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Association of glycosylated hemoglobin (HbA1C) level with diabetic retinopathy in type 2 diabetes patients at tertiary care hospital

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Abstract
Introduction: Diabetic retinopathy (DR) is a chronic progressive, potentially sight-threatening disease of the retinal microvasculature associated with the prolonged hyperglycemia and associated with other condition. HbA1C is an important predictor for early identification of diabetic retinopathy cases.
Materials and Method: It is a hospital based prospective observational study to assess association of HbA1Clevels with Diabetic retinopathy in type 2 Diabetes. The study included 160 DR cases. All calculations were performed using SPSS® version 15 (Statistical Packages for the Social Sciences, Chicago).
Results: Maximum cases 88(55%) were developed diabetic retinopathy after 10 year. Mean duration of diabetes in (years) study population was 12.28± 6.05 years. 77.27% of mild NPDR cases were in range of 6.5-8.5% range of HbA1C. 60.72% moderate NPDR were in range 8.6-10.5% of HbA1C. 80% severe NPDR were in range 10.6-12.5% of HbA1C, whereas 80% PDR cases were in 12.6-14.5% range of HbA1C. Hb1Ac range was statistically significantly associated with progression of diabetic retinopathy (P=.001).
Conclusion: Maximum number of patients 84 (52.5 %)were developed diabetic retinopathy after 60 years of life and maximum patients 88(55%) were developed diabetic retinopathy after 10 years duration of disease. Glycosylated hemoglobin value (HbA1C %) showed increasing trend according to severity of diabetic retinopathy cases hence prevalence and severity of diabetic retinopathy increased with increasing level of HbA1C

Keywords: diabetic retinopathy, glycosylated hemoglobin), proliferative diabetic retinopathy, nonproliferative diabetic retinopathy, hyperglycemia

Introduction

Diabetic retinopathy (DR) is a chronic progressive, potentially sight-threatening disease of the retinal microvasculature associated with the prolonged hyperglycemia and associated with other condition &related to diabetes mellitus such as hypertension. In India, 20% of the type 2 diabetes mellitus (T2DM) population is estimated to develop DR which suggests that by 2025 nearly 11.4 million adults with diabetes may develop DR [1, 2]. The main risk factors associated with the earlier onset and rapid progression of retinopathy are-duration of diabetes, high blood sugar level, arterial hypertension, hyperlipidaemia, severe nephropathy other risk factor are smoking, obesity and anaemia. Clinically, Diabetic retinopathy is diagnosed by the presence of the microanerusym, hard exudates, intraretinal microvascular abnormalities, venous alteration, neovascularization, vitreous hemorrhage and difusse and focal macular edema. Microanerusym are most typical diabetes- related lesion detected on fundus examination.The DR disease pathology is a complicated network of various pathways, which are triggered by chronic hyperglycemia[4].Blood-retinal barrier breakdown is a very crucial event in the pathogenesis of DR brought about by adhesion of leucocytes to the retinal endothelium due to β2 integrin and intercellular adhesion molecule (ICAM)-1 interaction. The pericytes and capillary endothelial cells together result in reduced blood flow to the retina which brings about tissue hypoxia [5, 6]. Hypoxia is known to induce the key modifier of retinal angiogenesis
HbA1C is an N-terminal valine residue of erythrocyte hemoglobin become irreversibly glycosylated in proportion to circulating glucose concentration and the resultant product is referred as HbA1C [3]. As the life span of glycosylated haemoglobin is 120 days, unlike fsting blood glucose (FBS) and posprandial blood glucose(PPBS), it gives us a long term glycemic values [2]. As it is the best indicator of glycemic value of past 8-12 weeks, it is chosen to help us to foresee end tissue damage and its progression. The relation between glucose control and development of diabetic complication remains an area of active investigation.

Materials and Method

It is a hospital based prospective observational study to assess association of HbA1C levels with Diabetic retinopathy in type 2 Diabetes patients. The study had done in Department of Ophthalmology Sardar Patel Medical College & Associated group of hospitals, Bikaner (Rajasthan). Patients having type 2 DM with diabetic retinopathy of either sex and those who give written informed consent were included in study. The number of subjects recruited into the study were 160. The study was

performed according to guidelines of declaration of Helsinki on Human experimentation and was approved by institutional ethical committee. Each patient underwent a complete ophthalmic examination including clinical examination and lab investigation including visual acuity, fundus examination by direct& indirect ophthalmoscopy and +90D slit lamp biomicroscopy after dilatation of pupil, fundus photography and ocular tomography (OCT). Diabetic retinopathy classified according to early treatment diabetic retinopathy study (ETDRS) classification. After confirmation of diagnosis and obtaining consent from the patient, 2 ml blood drawn in EDTA vial, labelled from number 1 to 160 over vial and send to central laboratory for FBS and HbA1C. Glycosylated HbA1C was measured by auto analyser and expressed in percentage. The continuous data was presented as mean ± SD or median and inter-quartile range, as appropriate. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using Chi-square or Fisher's exact test whichever applicable. A P value of <0.05 was considered to indicate statistically significant. All calculations were performed using SPSS® version 15 (Statistical Packages for the Social Sciences, Chicago).

