Population based assessment of diabetic retinopathy in an urban population in southern India

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Abstract

***Aim*—To assess the prevalence of diabetic retinopathy and the visual impairment caused by it in an urban population in southern India in order to determine its public health significance.**

***Methods*—2522 subjects (85.4% of those eligible), a representative sample of the population of Hyderabad city in southern India, underwent interview and detailed dilated eye examination during 1996–7 as part of the Andhra Pradesh Eye Disease Study.**

***Results*—124 subjects, all ⩾30 years old, reported that they had diabetes, an age-sex adjusted prevalence of 7.82% (95% confidence interval (CI) 5.76–9.88%) in this age group. Diabetes was diagnosed at age ⩾30 years in all but two subjects. The duration since diagnosis of diabetes was <10 years in 75.6% and ⩾15 years in 6.7%. Diabetic retinopathy was present in 28 subjects, 1.78% (95% CI 1.09–2.48%) of those ⩾30 years old. Most of the diabetic retinopathy was of the mild (50%) or moderate (39.3%) non-proliferative type; one subject (3.6%) had proliferative retinopathy. Multiple logistic regression revealed that the odds of having diabetic retinopathy were significantly higher in those ⩾50 years than in those 30–49 years old (odds ratio 7.78, 95% CI 2.92–20.73). Three subjects had visual impairment between 6/12 and 6/38 in either eye due to diabetic retinopathy, 0.19% (95% CI 0–0.41%) of those ⩾30 years old.**

***Conclusion*—Visual impairment due to diabetic retinopathy was relatively uncommon in this urban Indian population in 1996–7. However, this could change in the near future with an increase in duration of diabetes because of the anticipated aging of India's population and the recent suggestion of increase in diabetes prevalence in urban India, and therefore should be monitored.**

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It is being suggested that diabetic retinopathy (DR) is becoming an important cause of visual impairment in India.[1] However, population based data on the prevalence of DR in India and the visual impairment caused by it are not available. The public health significance of DR can be assessed only with population based data. We obtained these data in a sample representative of the population of Hyderabad city, as part of the Andhra Pradesh Eye Disease Study (APEDS), a population based epidemiology study in the state of Andhra Pradesh in southern India.[2–4]

Methods

Details of the sampling and methods of APEDS have been reported elsewhere.[2–4] This study was approved by the ethics committee of the LV Prasad Eye Institute, Hyderabad, India. The aspects relevant to this report follow.

The total sample for APEDS was determined as 10 000, 2500 each in one urban and three rural areas.[2] This sample size was calculated to get 5000 subjects each in the two age groups below and above 30 years because for an actual prevalence of 0.5% for an eye disease in either of these age groups this sample size would estimate it between 0.3–0.8% at the 95% confidence level.[2]

A multistage sampling procedure was used to obtain the APEDS urban sample representative of the 3.5 million population of Hyderabad city in southern India. The blocks (clusters) of Hyderabad were stratified by socioeconomic status and religion.[2 3] The socioeconomic strata were: extreme lower (monthly per capita income in rupees ⩽200 (£3.2)), lower (201–500), middle (501–2000), and upper (>2000). The religion strata were Hindu and Muslim. Twenty four clusters were chosen using stratified random sampling with equal probability of selection.[3] The selected clusters were mapped, and every third to fifth household was randomly systematically selected to obtain a similar number of households in the different clusters. Oversampling of those above 30 years of age was done by randomly assigning 10 of the selected clusters to have only subjects older than 30 years eligible, and the other 14 clusters to have all ages eligible.[2 3] Aiming for a recruitment rate of at least 85%, a total of 2954 subjects were sampled to obtain a minimum sample of 2500 subjects.

The sampled subjects were interviewed in detail.[2] This included systemic history about the diagnosis and treatment of diabetes and ocular history.

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 examination, and dilatation of pupil unless contrain-

Table 1 Age adjusted prevalence of self reported diabetes and diabetic retinopathy

	Percentage prevalence (95% CI) in those ⩾30 years old	
	Males	*Females*
Self reported diabetes	9.44 (6.48–12.40)	6.49 (4.30–8.68)
Diabetic retinopathy*	2.14 (1.00–3.27)	1.49 (0.60–2.38)

*Diabetic retinopathy diagnosed after detailed dilated fundus examination.

dicated because of risk of angle closure. After dilatation, stereoscopic fundus examination was done at the slit lamp using 78 dioptre lens and with the indirect ophthalmoscope using 20 dioptre lens.

