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Cataract in type 2 diabetes mellitus in Isfahan, Iran: Incidence and risk factors

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Abstract

BACKGROUND Evidence on the incidence of and risk factors for cataract in type 2 diabetes mellitus is scarce and mainly derived from studies in developed countries. Locally derived evidence is required for planning a well co-ordinated approach to this public health problem in developing countries.

OBJECTIVE The objective of the present study was to estimate the incidence of and risk factors for the development of cataract in type 2 (insulin-treated and non-insulin-treated) diabetes using routinely collected data from a clinical information system at Isfahan Endocrinology and Metabolism Research Center, Iran.

METHOD During the mean (standard deviation (SD)) follow-up period of 3.6 (2.7) (range 1–11) years, 3888 diabetic patients (1348 male and 2540 female) from Isfahan Endocrinology and Metabolism Research Center outpatient clinics have been examined. The mean (SD) age of the participants was 52.0 (10.5) years with a mean (SD) duration of diabetes of 12.6 (7.5) years at initial registration.

RESULTS Among the 3888 patients who were free of cataract at initial registration with at least one follow-up visit between 1992 and 2004, the incidence of cataract was 33.1 (95% confidence interval (CI): 30.2, 36.1) (64.8 (95% CI: 57.7, 72.0) in males and 17.9 (95% CI: 15.2, 20.5) in females per 1000 person-years based on 14012 person-years of follow-up. The age-adjusted incidence rate of cataract was 20% greater among insulin-treated than non-insulin-treated type 2 diabetes mellitus clinic attenders and it increased with age. Using a Cox's Proportional Hazards Model for insulin and non-insulin-treated type 2 diabetes separately, age, age at diagnosis of diabetes, duration of diabetes, and smoking were significant predictors of cataract for insulin

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and non-insulin-treated type 2 diabetes patients. When all variables were entered in the model, fasting blood glucose and insulin treatment were significant predictors of cataract. In the insulin-treated group, fasting blood glucose was a significant predictor of cataract. Systolic and diastolic blood pressure, gender, HbA_{1c}, proteinuria, body mass index, cholesterol, triglyceride and creatinine had no significant independent association with cataract when other covariates were considered.

CONCLUSION These data suggest that cataract in this population of Iranian type 2 diabetic patients is common. With an estimated incidence of 33.1 per 1000 person-years of observation after mean 3.6 years' follow-up, diabetic cataract clearly poses a formidable health threat to Iranian diabetic patients. The results of this study highlight the need for regular eye examination in people with diabetes.

Key words Cataract epidemiology; diabetes mellitus; cataract risk factors; Iran

Introduction Diabetic eye disease and its complications are a leading cause of blindness and visual dysfunction in adults worldwide.^{1,2} The relationship between diabetes and cataract is well established and consistent in most³⁻⁹ but not all¹⁰ studies and has been examined in many different populations in developed nations.³⁻¹⁰ The possible association between blood pressure, serum lipids, smoking and body mass index and cataract shows inconsistent results. The strength and significance of some of these findings have varied. Several of these clinic- and population-based studies showed no effect^{10,11} or a positive effect.^{3,8,12,13} Accurate information regarding the incidence of cataract and associated risk factors in people with diabetes is important in the prevention or delay of its development and of the visual impairment caused by this complication in these countries.

Diabetic cataract is a serious problem in Iran but to our knowledge, there have been no longitudinal studies describing its incidence or risk factors. The objective of this report was to estimate the incidence of and risk factors for cataract in type 2 (insulin-treated and non-insulin-treated) diabetes using routinely collected data from a clinical information system for diabetes at Isfahan Endocrinology and Metabolism Research Center, Iran.

Patients and methods

DATA COLLECTION The recruitment methods and examination procedures of the Isfahan Endocrinology and Metabolism Research Center outpatient clinics have been described before.¹⁴ In summary, clinical data are collected for all consecutive patients at the first attendance and at review consultations (usually annually) using standard encounter forms. These include an examination of the ocular fundus, lens, limbs, blood pressure and construction of a problem list by the clinician, measurement of fasting blood glucose, glycosylated hemoglobin (HbA_{1c}), urinary protein, serum triglycerides, cholesterol and

creatinine, and reporting of smoking as part of a completed questionnaire on demography, family history, and smoking by the patient. A registry clerk enters data from these forms into the computer after the clinic.

