

Research Article**Prevalence of Diabetic Retinopathy and Correlation with Systemic Risk Factors
in Type 2 Diabetes Mellitus in a Tertiary Care Hospital****D. Baba, V. Muthu krishnan, Sandeep Bhaskaran, Pranav S Kumar, R. Poovitha,**

Sri Lakshmi Narayana Institute of Medical Sciences (SLIMS), Kudapakkam, Puducherry, India

***Corresponding author**

V. Muthu Krishnan

Email: muthu2308@yahoo.co.in

Abstract: The objective of the study is to assess the prevalence of diabetic retinopathy and determine the correlation of incidence and severity of retinopathy with systemic risk factors in type 2 diabetes mellitus. 500 subjects of both sexes, with the mean age of 55 ± 8 years, with type 2 diabetes mellitus were included in the study. Patients were screened for presence of associated risk factors including duration and control of hyperglycemic status, hypertension, hyperlipidemia, HbA1C, nephropathy, neuropathy and anemia. Ophthalmoscopic examination was performed after pupillary dilatation and staging of diabetic retinopathy is done. 334 out of 500 patients (66.8%) had diabetic retinopathy and the prevalence was higher in elderly above 60 years and those with severe grades of systemic risk factors. Amongst the 1000 eyes studied, 573 were classified as non-proliferative diabetic retinopathy (NPDR) and 33 as proliferative diabetic retinopathy (PDR). Prevalence of mild non-proliferative, moderate non-proliferative, severe non-proliferative, very severe non-proliferative and proliferative diabetic retinopathy were 14%, 41.8%, 30.3%, 8.2% and 5.4% respectively. A significant association was observed between the duration of diabetes and the presence and severity of diabetic retinopathy. Prevalence of anemia, nephropathy, hyperlipidemia and peripheral neuropathy in patients with retinopathy was 42.5%, 12.2%, 75.4% and 9.3% respectively. Diabetic retinopathy and systemic complications run parallel in most patients. Prevalence and severity of diabetic retinopathy was more in patients with longer duration of diabetes and with more systemic complications. Hyperlipidemia is a major marker for retinopathy and these patients need ophthalmic evaluation at the earliest.

Keywords: Diabetic retinopathy, nephropathy, hyperlipidemia, neuropathy, hypertension, systemic complications.

INTRODUCTION:

Diabetes mellitus is a group of metabolic disorders producing hyperglycaemia [1]. The globally estimated number of diabetic patients is around 150 million. This prevalence rate (about 5.4%) is predicted to double by 2025, with most number of cases being expected in China and India [2]. The expected number of diabetic patients is to rise from 171 million in 2000 to 366 million in 2030 [3].

Diabetic retinopathy is found to be the leading cause for acquired blindness and one of the leading causes of visual deficit in the working population of both developed and developing countries [4]. It is the sixth cause of blindness in India and is increasing day by day [4]. Indians are also susceptible to the major complications related to diabetes like coronary artery disease, neuropathy, nephropathy and retinopathy. The important risk factors for the high prevalence of diabetes include high familial aggregation, central obesity, insulin resistance and lifestyle changes due to urbanization [5, 6, 7]. Prevalence of the complications is

higher in lower socio-economic groups due to lack of good control of diabetes and hypertension and also due to behavioral factors [7].

The direct and indirect costs involved in the treatment of the chronic disease especially when associated with the vascular complications are enormous. In order to reduce the high morbidity and mortality and also to reduce the cost burden to the patients and to the society, urgent preventive measures must be undertaken [7]. The presence of diabetic retinopathy may indicate the development of systemic complications. Early diagnosis and treatment of diabetic retinopathy is important for prevention of blinding complications. The objectives of the study were to estimate the prevalence of diabetic retinopathy and to determine the correlation of systemic risk factors with retinopathy.

