



## Systemic Co Morbidities, Visual Defect and Severity of Diabetic Retinopathy in Diabetics at Presentation

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### Abstract

**Aim:** To assess systemic co morbidities, visual defect and severity of DR at presentation in diabetics in a tertiary care center.

**Methods:** A cross sectional study conducted for a period of 18 months in 130 newly detected Diabetic Retinopathy cases (DR) in a tertiary care center. They were evaluated with a proforma for risk factors and staging of retinopathy was done with International Clinical Diabetic Retinopathy Disease Severity Scale.

**Results and Discussion:** The duration of diabetes had significant association with stage of DR at presentation ( $p=0.048$ ). Co morbidities like hypertension, dyslipidemia, CVA, CAD had no significant association with the stage of DR ( $P=0.001$ ). Previous cataract surgery had no association with the stage of DR at presentation. Patients with co-existing diabetic nephropathy had more prevalence of DR and they had more severe presentation at the beginning ( $p=0.004$ ).

**Conclusion:** The study found significant association between stage of diabetic retinopathy and age at diagnosis, mean duration of diabetes, co morbid nephropathy and low BMI in advanced cases. The study opened up a window to intensify the need for early diagnosis and management of DR cases, because it was found that there is progression of stage of DR, and deterioration of visual acuity as the time passed by.

**Keywords:** diabetic retinopathy, risk factor, clinical profile, visual outcome.

### Introduction

Diabetic Retinopathy (DR), a long-term complication of Diabetes Mellitus, is asymptomatic in its most treatable stages when the condition would be neglected due to ignorance or carelessness. Vision Threatening Diabetic Retinopathy (VTDR) is a major cause of blindness

among the working age group<sup>1,2,3,4</sup>. The estimated high prevalence of diabetes by 2030 in India is a matter of concern considering the potential of vision loss associated with increase in incidence of diabetic retinopathy. However, progression of diabetic retinopathy can be delayed by early detection of diabetes, proper screening to detect

retinopathy in early stages and timely treatment of the same, along with control of other contributing factors. Thus, timely detection and treatment can significantly reduce visual impairment, and thus improve quality of life. So, there is a need to assess the stage of retinopathy at diagnosis and the different factors contributing to the development of retinopathy. Although many epidemiologic studies conducted worldwide have clearly outlined the clinical-epidemiological profile of DR at presentation this study will give regional data which would be helpful to reassess the current status, identify any changing trends, create awareness among the study population and would serve as a baseline data for future research.

### Materials and Methods

The present study was conducted with an objective of (1) To assess visual defect, systemic comorbidities and severity of DR at the time of presentation (2) To describe the clinical profile of DR at the time of diagnosis. Sample size was calculated from a study conducted by Singh P et al<sup>5</sup> assessing prevalence of DR in diabetic patients of Vindhya region; 69.44% of DR cases were in pre-proliferative stage. A cross sectional study of 127 newly diagnosed diabetic retinopathy cases who attended OPD formed the sample. The study was conducted for a period of 18 months at a tertiary care center. Diabetic retinopathy cases (1) on treatment and follow up, (2) with significant hazy media preventing staging of retinopathy and (3) Diabetics with other retinal disorders like age related macular degeneration, hypertensive

retinopathy, venous occlusions, primary open angle glaucoma, optic atrophy etc. were excluded from the study.

### Procedure

After getting Institutional review board clearance, those who gave informed consent were evaluated by the principal investigator with the help of a structured proforma for socio demographic and disease related variables. Height and weight of the subjects were measured. Blood pressure recorded in the right arm in the sitting posture after taking rest for a period of five minutes. Comprehensive ocular examination was done. Fundus evaluation with indirect ophthalmoscopy with 20D lens and slit lamp biomicroscope using 90D lens was done. ICDRS classification were used to classify Diabetic retinopathy and Diabetic Macular Edema.

Fundus Fluorescein Angiography and Optical Coherence Tomography were used in cases with macular edema, suspicious macular ischemia, doubtful proliferative retinopathy and also to rule out other diagnosis.

Data was analyzed with IBM SPSS version 16 software. The study variables were assessed using chi-square test (for qualitative variables) and t test/ANOVA (for quantitative/continuous variables). The level of statistical significance was taken as p value less than 0.05.

### Results

Results are presented in Table 1.

