Retrospective analysis of risk factors for late presentation of chronic glaucoma

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Abstract

***Background*—Why some individuals present to the ophthalmologist in the early stages of chronic glaucoma but others present with very advanced visual field loss is a question which has received little attention. This study is an attempt to identify some basic characteristics of people who present with late glaucoma.**

***Methods*—A retrospective case-control study by medical record review was employed. 100 cases and 100 controls were identified from the notes of patients presenting to Moorfields Eye Hospital glaucoma service between July 1993 and July 1995. Cases were defined as new patients presenting with absolute field loss within five degrees of fixation and a cup to disc ratio of greater than 0.8 in one or both eyes. Controls were new patients with no absolute field loss within 20 degrees in either eye, but otherwise typical glaucomatous field loss and a cup to disc ratio of greater than 0.5 or a difference of 0.2 or more between the discs.**

***Results*—The ethnic origin, sex, referral source, presenting IOP, and age of the subjects studied were independently associated with late presentation. An African Caribbean patient is estimated to be four and a half times more likely to attend with advanced field loss than a white patient of similar age, sex, IOP, and referral source (adj OR: 4.55, 95% CI [1.57, 13.18]). A female patient is estimated to be one third (0.34, [0.15, 0.74]) as likely to attend late than a male patient of the similar age, IOP, ethnic origin, and referral source. A patient referred via any source other than an optometrist with the correct diagnosis is estimated to be greater than four times (4.32 [1.89, 9.88]) more likely to be a late attender than a patient of the same sex, ethnicity, and similar age but referred with a diagnosis of glaucoma. There was a trend of increasing odds of late presentation with increasing age (adj OR per 10 years, baseline 40–49 years 1.68 [1.22, 2.20]). A patient whose presenting IOP is 21–25 mm Hg is estimated to be a quarter (0.24, [0.09, 0.64]) as likely to attend with advanced field loss than a patient of the same ethnic origin, sex, age, referral source, but with presenting IOP of greater than 31 mm Hg**

***Conclusions*—These data strongly suggest that certain subgroups of patients with glaucoma are likely to be at greater risk of presenting with advanced and irremediable field loss.**

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Despite extensive research and new treatments glaucoma remains a major cause of blindness in the developing and developed world. Risk factors for the development of glaucoma have been extensively investigated but those for glaucoma blindness have received little attention.

A number of workers have shown that patients who present with advanced glaucoma are at a substantial risk of blindness.[1–3] Grant and Burke found that eyes with a visual field defect at the start of treatment were more likely to progress to blindness than eyes in which treatment is started at the stage where there is no field loss (although whether all the patients in the second group had glaucoma is difficult to ascertain).[1] Wilson *et al* looked at risk factors for rate of progression of glaucomatous visual field loss in 57 patients and found that initial visual field was the strongest determinant of rate of further visual field loss.[4] Patients in their study deteriorated 11.7 times faster in the more advanced eyes. Mikelburg *et al* measured scotoma mass of fields and compared them with the rate of subsequent decline.[5] They found that when scotoma mass was small (that is, early disease) rate of visual field loss was slow but when the scotoma mass was large, rapid linear progression of visual fields occurred. Miller and Karseras stated that, from their series, glaucoma is more benign in patients with considerable visual reserve.[6]

These studies suggest that late presentation is a considerable risk factor for glaucoma blindness.

Patients and methods

All patients referred from the primary care clinic at Moorfields Eye Hospital to the glaucoma service between July 1993 and July 1995 who had not previously been diagnosed as having chronic glaucoma were identified.

For simplicity, the first 100 consecutively identified cases and 100 controls that fitted the criteria were used. This study was a pilot, an objective of which was to provide estimates for use in sample size calculations in subsequent work.

