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Original Research Article

A Hospital-Based Study Assessing the Correlation of the Duration of Diabetes Mellitus, Microalbuminuria, Hyperlipidaemia with the Severity of Diabetic Retinopathy: An Observational Study

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Abstract

Aim: The present study was carried out with an aim to study the concordance and correlation of microalbuminuria, dyslipidemia with the severity of Diabetic Retinopathy in type II diabetes mellitus patient and to provide a possible basis for explanation of mechanisms governing this relationship

Material & Methods: This was a hospital based cross sectional study conducted in the Department of Ophthalmology, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India for one year . 200 patients were included in this study.

Results: A total of 200 subjects of either gender were included in our study, out of which 110 (55%) were females and rest were males 90 (45%). Majority of the patients lied in the age group of 40-60 years (55%) followed by 60-80 years (28%) and below 40 years (14%), while only 6 (3%) patients were aged above 80 years. 40% had diabetes <10 years followed by 30% having diabetes from last 10-20 years. 70% patients had grade 0 micro-albuminuria. 55% patients had total cholesterol level at borderline. Proportion of Group I (No retinopathy) was higher in younger patients. Another statistically significant association was found between the severity of retinopathy and duration of diabetes ($p < 0.001$). A statistically significant association between microalbuminuria grade and severity of retinopathy was observed ($p < 0.001$). Proportional difference in severity of retinopathy in patients with different total cholesterol levels was found to be statistically significant ($p = 0.001$).

Conclusion: Duration of diabetes and microalbuminuria had been found to be the independent risk factors for diabetic retinopathy, but serum cholesterol levels did not show an independent role in our study. The findings in present study endorsed the view that microalbuminuria poses a risk for diabetic retinopathy which is affected by duration of diabetes, level of glycemic control and lipid levels.

Keywords: Diabetes Mellitus; Diabetic Retinopathy; Microalbuminuria; Hyperlipidaemia

Introduction

Diabetes is one of the most common metabolic disease globally and hence one of the most challenging health concerns in modern era. [1] Diabetes is one of the largest global health emergencies of the 21st century. [2] The world has around 246 million people with diabetes. [3] It is recognized as a group of heterogeneous disorders with the common elements of hyperglycemia and glucose intolerance, due to insulin deficiency or impaired effectiveness of insulin action, or both. [4,5] Diabetes is characterized by metabolic abnormalities and long-term microvascular and macrovascular complications. While there are many risk factors associated with the development and progression of retinopathy, the duration of the disease and the age of the patient are said to be the most predictable. Several other factors, including high blood pressure, pregnancy, blood glucose control, and nephropathy have been linked with a greater risk for developing diabetic microangiopathy. The role of microalbuminuria, dyslipidaemia, body mass index (BMI), and smoking as predictors of diabetic retinopathy is not well.

Diabetic retinopathy (DR) and diabetic nephropathy (DN) (now called diabetic kidney disease [DKD]) are the most common microvascular complications of diabetes. DR and DKD are major causes of social and economic burden to individuals with diabetes and the healthcare system due to the risk of blindness [6] and end-stage renal disease. [7] Diabetic

retinopathy is the most common and probably the most serious of all ocular problems. Due to its microvascular complications, diabetic retinopathy accounts for 4.8% of the 37 million cases of blindness in the world. [3] Diabetic retinopathy is the most serious of the various complications of diabetes. [8,9] The incidence of diabetic retinopathy is 21% to 60%, respectively, in people with diabetes below five years and at least 15 years. Proliferative retinopathy ranges from 1.2% to 67% in people with diabetes for less than a decade and for 35 or more years. The incidence of blindness was 16% in patients with DM. The retinal changes can be broadly divided into proliferative (PDR) and nonproliferative diabetic retinopathy (NPDR) groups according to ETDRS classification. Further NPDR can be classified into 1) very mild NPDR2) mild NPDR 3) moderate NPDR 4) Severe NPDR and 5) very severe NPDR. PDR can be classified as mild to moderate PDR and high-risk PDR. [10]

The other microvascular complication associated with diabetes is diabetic nephropathy which is preceded by lower degrees of proteinuria, or "microalbuminuria". Without intervention, diabetic patients with microalbuminuria typically progress to proteinuria and overt diabetic nephropathy. As many as 7% of patients with type 2 diabetes may already have microalbuminuria at the time they are diagnosed with diabetes. [11] Apart from hyperglycemia and hypertension, hyperlipidemia is also a major risk factor for development of diabetes. Thus, the present study was carried out with an aim to study the concordance and correlation of microalbuminuria, dyslipidemia and Diabetic Retinopathy in type II diabetes mellitus patient and to provide a possible basis for explanation of mechanisms governing this relationship.

