Risk factors for diabetic retinopathy: Findings from The Andhra Pradesh Eye Disease Study

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Objective: To assess prevalence, potential risk factors and population attributable risk percentage (PAR%) for diabetic retinopathy (DR) in the Indian state of Andhra Pradesh.

Methods: A population-based study, using a stratified, random, cluster, systematic sampling strategy, was conducted in the state of Andhra Pradesh in India during 1996 and 2000. Participants from 94 clusters in one urban and three rural areas representative of the population of Andhra Pradesh, underwent a detailed interview and a comprehensive dilated ocular evaluation by trained professionals. DR was defined according to the international classification and grading system. For subjects more than or equal to 30 years of age, we explored associations of DR with potential risk factors using bivariable and multivariable analyses. Population attributable risk percent was calculated using Levin's formula.

Results: Diabetic retinopathy was present in 39 of 5586 subjects, an age-gender-area-adjusted prevalence of 0.72% (95% confidence interval (CI): 0.49%–0.93%) among subjects aged ≥ 30 years old, and 0.27% (95% CI: 0.17%–0.37%) for all ages. Most of the DR was either mild (51.3%) or moderate (35.9%) non-proliferative type; one subject (2.6%) had proliferative retinopathy. Multivariable analysis showed that increasing age, adjusted odds ratio (OR); 4.04 (95% CI: 1.88–8.68), middle and upper socioeconomic status group (OR); 2.34 (95% CI: 1.16–4.73), hypertension (OR); 3.48 (95% CI: 1.50–8.11) and duration of diabetes ≥ 15 years (OR); 8.62 (95% CI: 2.63–28.29) were significantly associated with increasing risk of DR. The PAR % for hypertension was 50%; it was 10% for cigarette smokers.

Conclusions: Extrapolating the prevalence of diabetic retinopathy in our sample to the Indian population suggests that there may be an estimated 2.77 million people with DR, approximately 0.07 million people with severe DR. As the population demographics change towards aging, this number is likely to increase further. Health care programs in India need to examine strategies to prevent diabetes and DR, as well as create the infrastructure required to manage this condition.

Keywords: diabetic retinopathy, risk factors, population attributable risk percent, population based cross-sectional study, southern India

Introduction

Diabetic retinopathy (DR) is the leading cause of visual impairment in the Western world, particularly among persons of working age (Klein et al 1984b). India has the largest number of diabetics in the world and DR is becoming an important cause of visual impairment (Kumar 1998). According to the latest World Health Organization (WHO) report, India has 31.7 million diabetic subjects, and the number is expected to increase to a staggering 79.4 million by 2030 (King et al 1998). The potential for blindness and vision impairment among persons with diabetes is well recognized. Standard treatment modalities are available and if instituted early may prevent blindness or maintain sight. Several risk factors have been implicated for onset and progression of blindness among diabetics. A better understanding of the risk factors, especially the modifiable risk factors, may help plan better strategies addressing diabetes and

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diabetic retinopathy care in India (Wild et al 2004). We report on some of the possible risk factors for DR and the estimated population attributable risk percentage (PAR) associated with these risk factors for DR in a representative sample of the population aged 30 years and older from a state of South India.

Methods

The details of the design of Andhra Pradesh Eye Disease Study (APEDS), conducted during 1996–2000, following the tenets of the Helsinki Declaration, have been described previously (Dandona et al 1997, 1998, 2001). Approval of the Ethics Committee of the Institute was obtained for the study design.

Study sample

A multistage sampling procedure was used to select the study sample of 10,000 persons, 5000 each below and above 30 years of age based on the assumption that a 0.5% prevalence of an eye disease in either of these groups may be of public health significance. This sample would estimate the prevalence as 0.3% to 0.8% at the 95% confidence level. One urban and three rural areas from different parts of the southern Indian state of Andhra Pradesh were selected, with the aim of including approximately 2500 participants in each area, such that these would roughly reflect the urban-rural and socioeconomic distribution of the population of this state. These four areas were located in Hyderabad (urban), West Godavari district (well off rural), and Adilabad and Mahabubnagar districts (poor rural).

