ORIGINAL ARTICLE

CLINICAL CORRELATION OF HBA1C AND DIABETIC NEPHROPATHY WITH DIABETIC RETINOPATHY

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ABSTRACT: To establish a relation between diabetic retinopathy and diabetic nephropathy in type II diabetes mellitus. To find out the relation between level of glycosylated haemoglobin (HbA1c) with diabetic retinopathy and diabetic nephropathy. An observational clinical study where 50 patients with diabetic retinopathy included. HbA1C, blood urea and serum creatinine levels of these patients were measured and the correlation between these values with the severity of retinopathy was assessed. Among 50 patients, 31 were males and 19 females. Mean age of patients was 62 years. Mean duration of diabetes mellitus was 6.9 years. None of the patients with severe NPDR and PDR had HbA1C under very good control. 64.3% with mild NPDR, 78.2% with moderate NPDR, 87.5% with severe NPDR and 100% patients with PDR had HbA1C under poor control. In mild NPDR group 14.3%, in severe NPDR group 50% and in PDR group 40% had blood urea >40. In mild NPDR group 14.3%, in severe NPDR group 50% and in PDR group 60% had serum creatinine>1. Glycosylated haemoglobin showed increasing trend as severity of diabetic retinopathy increased. Blood urea and serum creatinine also showed a positive correlation with diabetic retinopathy.

KEYWORDS: Diabetic Retinopathy, Diabetic Nephropathy, Glycosylated Haemoglobin, Blood Urea, Serum Creatinine.

INTRODUCTION: Diabetic Nephropathy & Diabetic Retinopathy are definitely the two most dreaded complications of diabetes. Together they contribute to visual and systemic morbidity and mortality. As they progress to end stage renal disease and blindness, they impose enormous medical, economical and social costs on both the patient and health care system[1.]

Diabetic retinopathy is a vascular disorder affecting the microvasculature of retina[2]. This is a leading cause of blindness among socioeconomically viable age group world wide[3]. It is estimated that about 5.5 million adult patients with diabetes have diabetic retinopathy. About 50,000 new cases of blindness occur per year, out of which 50% are caused by diabetes and most caused by diabetic retinopathy[4]. The prevalence of diabetes is elected to reach epidemic proportions with increasing burden of disease in developing countries. WHO estimates a three fold rise of disease in Asia[5'6]. According to WHO report, dated 2004, India has 31.7 million diabetics and the number is expected to increase to a staggering 79.4 million by 2030. In India with the epidemic increase in type 2 diabetes mellitus as reported by the World Health Organization, diabetic retinopathy is fast becoming an important cause of visual disability[2,7].

Diabetic nephropathy is a clinical syndrome characterized by persistent albuminuria, arterial blood pressure elevation, and decline in Glomerular Filtration Rate and a high risk of cardiovascular morbidity and mortality[1]. This major life threatening complication develops in approximately 20% to 40% of type I and <20% of type II diabetic patients[8].

As the pathologic mechanism of diabetic retinopathy and diabetic nephropathy is similar, most of the patients with diabetic retinopathy have diabetic nephropathy. Unlike in eye, the vasculature of kidney can't be directly visualized. So we have to depend on renal function tests and albuminuria to monitor kidney function.

Glycosylated haemoglobin measurement is a method for estimating the degree of hyperglycemia over a period of 2 to 3 months[6]. Diabetic nephropathy and diabetic retinopathy are more likely to develop in patients with poor glycemic control[1]. Previous studies have showed a positive correlation between severity of retinopathy and high levels of HbA1c[1].

This study aims to find out the relationship between diabetic nephropathy and severity of diabetic retinopathy in type II diabetic patients and also to find out the relation between HbA1c and severity of diabetic nephropathy and diabetic retinopathy. So by controlling the HbAIc level, we will be able to slow down or arrest the progression of diabetic retinopathy and diabetic nephropathy and thereby reduce the economic, social and psychological impact of diabetes mellitus on patients and society.

MATERIALS AND METHODS: 50 patients with diabetic retinopathy attending KIMS hospital ophthalmology department were included in the study.

Inclusion criteria:

- Patients of either sex with type II diabetes mellitus
- At least 1 year duration on treatment with OHA/Insulin

Exclusion Criteria:

- Pre-existing non diabetic retinopathy & maculopathy
- Non diabetic renal disorders
- Chronic liver diseases
- Undergone laser photocoagulation therapy

Ophthalmic evaluation comprises of measurement of best corrected visual acuity, Intra Ocular Pressure measurement and slit lamp examination. All fundus examination performed with Indirect Ophthalmoscopy and slit lamp biomicroscopy with 90D lens after pupil dilatation.

