Use of Conjunctival Vessel Width for Assessment of Severity of Retinopathy in Type-2 Diabetes Mellitus Patients

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ABSTRACT

Introduction: Diabetes mellitus is defined as a metabolic disorder of multiple etiologies characterized by chronic hyperglycaemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, insulin action, or both. The manifestations of diabetes in eye from conjunctiva to optic nerve have been studied in depth and well documented. The two most important visual complications of DR are diabetic macular edema (DME) and proliferative DR (PDR). The assessment of severity of retinopathy may be possible by means of evaluation of conjunctival microangiopathy in diabetic patients. So study aimed at assessment of width of the most prominent temporal bulbar conjunctival vessel in patients of type 2 DM with varying levels of retinopathy.

Material and Methods: This cross-sectional study involved 140 (280 eyes) diagnosed patients of diabetes mellitus with disease duration of 15 to 19 years. Using the Appasamy anterior segment imaging system, measurement of conjunctival vessel width was done. Using the ETDRS system the diabetic patients were divided based on the severity of retinopathy and analysis of conjunctival vessel width with varying severity of retinopathy was done.

Results: In the study population average conjunctival vessel width was 28.8 microns in diabetics without retinopathy and in patients with retinopathy the average width was 33.96 microns which increased with increasing severity of retinopathy. Increasing severity of diabetic retinopathy resulted in significant increase in the conjunctival vessel width [$p < 0.0001$]. Vessel engorgement and straightening due to macrovessel dilatation in diabetic patients is marked in cases with longer duration of disease.

Conclusion: Diabetic retinopathy (DR) is a microvascular complication of diabetes and research has clearly demonstrated that blindness from diabetes is almost entirely preventable with early diagnosis, optimization of risk factors and timely photocoagulation where appropriate.

Keywords: Conjunctival Vessel, Retinopathy, Type-2 Diabetes

INTRODUCTION

Recent estimates indicate that there were 171 million people in the world with diabetes in the year 2000 and this is projected to increase to 366 million by 2030.[1] India shelters the most number of people with diabetes mellitus worldwide. From 31 million in the year 2000, the number of persons with diabetes mellitus in India would register a 2.5 fold increase over the next 30 years so as to reach an alarming level of estimated 80 million by the year 2030.[2] Diabetes mellitus is defined as a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, insulin action or both.[3] Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. Diabetes mellitus affects every part of the body and eye is not an exception. The manifestations of diabetes in eye from conjunctiva to optic nerve have been studied in depth and well documented.[5] WHO has estimated that diabetic retinopathy is responsible for 4.8% of the 37 million cases of blindness throughout the world.[5,6] Diabetic retinopathy is becoming an increasingly important cause of visual impairment in India. Vision loss and blindness due to diabetic retinopathy are preventable to a large extent, with early detection and timely treatment.[7,8] The best predictor of diabetic retinopathy is the duration of the disease.[9] Klein et al.[9] reported that 10 years after the diagnosis of type 2 diabetes, 67% of patients had retinopathy and 10% had PDR.

The requirement of equipment and trained personnel is a major concern in assessment of target organ damage in diabetics by means of visualization of retinal vessels. So we need an alternative for it. The readily visible conjunctival vessels can serve as an alternative and 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 measuring the width of the conjunctival vessel in type-2 Diabetes Mellitus patients and analyzing the change in the vessel width with the severity of retinopathy. Study aimed at assessment of width of the most prominent temporal bulbar conjunctival vessel in patients of type 2 DM with varying levels of retinopathy.

MATERIAL AND METHODS

After obtaining clearance from ethical committee of the institute, 140 (280 eyes) diabetic patients willing to participate in this study were inducted. Written informed consent was taken from all the patients. First the general and ophthalmic history was obtained from study population. Complete ocular examination was conducted in all the enrolled patients inclusive of detailed mydriatic fundus examination. The level of diabetic retinopathy was assessed clinically based on the ETDRS classification. Using the Ophthalmic Slit Imaging System, the image of vessels on the most prominent temporal bulbar conjunctiva was captured by the image-net. A red free photograph of the same vessel was captured. The most prominent vessel on the red-free photograph was subjected to the assessment of the width using

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How to cite this article: Rishi Sharma, Alok Sati, Sandeep Shankar, V.S. Gurunadh. Use of conjunctival vessel width for assessment of severity of retinopathy in Type-2 diabetes mellitus patients. International Journal of Contemporary Medical Research 2017;4(5):1007-1010.

the measurement program of the system. The vessel width was measured in patients with different levels of retinopathy and the results were subjected to statistical analysis.