**Table 1** Incidence of Variables, Categories, Number of cases, Percentage, Chi square and ANOVA Test Results

| SL. No. | Variable                         | Category      | Number of Cases | Percentage | Chi Square / ANOVA test results |
|---------|----------------------------------|---------------|-----------------|------------|---------------------------------|
| 1       | Sex                              | Male          | 81              | 62.3       |                                 |
|         |                                  | Female        | 49              | 37.7       |                                 |
| 2       | Income                           | BPL           | 67              | 51.5       |                                 |
|         |                                  | APL           | 63              | 48.5       |                                 |
| 3       | Duration of Diabetics            | < 1 year      | 4               | 3.1        |                                 |
|         |                                  | 1 – 10 years  | 70              | 53.8       |                                 |
|         |                                  | > 10 years    | 56              | 43.1       |                                 |
| 4       | Stage of Diabetic Retinopathy at | Mild NPDR     | 103             | 39.61      |                                 |
|         |                                  | Moderate NPDR | 104             | 40         |                                 |
|         |                                  | Severe NPDR   | 16              | 6.15       |                                 |

|                         |                                |               |     |        |   |
|-------------------------|--------------------------------|---------------|-----|--------|---|
|                         | presentation                   | PDR           | 37  | 14.23  |   |
| 5                       | Stage of DME at presentation   | No            | 137 | 58     |   |
|                         |                                | Mild          | 58  | 22.3   |   |
|                         |                                | Moderate      | 60  | 23.07  |   |
|                         |                                | Severe        | 5   | 1.92   |   |
| 6                       | Status of Iris (NVI)           | Present       | 12  | 4.6    |   |
|                         |                                | Absent        | 248 | 95.4   |   |
| 7                       | Status of Lens                 | Normal        | 166 | 63.84  |   |
|                         |                                | Cataract      | 74  | 28.46  |   |
|                         |                                | IOL           | 20  | 7.69   |   |
| Chi Square Test Results |                                |               |     |        |   |
| 8                       | Nephropathy                    | Mild NPDR     | 1   | 9.1    | X <sup>2</sup> = 13.25<br>P=0.004<br>P<0.05 |
|                         |                                | Moderate NPDR | 2   | 18.2   |   |
|                         |                                | Severe NPDR   | 4   | 36.4   |   |
|                         |                                | PDR           | 4   | 36.4   |   |
|                         | No Nephropathy                 | Mild NPDR     | 48  | 40.3   |   |
|                         |                                | Moderate NPDR | 46  | 38.7   |   |
|                         |                                | Severe NPDR   | 8   | 6.7    |   |
|                         |                                | PDR           | 17  | 14.3   |   |
| 9                       | History of Cataract Surgery    | Mild NPDR     |     | 25     | X <sup>2</sup> = 12.02<br>P=0.061<br>p>0.05 |
|                         |                                | Moderate NPDR |     | 62.5   |   |
|                         |                                | Severe NPDR   |     | 12.5   |   |
|                         |                                | PDR           |     | 0      |   |
|                         | No History of Cataract Surgery | Mild NPDR     |     | 43.4   |   |
|                         |                                | Moderate NPDR |     | 40.7   |   |
|                         |                                | Severe NPDR   |     | 1.8    |   |
|                         |                                | PDR           |     | 14.2   |   |
| 10                      | Hypertension                   | Mild NPDR     |     | 32.7   | X <sup>2</sup> =3.553 P=0.314<br>P<0.05     |
|                         |                                | Moderate NPDR |     | 48.2   |   |
|                         |                                | Severe NPDR   |     | 3.44   |   |
|                         |                                | PDR           |     | 15.5   |   |
|                         | No Hypertension                | Mild NPDR     |     | 48.61  |   |
|                         |                                | Moderate NPDR |     | 38.88  |   |
|                         |                                | Severe NPDR   |     | 2.77   |   |
|                         |                                | PDR           |     | 9.72   |   |
| 11                      | Dyslipidemia                   | Mild NPDR     |     | 33.33  | X <sup>2</sup> =5.781 P=0.123<br>P<0.05     |
|                         |                                | Moderate NPDR |     | 41.02  |   |
|                         |                                | Severe NPDR   |     | 2.56   |   |
|                         |                                | PDR           |     | 23.07  |   |
|                         | No Dyslipidemia                | Mild NPDR     |     | 45.05  |   |
|                         |                                | Moderate NPDR |     | 43.95  |   |
|                         |                                | Severe NPDR   |     | 3.29   |   |
|                         |                                | PDR           |     | 7.69   |   |
| 12                      | Activity                       | Active        |     | 6.2    | X <sup>2</sup> = 13.25<br>P=0.004<br>p>0.05 |
|                         |                                | Moderate      |     | 84.6   |   |
|                         |                                | Sedentary     |     | 9.2    |   |
| ANOVA Test results      |                                |               |     |        |   |
|                         |                                |               |     | Mean   | ANOVA                                       |
| 13                      | Visual Acquity                 | Mild NPDR     |     | 0.0611 | P= 0.00<br>P<0.5                            |
|                         |                                | Moderate NPDR |     | 0.075  |   |
|                         |                                | Severe NPDR   |     | 0.3143 |   |
|                         |                                | PDR           |     | 0.7875 |   |
| 14                      | Mean BMI                       | Mild NPDR     |     | 24.55  | P=0.001<br>P<0.5                            |
|                         |                                | Moderate NPDR |     | 25.36  |   |
|                         |                                | Severe NPDR   |     | 26.95  |   |
|                         |                                | PDR           |     | 23.2   |   |
| 15                      | Mean Hb                        | Mild NPDR     |     | 13.43  | P=0.00<br>P<0.5                             |
|                         |                                | Moderate NPDR |     | 14.04  |   |
|                         |                                | Severe NPDR   |     | 13.73  |   |
|                         |                                | PDR           |     | 12.32  |   |
| 16                      | Mean HbA1C                     | Mild NPDR     |     | 6.708  | P=0.00<br>P<0.5                             |
|                         |                                | Moderate NPDR |     | 7.283  |   |
|                         |                                | Severe NPDR   |     | 7.3    |   |
|                         |                                | PDR           |     | 8.457  |   |