For the urban (Hyderabad) component of APEDS the blocks (clusters) of Hyderabad were stratified by socioeconomic status and religion. The socioeconomic strata were: extreme lower (monthly per capita income in Rupees $\leq$ 200 [$US 5.1]), lower (201–500), middle (501–2000) and upper (>2000); the religion strata were Hindu and Muslim. After this stratification, 24 clusters were chosen using stratified random sampling with equal probability of selection, such that the socioeconomic and religion distribution in the sample would be similar to that in the population. The selected clusters were mapped, and households were selected systematically using a sampling interval of three to five to obtain a similar number of households in the various clusters. A total of 2954 subjects were sampled with the aim of achieving a recruitment rate of at least 85% to obtain a minimum sample of 2500.

From three rural areas from different parts of Andhra Pradesh, 70 rural clusters were selected with the aim of having a study sample representative of the socioeconomic distribution of the rural population of the state. These three rural areas were located in (1) West Godavari (well-off rural), (2) Adilabad, and (3) Mahabubnagar districts (poor rural). For these three rural segments, a total of 8832 subjects were sampled of which 7771 eligible participants were interviewed by trained field investigators.

Interview

The sampled subjects were interviewed in detail by trained field investigators using a structured questionnaire in a masked manner (Dandona et al 1997). Questions included systemic history about the diagnosis and treatment of diabetes and ocular history and information on risk factors of systemic diseases and personal habits such as smoking. The questionnaire was designed to collect data on current and prior status of cigarette, beedi, hookah (both are local variants of cigarette), and chutta (home-rolled cigar, prepared and used extensively in the state of AP) smoking. The first question related to smoking was on the current status of smoking (yes/no). If the response was yes, the volunteer was asked how long he/she had been smoking (years) and current level (in terms of number per day for cigarettes/beedies / chuttas; hours per day for the hookah) of smoking. Similar information was also obtained from prior smokers. The structured questionnaire also had questions about alcohol consumption to ascertain the information on duration, quantity and frequency of alcohol consumption. Hypertension was deemed to be present, if a subject had a history of high blood pressure diagnosed by a physician and/or current usage of anti hypertensive medications and/or a blood pressure reading of $\geq$ 140/90 mm Hg. Diabetes was deemed to be present, if a subject had a history of diabetes or was on anti-diabetic medications. Subjects not providing a history of diabetes but with retinopathy presumably from diabetes were subjected to a random blood sugar test. If the random blood sugar was above 120 mg/dl, the subject underwent a fasting blood sugar estimation on a subsequent day after an overnight fast.

Ophthalmologic examination

Subjects were brought to a clinic specially set up for this study. Written informed consent was obtained from the subjects before examination. The examination was performed by two ophthalmologists and two optometrists who had received special training in the procedures of this study. It included presenting and best corrected distance and near logMAR visual acuity, complete anterior segment slit-lamp examina-

tion, and dilatation of pupil unless contraindicated because of risk of angle closure. After dilatation, stereoscopic fundus examination was done at the slit lamp using a 78 D lens and with the indirect ophthalmoscope using 20 D lens.

Subjects who were physically debilitated and unable to come to the APEDS clinic were examined at home with portable equipment. Examination with 78 D lens and photography were not done at home.

Definition of diabetic retinopathy

To grade DR a slight modification of a standard classification system (Olk et al 1993) was done for simplification. Diabetic retinopathy was classified as follows:

- Non-proliferative diabetic retinopathy (NPDR):
- Mild NPDR – microaneurysms, hard exudates and intraretinal hemorrhages present in fewer than four quadrants;
- Moderate NPDR – moderate intraretinal hemorrhages present in four quadrants;
- Severe NPDR – if any of the following three were present: severe intraretinal hemorrhages in four quadrants, venous beading in two quadrants, obvious intraretinal microvascular abnormalities (IRMA) in one quadrant;
- Very severe NPDR – if more than one of the three features listed for severe NPDR were present;
- Proliferative diabetic retinopathy (PDR) – if any of the following were present: neovascularisation of the retina or iris or angle, preretinal or vitreous hemorrhage, tractional retinal detachment.

Stereoscopic photographs of the macula and optic disc were obtained with a Zeiss fundus camera in subjects having any evidence of DR. Photographs of all the standard photographic fields of the fundus (Moss et al 1989) were not taken, though the major findings used to classify DR were photographed. The grading of DR was based on the clinical examination, with the photographs serving as documentation. The photographs were reviewed by another ophthalmologist in an unmasked manner (for diagnosis of diabetes) to check for any major discrepancies with the clinical grading.

