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The Evaluation of HbA1c Levels With Diabetic Retinopathy in Type 2 Diabetes Mellitus

KEYWORDS: Diabetes mellitus, Diabetic retinopathy, HBA1C, Oral hypoglycemic agents

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ABSTRACT *The metabolic deregulation associated with diabetes mellitus causes secondary changes in multiple organ systems. American Diabetes Association (ADA) recommends HbA1c of < 7 % as target for good glycemic control, higher levels were associated with micro and macrovascular complications. Duration of diabetes was the strongest predictor of retinal changes. The objective of our study was to determine the prevalence, frequency and severity of diabetic retinopathy in association with HbA1c levels in type 2 diabetics.50 diabetic patients who came for visual disturbance were assessed for presence of retinal changes using dilated fundoscopy, slit lamp microscopy with 78D lens and all the necessary investigations.This study shows male preponderance, long duration of diabetes, use of OHA, poor glycemic control, prehypertensive patients not on medication and patients with microalbuminuria had a significant advancement in retinopathy changes .Also dyslipidemia was also equally contributing factor.*

INTRODUCTION

Diabetes mellitus represents a syndrome of metabolic abnormalities characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The resulting chronic hyperglycemia is associated with damage and destruction of various organs especially eyes, kidneys, nerves, heart and blood vessels. In the 2nd century AD; describing the disease as a dreadful affliction resulting in short life .The sweetness of urine in this disease was first recorded in Sanskrit literature of 5th to 6th century.[1] India has the largest number of Diabetics in the world. According to the latest World Health Organization reports, India has 31.7 million Diabetic subjects, and the number is expected to increase to a staggering 79.4 million by 2030. Type 2 Diabetes in Indians differs from that in the western world: the onset is at a younger age, obesity is less common, and genetic factors appear to be stronger.[2] This increase has been attributed to the rapid economic, demographic, and nutritional transition experienced in India, which has led to lifestyle changes resulting in increased prevalence of diabetes. Furthermore, type 2 diabetes in Indians differs from that in Europeans in several aspects: the onset is at a younger age ,obesity is less common , and genetic factors appear to be stronger .These clinical differences and rising prevalence of diabetes in India warrant well-conducted epidemiologic studies on diabetes related complications in this population to assess the health services burden due to diabetes.[3]Diabetic retinopathy was described by Duke Elder as one of the major tragedies in ophthalmology in our present generation.[4]It is estimated that DR develops in more than 75% of diabetic patients within 15 to 20 years of diagnosis of diabetes, risk factors for the development and progression of diabetic retinopathy include, hyperglycemia, genetic factors, race, duration of disease, arterial hypertension, and proteinuria.[5]One of the pathogenic mechanisms in the development of complications in diabetes is the glycation end products of proteins. This process is indirectly reflected in the blood by the level of HbA_1c which is an indicator of the long term glycemic control of a patient. This study was done to look into the association between HbA_1c and FBG, PPBG with microvascular complications in type 2 diabetes mellitus and there reliability in controlling HbA_1c levels.

MATERIALS AND METHODS

Objectives of the study:To determine the incidence and frequency of diabetic retinopathy in association with raised HbA_1c and the epidemiological profile of diabetic patients with diabetic retinopathy changes and to correlate levels of HbA_1c with severity of retinopathy and classification of diabetic retinopathy according to its severity by correlating findings in relation with blood sugar levels, HbA_1C levels, duration of diabetes and other clinical variables

Subjects/Evaluation:50 diabetic patients who came for visual disturbance to Vydehi Institute of Medical Sciences and Research Centre, Bangalore were assessed for the presence of retinopathy and clinically significant macular edema using dilated fundoscopy and slit-lamp microscopy with a 78 D lens. Patients were evaluated clinically with parameters of age,gender,duration of DM,type of treatment and blood pressure measurement. They were evaluated paraclinically with level of Hemoglobin (g/l), HbA1c, FBS (mg/dl), PPBS (mg/dl), Urea (md/dl), Creatinine (mg/dl) and urine microalbumin.

Statistical methods: 1.Analytical methods: Descriptive and inferential statistical analysis.

2. Statistical methods: Chi-square/Fisher exact test

RESULTS

This study shows male sex, long duration of diabetes, use of OHA, poor glycemic control,presence of systemic hy-

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pertension and nephropathy as the significant risk factors for the advancement ofDR.Other factors which are contributing to development and progression of retinopathy are low hemoglobinand hyperlipidemia. Patients of 61-70 year constituted 38% compared to 28% of 40-50 year and only 8% in extreme age group.Male constituted 68% compared to 32% female population studied.DM of 6-10 were 54% compared to 10% of more than 15 year of diabetes. Microalbuminuria was present in 38% patients compared to 62% with no albuminuria. 60% patients had retinopathy compared to 40 % without retinopathy. In lipid profile evaluation of patients, 6% of patients had total cholesterol>200 (mg/dl) whereas 68%of them had Triglycerides (mg/dl)>150 and 38% of them were with LDL(mg/dl)>130 .Also 54% of our study group of patients, had HDL (mg/dl) <40.