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

To grade DR a slight modification of a standard classification system[5] was done for simplification. DR was classified as mild non-proliferative DR (NPDR) if, along with microaneurysms and hard exudates in the retina, mild intraretinal haemorrhages were present in fewer than four quadrants; moderate NPDR if mild to moderate intraretinal haemorrhages were present in four quadrants; severe NPDR if any of the following three were present: severe intraretinal haemorrhages in four quadrants, venous beading in two quadrants, obvious intraretinal microvascular abnormalities in one quadrant; and very severe NPDR if more than one of the three features listed for severe NPDR were present. DR was classified as proliferative DR (PDR) if any of the following were present: neovascularisation of the retina or iris or angle, preretinal or vitreous haemorrhage, tractional retinal detachment. If the two eyes of a subject had different grades of DR, the worse grade was considered for analysis.

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[6] were not taken. However, 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.

It was planned that subjects with fundus findings suggestive of DR who were not known diabetics would have random blood glucose tested with finger stick and glucometer (Bayer). If this was <120 mg/dl (6.7 mmol/l), fasting blood glucose would be tested on another day. If this was >120 mg/dl, the subject would be considered to have diabetes.[7]

The demographic structure of Hyderabad[8] was used for age-sex adjustment of the prevalence estimates of diabetes and DR. Design effect of the sampling strategy was calculated from the prevalence in each cluster,[9] and 95% confidence intervals of the estimates adjusted accordingly. The association of age, sex, socioeconomic status, and religion with DR was assessed with univariate χ^2 analysis and multiple logistic regression.[10]

Table 2 Univariate distribution of diabetic retinopathy

	Total in group	*Number with diabetic retinopathy*	*Prevalence (%)*
Age* (years)			
30–39	463	1	0.22
40–49	390	4	1.02
50–59	257	15	5.84
60–69	182	6	3.30
⩾70	89	2	2.25
Sex†			
Male	623	14	2.24
Female	758	14	1.85
Socioeconomic status‡			
Extreme lower	120	2	1.67
Lower	516	7	1.36
Middle	576	16	2.78
Upper	142	3	2.11
Religion§			
Hindu	871	18	2.07
Muslim	480	10	2.08
Other	30	0	0

In 18 of the 1399 subjects ⩾30 years old, fundus could not be seen in either eye because of media opacity or small pupil; these subjects are not included in this table.
In 28 of the 1399 subjects ⩾30 years old, information about socioeconomic status was not available; in one of these 28 subjects, fundus could not be seen in either eye.
p Values with χ^2 test: *p<0.001, †p=0.60, ‡p=0.42, §p=0.73.

Results

In all, 2522 subjects (85.4% of those eligible) were interviewed and examined between October 1996 and June 1997. The age range of these subjects was 1 month to 102 years. A total of 1399 (55.5%) were ⩾30 years old, and 1347 (53.4%) female; 23 (0.9%) subjects were examined at home. Some 124 subjects, all ⩾30 years old, reported that they had been diagnosed to have diabetes, an age-sex adjusted prevalence of 7.82% (95% confidence interval (CI) 5.76–9.88%, design effect 2.15) in those ⩾30 years old and 2.44% (95% CI 1.40–3.47%, design effect 2.94) in all age groups considered together. Their mean age was 54 years, median 53 years, and range 31–86 years. The prevalence of self reported diabetes was higher in males than in females ⩾30 years old (Table 1). In two subjects diabetes was diagnosed at age 25 and 29 years, respectively, while in the rest at age ⩾30 years. Another 32 years old female subject not known to be diabetic had what looked like typical DR, but she refused to have a blood glucose test. However, she was considered to be diabetic based on typical DR. Of the 124 self reported diabetics, 97 (78.2%) were taking oral hypoglycaemics, 11 (8.9%) were using insulin, and 16 (12.9%) were not using any medication for diabetes.

