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ORIGINAL ARTICLE

PRIMARY JUVENILE OPEN-ANGLE GLAUCOMA, CLINICAL FEATURES AT PRESENTATION TO TERTIARY EYE CENTER, MENELIK II HOSPITAL, ADDIS ABABA

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ABSTRACT

Background: *Primary juvenile open-angle glaucoma is a rare form of glaucoma that affects young individuals below the age of 40 years. It is characterized by rapid progression of the disease with severely high intraocular pressure.*

Objective: *The purpose of this study was to describe the clinical features of patients with primary juvenile open-angle glaucoma at the time of presentation to tertiary eye center.*

Methods: *A retrospective cross-sectional medical record review of patients with the diagnosis of primary juvenile open-angle glaucoma at the Glaucoma unit of the Department of Ophthalmology, Menelik II tertiary referral hospital, Addis Ababa, Ethiopia. We reviewed charts of cases that were seen over a five year period. Central tendency, measures of dispersion, frequency and percentage were calculated using Statistical Package of Social Sciences version 21 statistical software.*

Results*: A total of 55 cases were included during the study period, 12 were affected unilaterally. The mean age was 27.0 ± 7.7, range: 5 to 35 years. Family history of glaucoma among parents and /or siblings was documented in 12 cases. Vision reduction was the commonest presenting complaint in 26 (47.3%) cases, followed by blurring of vision in 7 (12.7%). Seventeen (30.9%) were identified while presenting for other complaints. The mean intraocular pressure of 98 eyes with glaucoma and without medication was 37.20 ± 11.3 mm Hg, range, 15 - 69 mm Hg. Bilateral and unilateral blindness was identified in 9 (16.4%) and 27 (49.1%) cases, respectively. Glaucomatous optic nerve head damage was advanced in 68 (69.4%) of the eyes.*

Conclusion: *Ethiopians with primary juvenile open-angle glaucoma largely presented with vision loss related complaints and at advanced stage of the disease and with very high intraocular pressure. We recommend that eye care professionals should examine the optic nerve head and measure the intraocular pressure at any age, and to raise public awareness to detect this rare but blinding disease.*

Key words: *Juvenile open-angle glaucoma, intraocular pressure, glaucomatous optic nerve head*

INTRODUCTION

Glaucoma is a heterogeneous group of optic neuropathy and potentially blinding disease that can be divided into childhood, juvenile onset and adult onset categories according the age of onset, open angle and closed angle based on gonioscopy evaluation; and primary and secondary based on presence or absence of underlying cause (1).

Primary juvenile open-angle glaucoma (JOAG) is a rare form of glaucoma occurring 1: 50,000 in various ethnic origins (2) and it has various definitions. Some define it as a subset of primary childhood glaucoma (CHG) that occurs between age 3 and 40 years, while others define it as a subset of primary open-angle glaucoma (POAG) that occurs between age 5 and 35 years (3, 4).

The European Glaucoma Society defines JOAG as open angle-glaucoma with onset between the ages of 10 and 35 years (5).Primary juvenile open-angle glaucoma differs from childhood glaucoma by the absence of eyeball enlargement and corneal changes, and from that of POAG by the presence of very high intraocular pressure (IOP) and early age of onset (6-10). The diagnosis of primary JOAG is straight forward in the presence of markedly elevated intraocular pressure and glaucomatous optic nerve damage (3, 5). The disease is related to mutation of myocilin gene (MYOC/TIGR) and CYP1B1 and can be inherited as an autosomal dominant trait with high penetrance (2, 8, 11, 12). However, having MYOC mutation does not necessarily mean that a patient has or will develop JOAG (2).

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Most patients with primary JOAG present and/or are identified late with advanced form of the disease due to the symptomless nature and rare occurrence of the disease that leads to less attention by both the affected individuals and eye care professionals (3,5).

The purpose of this study was to describe the clinical features of Ethiopian patients with primary JOAG at time of presentation to a tertiary center. The outcome may help us to know how and when patients seek medical attention, the level of IOP and stage of glaucoma at presentation. The report of this study will alert eye care professionals to case detection at an earlier stage. And it will also be a contribution to the literature on the disease, which is particularly scarce from Africa.

PATIENTS AND METHODS

The study was a retrospective cross-sectional medical record review of patients with the diagnosis of primary JOAG over a five-year period (2013-2017). It was conducted at the Glaucoma unit of the Department of Ophthalmology, Menelik II tertiary referral Hospital, Addis Ababa, Ethiopia.

