



ORIGINAL RESEARCH PAPER

Ophthalmology

A STUDY ON CLINICAL EVALUATION OF DIABETIC RETINOPATHY AND ITS CORRELATION WITH SERUM HbA1c LEVEL

KEY WORDS: diabetic retinopathy, retinal degeneration, serum HbA1c, ETDRS classification, NPDR, PDR

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ABSTRACT

This cross-sectional clinical study titled "A clinical evaluation of diabetic retinopathy and its correlation with serum HbA1c level" was conducted in Hi-Tech medical college, Bhubaneswar from September 2019 to May 2021 by taking 67 patients from ophthalmological OPD who were diagnosed as cases of diabetic retinopathy, but not taking laser therapy and not having other non-diabetic causes of retinal degeneration and having diabetic mellitus of at least one year without considering type of diabetes or treatment taken by the patients. These 67 patients diagnosed as cases of diabetic retinopathy are classified according to their severity basing upon their findings(microaneurysm, exudates, retinal hemorrhages, venous beading , IRMA, new vessels in disc or elsewhere in retina) as per ETDRS(Abbreviated early treatment diabetic retinopathy study) classification as mild NPDR, moderate NPDR, severe NPDR, very severe NPDR, PDR. Their serum glycosylated haemoglobin (HbA1c) level of each individual in each group is detected and then mean HbA1c level of each group derived and when correlated, we found that the mean HbA1c for mild grade of retinopathy was found to be 7.667, for moderate non-proliferative diabetic retinopathy(NPDR) 8.450, for severe NPDR 9.700, for very severe NPDR 11.447 and for Proliferative Diabetic Retinopathy(PDR) the mean HbA1c value was found to be 11.468. The P value obtained through ANOVA test for HbA1c vs. grade of diabetic retinopathy was statistically significant (Sig : 0.000). The Eta & Eta squared value for HbA1c vs grade of retinopathy was 0.695 and 0.483. So the present study reveals that more severe grades of diabetic retinopathy manifesting in patients with higher levels of HbA1c.

INTRODUCTION :-

Diabetic retinopathy is predominantly a microangiopathy in which small blood vessels are affected and it is so prevalent that almost all of type 1 and two third of all type 2 Diabetics are expected to develop diabetic retinopathy over a period of time¹⁻³. Severity of diabetic retinopathy increases over period of time and the severity is diagnosed and classified basing upon their findings (microaneurysm, exudates, retinal hemorrhages, venous beading , IRMA, new vessels in disc or elsewhere in retina) as per ETDRS classification^{4,5}. Serum glycosylated hemoglobin (HbA1c) estimates the average glycemic status over weeks to months as per the lifespan of RBCs and is a prognostic marker as well as known to be a marker to access the long term control of diabetes mellitus⁶⁻⁸. Studies in the past have also shown that HbA1c level could be correlated with the long term complications of Diabetes mellitus in general⁹. Here the correlative study has done more specifically between Diabetic retinopathy with that of serum HbA1c level to establish clearly the association between these two¹⁰.

MATERIALS AND METHODS :-

A cross-sectional study was conducted in the Department of Ophthalmology, Hi-tech Medical College & Hospital by taking 67 patients diagnosed as a case of diabetic retinopathy but not taking laser therapy and not having other non-diabetic causes of retinal degeneration and having diabetic mellitus of at least one year without considering type of diabetes or treatment taken by the patients. These 67 patients diagnosed as cases of diabetic retinopathy are classified according to their severity basing upon their findings(microaneurysm, exudates, retinal hemorrhages, venous beading , IRMA, new vessels in disc or elsewhere in retina) as per ETDRS (Abbreviated early treatment diabetic retinopathy study) classification as mild NPDR, moderate NPDR, severe NPDR, very severe NPDR, PDR. Their serum HbA1c level of each individual in each group is estimated and then mean HbA1c

level of each group derived and then correlated between level of serum HbA1c and severity of diabetic retinopathy. Study was conducted only after being duly approved and permitted by the ethical committee and cases will be considered after written consent being taken from the patients.

Statistical analysis:

All values are presented as mean ± standard deviation (SD) with 95% confidence intervals. Statistical differences between the parameters were tested using Chi-square test. The Statistical analysis of the study data was carried out using the SPSS statistical software (V. 16.0) (SPSS, Chicago, IL, USA).

