence of subtypes shows regional difference within the same country [16,17].

According to the population-based Namil study, the prevalence of POAG in Korea was 3.59% [18]. When 21

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mmHg was used as the cut-off value, the prevalence of POAG with intraocular pressure (IOP) ≤ 21 mmHg was 2.81% and >21 mmHg was 0.78%. The Namil study was conducted in rural areas, and the prevalence of glaucoma subtypes varies between rural and urban areas. Most Koreans live in cities (81.5% of total population, from Bureau of Korean Statistics). Therefore, knowledge of the subtypes prevalent in the urban areas is important. However, the investigation of the prevalence of glaucoma in urban Korean society proved to be difficult because of the low compliance and participation rates. In fact, several attempts have already failed.

Thus, in this multicenter study, we investigated the profile of newly diagnosed glaucoma subtypes in an outpatient ophthalmology clinic located in an urban area. With the enrollment of 20 major clinics located in urban area, we intended to review the clinical characteristics of main glaucoma subtypes. Most of the university-based ophthalmology outpatient clinics and 41 members of Korean Glaucoma Society participated in this study allowing us to generalize the results.

Materials and Methods

All participating hospitals and ophthalmology outpatient clinics were located in major cities in Korea. From January 1, 2001 to June 30, 2016, all newly diagnosed glaucoma patients visiting those clinics were enrolled. The study protocol was approved by the institutional review board of each university hospital, and subsequent investigations followed the tenets of the Declaration of Helsinki. Informed consent was waived due to retrospective nature of the study design. The newly diagnosed glaucoma patients were interviewed for a medical history that included a family history of glaucoma. Eye examinations were performed including refractive error measurement, standard visual acuity testing with determination of best refractive correction, slit-lamp examination including Van Herick measurement of anterior chamber depth, IOP measurement with Goldmann applanation tonometry, fundus examination including binocular optic disc evaluation, a gonioscopic examination followed by visual field testing (Humphrey Field Analyzer; Carl Zeiss Meditec, Dublin, CA, USA), and structural evaluation using Stratus optical coherence tomography (Carl Zeiss Meditec) and/or scanning laser polarimetry

(GDx Vcc, Carl Zeiss Meditec). Newly diagnosed glaucoma patients were classified according to the International Society of Geographical & Epidemiological Ophthalmology criteria. These classifications are divided into 26 subtypes: ocular hypertension (OHT); POAG; normal tension glaucoma (NTG); acute angle-closure glaucoma (AACG); subacute ACG; chronic angle-closure glaucoma (CACG); plateau iris syndrome; combined-mechanism glaucoma; congenital glaucoma; glaucoma associated with developmental anomaly (Axenfeld-Rieger syndrome, Peter anomaly, aniridia, and Sturge-Weber syndrome); steroid-induced glaucoma; glaucoma associated with corneal endothelial disorders (iridocorneal endothelial syndrome and Fuch's endothelial dystrophy); pigmentary glaucoma; exfoliation (pseudoexfoliation) syndrome; glaucoma associated with cataract; glaucoma associated with lens dislocation; neovascular glaucoma (NVG); glaucoma associated with retinal detachment or vitreoretinal abnormality; glaucoma associated with inflammation (Posner-Schlossman syndrome, uveitis, keratitis, episcleritis, and scleritis); angle-recession glaucoma; glaucoma associated with hemorrhage; ciliary block (malignant) glaucoma; glaucoma in aphakia or pseudophakia; glaucoma associated with corneal surgery; glaucoma associated with vitreoretinal surgery; and others. If both eyes were included, the eye most severely affected in terms of visual field mean deviation was used for classification.

Statistical analysis

Age, sex, involved eye, untreated IOP, family history of glaucoma, presence of diabetes or systemic hypertension, and type of newly diagnosed glaucoma were recorded. All data for newly diagnosed glaucoma patients were collected and analyzed by one designated author (HC). Overlapping patients were excluded. Statistical analysis was performed using PASW Statistics ver. 18.0 (SPSS Inc., Chicago, IL, USA). A *p*-value <0.05 level was considered as significant for all tests.