MATERIALS AND METHODS:

This study was approved by the institutional ethics committee. The diabetic patients referred to the

ophthalmology department of the tertiary hospital were included in the study. Type II diabetic patients including new and review cases (diagnosed according to ADA criteria) were recruited into the study for a period of 1 year. Informed consent was obtained from all patients. Clinical data of all patients which included age, sex and duration of diabetes were obtained from the medical records and direct patient interview. Patients of all age groups and both sexes diagnosed with Type II diabetes mellitus were included in the study. Subjects with type 1 diabetes mellitus, secondary diabetes and gestational diabetes were excluded.

Diabetic patients were diagnosed by blood sugar (fasting & post prandial) examination. Blood samples were collected into fluoride oxalate and EDTA bottles for fasting blood glucose (FBG), post prandial blood glucose (PPBG), serum creatinine, blood urea, hematocrit, hemoglobin concentration, HbA1C and lipid profile measurements. Diabetes was diagnosed by participant's self-report, fasting blood sugar level >126mg/dl, post prandial >155mg/dl and HbA1C values > 6.5%. The condition was confirmed by doing urine, blood sugar examination, and dilated fundus examination according to the criteria of American

Academy of Ophthalmology. Diagnosis was established and graded according to Early Treatment of Diabetic Retinopathy Study (ETDRS) criteria. Blood pressure was measured using the sphygmomanometer. The presence of anemia was defined by a hemoglobin level < 13.0 g/dL in men and <12.0 g/dL in women based on definition of World Health Organization (WHO) [18]. Hyperlipidemia was noted when total cholesterol was >200mg/dl. Blood urea levels >45mg/dl and serum creatinine >1.6mg/dl were considered to have nephropathy. Data was collected and analyzed with the help of a proforma for each patient including name, age, sex, duration of diabetes, treatment received and compliance, ocular and systemic factors mentioned above.

RESULTS:

With the above mentioned ranges, the result was calculated and analyzed by using Correlation test and "R" value. Out of 500 patients, 334 were diagnosed with diabetic retinopathy. Hence out of 1000 eyes, 573 were classified as non-proliferative diabetic retinopathy (NPDR) and 33 as proliferative diabetic retinopathy (PDR).

Table 1- Distribution of patients according to duration of diabetes mellitus and grades of diabetic retinopathy

DUARATION OF DIABETES MELLITUS	GRADE OF DIABETIC RETINOPATHY						TOTAL
	MILD NPDR	MODERATE NPDR	SEVERE NPDR	Very severe NPDR	Early PDR	High Risk PDR	
<1 year	13	59	10	-	-	-	82
1-5 YEARS	59	103	77	18	-	-	257
5-10 YEARS	13	33	40	19	8	2	115
>10YEARS	3	11	21	14	19	-	68
TOTAL	88	206	148	51	27	2	522

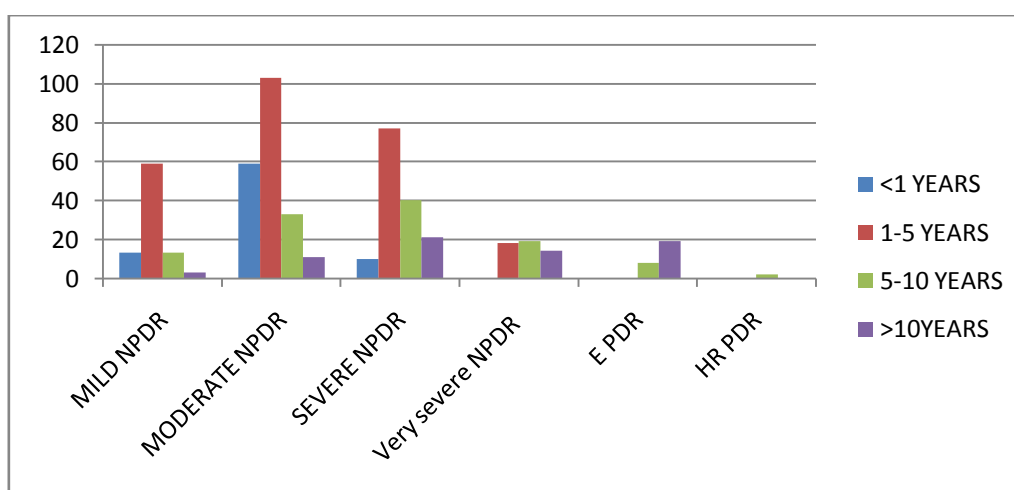


Fig 1: Correlation of diabetic retinopathy with duration

NPDR – Non Proliferative Diabetic Retinopathy, PDR – Proliferative Diabetic Retinopathy
E PDR – Early PDR, HR PDR- High Risk PDR