Results

A total 160 patients having diabetic retinopathy with type 2 diabetes mellitus had taken.

Table 1: Age distribution of diabetic retinopathy case

Age groups(years)	Case (n=160)
40-50	32(20%)
51-60	44(27.5%)
61-70	68(42.5%)
71-80	16(10%)

The age wise distribution of diabetic retinopathy cases showed 44(27.5%) patients were belong to 51-60 yrs, 68 (42.5%) patients were 61-70yrs, 32(20%) patients were 40-50yrs and 16(10%) patients belong to 71-80 yrs. Mean age of presentation in diabetic retinopathy in case group was 61.25 ±9.639 years (Table -1).

Table 2: Gender distribution of study group

Gender	No. of cases (n=160)	%
Male	92	57.5%
Female	68	42.5%
Total	160	100%

The gender wise distribution of 160 cases had shown, 92(57.5%) were male and 68(42.5%) were female (table-2). It was inferred that more number of male (92) patients had diabetic retinopathy than females (68). So diabetic retinopathy had more prevalent in male in our study group (M:F 1.35).

Table 3: Distribution of diabetic retinopathy cases according to ETDRs classification

Type of DR	No. of case(n=160)	%
Mild NPDR	44	27.5%
Moderate NPDR	56	35%
Severe NPDR	40	25%
PDR	20	12.5%
Grand Total	160	100%

The distribution of diabetic retinopathy cases according to ETDRs classification. Study included 160 patients with diabetic retinopathy. Of the 160 cases, 56(35%) had moderate NPDR, 44(27.5%) had mild NPDR, 40(25%) had severe NPDR and 20(12.5%) had PDR. Of 160 patients, 140(87.5%) patients were belonged to NPDR group (Table-3).

Table 4: Distribution of diabetic retinopathy cases according to duration of disease

Duration of DR	Type of diabetic retinopathy				No. of cases
	Mild NPDR	Moderate NPDR	Severe NPDR	PDR	
0-10 yrs	16(22.22%)	28(38.89%)	24(33.33%)	04(5.56%)	72
11-20 yrs	24(33.33%)	20(27.77%)	12(16.66%)	16(22.22%)	72
>20 years	04(25%)	08(50%)	04(25%)	00(0%)	16

In 160 cases, 72(45%) cases were developed diabetic retinopathy between 11 years and 20 years after onset of DM II, among them 24 had Mild NPDR, 20 Moderate NPDR, 12 severe NPDR and 16 had PDR. In our study maximum cases 88(55%) were developed diabetic retinopathy after 10 year. Mean duration (years) in our study population was 12.28± 6.05 years (Table-4).

Table 5: Distribution of cases according HbA1C range and type of diabetic retinopathy

HbA1C Range (%)	Type of Diabetic retinopathy				No. of cases (n=160)
	Mild NPDR (n=44)	Moderate NPDR (n=56)	Severe NPDR (n=40)	PDR (n=20)	
6.5-8.5	34(77.27%)	18(32.14%)	00(0%)	00(0%)	52
8.6-10.5	10(22.73%)	34(60.72%)	04(10%)	00(0%)	48
10.6-12.5	00(0%)	04(7.14%)	32(80%)	04(20%)	40
12.6-14.5	00(0%)	00(0%)	04(10%)	16(80%)	20
Total	44	56	40	20	160

There were 77.27% of mild NPDR cases and 32.14% of moderate NPDR cases in range of 6.5-8.5% range of HbA1C. 60.72% moderate NPDR cases, 22.73% mild NPDR cases and 10% severe NPDR were in range 8.6-10.5% of HbA1C. 80% severe NPDR cases, 20 % PDR cases were in range 10.6-12.5% of HbA1C whereas 80% PDR cases and 10% severe NPDR cases were in 12.6-14.5% range of HbA1C. Hb1Ac range was statistically significant in diabetic retinopathy group (P=.001;Table-5)

