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CORRELATION OF DURATION OF DIABETES MELLITUS AND GLYCOSYLATED HAEMOGLOBIN (HBA1C) LEVELS WITH DIABETIC RETINOPATHY

Ophthalmology

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ABSTRACT

Purpose - To correlate the duration of diabetes mellitus and glycosylated haemoglobin (HbA1c) levels with grades of diabetic retinopathy **Material & method-** An observational cross-sectional clinical study was conducted involving 100 diabetics. Detailed ophthalmic evaluation was done and data involving fasting blood sugar levels, post prandial blood sugar levels and glycosylated haemoglobin levels were collected. Any diabetic retinopathy related changes were documented & grading was done on the basis of severity using ETDRS classification. **Result-** Out of 100 diabetic patients evaluated, 58% patients had diabetic retinopathy (DR). There was no gender predilection. Strong association was found between duration of diabetes mellitus with presence & severity of Diabetic retinopathy. Chances of a diabetic patient developing DR & progression of DR increases as the duration of diabetes increases. Positive association was found between poor glycemic control as established by HbA1c levels with presence & severity of DR. Higher the HbA1c levels, higher the risk for DR. **Conclusion-** It was concluded that in diabetic patients, good glycemic control reduces the occurrence & progression of diabetic retinopathy.

KEYWORDS

diabetic retinopathy, HbA1c levels, diabetes mellitus

INTRODUCTION

Diabetic retinopathy (DR) occurs as a result of damage to the blood vessels of the retina due to uncontrolled diabetes. It is a leading cause of vision-loss globally. By the time of clinical diagnosis of DM, some individuals already show evidence of DR, indicating that diabetes may have been present for several years.[1] Duration of DM, glycemic control, hypertension, dyslipidemia, obesity & proteinuria play an important role for development of DR. [2]Clinically visible signs of DR are microaneurysms, flame- shaped haemorrhages, dot blot haemorrhaes, exudates, venous looping/ beading, intra retinal microvascular abnormalities, neovascularization & diabetic macular oedema. Depending on the severity of these lesions, grading of diabetic retinopathy is done. Most commonly used grading scale internationally is Early Treatment Diabetic Retinopathy Study (ETDRS) classification of diabetic retinopathy. This study was conducted to evaluate for any presence of diabetic retinopathy in diabetic patients & DR was graded on the basis of its severity as per ETDRS classification. Observations were made in correlation of duration of DM & glycosylated haemoglobin (HbA1c) levels with presence & severity of DR.

MATERIAL AND METHOD

Study design:

This was an observational cross–sectional study conducted over a period of one year from June 2017 to May 2018 under the Department of Ophthalmology, Index Medical College, Hospital and Research Centre, Indore (MP) after approval of institutional ethical committee**.**

Material: The study population included 100 diabetic subjects.

Inclusion Criteria:

- Patients of either sex
- Patients diagnosed as cases of Diabetes Mellitus with or without treatment.
- Both Type I and Type II Diabetes Mellitus.
- Patients with HbA1C levels >5.7 %

Exclusion Criteria:

- Any patient with corneal opacity or lenticular opacities which precluded proper fundus examination.
- Patients with other retinal degenerations.
- Patients with non diabetic renal disorders, chronic liver diseases or Haemoglobinopathies.
- Patient unwilling to participate in the study.

METHODS:

Written & informed consent was taken from all the participants. Patients' best corrected visual acuity was recorded using snellen's chart. Detailed history regarding duration of diabetes mellitus & intake of any anti- diabetic medication was noted. History regarding any systemic illness & other medications was documented. Detailed anterior segment examination was done using slit lamp. Intra ocular pressure was measured using *Goldmann applanation tonometer*. Pupils were dilated using 1% Tropicamide eye drops. Fundus was examined by slit lamp biomicroscopy using 78D lens. Any diabetic retinopathy related changes were documented & grading was done on the basis of severity using ETDRS classification. Blood investigations include: fasting blood sugar levels, post prandial blood sugar levels and glycosylated haemoglobin levels were collected.

Data analysis:

Unpaired't' test was applied for comparing the mean values between two groups. For comparison mean of more than two groups, one-way ANOVA followed by post-hoc tukey test was applied. Association between non-parametric variables was done using Pearson Chi-square test. A p value of < 0.05 was taken as statistically significant.