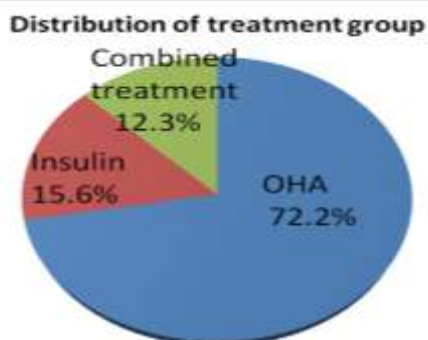


Fig 2: Distribution of patients based on type of anti-diabetic treatment
OHA – Oral Hypoglycemic Agents

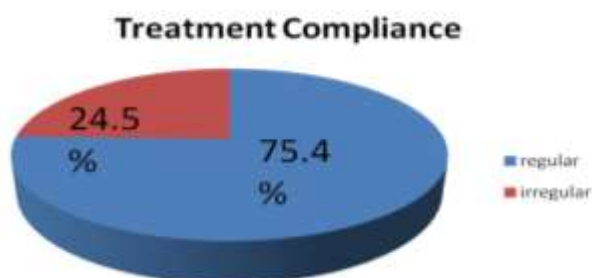


Fig 3: Correlation of diabetic retinopathy with patient compliance

Table 2: Correlation of diabetic retinopathy with glucose levels

Average glucose levels of different categories				
	Mild NPDR ($\bar{x} \pm \sigma$)	Moderate NPDR ($\bar{x} \pm \sigma$)	Severe NPDR ($\bar{x} \pm \sigma$)	PDR($\bar{x} \pm \sigma$)
Fbs	150.9±59.5	155.11±70.4	168.8±76.1	193.55±71.5
Ppbs	240.6±99.4	251.4±104.6	270.52±102.1	286.96±88.6
R value	0.735	0.826	0.782	0.733
P value	0.000	0.000	0.000	0.000

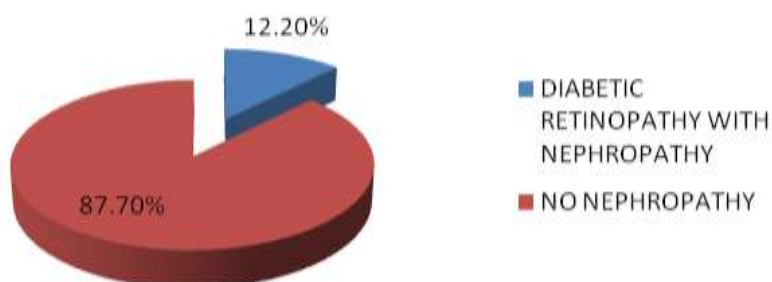


Fig 4: Correlation between diabetic nephropathy and retinopathy

Table 3: Distribution of patients according to blood urea, serum creatinine and grades of diabetic retinopathy

	GRADE OF DIABETIC RETINOPATHY					TOTAL
	MILD NPDR	MODERATE NPDR	SEVERE NPDR	Very severe NPDR	PDR	
Urea (mg/dl)(>45mg/dl)	4	12	18	9	3	46
Creatinine (md/dl)	6	20	15	8	4	53
	10	32	33	17	7	99
Both urea & creatinine	2	10	12	5	2	31