Subjects with fundus findings suggestive of DR who were not known diabetics had random blood glucose tested with finger stick and glucometer (Bayer). If this was >120 mg/dl (6.7 mmol/l), fasting blood glucose was tested on another day. If this was >120 mg/dl, the subject was considered to have diabetes (WHO 1980).

Data management

Data were initially documented on the APEDS data collection forms by the clinical examiners and the field investigators (Dandona et al 1997). This data collection was modified by the principal investigator and coinvestigator of the study and discussed with the clinical and field teams at regular intervals. The data were entered in a FoxPro database at the study headquarters in Hyderabad, and consistency checks were performed for these data (Dandona et al 1997).

Statistical analysis

The prevalence of DR and other estimates in our sample were adjusted for the estimated age and gender distribution of the population in India for the year 2000 (http://www.census.gov). The 95% confidence intervals were calculated by assuming a Poisson distribution (Rosner 1986 p 404–8) for prevalence <1%, and normal approximation of binomial distribution for prevalence of 1% or more. Variables of interest were first tested for associations with DR in bivariable analysis using the Fishers exact test or Chi-square test as appropriate and multivariable logistic regression was used to find potential risk factors after adjusting for potential confounders. Population attributable risk percentage for the individual factors identified in the multivariable logistic regression model were calculated using Levin's formula (Pearce 1989). The software SPSS version 14.0 for Windows (SPSS, Chicago, IL, USA) was used for statistical analysis. A two-tailed *P*-value of less than 0.05 was considered statistically significant.

Results

Study population

A total of 2522 (85.4%) of 2954 eligible participants from urban Hyderabad and 7771 (88%) of 8832 eligible participants from three rural Andhra Pradesh participated in the study. The study population was representative of both the urban and rural population of the state as a whole. In this study the data were analyzed for those more than or equal to 30 years old (n = 5586). The age range of the urban residents was 30 to 102 years (46.7 ± 12.9; median 45 years); 631 (45.1%) were men. The age range for rural residents was 30 to 95 years (47.8 ± 12.9; median 45 years) and 1964 (46.9%) were men.

Prevalence of diabetes

A total of 201 subjects, all above or equal to 30 years old, self reported diabetes, an age-gender-area-adjusted prevalence of 3.68% (95% confidence interval (CI): 3.18–4.17) and 1.34% (95% CI: 1.11–1.56) in all age groups considered together. The mean age of persons with diabetes was 55.3 ± 10.7 years

(median: 55 years; range 30–86 years) and was not significantly different between urban and rural areas (p = 0.103). The prevalence of self reported diabetes was similar in males and females (52.2 and 47.8% respectively) ≥ 30 years old. Age at diagnosis was less than 30 years for only one subject. Medications for diabetes were being used by 152 (75.6%) persons with diabetes.

DR prevalence and potential risk factors

The overall age-gender-area-adjusted prevalence of DR was 0.72% (95% CI: 0.49%–0.93%) in participants aged ≥ 30 years; it was 0.27% (95% CI: 0.17%–0.37%) in all age groups considered together. Among 201 subjects with diabetes, 39 (19.4%; 95% CI: 13.9–24.9) had DR. The mean age of the subjects with DR was 55.3 ± 9.4 years, (median: 56 years; range 31–70 years). DR was present in 68 eyes of 39 participants. Of the 39 subjects with DR, 20 (51.3%) had mild NPDR, 14 (35.9%) moderate NPDR, 3 (7.7%) severe NPDR and one (2.6%) PDR. The classification of DR was not mentioned for one subject. Nine subjects (25.7%) with DR were visually impaired as a consequence, but none were blind due to DR. Among persons with diabetes, the prevalence of DR did not vary substantially among gender, however, it was significantly different between urban and rural residents (21.6% vs 10.5%; p = 0.045).