The Fisher's exact test value obtained was 3.475 while the P value was .970 which was not statistically significant (P> 0.05). The Pearson chi-square showed a P value to be 0.962 which was also not significant. The degree of freedom was 8 for Pearson chi-square while for linear-by-linear association, the degree of freedom was one.

RESULT & DISCUSSION :-

In the study, the 67 number of patients diagnosed as cases of diabetic retinopathy are classified into different grades as per "abbreviated early treatment diabetic retinopathy study" as:-

Table 1: Frequency of different grades of diabetic retinopathy

Grades of diabetic retinopathy	Frequency
Mild NPDR	12
i. Microaneurysm	4
ii. Microaneurysm and retinal hemorrhages	5
iii. Microaneurysm and retinal hemorrhages and exudates(cotton wool spots)	3
Moderate NPDR	10
I. Severe retinal haemorrhages (20 medium – large per quadrants) in 1-3 quadrants	5

ii. significant venous beading in 1 quadrant	5
iii. mild IRMA (intraretinal microvascular anomaly)	0
Severe NPDR	13
i. Severe retinal haemorrhages in all 4 quadrants	6
ii. Significant venous beading in 2 or more quadrants	4
iii. Moderate IRMA in 1 or more quadrants	3
Very Severe NPDR	13
i. i&ii of Severe NPDR	5
ii. i&iii of Severe NPDR	5
iii. i,ii&iii of Severe NPDR	3
PDR	19
i. new vessels in the disc	10
ii. new vessels elsewhere	9

Table 2 :Prevalence of Different Grades of Diabetic Retinopathy

GRADE	FREQUENCY	PERCENTAGE(%)
Mild NPDR	12	17.91%
Moderate NPDR	10	14.92%
Severe NPDR	13	19.4%
Very severe NPDR	13	19.4%
PDR	19	28.35%
Total	n=67	n%=100%

According to the study as per Table No. 2, majority of the patients had NPDR amounting to 71.64%(48) as compared to PDR in 28.35%(19). Severe (13) and very severe(13) NPDR had an equal prevalence of 19.4%.

Again the serum HbA1c level of each individual in each grade is detected, then from these values the mean HbA1c level of the patients of each grade and the grand mean of all the grades is derived. Now from observed HbA1c value of each patient of each grade, mean HbA1c level of each grade and grand mean of all grades, the mean sum of squares between group and the mean sum of square within group derived and when put in ANOVA table by considering degree of freedom, we found the mean square, Eta squared, Eta, F statistic and finally the P value such as :-

Table 3: Relationship between severity of diabetic retinopathy and serum HbA1c level

Severity	HbA1c		
	Mean	N	Std. Deviation
Mild	7.667	12	1.9439
Moderate	8.450	10	2.0162
Severe	9.700	13	1.6010
Very severe	11.477	13	1.1512
PDR	11.468	19	1.6056
Total	9.996	67	2.2397

The mean HbA1c for mild grade of retinopathy was found to be 7.667, for moderate NPDR 8.450, for severe NPDR 9.700, for very severe NPDR 11.447 and for PDR the mean HbA1c value was found to be 11.468.

Table 4: Relationship between severity of diabetic retinopathy and serum HbA1c level

ANOVA TABLE						
		Sum of Squares	Df	Mean Square	F	Sig.
HbA1c* Severity	Between groups(combined)	159.853	4	39.963	14.4	.000
	Within Groups	171.216	62	2.762	71	
	Total	331.069	66			

Table 5 : Eta and Eta squared relationship between HbA1c vs. grades of retinopathy

Measures of Association		
	Eta	Eta Squared
HbA1c * Severity	0.695	0.483

The P value obtained through ANOVA test was statistically significant(sig:0.000) for HbA1c vs. grade of retinopathy. The Eta and Eta squared value for HbA1c vs. grades of retinopathy was 0.695 and 0.483 respectively.

However in this study, the 67 numbers of diabetic retinopathy cases taken irrespective of the type of treatment taken by the patients such as oral hypoglycaemic agents or insulin. when we try to establish the relation between the different grades of diabetic retinopathy to that of oral hypoglycemic agent and insulin therapy, we found that :-

Table 6: Relationship Between Different Grades of Diabetic Retinopathy and Anti-Diabetic Medication

Medication	Mild	Moderate	Severe	Very Severe	PDR	Total
Insulin	0(0%)	1(16.66%)	2(33.33%)	1(16.66%)	2(33.33%)	6(100%)
Antidiabetic OHA	11(19.64%)	9(16.07%)	10(17.85%)	11(19.64%)	15(26.78%)	56(100%)
Both	1(20%)	0(0%)	1(20%)	1(20%)	2(40%)	5(100%)
Total=67	12(17.9%)	10(14.9%)	13(19.4%)	13(19.4%)	19(28.35%)	67(100%)

Out of a total of 67 patients, 56 were under oral hypoglycaemic agents as compared to only 6 who were taking insulin at the time of study. In the PDR group, 15(26.78%) were taking OHA while 2(33.33%) were taking insulin to control their blood glucose level.