Cases were defined as typical glaucomatous field loss *within* five degrees of fixation but beyond 30 degrees in one or both eyes. The glaucoma could be of any chronic type as long as field loss was present. There had to be at least two consecutive fields confirming loss and a cup to disc ratio of more than 0.8. The only exception to this was when the field loss was so

Table 1 Study factors by case/control status

Study factor	*No of controls*	*No of cases*	*Total no of patients (%)*
Age (years):			
40–50	15	8	23 (11.5)
51–60	19	11	30 (15.0)
61–70	38	26	64 (32.0)
71–80	26	41	67 (33.5)
81–90	2	13	15 (7.5)
91 +	0	1	1 (0.50)
Sex:			
Male	47	58	105 (52.5)
Female	53	42	95 (47.5)
Ethnic origin:			
White (British)	77	45	122 (61)
African Carribean	8	19	27 (13.5)
Asian	9	9	18 (9)
White (other European)	2	6	8 (4)
Not ascertained	4	21	25 (12.5)
Referral source:			
Optometrist with correct diagnosis	85	51	136 (68)
Other	15	49	64 (32)
Presenting IOP (mm Hg):			
>31	26	57	83 (41.5)
26–30	31	25	56 (28)
21–25	34	13	47 (23.5)
<21	9	5	14 (7)
Glaucoma diagnosis:			
POAG	84	72	156 (78)
PXF	2	10	12 (6)
Chronic angle closure	6	12	18 (9)
Normal tension	7	5	12 (6)
Other	1	1	2 (1)
Ocular pathology:			
Not significant	91	75	166 (83)
Cataract	3	15	18 (9)
AMD	3	3	6 (3)
CRVO/BRVO	3	1	4 (2)
Corneal problem	0	4	4 (2)
Uniocular/amblyopic	2	0	2 (1)
Systemic disease:			
Generally in good health	60	59	119 (59.5)
Hypertension	23	29	52 (26)
Diabetes	6	5	11 (5.5)
Other chronic diseases	8	5	13 (6.5)
Hypertension and diabetes	3	2	5 (2.5)
Family history:			
Nil	67	75	142 (71)
Glaucoma in 1st or 2nd degree relative	33	25	58 (29)

advanced that field testing was not possible. Fields (Henson or Humphrey) were excluded if there were more than 20% fixation losses or false positives errors were more than 33%.[7]

Controls had typical glaucomatous field loss but *no* absolute scotomas within 20 degrees of fixation in either eye (therefore there was no doubt as to their glaucoma status). The glaucoma could be of any chronic type as long as field loss was present. There had to be at least two consecutive fields confirming this loss and a cup to disc ratio of greater than 0.5 must be present or a difference of more than 0.2 must have been noted. Fields (Henson or Humphrey) were excluded if there were more than 20% fixation losses or false positives errors were more than 33%.

For each case and control the following information was extracted from the notes:

(1) Basic data—age, sex, and ethnic origin.
(2) Referral source of the patient—this was initially divided into four groups:
   (i) from optometrist with a presumptive diagnosis of glaucoma
   (ii) from an optometrist but with no mention of glaucoma in the referral letter
   (iii) From a general practitioner with a presumptive diagnosis of glaucoma
   (iv) From a general practitioner with no mention of glaucoma in the referral letter

   In practice, a more meaningful comparison was between those patients referred with a presumptive diagnosis of glaucoma from their optometrist and those who had come from other sources (that is, (ii), (iii), and (iv) combined).
(3) Type of glaucoma diagnosed by ophthalmologist.
(4) Intraocular pressure (IOP) at presentation.
(5) Other significant ocular pathology present.
(6) Presence of systemic disease—for example, hypertension, diabetes.
(7) Family history of glaucoma.

The data were analysed using STATA[8] to investigate the effects of each study factor on the odds of being a late presenter. Estimates of the odds of being a late presenter with approximate 95% confidence intervals, by study factors were computed by logistic regression. In each case the first category of each study factor was used as a baseline, either because its selection appeared to give the most meaningful results or because it contained the greater number of observations and hence its choice favoured precision. Unadjusted and adjusted odds ratios are presented—adjustment being made for factors found to be statistically significant in the univariate models. A χ^2 test for trend was conducted to assess departure from linearity in the apparent trend of increasing odds of late presentation with increasing age.