Results

During the study period, a total of 198,671 patients visited the participating ophthalmology outpatient clinics. Among them, 5,530 (2.8%) were diagnosed with glaucoma

Table 1. Demographics and medical history of newly diagnosed glaucoma patients

Diagnosis	No. of patients	Mean age (yr)	Sex ratio (%)	Family history (%)	Diabetes (%)	Hypertension (%)
Ocular hypertension	612 (11.1%)	42.92 ± 16.51	47.06	6.37	8.50	13.73
Primary open-angle glaucoma	1,572 (28.4%)	52.74 ± 17.25	42.23	5.66	11.90	17.62
Normal-tension glaucoma	1,825 (33.0%)	51.38 ± 15.97	51.45	6.19	9.32	18.79
Acute angle-closure glaucoma	186 (3.4%)	64.28 ± 10.18	75.81	1.65	9.14	23.11
Subacute angle-closure glaucoma	37 (0.7%)	65.00 ± 11.38	75.68	5.41	10.81	37.84
Chronic angle-closure glaucoma	378 (6.8%)	64.88 ± 10.37	68.71	4.69	8.66	23.83
Plateau iris syndrome	2 (0%)	63.00 ± 4.24	50.00	0.00	0.00	0.00
Angle-recession glaucoma	23 (0.4%)	39.13 ± 15.33	13.04	8.70	4.35	8.70
Glaucoma associated with cataract	31(0.6%)	66.61 ± 18.40	54.84	3.23	6.45	16.13
Lens dislocation	10 (0.2%)	55.10 ± 16.50	10.00	0.00	20.00	10.00
Pseudoexfoliation syndrome	41 (0.7%)	66.90 ± 12.67	39.02	4.88	4.88	29.27
Steroid-induced glaucoma	67 (1.2%)	37.35 ± 16.20	49.25	1.49	7.46	8.96
Glaucoma associated with hemorrhage	19 (0.3%)	45.63 ± 18.01	26.32	0.00	10.53	15.79
Combined-mechanism glaucoma	13 (0.2%)	57.33 ± 21.19	46.13	0.00	7.69	23.08
Congenital glaucoma	37 (0.7%)	12.22 ± 11.88	37.84	8.11	0.00	0.00
Glaucoma associated with developmental anomaly	3 (0.1%)	18.00 ± 15.88	0.00	0.00	0.00	0.00
Glaucoma associated with corneal endothelial disorder	13 (0.2%)	42.85 ± 11.55	61.54	0.00	15.38	15.38
Pigmentary glaucoma	9 (0.2%)	47.33 ± 12.30	11.11	0.00	11.11	22.22
Neovascular glaucoma	289 (5.2%)	56.90 ± 15.72	41.18	2.08	47.40	31.49
Glaucoma associated with retinal detachment or vitreous abnormality	10 (0.2%)	49.90 ± 21.64	30.00	0.00	10.00	30.00
Glaucoma associated with inflammation	211 (3.8%)	48.50 ± 15.73	41.71	1.42	5.21	9.95
Ciliary black glaucoma	11 (0.2%)	61.27 ± 10.52	36.36	0.00	0.00	9.09
Glaucoma in aphakia or pseudophakia	121 (2.2%)	59.18 ± 13.90	28.93	3.31	14.05	19.01
Glaucoma associated with corneal surgery	9 (0.2%)	51.22 ± 15.06	33.33	0.00	33.33	11.11
Glaucoma associated with vitreoretinal surgery	23 (0.4%)	49.39 ± 18.00	43.48	0.00	30.43	17.39
Others	81 (1.5%)	48.23 ± 17.00	46.91	2.47	4.94	17.28
Total	5,530 (100%)					

