THE IMPACT OF SEVERITY OF DIABETIC RETINOPATHY IN CARDIOVASCULAR DISEASE RISK ASSESSMENT USING FRAMINGHAM RISK SCORE- A PILOT STUDY
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ABSTRACT: Diabetic retinopathy (DR) is the most common micro vascular complications of diabetes, estimated to affect approximately 100 million people worldwide, while cardiovascular disease (CVD) is the leading cause of death in individuals with type II diabetes. There is limited Indian data reporting the association of Diabetic retinopathy and its severity with CVD. AIM: To study the relation between the severity of DR and risk of CVD in central Indian subjects. METHODS: The subjects consisted of 50 patients with Diabetes mellitus type II having varying grades of diabetic retinopathy attending eye OPD of a tertiary care hospital in central India. 10 year risk of developing CVD was estimated using the Framingham Risk Score. RESULTS: The number of subjects with an increased risk of developing CVD increased with advancing age (28.57% in 40-49 years to 61.53% in > 60 years age group). The risk of CVD was slightly more in males (55.55%) compared to females (43.47%). Out of the 30 patients having sight threatening diabetic retinopathy, 13 had low risk of developing CVD while 17 had high risk of developing CVD. The prevalence of sight threatening retinopathy was more in the high risk group (56.67%) when compared to the low-risk group (40%). DISCUSSION: We found that more subjects having high risk of developing CVD had sight-threatening DR compared to those having low risk. CONCLUSION: Diabetic retinopathy may contribute to CVD risk in Indian population too. A careful cardiovascular assessment and follow-up may be required in individuals with diabetic retinopathy, using a larger sample size
KEYWORDS: Cardiovascular disease, Framingham Risk score, sight threatening diabetic retinopathy, non-sight threatening diabetic retinopathy.

INTRODUCTION: Recent years have shown a rapid increase in number of individuals suffering from diabetes. It is estimated that 79.4 million people in India will have diabetes by the year 2030,¹ while worldwide this figure may rise up to 366 million.² This will translate into similar increase in number of persons having various complications of diabetes. Diabetic retinopathy (DR) is the most common micro vascular complications of diabetes, involving damage to the microvasculature of the retina. It is one of the foremost causes of legal blindness and visual impairment in the working age population. It is estimated to affect approximately 100 million people worldwide when extrapolated to the world diabetes population in 2010.³ Cardiovascular disease (CVD) is the leading cause of death in individuals with type II diabetes accounting for 65% to 80% of deaths in diabetic patients.⁴ Diabetics are twice more likely to die of CVD than non-diabetics.⁵ CVD encompass atherosclerotic vascular diseases like coronary heart disease (CHD), cerebrovascular disease and peripheral arterial diseases. Diabetic retinopathy is a common chronic micro vascular complication of diabetes, while CVD is considered a macro vascular complication.⁶ While diabetic retinopathy is predominantly due to glucose dysregulation, the cardiovascular diseases are predominantly due to atherosclerosis.
Epidemiological data from previous studies have provided inconclusive evidence regarding the association of retinopathy with CVD in patients with type 2 diabetes. The predictive value of diabetic retinopathy for development of CVD is not fully defined, though several studies have shown that the presence and severity of retinopathy is associated with an increased risk of CVD. Indian data reporting the association of Diabetic retinopathy and its severity with CVD is limited. Identification of DR could add to the diabetic patient’s CV risk stratification Framingham risk score (FRS) is a widely recognized tool used to calculate the 10-year cardiovascular risk in an individual. It calculates the risk based on age, sex, smoking status, lipid profile and blood pressure. FRS can be categorized as low (<10%), and high (>10%). There are very few Indian studies in this respect, and none from central India. Therefore this study examined the relation between the severity of DR and risk of CVD in central Indian subjects.

**AIM**: The study was undertaken to assess whether severity of diabetic retinopathy predicts the risk of cardiovascular disease, using the FRS.

**MATERIALS AND METHODS**: The subjects consisted of 50 patients with Diabetes mellitus type II having varying grades of diabetic retinopathy attending eye OPD of a tertiary care hospital in central India. The fundi of patients was examined by a trained ophthalmologist after achieving pupillary dilatation by instilling a combination of tropicamide (0.8%) and phynylephrine (5%).

DR was diagnosed based on modified Klein classification of the Early Treatment Diabetic Retinopathy Study scale. Sight threatening DR included severe non-proliferative DR, proliferative DR and clinically significant macular edema, while non-sight threatening diabetic retinopathy included mild and moderate non-proliferative diabetic retinopathy. The level of retinopathy in the worst eye was used to classify the retinopathy status of each person. 10 year risk of developing CVD was estimated using the Framingham Risk Score. FRS is a widely used gender-specific algorithm, developed from the data obtained from the famous Framingham heart Study, to estimate the 10-year risk of developing coronary heart disease (CHD).