Investigations	Number of patients (n=50)	%
Hemoglobin(g/l)		
• <10	7	14.0
• 10-12	15	30.0
• 12-14	28	56.0
HbA_1c		
• <8.0	17	34.0
• 8.0-10.0	15	30.0
• >10	18	36.0
FBS (mg/dl)		
• <126	10	20.0
• 126-200	24	48.0
• >200	16	32.0
PPBS(mg/dl)		
• <200	10	20.0
• 201-300	25	50.0
• >300	15	30.0
Urea (mg/dl)		
• <30	18	36.0
• 31-60	29	58.0
• >60	3	6.0
Creatinine(mg/dl)		
• <1.20	25	50.0
• >1.20	25	50.0

Table 1: Investigations of patients studied

Clinical variables	Diabetic Retinopathy		p value
	No (n=20)	Yes (n=30)	
Age in years			
• 40-50	8(40%)	6(20%)	0.108
• 51-60	8(40%)	5(16.7%)	
• 61-70	4(20%)	15(50%)	
• 71-80	0(0%)	4(13.3%)	
Gender			
• Male	15(75%)	19(63.3%)	0.538
• Female	5(25%)	11(36.7%)	
Duration of DM(yrs)			
• 1-5	5(25%)	3(10%)	0.186
• 6-10	11(55%)	16(53.3%)	
• 11-15	4(20%)	6(20%)	
• >15	0(0%)	5(16.7%)	
Treatment			
• OHA	20(100%)	29(96.7%)	0.749
• Insulin	4(20%)	8(26.7%)	
Blood pressure			
• 1.Normal	1(5%)	2(6.7%)	0.058+
• 2.Pre hypertension	12(60%)	8(26.7%)	
• 3.Stage I hypertension	2(10%)	7(23.3%)	
• 4.Stage II hypertension	5(25%)	7(23.3%)	
• 5.Hypertensive crisis	0(0%)	6(20%)	
Microalbumin			
• No	19(95%)	12(40%)	<0.001
• Yes	1(5%)	18(60%)	
Hemoglobin(g/l)			
• <10	1(5%)	5(16.7%)	0.163
• 10-12	4(20%)	11(36.7%)	
• 12-14	15(75%)	14(46.7%)	

Table 2: Correlation of Incidence of Diabetic Retinopathy

Diabetic retinopathy	Number of patients(n=50)	HbA_1C			p value
		<8.0 (n=17)	8.0-10.0 (n=15)	>10.0 (n=18)	
1.Mild DR	14(28%)	3(17.6%)	6(40%)	5(27.8%)	0.390
2.Moderate DR	7(14%)	1(5.9%)	4(26.7%)	2(11.1%)	0.309
3.Severe DR	4(8%)	1(5.9%)	1(6.7%)	2(11.1%)	1.000
4.Very Severe DR	1(2%)	0(0%)	0(0%)	1(5.6%)	1.000
5.PDR early	3(6%)	2(11.8%)	0(0%)	1(5.6%)	0.633
6.High risk PDR	2(4%)	0(0%)	0(0%)	2(11.1%)	0.322
7.Macula	1(2%)	0(0%)	0(0%)	1(5.6%)	1.00

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Table 3:Incidence of Diabetic Retinopathy according to HbA_1c