All of our patients had been referred to an ophthalmology clinic. At each examination, pupils were pharmacologically dilated after an ocular examination. A slit-lamp examination of the anterior segment and lens was performed for assessment of lens opacities and it was noted whether each eye was phakic, aphakic, or had an intraocular lens implant. Cataract was evidenced by the presence of lens opacity in association with best visual acuity on Snellen's chart $\leq 20/70$ in the same eye. Subjects were considered to be at risk for cataract if they had not had a cataract in either eye at baseline. The date of diagnosis of cataract was established when the first eye showed lens opacity, even if the second eye did not have lens opacity at that time.

Many diabetic patients have cataract at diagnosis or develop it shortly afterwards. Since many patients were referred some years after diagnosis, we have no means of knowing the relationship between the onset of diabetes and the development of cataract among those with this complication at the time of referral. Also, the onset of type 2 diabetes may precede its diagnosis by some years. This study was therefore confined to those who were clinically free of cataract at initial registration, recording the rate of development of cataract over subsequent years.

PATIENTS Between 1992 and 2004, a total of 9897 type 2 diabetics were registered in the system. However, this study uses data for only the 3888 (1348 male and 2540 female) type 2 diabetic patients who were free of cataract at registration, had at least one subsequent review and for whom complete data were available. Those who participated have slightly lower fasting blood glucose (202.7 vs. 206.1 mg/dl; $P < 0.05$), HbA_{1c} (10.1 vs. 10.3%; $P < 0.01$), systolic blood pressure (125.4 vs. 127.7 mmHg; $P < 0.001$) and diastolic blood pressure (76.6 vs. 78.0 mmHg; $P < 0.001$) and have a lower proportion of current smokers (11.0% vs. 17.0%; $P < 0.001$), but have a higher proportion of females (65.3% vs. 53.1%; $P < 0.001$), insulin-treated diabetes (24.0% vs. 10.8%; $P < 0.001$), high blood pressure history (45.2% vs. 42.9%; $P < 0.05$) and proteinuria (33.4% vs. 29.3%; $P < 0.01$). The sample had similar distributions in age at diagnosis of diabetes, age, duration of diabetes, BMI, triglyceride, cholesterol and creatinine as those not selected. The 3888 patients had a mean (standard deviation [SD]) duration of diabetes of 12.6 (7.5) years and a mean age of 52.0 (10.5) years. The average duration of follow-up was 3.6 (2.7) years (range 1–11 years). The tenets of the Declaration of Helsinki were followed, institutional ethical committee approval was granted, and an informed consent was signed by each patient.

Risk factors for the development of cataract were assessed using the following data from the patient's registration consultation: gender, age at diagnosis, age, duration of diabetes (the time between diagnosis and the baseline examination), body mass index (BMI) (weight/height² [kg/m²]), smoking status (never, current), hemoglobin A_{1c} (HbA_{1c})

(measured by spectrophotometer as an indicator of diabetic control), fasting blood glucose, proteinuria, serum creatinine, triglycerides, cholesterol and blood pressure (BP) (systolic and diastolic) at registration. Diabetes treatment (insulin, oral hypoglycemic agent, and diet alone) used in the analysis was that recorded at the last clinic visit. Diabetes was defined as a previous history of diabetes treated with insulin, oral hypoglycemic agents, or diet. The physician defined the type of diabetes using the problem list. Hypertension was defined as a systolic blood pressure of 160 mmHg or more or diastolic blood pressure of 95 mmHg or more at the time of examination or a history of hypertension and current use of antihypertensive medication.⁵

