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Original Article / *Özgün Araştırma*

# Risk Factors for Primary Open-Angle Glaucoma in Western Turkey

## *Türkiye'nin Batısında Primer Açık Açılı Glokom için Risk Faktörleri*

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### *Summary*

**Purpose:** To evaluate the prevalence of primary open-angle glaucoma (POAG) in subjects aged over 40 years in Western Turkey and to quantify its association with several systemic risk factors.

**Material and Method:** The research was conducted in Afyonkarahisar, a middle Anatolian city, between November 2005 and February 2006. A total of 1533 subjects aged 40 years or more were included in the study. Diabetes mellitus, hypertension, atherosclerotic cardiac disease, obesity, smoking, alcohol consumption, and dietary habitus (meat, chicken, and fish consumption) were asked. Level of blood glucose, serum total cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein, very-low-density lipoprotein, Vitamin B12, and thyroid-stimulating-hormone were determined. Ophthalmic examination was performed, and intraocular pressure was measured by tonopen. Subjects with an IOP of 21 mmHg or more and/or with a cupping/disc ratio of 0.3 or more were told to come to the clinic for visual field analysis and gonioscopy. Subjects with a typical glaucomatous visual field defect and an open angle were recorded as POAG. Risk factors for POAG were determined by chi-square test.

**Results:** Prevalence of POAG was found to be 2% (30 subjects) and the only associated risk factor was age (p=0.05). Dietary habitus was also not associated with glaucoma (p>0.05).

**Discussion:** This study provides a population-based data about the prevalence and risk factors of POAG in Turkey. *(Turk J Ophthalmol 2013; 43: 87-90)*

**Key Words:** Age, diabetes mellitus, hypertension, obesity, primary open-angle glaucoma

### *Özet*

**Amaç:** Türkiye'nin batısında 40 yaşın üzerindeki primer açık açılı glokomun prevalansını belirlemek ve sistemik bazı risk faktörleri ile ilişkisini değerlendirmek.

**Gereç ve Yöntem:** Bu çalışma, Kasım 2005 ve Şubat 2006 tarihleri arasında bir orta Anadolu şehri olan Afyonkarahisar'da yapılmıştır. Çalışmaya 40 yaş ve üzerindeki toplam 1533 olgu dahil edildi. Diabetes mellitus, hipertansiyon, aterosklerotik kalp hastalığı, obezite, sigara ve alkol tüketimi ve beslenme alışkanlığı (kırmızı et, tavuk, veya balık tüketimi) sorgulandı. Açlık kan şekeri, total serum kolesterol, trigliserit, yüksek-dansiteli-lipoprotein, düşük-dansiteli lipoprotein, çok-düşük-dansiteli lipoprotein, Vitamin B12 ve tiroid-stimüle-edici-hormon seviyesi belirlendi. Oftalmik muayene yapıldı ve tonopen yardımı ile göz içi basıncı ölçüldü. Göz içi basıncı 21 mmHg veya üzerinde olan olgular ve veya çukurluk/disk oranı 0,3 veya üzerinde olan olgular görme alanı testi ve gonyoskopi yapılması için kliniğe çağrıldılar. Görme alanı testinde tipik glokomatöz görme alanı hasarı saptanan ve ön kamara açısı açık olan olgular primer açık açılı glokom olarak kaydedildi. Primer açık açılı glokom için risk faktörleri ki-kare testi kullanılarak değerlendirildi.

**Sonuçlar:** Primer açık açılı glokom prevalansı %2 idi ve ilişkili olan tek risk faktörü yaş olarak saptandı (p0,05). Beslenme alışkanlığınında etkisiz olduğu gözlendi (p>0,05).

**Tartışma:** Bu çalışma, Türkiye'de primer açık açılı glokomun prevalansı ve ilişkili risk faktörleri için topluma dayalı bilgi sağlamaktadır. *(Turk J Ophthalmol 2013; 43: 87-90)*

**Anahtar Kelimeler:** Diabetes mellitus, glokom, hipertansiyon, obezite, primer açık açılı glokom, yaş

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## Introduction

Primary open-angle glaucoma (POAG) is an important cause of vision loss which can be prevented if determined at an early stage. Because of this, the evaluation of risk factors play an important role in taking preventive care for POAG.

Glaucoma is a progressive optic neuropathy where intraocular pressure (IOP) is believed to be the main risk factor. Its incidence has been reported to be 0.9% -9.7% over the age of 40 years.[1-4] Some systemic and ocular risk factors like corticosteroid use and myopia are shown to play a role in the development of glaucoma, whereas smoking and the use of alcohol do not affect the development of glaucoma.[5,6]

In this study, we aimed to investigate the importance of a number of systemic conditions as risk factors for POAG in subjects aged over 40 years from Western Turkey.