Table 1 reports the distribution of DR. Increasing age, socioeconomic status, and duration of diabetes were positively associated with increasing risk of DR (Table 1). The potential risk factors evaluated in the bivariable analysis were age, socioeconomic status, place of residence, duration of diabetes, hypertension, and smoking (Table 1). In a multivariable logistic regression model that adjusted for potential confounders, age ≥ 50 years was associated significantly with higher odds of DR (Table 2). When age was entered in the logistic regression model as a covariate, for unit (a year) of increment of age, there were 1.01 (95% CI: 0.97–1.05; p = 0.859) odds ratio of increment of DR in this population. The odds of prevalence of DR were also significantly higher in the urban residents, adjusted OR 6.07 (95% CI: 2.84–12.98); middle and upper socioeconomic group, adjusted OR 2.34 (95% CI: 1.16–4.73) and in hypertensives, adjusted OR 3.48 (95% CI: 1.50–8.11) (Table 2). Duration of diabetes ≥ 15 years was also significantly associated with increased risk of DR, adjusted OR 8.62 (95% CI: 2.63–28.29). After adjusting for potential confounders in a multivariable logistic regression model that used systolic and diastolic blood pressures as continuous variables, the odds of DR were 1.03 (95% CI: 1.01–1.04; p = 0.001) for each unit increase in the systolic blood pressure, and 1.03 (95% CI: 1.01–1.05; p = 0.012) for each unit increase in the diastolic blood pressure. The odds for DR among cigarette and cigar smokers were higher than the "never smoker" reference group, but it was not statistically significant (Table 2). The PAR % for hypertension was 50% and was 10% for cigarette smokers. Table 3 shows the relation of duration of diabetes and diabetic retinopathy.

Discussion

Data from this population-based study demonstrated the expected association between increased duration of diabetes, age and DR. Urban residence, middle and upper socioeconomic status, and high blood pressure were also significantly associated with DR. Based on our results, high blood pressure, and possibly cigarette smoking were identified as modifiable risk factors.

The age-gender-area-adjusted prevalence of DR in this population was 0.72% (95% CI: 0.5%–0.9%) in participants aged ≥ 30 years. Our prevalence estimate of diabetic retinopathy was similar to that of previously published reports (Klein et al 1991; Lundbaek 1995). Our prevalence estimate of all DR is slightly higher than the estimate of previously published report from a different state of south India (0.5%; 95% CI: 0.3%–0.7%) (Nirmalan et al 2004). However, our estimate of DR is less than that previously published reports from other populations (Lopez et al 2002; Tapp et al 2003; Giuffre et al 2004; Kempen et al 2004; Varma et al 2004).

Patients diagnosed with diabetes by their physicians may be at higher risk of having more severe retinopathy present at the time of their diagnosis (Klein et al 1984b). They would be more likely to benefit from an immediate ophthalmologic examination. It is evident that many people with diabetes unaware that they may develop DR. Improved control of blood glucose levels, blood pressure, and serum lipid levels is likely to reduce the incidence, rate of progression, and/or severity of diabetic retinopathy. Improvements in the effectiveness of primary diabetes care over time could reduce the incidence of diabetic retinopathy and its rate of progression. However, improved diabetes care also could result in improved survival. Unlike other age-related eye diseases, diabetic retinopathy often causes blindness during working age years resulting in a large number of person-years of vision loss and correspondingly large economic cost.

If we project the DR prevalence of 0.27% to the 1027 million population in India, there could be 2.77 million people with DR inclusive of approximately 0.07 million people with severe DR, who would require definite treatment

Table 1 Associations between prevalence of DR, demographic factors, smoking and hypertension in the study population