No major discrepancy was found between the clinical grading of DR and that assessed by evaluation of the photographs taken as described in the methods section. DR was present in 28 subjects (22.4% of those with diabetes), all ⩾30 years old, an age-sex adjusted prevalence of 1.78% (95% CI 1.09–2.48%, no design effect) in those ⩾30 years old and 0.56% (95% CI 0.23–0.89%, design effect 1.25) for all age groups considered together. Like self reported diabetes, the prevalence of

Table 3 Association of demographic variables with diabetic retinopathy by multiple logistic regression

	Odds ratio for having diabetic retinopathy	*95% CI*
Age* (years)		
30–49	1.00	
⩾50	7.78	2.93–20.73
Sex		
Male	1.00	
Female	0.94	0.44–2.01
Socioeconomic status*		
Extreme lower or lower	1.00	
Middle or upper	1.86	0.83–4.17
Religion		
Hindu	1.00	
Muslim	0.85	0.39–1.89
Other	0.01	0 to >10[12]

*Categories for these variables were combined to increase power of the analysis.

DR was also more in males than in females ⩾30 years old (Table 1).

The univariate distribution of DR in the various demographic categories is shown in Table 2. Multiple logistic regression revealed that age ⩾50 years was associated with significantly higher odds of DR (Table 3). The odds of having DR were somewhat higher for the upper and middle than for the lower and extreme lower socioeconomic strata, but this difference did not reach statistical significance (Table 3).

Of the subjects using insulin for diabetes 70% had DR compared with 20.2% DR in those using oral hypoglycaemics for diabetes (p=0.004, Fisher's exact test) and 11.8% DR in those using no medication for diabetes (p=0.002, Fisher's exact test).

Of the 28 subjects with DR, 14 (50%) had mild NPDR, 11 (39.3%) moderate NPDR, two (7.1%) severe NPDR, none very severe NPDR, and one (3.6%) PDR. Of these 28 subjects, four (14.3%) had clinically significant macular oedema (CSMO). Three subjects had had partial mid-peripheral retinal photocoagulation in one or both eyes. One of these subjects had PDR. However, the other two subjects had moderate NPDR but did not have evidence of PDR or clear suggestion of previous PDR, indicating that this laser treatment may have been done for non-standard indications.

Table 4 Relation of duration since diagnosis of diabetes and diabetic retinopathy

Duration since diagnosis of diabetes	*Number (%) without DR*	*Number (%) mild NPDR*	*Number (%) moderate NPDR*
0–9 years	73 (61.3)	9 (7.6)	8 (6.7)
10–14 years	17 (14.3)	1 (0.8)	1 (0.8)
15–19 years	0	2 (1.7)	0
⩾20 years	1 (0.8)	2 (1.7)	2 (1.7)
Total	91 (76.5)	14 (11.8)	11 (9.2)
Duration since diagnosis of diabetes	*Number (%) severe NPDR*	*Number (%) PDR*	*Number (%) Total*
0–9 years	0	0	90 (75.6)
10–14 years	1 (0.8)	1 (0.8)	21 (17.6)
15–19 years	1 (0.8)	0	3 (2.5)
⩾20 years	0	0	5 (4.2)
Total	2 (1.7)	1 (0.8)	119 (100)

Of the 125 diabetics, fundus could not be examined in either eye in 4 owing to dense cataract or small pupil, and data regarding duration of diabetes were not available for 2. These 6 subjects are not included in this table.
NPDR=non-proliferative diabetic retinopathy; PDR=proliferative diabetic retinopathy.
Percentages do not add up exactly to the total because of rounding.

The relation between the duration since diagnosis of diabetes and DR is shown in Table 4.

Only in three subjects, could visual impairment of <6/12 in either eye be attributed to DR. In one subject visual acuity was 6/19 in both eyes as a result of diabetic maculopathy. In another, one eye had PDR and CSMO with acuity 6/15, and the other eye had PDR with acuity 6/11.5. In the third subject, both eyes had CSMO and acuity was 6/37.8 and 6/9.5 in the two eyes, respectively. No eye was blind (visual acuity <6/60) as a result of DR. The age-sex adjusted prevalence of this visual impairment in either eye was 0.19% (95% CI 0–0.41%) in those ⩾30 years old.

