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EFFECT OF GLYCEMIC CONTROL ON DIABETIC RETINOPATHY IN TYPE II DIABETES MELLITUS INDIVIDUALS

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ABSTRACT

Background:- Diabetic retinopathy is a major cause of blindness in population of working age. Chronic hyperglycemia is a major initiator of microvascular complications, poor glycemic control plays an important role in the development & progression of retinopathy.

Aims:- This study is aimed to find the role of glycemic control on the presence of retinopathy in type II diabetics and the relationship between glycemic control and retinopathy.

Settings and Design:- Prospective randomised cross sectional study.

Material & Methods:- The study comprised of 90 subjects within the age group of 40-60 years who were classified into 3 groups of 30 subjects each, Group I: HbA_{1c} < 7% - Controlled Diabetic Group, Group II: HbA_{1c} > 7 % - Uncontrolled Diabetic Group and Group III: Control Group - HbA_{1c}<6%. Glycosylated Hemoglobin was investigated in diabetic subjects and control groups, Retinopathy was detected and graded into Non-proliferative diabetic retinopathy (NPDR) and Proliferative diabetic retinopathy (PDR).

Statistical Analysis used:- The results were statistically analyzed by One-way ANOVA and chi-square test between the groups.

Results:- Uncontrolled diabetics with poor glycemic control (HbA_{1c}>7%) showed higher incidence of retinopathy (43.33%) when compared to controlled diabetics with good glycemic control (HbA_{1c}<7%) having retinopathy (10%).

Conclusion:- Uncontrolled hyperglycemia is associated with higher incidence of microvascular complication like retinopathy in diabetes. HbA_{1c} is an indicator of long-term blood glucose concentrations. Diabetic retinopathy patients should be under periodic ophthalmological surveillance for prevention of blindness & other diabetes related complications by stringent glycemic control.

Key words: Type II diabetes, glycemic control, retinopathy.

INTRODUCTION

Type II Diabetes Mellitus (DM) is a metabolic disorder primarily characterized by hyperglycemia caused by insulin resistance and/or relative insulin deficiency. Diabetic retinopathy is a major cause of blindness in population of working age. Diabetes is one of the leading causes of blindness in the industrialized countries[1,2] where the chances of loosing the sight are about 25 times higher than normal population. Poor glycemic control plays an important role in the development & progression of retinopathy with associated increase in morbidity & mortality.[3] This microvascular complication is predominantly seen in the age group of 40 to 60 years and is decreased by reduction of blood glucose concentrations.[4] Several studies have shown that severity of retinopathy depends on the sustained mean hyperglycemic level over a prolonged period.[5] Glycosylated hemoglobin reflects long-term glycemic control and is a more accurate & stable measure than fasting blood glucose levels.[6] Based on the DCCT and UKPDS the ADA recommends that a primary treatment goal in adults with diabetes should be near-normal glycemia with HbA_{1c} less than 7%.[7] The normal range of HbA_{1c} level in healthy persons is 4%-5.9%.[8] People with diabetes mellitus often have higher levels of HbA_{1c}. A diabetic person with good glucose control has an HbA_{1c} level that is close to or within 7% as per the American diabetes association.

The UKPDS showed significant reduction of progression of retinopathy with improvement in glycemic control.[9]

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The prevalence of diabetic retinopathy is about 34% in Indian studies.[10] The prevalence of diabetic retinopathy in Type II DM is 28% after 5years and 77% after 15years of onset of DM.[11] In India retinopathy was detected in 52% of patients with NIDDM of over 25years duration.[12] Early detection and treatment of diabetic retinopathy can save the vision in majority of the affected patients.[13]

The prestigious Early Treatment Diabetic Retinopathy Study (ETDRS) research group has classified diabetic retinopathy into the following.[14]

Nonproliferative diabetic retinopathy(NPDR)

Mild NPDR	Microaneurysms only
Moderate NPDR	More than just microaneurysms but less than severe NPDR
Severe NPDR	Any of the following:
	* >20 intraretinal hemorrhages in each of 4 quadrants
	* Definite venous beading in 2+ quadrants
	* Prominent intraretinal microvascular abnormalities in 1+ quadrant
	* And no signs of proliferative retinopathy.

