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CONJUNCTIVAL MICRO VASCULAR ABNORMALITIES IN YOUNG DIABETICS

Ophthalmology

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ABSTRACT

Purpose: To study the conjunctival microvascular changes in young diabetic patients and to know whether these changes has any corelation with the presence or severity of diabetic retinopathy**. Method Study design**: cross sectional descriptive study. Duration of the study - 2 years. Study population- 142 eyes of 71 young diabetic patients. Relevant data regarding age, sex, age of onset and duration were collected. Conjunctival changes were studied using slit lamp biomicroscopy and fundus examination was done. **Results**: 93 had retinopathy, 73 had NPDR and 20 had PDR. Male female ratio 1.08:1. Mean age of onset of diabetes was 31.79 years in the retinopathy group and 33 years in no retinopathy group.Mean duration of diabetes was 11.65 years in the retinopathy group and 6.65 years in no retinopathy group. Conjunctival vessels changes were observed in all the eyes. Straightening of vessels(72.5%) and thinning of vessels(53.5%) were most commonly noticed findings. Presence of irregular enlarged loop (p=0.037), avascular area (p=0.00), straightening of vessels (p=0.038) & thinning of vessels (p=0.023) in retinopathy group were found to be statistically significant. Avascular areas in the PDR group were statistically significant compared to NPDR group. **Conclusion**: Presence of conjunctival microvascular changes were significant in retinopathy group. The evaluation of conjunctival microvascular abnormalities may help in detecting retinopathy more easily and earlier. It may also help in predicting the severity of diabetic retinopathy in young diabetics.

KEYWORDS

Diabetes Mellitus in young, conjunctival microvascular abnormalities, diabetic retinopathy.

INTRODUCTION

The prevalence of diabetes mellitus amongst youngsters is increasing, with a significant impact on the individual, healthcare service delivery and planning. Early onset diabetes is grouped as pediatric (<19 years) and adult type (>19 years to 45 years).[1]This includes late onset type I DM, Maturity onset diabetes of young and type II DM. Lifetime exposure to hyperglycaemia combined with the presence of multiple cardiovascular risk factors in young onset diabetes results in a heightened risk of vascular complications.[2,3]

Ocular complications due to diabetes mellitus in one of the preventable causes of visual morbidity in our world. Diabetes being a microangiopathy, it can be hypothesised that microvascular changes can be expected in the conjunctival vessels as well. But the presence of conjunctival microvascular changes were rarely studied in any of those studies. This study intends to assess the prevalence and types of conjunctival microvascular changes in young diabetic patients (age 19-45 years) and to know whether these changes has any predictive role in the presence or severity of diabetic retinopathy.

MATERIAL AND METHODS:

A cross sectional descriptive study was conducted. Study approval was obtained from the institutional research board. There was no financial burden for the participants. A sample size of 140 was calculated based on the formula $n=4pq/d^2$. The cases were selected from those attending the ophthalmology OP for diabetic retinopathy screening and management. Diabetic individuals with age of onset between 19 to 45 years of age were included. Age of patients more than 45 years, Gestational diabetes mellitus, disease of exocrine pancreas, other endocrinopathies, drug induced diabetes mellitus and infections leading to diabetes mellitus were excluded. Genetic syndromes, dry eye syndrome, conditions that can affect the ocular surface, clinical diagnosis of glaucoma, retinal vascular occlusions or any other retinal, choroidal or optic nerve disease that could interfere with the staging of diabetic retinopathy, history of intraocular surgery and subjects on topical medications for more than two weeks were also excluded. Demographic profile and disease details (age of onset, duration) were noted.Conjunctival changes were studied using slit lamp biomicroscopy and retinal examination done using slitlamp biomicroscopy using 90D lens and indirect ophthalmoscope.

RESULTS:

142 eyes of 71 diabetics (19 to 45 years) were included in the study. Out of the 142 eyes, 93 had evidence of diabetic retinopathy. Male female ratio 1.08:1. Mean age of onset of diabetes was 31.79 years in the retinopathy group and 33 years in no retinopathy group.Mean duration of diabetes was 11.65 years in the retinopathy group and 6.65 years in no retinopathy group. Among the eyes showing features of diabetic retinopathy, nonproliferative retinopathy was observed in 73 eyes and proliferative diabetic retinopathy in 20 eyes.

The conjunctival changes observed were vessel tortuosity, isolated enlarged loop, irregular enlarged loop, architectural alteration (change in the dichotomous branching pattern of conjuctival vessels), presence of avascular areas, straigtening of vessels, cattle trucking, hemmorhages and thinning of vessels. The distribution of cases based on the presence of conjunctival microvascular abnormalities is given in table 1.

