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Five-year incidence of cataract in older persons with diabetes and pre-diabetes

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Abstract

PURPOSE To investigate longitudinal associations between diabetes and the 5-year incidence of cataract and cataract surgery. (A population-based, cohort study of 2335 persons with baseline ages 49 years or older resident in the Blue Mountains region, west of Sydney, Australia).

METHODS Baseline information on diabetes history was collected during an interviewer-administered questionnaire. Impaired Fasting Glucose (IFG) was defined as venous plasma glucose between 6.0 and 7.0 mmol/L and newly diagnosed diabetes as plasma glucose >7.0 mmol/L, using fasting blood glucose measurements taken at baseline. Retroillumination lens photographs from the baseline and 5-year follow-up examinations were graded for presence of cortical, posterior subcapsular (PSC) and nuclear cataract.

RESULTS We found a 2-fold higher 5-year incidence of cortical cataract in participants with IFG, multivariate adjusted odds ratio (OR) 2.2, 95% confidence interval (CI) 1.1–4.1. Incident PSC cataract was more frequent among persons with diabetes, but this association was statistically significant only for those with newly diagnosed diabetes, multivariate adjusted OR 4.5 (CI 1.5–13.0). There were no statistically significant associations found between incident nuclear cataract or cataract surgery and either diabetes or IFG.

CONCLUSIONS These epidemiological data suggest that IFG, a pre-diabetic condition, may be a risk factor for the development of cortical cataract.

Key words Cataract incidence; diabetes; impaired fasting glucose; elderly

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Introduction Relationships between diabetes mellitus and cataract have been demonstrated in different populations by a number of previous studies. Many studies have reported links between diabetes and prevalent cortical,[1–4] posterior subcapsular,[4] and nuclear[5] cataract and with a history of cataract surgery.[4,5] Few studies, however, have reported longitudinal associations between diabetes and cataract incidence.[6]

As temporal relations between risk factors and disease cannot usually be determined from prevalence data, we aimed in this report to examine the relationship between diabetes mellitus and 'pre-diabetes'[7] at baseline and the five-year incidence of cataract and cataract surgery in a cohort of older Australians attending the Blue Mountains Eye Study (BMES).

Materials and methods The Blue Mountains Eye Study is a population-based cohort study of vision and common eye diseases conducted in the urban population of the Blue Mountains region, west of Sydney, Australia. Details of recruitment methods are given elsewhere.[8,9] In brief, following a door-to-door census of the region, all permanent residents with birth dates prior to January 1, 1943 were invited to attend a local clinic for a detailed eye examination. Of 4433 eligible persons identified in a door-to-door census of two postal codes of the study region, 3654 (82%) attended the study clinic between January 1992 and January 1994 (BMES I). After 5 years, 2335 (75.1% of survivors) were re-examined in the follow-up study (BMES II).

Ethical approval for the study was obtained from the Western Sydney Area Health Service Human Research Ethics Committee and informed consent was obtained from all participants.

At both the baseline and 5-year visits, photographs of the lens of each eye were taken after pupil dilatation with 1% tropicamide and 10% phenylephrine eyedrops. The protocol for lens photography and grading closely followed the Wisconsin Cataract Grading System[10] developed for the Beaver Dam Eye Study.[11] Slit-lamp photographs were taken to assess the severity of nuclear lens cataracts using a Topcon SL-7E Photo Slit Lamp camera (Topcon Optical Co., Tokyo, Japan). Retroillumination photographs of the anterior and posterior lens were taken to assess the presence and severity of cortical and posterior subcapsular cataract using a Neitz Cataract CT-R camera (Neitz Instruments Co., Tokyo, Japan).[8]

The severity of nuclear cataract on a 5-point scale was assessed by comparing photographs of subjects' eyes with a set of four standard photographs. The presence and severity of cortical cataract was graded by placing over the Neitz photographs a circular grid divided into eight equal wedges and a central circle. Graders estimated the percentage of the area of each of these nine segments that was involved by cataract. These percentages were summed to give an estimate of the total area of the lens affected by cataract. Posterior subcapsular cataract was graded similarly. Photos taken with pupils less than 4 mm in either vertical or horizontal diameter were excluded from the cortical cataract analyses. The nuclear cataract standard photographs and the grid were provided by Dr. Barbara Klein of the University of Wisconsin,

Madison. All photographs were graded by one of two masked graders. The quadratic weighted kappas for inter-grader reproducibility were 0.79 for nuclear cataract (n = 260 eyes), 0.78 for cortical cataract (n = 379 eyes) and 0.57 for posterior subcapsular cataract (n = 383 eyes).[12] The cataract grading technique was identical for photographs taken at both the baseline and 5-year examinations, and graders were masked to the earlier grading when assessing the 5-year photographs.