which belonged to one of the above mentioned International Society of Geographical & Epidemiological Ophthalmology categories. The mean age of the newly diagnosed glaucoma patients was 52.0 ± 17.3 years (range, 6 to 89) of which 2,830 were male (51.2%). The mean IOP and vertical cup-to-disc ratio of the optic disc head in newly diagnosed

glaucoma patients were 22.1 ± 10.6 mmHg and 0.66 ± 0.22 , respectively. The proportions of the glaucoma subtypes are shown in Table 1. The most frequently observed glaucoma subtypes were NTG (33.0%), POAG (28.4%), OHT (11.1%), CACG (6.8%), NVG (5.2%), glaucoma associated with inflammation (3.8%), AACG (3.4%), and glaucoma in apha-

Table 2. Demographics and medical history of newly diagnosed glaucoma patients

Diagnosis	Mean IOP (mmHg)	Mean vertical cup-to-disc ratio
Ocular hypertension	21.81 ± 4.78	0.524 ± 0.210
Primary open-angle glaucoma	22.19 ± 8.17	0.696 ± 0.226
Normal-tension glaucoma	16.31 ± 3.48	0.691 ± 0.166
Acute angle-closure glaucoma	37.34 ± 19.41	0.492 ± 0.261
Subacute angle-closure glaucoma	21.81 ± 8.92	0.578 ± 0.227
Chronic angle-closure glaucoma	24.43 ± 12.53	0.679 ± 0.268
Plateau iris syndrome	12.50 ± 2.12	0.500 ± 0.424
Angle-recession glaucoma	31.04 ± 12.88	0.548 ± 0.254
Glaucoma associated with cataract	37.37 ± 18.84	0.511 ± 0.214
Lens dislocation	38.11 ± 13.19	0.483 ± 0.214
Pseudoexfoliation syndrome	21.12 ± 7.85	0.740 ± 0.228
Steroid-induced glaucoma	25.44 ± 8.76	0.604 ± 0.215
Glaucoma associated with hemorrhage	33.63 ± 14.03	0.692 ± 0.193
Combined-mechanism glaucoma	26.58 ± 8.70	0.741 ± 0.253
Congenital glaucoma	24.36 ± 9.80	0.718 ± 0.219
Glaucoma associated with developmental anomaly	37.33 ± 8.02	0.733 ± 0.306
Glaucoma associated with corneal endothelial disorder	27.00 ± 12.29	0.654 ± 0.163
Pigmentary glaucoma	27.78 ± 14.53	0.733 ± 0.233
Neovascular glaucoma	34.49 ± 16.87	0.686 ± 0.227
Glaucoma associated with retinal detachment or vitreous abnormality	24.40 ± 10.28	0.688 ± 0.253
Glaucoma associated with inflammation	28.66 ± 12.70	0.571 ± 0.236
Ciliary black glaucoma	41.55 ± 16.24	0.567 ± 0.301
Glaucoma in aphakia or pseudophakia	26.08 ± 11.47	0.716 ± 0.224
Glaucoma associated with corneal surgery	29.50 ± 9.20	0.600 ± 0.187
Glaucoma associated with vitreoretinal surgery	30.09 ± 14.34	0.693 ± 0.237
Others	20.85 ± 8.49	0.613 ± 0.194

IOP = intraocular pressure.

phia or pseudophakia (2.2%).