Proliferative diabetic retinopathy(PDR): One or more of the following:

* Neovascularisation
* Vitreous/preretinal hemorrhage.

Strong evidence exists that improved glycemic control is effective at lessening the risks of retinopathy, nephropathy and neuropathy in diabetes.[5] Glycosylated hemoglobin levels were used as a measure of glycemic control.

AIM OF THE STUDY

1) To study the relation between extent of glycemic control and the presence of retinopathy in Type II diabetics.

2) To investigate the relationship between glycemic control and retinopathy.

MATERIALS & METHODS

The study is conducted in a group of 90 individuals consisting of 30 normal healthy subjects as control and 60 diagnosed cases of Type II Diabetes Mellitus, irrespective of duration of diabetes and sex taken randomly from the outpatient and admitted patients of Medicine department of Sri Devaraj Urs Medical College (SDUMC), Kolar. The Diabetes mellitus patients were further divided into two sub-groups each consisting of 30 patients: Type II Diabetes mellitus patients with good glycemic control (HbA1c < 7%) in Group I - controlled diabetics and Type II Diabetes mellitus patients with poor glycemic control (HbA1c > 7%) in Group II – uncontrolled diabetics. The Research and Ethical committee of SDUMC has approved this study and Informed consent was obtained from all patients and control subjects participating in this study.

Exclusion criteria

Subjects suffering from hypertension, renal disease and persons on drugs affecting retina like chloroquine, thioridozine, chlorpromazine etc were excluded from this study. Personal history of smoking & alcohol consumption were also excluded.

Taking all aseptic and antiseptic precautions, 3 ml of blood is drawn from the Ante cubital vein, glycosylated hemoglobin level was estimated by cation-exchange resin method (Recombigen laboratories pvt. Ltd kits) using a Spectrophotometer and Retinopathy was detected/ruled out with the help of an ophthalmologist using direct and indirect ophthalmoscopy, three mirror slit lamp fundoscopy and classified as Non-proliferative, Proliferative according to ETDRS.[14]

Statistics

The results obtained were presented in Mean ± SD and then analysed statistically by one-way ANOVA followed by chi-square test. STATISTICA 5.0 version statistical package were used for the analysis of the data and Microsoft word and Excel have been used to generate tables.

Results

The test group comprises of 60 Type II diabetes mellitus patients within the age group of 40-60 years, mean age of controlled diabetic group (n=30) is 51.83±5.86yrs, uncontrolled diabetic group (n=30) is 56.17±4.18yrs and mean age group of control group (n=30) is

53.03±6.26yrs. Mean HbA_{1c} levels between the three groups were shown in Table 1 which shows an elevated level of HbA_{1c} in uncontrolled diabetic group compared to controlled diabetic group and Control group which is statistically significant. Our results from Table 2 shows 3 cases of NPDR(10%) in Controlled diabetics group and 13 cases of retinopathy (43.33%) in Uncontrolled diabetics group, out of which 10 were NPDR (33.33%) and 3 were PDR(10%) . Control group did not show any retinopathy. Chi-square analysis showed that occurrence of retinopathy in uncontrolled diabetic group was significantly higher as compared to controlled diabetic group ($p<0.05$) as seen in Table No. 3. Table 4 shows relation between HbA_{1c} levels and percentage distribution of retinopathy where uncontrolled diabetic group shows higher incidence of Retinopathy compared to controlled diabetic group.

Table No.1: Comparison of HbA1c levels between control group, controlled diabetic and uncontrolled diabetic group using one-way ANOVA

GROUPS	HbA_{1c} Value% mean±sd	MS Effect	MS Error	df Error	F	p Value
Control (n=30)	5.75±0.24	39.91	0.32	58	123.08	<0.001
Controlled Diabetics (n=30)	6.45±0.37					
Uncontrolled Diabetics (n=30)	8.01±0.83					

Table No. 2: Percentage distribution of retinopathy in control group, controlled diabetic and uncontrolled diabetic group