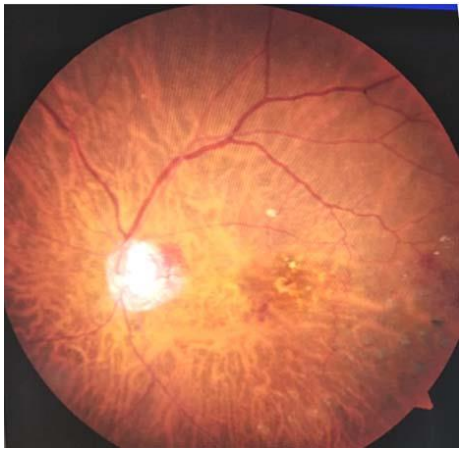

Fig 1: Fundus photograph Showing neovascularization on optic disc & Retina

Table 6: Distribution of cases according Mean and SD of HbA1C in retinopathy

Type of retinopathy	HbA1C (%)	
	Mean	SD
Mild NPDR	8.21	0.88
Moderate NPDR	8.93	1.24
Severe NPDR	11.67	1.11
PDR	12.65	0.38

The table shows mean and standard deviation with type of retinopathy group. The mean and SD HbA1C in mild NPDR group was 8.21 + .88, in moderate NPDR it was 8.93+1.24 and 11.67 +1.11 in severe NPDR group. In PDR group it was 12.65 and significantly high amongst diabetic retinopathy group. Mean and standard deviation was statistically significant with all diabetic retinopathy groups.

Discussion

Glycosylated HbA1C in diabetic retinopathy would be helpful both in the diagnosis and management of this disease. Present study included 160 diabetic retinopathies with type 2 DM cases who attended and referred to the department of ophthalmology between December 2018 to November 2019. Mean age of presentation in diabetic retinopathy cases was 61.25±9.639 years. In a study done by Awata T*et al* (2002) [7]. mean age of presentation was 58.4±11.7years, which was lower compared to our study.Another study done by Monika B *et al*. (2017) [8]. mean age of presentation was 58.6±9.4 years in diabetic retinopathy cases. Which was lower compared to our study. Study conducted by Suganthalaksmi B *et al* (2006) [9] found mean age of disease duration 63±7.2 yrs in DR. When it was compared to our study found higher.In our study there were 92 (57.50%) males and 68 (42.50%) females were enrolled. Male female ratio in our study was 1.35:1 hence male patients were predominant in number over female. Study conducted by Lokesh S *et al* (2018) [10] found males were 62.5% and females were 37.5%. When compared to our study were higher percentage of male patients and lower percentage of female patients were found. Another study done by Rajendra Prasad J *et al* (2016) [11] found male patients were 56% and females were 44%. When it was compared to our study male patient were slight lower and female were higher in number. In all study male patients were predominating over female in number.

The duration of diabetes has been recognized as an important factor in development and progression of diabetic retinopathy. In our study maximum cases 88(55%) were developed diabetic retinopathy after 10 year. Mean duration (years) in our study population was 12.28± 6.05 years. Study done by Khan *et al* (2008) [12] mean duration (years) of disease was 15±7.2 years in diabetic retinopathy when compared to our study it was higher.

Mean fasting blood glucose level in our study population was 180.63±56.517 mg/dl. Study conducted by Yang X *et al* (2011) [13] reported mean fasting blood glucose level was 166.14±53.46 mg/dl in diabetic retinopathy. It was lower when compared to our case group. Control of FBS is poor in our study so it may be responsible for earlier onset of diabetic retinopathy than other studies.

There were 77.27% of mild NPDR cases in range of 6.5-8.5% range of HbA1C. 60.72% of moderate NPDR cases were in range 8.6-10.5% of HbA1C. 80% severe NPDR cases were in range 10.6-12.5% of HbA1C whereas 80% PDR cases were in 12.6-14.5% range in our study. Study conducted by Lokesh S *et al*. (2018) [10] found that severe form of diabetic retinopathy are more commonly distributed among the patients with higher range of HbA1C compared to lower HbA1C group and it was similar results when compared to our study. Another study done by Rajendra Prasad J *et al*. (2016) [11] found increasing severity of retinopathy, increasing levels of HbA1C were noted significant correlation.

Conclusion

Maximum number of patients were developed diabetic retinopathy after 60 years of life and after 10 year of duration of disease. Glycosylated hemoglobin value (HbA1C %) showed increasing trend according to severity of diabetic retinopathy cases hence prevalence and severity of diabetic retinopathy increased with increasing level of HbA1C. All Diabetic retinopathy groups (Mild NPDR, Moderate NPDR, Severe NPDR and PDR) are statistically significant with HbA1C range above 6.5 %. HbA1C below 6.5% may reduce the risk of developing diabetic retinopathy. HbA1C and duration of diabetes are major predictor of diabetic retinopathy in type 2 diabetic mellitus. Higher HbA1C was associated with more severe diabetic retinopathy so control of blood sugar level is also important to prevent vision threatening complications.

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