## Materials and Methods

The study was approved by Clinical Research Ethics Committee at Afyon Kocatepe University Faculty of Medicine, and written informed consent was obtained from all participants. The research was conducted in Afyonkarahisar between November 2005 and February 2006.[7] A total of 1533 subjects aged 40 years or more from urban and province screening regions of Afyonkarahisar were detected according to the population records of the year 2000, which represent the population of the area appropriately. The records of the regional health institutions were used in order to determine the subjects and the subjects were selected randomly from the "Family Cards" of the primary health centers, regarding the gender and ages. Only one person was selected from every house. The subjects were informed about the study by telephone interviews one night before, their approvals were obtained and their transport to the health institutions, where the study would be conducted, was provided. The data were collected by a questionnaire in which face to face survey method was performed by the physicians. History of systemic disease like diabetes mellitus (DM), hypertension or atherosclerotic cardiac disease (ASCD), obesity, systemic or ocular drug use was asked. Five milliliters (ml) of venous blood was obtained from all subjects after fasting for at least 8 hours or overnight. Levels of blood glucose, serum total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), very low-density lipoprotein cholesterol (VLDL), Vitamin B12 and thyroid-stimulating hormone (TSH) were determined.

Subjects were divided into 4 groups according to their age as group 1 (40–49 years), group 2 (50–59 years), group 3 (60–69 years), and group 4 (70 years or more). The subjects were evaluated according to their living area as rural or urban area. The diagnosis of DM was made by a history of DM or measured fasting blood glucose level equal to or over 127 mg/dl, the diagnosis of hypertension was made by a history of hypertension or a blood pressure of 130/85 mmHg or more at the examination (at least 2 times). The diagnosis of ASCD was made by a previous history of myocardial infarction or prior stent placement, previous coronary artery by-pass surgery, or previous history of coronary angiography with plaques in coronary artery lumen.7 The diagnosis of obesity was made by a body mass index (BMI) (body weight (kg)/height2 ($m^2$)) of 30 or greater.[7-9] A total cholesterol level of 200 mg/dl or higher was accepted to be hypercholesterolemia, triglyceride level of 201 mg/dl or more to be hypertriglyceridemia, LDL level of 150 mg/dl or more to be high LDL, VLDL levels of 100 mg/dl or more to be high VLDL, and HDL levels of 35 mg/dl or less to be low HDL. Vitamin B12 level of 197 pg/ml was accepted to be hypovitaminosis B12. The reference range for TSH was 0.27 uIU/ml – 4.20 uIU/ml, levels below 0.27 uIU/ml were accepted to be hyperthyroidism, whereas levels over 4.20 uIU/ml were accepted to be hypothyroidism. The consumption of meat, chicken or fish was accepted to be positive if it was consumed at least once a week. Smoking and alcohol use was also asked. Subjects were divided as non-smokers and smokers (any number of cigarettes smoked per day currently or in the past) as well as nondrinkers or drinkers (any amount of alcohol intake currently or in the past).

Ophthalmic examination included measurement of visual acuity by Snellen chart, biomicroscopy (portable slit-lamp, SL15, Kowa, Japan) and fundus examination by direct ophthalmoscopy. Fundus examination in subjects with a visual acuity of 0.8 or less or in whom fundus could not be seen was completed by dilating the pupil with one drop of tropicamide and one drop of phenylephrine eye drops. Intraocular pressure was measured by tonopen (Tonopen XL, Medtronic, USA) by the same examiner. As the tonopen is internally calibrated, the instrument calibration was performed once daily prior to instrument use and when it was indicated by the LCD display according to the manufacturer instructions. After one drop of topical anesthetic was applied onto the eye, the patient was seated, and the tip of the tonopen was covered by ocufilm. Subjects with an IOP of 21 mmHg or more and/or with a cupping/disc ratio of 0.3 or more were told to come to the clinic for visual field analysis and gonioscopy. Visual field analysis was performed by Humphrey visual field analyser program SITA 24-2. Fixation losses, false-positive and false negative response rates higher than 33% were determined to be unreliable and the test was repeated. The subjects with a typical glaucomatous visual field defect and an open anterior chamber angle were diagnosed as POAG. Typical glaucomatous defect was considered if at least 2 of the followings were present: 1 - three or more nonedged points in a cluster depressed to $p<5\%$, 1 of which is depressed to $p<1\%$; 2 - glaucoma hemifield test outside normal limits; 3 - pattern standard deviation depressed to $p<5\%$.[10] The effect of the risk factors listed above on POAG was evaluated.

Statistical evaluation was performed by MedCalc statistical program version 7.3 (Belgium). Mean age between male and female subjects was evaluated by independent samples t-test. The affect of the risk factors on ocular disease development was evaluated by chi-square test and p-values <0.05 were determined to be statistically significant.

