Original Research Article

An observation of biochemical findings in cases of diabetic maculopathy

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Abstract

Diabetic maculopathy is a leading cause of decreased vision from diabetic retinopathy. Diabetic Retinopathy is a medical condition in which damage occurs to the retina due to diabetes mellitus. It is a leading cause of blindness. Diabetic retinopathy often has no early warning signs. Even macular edema, which can cause rapid vision loss, may not have any warning sign for some time. However, a person with macular edema is likely to have blurred vision. **Methods:** Most of the cases were selected from the outpatient department of Ophthalmology, and remaining were selected from the department of Medicine, Mata Gujri Memorial Medical College and L.S.K. Hospital, Kishanganj, Bihar, at random basis. Patients who had clinically diagnosed Diabetic Maculopathy were selected for this study. Patients with established diabetic macular edema were then selected and subjected to the following set of investigation- Post Prandial blood sugar (glucose), Glycated Haemoglobin and Lipid Profile. Total 50 patients were finally selected for the study it was done during the period of August 2018 to January 2019. **Results:** In the present study, there were 27 males (54%)and 23 females (46%). The mean value of post prandial blood glucose level was 127.44 mg/dl. It was found that maximum post prandial blood glucose level was 216.0 mg/dl and minimum was 71.0 mg/dl. In case of HbA1C the mean value was 8.6%. maximum and minimum HbA1C level found in this study was 10.1% and 5.8% respectively. The mean value of total cholesterol was 203.86 mg/dl, where as in case of Triglyceride the mean value was 213.84 mg/dl. In case of HDL and LDL the mean values were 42.5 mg/dl and 120.7 mg/dl. **Conclusion:** Duration of diabetes is a major risk factor for the development and progression of diabetic maculopathy, (P<0.01). In this study the average duration of diabetes is 12.24 years and poor metabolic control is a significant risk factor for the development of diabetic maculopathy as is evident from average HbA1c.

Key Word: Diabetic Maculopathy, Diabetic Retinopathy, Macular Edema.

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INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic disorders in which there is high blood sugar levels over a prolonged period.[1] Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger.[1] If left untreated, diabetes can cause many complications.[1] Acute complications may lead to diabetic ketoacidosis, hyperosmolar hyperglycaemic state, or death.[2] Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes.[1] Diabetes may be due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.[3] There are three main types of diabetes mellitus:[1]

- Type 1 DM results from the pancreas failure to produce enough insulin[1] This form was previously referred to as "Insulin Dependent Diabetes Mellitus" (IDDM) or "juvenile diabetes".[1]
- Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly.[1] As the disease progresses a lack of insulin may also develop.[4] This form was

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previously referred to as "Non Insulin Dependent Diabetes Mellitus" (NIDDM) or "adult-onset diabetes".[1] Diabetes may develop in pregnancy without any previous high blood sugar level.

Diabetic retinopathy affects up to 80 percent of those who have had diabetes for 20 years or more.[5] The longer a person has diabetes, higher are the chances of developing diabetic retinopathy.[6] The first stage, called non-proliferative diabetic retinopathy (NPDR)usually has no symptom. Patients may have 20/20 vision. The only way to detect NPDR is by direct and indirect ophthalmoscopy and fundus photography, in which microaneurysms can be seen.[7]If there is reduced vision, fluorescein angiography can show dynamic state of posterior pole of eye and elsewhere. Ischaemic Maculopathy is a sight threatening condition for which there are currently no effective treatments. When an individual has ischaemic maculopathy it is more difficult to treat with laser and it is unlikely to succeed when ischaemia of the macula is significant and if untreated, retinopathy is likely to worsen. Vision loss is common. One study reported that 58% of diabetics with ischaemic maculopathy had visual acuity of 20/100 (one fifth of normal visual acuity) after 3 years of disease.

The severity of macular edema is determined by:[8]

- The extent of the edema.
- The distribution in the macular area (i.e. focal versus diffuse).
- Central foveal involvement.
- Evidence of alteration of the Blood Retinal Barrier(BRB) and intraretinal cysts.
- Signs of ischemia.
- Presence or absence of vitreous traction.
- Increase in retinal thickness and cysts in the retina.
- Chronicity (i.e. time elapsed since initial diagnosis).