Material & Methods

This was a hospital based cross sectional study conducted in the Department of Ophthalmology, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India for one year. 200 patients were included in this study.

For the study, type II DM is defined as a fasting plasma glucose of more than or equal to 126 mg/dl or 2-hour post glucose load plasma glucose of more than or equal to 200 mg/dl or a random plasma glucose of more than or equal to 200 mg/dl in the presence of symptoms of hyperglycemia.

Inclusion Criteria

1. Age >18 years
2. Documented diagnosis of diabetes mellitus
3. HbA1c levels of >6.5%

Exclusion Criteria

1. All the Patients with Opaque/hazy ocular media preventing fundus visualization,
2. Co-existing ocular disorders likely to mask the findings of diabetic retinopathy.
3. Patients with presence of any of the confounding factors, like fever, active systemic infections, exercise, high protein intake, accelerated hypertension, congestive heart failure.
4. Patients not willing to participate in the study were excluded from the study.

Methodology

The patients underwent thorough history and ocular evaluation which included demographic details and medical history, which was recorded on a present proforma. Thorough ocular evaluation was done on all selected patients both clinically as well as with the help of diagnostic instruments. Both Uncorrected and best corrected visual acuity was recorded using a Snellen's chart. Anterior segment evaluation was done using slit lamp examination to look for any other ocular disease or ocular surgery. Amsler Grid Examination was also performed. The intraocular pressure was measured using an applanation tonometer. Fundus examination was performed by Direct Ophthalmoscopy,

Indirect Ophthalmoscopy and +90D lenses. Optical coherence tomography was performed using Cirrus 500 machine manufactured by Carl-Zeiss, Germany to measure the macular thickness, and Fundus Fluorescein Angiography by using Carl Zeiss fundus camera. Diabetic retinopathy was graded as per the ETDRS guidelines.

The biochemical evaluation was done by obtaining 2 ml of blood sample from the patient in a sterile vial and sent to the Department of Biochemistry. All the biochemical assessments were done using an Auto analyzer. All the patients were advised to undergo biochemical investigations for Blood sugar (fasting/pp), HbA1c taken as HbA1c:

Good Control: = 7.0%: grade1, Fair control: 7.1-8.5%: grade 2; poor control: > 8.5%: grade 3.[12] Urinary albumin to creatinine ratio in a random spot collection of urine and Lipid profile.

For the purpose of this study microalbuminuria was further sub graded as-Grade 0: < 2.5mg/mmol; Grade I: 2.5-12.5mg/mmol; Grade II: > 12.5-25mg/mmol and Grade III: > 25mg/mmol for men and Grade 0: < 3.5mg/mmol; Grade I: 3.5-12.5mg/mmol; Grade II: > 12.5-25mg/mmol and Grade III: > 25mg/mmol for women.[13]

Lipid profile was also sub graded as- Desirable (< 200); Border line high (200-239); High (≥240).[14]

Statistical Analysis

The data was analyzed using SPSS software version 15.0. Categorical data chi-square test was used whereas continuous data was analyzed using ANOVA and student "t-test". Multivariate assessment was done using logistic regression. The confidence level of the study was kept at 95% and hence a "p" value of less than 0.05 indicated a statically significant association.