Fasting plasma glucose measurements used the hexokinase method. Newly diagnosed Type 2 diabetes was defined using the American Diabetes Association criteria.[1] In subjects with no past history of diabetes or hyperglycaemia, diabetes was diagnosed when fasting blood glucose was ≥7.0 mmol/L. A pre-diabetes state termed Impaired Fasting Glucose (IFG) was diagnosed when the fasting glucose was 6.0 to <7.0 mmol/L.[7,13]

Participants were interviewed using a standard questionnaire that included details of past cataract surgery and any previous diagnoses by a medical practitioner of diabetes or hyperglycaemia. Participants with known diabetes were asked the year it was diagnosed and the type and duration of treatment received. The duration of diabetes was defined as the period from diagnosis to the clinic examination.

The interviewer-administered questionnaire also collected information about a wide range of possible risk factors for cataract, including smoking history, alcohol intake, use of oral and inhaled corticosteroids, history of hypertension and measures of socioeconomic status such as educational achievement. Sun-related skin damage was assessed at the examination by a single examiner as none, mild, moderate or severe.

Each cataract type was dichotomized (using criteria similar to the Beaver Dam Eye Study):[11,14] cortical (<5% vs ≥5% of the lens involved); posterior subcapsular (0% vs >0% of the lens involved) and nuclear (<grade 4 vs grades 4 or 5). We defined incidence as the development of opacity with the severity listed as the definition of each cataract type in an eye at risk. Each cataract type was analysed independently. The cataract status of each participant was defined by the level in the worse affected eye. Analyses (by subject) were initially performed controlling for age and sex and then in logistic regression models, after adjusting for the potential risk factors enumerated above (age, sex, smoking, alcohol, use of oral or inhaled corticosteroids, hypertension and education). The presence and severity of sun-related skin damage was also included in cortical cataract models.

The Cochran–Mantel–Haenszel method was used to test for trends in analyses, which were performed using SAS Version 8 statistical software (SAS Institute, Cary, NC). P-values <0.05 were taken to indicate statistical significance. Odds ratios (OR) and 95% confidence intervals (CI) are presented.

Results The 5-year incidence of cataract in any eye among the 2335 BMES II participants was 16.9%, 4.6%, 35.4 % and 5.7% for cortical, posterior subcapsular and nuclear cataract and for cataract surgery, respectively. Table 1 shows that the incidence of all types of cataract increased markedly with age. This was particularly marked for cataract surgery; persons with baseline ages 50–59 years had a 1.0% 5-year

TABLE 1. Five-year incidence as percent (number of cases) of different cataract types and cataract surgery by age group.

Cataract type	*Age group (years)*			
	50–59	*60–69*	*70–79*	*80+*
Cortical	10.4 (67)	19.1 (139)	22.6 (74)	32.6 (14)
Posterior subcapsular	2.3 (15)	4.9 (39)	7.2 (29)	7.4 (5)
Nuclear	16.2 (69)	35.7 (189)	61.2 (156)	76.5 (26)
Surgery	1.0 (7)	4.9 (45)	13.6 (72)	24.8 (27)

TABLE 2. Five-year incidence as percent (number of cases) of different cataract types and cataract surgery by gender.

Types of cataract	*Women*	*Men*	*Age-adjusted p-value*
Cortical	19.5 (193)	13.4 (101)	0.0009
Posterior subcapsular	4.8 (53)	4.4 (35)	0.78
Nuclear	37.6 (267)	32.5 (173)	0.15
Surgery	6.8 (89)	6.4 (62)	0.89

incidence of cataract surgery, while those aged 80+ years had a 5-year incidence of 24.8%. Table 2 shows gender differences in the 5-year incidence of cataract and cataract surgery. Women had a significantly higher incidence of cortical cataract (19.5%) compared to men (13.4%), and a non-significantly increased incidence of nuclear cataract (37.6% vs 32.5%).

Our study population included 83 participants with IFG and 36 participants in whom diabetes was diagnosed at the time of baseline examination. Diabetes had been diagnosed for less than 10 years in 80 participants and for 10 years or longer in 34 participants. Of the 83 participants with IFG at baseline, 75 returned for blood tests after 5 years; among these, 24 (32%) had been diagnosed with diabetes during the period.

Table 3 shows the relationship between categories of diabetes and the 5-year incidence of cortical cataract. Participants with IFG had a statistically significant increased risk of incident cortical cataract, age-sex adjusted OR 2.1 (CI 1.1–3.8). This association persisted after further adjustment for multiple potential confounders, OR 2.2 (CI 1.1–4.1). Participants with newly diagnosed diabetes also had non-significantly increased odds for cortical cataract, OR 2.2 (CI 0.8–5.5). Among persons with known diabetes, we found no association with the 5-year incidence of cortical cataract.

Table 3 also shows increased odds for 5-year incident posterior subcapsular cataract among persons with diabetes. However, the relationship was statistically significant only for persons with newly diagnosed diabetes, age-sex adjusted OR 5.5 (CI 2.1–14.5) and OR 4.5 (CI 1.5–13.1) after further adjustment for multiple potential confounders (data not shown).