Characteristic	Total population (n = 5,586)	DR no (%)	P-value
Age			
30–39	1863	1 (0.1)	<0.0001†
40–49	1424	8 (0.6)	
50–59	1047	17 (1.6)	
60–69	899	10 (1.1)	
70+	353	3 (0.8)	
Sex			
Male	2595	22 (0.8)	0.259§
Female	2991	17 (0.6)	
Socioeconomic status$			
Extreme lower	645	3 (0.5)	<0.0001†
Lower	2781	9 (0.3)	
Middle	1859	23 (1.2)	
Upper	215	4 (1.9)	
Place of residence			
Urban	1399	29 (2.1)	<0.0001§
Rural	4187	10 (0.2)	
Diabetes			
Yes	205	39 (19.0)	<0.0001§
No	5381	0 (0.0)	
Duration of diabetes			
0–9 years	155	21 (13.5)	<0.0001†
10–14 years	27	5 (18.5)	
15–19 years	12	7 (58.3)	
≥20 years	6	5 (83.3)	
Any smoking			
Yes	3700	29 (0.8)	0.313§
No	1885	10 (0.5)	
Beedi smoking			
Never a smoker	4577	35 (0.8)	0.218†
Current smoker	817	2 (0.2)	
Prior smoker	191	2 (1.0)	
Hooka smoking			
Never a smoker	5582	39 (0.7)	--
Current smoker	–	–	
Prior smoker	3	–	
Cigarette smoking			
Never a smoker	5121	32 (0.6)	<0.0001†
Current smoker	310	1 (0.3)	
Prior smoker	154	6 (3.9)	
Cigar smoking			
Never a smoker	4975	36 (0.7)	0.312†
Current smoker	455	1 (0.2)	
Prior smoker	155	2 (1.3)	
Hypertension			<0.0001§
No	3271	7 (0.2)	
Yes	2315	32 (1.4)	

Notes: †Chi-square test

§Fisher's exact test.

$Socioeconomic status defined according to monthly per capita income in Indian rupees: ≤ 200 extreme lower; 201–500 lower; 501–2000 middle and >2000 upper. Data on socioeconomic status were not available for 86 subjects.

Data on duration of diabetes were not available for one subject. Data on smoking were not available for one subject.

for DR. Tackling this burden will need a larger pool of trained personnel besides adequate infrastructure support. Training to treat vitreoretinal diseases (either lasers or surgical interventions) including diabetic retinopathy is currently not part of all ophthalmology residency programs; such training is often offered as post-residency fellowships in India (Fong et al 2004). A larger proportion of the persons with diabetes currently have the less severe forms of retinopathy or no

Table 2 Bivariate and multivariable logistic regression analyses for associations between potential risk factors and DR (n = 5586)

Characteristic	Total population	DR no (%)	Crude odds ratio (95% CI)	Adjusted odds ratio§ (95% CI)	PAR‡
Age$					
30–49	3287	9 (0.3)	1.00	1.00	
≥ 50	2299	30 (1.3)	4.81 (2.28–10.14)	4.04 (1.88–8.68)	--
Sex					
Male	2595	22 (0.8)	1.50 (0.79–2.82)	1.74 (0.83–3.67)	--
Female	2991	17 (0.6)	1.00	1.00	
Area					
Urban	1399	29 (2.1)	8.84 (4.30–18.19)	6.07 (2.84–12.98)	--
Rural	4187	10 (0.2)	1.00	1.00	
Socioeconomic status$					
Extreme Lower & Lower	3426	12 (0.4)	1.00	1.00	
Middle & Upper	2074	27 (1.3)	3.75 (1.90–7.42)	2.34 (1.16–4.73)	--
High BP					
No	3271	7 (0.2)	1.00	1.00	
Yes	2315	32 (1.4)	6.54 (2.88–14.83)	3.48 (1.50–8.11)	0.50 (0.17–0.74)
Duration of diabetes$					
0–9 years	155	21 (13.5)	1.00	1.00	
10–14 years	27	5 (18.5)	1.02 (0.32–3.23)	1.00 (0.25–2.65)	0.00
≥ 15 years	18	12 (66.7)	9.21 (2.98–28.41)	8.62 (2.63–28.29)	0.02 (0.0–0.11)
Cigarette smoking§§					
Never a smoker	5122	32 (0.6)	1.00	1.00	
Ever smoker	463	7 (1.5)	2.44 (1.07–5.56)	1.10 (0.44–2.79)	0.10 (0.0–0.14)
Cigar smoking§§					
Never a smoker	4975	36 (0.7)	1.00	1.00	
Ever smoker	610	3 (0.5)	1.00 (0.21–2.35)	1.37 (0.36–5.14)	0.04 (0.0–0.33)

Notes: §Cigarette and cigar smoking variables were replaced in the multivariable logistic regression model.
§Age adjusted odds ratios.
‡PAR estimates were derived from multivariable logistic regression model and therefore are not additive. In the parentheses, 95% CIs.
$Categories for these variables were combined to increase the power of the analysis.
Socioeconomic status defined according to monthly per capita income in Indian rupees: ≤ 200 extreme lower; 201–500 lower; 501–2000 middle and >2000 upper. Data on socioeconomic status were not available for 86 subjects. Data on duration of diabetes were not available for one subject. Data on smoking were not available for one subject.

retinopathy. Preventing the conversion of such persons to more severe forms of retinopathy is very important. This needs a concerted effort by ophthalmologists and internists who are engaged in the primary care for diabetes.

