

Assessment of Conjunctival Vessel Calibre in Type-2 Diabetes Mellitus Patients

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ABSTRACT

Background: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Every part of the eye from conjunctiva to the optic nerve has manifestations secondary to diabetes mellitus which have been well documented and studied. Evaluation of conjunctival angiopathy associated with diabetes may help in detecting changes in the retina more easily and even by paraclinical workers.

Methods: A cross-sectional, prospective study involving 70 patients of diabetes mellitus with disease duration of 15 to 19 years and equal number of age and sex matched controls were subjected to evaluation of conjunctival vessel width using the Appasamy anterior segment imaging system.

Results: In the study population average conjunctival vessel width was 36 μ and median width was 31.51 μ which was statistically different from the average width of 28.7 μ and median of 29 μ in controls [p < 0.002]. In patients with diabetes mellitus there was an increase in the calibre of conjunctival vessels which increased significantly with increasing severity of DR [p < 0.0001]. Macrovascular dilation associated with diabetes may result in vessel engorgement and straightening, especially among those with longer duration of disease. Increased tortuosity associated with diabetes among conjunctival capillaries mirrors established vessel changes observed in the retina

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia¹. Diabetes mellitus affects every part of the body and eye is not an exception. Every part of the eye from conjunctiva to the optic nerve has manifestations secondary to diabetes mellitus which have been well documented and studied.²The end organ damage in diabetes is assessed with the visualization of retinal vessels, however, the major concern is the requirement of equipment and trained personnel. So, do we have an alternative to it? We think the readily visible vessels i.e. conjunctival vessels can be easily visualized and documented even by the paramedical staff. However, there is paucity of literature about the effect of diabetes on the conjunctival vessels. This study therefore aims at assessment of conjunctival vessel morphology and width in patients with type 2 Diabetes Mellitus and correlates the same with retinal manifestations.

AIM AND OBJECTIVES

1. Assessment of conjunctival vessel morphology and width in patients with type 2 Diabetes Mellitus.
2. Correlation of the conjunctival changes with severity of retinopathy.

MATERIALS AND METHODS

This study adheres strictly to the tenets of the Declaration of Helsinki, and a prior approval of the institutional ethical committee had been taken. A total of 70 diagnosed patients of type 2 DM and 70 patients without diabetes willing to participate in this study were inducted. The patients were taken from Endocrinology and Ophthalmology Outpatients Departments. The type-2 DM patients were diagnosed in the Endocrinology OPD and referred to the Ophthal OPD for fundus evaluation. The subjects without diabetes mellitus were selected from those attending the ophthalmology opd for

routine eye checkup. Written, informed consent was taken from all the patients. The general and ophthalmic history was taken. Best corrected visual acuity was estimated. Complete ophthalmic examination was then done. The anterior segment was evaluated by means of slit lamp. Detailed mydriatic fundus examination was done by 90D slit lamp bio-microscopy, direct and indirect ophthalmoscopy. The level of diabetic retinopathy was assessed clinically based on the ETDRS classification. The 70 diagnosed patients of Type-2 were then subjected to assessment of diabetic retinopathy and subdivided into mild moderate and severe NPDR, PDR and those without any diabetic retinopathy based upon the ETDRS classification. Intra-ocular pressure was measured by Goldmann's applanation tonometry and patency of lacrimal passages was checked by syringing. On completion of the clinical examination, the subjects were taken up for the study of conjunctival vessels consisting of imaging of conjunctival vessel morphology by slit lamp imaging. The image of vessels on the temporal bulbar conjunctiva was captured by the image net. A red free photograph of the same was next captured. The most prominent vessel on the red-free photograph was subjected to the assessment of the width using the measurement program of the system. The findings of the conjunctival vessels were correlated with severity of retinopathy and the results were subjected to statistical analysis using the student's t test.

Inclusion criteria: Patients with diagnosed type-2 DM.

Exclusion criteria: 1. Patients with history of ocular surgery.

