

# Hyperlipidemia, Hypercholesterolemia and Glycemic Control as Risk Factor for Diabetic Retinopathy

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## ABSTRACT

**Objective:** To investigate the blood lipids, serum cholesterol and glycaemic control as risk factor for Diabetic retinopathy (DR).

**Study Design:** Cross sectional study

**Place and Duration of Study:** This study was conducted at Muhammad Medical College Hospital Mirpurkhas and Consultant Clinics Hyderabad from March 2014 to January 2015.

**Materials and Methods:** 100 cases of DR were selected for present study. Fundoscopy was performed by the physician followed by a Consultant ophthalmologist. Blood was collected from peripheral vein after a fasting state of 8 – 12 hours. Glycated hemoglobin A1 (A1C) and lipids were evaluated by standard assays. Volunteers were requested to sign to informed consent proforma. Research topic was approved by ethics committee of institute. Statistix 8.1 for data analysis and P-value  $\leq 0.05$  was considered significant.

**Results:** Of 100 patients, 58 (58%) were male and 42 (42%) were female patients. Mean  $\pm$  SD age in patients with and without DR was  $49.5 \pm 8.5$  and  $46.3 \pm 5.1$  years respectively. 21% frequency was noted for DR of any type. Age, male, A1C, hypercholesterolemia, hyperlipidemia and microalbuminuria proved positive correlated with DR. Correlation of DR was not found with VLDL, HDLc and triacylglycerols

**Conclusion:** The present study reports hyperlipidemia, hypercholesterolemia and poor glycaemic control as risk factors for diabetic retinopathy.

**Key Words:** Diabetes Retinopathy, Hypercholesterolemia, Hyperlipidemia, HbA1c

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## INTRODUCTION

Worldwide, the diabetes mellitus (DM) is approaching epidemic proportions and becoming a major public health challenge. In the millennium year, the DM burden was approximately 171 millions, which was reported to be 11% higher than previous reports.<sup>1</sup> Current estimates shows 8 million of diabetics in Pakistan and a same burden of those suffering from the impaired glucose tolerance. DM is characterized by microvascular complication, and Diabetic retinopathy (DR) is one of its type.<sup>3</sup> DR runs a natural course of progression from mild, moderate to severe non-proliferative retinopathy (NPR) and proliferative retinopathy (PR). Increased vascular permeability occurs in mild NPR. The microvasculature shows closure in moderate and severe NPDR. Neo-vascularization occurs over retina and behind vitreous humor in severe form of retinopathy called PR. Severe PR shows vascular exudates because of leaky

microvasculature and retinal thickening.<sup>4</sup> Previous studies had reported for screening of DR and its cost effectiveness which is essential for clinical prevention.<sup>5</sup> Type 2 diabetics (T2DM) show a prevalence of 5-35% of DR at the time of clinical diagnosis.<sup>6</sup> DR has become a major cause of blindness the World over.<sup>7</sup> Pakistan scenario shows an alarmingly increased incidence of newly diagnosed DM in various parts of countries. Newly diagnosed DM is reported from rural areas as 5% and 4.8% in male and female respectively; while urban areas show higher frequency of 5.1% and 6.8% in male and female respectively.<sup>8</sup> Unfortunately, national data on the prevalence of DR is lacking in particular in the newly diagnosed DM subjects.

Several risk factors had been pointed out in the development of DR in DM such as increased body mass index (BMI), reduced BMI, poor glycaemic control, hypercholesterolemia, hyperlipidemia and raised fasting glucose,<sup>9,10</sup> but have never been searched. Because of the high prevalence of type 2 DM in Sindh, it is worth to search the issue to make national baseline data regarding risk factors of DR among newly diagnosed patients. The present study analyzed the risk factors and frequency of Diabetic retinopathy among type 2 diabetics.