ANALYSIS Statistical methods used included Student's t-test, Chi-square test, and stepwise Cox's Proportional Hazards Model, which takes varying periods of follow-up and time-dependent changes of covariate values into account, to test associations between baseline variables and cataract outcomes.¹⁵⁻¹⁸ Two types of statistical analyses are presented in this report: crude relative risk based on incidence rates and adjusted relative risk determined by a forward stepwise Cox's Proportional Hazards Model using the SPSS for Windows computer package which simultaneously adjusts for other covariates. For this analysis, follow-up time, age, age at diagnosis, duration of diabetes, fasting blood glucose, HbA_{1c}, systolic and diastolic blood pressure, BMI and creatinine were included as continuous variables. Gender, proteinuria and cigarette smoking (never and current) were entered as dichotomous variables. Therapeutic regimen (diet, oral agents and insulin) was included as trichotomous variable. Incidence was expressed as the number of cases of cataract per 1000 person-years of observation (in order to fully utilize the period of observation for each individual and properly weight their contribution to the study). The numerator was the number of patients who had cataract diagnosed between 1992 and 2004, and the denominator was person-times. The period of risk began on the date of first registration for patients entering the study after this date; it extended to the date of diagnosis of cataract, date of last contact with registry, or end of the study. Patients who registered during the study period began to accumulate person-time from the date of registration. Relative risks and 95% confidence interval (CI) for incidence rates were estimated from the Cox regression analysis and 95% CIs for mean and proportion differences by confidence interval analysis software.¹⁹

Results

INCIDENCE Of the 3888 patients, 464 (11.9%; 169 men and 295 women) developed cataract in 14012 (4552 male and 9460 female) person-years of follow-up. The overall incidence of subsequent cataract was 33.1 (95% CI: 30.2, 36.1) per 1000 person-years. Incidence rates were lower in women (17.9 (95% CI: 15.2, 20.5) per 1000 person-years) than in men (64.8 (95% CI: 57.7, 72.0)). This difference was statistically

<i>Variables</i>	<i>Cataract Mean (SD)</i>	<i>No cataract Mean (SD)</i>	<i>Difference (95% CI)</i>
Age at registration (yr.)	56.1 (9.2)	51.4 (10.6)	4.6 (3.6, 5.6)**
Duration of diabetes (yr.)	14.5 (7.8)	12.4 (7.4)	2.1 (1.4, 2.8)***
Age at diagnosis (yr.)	48.5 (10.4)	45.1 (10.5)	3.4 (2.3, 4.4)**
BMI (kg/m ²)	27.1 (4.2)	27.6 (4.5)	-0.5 (-0.9, -0.03)*
Systolic BP (mmHg)	129.2 (22.0)	124.9 (21.7)	4.2 (2.3, 63.5)**
Diastolic BP (mmHg)	77.9 (12.4)	76.4 (11.9)	15.5 (0.4, 2.7)*
Fasting blood glucose (mg/dl)	209.0 (78.1)	201.8 (72.7)	7.2 (-0.1, 14.6)
HbA _{1c} (%)	10.3 (2.3)	10.1 (2.3)	0.2 (-0.02, 0.4)
Creatinine (μM/l)	0.98 (0.8)	0.98 (1.0)	0.00 (-0.09, 0.11)
Triglycerides (mg/dl)	228.7 (153.5)	229.7 (153.0)	-1.0 (-16.3, 14.4)
Cholesterol (mg/dl)	229.6 (58.7)	226.2 (53.3)	3.4 (-2.0, 8.8)
	<i>No. (%)</i>	<i>No. (%)</i>	
Gender			
Male	169 (36.4)	1179 (34.4)	2.0 (-2.7, 6.7)
Female	295 (63.6)	2245 (65.6)	-
Smoking			
Never smoked	376 (88.7)	2763 (89.1)	-0.4 (-3.6, 2.8)
Current smoker	48 (11.3)	339 (10.9)	-
Proteinuria			
Present	107 (36.4)	512 (32.9)	3.5 (-2.5, 9.5)
Absent	187 (63.6)	1045 (67.1)	-
Therapeutic regimen			
Diet	52 (11.2)	609 (17.8)	-6.6 (-9.7, -3.4)**
Oral agent	231 (49.8)	2065 (60.3)	-10.5 (-15.3, -5.7)**
Insulin	181 (39.0)	752 (21.9)	17.1 (12.4, 21.7)**

*P < 0.05, **P < 0.01, ***P < 0.001. CI = Confidence interval. The difference in the mean or percentage of the variables between cataract and no cataract.

significant (P < 0.01). Of the 933 patients who were insulin-treated but were free of cataract at initial registration, 181 subsequently developed cataract, giving an incidence of 43.5 (95% CI: 37.3, 49.7) per 1000 person-years. This was higher than the incidence rates seen for non-insulin-treated patients: 28.7 per 1000 person-years (95% CI: 25.4, 32.0) (P < 0.001).