In Table 3, no statistically significant associations were found between any of the three diabetes categories and the 5-year incidence of nuclear cataract, although increased odds were found for newly diagnosed dia-

Cataract type	*Diabetic status*	*Incident cataract % (number)*	*Age-sex adjusted odds ratio (95% CI)*	*Multivariate-adjusted odds ratio (95% CI)*
Cortical	None	15.9 (237)	1.0 (ref)	1.0 (ref)
	IFG	27.1 (16)	2.1 (1.1–3.8)	2.2 (1.1–4.1)
	Diabetes	20.8 (20)	1.5 (0.9–2.5)	1.5 (0.9–2.6)
PSC	None	4.3 (69)	1.0 (ref)	1.0 (ref)
	IFG	1.4 (1)	0.3 (0.0–2.2)	0.3 (0.0–2.2)
	Diabetes	6.7 (7)	1.5 (0.7–3.5)	1.4 (0.6–3.3)
Nuclear	None	34.9 (369)	1.0 (ref)	1.0 (ref)
	IFG	40.0 (18)	1.0 (0.5–2.0)	0.9 (0.4–1.9)
	Diabetes	46.3 (31)	1.4 (0.8–2.3)	1.3 (0.7–2.2)
Cataract Surgery	None	6.6 (125)	1.0 (ref)	1.0 (ref)
	IFG	6.2 (5)	0.7 (0.3–1.9)	0.8 (0.3–2.2)
	Diabetes	10.0 (14)	1.4 (0.8–2.6)	1.2 (0.6–2.4)

TABLE 3. Associations between diabetes status and the 5-year incidence of cataract and cataract surgery.

betes. The table shows that there were also no significant associations between any diabetes category and the 5-year incidence of cataract surgery. In stratified analyses, there were no statistically significant differences found in the associations with incident lens opacity among persons with known duration of diabetes for less than or greater than 10 years. However, participants with diabetes for less than 10 years had a borderline increased risk of 5-year incident cortical cataract, age-sex adjusted OR 1.7 (CI 1.0–3.0) and a non-significant higher risk of 5-year incident posterior subcapsular cataract, age-sex adjusted OR 2.1 (CI 0.9–4.9).

Discussion This study provides evidence that IFG may be a risk factor for the development of cortical cataract. As IFG is considered to be a risk factor for progression to frank diabetes,[7] these data suggest that persons with pre-diabetes have an increased risk of developing cortical cataract. To our knowledge, there have been no previous reports implicating IFG as a risk factor for cataract.

Our data provide relatively weak support for the role of diabetes as an independent risk factor for incident posterior subcapsular cataract, as has been previously reported by some population based studies, including the Beaver Dam Eye Study.[6] We could also not confirm a statistically significant association between diabetes and incident cataract surgery, as also reported by some previous studies, including our own.[1,6]

In stratified analyses, a known duration of diabetes of less than 10 years was significantly associated with the development of cortical cataract while a similar, weaker relationship was found with the development of posterior subcapsular cataract. It is possible that no relationship was found for participants with diabetes for 10 or more years as this group may have been more likely to have developed cataract at the time of the baseline study.

Our finding of non-significantly increased odds for incident posterior subcapsular cataract in persons with diabetes provides only weak support for the cross-sectional association described in our previous Blue Mountains Eye Study report.[1] Participants with known diabetes had a higher prevalence of posterior subcapsular cataract, after adjustment for age, sex and multiple confounders. This association was prominent in diabetic subjects treated with oral hypoglycaemic agents. Because of the small numbers in the different treatment groups in the incidence data, however, we were unable to perform similar stratified analyses for incident cataract.

Many biological mechanisms for the relationship between diabetes and cataract have been postulated, including oxidative damage to lens structural proteins and membrane lipids,[15] and an increase in the production of malonic dialdehyde, a breakdown product of lipid peroxides in cortical cataract, particularly among persons with diabetes.[16,17]

Limitations of our study include the relatively small number of cases for some subgroups, loss of data due to ungradable photographs (particularly for nuclear cataract) and the possibility of confounding from unknown factors. The likely effects of this have been discussed previously.[18,19] Diabetes could have resulted in selective survival (or participation), leading to a relative underestimation of the relationship with cortical cataract; selective survival could be an explanation for the failure to confirm an association with PSC cataract. Strengths of our study include its population base with relatively high participation rates, cataract diagnosis based on detailed grading of lens photographs that were shown to have high reproducibility, and control for several important confounders.

In conclusion, Blue Mountains Eye Study data indicate statistically significant associations between a pre-diabetic state (IFG) and incident cortical cataract. The data provide limited support for an association between diabetes (particularly newly diagnosed cases) and incident posterior subcapsular cataract. These data suggest a potential area for cataract prevention, as blood glucose levels are potentially modifiable via dietary prevention of diabetes, its early detection and the institution of measures to achieve tight glycaemic control among persons with diagnosed diabetes.

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