Table 1 - The distribution of cases based on the presence of conjunctival microvascular abnormalities

	Conjunctival microvascular abnormalities (N=142)	n	%
1	Vessel tortuosity	61	43
2	Isolated enlarged loop	41	28.9
3	Irregular enlarged loop	20	14.1
4	Architectural alteration	6	4.2
5	Presence of avascular areas	19	13.4
6	Straightening of vessels	103	72.5
7	Cattle trucking,	13	9.2
8	Hemmorhages	4	2.8
9	Thinning of vessels	76	53.5

Straightening of vessels was the most common finding, followed by thinning of vessels and vessel tortuosity. Hemmorhages were least observed.

The distribution of cases (with and without retinopathy) based on the presence of conjunctival microvascular abnormalities is given in table 2.

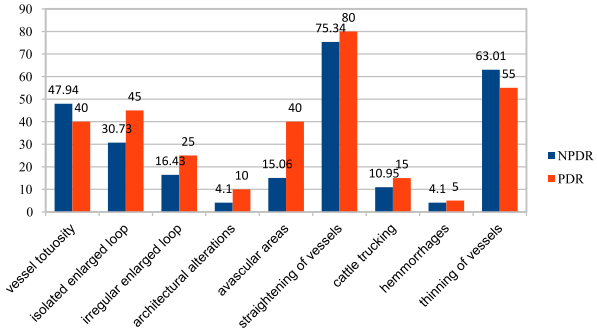
Table 2- The distribution of cases (with and without retinopathy) based on the presence of conjunctival microvascular abnormalities

Conjunctival microvascular abnormalities (N=142)	No diabetic retinopathy	Diabetic retinopathy	P value
Vessel tortuosity	18	43	0.182
Isolated enlarged loop	10	31	**0.076**
Irregular enlarged loop	3	7	**0.037*****

Architectural alteration	1	5	0.323
Presence of avascular areas,	0	19	**0.001*** **
Straightening of vessels,	32	71	**0.038*** **
Cattle trucking,	2	11	0.109
Hemmorhages	0	4	0.185
Thinning of vessels	19	57	**0.023*** **

Retinal changes in those with conjunctival microvascular abnormalities is give in figure 1. Straightening of vessels was the most common finding, followed by thinning of vessels and vessel tortuosity. Hemmorhages were least observed. Microvascular changes were observed more among those with retinopathy. Of the findings, presence of isolated enlarged loops, irregular enlarged loops, straightening of vessels and thinning of vessels among subjects with retinopathy was found to be statistically significant, hemmorrhages (p 0.185) and avascular areas (p 0.001) were seen only among those with retinopathy.

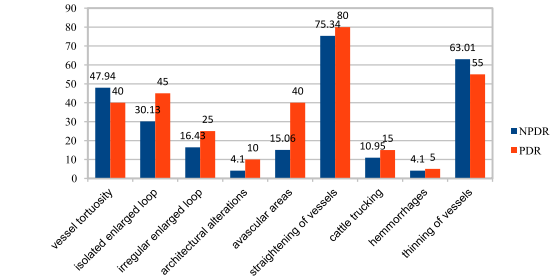
figure 1 - Retinal changes in those with conjunctival microvascular abnormalities



Retinopathy was further classified as NPDR and PDR. The distribution of cases of retinopathy (NPDR & PDR) with conjunctival changes is given in table 3.

Conjunctival microvascular abnormalities	NPDR (N 73)		PDR (N 20)		P value
	n	n/N %	n	n/N %	
Vessel tortuosity	35	47.94	8	40	0.354
Isolated enlarged loop	22	30.13	9	45	0.163
Irregular enlarged loop	12	16.43	5	25	0.282
Architectural alteration	3	4.10	2	10	0.292
Presence of avascular areas	11	15.06	8	40	**0.020*** **
Straightening of vessels	55	75.34	16	80	0.458
Cattle trucking	8	10.95	3	15	0.435
Hemmorhages	3	4.10	1	5	0.627
Thinning of vessels	46	63.01	11	55	0.344

figure 2 - Conjunctival microvascular abnormalities and type of retinopathy



Straightening of vessels was the most common finding, followed by thinning of vessels and vessel tortuosity. Hemmorhages were least observed. Architectural alterations and presence of hemmorrhages were rare. Conjunctival microvascular changes were more common among PDR cases except Vessel tortuosity and thinnning. Presence of PDR in subjects with avascular areas in the conjunctiva was statistically significant . The rest of the observations were not statistically significant.

DISCUSSION:

Diabetes mellitus is a microangiopathy. Diabetes affects the cappilaries of all tissues in the body especially retina, glomeruli of the kidney and the islets of langerhans of the pancreas.[4] Blood to the bulbar conjunctiva is primarily derived from the ophthalmic artery. The blood supply to the palpebral conjunctiva (the eyelid) is derived from the palpebral arteries which are branches of external carotid system. There is a rich anastamosis between palpebral and bulbar conjunctival vessels as well as between conjunctival and ciliary vessels at the limbal areas. Inspite of these factors , microangiopathy of diabetes has been found to involve conjunctival vessels. Conjunctiva is accessible to direct visualisation. Hence understanding the morphological patterns and their extent of involvement along with the corelation to the retinopathy is important. This was the rationale of the study. The ocular surface changes expected of age and age related ocular diseases and systemic diseases like hypertension, thyroid diseases etc were excluded by enrolling diabetic patients between 19 – 45 years of age.