For all selected patients, HbA1C, blood urea, serum creatinine estimation were done. According to the level of HbA1C, patients were grouped into very good control group (HbA1C<6), good control group (HbA1C between 6 and8) and poor control group (HbA1C>8). Blood urea value >40 and serum creatinine value>1 considered as abnormal. Proteinuria was not considered in this study. Relationship between glycosylated haemoglobin and severity of diabetic retinopathy assessed. Relationship between diabetic retinopathy and diabetic nephropathy assessed by finding the correlation between blood urea and serum creatinine value with severity of diabetic nephropathy.

Statistical Analysis: Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. 95% Confidence Interval has been computed to find the significant features.

RESULTS: In our study, 31 patients were males and 19 patients were females. The age of our study population ranges from 46 to 74 years with the mean of 62 years. Mean duration of diabetes mellitus ranged from 2 to 28 years with the mean of 6.9 years. Among 50 patients, 46% were diagnosed with moderate NPDR(Non Proliferative Diabetic Retinopathy) followed by mild NPDR (28%), severe NPDR(16%) and PDR (Proliferative Diabetic Retinopathy) (10%). 8% of patients had HbA1C under very good control (HbA1C <6). 14% had HbA1C under good control (HbA1C between 6 and 8). 78% of patients had HbA1C under poor control (HbA1C>8). 31 patients (62%) had blood urea <40 whereas 19 patients (38%) had blood urea >40. Serum creatinine was <1 in 26 patients (52%) and>1 in 24 patients (48%).

Table number 1 shows the relation of HbA1C, blood urea and serum creatinine with severity of diabetes. 21.4% patients with mild NPDR and 4.3% patients with moderate NPDR had HbA1C under very good control. None of the patients with severe NPDR and PDR had HbA1C under very good control. 64.3% with mild NPDR, 78.2% with moderate NPDR, 87.5% with severe NPDR and 100% patients with PDR had HbA1C under poor control). CSME was present in 24 patients (48%). None of the patients with CSME had HbA1C under very good control. 2 patients with CSME had HbA1C under good control and remaining 22(91.6%) had HbA1C under poor control. Table number 2 shows that average value of HbA1C increases as severity of diabetic retinopathy increases.

Table number 1 shows that in mild NPDR group only 14.3% had blood urea >40 whereas in moderate NPDR it is 47.8%, in severe NPDR it is 50% and in PDR it is 40%. In mild NPDR group only 14.3% had serum creatinine >1, whereas it is 65.2% in moderate NPDR group, 50% in severe NPDR group and 60% in PDR group. Table number 2 shows that the average value of blood urea increases as severity of diabetic retinopathy increases. Serum creatinine value also showed increase with severity of diabetic retinopathy (p value = 0.018).

Relationship between blood urea and HbA1C showed that of 19 patients with blood urea>40,14 patients(73.6%) had HbA1C>8. Of 24 patients with serum creatinine >1, 20 patients (83.3%) had HbA1C >8.

DISCUSSION: Diabetic retinopathy and diabetic nephropathy is more likely to develop in patients with poor glycemic control. Previous studies have shown that patients with HbA1C >8% are at higher risk for renal diseases[1]. In our study 73.6% patients with blood urea>40 and 83.3% patients with serum creatinine >1 had poor control of HbA1C. This shows that uncontrolled HbA1C has a relation with diabetic nephropathy.

Randomized clinical trials have confirmed the predictive value of poor glycemic control compared with good control in determining the risk of nephropathy and retinopathy[1]. DCCT showed 76% reduction in the rate of development of any retinopathy and an 80% reduction in progression of established retinopathy in patients with strict control of diabetes[1]. Wisconsin epidemiological study of diabetic retinopathy showed a positive correlation between severity of retinopathy and high level of HbA1C after 10 years of diabetes mellitus[9]. In the CURES Eye study for every 2 % elevation of HbA1C, the risk of diabetic retinopathy increases by a factor of 1.7[1, 10]. In the UKPDS, the risk reduction in eye complications for every 1% decrease in HbA1C was 19%. In our study (87.5%) with severe NPDR and (100%) patients with PDR had HbA1C under poor control. Table number 2 shows that value of HbA1C shows an increasing trend as severity of diabetic retinopathy increases.

Also patients with CSME had uncontrolled HbA1C suggesting a relationship between CSME and uncontrolled diabetes mellitus.