## Results

Nine-hundred-and-ten (59.4%) subjects were female and 623 (40.6%) subjects were male. Mean age of all subjects was 53.35±9.8 years (40 – 90 years) which was 53.09±9.7 years in females and 53.73±9.9 years in males (p=0.21). Sex distribution did not differ among age groups (p=0.80, chi-square test) (Table 1). Some of the risk factors could not be evaluated in all subjects because the subjects did not want to answer the questions, because of inadequate sera or because the kits came to an end.

Primary open-angle glaucoma was seen in 30 (2%) patients. Five (0.8%) of the POAG subjects were in age group 1, 9 (1.7%) were in age group 2, 6 (2.3%) were in age group 3, and 10 (8.0%) were in age group 4 (Table 2). The prevalence of glaucoma increased

significantly with age (p<0.001, chi-square test). Prevalence of glaucoma was significantly higher in age group 4 compared to age groups 1, 2, and 3 (p<0.001, p<0.001, p=0.009, respectively). There was no significant difference between group 1 and group 2, group 1 and group 3, group 2 and group 3 (p=0.200, p=0.069, p=0.52). Thirteen of POAG subjects (43.3%) were female and 17 (56.7%) were male (p=0.11). Living in a rural area, hypertension, DM, ASCD and obesity did not have an influence on the prevalence of POAG (p=0.43, p=0.53, p=0.73, p=0.92, p=0.55, respectively) (Table-3). Level of plasma cholesterol, VLDL, LDL, HDL, Vitamin B12, and TSH had also no affect on the prevalence of POAG (p=0.17, p=0.73, p=0.23, p=0.54, p=0.57, p=0.61, respectively) (Table-4). Similarly, smoking, alcohol consumption and nutrition had no influence on POAG (for smoking p=0.10, for alcohol consumption p=0.23, for meat consumption p=0.88, for chicken consumption p=0.43, for fish consumption p=0.73) (Table 5).

## Discussion

This study provides a population-based data about the prevalence of POAG in Turkey. Prevalence of POAG in subjects aged over 40 years was found to be 2% which is compatible with the literature.[1-4,11,12] The only associated risk factor was found to be increasing age. Other systemic risk factors did not have a statistically significant affect on POAG. It has been shown that several risk factors can play an important role in the development of POAG. Similarly with the results of our study, POAG has been shown to increase significantly with age.[11,13-16] The drawback of our study is that we did not evaluate central corneal thickness and we did not measure diurnal changes in IOP. So, some POAG subjects can have been dismissed. Nevertheless, though diurnal fluctuation of greater than 10 mmHg is suggestive of glaucoma, the impact of IOP fluctuations on optic nerve still remains unknown.[17] We used tonopen during the study. It is known that Goldmann applanation tonometer is the gold standard of IOP measurement and tonopen can overestimate or underestimate measurements.[18] In contrast, Öztürk et al.[19] have shown that IOP measurements with tonopen were not affected by central corneal thickness and also they reported similar measurement results with Goldmann applanation tonometer and tonopen.

Gender had no influence on POAG in our study. There are conflicting reports about the effect of gender on glaucoma. Vijaya et al.[11,13,20] could find no association with gender, whereas other studies reported POAG and ocular hypertension to be more frequent in females.

Obesity and BMI did not have an influence on the development of POAG. Primary open-angle glaucoma has been reported to be significantly associated with high BMI.[21] We could not find a significant association between nutrition and POAG. We could not find any study about the effect of meat, chicken or fish consumption on POAG.

Diabetes mellitus and hypertension did not have an influence on the development of POAG. Though systemic hypertension is

**Table 1.** Sex distribution

| Sex | n (%) | | | | |
|---|---|---|---|---|---|
| | 40-49 years | 50-59 years | 60-69 years | 70+ years | Total |
| Female | 371 (60.7) | 312 (57.9) | 152 (58.9) | 75 (60.0) | 910 (59.4) |
| Male | 240 (39.3) | 227 (42.1) | 106 (41.1) | 50 (40.0) | 623 (40.6) |

**Table 2.** The distribution of subjects with glaucoma according to age group

| Age group | Glaucoma + n (%) | Glaucoma – n (%) | Total n |
|---|---|---|---|
| 40 – 49 years | 5 (0.8) | 606 (99.2) | 611 |
| 50 – 59 years | 9 (1.7) | 530 (98.3) | 539 |
| 60 – 69 years | 6 (2.3) | 252 (97.7) | 258 |
| 70+ | 10 (8.0) | 115 (92.0) | 125 |