2. Patients On anti-glaucoma medications.

RESULTS

The data collected was entered and analysed in SPSS version 16. Data analysis was done by using student t test to compare the conjunctival vessel width in non-diabetic and diabetic patients. The conjunctival vessel width was correlated with the severity of retinopathy and duration of diabetes and p-value < 0.05 was considered as significant.

1. Age distribution

- a. The maximum number of patients were between 56 – 65 years of age 33/70 (45.1%) and if the next group is also included it would amount to 44/70 (62.85%). This indicates that the usual age of diabetics who attend an eye OPD range from 56 to 65 years and beyond. This is in consonance with the global prevalence as given in the study of Wild et al.³
- b. The same is true with the non-diabetics [31/70 (44.28%) and 37/70 (52.85%)].

2. Duration of Diabetes

- a. The maximum number of patients were having disease duration between 15 to 19 years. Diabetic retinopathy usually sets in by about 15 years in patients with type 2 disease⁴. It is worth noting that patients with disease duration of more than 20 years (18.57% in this study) are less.

3. Severity of Diabetic Retinopathy

The total number of patients with mild and moderate is 46/70 which amounts to (65.71%). This indicates that in a population of diabetics about two thirds of the patients may have mild to moderate NPDR. This figure also is more than the global prevalence.⁵ Patients with no retinopathy constituted 5/70 (7.14%). Since the figure is small it cannot be compared. Severe NPDR and PDR constitute 19/70 (27.14%) This is more than the global prevalence of PDR as per the global survey 6.96 PDR + 10.2 VTDR (visually threatening DR)⁵

4. Conjunctival vessel Width

- a. The average conjunctival vessel width in the non-diabetic subjects was 28.7 micron and the median was 29 micron. Compared to this the average width in the study population was 36 micron and the median was 31.51 micron. This difference is statistically strongly significant with a p value of 0.002 (Using Chi Square test).
- b. This indicates that in patients with diabetes mellitus there is an increase in the calibre of conjunctival vessel. The line diagram emphasizes this point amply. It may also be seen in the line diagram that in patients of diabetes mellitus conjunctival widening has a plateau whereas in non-diabetic subjects the line shows an acute peak.
- c. The bar diagram shows that maximum width in the non-diabetic subjects stops at 39 microns whereas in the study population it stops at 36 microns, further corroborating the fact that the width of the conjunctival vessels increases with diabetes.
- d. There is no difference in males or females with respect to conjunctival changes in both groups.

5. Difference in Conjunctival width between Fellow eyes in Non-Diabetic and Diabetic patients

The difference in conjunctival width between fellow eyes was also studied. The difference varied from 01 micron to 03 microns in both the normal subjects and the study population. The difference of 01 micron in conjunctival width between fellow eyes of normal subjects was seen in 37/70(52.85%). In the study group difference of 01 microns between fellow eyes was seen in 27(38.57%) cases. A difference of 02 microns was seen in 26(37.14%) normal subjects and in 32(45.71%) of the study population. A difference of 03 microns was seen in 7(10%) normal subjects and in 11(15.71%) of the study population. This data only proves that the difference of conjunctival width between the two eyes is not significant enough to affect the outcomes of the study and this was corroborated by statistical analysis. (p value of 0.2152)

6: Relationship between Severity of Diabetic Retinopathy and Conjunctival width

The line diagram indicates that the conjunctival width in patients with mild diabetic retinopathy shows a peak between 30-34 microns (Mean -33.94). The peak in case of moderate diabetic retinopathy falls between 35- 39 microns (Mean – 37.21) while in severe diabetic retinopathy the peak falls between 40-44 microns (Mean – 41.35). The peak in proliferative diabetic retinopathy falls between 40-44 microns (Mean – 44.61). With increasing severity of DR there is an increase in the width of the conjunctival vessels. This difference is statistically extremely significant with p value of < 0.0001 using the Chi-Square test.

7. Difference in Conjunctival width between Non-Diabetics and Diabetics without Retinopathy

An attempt has also been made to study the difference in conjunctival width between non-diabetic subjects and patients with no diabetic retinopathy. It was observed that patients with no diabetic retinopathy had minimum conjunctival width of 25 microns compared to 21 microns in normal subjects. However, due to mismatch between the number of subjects without diabetic retinopathy and non-diabetic subjects p value <0.0790 is insignificant. The raw data however does suggest that even with no retinopathy patients of diabetes do have a larger calibre vessel in the conjunctiva when compared to non-diabetics.