We found with multivariable analysis that subjects belonging to the middle or upper socioeconomic strata had a 2.3 fold higher risk of having DR than those belonging to lower or extreme lower strata and it was statistically significant (Table 2). One could speculate that this trend could be the result of less predisposition of the lower socioeconomic strata to DR or higher mortality at relatively younger age or a combination of these two. Further

Table 3 Relation of duration since diagnosis of diabetes and DR (n = 200)

Duration since diagnosis of diabetes	Number (%) without DR	Number (%) mild NPDR	Number (%) moderate NPDR	Number (%) severe NPDR	Number (%) PDR
0–9 years	134 (67.0)	12 (6.0)	9 (4.5)	0	0
10–14 years	22 (11.0)	1 (0.01)	2 (1.0)	1 (0.01)	1 (0.01)
15–19 years	5 (2.5)	5 (2.5)	1 (0.01)	1 (0.01)	0
≥20 years	1 (0.01)	2 (1.0)	2 (1.0)	1 (0.01)	0
Total	162 (81.0)	20 (10.0)	14 (7.0)	3 (1.5)	1 (0.01)

Notes: Data on duration of diabetes were not available for one subject. NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

study would be needed for verification of this finding and its implications.

We found a statistically significant association between hypertension and DR, which is in accordance with previously published reports (Klein 1989; Tapp et al 2003; Van Leiden 2003; Hove et al 2004; Leske et al 2005; Rema, Premkumar et al 2005; Wong et al 2006). Though a lot of studies have shown the association between hypertension and DR, the exact pathogenesis is not known. However, the available evidence supports the theory that (a) hemodynamic alternations in retinal microvasculature and (b) hypertension induced increased expression of vascular endothelial growth factor could be the probable mechanisms involved in the progression of DR. The pathogenesis of renal microangiopathy may be very similar to that of retinal microangiopathy, and both may be accelerated by high blood pressure. This study demonstrates that the blood pressure of persons with diabetes should be monitored in addition to their glucose control. Population attributable risk (PAR) percentage for associated risk factors varied between 10%–50%. The prevalence of hypertension in this population seems high and may reflect error in the diagnosis. If we take a conservative definition of hypertension (if a subject had a history of high blood pressure diagnosed by a physician and/or current usage of anti hypertensive medications), the prevalence decreases to 9% and the PAR to 18%. The prevalence of hypertension in other studies has been reported to vary from 20% to 40% in urban adults and 12%–17% in rural residents (Gupta 2004). If we consider these prevalence estimates, the PAR% for hypertension in urban adults could be as low as 33% and as high as 50%. The PAR% for hypertension in rural residents could vary from 23% to 30%. Either way, the high PAR% for hypertension in this population is an additional reason for modifying this risk factor as a public health intervention. A PAR% of 10% for smoking provides another reason to encourage people to give up this habit.

The association of longer duration with a higher the risk of DR was in accordance with previously published reports (DCCT 1993; Klein et al 1995; Shriwas et al 1996; UKPDS 1998a, 1998b; Larsson et al 1999; Tapp et al 2003; Giuffre et al 2004; Jenchitr et al 2004; Varma 2006; Wong et al 2006). In the present study, the prevalence of DR was 19% among diabetes subjects, which is similar to that previously published report from a different state of southern India (Rema, Sujatha et al 2005). Changing demographics in India, shift towards aging, higher prevalence of diabetes, translates to a lot more persons with diabetes possibly living longer, thus more persons at risk for DR.