RESULT

In total 100 diabetic patients who met the inclusion criteria were included in this study. All patients had type 2 DM. Out of these, 58 patients had diabetic retinopathy.29 were males & 29 were females. Diabetics with no diabetic retinopathy were 16 males & 26 females. The observations on the basis of gender in patients with diabetic retinopathy & in patients with no diabetic retinopathy was not found to be statistically significant ($p > 0.05$). Most of the patients were in the age group 41-60 years. [Table -1]

Table-1: Distribution of diabetic patients according to ageAge GroupNumber Percentage

Age Group	Number	Percentage
≤40 years	2	2.0
41-60 years	62	62.0
61-80 years	32	32.0
>80 years	4	4.0
Total	100	100.0

DR was noted to be more in older age group and was statistically significant. ($p<0.05$) [Table -2]

Table-2: Comparison of mean age between patients with DR and no DR

DR / No DR	Number	Age (in years) [Mean ± SD]	't' value	P value
Patients with DR	58	61.05 ± 10.32	2.153, df=98	0.0337
Patients with No DR	42	56.74 ± 9.23		

In 42 (42.0%) patients there was no diabetic retinopathy. In 8 (8.0%) patients there was very mild NPDR, in 12 (12.0%) patients there was mild NPDR, in 23 (23.0%) patients there was moderate NPDR, in 7 (7.0%) patients there was severe NPDR and in 2 (2.0%) patients there was very severe NPDR, while in 6 (6.0%) patients there was early PDR. Majority of the patients were having mild to moderate NPDR in our study. Only 8 patients had macular oedema.

Most of the diabetic patients were having duration of diabetes mellitus between 1-5 years. [Table -3]

Table-3: Distribution of patients according to duration of diabetes mellitus

Duration of diabetes mellitus	Number	Percentage
< 1 year	14	14.0
1-5 years	43	43.0
6-10 years	22	22.0
11-15 years	11	11.0
>15 years	10	10.0
Total	100	100.0

This study showed mean duration of diabetes was higher in patients with DR in comparison to diabetics with no DR which was statistically significant ($p<0.05$) [Table- 4].

Table- 4: Comparison of mean duration of diabetes between Patients with diabetic retinopathy and no diabetic retinopathy

DR / No DR	Number	Duration [Mean ± SD]	't' value	P value
Patients with DR	58	9.47 ± 6.74	5.81, df=98	0.000*
Patients with no DR	42	2.95 ± 3.15		

Table-5 shows that severity of diabetic retinopathy is dependent on the duration of diabetes mellitus. As the duration of diabetes mellitus increases the severity of the diabetic retinopathy also increases.

Table-5: Association between duration of diabetes and diabetic retinopathy grading

Duration of diabetes mellitus	Diabetic Retinopathy Grading						
	Nil	Very mild NPDR	Mild NPDR	Moderate NPDR	Severe NPDR	Very severe NPDR	Early PDR
<1 year	13 30.95%	0 0.00%	1 8.33%	0 0.00%	0 0.00%	0 0.00%	0 0.00%
1-5 years	22 52.38%	4 50.00%	8 66.67%	7 30.43%	0 0.00%	0 0.00%	2 33.33%
6-10 years	7 16.67%	2 25.00%	2 16.67%	8 34.78%	3 42.86%	0 0.00%	0 0.00%
11-15 years	0 0.00%	1 12.50%	0 0.00%	5 21.74%	1 14.29%	2 100.0%	2 33.33%
>15 years	0 0.00%	1 12.50%	1 8.33%	3 13.04%	3 42.86%	0 0.00%	2 33.33%
Total	42 100.0%	8 100.0%	12 100.0%	23 100.0%	7 100.0%	2 100.0%	6 100.0%

The difference in HbA1c was found to be statistically significant showing that the mean HbA1c was higher in diabetics with retinopathy in comparison to diabetics with no diabetic retinopathy. [Table-6]

Table- 6: Comparison of mean HbA1c levels in patients with diabetic retinopathy and no diabetic retinopathy

DR / No DR	Number	HbA1c [Mean ± SD]	't' value	P value
Patients with DR	58	8.62 ± 1.65	5.79, df=98	0.000*
Patients with no DR	42	6.89 ± 1.19		

This study showed significant association between HbA1c grading and the type of diabetic retinopathy ($p<0.05$).

With higher HbA1c grade (>10%), there are increased chances of having Moderate to very severe NPDR and Early PDR. [Table-7,8]

Table-7: Association between HbA1c levels and diabetic retinopathy grading

HbA1c Grading	Diabetic Retinopathy Grading						
	Nil	Very mild NPDR	Mild NPDR	Moderate NPDR	Severe NPDR	Very severe NPDR	Early PDR
5.7-8%	34 80.95%	5 62.50%	7 58.33%	11 47.83%	1 14.29%	0 0.00%	0 0.00%
8-10%	7 16.67%	1 12.50%	4 33.33%	10 43.48%	3 42.86%	0 0.00%	0 0.00%
>10%	1 2.38%	2 25.00%	1 8.33%	2 8.70%	3 42.86%	2 100.0%	6 100.0%
Total	42 100.0%	8 100.0%	12 100.0%	23 100.0%	7 100.0%	2 100.0%	6 100.0%