All the diabetic cases who participated in the study had evidence of microvascular abnormalities in the bulbar conjunctiva. The conjunctival changes observed were vessel tortuosity, isolated enlarged loop, irregular enlarged loop, architectural alteration (change in the dichotomous branching pattern of conjuctival vessels), presence of avascular areas, straigtening of vessels, cattle trucking, hemmorhages and thinning of vessels. Straightening of vessels was the most common finding, followed by thinning of vessels and vessel tortuosity. Hemmorhages were least observed.

R. Van Zijderval et al also showed that the conjunctival microvessel changes were more frequently found in the diabetic group.[5] The most common changes they observed were capillary elongation , sludging and vessel distension. Christopher G Oven et al reports that conjunctival microvessel dilatation may result in the straightening of vessels.[6] Rishi Sharma et al also observed straightening of vessels in patients with longer duration of diabetes.[7] According to Touka Banaee et al , diabetes mellitus is associated with contraction of large sized vessels and increased small sized vessels. Tortousity of vessels were found in 43% of their patients.[8] R van Zijderval et al found more vessel distension and tortousity in the diabetic group compared to the normal individuals.[5] Dilated and tortuous conjunctival vessels were also reported by Adeoti et al, Clement Mcculloh et aland Nicol Stuebiger et al.[4.9.10] Clement Mc Culloh et al reports that these changes were more common in veins.[4] Nicol Stuebiger et al observed changes in temporal conjunctiva.[10]

Microvascular changes were observed more among those with retinopathy. Of the findings, presence of isolated enlarged loops, irregular enlarged loops, straightening of vessels and thinning of vessels among subjects with retinopathy was found to be statistically significant. Hemmorrhages and avascular areas were seen only among those with retinopathy. According to Clement Mcculloch et al conjunctival aneurysms are common in patients with retinopathy.[4] Worthen DM et al reports decreased vascularity in the capillary bed in diabetic patients.[11] Loss of conjunctival capillaries was noted by Owen CG et al and Touka Banee et al . They also observed increased prevalence of conjunctival hemmorrhages. Similar observations were made by Clement Mcculloch et al.

Khansari et al reports that Wall sheer stress (WSS) was lower in conjunctival arterioles of subjects with no diabetic retinopathy and in venules at all stages of DR, as compared to non-diabetic subjects. WSS is an important hemodynamic parameter which affects endothelial functions, such as migration of leukocytes, adhesion, control of vessel diameter, cytoskeletal structure, and energy metabolism. Reduced WSS in the retinal arterioles of subjects with early DR and in the carotid and branchial arteries of diabetic subjects was previously reported.[12,13]

Among those with retinopathy, straightening of vessels was the most common microvascular abnormality. This was followed by vessel tortuosity and thinning of vessels. Architectural alterations and presence of hemmorrhages were rare. Conjunctival microvascular changes were more common among PDR cases except Vessel tortuosity and thinnning. Increased vascular endothelial growth factor (VEGF) expression is responsible for vasodilation. VEGF expression has been reported to be elevated in conjunctival macrophages, epithelial, endothelial, and fibroblast cells in NPDR and PDR subjects.[14]

Presence of PDR in subjects with avascular areas in the conjunctiva was statistically significant . Khan et al observed that conjunctival

vessel tortousity had a significant correlation with the severity of diabetic retinopathy.[15] Nicol stuebiger et al commented that lower number of vessels with lesser branching were seen in eyes of diabetic patients before the development of diabetic retinopathy. Similar observations were made by Cheung A T et al.[16] Touka Banee et al observed that reduced conjunctival vascularity corelated with progression of retinopathy. Cattle trucking, box car blood flow phenomenon, sludging of vessels and enlarged cappillaries were associated with progression of the diabetic retinopathy and increased duration of the disease.[17]

Absence of a control group of non diabetic subjects is a major limitation of the study. Lack of equal numbers in each subgroup might have contributed to the low statistical power. Further studies are warranted to identify the correlation between conjunctival changes and types of NPDR, PDR and maculopathy.

CONCLUSION:

Presence of conjunctival microvascular changes were significant in the young onset diabetic subjects with retinopathy. Morphological changes may be indicative of hypoxia. Sludging of circulation, hemmorrhages and avascular areas were suggestive of severe ischemia and corelated well with presnce of retinal ischemia in terms of PDR. Assessment of conjunctival hemodynamic alterations has the potential for screening, diagnostic evaluation and prognostication among young onset diabetic subjects with retinopathy.

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