Glaucoma patients are referred to the Glaucoma unit from the different clinics of the eye department, eye centers in Addis Ababa and various areas of the country. Routine glaucoma evaluation for all new patients coming to the unit is done using evaluation format sheets that are attached to the patients' chart. Evaluation includes history taking, visual acuity including pinhole or with correction using Snellen chart on LCD display screen, intraocular pressure (IOP) measurement with I-care or Goldmann applanation tonometer, thorough eye evaluation under slit-lump microscope including gonioscopy, and optic nerve head and retina examination using 90D lens.

Staging of severity of glaucoma is made based on the extent of glaucomatous optic nerve head damage. Diagnosis of early, moderate or advanced glaucoma is made when the vertical cup: disc (VCD) ratio is 0.65 or less, 0.7 to 0.85 and 0.9 or greater, respectively according to the Canadian glaucoma strategy (13). Visual field is determined using Humphrey Frequency Doubling Technology (Welch Allyn, Carl Zeiss Meditech, Calif.) for those who have visual acuity better than 3/60.

The registration book of the Glaucoma unit was used to identify cases with the diagnosis of JOAG and to retrieve their charts. Those with the diagnosis of primary juvenile open-angle glaucoma who had completed evaluation format sheets were included in the study.

Relevant data was collected from the evaluation format sheets of each patient's chart into prepared data collection sheet. The data was entered to Epi-Data version 3.1 (The EpiData Association Company) and after being cleared, it was transferred to Statistical Package of Social Sciences (SPSS) version 21 statistical software. Descriptive statistics such as frequency, percentage and ratio were used for summarizing the data of categorical group. Mean and standard deviation was calculated for total numbers of variables of all eyes with glaucoma, and for the bilateral and unilateral cases. The mean difference between bilateral and unilateral cases was compared using independent t-test and statistical significance was declared if $P< 0.05$.

Operational classification and definition: Distance vision impairment for individual eye was classified based on the World Health Organization (WHO) classification (14). Visual acuity that was documented with either pin hole or correcting eyeglasses for those eyes with vision less than 6/6 was taken as the best visual acuity. Vision impairment was classified as mild, moderate, sever and blind when the visual acuity was less than 6/12, 6/18, 6/60 and 3/60, respectively. Visual field involving the central fixation or the central 10 degree among eyes with visual acuity better than 3/60 were considered as blind.

Ethical clearance: The study was approved by the research and publication ethics committee of the Department of Ophthalmology, School of Medicine, College of Health Science, Addis Ababa University. And patients' charts were handled confidentially.

RESULTS

A total of 62 cases with the diagnosis of primary JOAG were identified during the five-year period, and 55 with complete data were included in this study. Details of demographic characteristics are described in Table 1. The mean age of all study cases was 27.0 ± 7.7, ranging from 5 to 35 years. The mean age of those who had bilateral glaucoma was 27.2 ± 7.7, while for those presenting with one eye affected was 25.8 ± 8.8, (P-value: 0.53). Males were larger in number than females (34/21), making 1.6:1 ratio. The male:female ratio was even higher among the bilateral 43 cases, 2.3:1. On the other hand, among the unilateral 12 cases, females were twice as many as males, 2:1. Addis Ababa was the residential place for 26 (47. 3%) cases, while the rest were from other areas of the country. Family history of glaucoma among parents or siblings was documented in 12 cases. Eight had affected parents, while siblings were the affected in the others. Four of the unilateral cases with positive family history had affected siblings.

Table 1: Demographic Characteristics of Primary Juvenile Open Angle Glaucoma Patients, Menelik II Hospital, Addis Ababa, 2013-2017.

Characteristic	Frequency number	Percent
Age		
< 10	1	1.8
10 - 19	11	20.0
20 - 29	18	32.7
Above 30	25	45.5
Sex		
Male	34	61.8
Female	21	38.2
Address		
Addis Ababa	26	47.3
Others	29	52.7
Occupation		
Student	15	27.3
Farmer	7	12.7
Employed	23	41.8
Non-employed	10	18.2
Family history		
Yes	12	21.8
No	43	78.2

The initial presenting complaints of all the cases are listed in Table 2. Many of the cases, 26 (47.3%) came to the eye care service when they had either vision reduction or loss. The second vision related complaint that was documented in seven cases was blurring of vision.

These two complaints were the reasons for the 30 (69.8%) bilaterally affected cases for seeking attention, while 9 (75%) of the unilaterally affected cases were detected during evaluation for other complaints.