The demographics and concurrent medical conditions of the newly diagnosed glaucoma patients are also shown in Table 1. POAG, NVG, angle-recession glaucoma, lens dislocation, pseudoexfoliation syndrome, glaucoma associated with hemorrhage, congenital glaucoma, pigmentary glaucoma, glaucoma associated with inflammation, and glaucoma associated with aphakia or pseudophakia showed significant male predominance (assuming 50% as an esti-

mated sex ratio, $p < 0.05$ by chi-square test). In contrast, AACG, CACG and glaucoma associated with corneal endothelial disorder showed female predominance (assuming 50% as an estimated sex ratio, $p < 0.05$ by chi-square test) (Table 1). The presence of diabetes and hypertension varied widely (ranges, 0.0% to 47.4% and 0.0% to 37.8%, respectively) in glaucoma subtypes. The presence of family history also showed a range of variation (range, 0.0% to 8.7%) (Table 1). The ocular information for newly diag-

nosed glaucoma patients is presented in Table 2. Mean IOP and vertical cup-to-disc ratio varied widely with glaucoma subtypes.

Of the newly diagnosed glaucoma patients, the 8 most frequently observed glaucoma subtypes accounted for 92.1% of the total. In the age distribution, CACG, AACG, NVG and glaucoma associated with aphakia or pseudophakia did not show significant differences ($p > 0.05$ by Student's *t*-tests); however, all other glaucoma subtypes showed significant differences ($p < 0.05$ by Student's *t*-tests). In terms of IOP, NVG and AACG did not show a significant difference ($p > 0.05$ by Student's *t*-test); however, all of the other glaucoma subtypes showed significant differences ($p > 0.05$ by Student's *t*-test). In cup-to-disc ratio, NTG, POAG, CACG, NVG, and glaucoma associated with aphakia or pseudophakia showed no significant difference ($p = 0.504$ by one-way analysis of variance); however, all other glaucoma subtypes showed a significant difference ($p < 0.05$ by Student's *t*-test).

In relation to the incidence rate of diabetes, NTG, OHT, CACG, glaucoma associated with inflammation, AACG, and glaucoma associated with aphakia or pseudophakia did not show any significant difference ($p = 0.102$ by chi-square test). However, POAG showed a significantly higher incidence rate of diabetes than did NTG or glaucoma associated with inflammation ($p < 0.05$ by chi-square tests). NVG showed a significantly higher incidence rate of diabetes than did any of the other glaucoma subtypes ($p < 0.05$ by chi-square test).

Regarding the incidence rate of systemic hypertension, glaucoma associated with inflammation showed a significantly lower incidence rate than did any of the other glaucoma subtypes ($p < 0.05$ by chi-square test); but NVG showed a significantly higher incidence rate than did any of the other glaucoma subtypes except for AACG ($p < 0.05$ by chi-square test). NTG, POAG, NVG, CACG, and AACG did not show significant differences in terms of incidence rate of hypertension ($p > 0.05$ by chi-square test).

Discussion

In the current study, the sex distribution of AACG, subacute ACG, CACG, and glaucoma associated with corneal endothelial disorder exhibited significant female predominance. This finding is consistent with previous studies [19-

23]. In contrast, POAG, OHT, NVG, glaucoma associated with inflammation, glaucoma in aphakia or pseudophakia, angle-recession glaucoma, lens dislocation, and glaucoma associated with hemorrhage exhibited significant male predominance. We speculate that the male predominance among cases of angle-recession glaucoma, lens dislocation, and glaucoma associated with hemorrhage could be explained by the fact that these subtypes of glaucoma are usually associated with trauma. However, significant male predominance among POAG, OHT, NVG, glaucoma associated with inflammation, and glaucoma in aphakia or pseudophakia require further investigation. In the comparison of NTG with POAG, NTG showed a significantly higher female proportion and a lower age. Previous publications also reported a higher percentage of women in the NTG classification; thus our result was in line with these publications [24-26]. A higher proportion of lower age in NTG may be related to the recent observation that greater proportion of myopia is noted in the younger age group, and myopia is a risk factor for NTG [27]. This speculation requires further investigation. The reported association between diabetes and glaucoma remains controversial [28-38]. According to official statistics from the Korean government (Korean National Health and Nutrition Examination Survey IV), the prevalence of systemic hypertension and diabetes in the general Korean population (age equal to or more than 30 years) were 24.9% and 9.5%, respectively. The incidence rate of diabetes in glaucoma associated with inflammation was 5.2%, which was lower than that of general Korean population. Meanwhile, the incidence rate of diabetes in POAG and glaucoma in aphakia or pseudophakia were found to be higher than that of the general Korean population (11.9% and 14.1% vs. 9.5%). However, we cannot directly compare these results because our results, based on outpatient clinic visits, may be prone to selection bias. The association between systemic hypertension and glaucoma, usually attributed to ocular perfusion pressure, is also debatable [39,40]. In this study, various subtypes of glaucoma showed a wide range of incidence rates in systemic hypertension (0.0% to 31.5%). However, all glaucoma subtypes except NVG had a lower incidence rate of systemic hypertension than the general Korean population (24.9% according to official Korean records—Korean National Health and Nutrition Examination Survey IV). Among the most frequently observed subtypes of glaucoma, CACG and AACG had a signifi-

