Original article:

Study of correlation of severity of diabetic retinopathy with levels of haemogloelbin A1c in patients with type II Diabetes Mellitus

[1]Dr Apoorva* ,[2] Dr Sabhia Jan

[1]Senior Resident, [2]Senior Resident

Shaheed Hasan Khan Mewati Govt. Medical College, Nalhar , Nuh

Corresponding author *

Abstract:

Introduction: Diabetes mellitus is a major cause of avoidable blindness in both the developing and the developed countries. Diabetes is the disorder with acute metabolic and chronic macrovascular & microvascular complications such as diabetic retinopathy

Methodology: 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 was also 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 slit lamp bimicroscopy with +90 D lens. All the findings were documented in the Performa and verified by the guide.

Results: he means of FBS in each level of severity of diabetic retinopathy. The mean of FBS in mild NPDR was 144.47 ± 38.08,in moderate NPDR was 165.33 ± 48.69,in severe NPDR was 182.72 ± 67.02,in Early PDR was 172.37 ± 41.58 and in High risk PDR was 170.2 ± 42.18.Therefore,as the severity of retinopathy increased, the mean FBS for the level of severity also increased .The standard deviation(S.D)in each group being considerably large.

Conclusion: Severity of retinopathy also increases with increase in the duration of diabetes, the two having a statistically significant relation from our present study work.

INTRODUCTION

Diabetes mellitus is a major cause of avoidable blindness in both the developing and the developed countries. Diabetes is the disorder with acute metabolic and chronic macrovascular & microvascular complications such as diabetic retinopathy (DR) . Patients with diabetic retinopathy (DR) are 25 times more likely to become blind than non-diabetics. [1] The estimated population of diabetic retinopathy is 5.8 million. The pathogenesis of DR revolves around the retinal microvascular changes which result in the development of non-proliferative and proliferative retinopathy with or without maculopathy. Microvascular complications due to microangiopathy have been directly linked to glycemic control & affect the kidneys, eyes and peripheral nerves. DR is the most frequent cause of blindness among adults aged 20-75 years and it remains a significant health problem worldwide as reported by the ADA.(1) Improvements in diabetic care and earlier detection of the disease can reduce the incidence of visual impairment and blindness. Some people may already show evidence of DR, indicating that diabetes may have been present for several years, even before the clinical diagnosis of diabetes.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Glycosylated haemoglobin (HbA1c) serves as an integrator of the mean blood glucose over several preceding weeks. Hemoglobin undergoes nonenzymatic glycosylation in the presence of plasma glucose. Normal levels of glucose produce a normal amount of glycated hemoglobin. As the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a predictable way. This serves as a marker for average blood glucose levels over the previous months prior to the measurement. Normally 5% of total hemoglobin is glycosylated.[2] With this view present study was planned to study the severity of diabetic retinopathy with levels of haemogloelbin A1c in patients with type II Diabetes Mellitus .

MATERIALS AND METHODS

This cross-sectional study was comprised of all the patients of DR attending the OPD, in-patients & referrals to ophthalmology department at Rohilkhand Medical College & Hospital .

Inclusion criteria:

1. Participants diagnosed to have type II DM with retinopathy changes in the fundus were included in this study.

Exclusion criteria:

1. Participants with very hazy ocular media (i.e. ocular fundus not clearly visible by indirect ophthalmoscopy) were excluded from the study.
2. Participants who did not accept the informed consent
3. Pregnant women

Patients were divided into three groups depending upon the duration of diabetes upon presentation-

GROUP A - patients with diabetes for less than 5yrs

GROUP B - patients with diabetes for a period of 6-15yrs

GROUP C - patients with diabetes for more than 15 years

In each group the correlation between HbA1c levels and severity of diabetic retinopathy was compared.

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 was also 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 slit lamp bimicroscopy with +90 D lens. All the findings were documented in the Performa and verified by the guide.

The retinopathies were documented in accordance with the modified ETDRS classification as follows:

1. Mild NPDR
2. Moderate NPDR
3. Severe NPDR
4. Very severe NPDR
5. PDR
6. High Risk PDR

All patients were subjected to seven field fundus photography. Fundus Fluorescein Angiography was performed only when clinically necessary.

Laboratory investigations done:

1. FBS levels
2. Glycosylated haemoglobin (HbA1c) levels to determine the glycemic control

Examination of HbA1c:

Glycosylated haemoglobin was measured by Immunoturbidimetric method using Quantia HbA1c which is a turbidimetric immunoassay for the direct

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

determination of HbA1c in human blood without the need to estimate total haemoglobin. It is expressed in %.

Statistical method:

Data obtained was analyzed using SPSS version 12.0 of computer analysis.