8. Difference in Conjunctival width between Mild and Moderate Diabetics and Severe NPDR and PDR

A comparison was made in the conjunctival width of patients of mild and moderate diabetic retinopathy with patients of severe diabetic retinopathy and proliferative diabetic retinopathy as these two groups have generally different management protocols. In cases with severe NPDR and PDR pan-retinal photocoagulation is usually performed. It was seen that in cases of mild and moderate retinopathy maximum number of eyes 32/92(34.78 %) fall between 35-39 microns, while in cases of severe and proliferative diabetic retinopathy 16/38(42.10%) fall in the range of 40-44 microns. This difference is statistically extremely significant with a p value of < 0.0001.⁶

DISCUSSION

.Macro vessel dilatation associated with diabetes may result in vessel engorgement and straightening, especially among those with longer duration of disease⁷. Increased tortuosity associated with diabetes among conjunctival capillaries mirrors established vessel changes observed in the retina⁸. Danilova et al⁹ in their study recommended microphotography of conjunctival vessels in diabetes mellitus for early diagnosis of micro hemodynamic disturbances. Worthen DM et al¹⁰ using newly developed morphometric techniques showed greater venous dilatation in conjunctival vessel in diabetics. In the present study we analysed and compared the conjunctival vessel width using slit lamp imaging system in diabetics and normal population. Computer-assisted intravital microscopy (CAIM) was used by Cheung AT et al¹¹ to study conjunctival microcirculation in 14 patients with T2DM and in age-matched healthy control subjects without diabetes .The authors found that patients with T2DM had significantly wider conjunctival vessel diameter than healthy non diabetic control subjects. In the study patients, microvascular distribution was significantly abnormal and the vessel distribution was found to be uneven on the surface of the bulbar conjunctiva. In this study we also found that average width of conjunctival vessel in the diabetic population was 36 micron compared to normal subjects in which the vessel width was 28.7 micron. This difference is statistically strongly significant with a p value of 0.002(Using Chi Square test). This indicates that the calibre of conjunctival vessel increases in patients with diabetes mellitus. **The findings of this study are in consonance with the studies of AT Cheung et al. However the study methodology is different, the study numbers are 70 compared to 14 and co-relation has been done with severity of DR.**

Laguerre G et al¹² studied conjunctival vessels in non insulin dependent diabetes mellitus and found significant venous dilatation in conjunctival vessels¹⁴ in diabetics . CG Owen et al¹³ had studied tortuosity of conjunctival vessels and R. van

Zijdeveld et al had studied conjunctival micro-circulation abnormalities. **Both these studies indirectly stated about the dilatation of conjunctival vessels in diabetics which has been studied in detail in the present study.**

This study indicates that in diabetic patients there is an increase in the calibre of conjunctival vessel and it further increases with increasing severity of DR ($p < 0.0001$). The difference in conjunctival width in eyes with Mild & Moderate NPDR and Severe NPDR & PDR ($p < 0.0001$) was extremely significant. The raw data also suggests that even with no retinopathy, diabetics have larger calibre of conjunctival vessel as compared to non-diabetic population.

Summary and Conclusion: In patients with Diabetes Mellitus there is an increase in the calibre of conjunctival vessels which shows extremely significant increase with severity of DR ($p < 0.0001$). Also extremely significant is the difference in the conjunctival width in eyes with Mild & Moderate NPDR (35-39 microns) and Severe NPDR & PDR (40-44 microns) [$p < 0.0001$]. These two groups have generally different management protocols as in cases with severe NPDR and PDR pan-retinal photocoagulation is usually performed. The raw data also suggests that even with no retinopathy patients of Diabetes do have a larger calibre vessel in the conjunctiva when compared to normal population.

