The epidemiology of acute angle closure in Scotland: a prospective survey.

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Abstract:

Purpose:

To estimate the incidence, and describe the clinical features and short term clinical outcomes of acute angle closure (AAC).

Methods:

Patients with newly diagnosed AAC were identified prospectively over a 12-month period (November 2011 to October 2012) by active surveillance through the Scottish Ophthalmic Surveillance Unit reporting system. Data were collected at case identification and at 6 months follow up.

Results:

There were 114 cases reported, giving an annual incidence of 2.2 per 100,000 (95% CI 1.9–2.6) in the whole population and 3.4 per 100,000 for those age ≥30 years old (95% CI 2.9–3.9) in Scotland. Precipitating factors were identified in 40% of cases. Almost 1 in 5 cases was associated with topical dilating drops. Best corrected visual acuity (BCVA) at presentation ranged from 6/6 to perception of light. The mean presenting intraocular pressure was 52 mmHg (SD 11). Almost 30% cases had a delayed presentation of 3 or more days. At 6 months follow up, 75% had BCVA of 6/12 or better and 30% were found to have glaucoma at follow up. Delayed presentation (>2 days) was associated with higher rate of glaucoma at follow up (22.6% vs 60.8%, *p<0.001*), worse VA (0.34 vs 0.74 LogMAR, *p<0.0001*) and need for more topical medication (0.52 vs 1.2, *p=0.003*) to control IOP.

Conclusion:

The incidence of AAC in Scotland is relatively low compared to the Far East countries, but in line with previous European data. Almost 1 in 5 cases were associated with pupil dilation for retinal examination.

(word count: 250)

Introduction:

Glaucoma is the leading cause of irreversible blindness.[1] While primary angle-closure glaucoma (PACG) is thought to account for a quarter of all primary glaucoma cases compared to three quarters for primary open angle glaucoma (POAG), it is more visually destructive, with the proportions of blindness caused by each being almost equal[1]. Current estimates suggest 19-42% cases of primary angle closure disease in European derived population present acutely[2 3].

The epidemiology of acute angle closure (AAC) in Europeans is not well described. Current reported incidence rates are estimated from retrospective reviews of patient attendances and subsequent extrapolation of results[4-6] or from Hospital Episode Statistics (HES) data[7]. The reported incidence in European countries ranged from 1.4 to 4.2 per 100 000 per year.[4-6]

The main aims of this study were to estimate the incidence of AAC in Scotland, investigate the ocular and demographic risk factors associated with AAC and the short term clinical outcomes of AAC. This is the first prospective epidemiological study of AAC in Europe.

Methods:

Patients with newly diagnosed AAC were identified prospectively through active surveillance by the Scottish Ophthalmic Surveillance Unit (SOSU) during a 12-month period between 1st of November 2012 to 31st October 2013. This methodology is commonly used by the sister organisation British Ophthalmic Surveillance Unit (BOSU)[8]. Reporting ophthalmologists were sent a baseline questionnaire by post to gather information on patient's demographic data, clinical findings, and management. Another follow up questionnaire was sent to reporting ophthalmologist again by post at 6 months. Only residents within Scotland with a new diagnosis of acute angle closure were included in the study.

The inclusion criteria are: any two of the symptoms: blurring of vision; ocular or peri-ocular pain; nausea or vomiting; and antecedent history of intermittent blurring of vision with haloes; any of the signs: corneal edema; unreactive mid-dilated pupil; iris bombe; conjunctiva injection and IOP≥30.[9] The examining ophthalmologist also need to perform gonioscopy examination to confirm the presence of occluded angle in the affected eye. The presence of occludable angle in the fellow eye was acceptable if the clarity of the affected eye was not satisfactory. 'Occludable angle' was defined as an angle in which ≥180° (about 2 quadrants) of the posterior trabecular meshwork could not be seen. Exclusion criteria included neovascularisation and pseudophakia. The 2011 Scottish census was used to calculate the annual incidence per 100 000 of the population and cases for 100,000 for those age ≥30 years old.

