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Original research article

To Study the Prognosis of Non Proliferative Diabetic Retinopathy In Association with Risk Factors Like Hba1c, Lipid Profile and Urine Microalbumin

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Abstract

Background: Diabetes mellitus is a common and serious disease with chronic complications and constitutes a substantial burden for both patient and health care system. Objectives: To find out the association between the level of Glycosylated Heamoglobin [HBA1c] With the prognosis of Non Proliferative Diabetic Retinopathy (NPDR).

Material and methods: 100 patients with type 2 diabetes visiting the Opthalmology OPD and IPD from Sept 2020 to July 2022 .at, SKMCH, Muzaffarpur. were taken up for the study.

Conclusion: The present study shown that elevated level HBA1C levels are found to be the potent predictors of progression of diabetic retinopathy . Hypercholesterolemia was found to be significantly associated with severe NPDR, very severe NPDR . Raised serum cholesterol level was also significantly associated with CSME. patients with urine Microalbuminuria are more likely to have severe diabetic retinopathy . Early diagnosis and prompt treatment in these patients can reduce the onset and progression of retinopathy.

Keywords: NPDR –Non proliferative Diabetic Retinopathy .HBA1C-Glycated Haemoglobin.

Introduction

Worldwide, Diabetic retinopathy is a leading cause of vision loss[1] and globally 34.6% of diabetes are estimated to have Diabetic retinopathy[2]. It is estimated that the global magnitude of diabetic retinopathy will increase from 126.6 million in 2010 to 191 millionby 2030[3].The prevalence of diabetic retinopathy in India ranges from 17.6% to 28.2%[4]. The prevalence of type 2 diabetes mellitus has gone beyond an epidemic form to pandemic onewith every 5th diabetic in the world is an Indian estimated 31.7 million diabetes in the year2000 and projected that 79.4 million people in India will have diabetes by the year 2030 in India [5].The rapid number of person increases with diabetes is expected to increase with ocular complications. It is a major cause of avoidable blindness in developing country in India with the epidemic increases in type 2 Diabetic Mellitus as reported by the WHO, Diabeticretinopathy is fast becoming an important cause of visual disability [6].Diabetic retinopathyis vascular disorder affecting the microvasculature of retina [7.] The prevalence of Diabetic retinopathy in diabetic patient is 40%[8.] It is estimated that 5.5million adult patient with type 2 diabetes have Diabetic

retinopathy. About 50,000 new case of blindness occur per year out of which 50% are caused by diabetic retinopathy[9].Improvement in diabetic care and earlier detection by using new noninvasivemethod like OCT the incidence of visual impairment and blindness can be reduced up to 90%[10,]. Diabetes mellitus is defined as a syndrome characterized by hyperglycemia resulting from absolute or relative impairment in insulin secretion or insulin action.It is the mostcommon endocrine disease ,causing metabolic abnormalities and long term complications involving the Eyes ,kidney ,nerves ,and blood vessel . Diabetes mellitus (DM) is a complex metabolic disease caused by a variable interaction between hereditary and environmental factors. It is associated with a considerable mortality from a variety of complications, which tend to worsen over time and carries a significant premature mortality risk. Its main features are abnormal insulin secretion, high levels of blood glucose and variety of complications such as retinopathy, nephropathy, neuropathy and arteriosclerosis. Diabetic retinopathy (DR) is a sight threatening complication of Diabetes Mellitus and is one of the leading causes of acquired blindness in adults. According to WHO, diabetic retinopathy is responsible for 3-7% total blindness in Asia(11).In India the prevalence of diabetic retinopathy in general population is 3.5% and the prevalence of diabetic retinopathy in the population with diabetic mellitus is 18.0%. The chance of loosing the sight is about 25 times higher compared to normal individuals. The treatment of diabetic retinopathy is laser photocoagulation, strict glycemic control ,with systemic lipid lowering therapy over the last decade .there is evidenceof the effect of lipid lowering in reducing hard exudates[12.] Several studies have been done to study the influence of these individual risk factors on the progression of retinopathy. However, very few studies have been done to study the correlation between all these risk factors in diabetic patients with retinopathy.

Objectives

To find out the association between the level of Glycosylated Heamoglobin[HBA1c] With the prognosis of Non Proliferative Diabetic Retinopathy (NPDR). To evaluate the association of elevated Serum Lipid level with the severity of Diabetic Retinopathy and its association with the prognosis of Non proliferative Diabetic Retinopathy.