RISK FACTORS Table I shows the group means (SD) and proportions for those participants who did and did not develop cataract. Those who developed cataract had higher systolic (129.2 vs. 124.9 mmHg; P < 0.01) and diastolic blood pressure (77.9 vs. 76.4; P < 0.05), longer duration of diabetes (7.6 vs. 6.2 years; P < 0.001), and lower BMI (27.1 vs. 27.6; P < 0.05) and were older at registration (56.1 vs. 51.4; P < 0.01) and diagnosis (48.5 vs. 45.1; P < 0.01). A lower proportion of those who developed cataract had used diet (11.2% vs. 17.8%; P < 0.01) or an oral

TABLE I. Group means and proportions for selected variables between 464 participants who did and 3424 who did not develop cataract.

TABLE 2. Incidence rates of cataract by baseline variables.

Variables	At risk (No.)	Cases (No.)	Person-years	Incidence per 1000 person-years	Crude relative risk (95% CI)	Age-adjusted relative risk (95% CI)†
Gender						
Female	2540	169	9460	17.9	1.0	1.0
Male	1348	295	4552	64.8	3.6 (3.0, 4.4)**	1.04 (1.01, 1.08)*
Age at registration (yr.)						
<40	435	19	1559	12.2	1.0	—
40–49	1129	94	4202	22.4	1.8 (1.1, 3.0)*	—
50–59	1268	166	4784	34.7	2.8 (1.8, 4.6)**	—
60–69	826	151	2862	52.8	4.3 (2.7, 6.9)**	—
≥70	201	33	564	58.5	4.8 (2.8, 8.4)**	—
Age at diagnosis (yr.)						
<30	200	14	720	19.4	1.0	1.0
30–59	3250	376	12009	31.3	1.6 (0.9, 2.7)	0.9 (0.86, 0.97)**
≥60	365	69	1136	60.7	3.1 (1.8, 5.5)**	1.09 (0.98, 1.2)
Duration of diabetes (yr.)						
<5	341	19	560	33.9	1.0	1.0
5–7	719	65	1884	34.5	1.02 (0.6, 1.7)	1.2 (1.1)*
8–11	931	98	3607	27.2	0.8 (0.5, 1.3)	0.74 ()*
≥12	1855	278	7858	35.4	1.04 (0.7, 1.7)	0.59 ()
Fasting blood glucose (mg/dl)						
≤120	340	40	1139	35.1	1.0	1.0
121–140	358	41	1391	29.5	0.8 (0.5, 1.3)	0.96 (0.88, 1.04)
141–200	1191	144	4669	30.8	0.9 (0.6, 1.2)	0.95 (0.89, 1.005)
>200	1625	214	6109	35.0	1.0 (0.7, 1.4)	0.99 (0.94, 1.05)
HbA1c (%)						
≤9	1180	158	4010	39.4	1.0	1.0
9.1–11	994	145	4091	35.4	0.9 (0.7, 1.1)	1.08 (1.01, 1.2)*
11.1–13	530	69	2353	29.3	0.7 (0.6, 1.0)	0.99 (0.91, 1.1)
13.1–15	262	44	1274	34.5	0.9 (0.6, 1.2)	0.88 (0.79, 0.98)*
>15	102	17	550	30.9	0.8 (0.5, 1.3)	0.77 (0.66, 0.91)**
Systolic BP (mmHg)						
<140	2806	300	10055	29.8	1.0	1.0
140–159	629	96	2316	41.5	1.4 (1.1, 1.7)*	0.98 (0.92, 1.04)
≥160	445	68	1629	41.7	1.4 (1.1, 1.8)*	0.99 (0.92, 1.06)
Diastolic BP (mmHg)						
<70	628	68	2266	30.0	1.0	1.0
70–90	2484	281	8824	31.8	1.1 (0.8, 1.4)	1.03 (0.98, 1.1)
≥90	734	112	2846	39.4	1.3 (1.0, 1.8)	0.93 (0.88, 0.99)*
BMI (kg/m ²)						
<27	1867	234	6827	34.3	1.0	1.0
27–33	1643	193	5916	32.6	0.9 (0.8, 1.1)	0.99 (0.94, 1.04)
≥34	294	27	1009	26.8	0.8 (0.5, 1.2)	1.06 (0.98, 1.1)
Smoking						
Never smoked	3139	376	11591	32.4	1.0	1.0
Current smoker	387	48	1409	34.1	1.1 (0.8, 1.4)	1.01 (0.95, 1.06)
Proteinuria						
Absent	1232	187	5766	32.4	1.0	1.0
Present	619	107	3054	35.0	1.1 (0.9, 1.4)	0.96 (0.92, 1.01)
Creatinine (μM/l)						
≤1.5	2696	391	10777	36.3	1.0	1.0
>1.5	119	17	498	34.1	0.9 (0.6, 1.2)	0.96 (0.87, 1.05)
Therapeutic regimen						
Diet alone or Oral agent	2957	283	9854	28.7	1.0	1.0
Insulin	933	181	4161	43.5	1.5 (1.3, 1.8)**	1.2 (1.14, 1.22)***