The definition of glaucoma was based on the International Society for Geographical and Epidemiological Ophthalmology (ISGEO) classification[10], namely:

- "Glaucoma: "glaucoma" is reserved for people with established, visually significant end organ damage. It is defined as structural optic disc damage exceeding the specified limit (glaucomatous optic neuropathy) and glaucomatous visual field loss. Patient with AAC attack may not develop "glaucoma" as defined above.
    1. Glaucomatous optic neuropathy: Eyes with a vertical cup/disc ratio (vCDR) of ≥0.70 (≥97.5th percentile of normal population) or a neuroretinal rim width reduced to <0.1 CDR (between 11 to 1 o'clock or 5 to 7 o'clock).
    2. Glaucomatous visual field loss: The glaucoma hemifield test graded "outside normal limits" and a cluster of three contiguous points at the 5% level on the pattern deviation plot, using the threshold test strategy with the 24-2 test pattern.

- If the subject could not satisfactorily complete visual field testing but had a CDR or CDR asymmetry >99.5th percentile for the normal population (vCDR>0.8), glaucoma was diagnosed solely on the structural evidence. And, there should be no alternative explanation for CDR abnormality finding.

- If the optic disc is not seen and field test is impossible, glaucoma is diagnosed (A) The visual acuity <3/60 and the IOP >99.5th percentile, or (B) The visual acuity <3/60 and the eye shows evidence of glaucoma filtering surgery."

Visual acuity was recorded at presentation and at 6-month follow-up. In line with previous studies, a VA of <6/60 Snellen in the affected eye was classified as severe visual impairment.[11 12] Reporting ophthalmologists were also asked if cases were eligible for registration as partial sighted (sight impaired) or blind (severely sight impaired) according to the criteria defined by the Department of Health on Certificate of Vision Impairment.[13]

The clinical outcomes were compared between those who had delayed presentation of 3 days or more and those who presented less than 3 days. Chi-square test was used to compare number of co-existing glaucoma and the need for surgical intervention between the two groups. An independent t-test was applied to compare the mean corrected distant visual acuity, mean number of topical medications and mean durations of hospital admissions between 2 groups. A *p*-value of <0.05 was considered significant. Analysis was performed using Statistical Package for Social Sciences software version 20.0 (SPSS, Chicago, IL, USA). Caldicott approval and ethics permission were granted.

Result:

Incidence

There were 118 AAC cases reported during the 12-month period between 1st November 2012 and 31st October 2013 and the SOSU card return rates for the study was 68%. The reporting ophthalmologist did not return the subsequent questionnaires for 19 cases, 4 cases were excluded as having secondary mechanisms (aqueous misdirection, n=2; pseudophakic pupil block, n=1; neovascular glaucoma, n=1). Incidence rates were calculated on the basis of 118 reported cases. Clinical outcomes were reported using data from 95 cases with available data. In 2011 census, Scotland has a population of 5,295,403 and 65% (n=3,460,281) were 30 years and older.[14] With 114 primary AAC cases (included 19 cases for whom the follow-up questionnaire was not returned) over 12 months, the estimated annual incidence of AAC in Scotland was 2.2 cases per 100,000 (95% CI 1.9 – 2.6) of the whole population and 3.4 per 100 000 per year (95% CI 2.9 – 3.9) for population of ≥ 30 years old.

Presenting features:

Table 1 summarises the baseline characteristics of the 95 eyes of 89 patients. Eighty-three patients presented with unilateral AAC attack and six patients presented with bilateral AAC. Mean patient age was 70.9 (SD 9.1, range 53 to 91 years old). The ratio of males to females was 1:1.6. The incidence of AAC was higher during winter 2012 and autumn 2013, with 28 cases (29%) and 29 cases (31%) respectively. Precipitating factors were identified in 38 cases (40%) (table 1), the common precipitating factors were topical eye drops for pupil dilatation (n=18), beta-2 agonist (n=6) and selective serotonin receptor inhibitor (n=5)**.** 53% of patients were symptomatic for 1-2 days before presenting to ophthalmologist. 14 patients (15%) were seen within 24 hours of their symptoms, and 27 (28%) had delayed presentations of 3 days or more.