OBSERVATIONS AND RESULTS

Table. 1. Correlation of severity of retinopathy and duration of diabetes:

Duration of diabetes (years)	Severity of retinopathy					
	Mild NPDR	Moderate NPDR	Severe NPDR	Early PDR	High Risk PDR	Total
0 -5	3(18%)	2(4%)	3(14%)	1(13%)	0	9
6-15	12(71%)	36(75%)	11(50%)	2(25%)	2(40%)	63
> 15	2(12%)	10(21%)	8(36%)	5(63%)	3(60%)	28
Total	17(100%)	48(100%)	22(100%)	8(100%)	5(100%)	100

P= 0.0409(significant)

From the above table it can be observed that while the mild NPDR cases progressively reduced from 18% to 12% as the duration of diabetes increased from 0-15 years to more than 15 year, severe NPDR and early PDR cases increased from 4% to 21% and 14% to 36% respectively as the duration of diabetes increased from 0-15 years to more than 15 year. The distribution of retinopathy along the duration of diabetes was found to be statistically very significant

Table. 2. Correlation of vision with severity of retinopathy

Visual acuity (Snellen's)	Severity of retinopathy					
	Mild NPDR	Moderate NPDR	Severe NPDR	Early PDR	High Risk PDR	Total
< 6 /18	10	32	10	5	0	57
6/18 - 6/36	6	12	8	1	2	29
> 6 /36	1	4	4	2	3	14
Total	17	48	22	8	5	100

P=0.0358(Significant)

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

The above table reveals a significant association between best corrected visual acuity of the patient and the severity of retinopathy. Higher the level of retinopathy, lesser is the vision. These observations include all the cases with CSME also.

Table. 3. Association of HbA1c with severity of retinopathy: Mean and standard deviation (S.D) of HbA1c in retinopathy:

Hb A1c range (%)	Severity of retinopathy					
	Mild NPDR	Moderate NPDR	Severe NPDR	Early PDR	High Risk PDR	Total
6.5 - 8.5	13(76%)	35(73%)	6(27%)	2(25%)	1(20%)	57
8.6 - 10.5	4(24%)	10(21%)	10(45%)	4(50%)	3(60%)	31
10.6 - 12.5	0	3(6%)	5(23%)	2(25%)	1(20%)	11
12.6 - 14.5	0	0	1(5%)	0	0	1
Total	17(100%)	48(100%)	22(100%)	8(100%)	5(100%)	100

The table shows the means of HbA1c in each level of severity of diabetic retinopathy. The mean of HbA1c in mild NPDR was 7.82 ± 1.35, in moderate NPDR was 8.46 ± 1.34, in severe NPDR was 9.96 ± 1.51, in Early PDR was 9.13 ± 1.48 and in High risk. PDR was 9.28 ± 1.13.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.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Table. 4. Means and S. D. of FBS and severity of retinopathy

Retinopathy	MEAN	S.D.
MILD NPDR	144.47	38.08
MODERATE NPDR	165.33	48.69
SEVERE NPDR	182.72	67.02
Early PDR	172.37	41.58
High Risk PDR	170.2	42.18

The table shows the means of FBS in each level of severity of diabetic retinopathy. The mean of FBS in mild NPDR was 144.47 ± 38.08,in moderate NPDR was 165.33 ± 48.69,in severe NPDR was 182.72 ± 67.02,in Early PDR was 172.37 ± 41.58 and in High risk PDR was 170.2 ± 42.18.Therefore,as the severity of retinopathy increased, the mean FBS for the level of severity also increased .The standard deviation(S.D)in each group being considerably large.

DISCUSSION

The present study included 100 cases of retinopathy which constituted 17% mild NPDR, 48% moderate NPDR, 22% severe NPDR, 8% PDR and 5% high risk PDR. Out of 100 retinopathy patients studied moderate NPDR accounted for nearly half the patients while other half consisted of PDR, mild and severe NPDR, the latter being higher than the former. Regardless of the severity of retinopathy, 22% cases had CSME.

Patients were divided into 3 groups in this study. 70% of mild NPDR and 75% of moderate NPDR cases were seen in patients with 6-15 years of duration of diabetes and 63% of early PDR and 60% high risk PDR were seen in diabetic duration of more than 15 years. It was seen that the distribution of retinopathy along the duration of diabetes is statistically significant. And it was evident from the findings that there was worsening of the retinopathy with increasing duration of diabetes in these individuals.

The significant relation between duration of diabetes and severity of retinopathy was also proved in a study done by HS Bajpai et al[3] at Varanasi in which it was seen that 51% of diabetics with less than 10 years of duration, had grade I changes while only 11.7% had grade I changes with diabetes of more than 10 years duration.

This observation also had favorable correlation with another longitudinal study by Palmberg[4] and crosss-sectional study by Bendu AP[5] which noted similar findings.