cantly higher incidence rate of systemic hypertension; however, this finding may be related to the observation that patients with CACG and AACG patients are relatively older.

In the Namil study, POAG with IOP ≤ 21 mmHg (2.81%) was the most frequent subtype of glaucoma, followed by POAG with IOP > 21 mmHg (0.78%), PACG (0.65%), OHT (0.59%), and secondary glaucoma (glaucoma associated with surgery, 0.26%). In this study, based on a hospital-visiting population, POAG with IOP ≤ 21 mmHg was the most frequently observed glaucoma subtype as in the Namil study. However, the proportion of POAG in this study was much greater than that of the Namil study. This can be explained by the fact that participants in this study were recruited from the clinic and thus may have had symptoms related to elevated IOP. However, because the Namil study was population-based, the study included asymptomatic patients. In the current study, the proportion of NVG and glaucoma associated with inflammation were much higher than that of Namil study. We speculate that this result reflects that more intractable types of glaucoma like NVG or glaucoma associated with inflammation are prone to manifest serious symptoms and signs. This results in more presentations to major glaucoma clinics.

This study had several limitations. First, this study included the patients who visited an ophthalmology outpatient clinic during the study period. Therefore, the subjects were enrolled in a hospital-based setting, which can be quite different from population-based studies. In addition, our study had a potential for referral bias: patients in tertiary medical centers were considerably different from the general population. The referral bias may have significantly affected the clinical characteristics and profiles of newly diagnosed glaucoma subtypes in this study. Also, analysis of the demographic and ocular factors that influence the referral of patients is necessary and should be performed in future analyses. Finally, the family history of various glaucoma types showed different profiles which can be a potentially interesting finding. Since family history was obtained by questionnaire, future study is warranted to reinforce our results.

In conclusion, a total of 198,671 patients were enrolled, 5,530 (2.8%) of whom were newly diagnosed with glaucoma. NTG, POAG, OHT, CACG, NVG, glaucoma associated with inflammation, AACG, and glaucoma in aphakia or pseudophakia were the most frequently observed glauco-

ma subtypes in the urban ophthalmology outpatient clinics included in this study. The incidence rate of diabetes in POAG and glaucoma in aphakia or pseudophakia were higher than that of the general Korean population. This is one of the largest studies investigating the profiles and clinical characteristics of glaucoma subtypes in urban clinics and thus can provide insight into the profile and clinical characteristics of those who visit urban ophthalmology outpatient clinics. Profiles of specific diseases in hospitals may reflect the corresponding prevalence of the general population. However, this prevalence may also be affected by many factors such as socioeconomic status and ethnicity, public health systems, and hospital access. Therefore, the findings in this study may not be representative of the general urban population in Korea. Moreover, as mentioned earlier, this was not a population-based study. Thus, the proportions of glaucoma reported herein should be interpreted with caution. Further population-based studies are warranted to determine the true prevalence of glaucoma subtypes in South Korean cities.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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