Table 7: Relationship between different grades of diabetic retinopathy and anti-diabetic medication

	Chi-Squre Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	3.024 ^a	8	.933	.962		
Likelihood Ratio	4.707	8	.788	.944		
Fisher's Exact Test	3.475			.970		
Linear-by-Linear Association	.023 ^b	1	.878	.920	.480	.079
No. of Valid Cases	67					

a. 10 cells (66.7%) have expected count less than 5. The minimum expected count is 0.75.
b. The standardized statistic is 0.153

Relationship between diabetic retinopathy and age:

Klein and Klein observed that there was no relationship between patient's age and the severity of diabetic retinopathy¹¹. The present study also showed that it was not statistically significant either.

Relationship between diabetic retinopathy and hypertension:

Klein and his coworkers in their study found that there was no relationship between the severity of retinopathy with the blood pressure levels. Hypertension did not have any effect on the course of disease or its severity¹². Our study also found a negative association between these two factors and it was statistically nonsignificant (P>0.05).

Relationship between diabetic retinopathy and gender:

This study showed that there is no correlation between the gender of the patient with the severity of diabetic retinopathy and that it was, statistically non-significant. Santos *et al*¹³ had concluded in their study that there was a trend towards a higher frequency of diabetic retinopathy in men than in women. In contrast, Tapp *et al*¹⁴ and Nakagami *et al*¹⁵ had found

no association.

Relationship between diabetic retinopathy and hyperlipidemia:

Chen *et al*¹⁶ and Van Leiden *et al*¹⁷ found no correlation between diabetic retinopathy and hyperlipidemia. The present study also found the relationship between these two factors to be clinically and statistically non-significant.

Relationship between diabetic retinopathy and duration of diabetes:

In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), the widest and 'most. prolonged population based ophthalmologic survey, reported that higher prevalence of DR was associated with longer duration of diabetes.¹⁸

41.8 % had diabetic retinopathy after 15 yr of diabetes in the CURES study. Also, the risk of diabetic retinopathy increased by 1.89 times with a five year increase in the duration of diabetes. [64] In our study, a statistically significant correlation was found between the severity of DR with the duration of diabetes.(P<.000) Mild NPDR was seen after a mean duration of 5.5 years while moderate NPDR was seen after a mean duration of 8.6 years. Severe and very severe NPDR were seen after a mean duration of 12.4 and 11.8 years respectively. For. PDR, the mean duration was 9.8 years.

Relationship between diabetic retinopathy and HbA1c:

In our study, the mean HbA1c for mild grade of retinopathy was found to be 7.667, for moderate DR 8.450, for severe DR 9.700, for very severe DR 11.447 and for PDR the mean HbA1c value was found to be 11.468. There was a statistically significant correlation between the two. In patients with poor glycemic control, the risk of PD.R increased to about 6 times according to one of the study.¹⁹

Another similar study showed that the HbA1c levels correlated with prevalence of retinopathy status in diabetic patients on insulin therapy,²⁰ The DCCT confirmed that a strict glycemic control reduces both the risk of onset and the progression of diabetic retinopathy and other microvascular complications of diabetes.

Relationship between grades of diabetic retinopathy and CSME:

Kojima and Espiritu,²¹ concluded in their study that severity of retinopathy was significantly associated with maculopathy (p=0.001). In our study, we found statistically significant correlation between the grades of retinopathy and CSME. No patient in the mild grade of diabetes had CSME, while 33.33% in very severe and 29..16% in severe grades of NPDR had CSME.

CONCLUSION:-

NPDR cases which are more prevalent, if diagnosed early and treated timely then many cases of blind disorders can be prevented. A statistically significant correlation was found between HbA1c levels and the severity of diabetic retinopathy with more severe grades of diabetic retinopathy manifesting in patients with higher levels of HbA1c. However this study reveals that diabetic medications can not alter the severity of diabetic retinopathy.

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