Table 2: Presenting complaints of Primary Juvenile Open-Angle Glaucoma patients, Menelik II Hospital, Addis Ababa 2013-2017.

Complaint	Total n=55 (%)	Bilateral n=43 (%)	Unilateral n=12(%)	P-value
Vision reduction/loss	26 (47.3)	24 (55.8)	2 (16.7)	< 0.05
Blurring of vision	7 (12.7)	6 (14.0)	1 (8.3)	> 0.05
Redness of eye	4 (7.3)	4 (9.3)	-	-
Eye pain	1 (1.8)	1 (2.3)	-	-
Evaluation for other complaints	17 (30.9)	8 (18.6)	9 (75.0)	< 0.001

The clinical characteristic of the eyes with glaucoma is depicted in Table 3. The mean intraocular pressure of all eyes with glaucoma was 37.2 $\pm$ 11.3 mm Hg, range 15 - 69 mm Hg.

The mean intraocular pressure was higher (42. 5 $\pm$ 10.9 mm Hg) among 75 eyes without medications than those on medications (30.28 $\pm$7.57 mm Hg), P-value < 0.001. The mean number of medications was 1.8 $\pm$ 0.66.

The visual acuity (VA) was severely impaired (VA < 6/60) in six eyes, while 31 eyes were blind (VA < 3/60). Bilateral blindness was identified in three cases. Among 14 eyes with visual field involving the central 10^0, two were that of a bilateral case and four were of those who had a second eye with visual acuity < 3/60, making the total number of bilateral blind cases 9 (16.4%). Twenty-seven cases (49.1%) were unilaterally blind by either visual acuity or visual field. Among the 12 unilateral cases, 5 (41.7%) were blind by visual acuity or visual field.

Mean vertical cup to disc ratio (VCD) was 0.88 $\pm$ 0.20. Severe or advanced glaucomatous optic nerve head damage (VCD $\geq$ 0.9) was documented in 68 (69.4%) eyes. The bilateral cases had advanced damage bilaterally in 24 eyes and unilaterally in 16 eyes. Half of the unilateral cases had advanced optic nerve head damage.

Gonioscopy, which was documented in all cases revealed the presence of iris processes with high insertion in 18 eyes, of which 15 were that of the bilateral cases.

Table 3: Clinical characteristics of eyes with Primary Juvenile Open-Angle Glaucoma, Menelik II Hospital, Addis Ababa, 2013-2017.

Variables	Frequency (n=98)	Percent
Intraocular pressure, mm Hg		
Below 21	3	3.1
21-30	25	25.5
31 – 40	29	29.6
Above 40	41	41.8
Visual Impairment		
Mild (< 6/12)	9	9.2
Moderate (< 6/18)	14	14.3
Severe (< 6/60)	6	6.1
Blind (< 3/60)	31	31.6
Glaucomatous optic disc damage		
Early	13	13.3
Moderate	17	17.3
Advanced	68	69.4
Visual field		
Central 10 degree involved	14	14.3
Central 10 degree not involved	84	85.7
Gonioscopy		
Normal appearing	80	81.7
Iris processes with high insertion	18	18.4

There was no statistically significant difference between the bilateral and unilateral cases when comparing the clinical characteristics including, mean age (P = 0.53), mean IOP with medication (P = 0.097) and without medication (P = 0.053), severity of visual loss (P = 0.466), tunnel visual field involving the central 10 degree (P = 0.562), and the mean of cup to disc ratio (P = 0.823). Table 4 shows the mean difference in intraocular pressure and vertical cup-disc ratio between the bilateral and unilateral affected eyes.

Table 4: Intraocular pressure and optic nerve head status of bilateral and unilateral eyes with primary juvenile open-angle glaucoma, Menelik II Hospital, Addis Ababa 2013-2017.

Character, Mean (SD)	All eyes n = 98	Bilateral n = 86	Unilateral n = 12	P-value
Intraocular pressure				
With and without medication	37.2 (11.30)	37.2(10.99)	37.2 (13.96)	0.986
With medication	30.3 (7.57)	31.2 (7.43)	25.0 (7.71)	0.097
Without medication	42.5 (10.94)	42.1 (10.9)	44.6 (11.56)	0.0533
Optic disc cup-disc ratio	0.88 (0.20)	0.88 (0.21)	0.89 (0.17)	0.823

DISCUSSION

This study demonstrates the presenting complaints, sex and age distribution, level of eye pressure, severity of glaucomatous optic nerve head damage and vision loss of Ethiopian patients with primary juvenile open angle-glaucoma, presenting at tertiary eye care level. The rare nature of the disease in young individuals is seen in the low number of cases over a five-year period, which is true elsewhere as well (4, 6, 8). The opportunity to get even this number was due to the referral of cases to the Glaucoma unit from various eye centers.