Results

Table 1: Demographic data

Parameter	No. of Cases	Percentage
Gender		
Male	90	45
Female	110	55
Age group (years)		
Below 40	28	14
40-60	110	55
60-80	56	28
Above 80	6	3
Duration of diabetes		
<10 years	80	40
10-20 years	70	35
20-40 years	30	15
>40 years	20	10
Micro- AlbuminuriaGrade		
Grade 0	70	35
Grade I (2.5-12.5 mg/mmol)	60	30
Grade II (>12.5-25 mg/mmol)	40	20
Grade III (>25 mg/mmol)	30	15
Total cholesterol Level		
Desirable (<200)	60	30
Borderline high(200-239)	110	55
High (>=240)	30	15

A total of 200 subjects of either gender were included in our study, out of which 110 (55%) were females and rest were males 90 (45%). Majority of the patients lied in the age group of 40-60 years (55%) followed by 60-80 years (28%) and below 40 years (14%), while only 6 (3%) patients were aged above 80 years. 40% had diabetes <10 years followed by 30% having diabetes from last 10-20 years. 70% patients had grade 0 micro-albuminuria. 55% patients had total cholesterol level at borderline.

Table 2: Correlation of severity of retinopathy with age

Age Group (In Years)	Group I (No Retinopathy) (n=100, 50%)		Group Iia (Very Mild to Moderate) (n =50, 25%)		Group Iib (Severe to very Severe) (n = 28, 14%)		Group Iic (Proliferative Diabetic Retinopathy) (n = 22, 11%)	
	NO.	%	NO.	%	NO.	%	NO.	%
<40 (n=28)	20	71.43	3	10.72	5	17.85	0	0
40-60 (n=110)	52	47.27	34	30.90	14	12.72	10	9.09
60-80 (n=56)	22	39.28	13	23.21	9	16.07	12	21.42
>80 (n=6)	6	100	0	0	0	0	0	0

Proportion of Group I (No retinopathy) was higher in younger patients i.e. below 40 (71.43%) and 40-60 (47.27%) as compared to elderly cases i.e. 60-80 (39.8%) and this difference was found to be statistically significant ($p < 0.001$).

Table 3: Correlation of severity of retinopathy and duration of diabetes mellitus

Duration Of Diabetes (Years)	Group I (No Retinopathy) (n=100, 50%)		Group Iia (Very Mild to Moderate) (n =50, 25%)		Group Iib (Severe to verySevere) (n = 28, 14%)		Group Iic (Proliferative DiabeticRetinopathy) (n = 22, 11%)	
	NO.	%	NO.	%	NO.	%	NO.	%
<10 years (n= 80)	58	72.50	10	12.50	8	10	4	5
10-20 years (n= 70)	35	50	12	17.14	10	14.28	13	18.57
20-40 years (n=30)	3	10	12	40	10	33.34	5	16.66
>40 years (n=20)	4	20	16	80	0	0	0	0

Another statistically significant association was found between the severity of retinopathy and duration of diabetes ($p < 0.001$). It was found that proportion of Group I (non-retinopathy) patients was higher in patients with duration of diabetes < 10 years (72.50%) as compared to patients with duration 10-20 years (50%), 20-40 years (10%) and > 40 years (20%).

Table 4: Correlation of Retinopathy and Microalbuminuria

Micro-Albuminuria Grade	Group I (No Retinopathy) (n=100, 50%)		Group Iia (Very Mild toModerate) (n =50, 25%)		Group Iib (Severe to very Severe) (n = 28, 14%)		Group Iic (Proliferative Diabetic Retinopathy) (n = 22, 11%)	
	No.	%	No.	%	No.	%	No.	%
Grade 0 (n=70)	60	85.71	8	11.42	2	2.85	0	0
Grade I(n=60) (2.5-12.5 mg/mmol)	30	50	24	40	6	10	0	0
Grade II (n=40)(>12.5-25 mg/mmol)	10	25	16	40	6	15	8	20
Grade III (n=30) (>25 mg/mmol)	0	0	2	6.66	14	46.66	14	46.66

Majority of patients (85.71%) of Grade 0 microalbuminuria (< 2.5 mg/mmol) had no Retinopathy. It was found that higher the level of microalbuminuria more is the severity of retinopathy. Proportion of Severe to very severe retinopathy and proliferative diabetic retinopathy were higher in higher grade of microalbuminuria (Grade II and Grade III). A statistically significant association between microalbuminuria grade and severity of retinopathy was observed ($p < 0.001$).