DISCUSSION

A prospective study was conducted over a period of 2 years to look at correlation between fasting plasma glucose, postprandial plasma glucose, HbA_1c levels, blood pressure, microalbuminuria and their relation to diabetic retinopathy. Of 50 patients included in the study 68% were males and 32% were female .There was preponderance of males with retinopathy(63.3%) compared to 36.7% in female. 50% of the patients were from 61-70 year with the mean age of study population was 65.5 year (Table 2). This advanced in age of development of retinopathy in our study could be because of awareness about the disease and good blood sugar control compared to Tanaka et al study where it was 53.26 year.[10]Mean FBS and post PPBS levels of the study population were 165 mg /dl and 250 mg/dl respectively indicating that majority of the type 2 diabetes had poorly controlled higher than recommended blood glucose levels.This fact is reinforced by the fact that the mean glycated hemoglobin was 9% was beyond the recommended < 7 % of the normal values in our laboratory range being 4.5-6.4% .The predominant mode of therapy was with oral hypoglycemic drugs 96.7% with only 3.3 % using insulin (Table 2). This inspite of the poor glycemic control of the population is probably due to the inherent resistance in patients and sometimes physicians to start patients on insulin. On analyzing the association of various markers of glycemic status only PPBG was significantly associated with all three microvascular complications and also with macrovascular disease. PPBG had a significant correlation with macrovascular complications. With the present study showing a significant association of PPBG with levels of glycated hemoglobin it becomes imperative that it be considered a part of routine follow-up measure for glycemic control in diabetes.[10] The postprandial state is an important contributing factor to the development of atherosclerosis the generation of an oxidative stress may be the common pathway through which postprandial hyperglycemia may adversely modify atherosclerotic risk factors as lipids coagulation system and endothelial function.[11,12]Many studies have shown that the duration of diabetes was the strongest predictor for the development and severity of retinopathy,hard exudates formation,macular edema and poor visual outcome, but our study has shown that 6-10 year of diabetic with uncontrolled plasma sugars are more prone for development of retinopathy compared with 16.7% with good sugar control. Microalbuminuria with p value < 0.001 has been shown to be significant predictor of microvascular damage. In our study, among 19 patients with microalbuminuria 60% of patients had retinopathy.[7]26.7% of patients who had prehypertension and not on any antihypertensive medications have developed retinopathy compared to 23% of stage 1 & 2 hypertensive who were on medications .So constant high normal blood pressure might have contributed for the development of retinopathy.In our study, higher levels of hemoglobin patients had more incidence of retinopathy compared with lower Hb% which is contrary to ETDR study where anemia was found to be significantly associated with presence of severe retinopathy, hard exudates, CSME and visual loss.[8] Diabetic retinopathy Indian prospective study showed that for every 1% reduction there was 37% reduction in microvascular complications. But our study has shown higher levels of HbA_1c 8-10% were associated with microvascular complications than HbA_1c of 6.5-7 % at which retinopathy,chronic kidney disease,albuminuria,dyslipidemia are less detected. It is also concluded from the results that HbA_1c can be used as a predictor of dyslipidemia in type 2 DM. Our study has also showed the association of total cholesterol and LDL-cholesterol with severity of retinopathy.UKPDS group study the tight blood pressure control was associated with significant reduction in microvascular complications.Our study has also revealed that un identified high blood pressure and uncontrolled blood pressure patients had significant retinal changes with p value of 0.058.[9] Chew EY et al showed that significant association of retinopathy among insulin users with p<0.001[6] but our study has showed higher incidence among OHA' users and it less in insulin users through the use of insulin associated with intensive sugar control and improve diabetic retinopathy outcome it has not been well documented.

The other significant risk factors noted were the presence of hypertension chronic renal failure, microalbuminuria and raised HbA_1c.[13] UKPDS follow-up data showed that intensive treatment was associated with reduced risk for all diabetes related end points. The HbA_1c of 7.5% was associated with lowest progression of large vessel events.[14,16]The ADVANCE study showed intensive blood pressure and glucose control HbA_1c<7.5% reduced frequency of microvascular complications.[15]The TG/HDL –cholesterol ratio was positively associated with an increased risk of retinopathy independent of duration of diabetes ,HbA1c, hypertensionand albuminuria. However our study has showed more positive relation with triglycerides in which 68% had TG >150mg/dl and 54% had HDL of<40mg/dl and LDL > 130 in 38% of people so there is a definite relation dyslipidemia with retinopathy.[17]

CONCLUSION

Diabetic retinopathy is one of most common cause of blindness, the associated comorbidities significantly contribute for rapid progression of disease. Early detection intervention and treating underlying comorbid conditions significantly bring down the incidence as well as progression of retinopathy. Although various risk factors are implicated for the development and progression of diabetic retinopathy, duration of diabetes remains to be the most important. Our study also shows CSME in long term diabetics. Our study did not show significant changes in retinopathy with anemic as shown by other studies rather high Hb% people had more incidence of retinopathy.

Microalbuminuria and pre-hypertensive who were not on any medications had more incidence of retinopathy, PDR and CSME. There is a significant association of serum triglycerides, LDL –cholesterol with DR and CSME.This study also found HbA_1c had a positive correlation with fasting and postprandial blood sugar, triglycerides and cholesterol so HbA_1c can be used as a predictor of dyslipidemia in DM-2 .As this study looks at a small number of patients and only at a short duration of patients glycemic status and does not represent the overall glycemic status for their actual duration of diabetes.It would be necessary to conduct long term studies with larger numbers to look at association of different variables. Most of the patients in this study had no regular ophthalmic assessments and the prevalence of DR was found to be higher in these patients. In this context,regular ophthalmic screening in diabetics for early detection of non-proliferative retinopathy and increasing public awareness are highly recommended.

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