Total number of person-years and at risk is not the same for each variable because of missing values. †Relative risks (with 95% CI) calculated by Cox's Proportional Hazard Model.²³ *P < 0.05, **P < 0.01, ***P < 0.001.

agent (49.8% vs. 60.3%; $P < 0.01$), but a higher proportion had used insulin (39.0% vs. 21.9%; $P < 0.01$).

A univariate analysis (Table 2) showed that male gender, age at registration and diagnosis, duration of diabetes, systolic blood pressure and therapeutic regimen were significantly associated with the risk of developing cataract. For all variables there was a fairly consistent 'dose response' across the range of values; for example, the risk of cataract was higher in older age groups, among patients with a longer duration of diabetes, and those with higher systolic blood pressure. The insulin-treated type 2 diabetic patients were more likely to develop cataract than non-insulin-treated patients in this univariate analysis. Age-adjusted Cox regression coefficients among those free of cataract at registration showed that significant risk factors for developing cataract were gender, age at diagnosis of diabetes, HbA_{1c} and insulin treatment.

The incidence of cataract was also analyzed with a multivariate model. A stepwise Cox's Proportional Hazard Model was performed. Since 799 subjects were excluded from these analyses because of missing data on risk factors, 3089 people remained to be analyzed for any incident cataract. Three separate models were computed for insulin-treated and non-insulin-treated type 2 diabetic patients and all type 2 diabetes together. Table 3 shows the association of these variables in order of their entry into the regression equation in each group. Older age at registration, shorter duration of diabetes, younger age at diagnosis of diabetes and smoking significantly increased the risk of developing cataract in all models. As expected, there was a statistically significant interaction between age and duration of diabetes. For the non-insulin-treated group, fasting blood glucose also increased the risk of developing cataract significantly. In the model, which included all types of diabetes, insulin-treated diabetes also significantly increased the risk of developing cataract. No other variables were significant.

Discussion In this follow-up study of 3888 diabetes clinic attenders, we found an overall incidence of cataract of 33.1 per 1000 person-years (464 patients) over an average follow-up of 3.6 years. To the best of our knowledge, no other incidence rates for cataract among Iranian people have been reported. Incidence rates in various studies from around the world show considerable variation. Incidence rates of cataract are difficult to compare because of differing assessment methods. However, the estimates of the incidence of cataract varied widely in other studies too as a result of variations in study design, detection methods, or the definition of cataract, the examination of patients at different stages in the natural history of diabetes and the study of selected populations of diabetic individuals. A very similar study to this, from Nottingham UK, showed that the incidence of diabetic cataract in a clinic population was 11.7 per 1000 person-years in non-insulin-treated and 17.8 per 1000 person-years in insulin-treated type 2 diabetics.³ In Wisconsin, USA after 10 years of follow-up, the observed cumulative incidence of diabetic cataract surgery was 8.3%²⁰ and 24.9% for the younger- and older-onset groups, respectively.