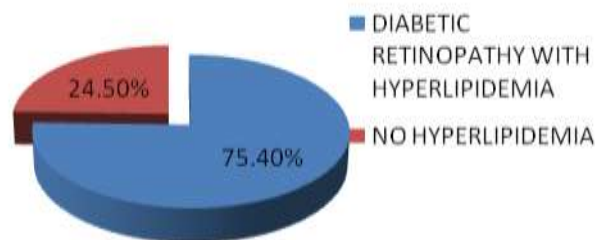


Fig 5: Correlation of diabetic retinopathy with hyperlipidemia

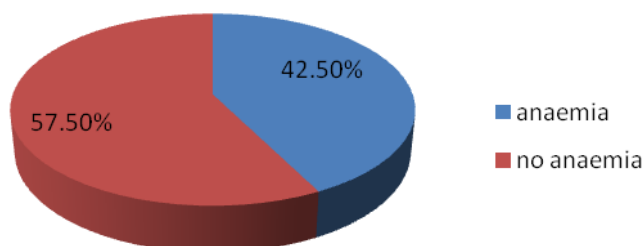


Fig 6: Correlation of diabetic retinopathy with anemia

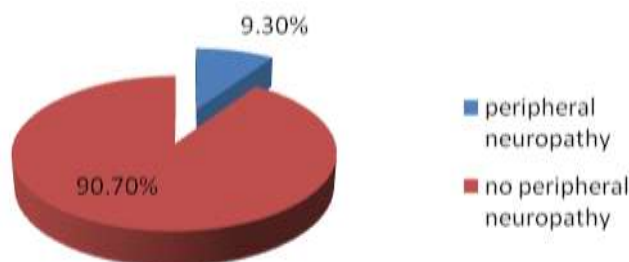


Fig 7: Correlation of diabetic retinopathy with peripheral neuropathy

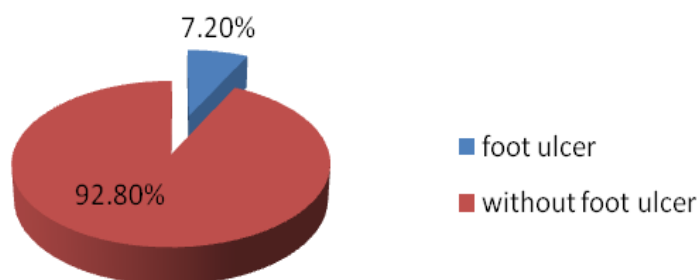


Fig 8: Correlation of diabetic retinopathy with foot ulcer

DISCUSSION

Diabetic retinopathy is found to be the leading cause for acquired blindness and one of the leading causes of visual deficit in the working population of both developed and developing countries [4]. The prevalence of diabetic retinopathy was 66.8% in type 2 diabetic patients. This was significantly higher with longer duration of diabetes and severe systemic risk factors. This study provides an improved estimate regarding diabetes mellitus and its long term complications.

Many people were diagnosed as glucose intolerance rather than diabetes mellitus since they did not match

the national diabetes data group criteria [8]. Our study provides a comprehensive assessment of the frequency and staging of retinopathy. We found 66.8% of retinopathy among 500 diabetic patients. Similarly Dyck *et al.*; in their study observed 79% of the IDDM patients and 55% NIDDM patients had retinopathy [9, 10]. The differences obtained may be due to use of different criteria for diabetes mellitus, a different geographic location or failure to detect all diabetic cases in the population. It is commonly inferred that the prevalence of diabetes mellitus and its complications is greatly underestimated because of the many undetected patients in the community [4]. Our data, based on a

patient population that is almost completely surveyed for hyperglycemia, does not support such an underestimate.

Percentages of mild non-proliferative, moderate non-proliferative, severe non-proliferative, very severe non-proliferative and proliferative diabetic retinopathy were 14%, 41.8%, 30.3%, 8.2%, 5.4% respectively. This was also studied in the Rochester diabetic neuropathy study where the percentages of early non-proliferative, late non-proliferative, proliferative type were 16%, 24%, 3% respectively [9, 10]. Klein *et al* found prevalence values similar to those found in this study [11, 12, 13]. Our estimate of the frequency of nephropathy, on the other hand, is suboptimal since we did not systematically assess 24 hour urine albumin levels. Diabetic nephropathy, an important complication of long standing diabetes mellitus, has been extensively studied [14, 15].