The incidence of retinopathy was also observed to be increased with the increase in the duration of DM, from 16.7% in less than one year duration to 100% where the duration of diabetes was above 16 years[73]. And it has been already proved in WESDR Study that the prevalence of DR raised from 17% to 97.5% in patients with diabetes for less than 5 years duration and 15 or more years, respectively. Proliferative

Retinopathy varied from 1.2% to 67% in patients with DM for less than 10 years and 35 or more years, respectively, concluding a direct connection between the frequency and severity of DR and the duration of DM.

The present study revealed a significant association between visual acuity of the patient and the severity of retinopathy. Higher the level of retinopathy, lesser is the vision. These observations include all the cases with CSME also.

Although the main cause of decreased visual acuity in diabetic retinopathy is macular edema which can cause significant visual loss. As proved by ETDRS, the risk of moderate visual loss (a doubling of initial visual angle e.g. 20/30 to 20/60 or a decrease of 3 lines or more on a logarithm visual acuity chart) was 32%. Decreased visual acuity is one of the major risk factors responsible for progression to high risk PDR. A study done in middle east in 2006, showed significant correlation between OCT patterns of CSME and severity of retinopathy & visual acuity ($p = 0.002$).[6]

HbA1c and severity of retinopathy

The Early Treatment Diabetic Retinopathy Study identified the HbA1C as one of the most important risk factors for the prognosis to high risk proliferative retinopathy. The Diabetes Control and Complication Trial results were stratified by HbA1c levels, there was a 35% to 40% reduction in the risk of retinopathy progression for every 10% decrease in HbA_1C (e.g. from 8% to 7.2%), indicating a fivefold increase in the risk for patients with HbA_1C of about 10% versus those with 7% .

Epidemiologic analysis of the UKPDS data showed a continous relationship between the risk of microvascular complications and glycemia, so for every percentage point decrease in HbA1C (e.g. 9% to 8%), there was a 35% reduction in the risk of microvascular complications. And a clear relationship was seen between the increasing HbA1c values and increasing proportion of patients with non-sight threatening diabetic retinopathy and sight threatening diabetic retinopathy ($p < 0.0001$) in a study done on 1414 subjects in Chennai in 2010 which also gave a targeted value of HbA1c as >8% (which would give maximum yield of sight threatening diabetic retinopathy.

The WESDR also found that HbA1c correlated with a consistent increase in retinopathy from the lowest (5.4- 8.5%) to the highest quartile (11.6-20.8%).[7]

Similarly, in our study, the mean values of HbA1c in non-proliferative levels of diabetic retinopathy have indisputable difference. The S.D. of each level being considerably small, made the difference more relevant.

In this study, the glycemic status of the patients 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. There were 76% of mild NPDR cases, 73% of moderate NPDR cases and 27% of severe NPDR cases in 6.5% -8.5% range of HbA1c. Whereas in HbA1c range 8.6%-10.5%, mild & moderate NPDR cases reduced to 24% and 21% respectively and severe NPDR cases increased to 45%. And high-risk PDR raised from 20% to 60% when HbA1c raises from 6.5%-8.5% range to 8.6%-10.5%. This revealed an increasing trend of severity of retinopathy with raise inHbA1c. Therefore, it was noted that poor glycemic control, indicated by high HbA1c levels, led to the worsening of the retinopathy. Mean value of HbA1c was found to be

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

higher in proliferative retinopathy in study done in 1991.[8]

CONCLUSION

Severity of retinopathy also increases with increase in the duration of diabetes, the two having a statistically significant relation from our present study work.

REFERENCES:

1. Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Klein R, et al. Diabetic Retinopathy. Diabetes Care 2003;26(Suppl 1):s99-102.
2. Davis RE, Nicol DJ, McCann VJ, Calder JS. Glycosylated haemoglobin levels in patients with diabetes mellitus. Med J Aust.1978;1(10):530-2.
3. Bajpai HS, Mehra KS, Singh VP, Tikko SK, Agrawal JK, Sharma A. Diabeticretinopathy (a clinico-biochemical study). Indian J Ophthalmol. 1979;27(3):12-5.
4. Klein R, Klein BE, Moss SE. The Wisconsin Epidemiologic Study of DiabeticRetinopathy, II: Prevalence and high risk of diabetic retinopathy when age atdiagnosis is less than 30 years. Arch Ophthalmol. 1984;102:520-6.
5. Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M.Guidelines and recommendations for laboratory analysis in the diagnosis andmanagement of diabetesmellitus. Clin Chem. 2002;48:436-72.
6. Huisman T, Dozy A. Studies on the heterogeneity of hemoglobin. V. Binding of hemoglobin with oxidized glutathione. J Lab Clin Med. 1962;60:302–19.
7. Schnek A, Schroeder W. The relation between the minor components of whole normal human adult hemoglobin as isolated by chromatography and starch block electrophoresis. J Am Chem Soc 1961;83:1472–8.
8. Fitzgibbons J, Koler R, Jones R. Red-cell age-related changes of hemoglobins AIa+b and AIc in normal and diabetic subjects. J Clin Invest 1976;41:820–4.