Diagram1. Age Distribution

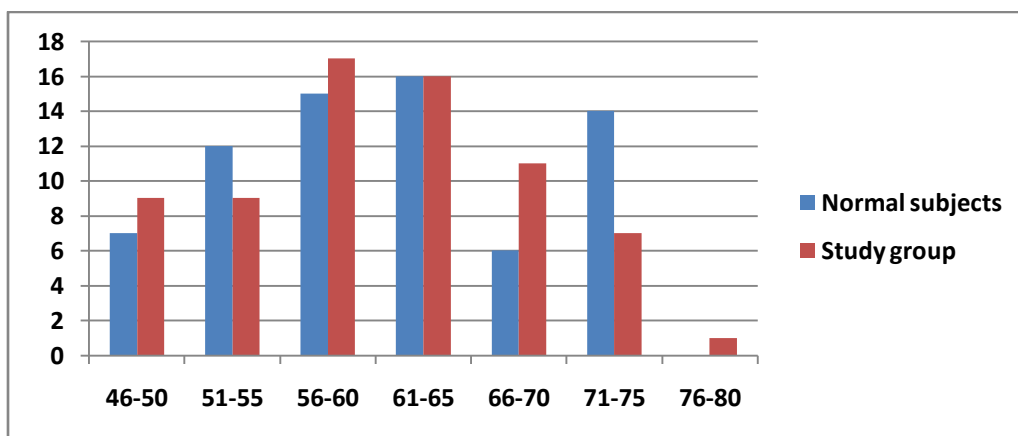


Table 2a: Sex Distribution- Diabetics

Age range	Study group	
	Male	Female
46-50	4 (11.41%)	4(11.41%)
51-55	6 (17.1%)	3 (4.2%)
56-60	9 (25.7%)	8 (22.5%)
61-65	6 (17.1%)	10 (28.55%)
66-70	6 (17.1%)	5 (14.2%)
71-75	4 (11.41%)	4 (11.41%)
76-80	1(1.4%)	1(1.4%)
Total	35	35

Table 2b: Sex Distribution-Normal Subjects

Age range	Normal(Non-Diabetic) subjects	
	Male	Female
46-50	4(11.41%)	3 (4.2%)
51-55	6 (17.1%)	6 (17.1%)
56-60	8 (22.5%)	7 (20%)
61-65	7 (20%)	9 (25.7%)
66-70	3 (4.2%)	3 (4.2%)
71-75	7 (20%)	7 (20%)
Total	35	35

Table 3: Duration of Diabetes with Sex Distribution

Duration of diabetes (yrs)	Study group		Total
	Male	Female	
5-9	4(5.71%)	7(10%)	11(15.71%)
10-14	8(11.42%)	9(12.85%)	17(24.28%)
15-19	15(21.42%)	14(20%)	29(41.42%)
20-24	7(10%)	4(5.71%)	11(15.71%)
25-29	1(1.42%)	1(1.42%)	02(2.85%)
Total	35	35	70

Table 4: Severity of Diabetic Retinopathy with Sex Distribution

SEVERITY OF DIABETIC RETINOPATHY	STUDY GROUP		
	Male	Female	Total
NO DR	1(1.42%)	04(5.71%)	05 (7.14%)
MILDNPDR	15(21.42%)	12(17.14%)	27 (38.5%)
MODERATE NPDR	8(11.42%)	11(15.71%)	19 (27.14%)
SEVERE NPDR	05 (7.14%)	05 (7.14%)	10 (14.28%)
PDR	06(8.57%)	03(4.28%)	09 (12.85%)
Total	35	35	70

Table 5a: Conjunctival Vessel Width in Eyes of Diabetic Patients and Non-Diabetics

Range of conjunctival vessel width μ	NON-DIABETICS	DIABETICS
20-24	23(16.42%)	01(0.71%)
25-29	56(40%)	18(12.85%)
30-34	49(35%)	32(22.85%)
35-39	12(8.57%)	41(29.28%)
40-44	0	32(22.85%)
45-49	0	12(8.57%)
50-54	0	04(2.85%)
Total no of eyes	140	140
Average	28.47 μ	36.9 μ
Median	29 μ	31.5 μ