Results

Table 1 shows the characteristics of the study population. The majority (73.5%) of patients were over 60 years and similar numbers of men and women were studied. More than half of the study patients were white (61%), 13.5% were African Caribbean, and 9% were Asian; 12.5% of the group did not have their ethnic origin recorded in their notes. The majority of patients (68%) had been referred to the hospital eye service by optometrists with a presumptive diagnosis of glaucoma. The remaining 32% had either come from their general practitioner or from their optometrist but without a diagnosis of glaucoma mentioned in the referral letter. A total of 41.5% of patients studied had a presenting IOP of greater than 31 mm Hg, only 7% had an IOP of less than 21 mm Hg at presentation. The most common glaucoma diagnosis made by the ophthalmologist was primary open angle glaucoma (POAG); 78% of the patients were diagnosed with POAG compared with 9% chronic angle closure (CACG), and 6% each of pseudoexfoliation (PXF) and normal tension glaucoma (NTG). Most patients (83%) had no other significant ocular pathology mentioned in the notes and 59.5% were generally in good health; 29% of the patients had a family history of glaucoma mentioned in their notes.

Table 2 shows the estimated effect of each study factor on late presentation. These data provide strong evidence of independent associations between late presentation and the age,

Table 2 Estimates of the effect of each study factor on late presentation

Study factor	*Odds of being a late presenter*	*95% CI*	*OR*	*95% CI*	*Adj OR***	*95%CI*
Age per 10 years:						
40–50	0.53	(0.23,1.26)	1			
51–60	0.58	(0.28,1.22)	1.09	(0.35,3.38)		
61–70	0.68	(0.42,1.23)	1.28	(0.48,3.46)		
71–80	1.58	(0.97,2.58)	2.96	(1.10,7.95)		
81–90	6.50	(1.47,28.80)	12.19	*(2.19,67.95)		
91 +						
Baseline 40–50 years			1.68	(1.28,2.20)	1.78	(1.22,2.60)
Sex:						
Male	1.23	(0.84,1.81)	1			
Female	0.79	(0.53,1.19)	0.64	(0.37,1.12)	0.34	(0.15,0.74)
Ethnic origin:						
White (British)	0.58	(0.41,0.84)	1			
African Caribbean	2.38	(1.04,5.43)	4.06	(1.65,10.04)	4.55	(1.57,13.18)
Asian	1.00	(0.40,2.52)	1.71	(0.63,4.63)	1.22	(0.36,4.11)
White (other European)	3.00	(0.61,14.86)	5.13	(0.99,26.52)	2.01	(0.26,15.61)
Referral source:						
Optometrist with correct diagnosis	0.60	(0.42,0.85)	1			
Other	3.27	(1.83,5.83)	5.44	(2.77,10.68)	4.32	(1,89,9.88)
Presenting IOP (mm Hg):						
>31			1			
26–30			0.37	(0.18, 0.74)	0.43	(0.18,1.03)
21–25			0.17	(0.18, 1.03)	0.24	(0.09,0.64)
<21			0.25	(0.08, 0.38)	0.24	(0.09, 0.64)
Glaucoma diagnosis:						
POAG	0.86	(0.63,1.17)	1			
PXF	5.00	(1.10,22.82)	5.83	(1.24,27.49)	3.47	(0.62,19.50)
Chronic angle closure	2.00	(0.75,5.33)	2.33	(0.83,6.53)	2.48	(0.69,8.90)
Normal tension	0.71	(0.23,2.25)	0.83	(0.25,2.74)		
Ocular pathology:						
Not significant	0.82	(0.61,1.12)	1			
Cataract	5.00	(1.45,17.27)	6.06	(1.69,21.75)	4.20	(0.93,19.00)
AMD	1.00	(0.20,4.96)	1.21	(0.24,6.19)	0.72	(0.10,5.11)
Systemic disease:						
Generally in good health	0.98	(0.69,1.41)	1			
Hypertension	1.26	(0.73,2.18)	1.28	(0.67,2.47)	0.76	(0.32, 1.81)
Diabetes	0.83	(0.25,2.73)	0.85	(0.25,2.93)	0.46	(0.09, 2.25)
Other chronic diseases	0.63	(0.20,1.91)	0.64	(0.20,2.06)	0.28	(0.06, 1.37)
Hypertension and diabetes	0.67	(0.11,3.99)	0.68	(0.11,4.20)		
Family history:						
Nil	1.19	(0.81,1.56)	1			
Glaucoma in 1st or 2nd degree relative	0.76	(0.45,1.27)	0.68	(0.37,1.25)	0.86	(0.37,2.04)