There were 33 patients (35%) with a visual acuity worse than 6/60 at presentation. The mean IOP was 52mmHg (range, 30-78). All cases had IOP of ≥30 and unreactive mid dilated pupil.

Table 1: Epidermiology and predisposing factors of acute angle closure in 95 cases

Clinical Characteristics at Presentation	
Age, mean (range)	71 (53-91)
Gender	
Male	36 (38)
Female	59 (62)
Ethnics	
White	94 (99)
Asian or British Asian	1 (1)

Seasonal variation	
Winter (Nov, Dec, Jan)	28 (29)
Spring (Feb, Mar, Apr)	16 (17)
Summer (May, Jun, Jul)	22 (23)
Autumn (Aug, Sep, Oct)	29 (31)
Precipitating factors	
None	57 (60)
Yes	38 (40)
Topical dilating drops	18 (19)
Beta 2 agonist	6 (6)
Selective serotonin receptor inhibitor	5 (5)
Tricyclic antidepressant	3 (3)
Anticholinergic bronchodilator	2 (2)
Nasal decongestant	1 (1)
Anti-histamine	1 (1)
Other systemic*	2 (2)
Symptoms at presentation	
Ocular or peri-ocular pain	79 (83)
Nausea and vomiting	42 (44)
Blurring of vision	82 (86)
Antecedent history of intermittent blurring of vision with haloes	22 (22)
Duration of symptoms	
Unknown	4 (4)
< 24 hours	14 (15)
1 – 2 days	50 (53)
≥ 3 days	27 (28)
Presenting vision	
6/6 to 6/12	26 (27)
6/15 to 6/60	36 (38)
>6/60	33 (35)
Mean IOP at presentation, (range)	52 (30- 78)
Clinical signs at presentation.	
Corneal epithelial edema	76 (80)
Unreactive mid dilated pupil	95 (100)
Iris bombe	9 (10)
Conjunctiva injection	71 (75)
IOP≥30	95 (100)

Data are expressed as n (%) of 95 eyes, unless otherwise noted. *Levodopa (n=1) and Mirtazepine (n=1)

Treatment:

Table 2 shows the management of AAC in the first 72 hours and during the 6 months follow up. Every patient had topical medications at presentation to lower pressure. Majority of patients had laser peripheral iridotomy (87%), IV acetazolamide (85%) and oral acetazolamide (85%). IV mannitol was only used in 15% of patients. Rarely, patients needed surgical peripheral iridectomy (n=1), cyclodiode

laser (n=1) and phacoemulsification and IOL implant (n=1) within the first 72 hours of management. Only 68% of patients had prophylactic laser peripheral iridotomy on the fellow eye.

During the 6 months follow up, 38% of patients were still on topical pressure lowering medications and 35% of patients had undergone phacoemulsification and IOL implant on the affected eye.

Table 2: Management of the affected eye and the fellow eye:

	Within 72 hours (95 eyes)	**At 6 months follow up (89 eyes)**
Affected eye		
Topical medication	95 (100)	34 (38)
Laser peripheral iridectomy	83 (87)	3 (3)
IV Acetazolamide	81 (85)	0
Oral Acetazolamide	68 (72)	0
IV Mannitol	14 (15)	0
Laser peripheral iridoplasty	2 (2)	0
Supine position	2 (2)	0
Phaco+ IOL	1 (1)	33 (35)
Surgical iridotomy	1 (1)	2 (2)
Cyclodiode laser	1 (1)	1 (1)
Paracenthesis	0	0
Primary trabeculectomy	0	2 (2)
ECCE	0	1 (1)
Fellow eye		
Laser peripheral iridotomy	65 (68)	9 (10)
Topical medication	22 (23)	___
Laser peripheral iridoplasty	2 (2)	0
Surgical peripheral iridotomy	2 (2)	2 (2)
Phaco + IOL	5 (5)	5 (5)

