IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 7 Ver. XI (July. 2016), PP 48-53
www.iosrjournals.org

Association of Diabetic Retinopathy in Type II Diabetes Mellitus with Hba1c Levels: A Study

Dr. Rajendra Prasad. J[(1)], Dr. Nayana. G[(2)]
[(1)]*Associate Professor, Department of Ophthalmology, Dr. Psims & Rf, Chinnaoutpalli, India*
[(2)]*Resident Department of Ophthalmology, Dr. Psims & Rf, Chinnaoutpalli, India*

Abstract :
Purpose :*To assess the association of Diabetic Rtinopathy in Type – II Diabetes Mellitus with HbA1c (Glycosylated Haemoglobin) levels.*
Materials and Methods :*Present study was carried out in type – II Diabetes Mellitus patients at Dr. PSIMS & RF, Chinnaoutpalli.*
***Results** : Out of 100 patients in the study the mean age of Diabetes Mellitus is 15.99 years + 5.68 years. The mean of HbA1c is in the study population was 9.25 + 1.59. The severity of Diabetic Retinopathy is increased with age and duration of Diabetes Mellitus. The range of HbA1cwas8.6% to 10.5%.*
***Discussion :** Among the 100 patients in this study the male to female ratio is 1.27:1. The mean HbA1c levels was 9.25+1.59. An earlier study showed the mean age of diagnosis of Diabetes Mellitus is 46.5years and the mean duration of Diabetes Mellitus is 7.6+5 years with mean HbA1c levels of 8.6%. These values are close to our study.*
***Conclusion** : The HbA1c levels showed an increase with the severity of Diabetic Retinopathy. The high HbA1c levels showed the presence of CSME, a severe form of Diabetic Retinopathy.*
***Keywords**: Diabetes milletus, Diabetic retinopathy, Nonproliferative daibetic retinopathy [NPDR], proliferative diabetic retinopathy[PDR],Glycosylated haemoglobin[HbA1c]*

I. Introduction

Diabetes is a Group of metabolic diseases characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both. It is single most important disease which can affect nearly every organ system in the body.[1]

Diabetes is the commonest metabolic abnormality in the humans.[2] Type 2 diabetes is the commonest form of diabetes constituting nearly 90% of the diabetic population.[3] India with largest number of diabetic subjects earned the title Diabetes capital of the world.

1.1 Diabetic retinopathy: It is the chronic progressive sight threatening disease of retinal microvasculature associated with prolonged hyperglycemia. The presence of diabetic retinopathy indicates microcirculatory dysfunction in the other organ systems.[4]

Diabetic retinopathy is a leading cause of preventable blindness in working aged people.[5] It used to be 17th cause of blindness but now ascended to 6 position with estimated 5.8 million affected diabetic retinopathy patients.[6]

1.2 HbA1c: N terminal valine residue of erythrocyte hemoglobin become irreversibly glycosylated in proportion to circulating glucose concentrations and the resultant product is referred to as hemoglobin A1C (HbA1c).[7] As the life span of glycosylated HB is 120 days, unlike FBS and PPBS, it gives us a long term glycemic values.[8]

Hence forth to diagnose prediabetes and diabetes, American Diabetic association is recommending HbA1c is to be considered. 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 relationship between glucose control and development of diabetic complications remains an area of active investigation. As the relationship between HbA1c and risk of microvascular complications is exponential with no obvious "threshold" value, it means that targets aimed for are still to some extent arbitrary. The trend to lower targets seems to be continuing.[9]

The present study is to investigate the relationship of glycosylated haemoglobin (HbA1c) with the severity of diabetic retinopathy.

II. Alms & Objectives

1. To determine the association of blood levels of haemoglobin A1c in the presence of diabetic retinopathy in patients with type II diabetes mellitus.
2. To correlate the severity of diabetic retinopathy with the levels of haemoglobin A1c.

III. Materials And Methods

The present study was carried out as a one year cross sectional descriptive observational design to correlate the levels of HbA1c with the severity of diabetic retinopathy in patients with type2 diabetes mellitus at DR PSIMS & RF Chinnoutpalli.

Patients attending the out-patient, in-patient and referrals to ophthalmology department at DR PSIMS&RF Chinnoutpalli, between January 1, 2014 and December 31, 2014 were included in the study.