Macular Edema, in which blood vessels leak their contents into the macular region, can occur at any stage of NPDR. Its symptoms are blurred vision and darkened or distorted images that are not the same in both eyes. Ten percent (10%) of diabetic patients will have vision loss related to macular edema. Optical Coherence Tomography(OCT) can show areas of retinal thickening due to fluid accumulation from macular edema.[9] In the second stage, abnormal new blood vessels (neovascularisation) form at the back of the eye as part of proliferative diabetic retinopathy (PDR); these can burst and bleed causing vitreous haemorrhage and blur the vision, as these new blood vessels are fragile. Macular edema results from the breakdown of the blood-retinal barrier in the retinal capillaries. The tight endothelial cell junctions break down resulting in increased vascular permeability and increased fluid accumulation in the outer layers of the retina. Microaneurysms are believed to play a significant role by acting as sources for fluid and lipid transudation. Factors that are believed to cause microaneurysms are loss of pericytes and supporting astrocytes in the retina, increased capillary transmural pressure and local production of vasoproliferative factors such as vascular endothelial growth factor (VEGF). Hyperglycaemia is believed to be the main factor that causes increased oxidative stress and diacylglycerol accumulation. This substance activates protein Kinase C which in turn increases VEGF expression.

Clinically significant macular edema (CSME) is defined as:

1. Retinal thickening at or within 500 µm of the centre of the macula.
2. Hard exudates at or within 500 µm of the centre of the macula associated with retinal thickening(which may be outside 500µm) or
3. An area or areas of retinal thickening at least 1 disc diameter in size a part of which is within 1disc diameter of the centre of macula.

Risk Factors:

- Duration of diabetes mellitus.
- Poor glycaemic control.
- Hypertension.
- Hyperlipidaemia

METHODS

Patient selection: Most of the cases were selected from the outpatient department of Ophthalmology, Mata Gujri Memorial Medical College and L.S.K. Hospital, Kishanganj, Bihar, at random basis. Others were selected from Diabetic Clinic of this institution.

Inclusion criteria

Patients who had clinically diagnosed Diabetic Maculopathy were selected for this study.

Exclusion criteria

1) Corneal opacity obscuring visualization of fundus.
2) Significant cataract obscuring visualization of fundus.
3) Vitreous opacities or haemorrhage in both eyes.
4) Patients whose pupil did not dilate.

Recording of visual acuity: For distant vision Snellen's Test Types were used and Roman Test Types were used for near vision.

The following points were noted

1) Duration of diabetes.
2) Any history of previously diagnosed neuropathy or nephropathy.
3) Presence of hypertension.

4) Any history of tingling, numbness, loss of sensation, sweating, foot disease etc.
5) Any history of swelling, puffiness consistent with nephropathy.
6) Presence of Xanthalesma.
7) History of visual loss and duration of visual loss.

Patients with established diabetic macular edema were then selected and subjected to the following set of investigation

Biochemical parameters:

a) Post Prandial blood sugar (glucose) The method used to test glucose is GOD-PAP[10] Method. (Enzymatic colorimetric Test for glucose). Normal value is PPPG < 145 mg%.
b) Glycated Haemoglobin (HbA_1c)[11] It is tested using chromatographic method. Normal < 6.0 – 7.3%.
c) Lipid Profile

I. Cholesterol (serum) Tested by CHOD-PAP method[12.] Normal < 200 mg/dl. Borderline high - 200-239 mg/dl. High > 240 mg/dl.
II. LDL - Tested by selective precipitation method[13]. Normal < 130 mg/dl (without CHD, diabetes) < 100 mg/dl (with CHD, diabetes)
III. Triglycerides- Measured by Enzymatic DHBS colorimetric method[86].Expected value 30- 170 mg/dl.

RESULTS

Table 1: Sex wise Distribution

Sex	No of Patients	Percentage (%)
Male	27	54
Female	23	46

In the present study, there were 27 males (54%) and 23 females (46%).

Table 2: Distribution of Diabetes Mellitus Type –I and Type II among retinopathy With maculopathy

Diabetes Mellitus	No of Patients	Percentage (%)
Type-I	10	20
Type-II	40	80

Figure 2: Distribution of Diabetes Mellitus Type-I and Type II among retinopathy with maculopathy.

The present study included 50 cases. Clinical assessment was done in all 50 patients havingretinopathy with maculopathy which further segregated into two groups DM Type I and DM Type II among which20% patients were D.M. Type-I and 80% patients were D.M. Type-II.

Table 3: Duration of diabetes

Duration of diabetes (years)	Type I	Type II
0-5	0	4
6-10	1	15
11-15	4	11
16-20	3	8
21-25	1	2
> 25	1	0

From Table no 3 it was interpreted that majority of patients i.e. 40 (80%) patients had type II DM and 10 (20%) patients had type I DM. Among type II DM patients 6-10 years duration group consisted maximum 15 (30%) patients. Only 1 patient was suffering from Type I DM for more than 25 years.