The components of the score are 1. Age 2. Gender 3. Total Cholesterol in mmol/L 4. Cigarette smoking 5. High Density lipoprotein (HDL) cholesterol in mmol/L 6. Systolic blood pressure in mmHg 7. Medication for hypertension Score less than 10 was considered as low risk (low FRS) and score more than 10 as high risk (high FRS). The study protocol was approved by the Institutional Review Board. A written consent was obtained from the subjects as per the Helsinki Declaration.

**RESULTS**: 50 patients with varying severity of diabetic retinopathy were included in the study. The age ranged from 40 years to 75 years. (Table 1) Most of the subjects belonged to the age group 50-59 years. The number of subjects with an increased risk of developing CVD increased with advancing age (28.57% in 40-49 years to 61.53% in > 60 years age group).

(Table 1) Age distribution of patients according to low and high risk of developing cardiovascular disease (low and high FRS).

|          | 40-50 N (%) | 50-60 N (%) | >60 N (%) |
|----------|-------------|-------------|-----------|
| Low FRS  | 10 (71.42)  | 10 (43.47)  | 5 (38.46) |
| High FRS | 4 (28.57)   | 13 (56.52)  | 8 (61.53) |
| **Total**| **14**      | **23**      | **13**    |

Table 1
There were almost an equal number of males (27) and females (23) in the study. (Table 2). The risk of CVD was slightly more in males compared to females.

**Table 2:** Distribution of male and female patients according to FRS.

|                | Males N (%) | Females N (%) |
|----------------|-------------|---------------|
| Low FRS        | 12 (44.44)  | 13 (56.52)    |
| High FRS       | 15 (55.55)  | 10 (43.47)    |
| **Total**      | **27**      | **23**        |

30 patients had sight threatening diabetic retinopathy (STDR) Out of these, 13 had low risk of developing CVD while 17 had high risk of developing CVD. 20 patients in the study had non sight threatening diabetic retinopathy. Out of these 12 patients had low FRS, while 8 had high FRS. The prevalence of sight threatening retinopathy was more in the high risk group (56.67%) when compared to the low-risk group (40%). (Table 3).

**Table 3:** Distribution of patients according to severity of diabetic retinopathy and FRS.

|                | STD N (%) | Non STD N (%) |
|----------------|-----------|---------------|
| Low FRS        | 13(43.33) | 12(60)        |
| High FRS       | 17(56.67) | 8(40)         |
| **Total**      | **30**    | **20**        |

**DISCUSSION:** We studied the 10 year risk of developing CVD among type II diabetic subjects having varying grades of diabetic retinopathy in a hospital based study in central India. We found that, in the 40-50 years age group, most subjects had low risk of developing CVD. Number of subjects with high risk of developing CVD increased with age, with 61.53% of patients aged above 60 years having high FRS. However, since age is one of the factors taken into account while calculating the risk of CVD using the FRS, its predictive ability when applied in younger subjects may be limited. Konstantinou DM also noted the limitation of predictive ability of FRS when applied in younger individuals.⁸ We found that the risk of developing CVD was more in males compared to females. Similar to our study, Damkondwar et al, in a population based study in south India, found the same sexual predilection.⁷

We found that more subjects having high risk of developing CVD had sight-threatening DR compared to those having low risk. The association between diabetic retinopathy and risk of developing CVD has been reported in various studies. Klein et al in a population based study, found an association of cardiovascular disease with diabetic retinopathy.⁹ The ARIC study found that in individuals with type 2 diabetes, the presence of signs of retinopathy was associated with a twofold higher risk of incident CHD. They also found the association to be graded with retinopathy severity.¹⁰ Gimeno-Orna et al. also found that the presence of baseline retinopathy was associated with CVD irrespective of other cardiovascular risk factors.¹¹ Kramer et al reported that persons with any degree of DR are at 61% higher risk of CVD events and all-cause mortality independent of traditional risk factors based on the meta-analysis data of 20 epidemiological studies.¹² Kawasaki et al in a study of
Japanese subjects found that the risk of CVD is increased even with a mild stage DR in type 2 diabetic Japanese persons. Damkondwar et al in a study on south Indian subjects, also found that the severity of DR and sight threatening DR was more in subjects in the high-risk group than in the low-risk group.

Cardiovascular diseases are the most common causes of mortality and morbidity in the type 2 diabetic population. Most CVD sufferers in India are in their productive age which may potentially impose huge socioeconomic burden and devastating consequences over the coming years. Our study, conducted in subjects from central India, also showed that FRS may be related to severity of diabetic retinopathy.

The major limitation of our study is a small sample size. The risk of CVD in patients having DR in Indian eyes should be further studied in a larger study.

CONCLUSION: Diabetic retinopathy may contribute to CVD risk in Indian population too. A careful cardiovascular assessment and follow-up may be required in individuals with diabetic retinopathy. Studies with larger sample size are needed to further support this conclusion.

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