WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 8, 1888-1894. Research Article ISSN 2277– 7105

STUDY OF THE RISK FACTORS FOR THE DEVELOPMENT OF RETINOPATHY IN TYPE 2 DIABETIC PATIENTS WITH AND WITHOUT FAMILY HISTORY

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Article Received on
26 May 2015,

Revised on 21 June 2015,
Accepted on 14 July 2015

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ABSTRACT

Diabetic retinopathy (DR) is one of the most common and specific complications of type 2 diabetes mellitus (T2DM).[1-3] It is estimated that almost half of the patients with T2DM have some degree of retinopathy at any given time and 75 % of T2DM develop DR after 15 year duration of diabetes.[4,5] Even though visual morbidity from diabetes is a significant public health problem, this is largely preventable and treatable if managed with timely intervention, and thus the quality of life can be preserved. Hence it is important to precisely identify the risk factors for the development and progression of DR. Though risk factors of DR such as duration of diabetes, glycemic control, hypertension and dyslipidemia are extensively studied, other incompletely defined factors also may be involved in the development of complications because many people with long standing diabetes never develop any complications like nephropathy or retinopathy.[5] A few previous studies in the Western population investigated the role of heredity in the development and progression of DR.[6] Very few data are available from the Indian subcontinent.[7] This study examined the role of family history in the prevalence and severity of DR and, analysed whether there is any difference in the risk factor pattern like hyperglycemia, Hb A_1C, microalbuminuria, dyslipidemia and obesity in patients with DR in relation to family history.

KEY WORDS: Diabetic retinopathy, family history, microalbuminuria, hyperglycemia, HbA_1C, dyslipidemia, obesity.

INTRODUCTION

The prevalence of chronic, non-communicable diseases is increasing at a frightening rate. Diabetes with its devastating complications is rapidly emerging as a global health problem that threatens to assume a pandemic level by 2030 by involving 366 million population.[1] In India an epidemic increase in T2DM has been reported by the World Health Organization.[2] T2DM is a leading cause of morbidity and mortality due to its macro vascular and micro vascular complications. Diabetic retinopathy (DR) is one of the most common and specific complications of T2DM [3]. It is estimated that almost half of the patients with T2DM have some degree of retinopathy at any given time and 75 % of T2DM develop DR after 15 year duration of diabetes.[4, 5] The UK Prospective Diabetes Study reported 35% prevalence of DR in diabetes population.[6] Visual morbidity from diabetes is a significant public health problem; however this is largely preventable and treatable if managed with timely intervention, the quality of life can be preserved hence it is important to precisely identify the risk factors for the development and progression of DR.

Many of the risk factors of DR are extensively studied and which emphasis the role of duration of diabetes, glycemic control, hypertension and dyslipidemia.[7] But other incompletely defined factors also may be involved in the development of complications because many people with long standing diabetes never develop any complications like nephropathy or retinopathy. A Few previous studies mention about the role of heredity in the development and progression of DR.[8, 9] Moreover, the data about the risk factors are mostly derived from the studies on Western population. The data available from the Indian subcontinent are almost scanty.[10] This study examined the role of family history in the prevalence and severity of DR and whether there is any difference in the risk factor pattern like hyperglycemia, Hb A_1C, microalbuminuria, dyslipidemia and obesity in patients with DR in relation to family history.

MATERIALS AND METHODS

Subjects

A cross-sectional study was undertaken on 200 known diabetic patients attending the Medicine OP Clinic of the Department of General Medicine, Government Medical College, Thrissur. Each patient was examined by the attending physician and detailed family history

about the diabetes and other basic demographic data were collected using a questionnaire. Informed consent was obtained from all study subjects. Anthropometric measurements like height, weight and body mass index (BMI) were carried out using standard techniques.[8] Blood pressure (BP) was recorded twice (5 min apart) in the sitting position in the right arm to the nearest 2 mm Hg with a mercury sphygmomanometer and the mean was taken as the final reading. Hypertension was diagnosed in subjects who were on anti-hypertensive medication or had systolic BP ≥140 mmHg or diastolic BP ≥ 90 mmHg.[9]

Methods

A fasting blood sample of 8 ml was obtained after an overnight fast of 8 hrs. by venipuncture for fasting blood glucose, lipid profile, glycated hemoglobin (HbA_1C) and, a 90-minutes post prandial sample was obtained after a standard South Indian breakfast, for investigations like hyperglycemia, HbA_1C, microalbuminuria, dyslipidemia and obesity. Fasting urine samples were also collected for microalbumin determination. Estimation of plasma glucose and serum lipids were carried out in EM 360 Fully Automated Biochemistry Analyser of M/s. Erba-Manneihm utilizing the kits, calibrators and controls supplied by M/s. Transasia Diagnostics, Mumbai. Hb A_1C was estimated by column chromatography. Low-density lipoprotein (LDL-C) cholesterol was calculated using the Friedewald formula. Microalbumin concentration was measured using an immuno turbidimetric assay. The diagnostic criterion for macroalbuminuria was albumin excretion ≥300 mg/g creatinine.[10]

A comprehensive ocular examination was carried out in all study subjects by an Ophthalmologist. The patients were categorized with a score of 0 to 5 according to the degree of their retinopathy as follows: 0-No retinopathy, 1-Mild non-proliferative diabetic retinopathy (NPDR), 2-Moderate NPDR, 3-Severe NPDR, 4-Very severe NPDR and 5-Proliferative diabetic retinopathy (PDR). Statistical analyses were done using Chi square test and two-tailed, independent ‘t’ test using SPSS version 17.0 software program.[11]

RESULTS

The study population in the present study constituted almost equal number of males and females. There was no statistically significant difference between the family histories of diabetes in both sexes. In this study, it was noticed that the incidence of development of DR is less in patients without family history.