Inclusion criteria: Diagnosed patients of Type-2 DM

Exclusion criteria:

1. Patients with history of ocular surgery and use of anti-glaucoma medications.
2. Patients with media opacities which prevented visualization of the fundus.

STATISTICAL ANALYSIS

Using 20:0 version of SPSS (Statistical Package for Social Sciences) data was analysed. The conjunctival vessel width was correlated with the severity of retinopathy and duration of diabetes and p-value < 0.05 was considered as significant.

RESULTS

Majority population of the study group were having diabetes for the last 15-19 years which was same as the duration of 15 years usually by which diabetic retinopathy sets in type 2 DM. Mild to moderate NPDR was found in 65.71% (184/280 eyes) of the study population and Severe NPDR was seen in 14.28% (40 eyes)and 36 eyes out of 280 (12.8%) had PDR. Using the Pearson Correlation coefficient strong positive correlation was established between the conjunctival vessel width and duration of diabetes with p value less than 0.001.

In patients with mild diabetic retinopathy the conjunctival vessel width 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 which was established using Fisher's exact test and is statistically extremely significant with p value of < 0.0001.

Severity of Diabetic Retinopathy	Number of Eyes
NO DR	20 (7.14%)
MILDNPDR	108 (38.5%)
MODERATE NPDR	76 (27.14%)
SEVERE NPDR	40 (11.42%)
PDR	36 (12.87%)
Total	280

Table-1: Severity of diabetic retinopathy

DISCUSSION

Involvement of the conjunctiva in patients with diabetes has been an area of study since long. Capillary loss and Macro-vessel dilatation has been seen in the conjunctiva and similar changes have been noted in the retina in diabetic patients.[10] A study by Danilova compared the conjunctival and retinal vessels and found that in 68% patients with normal fundus and all patients with diabetic retinopathies there was disturbance in the conjunctival microcirculation. He therefore recommended that for early diagnosis of micro hemodynamic disturbances

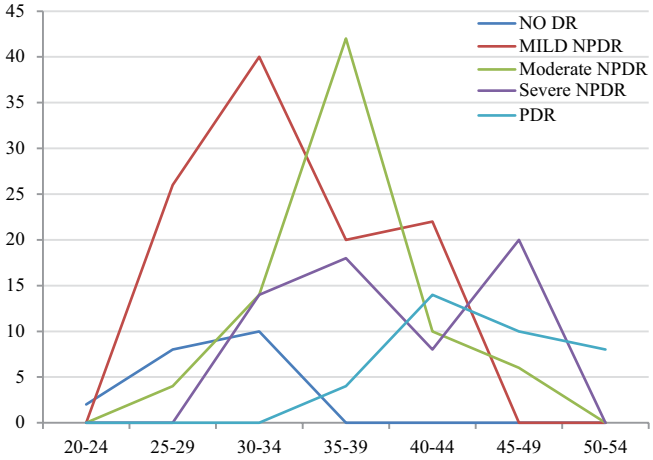

Diagram-2: Relationship between severity of diabetic retinopathy and conjunctival width

Figure-1: Image of temporal bulbar conjunctival vessel on diffuse illumination

Range of conjunctival width	NO DR	MILD NPDR	Moderate NPDR	Severe NPDR	PDR	Total
20-24	2(0.71%)	0	0	0	0	2(0.71%)
25-29	8(2.85%)	26(8.57%)	4(1.42%)	0	0	36(12.85%)
30-34	10(3.57%)	40(14.28%)	14(5%)	0	0	64(22.85%)
35-39	0	20(7.85%)	42(15%)	14(5%)	4(1.42%)	82(29.28%)
40-44	0	22(7.85%)	10(3.57%)	18(6.42%)	14(5%)	64(22.85%)
45-49	0	0	6(2.14%)	8(2.85%)	10(3.57%)	24(8.57%)
50-54	0	0	0	0	8(2.85%)	8(2.85%)
Total	20(7.1%)	108(38.57%)	76(27.14%)	40(14.28%)	36(12.8%)	280
Mean	28.8	33.94	37.21	41.35	44.61	-
The two-tailed P value is less than 0.0001						