Data are expressed as n (%), unless otherwise noted

Outcomes/ follow up:

The 6-month follow-up questionnaire return rate was 94% (89/95). Table 3 summarises the clinical characteristics. 75% of patients achieved vision of 6/12 or better in 6 months. Unfortunately, six patients (7%) had vision of 6/60 or worse. Of those patients, 5 had glaucoma at follow up and 1 had retina vein occlusion. Mean IOP had also improved from the mean of 52 mmHg to 16 mmHg. The average days of hospital admission and outpatient visits were 1.6 days and 3.7 visits respectively. 33% of patients were found to have glaucoma during follow up. None of the patients was eligible for sight impairment registration after AAC attacks.

Table 3: Clinical characteristic at 6 months follow up of 89 cases

Clinical characteristics at 6 months follow up	
Vision of 6/12 or better	65 (75)
Vision worse than 6/60	6 (7)
Mean IOP, (range)	16 (4-55)
Mean days of hospitalisation, (range)	1.6 (0-15)
Mean outpatient clinic visits over the last 6 months (range)	3.7 (0-18)
Further AAC attack after 72 hours	8 (9)
Clinical outcomes:	
Previous AAC but no glaucoma	60 (67)
Previous AAC and glaucoma	29 (33)
Sight impairment registration	
Not eligible	88 (99)
Already registered before AAC attack	1 (1)
Registered after AAC attack	0

Data are expressed as n (%) of 89 eyes, unless otherwise noted

As shown on table 4, patients with delayed presentation of 3 days or more had a significantly higher rate of glaucoma at follow up (22.6% vs 60.8%, *p<0.001*), worse BCVA (0.34 vs 0.74 LogMAR, *p<0.0001*) and depended on more types topical medication (0.52 vs 1.2, *p=0.003*) to control IOP.

Table 4: Difference in clinical outcomes (at 6 months) between patients with symptoms of less than 72 hours and more than 72 hours at presentation.

	<72 hours (n= 62)	≥72 hours (n=23)	p= value
% With glaucoma	22.6% (14)	60.8% (14)	***0.001*** (chi- square)
% Need topical medication(s) to control IOP	34% (21)	56% (13)	0.058 (chi- square)
% Need for surgical intervention	38.7% (24)	47.8% (11)	0.450 (chi-square)
Mean BCVA (LogMAR equivalent)	0.34	0.74	***0.000*** (student t-test)
Mean no of topical medication	0.5	1.2	***0.003*** (student t-test)
Mean no of days in hospital	1.8	1.5	0.185 (student t-test)

Discussion:

This is the first prospective epidemiological study of AAC in the Europe. Our study estimates an annual incidence of 2.2 cases per 100,000 in general population and 3.3 per 100,000 in population for those ≥30 years old.

There is minimal contemporary data for comparison, with historical incidence rates of 4.2 per 100,000 population in Israel in 1985; 3.8 per 100,000 population in Finland for the period between 1973 and

1986. Interestingly our incidence rate is similar to that estimated in a recent analysis of AAC cases presenting to a single tertiary referral hospital with subsequent extrapolation to Scotland as a whole, whereby the expected annual incidence was 1.4 cases per 100,000 per year in Scotland.