Table 1: Incidence of DR in T2DM Patients with and without Family History.

Family History	No DR	Mild DR	Moderate DR	Severe DR	PDR
With Family History(N=140)	27 (13.5%)	50 (25%)	60 (30%)		3 (1.5%)
Without Family (N= 60)	51 (25.5%)	7 (3.5%)	2 (1%)	0 (0%)	0 (0%)

Table 2: Age and Gender-wise Distribution of T2DM Patients with and without Family istory

Family History	Gender		Age Groups	
		41-50 yrs.	51-60yrs.	61-70yrs.
With (N=140)	Men	18	27	25
	Women	22	34	14
Without (N= 60)	Men	10	10	9
	Women	11	12	8

Out of 200 patients, 60 patients were without family history and 140 patients with family history. Out of 140 (80.7%) 113 developed DR against 9 (15%) out of 60 patients in the group without family history of T2DM ($p<0.0001$).

Table 3: Gender-wise Distribution of T2DM Patients with and without Family History.

Sex	Without family history of Diabetes	With family history of Diabetes	Total
Male	29 (14.5%)	70(35%)	99
Female	31(15%)	70(35%)	101
Total	60	140	200

Table 4: Age-wise Distribution of T2DM patients with and without Family History

Age	With family history of Diabetes	Without family history of Diabetes	Total
40-50	40 (28.5.5%)	21 (34.6%)	61
51-60	61(43.57%)	22 (36%)	83
61-70	39 (27.8%)	17 (26.6%)	56
Total	140	60	200

Table 5- Comparison of the Clinical and Biochemical Characteristics of T2DM patients (Mean ± SD) using the Student's "t" Test

Variables	No DR	DR	p value
Age	53.10 ± 9.34	56 ± 9.4	0.018
BMI	24.05±3.15	24.45±2.95	NS
FBG	145.14 ± 38.86	171.10 ±56.77	0.0001
PPBG	179.63 ± 56.27	206.47± 69.17	0.005
HbA1C	7.72±1.78	8.58 ± 1.92	0.002
Microalbumin	26±49.5	137.05 ±81.47	0.001
TC	222.63±44.38	230.62±49.82	NS
HDL-C	58.5 ±16.95	52.44±14.51	0.008
LDL-C	131.05±42.17	143.43±46.63	<0.05
TG	165.40 ±58.69	173.77±62.12	NS

ApoA1	136.72 ± 35.33	147.28 ±66.07	NS
ApoB	112.72 ± 45.87	109.95±43.04	NS

In patients without family history 78% had mild DR and none had severe DR or PDR where as 54.4% of patients showed moderate to severe PDR and PDR.A total of 122 patients had DR which constitutes 61%. There is a significant difference between the groups with DR and without DR in the risk factor pattern.

DISCUSSION

In the present study, 200patients with T2DM were studied out of which 61% had DR. Out of these, 140 patients were having a family history of diabetes for the first degree relatives. Previous studies from India reported prevalence of DR ranging from 17.6-26.8%.[12, 13] The finding from our study is comparable with the reports from Liverpool Diabetes Eye Study (33.6%) and Diabetic Eye Disease in Tayside-Sctotland study (55.5%). The higher percentage of DR in the present study may be explained by strong genetic component in the etiology of T2DM and its complications. About 92%of patients with DR had a family history of diabetes for the first degree relative. The severity of DR was also found to be associated with family history. Majority (77.8%) of patients without family history was in the mild DR group and none had severe DR or PDR. But in patients with family history, moderate to severe DR accounted for 53.1% and PDR for 2.7%. Previous studies on parental influence on T2DM in the off springs observed a younger age of onset of T2DM and a greater chance of developing later complications.[14-17] The other findings on the major risk factors for the development of DR are consistent with previous studies. The role of glycemic control indicated by FBG, PPBG and HbA_1C is well recognized. Our study also shows a significant association between DR and glycemic control. But contrary to the previous studies, the duration, gender and blood pressure do not show significant association with DR. Dyslipidemia as an additional risk factor had been attempted in several studies but results were inconsistent. The preset study observed a significant association between HDL-C and LDL-C but not with TC, TG, apo-A and apo-B. Role of micro-albuminuria as a risk factor is also a matter of dispute.[18-20] The present study is in favour of micro-albuminuria substantiating the fact that urinary albumin is a marker of generalized vascular involvement in T2DM.

CONCLUSIONS

In the present study, a significant association between the prevalence and severity of DR with family history was found. Hence a more prudent control of other risk factors like glycemic

indices, dyslipidemia and micro-albuminuria may be advised for diabetic patients with family history as they are at greater risk for the development and progression of DR.

ACKNOWLEDGEMENTS

The authors acknowledge the invaluable help from Dr. Sudha V., Associate Professor, Department of Ophthalmology and Dr. Andrews M.A., Professor, Department of Medicine, Govt. Medical College, Thrissur in the completion of the study. Thanks to the technicians and other laboratory staff who extended assistance in laboratory investigations. Due acknowledgements are to all staff in the Department of Ophthalmology and all subjects who participated in the study.

FUNDING

This study was funded by the State Board of Medical Research, Kerala & Institutional Research Committee, Govt. Medical College, Thrissur.

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