Table 4: Visual acuity of the patients studied.

Visual acuity	RE	LE
6/6	5	3
6/9	11	12
6/12	11	12
6/18	15	5
6/24	0	5
6/36	7	10
6/60	1	2
Worse than 6/60	0	1

From the table no.4, it was interpreted that 45 patients (90%) had visual acuity of 6/12 or worse in at least one eye.

Table 5: Mean value of Post Prandial Blood Glucose and HbA1c

Post Prandial Blood Glucose and HbA1c Level	Minimum	Maximum	Mean
Post Prandial Blood Glucose	71.0 mg/dl	216.0 mg/dl	127.44
HbA1c	5.8%	10.1 %	8.60

Table No. 5 showed the mean value of post prandial blood glucose and HbA1C level of the patients. The mean value of post prandial blood glucose level was 127.44 mg/dl. It was found that maximum post prandial blood glucose level was 216.0 mg/dl and minimum was 71.0 mg/dl. In case of HbA1C the mean value was 8.6%. maximum and minimum HbA1C level found in this study was 10.1% and 5.8% respectively.

Table 6: Mean, Maximum and Minimum value of Lipid profile

Lipid Profile	Minimum	Maximum	Mean
Total Cholesterol	168 mg/dl	263 mg/dl	203.86
Triglyceride	67mg/dl	586 mg/dl	213.84
HDL	29mg/dl	78 mg/dl	42.5
LDL	72 mg/dl	186 mg/dl	120.74

Table No. 6 showed the mean value of lipid profile of the patients. The mean value of total cholesterol was 203.86 mg/dl, where as in case of Triglyceride the mean value was 213.84 mg/dl. In case of HDL and LDL the mean values were 42.5 mg/dl and 120.7 mg/dl respectively.

Table 7: Relationship of Maculopathy with Type of Diabetes

Type of Maculopathy	Type I DM	Type II DM
Focal	2	19
Diffuse	7	15
Focal maculopathy along with Diffuse maculopathy	0	2
Ischaemic	**1**	4
Total	10	40

Table No. 7 shows the relationship of maculopathy with type of diabetes. In Type I DM there were 2 cases of focal, 7 cases of diffuse and 1 cases of ischaemic maculopathy were seen. In Type II DM there were 19 cases of focal, 15 cases of diffuse,2 cases presented with both focal maculopathy in one eye and diffuse maculopathy in other eye and 4 cases presented with ischaemic maculopathy.

Table 8: Relationship between type of Maculopathy and duration of Diabetes.

Maculopathy	0-5 years	6-10 years	11-15 years	16-20 years	> 20 years
Focal	3	11	5	2	0
Diffuse	1	4	9	6	2
Focal maculopathy along with Diffuse maculopathy	**0**	**1**	**1**	**0**	0
Ischaemic	**0**	**0**	**0**	**3**	2

Table No. 8 shows the relationship between type of maculopathy and duration of diabetes. The duration of diabetes was divided into 5 groups i.e. 0-5 years, 6-10 years, 11-15 years, 16-20 years and >20 years duration.0-5 years duration group consisted 3 patients of focal maculopathy and 1 patient of diffuse maculopathy. 6-10 years duration group consisted 11 and 4 patients of focal and diffuse maculopathy respectively and 1 patient presented with both focal maculopathy in one eye and diffuse maculopathy in other eye. 5 patients of focal maculopathy and 9 patientsof diffuse maculopathy belonged to 11-15 years duration group and 1 patient presented with both focal maculopathy in one eye and diffuse maculopathy in other eye. 16-20 years duration group consisted 2,6 and 3 patients of focal, diffuse and ischaemic maculopathy respectively. More than 20 years duration group had 2 patients each who had diffuse maculopathy and ischaemic maculopathy.

DISCUSSION

In this study 50 cases of diabetic maculopathy evaluated. Out of 50 cases there were 27 males sex ratio of Male: Female in this study was 1:1.73 which is mentioned in Table 1 In Table 2 it has been mentioned that out of 50 cases observed in this study 10 patients were found to have Type 1 diabetes mellitus and 40 patients were found to have Type 11 diabetes mellitus. From the Wisconsin Epidemiologic study of Diabetic Retinopathy it was concluded that a) The duration of Type I and Type II diabetes is a risk factors for diabetic retinopathy. b) Diabetes duration of 10 years has 77.4% sensitivity for detecting the presence of retinopathy in Type I diabetic.