*Test against departure from linearity: χ^2 (3 df) 4.39, p=0.222. **Adjusted for age, ethnic origin, referral source, and presenting IOP.

sex, ethnic origin, referral source, and presenting IOP of the study patient. We estimate a trend of increasing odds of late presentation with increasing age over 40 years (adj OR: 1.68 [1.22,2.20) in sufferers of the same sex, ethnic and IOP group, and referral source. A woman is estimated to be one third (0.34 [0.15, 0.74]) as likely to be a late presenter than a man of the same ethnic, group, referral source and similar age, and presenting IOP. These data provide strong evidence of association between ethnicity and late presentation that is not explained by differences in age, sex, IOP, or referral source. An African Caribbean patient is estimated to be four and a half times (4.55 [1.57, 13.18]) more likely to present with advanced loss than a white patient of the same sex and referral source and similar age and IOP. These data suggest also that Asian patients may be at slightly increased odds of late presentation than the white patients, although numbers were small and the confidence interval includes the unity of no association. Referral source is shown by these data to be strongly associated with late presentation. A patient referred via any source other than an optometrist with the correct diagnosis is estimated to be greater than four times (4.32 [1.89, 9.88]) more likely to be a late attender than a patient so referred of the same sex, ethnicity and similar age, and IOP. These data provide evidence too of association between presenting IOP and field loss. Estimated at greatest odds of late presentation are patients with presenting IOP of greater than 31 mm Hg. A patient with a presenting IOP of 21–25 mm Hg is estimated to be a quarter (0.24 [0.09, 0.64]) as likely to attend with advanced field loss as a patient with presenting IOP of greater than 31 mm Hg but of the same sex, age, ethnic origin, and referral source.

These data provide little evidence of association between late presentation and any of the other factors studied, but this may well be a consequence of the low power associated with a pilot study of this size.

Discussion

There have been a number of hospital based studies that have estimated the proportion of glaucoma patients who present with substantial visual field loss. Grant and Burke calculated that one third of the patients who had become blind from glaucoma had done so before they had sought medical attention for their eyes.[1] Elkington *et al* and Sheldrick *et al* gave respectively figures of 33% and 20% presenting late.[9 10] The West of Ireland population based study found that 10% of people with glaucoma were severely visually impaired at first examination.[11]

It is of note that of these, only Grant and Burke's study included non-white patients and that their estimate of late presentation was greater than the other studies. Our data suggest that patients of African Caribbean origin are

over four times more likely to present late than comparable white patients. There are a number of possible reasons for this including a more rapid disease progression, earlier onset of disease (which is also when glaucoma testing is less likely during routine sight testing), and poorer access/uptake of eye care services.[12–14]

Our results provide strong evidence of an association between age and late presentation. The risk of late presentation appears to increase linearly with increasing age over 40 years. This seems plausible since both the prevalence and incidence of glaucoma rise with age—as does the incidence of blind registrations from glaucoma.[15] Other factors such as difficulties with mobility and social isolation can reduce access to sight (and therefore glaucoma) testing may also contribute to the later presentation.