With the availability of the tools like the Diabetes Risk Score (Mohan et al 2005), it is possible to identify those at high risk of diabetes in the general population. Primordial preventive measures like weight control and lifestyle changes can prevent the progression of diabetes and its complications like DR. Maintaining a strict glycaemic control and regular ophthalmic examinations of those identified as diabetic to detect early retinopathy are the ways to prevent blindness from retinopathy in people with diabetes (Narendran et al 2002). Treatment modalities exist that can prevent or delay the onset of diabetic retinopathy, as well as prevent loss of vision, in a large proportion of patients with diabetes. Timely laser photocoagulation therapy can also prevent loss of vision in a large proportion of patients with severe NPDR and PDR and/or macular edema. Because a significant number of patients with vision-threatening disease may not have symptoms, ongoing evaluation for retinopathy is a valuable and required strategy (Fong et al 2004). This is yet another reason to insist on a comprehensive eye exam, especially in a country where this is not always the norm.

The many strengths of this study include use of standardized methods for collecting and grading of fundus photograph, the representativeness of the study population, and the high response rate. A limitation of study is that all standard photographic fields of the stereo fundus photographs were not taken and graded by masked observer(s). Although the two ophthalmologists who graded DR clinically were trained specially for the study, it is possible that some misgrading of DR could have occurred. If any cases of DR were missed, however, these would have most likely been mild NPDR. The other limitations of our study include the ascertainment of diabetes by history, and the relatively few cases of DR. It is possible that we may have missed some important risk factors.

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References

Dandona R, Dandona L, Naduvilath TJ, et al. 1997. Design of a population study of visually impairment in India: The Andhra Pradesh Eye Disease Study. *Indian J Ophthalmol*, 45:251–7.

Dandona L, Dandona R, Naduvilath TJ, et al. 1998. Is eye-care-policy focus almost exclusively on cataract adequate to deal with blindness in India? *Lancet*, 2l:1312–16.

Dandona L, Dandona R, Srinivas M, et al. 2001. Blindness in the Indian State of Andhra Pradesh. *Invest Ophthalmol Vis Sci*, 42:908–16.

[DCCT] The Diabetes Control and Complications Trail (DCCT) Research Group. 1993. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes. *N Engl J Med*, 329:977–86.

Ferris FL III. 1993. How effective are treatments for diabetic retinopathy? *JAMA*, 269:1290–1.

Fong DS, Aiello L, Gardner TW, et al. 2004. Retinopathy in diabetes. *Diabetes Care*, 26:S84–7.

Giuffre G, Lodato G, Dardanoni G. 2004. Prevalence and risk factors of diabetic retinopathy in adult and elderly subjects: The Casteldaccia Eye Study. *Graefes Arch Clin Exp Ophthalmol*, 242:535–40.

Gupta R. 2004. Trends in hypertension epidemiology in India. *J Hum Hypertens*, 18:73–8.

Hove MN, Kristensen JK, Lauritzen T, et al. 2004. The prevalence of retinopathy in an unselected population of type 2 diabetes patients from Arhus County, Denmark. *Acta Ophthalmol Scand*, 82:443–8.

Jenchitr W, Samaiporn S, Lertmeemongkolchai P, et al. 2004. Prevalence of diabetic retinopathy in relation to duration of diabetes mellitus in community hospitals of Lampang. *J Med Assoc Thai*, 87:1321–6.

Kempen JH, O'Colmain BJ, Leske MC, et al. 2004. The prevalence of diabetic retinopathy among adults in the United States. *Arch Ophthalmol*, 122:552–63.

King H, Aubert RE, Herman WH. 1998. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and proportions. *Diabetes Care*, 21:1414–31.

Klein R, Barrette-Connor EL, Blunt BA, et al. 1991. Visual impairment and retinopathy in people with normal glucose tolerance, impaired glucose tolerance, and newly diagnosed non-insulin-dependent diabetes mellitus. *Diabetes Care*, 114:914–18.

Klein R, Klein BE. 1995. Vision disorders in diabetes. In: Harris MI, Cowie CC, Stern MP, et al eds. Diabetes in America. 2nd ed. NIH Publication 95-1468. Bethesda, MD: National Institute of Health p 293–338.

Klein R, Klein BE, Moss SE. 1984a. Visual impairment in diabetes. *Ophthalmology*, 91:1–9.

Klein R, Klein BEK, Moss SE, et al. 1984b. The Wisconsin Epidemiologic Study of Diabetic Retinopathy III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol*, 102:527–32.

Klein R, Klein BEK, Moss SE, et al. 1989. Is blood pressure a predictor of the incidence or progression of diabetic retinopathy?. *Arch intern Med*, 149:2427–32.