The beginning of the disease could be much earlier than the age at presentation (mean 27.0 $\pm$ 7.7) because at the time of presentation the majority (68, 69.4% eyes) had an advanced stage of the disease. Lower average ages of 18 and 18.5 years, at diagnosis have been reported in studies done by Johnson AT et al and Wiggs JL et al respectively (11, 8). In the literature, some stated that primary JOAG is a form of childhood glaucoma while others argued it is a subset of primary open-angle glaucoma (4, 5). Based on our findings, where 25 (45.5%) were older than 30 years and normal appearing gonioscopy that was seen in 80 (81.7%) of the affected eyes, we would support the view that it is a variant of POAG.

There were more males than females (34/21, 1.6:1) in this study, similar to the male predominance of 64% in a study from Korea (9). However, a report from the United State found both sexes to be affected equally (5). The majority of the cases 43 (78.2%) had bilaterally affected eyes, which is comparable to 79.2% in the medical record review study of 72 cases with JOAG in Korea (9). The bilateral nature of the disease is similar to that of primary childhood glaucoma and primary open-angle glaucoma and the relation of the disease to gene mutations.

The inheritance pattern of primary juvenile open angle glaucoma is autosomal dominance related to myocilin gene mutations (1,2,3,5). However, in this study, family history was obtained in only 12 cases (4 siblings and 8 parents), which could be actual fact or due to the absence of family screening and pedigree study.
Vision reduction (26, 47.3%) and blurring of vision (7,12.7%) were the common presenting complaints for seeking ophthalmic evaluation in 33 (60%) cases; and 17 (30.9%) presented with other complaints. In the study from Korea, 42 (58%) cases presented with complaints of symptoms associated with vision and pain; and one-third presented with no definitive symptoms (9). The results of the two studies may indicate that affected cases come to attention by the time the glaucoma is at an advanced stage and /or with severely elevated IOP causing vision loss, blurring of vision and pain.

Those who were identified on evaluation for other complaints indicates the importance of evaluation of the optic nerve head and measuring IOP in patients coming for other complaints regardless of patient's age to detect this blinding disease. The presentation of a larger number of the unilateral cases (9/12) with other complaints could be explained by the presence of good vision with the unaffected eye and unnoticed progressive vision reduction of the affected eye, which is true in the other forms of ocular diseases, in which vision loss in one eye is found during routine examination or during driving license or medical fitness check-ups.

The level of IOP was above 30 mm Hg in 78 (71.4%) of the affected eyes, which is similar to the study done in the United States that has reported average IOP of 38.5 mm Hg at time of diagnosis (8). It has also been shown in different studies that severely elevated intraocular pressure to be characteristic of primary JOAG (2, 5, 11). The magnitude of the blindness, that is bilateral in 9 (16.4%) and unilateral in 27 (49.1%) cases can be explained by the presence of advanced glaucomatous optic nerve head damage that was recoded in 68 (69.4%) eyes and the severely high IOP level, and symptomless nature of the disease that leads to late presentation with vision loss (3,5). The normal appearing gonioscopic angle drainage structures in 80 eyes of our cases is an indication of absence of overt angle anomaly, unlike the childhood glaucoma and similarity to that of POAG (5,10,11).

Comparing the level of IOP with and without medication, it is similarly high in both bilateral and unilateral cases without statistically significant difference. This is an indication of the high level of pressure in these cases whether they are bilaterally or unilaterally affected. Even if there was reduction with medication, the pressure remained high because the disease is less responsive to medical treatment (3). The severity of optic nerve head damage was similar in both bilateral and unilateral cases, which can obviously be explained by the presence of high IOP irrespective of laterality.
Limitations of the study: Although this study shows the presenting clinical features of cases with primary JOAG, the fact that it was a retrospective study has limited the variety of data and further details that could have been collected; and cases with incomplete data were excluded.

***Conclusion*:** Ethiopians with primary Juvenile open -angle glaucoma largely presented with vision loss related complaints at an advanced stage of the disease and with very high intraocular pressure. We recommend eye care professionals to examine the optic nerve head and measure the intraocular pressure at any age, and to raise public awareness to detect this rare but blinding disease.

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Conflict of interest

The authors have declared that no competing interests exist.

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