Table 5: Correlation of Severity of Retinopathy and Total cholesterol

Total cholesterol Level	Group I (No Retinopathy) (n=100, 50%)		Group Iia (Very Mild to Moderate) (n =50, 25%)		Group Iib (Severe to very severe) (n = 28, 14%)		Group Iic (Proliferative DiabeticRetinopathy) (n = 22, 11%)	
	NO	%	No	%	No	%	NO	%
Desirable (<200) (n=60)	36	60	12	20	8	13.34	4	6.66
Borderline high (200-239) (n=110)	54	49.09	28	25.45	15	13.63	13	11.81
High (>=240)(n=30)	10	33.33	10	33.33	5	16.66	5	16.66

Prevalence of retinopathy was 60%, in patients having high total cholesterol levels. Proportional difference in severity of retinopathy in patients with different total cholesterol levels was found to be statistically significant ($p = 0.001$).

Discussion

Among the multiple risk factors for diabetic retinopathy (DR), the duration of diabetes is probably the strongest predictor for the development and progression of retinopathy. [15-17] The vast majority of patients with diabetes fall into two broad categories: absolute insulin deficiency and insulin secretion, characterized by type 2 diabetes, insufficient type of growth compensation and the presence of insulin resistance. In addition to the two main types, pregnancy and pancreatic disorders, endocrinopathies and drugs, etc are also the causes.3 Prolonged hyperglycemia promotes glucose reactions with components of the artery wall, resulting in an increase in glycation end products. [18] Microalbuminuria is a nephrotic disorder which if remains untreated progresses to proteinuria and overt diabetic nephropathy. It has been reported that as many as 7% of patients with type 2 diabetes already have microalbuminuria at the time they are diagnosed with diabetes.16 Thus microalbuminuria is a microvascular complication that is often accompanied with the diagnosis of type 2 diabetes and in effect may have a crucial role in determining the future course of disease and per se complications associated with it. [4]

A total of 200 subjects of either gender were included in our study, out of which 110 (55%) were females and rest were males 90 (45%). Majority of the patients lied in the age group of 40-60 years (55%) followed by 60-80 years (28%) and below 40 years (14%), while only 6 (3%) patients were aged above 80 years. Chung et al [19] (2011) had majority of male patients (54%) with a mean age of 64.9 ± 10.8 years in the study population, thus, showing the patients in their series to be older than in present study. Similarly, a study done on Indian population by us in 2016 showed that prevalence of diabetic retinopathy is significantly higher in men (68.5%) than in women and in those who were 50-70years of age (75.5%). [20]

40% had diabetes <10 years followed by 30% having diabetes from last 10-20 years. 70% patients had grade 0 micro-albuminuria. 55% patients had total cholesterol level at borderline. Proportion of Group I (No retinopathy) was higher in younger patients. Another statistically significant association was found between the severity of retinopathy and duration of diabetes ($p < 0.001$). A statistically significant association between microalbuminuria grade and severity of retinopathy was observed ($p < 0.001$). It was observed that in general, prevalence as well as severity of diabetic retinopathy increased significantly with increasing duration of diabetes. This finding eventually correlates well with the observations of other clinical studies [19,21,22] as well as population studies [23] which have laid emphasis that early onset of diabetes (≈ longer duration of diabetes) poses increased risk for diabetic retinopathy in general and that in patients with microalbuminuria in particular. We also conducted a study in past in which we found that albuminuria was significantly higher in our patients with diabetic retinopathy than in those without retinopathy. [24]

Proportional difference in severity of retinopathy in patients with different total cholesterol levels was found to be statistically significant ($p = 0.001$). Hyperlipidemia is regarded as one of the major factors responsible for diabetic retinopathy apart from hyperglycemia and hypertension. [25] A significant association between retinal hard exudate secretion and elevated serum lipid levels has also been reported. [6,26]

Conclusion

Duration of diabetes and microalbuminuria have been found to be the independent risk factors for diabetic retinopathy, but serum cholesterol levels did not show an independent role in our study. The findings in present study endorsed the view that microalbuminuria poses a risk for diabetic retinopathy which is affected by duration of diabetes, level of glycemic control and lipid levels.

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