Discussion

India has a large burden of visual impairment, including blindness. It is estimated that of the population of about a billion 1–1.5% are blind.[3 11 12] To deal with such a large burden of blindness, the priorities have to be based on reliable population based data. It is felt by some in India that DR is becoming a significant cause of visual impairment.[1] This paper evaluates the public health significance of DR based on population based data from the urban segment of the ongoing epidemiological study, APEDS, in southern India.

In the urban population studied, the prevalence of self reported diabetes was 7.8% in those ⩾30 years old or 2.4% of the population. This is very likely much lower than the actual prevalence of diabetes in this population because of undiagnosed diabetes. Almost all of the self reported diabetes was diagnosed at ⩾30 years of age. DR was present in 22.4% of the self reported diabetics. In comparison, 22.8% of those with self reported diabetes had DR in the Melbourne Visual Impairment Project,[13] and 32.4% of the diabetics in Blue Mountains Eye Study,[14] 26% in Rotterdam Study,[15] 52% in Melton Study,[16] and 36.8% in Beaver Dam Eye Study.[17] In a large series of diabetics attending a diabetes centre in southern India, 34.1% were reported recently to have DR.[18]

In the present study, 1.8% of the population ⩾30 years old had DR. The vast majority of those with DR had mild or moderate NPDR (89.3%); severe NPDR or PDR was present in only 10.7%. Twelve per cent (three of 25) of those with mild or moderate NPDR had CSMO of which one third was associated with visual impairment (acuity <6/12). Visual impairment in either eye as a result of DR was present in one tenth of those with DR; this translates into one out of 525 people ⩾30 years old or one out of 1700 population. Visual impairment in the better eye due to DR was one third of this rate. No eye was blind (acuity <6/60) due to DR in the sample studied. A higher occurrence of blindness due to DR has been reported from the developed countries.[19–21] One reason for this difference could be that diabetics in India may be dying younger and therefore the duration of diabetes may not be as much as in the developed countries. This may in turn result in less chance of

advanced DR developing which could result in blindness. Increase in duration of diabetes has been shown to be associated with higher risk of blindness which increases particularly after about 15 years of diabetes.[19] In our sample, 87.5% of those with duration of diabetes since diagnosis ⩾15 years had DR compared with 18.9% of those with duration <15 years. However, none of those with duration of diabetes since diagnosis ⩾15 years had advanced DR which could have resulted in blindness. This could be due to the small number of subjects in this group (eight) or to some other unidentified reason. Another reason for not finding blindness caused by DR in our sample could be that the majority of the diabetes (98.4%) had been diagnosed at ⩾30 years of age. It has been reported that diabetes diagnosed at <30 years of age is more common in developed countries,[22] and it is associated with a higher chance of blindness caused by DR.[19]

We found with multivariate analysis that subjects belonging to the upper or middle socioeconomic strata had a 86% higher chance of having DR than those belonging to the lower or extreme lower strata though this did not reach statistical significance. 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 in these strata before DR can develop or a combination of these two. Further study would be needed for verification of this finding and its implications.

A limitation of our study is that all standard photographic fields of the fundus were not photographed and graded by masked observer(s). Although the two ophthalmologists who graded DR clinically were trained specifically 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.

In this urban population in southern India 1% had blindness, the causes of which were varied, including cataract, retinal diseases (retinitis pigmentosa, chorioretinitis scar, atrophic macula, myopic degeneration, retinal detachment), corneal diseases, refractive error, glaucoma, and optic atrophy.[3] DR did not contribute to this blindness. In this same population, moderate visual impairment was present in 7.2%,[4] to which DR contributed only a minute fraction (0.013%). In brief, compared with other causes DR contributed very little to visual impairment in this urban population in southern India in 1996–7. However, these results should be interpreted with extreme caution. It is anticipated that the population of India will age over the next few decades—that is, the proportion of older people in the population will increase. It is possible that this would result in increase in the number of years that people would live with diabetes, thereby, increasing the chance of visual impairment due to DR. In addition, there is evidence that the prevalence of diabetes has recently been increasing considerably in urban India.[23] This, along with aging of the population, may increase the predisposition to visual impairment due to DR significantly in urban India over the next decade or two. Therefore, in order to monitor the relative public health importance of visual impairment due to DR and other causes in India, new reliable population based data will be needed in the future.[24]

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