Review of Literature

In 1846,French ophthalmologist Apollinaire Bouchardat(1806-1886) reported development ofvisual loss in absence of cataract in diabetics.It was Edward jaguar (1818-1884) who first observed diabetic macular changes in 1855 [13] .It is estimated that diabetes mellitus affects 4 percent of the worlds population ,almost half of whom have some degree of diabetic retinopathy at any given time**.** Diabetes Mellitus is a common and potentially disabling chronic disease. Persons with diabetes mellitus are at an increased risk of number of complications including retinopathy,renal disease, heart disease and neuropathy. These complic8ations can progress to end stage outcomes such as blindness, end stage renal disease and amputation. Diabetes Mellitus is one of the main threats to human health in the 21st century. The prevalence of diabetic mellitus is growing rapidly worldwide . The WHO has estimatedthat there were 135 million diabetes mellitus cases in 1995 and this would increase to 300 million by the year 2025 and 438million by the year 2030.the major proportion of this increase will occur in developing countries of the world . Increasing urbanization and Industrialization are the chief reasons for the rapid increase in the prevalence of type 2 diabetes mellitus.[14] In recent years, India has witnessed a rapidly exploding epidemic of diabetes mellitus. India leads the world today with the largest number of diabetics in any given country. The prevalence of type 2 diabetes mellitus in urban Indian adults has increased from <3%in 1970s to > 12% by 2000; while that in the rural population it has increased to almost7%. Moreover there is equally

large pool of individuals with impaired glucose tolerance, many of whom will develop type 2 diabetes mellitus in the future. There is an urgent need for strategies to prevent the emerging global epidemic of diabetes mellitus, apart from treating diabetes mellitus and the associated complications. Better education, improved nutrition, increased physical activity, weight reduction; early diagnosis and prompt treatment are all means of curbing the impact of diabetes mellitus. Raman et .al.,(2009) the sankara nethralaya Epidemiologic and molecular Genetic study evaluated a sample of 5999 patient in southern India .the prevalence rate of DR in an urbandiabetic population was found to be 18%.[15] Niveditha H et.al at 2015 conducted a study .Clinical correlation of HBA1c and Diabetic retinopathy .It was observational clinical study ,where 50 patients with diabetic retinopathy wasincluded and she found that none of the patient with severe NPDR and PDR had HBA1c under goodcontrol ,64.3% with mild NPDR, 78.2% with moderate NPDR,87.5% with severe NPDR and 100%with PDR had HBA1C poor control. Singh et al.,(2012) conducted cross sectional study on 202 patient ,out of which 130 were diabetic .out of those 94 were having no retinal changes whereas 25 had preproliferative changes 7 had proliferative changes ,4 had complete loss of vision .the overall prevalence of diabetic retinopathy was 27.69%.26 Chen et al. suggested that dyslipidemia but not hyperglycemia induces inflammator adhesion molecules in human retinal vascular endothelial cells which are suppose to play a very important role in development of early diabetic retinopathy. Diabetic dyslipidemia serves as an inflammatory stimulus that initiates and contributes to microvascular complications27 Ucgun et al studied the importance of serum lipids in Exudative Macular Edema and found that total serum cholesterol and LDL levels were elevated in patients with macular edema and high hard exudates. Triglyceride, HDL,VLDL levels were not different between the two groups· Eckhard Zander et.al., have demonstrated that irrespective of the type of diabetes mellitus, there was significant association of maculopathy with factors such as duration of diabetes mellitus, HbA_{1c} levels, protienuria, triglyceride and total cholesterol levels. K.G Santos et.al., emphasized the need for good glycemic control in order to prevent or delay the onset of diabetic retinopathy, since duration of diabetes mellitus, glycosylated hemoglobin and albumin excretion rate were independently related to diabetic retinopathy.[16]

Material and methods

Prospective type of study, 100 patients with type 2 diabetes visiting the Opthalmology OPD and IPD from Sept 2020 to July 2022 .at, SKMCH, Muzaffarpur, were taken up for the study. Data Was collected from type 2 diabetic patients visiting OPD and IPD in the Department of Ophthalmology in, Sri Krishna medical college & Hospital (SKMCH), Muzaffarpur, Bihar. The age of patients varied from 35-75years. The cases were selected on the basis of simple random sampling method.

Inclusion Criteria

Patients of either sex, Patient diagnosed with NPDR.
Patient with diabetes mellitus more than 5 year duration.
All type 2 Diabetes mellitus patients.

Exclusion Criteria

Patient with pathological myopia.
Who have undergone pan retinal photocoagulation therapy.
Chronic liver disease & vitamin B12 deficiency.
With Renal causes of retinopathy.
Patient with hypertensive retinopathy.