Table-2: Conjunctival width with severity of diabetic retinopathy

in diabetic patients microphotography of the conjunctival vessels should be performed. Disturbances of the conjunctival microcirculation observed from the first years of diabetes mellitus onset reached the maximum in the moderately severe form of diabetes over 10 years in duration with intense diabetic microangiopathies.[11] A Russian study was conducted on the basal blood flow and responses of the microcirculatory channel to physiological and pharmacological loads in health and diabetes mellitus using the method of photon-correlation spectroscopy in the light fiber variant. The rate of the basal blood flow in patients with diabetes mellitus (irrespective of the diabetes type) as compared to that in health was significantly lower in the fingertip and tended toward reduction in the inner side of the forearm, lobule of the auricle and in the conjunctiva. The presence of retinopathies in patients with diabetes mellitus resulted in a significant decrease in the rate of the blood flow in the conjunctiva as compared to those in health and diabetes mellitus without retinopathy.[12] It was earlier hypothesized that that the vessels of the fundus of the eye were closely connected to the circulation of the cerebral flow whereas the changes of the conjunctival vascular bed might possibly correlate in a better way with the peripheral vessels and that majority of the patients with a high index at the bulbar conjunctiva suffer from peripheral occlusive disease.[13] However, Vasiutkova LA[14] applied conjunctival biomicroscopy for the study of microcirculation in 30 healthy persons and in 112 patients suffering from diabetes mellitus before and after the treatment. Marked derangement of the end blood flow was expressed in the appearance of perivascular, vascular, and intravascular lesions, increasing with the progress of diabetes mellitus. Adequate therapy gave positive results with the disappearance or reduction of perivascular lesions in the microcirculation, and also improvement of the rheological properties of the blood. Several teams have emphasized the value of conjunctival angioscopy (CA) and peri-ungual capillaroscopy (PUC), describing suggestive anomalies: microectatic venous dilatation (V/A greater than 4.5), sludge on CA, "fish shoal" capillaries.[15] To WJ et al hypothesized that T2DM vasculopathy can be revealed and quantified in the bulbar conjunctiva prior to its pathologic presentation in the retina. Using computer-assisted intravital microscopy (CAIM), an objective, non-invasive approach can provide a viable complement to retinal fundus photography to possibly screen patients for early signs of real-time, in vivo T2DM vasculopathy. The results of this study are indicative of the presence of a time window for early intervention of T2DM before non-proliferative retinopathy develops, and the real-time availability of the conjunctival microvasculature as an in vivo platform to monitor disease progression.[16] Cheung AT[17] et al studied conjunctival microvascular abnormalities in the bulbar conjunctiva of 14 patients with T2DM and in age-matched healthy control subjects without diabetes using computer-assisted intravital microscopy (CAIM). They found that in patients with T2DM (N = 14) the conjunctival vessel diameters (71.9 +/- 5.2 mm) were wider than the healthy nondiabetic control subjects (54.0 +/- 4.4 mm). In the study patients, microvascular distribution was significantly (P<0.01) abnormal (36.7 +/- 18.2 versus 45.3 +/- 9.6 cm per unit area, patients versus control subjects), and vessel distribution was uneven on the surface of the bulbar conjunctiva. The arteriole: venule (A:V) ratio in patients with T2DM was extremely variable and differed significantly (P<0.01) from that in the nondiabetic control subjects (A:V approximately 1:2). In addition, a unique sinusoidal (hypertensive) vascular pattern frequently existed in some of the large veins of all study patients with T2DM but in none of the nondiabetic control subjects. The sum total of the microvascular changes (abnormalities) in the conjunctival microcirculation in each patient correlated significantly with disease severity, as noted in the medical records. Owen CG[18] et al conducted a case-control study on fifty-three patients with diabetes (17 with type 1 diabetes, 36 with type 2 diabetes) and 60 controls (all aged 20-94 years). Digital red-free images of conjunctivae were analyzed using an automated computer algorithm to identify vessel axes and to quantify vessel tortuosity. They found that in diabetes mellitus simililar to the changes in the retinal blood vessels there was capillary loss and macrovessel dilation in the conjunctiva. The dilatation of conjunctival vessels in diabetics was also studied by R. van Zijderveld et.[19] The present study has dealt with the conjunctival vessel changes in diabetics and variation in vessel width with severity of retinopathy in detail.

CONCLUSION

In diabetic patients with increasing severity of retinopathy there is significant increase in vessel width. In patients with Mild and Moderate NPDR conjunctival vessel width was 35-39 microns compared to 40-44 microns in eyes with Severe NPDR and PDR ($p < 0.0001$). The management protocol in mild and moderate NPDR differs from cases with severe NPDR and PDR wherein timely laser photocoagulation of diabetic retinopathy can reduce severe visual loss by 95%.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 17-03-2017; **Accepted:** 20-05-2017; **Published:** 28-05-2017