3.1Sample Size: 100

3.2Inclusion criteria:

1. Participants diagnosed to have type 2 diabetes mellitus with retinopathy changes in the fundus are included in this study.
2. Recent HbA1 c levels of the participants known.

3.3Exclusion criteria:

1. Participants with known other systemic diseases which could manifest as retinal pathology.
2. Participants with very hazy ocular media (i.e. ocular fundus not clearly visible by indirect ophthalmoscopy) are excluded from the study.
3. Gestational diabetics and juvenile diabetics
4. Undergone laser photocoagulation therapy
5. Participants not accepting the informed consent

3.4 Evaluation of patients:

After taking informed consent all patients were examined according to a predesigned proforma. Relevant history regarding the diabetes with respect to age of onset, duration, nature and effect of treatment received were taken.

A general physical examination was performed followed by a complete ophthalmic examination. A detailed fundus evaluation was performed using a direct ophthalmoscopy, indirect ophthalmoscopy along with slitlamp biomicroscopy with +90D lens.

The retinopathies were observed and documented in accordance with the modified ETDRS classification ie International Clinical Disease severity scale for Diabetic Retinopathy which has been proposed to facilitate simple to use in clinical practice and easy to remember is as follows:

1. MildNPDR.
2. Moderate NPDR.
3. Severe NPDR.
4. Early PDR.
5. High Risk PDR.

All patients were subjected to fundus photography. Fundus fluorescein angiography was performed only when clinically necessary.

3.5 Laboratory investigations observed were as follows:

- FBS
- Glycosylated hemoglobin (HbA1c)

3.6 Estimation of HbA1c :

Glycosylated haemoglobin (HbA1c) was measured by Daytona auto analysis set.lt is expressed in percentage (%).

3.7 Statistical methods :

Analysis of variance test was used to determine the relationship between HbA1c and severity of retinopathy in patients of type 2 DM.

Chi Square test was used to determine the relationship between severity of diabetic retinopathy with visual acuity and duration of diabetes.All the calculations were done using NCSS statistical data package editor, version 9.

IV. Observations And Results

Table1: Demographic and clinical data of study population

Parameters	Observation
Total number included	100
M:F	1.27:1
Mean age (years)	63.79 +- 8.47
Mean age at diagnosis (years)	49+-5.95
Mean duration of diabetes (years)	15.99 +-5.68
Mean HbA1c(%)	9.25 +- 1.59

The above table shows the demographic data of 100 patients included in our study. The mean age of participants in this study was 63.79 + 8.47 and out of the 100 participants, M:F ratio was 1.27:1 . The mean age of 100 patients at diagnosis was 49 + 5.95 and mean duration of diabetic age was 15.99 + 5.68. The mean of Glycosylated haemoglobin (HbA1c) in the study population was 9.25 + 1.59.

Table2: Gender distribution

Gender	Total	M:F
Male	56	1.27:1
Female	44	
Total	100	

There were 56 males and 44 females in our study group, revealing a male predominance in our recruited study population. The male : female ratio was 1.27 : 1.

Table3: Prevalence of retinopathy

Retinopathy	No of patients	Percentage (%)
Mild NPDR	17	17
Moderate NPDR	18	18
Severe NPDR	48	48
Early PDR	13	13
High risk PDR	4	4