**Table 3.** The effect of living area and systemic diseases on POAG

| Systemic disease | | POAG (n) | | |
|---|---|---|---|---|
| | | - | + | p |
| Living area | Urban | 787 | 13 | 0.43 |
| (n=1533) | Rural | 1057 | 19 | |
| Hypertension | - | 1057 | 19 | 0.53 |
| (n=1533) | + | 446 | 11 | |
| Diabetes mellitus | - | 1263 | 24 | 0.73 |
| (n=1533) | + | 240 | 6 | |
| ASCD | - | 1385 | 28 | 0.92 |
| (n=1533) | + | 118 | 2 | |
| Obesity | - | 920 | 20 | 0.55 |
| (n=1462) | + | 514 | 8 | |

POAG: primary open-angle glaucoma; ASCD: atherosclerotic cardiac disease; p=chi-square test

**Table 4.** The effect of serum lipid profile, Vitamin B12 and TSH level on POAG

| Systemic disease | | POAG (n) | | |
|---|---|---|---|---|
| | | - | + | p |
| Cholesterol | Normal | 884 | 22 | |
| (n=1533) | High | 619 | 0 | 0.17 |
| VLDL | Normal | 1313 | 26 | |
| (n=1382) | High | 43 | 0 | 0.73 |
| LDL | Normal | 1155 | 25 | |
| (n=1369) | High | 188 | 1 | 0.23 |
| HDL | Normal | 988 | 17 | |
| (n=1384) | Low | 370 | 9 | 0.54 |
| Triglyceride | Normal | 964 | 20 | |
| (n=1382) | High | 392 | 6 | 0.67 |
| Vitamin B12 | Normal | 888 | 19 | |
| (n=1376) | Low | 462 | 7 | 0.92 |
| TSH | Normal | 1242 | 25 | |
| (n=1377) | Low | 61 | 1 | 0.55 |

POAG: primary open-angle glaucoma; ASCD: atherosclerotic cardiac disease; VLDL: very low-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; TSH: thyroid-stimulating hormone; p=chi-square test

**Table 5.** Effect of diet on POAG

| Systemic disease | | POAG (n) | | |
|---|---|---|---|---|
| | | - | + | p |
| Smoking | - | 807 | 11 | |
| (n=1533) | + | 696 | 19 | 0.10 |
| Alcohol | - | 1381 | 26 | |
| (n=1502) | + | 91 | 4 | 0.23 |
| Meat | - | 1031 | 22 | |
| (n=1182) | + | 126 | 3 | 0.88 |
| Chicken | - | 1114 | 23 | |
| (n=1349) | + | 210 | 2 | 0.43 |
| Fish | - | 1039 | 26 | |
| (n=1148) | + | 82 | 1 | 0.73 |

POAG: primary open-angle glaucoma, p=chi-square test

defined as a systolic blood pressure of 140 mmHg and a diastolic blood pressure of 90 mmHg or more, we included subjects with a systolic blood pressure of >130 mmHg and diastolic blood pressure of 85 mmHg or more in the hypertensive group as cardiovascular disease has been shown to be more frequent in these patients.[9,22] Systemic hypertension and DM did not affect the development of POAG in the study performed by Vijaya et al.20 In contrast, some studies have shown that DM increased the risk of developing POAG.[21,23] Similarly, Pasquale et al.[24] reported that POAG increased with type 2 DM in women. Glaucoma patients have been shown to have a lower diastolic blood pressure.[12] No associations with POAG were identified for total serum cholesterol, triglycerides and LDL, VLDL and HDL. Newman-Casey et al.[23] showed that hyperlipidemia alone decreased the risk of POAG, whereas comorbid hyperlipidemia with hypertension or DM increased the risk of POAG. Plasma Vitamin B12 level did not influence the development of POAG in our study. Similarly, Cumurcu et al.[25] could detect no difference in serum Vitamin B12 levels in POAG subjects. Though we could not detect an association between plasma TSH level and POAG, we could not find a study evaluating the correlation between plasma TSH level and POAG in the literature.

The prevalence of POAG in subjects living in urban areas or rural areas did not change in our study. In contrast to our study, the prevalence of POAG has been reported to be higher in urban population.[11,16]

Recently, Wise et al[21] reported that smoking might be associated with increased risk of early-onset POAG. In contrast to this, Buys et al.[26] showed that smoking decreased the risk of open-angle glaucoma. In our study, no association was found between smoking, alcohol consumption and POAG. Alcohol consumption has been reported to be an independent risk factor for POAG.[21] In our study, smoking and alcohol consumption did not have an influence on the development of POAG.

In summary, this study provides the prevalence rate and risk factors for POAG in Western Turkey. Additional studies are required to incorporate these findings into future investigations for interpretation and prevention of risk factors for POAG in Turkey.

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