A link between renal and retinal angiopathy in diabetes has been long recognized, an effect that may be mediated through an increase in Blood pressure, fibrinogen levels and lipoproteins[11]. Cross-sectional and longitudinal studies report a relationship between diabetic retinopathy and diabetic nephropathy. In our study among patients with severe NPDR, 50% had blood urea>40 whereas in patients with mild NPDR and moderate NPDR, this percentage is 14.3% and 47.8 respectively. 50% of patients with severe NPDR had serum creatinine>1 and 60% of patients with PDR had serum creatinine >1 which shows that there is a correlation between severity of diabetic retinopathy and diabetic nephropathy.

CONCLUSIONS: The value of glycosylated haemoglobin showed an increasing trend as severity of diabetic retinopathy increases. Blood urea and serum creatinine showed a significant relation with severity of diabetic retinopathy. This suggests a positive relation between diabetic retinopathy and diabetic nephropathy.

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Clinical variables	Diagnosis				Total	P value
	Mild NPDR (n=14)	Moderate NPDR (n=23)	Severe NPDR (n=8)	PDR (n=5)		
Gender						
Female	6(42.9%)	9(39.1%)	1(12.5%)	3(60%)	19(38%)	0.355
Male	8(57.1%)	14(60.9%)	7(87.5%)	2(40%)	31(62%)	
HbA1c						
<6	3(21.4%)	1(4.3%)	0(0%)	0(0%)	4(8%)	0.838
6-8	2(14.3%)	4(17.4%)	1(12.5%)	0(0%)	7(14%)	
>8	9(64.3%)	18(78.2%)	7(87.5%)	5(100%)	38(78%)	
Blood Urea						
<40	12(85.7%)	12(52.2%)	4(50%)	3(60%)	31(62%)	0.174
>40	2(14.3%)	11(47.8%)	4(50%)	2(40%)	19(38%)	
Serum Creatinine						
<1	12(85.7%)	8(34.8%)	4(50%)	2(40%)	26(52%)	0.018*
>1	2(14.3%)	15(65.2%)	4(50%)	3(60%)	24(48%)	

Table 1: Correlation of clinical variables with diagnosis

Bio-Chemical variables	Diagnosis				Total (n=50)	P value
	Mild NPDR (n=14)	Moderate NPDR (n=23)	Severe NPDR (n=8)	PDR (n=5)		
HbA1c	9.08±3.01	9.32±0.42	10.01±0.55	9.04±0.48	9.34±0.31	0.800
Blood urea	31.93±17.33	41.22±4.15	44.25±8.63	59±30.95	40.88±3.98	0.314
S Creatinine	1.16±1.04	1.43±0.23	1.18±0.17	1.04±0.12	1.28±0.13	0.750

Table 2: Correlation of Bio-chemical variables (mean values) with diagnosis

REFERENCES:

1. Ali Jawa, Juanita KC, Vvian A, Fonesca (2004) Diabetic Nephropathy and Retinopathy. Med Clin N Am:1001-1036.
2. M Rema, R Pradeepa (2000) Diabetic Retinopathy-An Indian Perspective. Indian J: 297-310.
3. Park CY, Park SE, Bae JC, Kim WJ et al (2012) Prevalence and risk factors for Diabetic Retinopathy in Koreans with type 2 Diabetes Mellitus. British J: 151-155.
4. R&B legend Gladys Knight (2003) Sings praises of early detection and management of diabetes. Schaumberg (IL). Prevent Blindness America.
5. PS Mallika, PY Lee, WL Cheah, JS Wong et al (2011) Risk factors for Diabetic Retinopathy in diabetics screened using fundus photography at a primary health care setting in east Malaysia. Malaysian Family Physician: 1985-2274.
6. King H, Auber RE, Herman WH (1998) Global burden of diabetes prevalence, numerical estimates, and projections. Diabetes Care: 1414-1431.
7. Wild SRG, Green A, Sicree R, King H (2004) Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. Diabetes Care: 1047-1053.
8. Skyler JS (2004) Microvascular complications retinopathy and nephropathy. Endocrinol Metab CLIN North Am: 833-856.
9. Klein r, Klein BE, Moss SE, Davis MD, DE Mets DL(1984)The Wisconsin Epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. Arch Ophthalmol: 520-526.
10. Rema M, Premkumar S, Anitha B, Deepa R et al(2003) Prevalence of diabetic retinopathy in urban India.The Chennai Urban Rural Epidemiologic Study– study design and Methodology Urban component. J Assoc Physicians India: 863-70.
11. Root F, Pote WH, Frehner H(1954) Triopathy of diabetes; sequence of neuropathy, retinopathy, and nephropathy in one hundred fifty-five patients. AMA Arch Intern Med : 931-941.

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