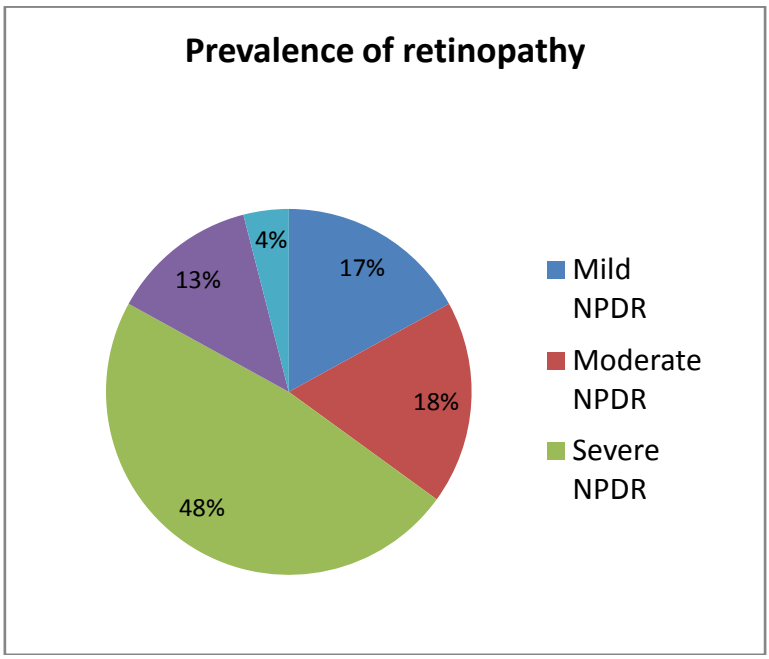


Figure – 1 : Prevalence of Retinopathy

The present study constituted 17% mild NPDR, 18% moderate NPDR, 48% severe NPDR, 13% PDR and 4% high risk PDR. Out of 100 retinopathy patients studied severe and very severe NPDR accounted for nearly half the patients while the other half consisted of early PDR, mild and moderate NPDR, the latter being higher than the former.

Table 4 : Correlation of HbA1c with severity of Retinopathy

HbA1c range (%).	Severity of retinopathy				
	Mild NPDR	Moderate NPDR	Severe NPDR	Early PDR	High Risk PDR
6.5-8.5	13	12	6	4	1
8.5-10.5	1	7	26	7	2
10.6-12.5	0	2	13	2	1
12.6-14.5	0	1	2	0	0
Total	**14**	**22**	**47**	**13**	**4**

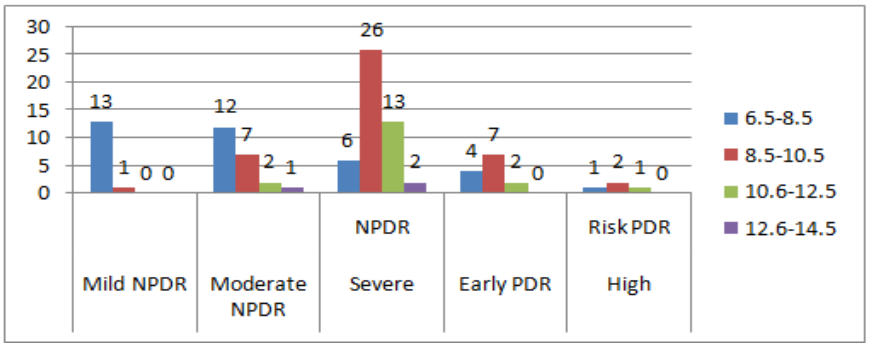
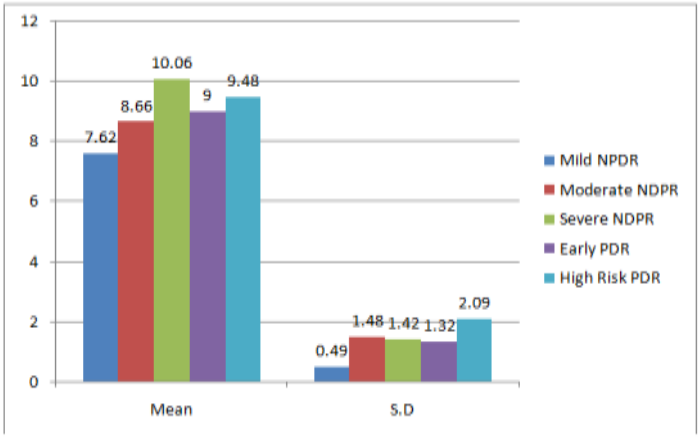


Figure – 2 : Distribution of Retinopathy

The above table reveals that there were 85% of mild NPDR cases, 62% of moderate NPDR cases and 14% of PDR cases in 6.5% - 8.5% range of HbA1c.Whereas in HbA1c range of 8.6 % - 10.5%, mild and moderate NPDR cases reduced to 15% and 29% respectively and severe NPDR cases increased to 53%. Early PDR cases raised from 38% in 6.5% - 8.5% range of HbA1c to 46% in 8.6 % -10.5%. And high-risk PDR cases raised from 25% to 50% when HbA1c raises from 6.5% - 8.5% to 8.6 %- 10.5%. This revealed an increasing trend of severity of retinopathy with raise in HbA1c levels.