TABLE 3. Risk factors related to incidence of cataract for patients with insulin-treated, non-insulin-treated and both insulin- and non-insulin treated together (Cox's Proportional Hazard Model).

<i>Variables</i>	<i>Relative Risk (95% Confidence Interval)</i>
Total	
Age (yr.)	1.27 (1.25, 1.30)***
Duration of diabetes (yr.)	0.80 (0.78, 0.81)***
Fasting blood glucose (mg/dl)	1.0006 (1.0001, 1.001)*
Age at diagnosis (yr.)	0.80 (0.77, 0.80)*
Therapeutic regimen	
Diet	1.0
Oral agent	0.80 (0.75, 0.85)***
Insulin	1.04 (0.99, 1.1)
Smoking	
Never smoked	1.0
Current smoker	1.1 (1.04, 1.2)***
Non-insulin-treated	
Age (yr.)	1.34 (1.31, 1.37)***
Duration of diabetes (yr.)	0.76 (0.74, 0.76)***
Fasting blood glucose (mg/dl)	1.001 (1.0004, 1.002)**
Age at diagnosis (yr.)	0.75 (0.73, 0.77)***
Smoking	
Never smoked	1.0
Current smoker	1.10 (1.03, 1.19)**
Insulin-treated	
Age (yr.)	1.49 (1.43, 1.57)***
Duration of diabetes (yr.)	0.68 (0.65, 0.71)***
Age at diagnosis (yr.)	0.67 (0.64, 0.70)***
Smoking	
Never smoked	1.0
Current smoker	1.14 (1.005, 1.29)*

*P < 0.05, **P < 0.01, ***P < 0.001.

One study from China among type 2 diabetics found the incidence of diabetic cataract to be 62.4%, which was significantly related to the duration of the disease.⁴ Our clinic-based figure is higher than the values reported by the Wisconsin population-based epidemiologic study and Nottingham clinic-based study, but lower than the study in China. Our figure is also higher than the age-specific incidence rates of cataract in type 2 diabetic patients found in the Oxford Community Diabetes Study.²¹ The higher rates in our study could have been due to the perception of diabetics and decision makers in Iran, which could have resulted in earlier surgery for cataract in other developed countries. The lower rates in our study than in the Chinese study could have been due to less complete follow-up of people with more severe diabetes or other factors. Because our patients were less likely to return for follow-up visits, our rates are likely underestimates of the true rates in this population. However, it seems that the incidence of cataract among Isfahanian diabetic patients was high.

Univariate analysis (Table 2) shows an expected pattern of association for many variables with the development of cataract. In multivariate analysis, fewer remain independently associated. In this study, males seemed to be at a higher risk of developing cataract in univariate analysis. After adjusting for other confounders, however, gender was not a significant independent predictor. This has also been reported by others.³

In univariate analysis, we found that the incidence of cataract was higher in insulin-treated type 2 diabetic patients than in non-insulin-treated patients. Insulin treatment may indicate a more severe disease process. After adjustment for other covariates in the multivariate analysis, the type of treatment was still significant. A higher incidence of cataract among insulin-treated patients could be attributable to their longer duration of diabetes, younger age at onset and poorer metabolic control than in non-insulin-treated type 2 diabetes.

In this study, a longer duration of diabetes was associated with the incidence of cataract. However, adjustment for other risk factors by multivariate analysis substantially changed the ordering of risk associated with duration of diabetes. When adjusting for other risk factors by multivariate analysis, a shorter duration of diabetes became a significant risk factor for cataract. However, there was statistically significant interaction between age and duration of diabetes and the effects of both variables are not independent.