## Discussion

The global increase of diabetes has a significant impact on the prevalence of diabetic complications among which diabetic retinopathy takes an important place. DR is a leading cause of acquired blindness in working age adults and has been estimated to represent 12% of blindness in developed countries. In the study the stage of diabetic retinopathy at which patients present to us for the first time was found out and the associated risk factors of DR were also assessed. The present study indicates that factors like age, duration of DM, nephropathy, and BMI are influencing DR.

Male gender was observed to be associated with the presence of DR, but not its severity. In this study out of 130 patients 81 (62.3%) were males and 49 (37.7 %) were females. Similar observations were made by Pradeepa et. al.<sup>6</sup> in an urban Indian population. In a study conducted by Rani P K et al<sup>7</sup> in Southern districts of Tamil Nadu male gender was considered as a risk factor associated with development of any DR. The age group of present study ranged from 25 to 72 years with the maximum patients (37.7%) coming under the range of 60 to 70 years. Results indicates that increasing age was significantly associated with increasing risk of diabetic retinopathy( $p < .05$ ).

Of the 130 patients 4 (3.1%) had duration of DM less than 1 year, 70 (53.8%) had duration of DM between 1 to 10 years and 56(43.1%) had duration more than 10 years. The relation between duration of DM and development of DR was statistically significant both in the 1 to 10 years group ( $p = .04$ ) and more than 10 years group ( $p = .03$ ). It shows that duration of diabetes is an important risk factor for development of diabetic retinopathy. Similar findings were seen in the studies conducted in Andhra Pradesh by Sannapaneni Krishnaiah et al<sup>8</sup> and also by Rani P K et al<sup>7</sup>.

According to the income status patients were divided into two categories APL and BPL; APL were 48.5% and BPL were 51.5%. The present study indicates that socio economic strata is not influencing DR occurrence. The study sample included 6.2 % of physically active subjects, 84.6

% of moderately active subjects, and 9.2 % with sedentary lifestyle. DR was found to be highest in moderately active group irrespective of its stages. Present study further substantiates the fact that DR is a complication found in active working population. This finding is contradicting with that of Anna Praidou et al<sup>9</sup> which indicates that lack of physical activity is a risk factor in the development of DM as well as DR.

At presentation out of 260 eyes of 130 cases 39.61% (103 eyes) showed mild NPDR changes, 40% (104 eyes) showed moderate NPDR changes, 6.15% (16 eyes) showed severe NPDR changes and 14.23% (37 eyes) showed PDR changes. Sannapaneni Krishnaiah et al.<sup>8</sup> population-based study in the state of Andhra Pradesh in India found out that the diabetic retinopathy is more in mild NPDR (51.3%), then moderate NPDR (35.9%), and proliferative retinopathy (2.6%) stages. Narendran et al's<sup>10</sup> population-based prevalence survey of DR in Palakkad district of Kerala also showed similar finding. NPDR (94.1%) was the most common form of retinopathy seen. So, the stage of DR at presentation is comparable to the findings obtained in other similar studies.

The relation between comorbidities like hypertension, dyslipidemia, neuropathy, nephropathy, CAD, CVA etc and stage of DR was assessed. Only nephropathy showed a statistically significant relation with diabetic retinopathy ( $p = .004$ ). 72.8% of patients with nephropathy had severe stages of retinopathy at presentation. Hypertension was considered as established risk factor for the progression of DR according to a study by Krishnaiah<sup>8</sup> in the state of Andhra Pradesh. But in the current study no significant association could be found between hypertension and DR ( $p > .05$ ). Narendran et al in Palakkad district of Kerala also presented a similar finding ( $p = .658$ ).