Table 5 : Mean and standard deviation (S.D) of HbA1c in retinopathy:

Retinopathy Severity	HbA1c	
	MEAN	S.D
MILD NPDR	7.62	0.49
MODERATE NPDR	8.66	1.48
SEVERE NPDR	10.06	1.42
Early PDR	9.00	1.32
High Risk PDR	9.48	2.09



Figure–3 : Mean and standard deviation (S.D) of HbA1c in retinopathy

The table shows the means of HbA1c in each level of severity of diabetic retinopathy. The mean of HbA1c in mild NPDR was 7.62 + 0.49. In moderate NPDR it was 8.66 + 1.48. In severe NPDR 10.06 + 1.42. In Early PDR 9.0 + 1.32 and in High risk PDR 9.48 + 2.09. Therefore, as the severity of retinopathy increased,

the mean HbA1c for that level of severity also increased. The standard deviation (S.D) in each group being small.

V. Discussion

The present study was conducted as a descriptive observational study to determine the correlation of HbA1c levels with diabetic retinopathy.

5.1 Prevalence of retinopathy:

The present study included 100 cases of retinopathy which constituted 17% mild NPDR, 18% moderate NPDR, 48% severe NPDR,13% PDR and 4% high risk PDR.

Out of 100 retinopathy patients studied severe & very sever NPDR accounted for nearly half the patients while the other half consisted of PDR, mild and moderate NPDR, the latter being higher than the former. Regardless of the severity of retinopathy, 23% cases had CSME.

A south Indian study by Mohan R. reported an overall prevalence of 14 per cent, NPDR 6%, while 4% had macular oedema and 4% had PDR.[9]A Chennai study revealed the prevalence of DR was 34.1%. The prevalence included 30.8% with NPDR, 3.4% with PDR and 6.4% had DME.[10]

The differences in the findings could be attributed to variable population Characteristics as age of onset, diabetic duration, treatment and its adherence.

5.2 HbA1c and severity of retinopathy:

Our study revealed that mean values of HbA1c in non-proliferative types of diabetic retinopathy have indisputable difference. The standard deviation of each level being considerably small, made the difference more relevant.

One way distribution of HbA1c in our study among the levels of retinopathy revealed significant non homogeneity and further revealed that the transition from mild to severe NPDR was statistically highly significant and that from moderate to severe NPDR was significant.

Two way distribution of retinopathy among ranges of HbA1c revealed significant association with the severity of retinopathy. The glycemic status of the patients in this study was studied by measuring HbA1C levels. When the HbA1C values were compared in the groups with increasing severity of retinopathy, increasing levels of HbA1C were noted showing a significant correlation. Therefore it was noted that poor glycemic control led to the worsening of the retinopathy.

The Diabetes Control and Complications Trial (DCCT) and the U.K. Prospective Diabetes study (UKPDS) were two randomized clinical trials which conclusively showed the efficacy of glycemic control in preventing diabetic retinopathy. These studies mentioned that glycemic control was protective for all levels of retinopathy and there was no glycemic threshold below which a reduction in microvascular complications was not observed.[13]

5.3 HbAlc with CSME:

Comparision of the means of HbA1c in patients with and without CSME revealed statistically significant association of CSME with HbA1c. High glycosylated hemoglobin (HbA1c) level is a well-known risk factor for diabetic macular oedema. In addition, the DCCT had demonstrated that intensive treatment to maintain blood glucose levels at a normal range reduced the risk of clinically significant macular oedema at the rate of 23%.[14,15]

A recent study in this regard has shown that mean HbA1c in patients with persistent unilateral CSME was 8.6% and that in bilateral CSME was 9.1%. Same study also revealed that type2 diabetics with persistent CSME have higher HbA1c at the time of their disease than patients with resolved CSME.

VI. Conclusions

The value of glycosylated haemoglobin (HbA1c) showed an increasing trend as severity of diabetic retinopathy increases. The poor metabolic control as demonstrated by high HbA1c is significantly associated with severity of retinopathy and presence of CSME. From the analysis of our study, we recommend to maintain HbA1c levels below 7.5% which may reduce the risk of development and progression of diabetic retinopathy. Duration of diabetes and high HbA1c levels are found to be the major predictors of diabetic retinopathy in type II diabetes mellitus.

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