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## MATERIALS AND METHODS

The present study of cross sectional design was conducted at Muhammad Medical College Hospital Mirpurkhas and Consultant Clinics - Hyderabad over duration of March 2014 - January 2015. The patients were selected through non-probability purposive sampling. The criteria for diagnosis of type 2 DM were according to WHO guidelines 1994. A sample of 100 subjects was selected through non-probability purposive sampling as per pre-defined inclusion and exclusion criteria. Volunteer diagnosed type 2 diabetics with retinopathy of age 20-50 years were included. Diabetics with chronic liver disease, renal failure and other major systemic illness were excluded. Data were collected and noted in a structured proforma. Written informed consent was signed by volunteer subjects. A consultant ophthalmologist was asked to perform Fundoscopy once physician has completed his interest. Anterior eye ball segment was examined using slit lamp and measured; the intraocular pressure (applanation tonometer) was measured and fundoscopy.<sup>10</sup>

In this study, it was not possible to assess retinal thickening/elevation as a consequence of non availability of stereo retinal micro-photographs. Therefore, maculopathy *per se* was not gradable. Mild retinopathy cases managed, while moderate - severe retinopathy and proliferative or photocoagulated cases were referred to an ophthalmology service. The patients were assessed for the presence of risk factors: sex, age, duration, systolic & diastolic blood pressure, hyperglycemia, nephropathy, hypertension, cholesterol, triglycerides, smoking and obesity. Joint National Committee (JNC) VIII criteria were followed for diagnosis of hypertension.<sup>3</sup>

Patients were instructed for 12 hour fasting for determination of blood lipids according to WHO criteria<sup>7</sup>. The BMI was calculated by formula weight/height. A BMI of 25-29 kg/m<sup>2</sup> was regarded as overweight and  $\geq 30$  kg/m<sup>2</sup> as obesity<sup>10</sup>. The patients were divided into 2- groups: a). group I. those with any DR and; b). group II. those without DR. The degree of glycaemic control was evaluated by measuring HbA1c concentration. Ideal glycaemic control was considered an A1C of < 7%. Microalbuminuria was measured in early morning urine first void sample after exclusion of other causes. Blood lipids criteria were counted as per standards of ATP III; total cholesterol >200mg/dL, LDLc >130mg/dL, HDL <40mg/dL, VLDL>30mg/dL, and triglycerides >150mg/dL.<sup>11</sup> Data was analyzed on *Statistix 8.1* (USA). Normality of data was checked by Shapiro Wilk testing. Continuous and categorical variables were analyzed (student's t test & chi square test). Significant p-value was taken at  $\leq 0.05$ .

## RESULTS

Of 100 patients, 58 (58%) were male and 42 (42%) were female patients. Mean  $\pm$  SD age in DR was 49.5 $\pm$ 8.5 versus 46.3 $\pm$ 5.1 years without DR. Any type of retinopathy was noted in 21 (21%). Prevalence of mild retinopathy was 12% and moderate-severe retinopathy was 18%.

**Table No.I. Baseline characteristics of diabetic study population (n=100)**

|                                     | Retinopathy    |                | p-value |
|-------------------------------------|----------------|----------------|---------|
|                                     | Yes (n=21)     | No (n=79)      |         |
| Age (years)                         | 49.5 $\pm$ 8.5 | 46.3 $\pm$ 5.1 | 0.03    |
| Male                                | 15             | 43             | 0.09    |
| Female                              | 06             | 36             | 0.13    |
| BMI (kg/m <sup>2</sup> )            | 26.5 $\pm$ 7.8 | 27.7 $\pm$ 9.5 | 0.043   |
| BMI                                 | 19             | 35             | 0.03    |
| SBP (mmHg)                          | 152 $\pm$ 11   | 136 $\pm$ 11   | 0.03    |
| DBP (mmHg)                          | 91 $\pm$ 11    | 76 $\pm$ 9     | 0.61    |
| Smoking (5 packs year)              | 4              | 29             | 0.03    |
| Obesity (BMI >30kg/m <sup>2</sup> ) | 17             | 39             | 0.12    |
| Blood glucose (mg/dl)               | 279 $\pm$ 23.5 | 241 $\pm$ 13.7 | 0.012   |
| Serum creatinine(mg/dl)             | 3.1 $\pm$ 0.51 | 2.1 $\pm$ 0.11 | 0.12    |
| HbA1c ( $\geq$ 7%)                  | 19             | 35             | 0.013   |
| Microalbuminuria                    | 17             | 06             | 0.023   |