The two-tailed P value is less than 0.0001

Diagram 5a: Conjunctival Vessel Width in Eyes of Diabetic Patients and Normal Subjects (Line diagram)

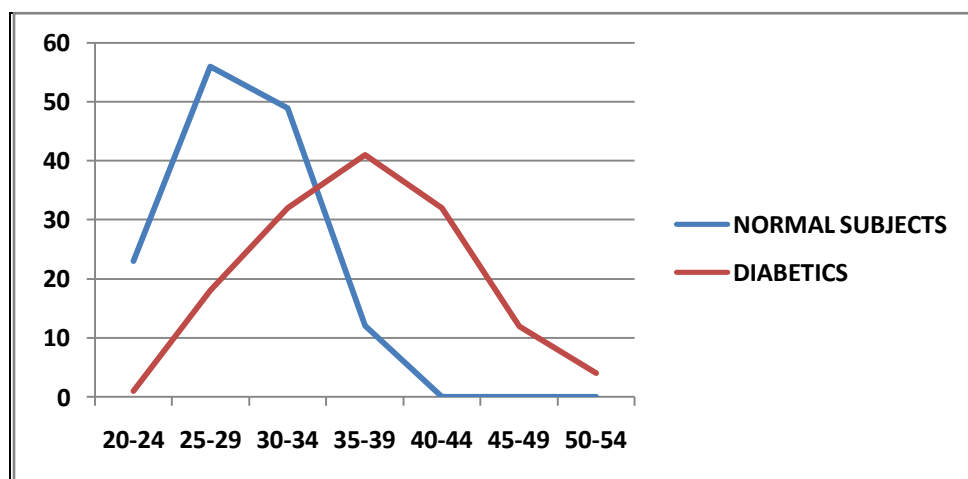


Diagram 5b: Conjunctival Vessel Width in Eyes of Diabetic Patients and Non-Diabetics (Bar diagram)

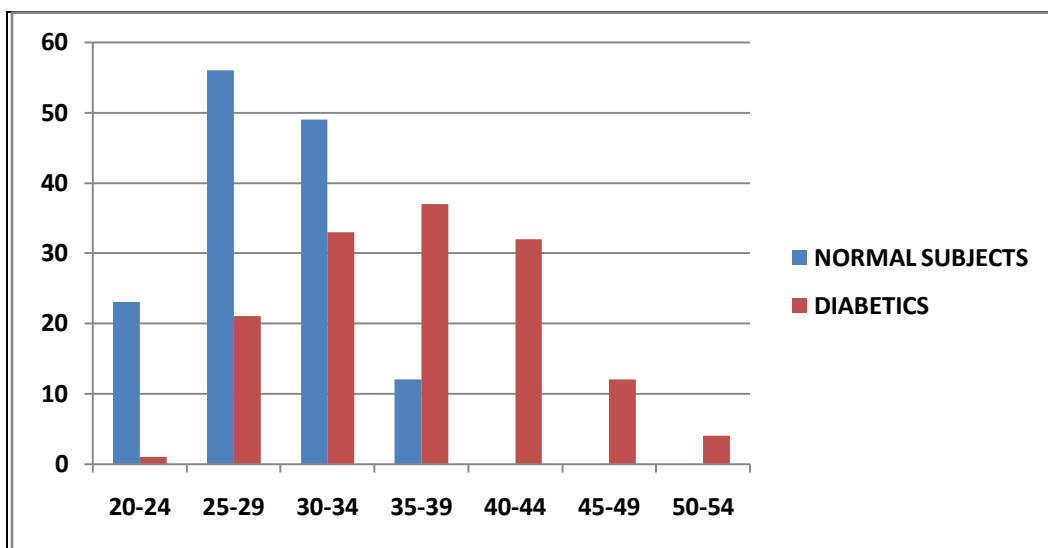


Table 6: Difference in Conjunctival Width between Fellow Eyes in Normal and Diabetic Patients

DIFFERENCE IN CONJUNCTIVAL WIDTH	NORMAL SUBJECTS	STUDY GROUP
1microns	37(52.85%)	27(38.57%)
2 microns	26(37.14%)	32(45.71%)
3 microns	7(10%)	11(15.71%)