An increased BMI was considered as a risk factor for development of diabetes and other life style diseases such as hypertension and dyslipidemia. But in present study the relation of BMI to the

stage of DR showed a statistically significant relation ( $p=.001$ ). The PDR stage showed a mean BMI of 23.2. The present study is more in accordance with Rani PK<sup>7</sup> which projects Lean BMI as a significant risk factor associated with development of retinopathy. This inverse relation between BMI and DR could be due to the catabolic effect of lack of insulin over a long duration of hyperglycemia, resulting in lean individuals. There are evidences that South Asians have abdominal obesity despite normal BMIs, the so called "Asian Indian phenotype"; which may explain the paradox<sup>11</sup>. Further, it is interesting to note that in Caucasians, high BMI is observed in DM subjects, but in Asian population subjects with DM are lean<sup>12</sup>. This may be linked to the fact that Asians with type 2 DM show lesser insulin secretion, but greater insulin sensitivity as compared to Caucasian diabetic patients.<sup>13,14</sup>. But in another study by Narendran<sup>11</sup> in Southern India, BMI was found to be not associated with DR ( $p=0.317$ )

The status of iris and lens at presentation were assessed in the study and 4.6% of eyes had neovascularization of iris and 95.4% had no neovascularization of eyes at the time of presentation. The status of lens was assessed and 166 eyes (63.84%) were normal, 74 eyes (28.46%) had cataract and 20 eyes (7.69%) had intraocular lens implanted. The association between cataract surgery and stage of retinopathy was assessed and found to be not significant in the study. However, cataract surgery was found to have a significant correlation with progression of diabetic retinopathy in a study conducted by Chew EY, et al<sup>15</sup> in the National Institute of Health, Bethesda.

The proportion of DME cases at presentation was found out from different stages of DR and it was found to be no DME in 52.69%, mild DME in 22.3 %, moderate DME in 23.07 % and severe DME in 1.92%. Similar finding of diabetic maculopathy was observed in a study carried out in Department of Ophthalmology of Douala General Hospital, Cameroon by Ahmadou M Jingi et al.<sup>16</sup>. The mean visual acuity at presentation was

assessed for different stages of retinopathy and was found to be .0611 for mild, .0750 for moderate, .3143 for severe NPDR and .7875 for PDR cases which showed a statistically significant decrease in mean visual acuity as DR progressed with a p value of  $p=.000$ . Similar risk association of DR with moderate visual impairment was found in accordance with studies conducted by Rani PK and Raman R<sup>7</sup>.

Mean hemoglobin and HbA1C levels in the blood was calculated at the time of presentation and its association with stage of DR was found out. Mean Hb at presentation was 13.43mg/dl for mild, 14.04mg/dl for moderate, 13.73mg/dl for severe NPDR and 12.32mg/dl for PDR cases which had a significant p value ( $p= .00$ ) with mean hemoglobin least for severe cases. Such a significant association was not found in reviewed studies. Nephropathy may be the contributory factor for this association . Mean HbA1C levels also showed a significant relation with the stage of DR with p value  $<.05$ . The mean values of HbA1C were 6.708 for mild NPDR, 7.283 for moderate NPDR, 7.3 for severe NPDR and 8.457 for PDR cases. The mean HbA1C were lesser for mild cases and it increased as the stage of DR worsened. A significant association was found between HbA1C levels and DR in a study conducted by Axer- Siegel and Herscovici in Israel<sup>17</sup>.

### Conclusion

The study indicates that increasing age has significant association with the development of DR. Duration of diabetes was found to be the significant factor associated with development of DR, and for those with duration of diabetes of more than ten years the risk is very high. At presentation 79.6 % of the eyes were at a stage of either mild (39.61%) or moderate (40%) DR. This warrant the need of early diagnosis, interventions and regular follow up for a good visual outcome. Of the co morbidities only nephropathy was found to be having significant association, as persons with nephropathy had a more severe stage of



retinopathy. Other factors like dyslipidemia, hypertension, CAD, CVA was found to have no significant association. In our study it was found that a lean BMI has significant association with advanced stages of DR, which was shown in few studies conducted in India and is a significantly different finding from western countries where the patient is more obese. This interesting disparity was found to be due to relative insulin deficiency in Asian population compared to those in the west which leads to an increased catabolism and low BMI. Only few had neovascularization of iris (4.6%) at presentation, which is an indication of less severity at the beginning. It was found that there is no significant association between cataract surgery and DR. It was found that visual acuity is worsening with progression of retinopathy. So, it is possible to halt the progress of retinopathy and resulting visual impairment with early identification and treatment. Almost 50% had DME at presentation. These patients can be properly assessed and treated resulting in better prognosis. The study opens our view towards the need for regular screening, early detection and management of retinopathy for preventing blindness.

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