GROUPS	% occurrence of Retinopathy		
	NPDR	PDR	TOTAL
Control (n=30)	0	0	0
Controlled Diabetics (n=30)	10 (n=3)	0	10 (n=3)
Uncontrolled Diabetics (n=30)	33.33 (n=10)	10 (n=3)	43.33 (n=13)

Table No. 3: Comparison of occurrence of retinopathy in controlled diabetic vs uncontrolled diabetic group using Chi-square test

GROUPS	Retinopathy Frequency	χ^2	p Value
Controlled Diabetics (n=30)	3	6.25	<0.05
Uncontrolled Diabetics (n=30)	13		

Table No. 4: HbA1c levels and percentage distribution among subjects with retinopathy

GROUPS	HbA_{1c} Value% (mean±sd)	Percentage
Total Subjects with retinopathy (n=16)	8.30±1.06	26.67%
Retinopathy in controlled diabetics (n=3)	6.80±0.29	10%
Retinopathy in uncontrolled diabetics (n=13)	8.64±0.83	43.33%

DISCUSSION

Glycosylated hemoglobin has been firmly established as an index of long-term blood glucose concentrations and a measure of the risk for the development of complications in patients with diabetes mellitus.[15] The DCCT has documented that there is a direct relation between blood glucose concentrations as measured by HbA_{Ic} and the risk of complications.[16] Analogous correlations between HbA_{1c} and complications were observed in patients with diabetes type 2 mellitus in the UKPDS trial. Each 1% reduction in HbA_{1c} (e.g. from 8% to 7%) was associated with risk reduction of 37% for micro vascular complications[17] an increase of 1% in HbA_{1c} was associated with a 28% increase in the risk of death.[18]

Based on the DCCT and UKPDS the ADA recommends that a primary treatment goal in adults with diabetes should be near-normal glycemia with HbA_{1c} less than 7%.[19]

An effort has been made in this study to evaluate the effect of glycemic control on the presence of retinopathy by comparing their occurrence in controlled diabetics ($HbA_{1c}<7\%$) and uncontrolled diabetic patients ($HbA_{1c}>7\%$) with that of healthy controls($HbA_{1c}<6\%$).

The Wisconsin eye study (Klein et al, 1996): showed that the incidence and progression of retinopathy was related to the glycemic status of patients.[3] In our study retinopathy was present in 16 subjects (26.67%) (both controlled diabetics & uncontrolled diabetics) [Table No. 4] correlated with earlier studies which reported incidence of retinopathy in Type II diabetes between 16 to 53.4%.[20-25]

None of the subjects of controlled diabetic group (Group I) showed PDR. PDR was seen in 3 cases in uncontrolled diabetic group (Group II) and all had HbA_{1c} values above 8.48%. However no statistical comparisons were made for this finding because of less number of patients with PDR.

10 subjects with NPDR had HbA_{1c} values lower than 8.48% (7 in uncontrolled diabetic group and 3 in controlled diabetic group). However 3 subjects with NPDR showed HbA_{1c} values higher than 8.48%. Therefore HbA_{1c} level per se does not seem to have a direct bearing on NPDR or PDR as other associated factors may be playing role.

Moreover our study shows poor glycemic control HbA_{1c} (8.30±1.06) is associated with higher incidence of Retinopathy (26.67%) in both Group I & II. Uncontrolled diabetic group (Group II) have higher incidence of retinopathy (43.33%) with mean HbA_{1c} 8.64±0.83 when compared to controlled diabetic group (Group I) 10% with mean HbA_{1c} 6.80±0.29 [Table No. 4].

CONCLUSION

Uncontrolled diabetics with poor glycemic control (HbA_{1c}>7%) showed higher incidence of retinopathy when compared to controlled diabetics with good glycemic control (HbA_{1c}<7%). There was a significant association of retinopathy in uncontrolled diabetics. Retinopathy showed a direct relationship with glycemic control. HbA_{1c} value above 7% is associated with higher occurrence of retinopathy. Retinopathy serves as a warning to achieve good glycemic control and prevent further worsening of diabetes related complications. Diabetic retinopathy patients should be under periodic ophthalmological surveillance for prevention of blindness & other diabetes related complications by stringent glycemic control.

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