There have been recent reports that the incidence of AAC may be reducing with time. An analysis of Hospital Episode Statistics data from England reported in 2010 that the incidence of AAC appeared to have halved over the past decade presumably due to increasing number of laser peripheral iridotomies performed, phacoemulsification cataract surgery and greater awareness of angle-closure mechanisms as an important, treatable cause of glaucoma disease[7 15] A similar analysis using data from the Information Service Division (ISD) Scotland reported the rate of AAC to have reduced by 46% over the period between 1998 and 2012.[15]. In the far east, Singapore has much higher incidence of AAC, Seah et al reported 12.2 per 100 000 in populations over 30 years old. This is most likely secondary to different ethnic groups. Scotland has 96% of white population and Singapore has 80% of Chinese origin. It is well established that Chinese has higher rate of PACG.[9 16]

Precipitating factors were identified in 40% of cases. Almost 1 in 5 of overall cases were associated with recent topical dilating drops administered as part of a recent routine community Optometric examination. Another 1 in 5 cases were associated with prescribed and/ or over the counter medications, thus highlighting the importance of careful clinical history taking including detailed drug history when assessing patients with AAC. For prescribed medications, beta-2 agonist (n=6), anti-selective serotonin receptor inhibitor (n=5) and tricyclic antidepressant (n=3) were the frequent causes in our cases. There was only two AAC precipitated by over the counter medications, namely nasal decongestant (n=1) and antihistamine (n=1). For comparison, the case series by Choong and co-workers identified possible precipitating factors in only 19% of cases.[17]

In our study, 28% of AAC cases were diagnosed 3 or more days after the onset of symptoms. Compared to those who presented less than 3 days, they were more likely to be found to have glaucoma at follow up ($p<0.001$) and have worse corrected distant visual acuity ($p<0.001$). This is similar to the previous report on the outcomes acute angle closure in Asian population. Tan et al found that longer duration of symptoms and time taken to break acute attack are associated with primary angle closure glaucoma.[18]

There is limited evidence about the percentage of AAC eyes that develop PACG in the white Caucasian population. Our study shows that at 6 months follow up, 33% have glaucoma and 38% were still on topical IOP-lowering medication. This result is consistent with previous publications on White Caucasians.[5 17] However, a more recent study by Andreatta et al suggested a lower rate of 15% on

a long term follow up, this may be explained by the exclusion of PACG at presentation in their study.[19]

At 6 months follow up, our study showed that only 6 patients (7%) had corrected distant visual acuity of <6/60, compared to 35% at presentation. Glaucomatous optic neuropathy is responsible for 5 out of 6 patients (83%) in our study. Previous studies on Caucasians reported reduced BCVA of <6/60 in 12-15% of eyes in short and long term follow up.[11 17 19 20] Interestingly, Tan et al showed that 90.5% of their cohort had BCVA >6/12 at final follow up and none had BCVA of worse than 6/60.[18] The inconsistent results may be due the variability of follow up durations, different racial origin and different inclusion criteria. Based on the criteria specified by Department of Health on Certificate of Vision Impairment, none of our patients were eligible for sight impairment registration following AAC attack.

This study used a proven method of active case ascertainment to identify incident cases,[8] however, there are several limitations. Firstly, there are likely to be source of under-ascertainment such as cases not being made aware to the consultant ophthalmologist, non-participation and unreported cases. Hence, the incidence reported in this study is a minimum rate. Secondly, we modified inclusion criteria for AAC used by other population study.[9] We only included patients with IOP>30 at presentation instead of 19 and subjects did not necessary have to have 4 out of 5 of the signs as suggested.[9] We believed that if we were to follow the inclusion criteria as Seah et al, true AAC cases would have been missed. All our patients, however, have unreactive mid-dilated pupils, IOP>30 and occluded angle on the affected eye or occludable angle on the fellow eye.

In conclusion, this is the first prospective incidence study of AAC in Scotland. We estimate the incidence to be 2.2 cases per 100,000 of the general population or 3.4 per 100,000 for those ≥30 years old for 2011-12, where 96% of the populations are White Caucasian. Almost 1 in 5 cases were associated with pupil dilatation for retinal examination.

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