Kumar A. 1998. Diabetic blindness in India: the emerging scenario. *Indian J Ophthalmol*, 46:65–6.

Larsson LI, Alm A, Bergenheim T, et al. 1999. Retinopathy in diabetic patients aged 15–50 years in the county of Umea, Sweden. *Acta Ophthalmol Scand*, 77:430–6.

Lopez IM, Diez A, Velilla S, et al. 2002. Prevalence of diabetic retinopathy and eye care in a rural area of Spain. *Ophthalmic Epidemiol*, 9:205–14.

Leske ME, Wu SY, Hennis A, et al. 2005. Hyperglycemia, blood pressure, and the 9-year incidence of diabetic retinopathy: the Barbados Eye Studies. *Ophthalmology*, 112:799–805.

Lundbaek K. 1955. Diabetic retinopathy in newly diagnosed diabetes mellitus. *Acta Med Scand*, 152:53–60.

Mohan V, Deepa R, Deepa M, et al. 2005. A simplified Indian Diabetes Risk Score for screening for undiagnosed diabetic subjects. *J Assoc Physicians India*, 53:759–63.

Moss SE, Meuer SM, Klein R, et al. 1989. Are seven standard photographic fields necessary for classification of diabetic retinopathy?. *Invest Ophthalmol Vis Sci*, 30:823–8.

Nirmalan PK, Katz J, Robin AL, et al. 2004. Prevalence of vitreoretinal disorders in a rural population of southern India: the Aravind Comprehensive Eye Study. *Arch Ophthalmol*, 122:581–6.

Olk RJ, Lee CM. 1993. Diabetic retinopathy: practical management. Philadelphia: JB Lippincott 3–20.

Pearce N. 1989. Analytical implications of epidemiological concepts of interaction. *Int J Epidemiol*, 18:976–80.

Rema M, Premkumar S, Anitha B, et al. 2005. Prevalence of diabetic retinopathy in urban India: The Chennai Urban Rural Epidemiology Study (CURES) Eye Study, I. *Invest Ophthalmol Vis Sci*, 46:2328–33.

Rema M, Sujatha P, Pradeepa R. 2005. Visual outcomes of pan-retinal photocoagulation in diabetic retinopathy at one-year follow-up and associated risk factors. *Indian J Ophthalmol*, 53:93–9.

Rosner B. 1986. Fundamentals of Biostatistics, 2nd ed. Boston: PWS Publishers p 84–92, 404–08.

Shriwas SR, Rahman Isa AB, Reddy SC, et al. 1996. Risk factors for retinopathy in diabetes mellitus in Kelantan, Malaysia. *Med J Malaysia*, 51:447–52.

Tapp RJ, Shaw JE, Harper CA, et al. 2003. The prevalence of and factors associated with diabetic retinopathy in the Australian population. *Diabetes Care*, 26:1731–7.

Tewari HK, Venkatesh P. 2004. Diabetic retinopathy for general practitioners. *Indian Med Assoc*, 102:722–3.

[UKPDS] UK Prospective Diabetes Study Group. 1998a. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk complications in patients with type 2 diabetes. UKPDS 33. *Lancet*, 352:837–53.

[UKPDS] UK Prospective Diabetes Study Group. 1998b. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes. UKPDS 38. *BMJ*, 317:703–13.

Van Leiden HA, Dekker JM, Moll AC, et al. 2003. Risk factors for incident retinopathy in a diabetic and nondiabetic population: the Hoorn study. *Arch Ophthalmol*, 121:245–51.

Varma R. 2006. Diabetic retinopathy: challenges and future directions. *Am J Ophthalmol*, 141:539–41.

Varma R, Torres M, Pena F, et al. 2004. Prevalence of diabetic retinopathy in adult latinos; the los angeles latino eye study. *Ophthalmology*, 111:1298–306.

WHO. 1980. Expert Committee on Diabetes Mellitus. Technical Report Series 646. Geneva: WHO

Wild S, Roglic G, Green A, et al. 2004. Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. *Diabetes Care*, 27:1047–53.

Wong TY, Klein R, Islam A, et al. 2006. Diabetic Retinopathy in a Multiethnic Cohort in the United States. *Am J Ophthalmol*, 141:446–55.