Also from the Knopia University study[14], Finland it was concluded that the frequency of maculopathy in Type II diabetes was low at the time of diagnosis, but increased sharply after 5 years of the disease and at the 10 years examination. In this study, from Table 3, it is evident that the cluster of cases starts at 0-5 years age group and starts increasing as the duration of diabetes increases with peak between 6-15 years age group. There after it declines but this may be due to the fact that after 20 years we get a reduction in the number of cases as the life expectancy gets crossed in that age group. The average duration of diabetes found in this study is 12.224 years and SD value was ±5.70 years. The data is significantly on its higher side. Hence duration of diabetes is a major risk factor for the development of diabetic maculopathy (statistically significant, $p<0.01$). In this study the average glycosylated haemoglobin (HbA1c) is 8.6% (normal <7.3%) which signifies that the studied patients had poor glycaemic control which was mentioned in table 5. Most (eg. HDS/UKPDS study, The EUCLID study, the WESDR) studies report an association of hypertension and retinopathy. There was a continuous relationship between the risk of diabetic retinopathy and systolic blood pressure (> 130 mm Hg) observed in the UKPDS. In both the 4 and 10 years follow-up studies of the WESDR, increased systolic blood pressure (independent of other risk factors), predicted proliferative diabetic retinopathy in people with Type I but not Type 2 diabetes. In both types of diabetes elevated diastolic blood pressure was a risk factor for macular edema and elevated systolic blood pressure was a risk factor for loss of vision. In conclusion, elevated blood pressure is an independent risk factor for any retinopathy, macular edema, and loss of vision in both Type I, and Type 2 diabetes[14-16] and for proliferative retinopathy is Type I diabetes[17]. In the DCCT conventional treatment group, patients with Type I diabetes in the higher quartile of baseline triglycerides had a twofold rate of progression of retinopathy compared with those in the lower- quartile. The severity of hard exudates was directly related to the risk of visual decrease even after adjustment for retinal thickening. Elevated serum cholesterol > 6.2 mmol/L at base line increased the risk of visual loss by 50% when compared with a low serum cholesterol level < 6.21 mmol/L. In the ETDRS, the development and severity of retinal hard exudates in the macula were directly associated with elevations in serum total cholesterol[18-20] and LDL[21,22]. Patients with total serum cholesterol $\geq$ 6.21 mmol/L or triglyceride > 4.50 mmol/Ldeveloped hard exudates approximately 50% faster than patients with serum cholesterol < 5.17 mmol/L or triglyceride <2.3 mmol/L. So it may be concluded that dyslipidemia is a risk factor for visual loss.[23,24]. In this study of 50 patients the average lipid profile obtained (Table -6) were found to be Total Cholesterol – 203.86 mg/dl.(5.27mmol/L), Triglyceride- 213.84 mg/dl.(2.37mmol/L), LDL - 120.74 mg/dl.(3.09mmol/L) Table-7 it is evident that cases with Type II diabetes mellitus are more prone to develop diabetic maculopathy than Type I diabetes mellitus ($P < 0.05$). This rejects the null hypothesis at 5% level of confidence but there is no correlation between type of diabetes and type of diabetic maculopathy. In Table No-8, it was seen that diffuse and ischaemic maculopathy occurs more as duration of diabetes increases as compared to focal maculopathy.

CONCLUSION

Duration of diabetes is a major risk factor for the development and progression of diabetic maculopathy,($P< 0.01$). In this study the average duration of diabetes is 12.24 years. The data is significant. we see that the cluster of cases start at 0-5 years duration group and starts increasing with peak between 6-15 years duration. Thereafter it declines, but this may be due to the fact that after 20 years we get a reduction in the number of cases as the life expectancy gets crossed in that age group. It appears that diffuse and ischaemic maculopathy tend to occur more as duration of diabetes increases as compared to focal maculopathy. Poor metabolic control is a significant risk factor for the development of diabetic maculopathy as is evident from average HbA1c which is 8.60% in this study. The data is significant. Dyslipidemia is a major risk factor for the development of diabetic maculopathy. From the percentile raw score it is evident that 30% of the subjects have serum LDL level nearly 103.35 mg/dl, 70% under 133.2 mg/dl (130 mg/dl being regarded as normal for LDL). Interesting point to be noted is that 90% of the patients are under 160 mg/dl serum LDL which is thought to be moderately controlled and yet they developed diabetic maculopathy. This perhaps indicates towards the importance of tight control of serum LDL below 100mg/dl in diabetic patients to prevent or at least delay the development of diabetic maculopathy.

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