**Table No.2: Lipid profile in diabetic study subjects (n=100)**

|                           | Retinopathy       |                  | p-value |
|---------------------------|-------------------|------------------|---------|
|                           | Yes (n=21)        | No (n=79)        |         |
| Triglycerides (mg/dl)     | 231.1 $\pm$ 110.7 | 132.9 $\pm$ 45.7 | 0.001   |
| Cholesterol-Total (mg/dl) | 211.1 $\pm$ 44.9  | 158.3 $\pm$ 25.9 | 0.0001  |
| HDLc (mg/dl)              | 32.5 $\pm$ 7.3    | 39.9 $\pm$ 8.5   | 0.02    |
| LDLc (mg/dl)              | 126.6 $\pm$ 17.3  | 96.3 $\pm$ 19.6  | 0.001   |
| VLDL (mg/dl)              | 29.3 $\pm$ 8.1    | 41 $\pm$ 14      | 0.00    |

There were 6 cases of proliferative or photocoagulated retinopathy (6%). The frequency of risk factors in patients with & without retinopathy is shown in table I. DR was found increased with aging (Table II). Any type of DR showed +ve correlation with age, male gender, HbA1c, microalbuminuria and LDLc (table III). HDLc, triglycerides and VLDL showed -ve correlation with DR.

**Table No.3: Correlation of risk factors with Diabetic retinopathy (n=100)**

|                         | r-value | p-value |
|-------------------------|---------|---------|
| Age                     | +0.47   | 0.001   |
| Gender- male            | +0.45   | 0.001   |
| Smoking                 | +0.61   | 0.001   |
| HbA1c (%)               | +0.87   | 0.001   |
| Microalbuminuria (mg/L) | +0.83   | 0.001   |
| Cholesterol (mg/dl)     | +0.89   | 0.031   |
| LDLc (mg/dl)            | +0.52   | 0.032   |
| Triglycerides (mg/dl)   | -0.39   | 0.0001  |
| HDLc (mg/dl)            | -0.57   | 0.001   |
| VLDL (mg/dl)            | -0.27   | 0.001   |

## DISCUSSION

Frequency of DR was noted as 21% in present study. A previous study reported a prevalence of 15.7%<sup>11</sup> which is less to present finding, while another study had reported a prevalence of 15% of DR.<sup>12</sup> The high prevalence of present study is most probably because of long duration of DM of our study subjects as shown in table I. Our findings of age, smoking, blood sugar, HbA1c, cholesterol, triglycerides, LDL, HDLc, VLDL, BMI, and serum creatinine are consistent with previous study.<sup>12</sup>

Another previous study has reported similar results of the older age, insulin therapy, HbA1c, hypercholesterolemia, triglycerides, microalbuminuria and duration of diabetes significantly related to the DR.<sup>10</sup> Findings of above study are consistent with our present study. Previous studies by Talu et al<sup>13</sup> and Tzeng TF et al<sup>14</sup> had reported DR prevalence of 14.37% and 25.5% respectively. The findings are comparable to present study. However, another previous study<sup>15</sup> has reported a prevalence of 59.3% of DR which is very high. Several studies had reported differing prevalence of DR, and this might be because of various factors such as: different study populations, race, ethnicity, age, study designs, primary and secondary health care facilities, and other risk factors.

Some studies have shown that older age at diagnosis of DM is a risk factor for DR, this is most probable differences of reported frequency of DR<sup>13-15</sup>. Male gender is proved as risk factor for DR which is similar to a previous report by Liu et al.<sup>16</sup> A1c level is an established gold measure of diabetic glycaemic control. It was reported that a 1% reduction reduces diabetic microvascular complications by 25%. Systemic hypertension and micro-albuminuria proved of having a +ve correlation with DR in present study, the findings support the previous work.<sup>6,10,13,14</sup> Smoking proved risk factor for DR which is consistent to reported studies.<sup>10,17</sup> Hyperlipidemia, hypercholesterolemia and poor glycaemic control were proved as risk factors for DR. The principal limitation of present study is the small sample size; however, the findings are of clinical

importance. Further studies with large sample size are recommended to quantify the prevalence of and to identify the risk factors of DR in our population.

## CONCLUSION

The present study reports hyperlipidemia, hypercholesterolemia and poor glycaemic control as risk factors for diabetic retinopathy. Treating physicians and ophthalmologist must consider of the risk factors. It is essential to perform ophthalmological examination and treat risk factors to prevent retinopathy and blindness.

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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