The two-tailed P value equals 0.2152

Table7a: Relationship between Severity of Diabetic Retinopathy and Conjunctival Width

Range of conjunctival width	NO DR	MILD NPDR	MODERATE NPDR	SEVERE NPDR	PDR	TOTAL
20-24	1(0.71%)	0	0	0	0	1(0.71%)
25-29	4(2.85%)	13(8.57%)	2(1.42%)	0	0	18(12.85%)
30-34	5(3.57%)	20(14.28%)	7(5%)	0	0	32(22.85%)
35-39	0	10(7.85%)	21(15%)	7(5%)	2(1.42%)	41(29.28%)
40-44	0	11(7.85%)	5(3.57%)	9(6.42%)	7(5%)	32(22.85%)
45-49	0	0	3(2.14%)	4(2.85%)	5(3.57%)	12(8.57%)
50-54	0	0	0	0	4(2.85%)	4(2.85%)
Total	10(7.1%)	54(38.57%)	38(27.14%)	20(14.28%)	18(12.8%)	140
Mean	28.8	33.94	37.21	41.35	44.61	-

The two-tailed P value is less than 0.0001

Diagram7a: Relationship between Severity of Diabetic Retinopathy and Conjunctival Width (Bar Diagram)

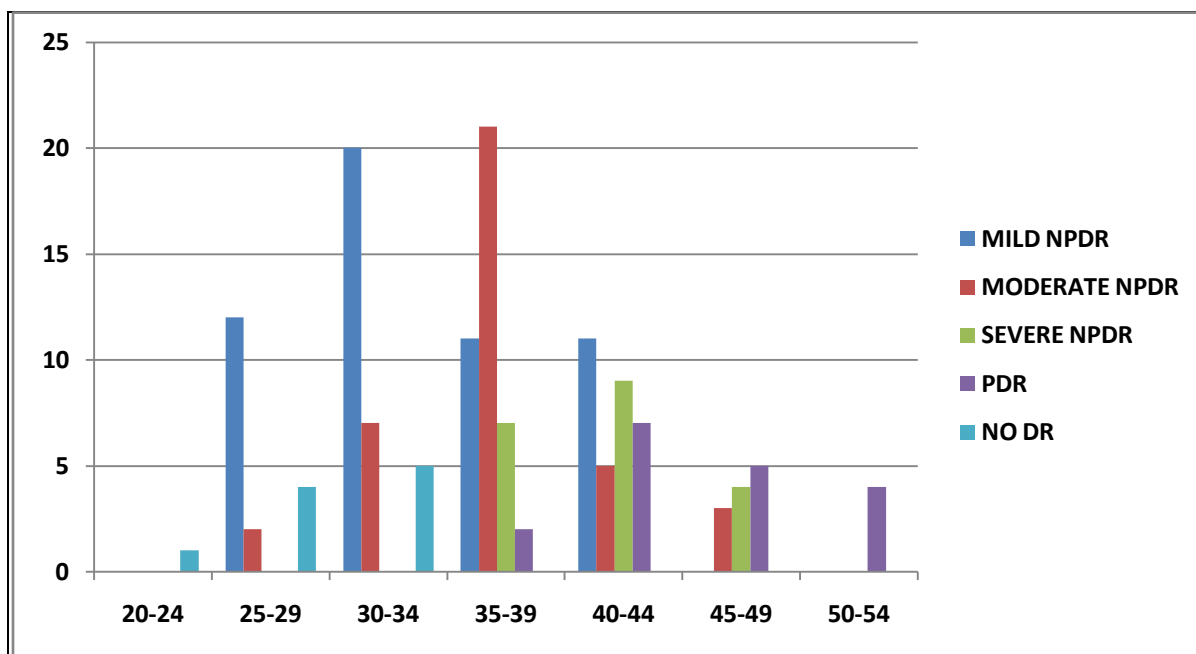


Fig 1: Image of temporal bulbar conjunctival vessel on diffuse illumination



Fig 2: Red free light image of temporal bulbar conjunctival vessel

Conflicts of interest

All authors have none to declare.

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