In univariate analysis, HbA_{1c} was not associated with a significant increase in the risk. After adjustment for age, the level of hyperglycemia, as measured by a single assessment of glycosylated hemoglobin at baseline, was found to be a negative predictor of diabetic cataract. After adjustment for other covariates in the multivariate analysis, the level of glycosylated hemoglobin was non-significant. The negative association of higher levels of glycosylated hemoglobin with cataract after adjustment for age is not surprising. However, lens opacity was associated with duration of diabetes and age. In the Beaver Dam Eye study, the level of glycemia at baseline was also not a predictor of cataract.⁵ In data from the Wisconsin Epidemiological Study of Diabetic Retinopathy,²⁰ the level of glycemia at baseline was an important predictor of cumulative incidence of cataract surgery. This has also been reported by Janghorbani et al.³ and Dobbs et al.²²

The effect of blood pressure on the risk of cataract is an important but difficult issue because blood pressure rises as duration of diabetes and age increase. Previous studies have yielded conflicting results and are not well established. Some studies find no relationship;^{3,23} in some other studies, however, the incidence of cataract was related to blood pressure.^{11,24,25} In this study, systolic and diastolic blood pressure was not associated with a significant increase in the risk. This has also been reported by Klein et al.²⁰ and Janghorbani et al.³

In this study, smoking (classified in two simple categories of never and current) was related to the incidence of cataract. Although data from some studies suggest a positive relationship between cigarette smoking and cataract,^{20,25-32} some other studies have failed to confirm this relationship.^{10,24}

Previous studies differ in relation to the importance of obesity as a risk factor. A higher BMI was an independent predictor of self-reported cataract in a prospective cohort study,³³ whereas a lower BMI was associated with increased risk of nuclear^{24,27} and mixed²⁷ cataract in case-control studies. Additionally, lower weight and shorter height were associated with an increased cataract risk in a survey in India.³⁴ In the Barbados Eye Study, BMI was not related to the risk of lens opacities.³⁵ However, we found no association between BMI and cataract.

Although we have not carried out any special studies of the validity or reliability of data for this analysis, a clerk was employed to check consistency and, where possible, to ensure completeness of data. Previous studies show that these patients are a representative sample of known diabetic patients in Isfahan.^{36,37} Our experience with other parts of the data set gives us some confidence that the data quality is sufficient for this type of study and that our results provide useful additional evidence on the incidence of and risk factors for cataract. The study was clinic-based rather than population-based, and so may not contain a clinical spectrum representative of diabetic patients in the community. Many patients requiring only oral or dietary treatment may never attend the clinic.³⁸ Clinic-based estimates of the incidence or prevalence of complications are most likely to be affected by referral patterns. Selection bias is less likely to affect incidence rates and associations between risk factors and complications³⁹ as investigated in this study.

In this study, cataract was diagnosed by ophthalmologists. Our diagnosis of cataract was not based on a single examination but on continuing examination during follow-up, using a problem list as the basis for further clinical decisions. All of those with cataract will have been referred to an ophthalmology clinic and so had their diagnosis of cataract confirmed, or not, by an ophthalmologist. Nevertheless, four ophthalmologists made observations over the years, and problems of observer error need to be considered. It seems reasonable to assume that observer error is independent of such variables as age, duration of diabetes, blood pressure and type of treatment of the patient. If this is so, misclassification resulting from observer error will tend to reduce rather than increase the significance of differences between groups of patients. If, therefore, a significant difference is found between two otherwise comparable groups of patients, it is reasonable to infer that it is not due to observer error but must reflect a true difference. Slight differences in baseline systolic and diastolic blood pressure, fasting blood glucose, HbA_{1c}, gender, smoking status and therapeutic regimen between study participants and the entire population of registered diabetic patients could limit slightly the generalizability of our findings.

In summary, our study indicates that the occurrence of cataract in people with diabetes is associated with older age, younger age at diagnosis of diabetes, smoking, duration, and type of treatment of diabetes. With an estimated incidence of 33.1 per 1000 person-years of observation, diabetic cataract clearly poses a formidable health threat to Iranian diabetic patients. The results of this study highlight the need for regular eye examination in people with diabetes.

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