All the study subjects had a thorough ophthalmic evaluation which included slit-lamp biomicroscopic examination of anterior segment, best corrected visual acuity (BCVA) of each eye recorded using Snellen chart, complete fundus examination after mydriasis with 1% tropicamide and 5% phenylephrine eye drops using direct ophthalmoscopy, indirect ophthalmoscopy with +20D lens and stereoscopic slit lamp biomicroscopy of the disc and macula using + 78D Volk lens. All cases were examined for the presence or absence of diabetic retinopathy. Those cases with fundus showing features of diabetic retinopathy were graded into four classes on the basis of ETDRS classification. Thus, a total of four categories were made based on the fundus pictureof the patients.

5ml of fasting blood sample was collected under asepsis from the anterior cubital vein using disposable syringe to assess hba1c , lipid profile and blood sugar level. The following tests were carried out by enzymatic method using autoanylyser in the Central Laboratory with the help of the department of Biochemistry.
Undiluted sample is added to a buffer containing antibody specific for human serum albumin. The absorbance (340 nm) of the resulting turbid solution is proportional to the concentration of albumin in the sample urine. Expected Values

Table 1:

Category	24hr Collection(Mg/24hr)	Timed Collection (□G/Min)	Spot Collection □G/Mg OfCreatinine
Normal	<30	<20	<30
Microalbuminuria	30-299	20-199	30-299
Clinical Albuminuria	300	200	300

Results
Descriptive statistics such as mean, SD and percentage was used to present the data. Association between variables was assessed by using Chi-square test. Pearson's correlation coefficient was used to find out correlation between Microalbuminuria and development of Retinopathy in type 2 Diabetic Mellitus patients. A p-value less than 0.05 were considered as significant.

Table 2:

	Minimum	Maximum	Mean	Std. Deviation
Age	47	74	58.53	6.12
Duration_of_DM	10	74	15.52	7.21
HBA1C	6.78	13.60	9.83	1.93
TOTAL_CHOLESTROL	141.00	570.08	282.62	89.74
TRIGLYCERIDE	81.80	738.60	259.55	133.32
LDL	40.00	243.07	147.93	41.69
VLDL	16.40	200.00	57.18	27.19
URINE_MICROALBUMINURIA	.00	975.00	98.19	125.35

Age Distribution
Study involved 100 patients of different age group ranging from age 47 yrs to age 77yrs.with mean age group of 58.53.maximum no of patients involved age group is 57 to 61 years (30%).

SEX DISTRIBUTION

Table 3:

Sex	Number	Percentage%
Female	42	42.0
Male	58	58.0

Our study contain 58% male and 42% female .the mean age was 58.53+/- 1.5 .
In the study patients, the duration since diagnosis of diabetes mellitus (diabetic age) ranged from 10-25 years. The mean duration 15.25 ± 1.29 years respectively.in our study 42% patients had duration of diabetes 10 to 13 years .28% patients had 14 to 17 year duration.22% had 18 to 21 years of duration of diabetes mellitus .8% had 22 to 25 year of duration of diabetes mellitus.

GLYCATED HEAMOGLOBIN(HBA1C)

Table 4:

HBA1C	Number	Percentage
Good	6	6.0
Poor	94	94.0

showing number and percentage of patients with good andpoor HBA1C in the study .6%t were with normal HBA1C and 94% patients had poor values of HBA1C.
In the study conducted Serum total cholesterol concentrations were higher in subjects with severe NPDR, very severe NPDR (p =0.046) compare to mild to moderate NPDR .In our study among 100 patients 12 % had total cholesterol within normal limits . 21% had borderline control of total cholesterol .67% had poor control of total cholesterol.

LDL LEVELS

Table 5:

LDL	Number	Percentage
Normal	14	14.0
High	86	86.0

showing number of patients with high VLDL and normal VLDL inthe study conducted. 14% had normal VLDL levels and 86% patients were with high VLDL.

URINE MICROALBUMINURIA

Table 6:

URINE_MICROALBUMINURIA	Number	Percentage %
Normal	31	31.0
Microalbuminuria	68	68.0
Macroalbuminuria	1	1.0

showing number of patients with normal Microalbuminuria andmacroalbuminuria in the study conducted. 31% had normal values,68% patients had microalbuminuria and 1% patient had macroalbuminuria.
In the study borderline control of cholesterol 11 had mild NPDR ,9 had moderate 1 had severe NPDR .with high cholesterol level 3 had mild NPDR ,29 had moderate NPDR ,25 anssevere

NPDR and 10 had very severe NPDR .the severity of retinopathy was associated with increasingly total cholesterol is statistically significant ($p<0.0001$). In the study among 100 patients good control of LDL involved 14 pateints and 86 patientswith poor control of LDL showed severity of diabetic retinopathy .the asscociation of diabetic retinopathy with LDL level is statistically significant ($p<0.0001$).$\chi^2 = 14.49$, df=1, p=0.0001In the study among 100 patients with Microalbuminuria 4 had mild NPDR ,30 had moderate NPDR ,24had severe NPDR ,10 had very severe NPDR .the severity of diabetic retinopathy with Microalbuminuria is statistically significant($p<0.0001$) In the study among 100 patients, duration of diabetes ,HBA1C, total cholesterol , and urine Microalbuminuria is clinically significant with the severity of diabetic retinopathy .