Table-8: Comparison of HbA1c levels among different grades of diabetic retinopathy

Diabetic Retinopathy Grading	Number	HbA1c [Mean ± SD]	F value	P value
No diabetic retinopathy	42	6.89 ± 1.19	16.33	0.000*
Very mild NPDR	8	7.68 ± 1.99		
Mild NPDR	12	7.92 ± 1.41		
Moderate NPDR	23	8.17 ± 0.92		
Severe NPDR	7	9.60 ± 1.19		
Very severe NPDR	2	10.90 ± 0.71		
Early PDR	6	11.17 ± 0.91		
Total	100			

The mean HbA1c varied between duration of diabetes mellitus and was found to be higher in patients with longer duration of diabetes mellitus. ($p<0.05$) [Table-9]

Table-9: Comparison of mean HbA1c levels in relation to duration of diabetes mellitus

Duration of diabetes mellitus	Number	HbA1c [Mean ± SD]	F value	P value
< 1 year	14	7.38 ± 1.60	7.70	0.000*
1-5 years	43	7.46 ± 1.53		
6-10 years	22	7.56 ± 1.15		
11-15 years	11	9.25 ± 1.72		
>15 years	10	9.78 ± 1.75		
Total	100			

DISCUSSION

According to the WHO, 31.7 million people were affected by Diabetes in India in the year 2000. This figure is estimated to rise to 79.4 million by 2030, the largest number in any nation in the world.[3] DR is a microangiopathy resulting from the chronic effects of Diabetes mellitus. Almost two-thirds of Type 2 and almost all Type 1 diabetics are expected to develop DR over a period of time. [4] Gadkari et al conducted a nationwide population based cross-sectional study of diabetic patients as an initiative of the AIOS from 14th November to 21st November 2014 & stated that the prevalence of DR was 21.7% in India.[3] Globally, diabetic retinopathy is responsible for 1% of visual impairment & blindness.[5]

Present study was an observational, cross- sectional study conducted on diabetic patients. Our observation showed the prevalence of diabetic retinopathy as 58%. This was in line with studies conducted by Baba et al. [6] & Priyadharshini et al. [7] showing similar results regarding prevalence of DR i.e. 66.8% and 63 % respectively. In our study, DR was noted to be more in older age group and was statistically significant ($p<0.05$). Stratton et al (2001) [72] concluded in their study that in patients who already had DR, progression was associated with older age of the patients.

In this study, the prevalence of diabetic retinopathy was not significantly associated with gender. Similar result was found in a study conducted by Narendran et al (2002) [8]. But CURES-1 by Mohan et al. (2005) [9] & SN-DREAMS III by Raman et al. (2014) [10] reported

that the prevalence of diabetic retinopathy was more in male gender. It was observed in our study that increased duration of diabetes increases the incidence of diabetic retinopathy. A 4 years follow up study in Iranian population conducted by Manaviat et al. (2008) [11] showed similar results. SN-DREAMS III study by Raman et al (2014) [10] established that the strongest predictor for severity of retinopathy was the duration of diabetes.

Our study indicated statistically significant difference in the mean HbA1c between the various grades of diabetic retinopathy ($p<0.05$), showing that higher the HbA1c levels higher the severity of diabetic retinopathy. UKPDS (1970) [12] demonstrated that any improvement in glycaemic control and blood pressure reduces diabetes related complication like retinopathy & nephropathy. DCCT (1993) [13] conclusively showed the efficacy of glycemic control in preventing DR. It showed that intensive glycaemic control reduces the incidence and progression of microvascular complications (retinopathy, nephropathy and neuropathy) in type 1diabetes. Whether the same holds true in type 2 diabetes remained uncertain. Klein et al (1998) [14] did the WESDR study having a follow up period of 14 years. The study concluded that a reduction of hyperglycemia may result in beneficial decrease in the progression to proliferative retinopathy. Lower HbA1c levels at baseline were associated with improvement in DR.

CONCLUSION

Strong association was found between duration of DM with presence & severity of DR. The chances of a diabetic patient developing DR & progression of DR increases as the duration of diabetes increases. Positive association was found between poor glycemic control as established by HbA1c levels with presence & severity of DR. Higher the HbA1c levels, higher the risk for DR. It was concluded that in diabetic patients, good glycemic control reduces the occurrence & progression of diabetic retinopathy. Hence clinicians should always document the duration of diabetes & grade of diabetic retinopathy. HbA1c levels should be investigated in all diabetics. HbA1c levels helps in planning anti- diabetic treatment for the patient & further progression of DR can be delayed or prevented by maintaining good glycemic control.

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