In Britain, the optometrist plays a pivotal role in glaucoma detection. One study showed that 90% of glaucoma patients are referred to hospital on the basis of abnormal findings by an optometrist.[10] Our results estimate that a patient who has not been correctly referred to the hospital by an optometrist is over four times more likely to be a late presenter than a comparable patient who has. Patients referred from optometrists with a diagnosis of glaucoma are more likely to be in the earlier stages of the disease. This suggests that late presenters attend optometrists who do not test for glaucoma, or more probably, late presenters are people who tend not to go for regular sight tests.

We estimate that women are more likely to present in the early stages of glaucoma than men of similar age, presenting IOP, ethnic origin, and referral source. There is no firm evidence of a difference in the prevalence of glaucoma in men and women.[12] Glaucoma is not known to be a more rapidly progressive disease in men so the most plausible explanation for the earlier presentation of women is that their rate of sight testing (and general use of all preventative health services) is higher and this is supported by evidence from the General Household Survey.[16]

Whether an individual presents late in the course of their glaucoma is likely to be a function of the rapidity of their visual field deterioration and the frequency of their sight tests. An individual with a rapid decline can lose significant field even with two yearly sight tests—unless tested during an early, but detectable, phase of the disease. Conversely, an individual with a slowly declining field but who does not attend for sight testing for some years (or does not have a glaucoma examination during their sight tests) is at risk of late presentation for a different reason.

Individuals with rapid field loss are likely to be those with higher IOPs.[2] The influence of rapidity of field loss on late presentation is thus supported by our study in that we estimate that patients with presenting IOPs of greater than 31 mm Hg are at greatest risk of late presentation. Further support for this is that patients with PXF and CACG appear at greater risk of late presentation, although the confidence intervals are wide reflecting the small numbers.

NTG might be expected to be associated with late presentation since detection relies on visual field analysis by the optometrist or recognition of suspicious discs rather than raised IOP. One survey showed perimetry was only performed by 10% of optometrists.[12] Our data do not support this, suggesting perhaps that visual field deterioration is slower in NTG patients than other types of glaucoma. It is important to treat the NTG data with some caution as the numbers are small.

Our data provide little evidence of any association between late presentation and other pathology—be it systemic or ocular. Patients with cataract do appear to be slightly, albeit not statistically, significantly at greater risk of late presentation but we would advise cautious interpretation since "significant" cataract was only defined as mention of lens opacity in the clinical notes and was thus highly subjective.

Family history is well recognised as a risk factor for glaucoma and one might well expect it to be protective against late presentation because of increased awareness of the condition and eligibility for free sight tests. Our data are consistent with a weak protective effect although this was not statistically significant—perhaps a reflection of recall bias.

There are a number of potential biases in the study, the first of which is that it relied on information taken from medical notes. In some cases this was incomplete—for example, the ethnic origin of the patient, and in others it may have been inaccurate—for example, systemic disease. Another potential bias in the study could have arisen because case/control status was decided from the notes before the other information was extracted, which may have influenced the subsequent collection of information. While plausible, consideration should be given as to whether these observed associations might be due to residual confounding or perhaps bias. While this study has enabled adjustment for several potential confounders, bias due to unmeasured confounders such as socioeconomic status cannot be excluded.

As mentioned above, late presentation is a function of rapidity of visual field loss and frequency of sight testing. It is not possible in this pilot study to assess the relative influence of these two determinants in the risk factors that have been isolated but in the prospective study currently being undertaken this will be possible. The prospective study will also remove the bias of medical record review and be able to look at a far greater range of potential risk factors.

Conclusions

These data provide strong evidence that the risk of a patient over 40 years with chronic glaucoma presenting to the hospital eye service with advanced visual field loss is independently associated with sex, age, ethnic origin, referral source, and presenting IOP. Certain subgroups of patients with glaucoma are likely to be at greater risk of permanent visual impairment.

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