Discussion

Diabetic Retinopathy is definitely the most dreaded complications of diabetes. It is believed that the Indian population generally has an unusually efficient glucose metabolism. high prevalence of diabetes is a concern that the complications of diabetes, mainly diabetic retinopathy is increasing[17].Diabetic Retinopathy is a sight threatening complication of diabetes mellitus and is one of the leading causes of acquired blindness. It is due to microangiopathy affecting the retinal arterioles, capillaries and venules. Damage is caused by both microvascular leakage and microvascular occlusion. A series of risk factors have been related to the development and progression of retinopathy in diabetic patients. 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 costson both the patient and health care system. Diabetic retinopathy is a vascular disorder affecting the microvasculature of retina·This is a leading cause of blindness among socioeconomically viable age group world wide[18 ·] In this study an attempt was made to quantify specify the role of HBA1C , and role of various components of serum lipids and urine Microalbuminuria in asscociation with progression of NPDR .In the present study, 100 patients having type II diabetes mellitus of age group ranging from 47 to 74 years were studied. 42 patient female and 58 patient were male .patients were subcategorised depending on the severity / grade of retinopathy and presence or absence of CSME. The present study had a near equal sex distribution with only a slight male predominance. The male to female ratio [M : F] was 58 : 42. In a clinical cohort in Chennai diabetic retinopathy appeared to be prevalent more in the males compared to females (sex ratio 2 : 1). Similar male preponderance was also seen in the CURESEye study UKPDS study. Gupta et al and the Andra Pradesh Eye Disease study(APEDS)[19] However the difference with respect to the sex distribution was not statistically significant in the currentstudy. In this study, the mean duration of diabetes mellitus in diabetic patients with retinopathy was 15.25 ± 4.66 years. Our findings are comparable with the study done by M Remaet.al., who have proposed that duration of diabetes mellitus is probablythe strongest predictor for the development of retinopathy. Studies have also shown that for every 5-year increase in the duration of diabetes mellitus, the risk of diabetic retinopathy increases by 1.89 times. Studies done by Farhan K H et.al. have also shown that duration of diabetes mellitus can increase the risk for the development of diabetic retinopathy. The above findings show that duration of diabetes mellitus is one of the importantrisk factors in the development of diabetic retinopathy In the present study, there was a significant increase in the HbA_{1c} levels in diabetic patients with retinopathy .The mean HbA_{1c} levels in patients with diabetic retinopathy was 9.83 ± 1.44%. 6%patient were in good control and 96 % patients were in poor control .mild to moderate type diabetic retinopathy patient were in good control of HBA1C and severe n very severe type of diabetic retinopathy patient were poor control of HBA1C level . Glycosylated haemoglobin measurement is a method for estimating the degree of hyperglycemia over a period 2 to 3

months[20]. Diabetic nephropathy and diabetic retinopathy are more likely to develop in patients with poor glycemic control. Previous studies have showed a positive correlation between severity of retinopathy and high levels of HbA1c[1]. Our findings are comparable with the previous studies done by Ishratkareemet.al., who have observed increased HbA1c levels in diabetic patients with retinopathy associated with progression of severity of diabetic retinopathy .[21] Studies have also shown that in patients with type 2 diabetes mellitus, every 1%increase in HbA1c would result in an increase in the microvascular complications by 37%. K G Santos et.al., have demonstrated a significant increase in HbA1c levels in diabeticpatients with retinopathy.[22] Studies have suggested that increased capillary permeability, microangiopathy and retinal ischemia are probably due to the combined effects of various risk factors. Early diagnosis and prompt treatment in these patients can reduce the onset and progression of retinopathy.In the present study, we found that there was statistically significant correlation between the various parameters i.e.,HbA1c, total cholesterol triglyceride and microalbuminuria.

Conclusion

Based on the results of the present study and data available from literature, it can be implicated that HbA1c, lipid profile and microalbuminuria are involved in the development of diabetic retinopathy. The value of glycosylated haemoglobin showed an increasing trend as severity of diabetic retinopathy increases.Total glycemic exposure was dominant factor associated with risk of retinopathy progression .duration of diabetes and HBA1C concentration were the two major predictors of the presence of retinopathy and its progression

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