The incidence of anemia in our study (42.5%) may be due to smaller sample size, which was largely those who had poorly controlled diabetes, who may be susceptible to impaired erythropoietin production due to diabetic neuropathy. In contrast, prevalence of 20% has been reported in diabetes with renal insufficiency [16, 17].

A reason for the difference is that we used the national diabetes data group criteria for the diagnosis of diabetes mellitus, unlike other studies [4]. Many people were diagnosed as glucose intolerance rather than diabetes mellitus since they did not match the national diabetes data group criteria [8]. We observed a strong association between the duration of diabetes and the onset of retinopathy. 56.3% acquired retinopathy in the first 5 years after diagnosis.

Patients with less treatment compliance had a higher rate of retinopathy (75.4%). On comparison with other systemic risk factors it was found to have a higher correlation with the progression of retinopathy.

Hyperlipidemia is an important risk factor for development of retinopathy in diabetes. Our study shows a prevalence of 75.4% which was also observed in A Ramachandran *et al.*; in their study which showed a prevalence of 57% in males and 5% in females [18]. This difference may be due to lesser number of patients recruited in our study.

It is a proven fact that diabetic autonomic neuropathy is a complication of poor glycemic control. It is established that diabetic polyneuropathies can cause a high morbidity and even death. Most diabetic patients develop these complications in due course of time, and amongst all neuropathies, diabetic varieties are among the most frequent and disabling [19, 20]. As noted by

Lundbeck, Melton and Dyck, the data underlying such assumptions are of poor quality. We assume that the rate of problematic cases of neuropathy might be somewhat higher if premature death had not occurred among Rochester diabetic patients. The prevalence of peripheral neuropathy among diabetics was 9.3% as compared to 6% of NIDDM in Rochester study [21, 22].

Other factors which have been reported to increase the risk of anemia include systemic inflammation; damage to renal architecture produced by chronic hyperglycemia and formation of advanced glycation end products and depressed androgen levels induced by diabetes [18, 23, 24]. It is speculated that these conditions may be aggravated in poorly controlled diabetes than in controlled diabetes.

CONCLUSION:

The study shows that patients with longer duration of diabetes, uncontrolled hyperglycemia and those with associated systemic manifestations have a higher prevalence and severity of diabetic retinopathy. Diabetic retinopathy and systemic complications appear to be strongly associated. Hyperlipidemia is a major marker for retinopathy and these patients need ophthalmic evaluation at the earliest. Prevalence and severity of diabetic retinopathy was more with the increasing duration of diabetes and with systemic complications like nephropathy and neuropathy. Further studies need to be undertaken to strengthen the etiological relationship. However, it should be emphasized that examination of systemic risk factors should be an integral part of the assessment of diabetic eye disease.

REFERENCES:

1. Alvin CP; Harrison's Principles of Internal Medicine. 18th Edition, The McGraw-Hill publishers, United States of America, 2968.
2. Diet, nutrition and the prevention of chronic diseases. World Health Organ Tech Rep Ser. 2003;916:i-viii, 1-149, back cover
3. Wild S, Roglic G, Gren A, Sicree R, King H; Global prevalence of Diabetes. Diabetes Care 2004; 27(5):1047-1053.
4. Mohan V, Shanthirani S, Deepa R, Premalatha G, Sastry NG, Saroja R; Intra-urban differences in the prevalence of the metabolic syndrome in southern India -- the Chennai Urban Population Study (CUPS No. 4). Diabet. Med., 2001, 18(4), 280-287
5. Viswanathan M, McCarthy MI, Snehalatha C, Hitman G, Ramachandran A; Familial aggregation of type 2 (non-insulin-dependent) diabetes mellitus in south India; absence of excess maternal transmission. Diabet. Med, 1996; 13(3): 232-237.
6. Mohan V, Sharp PS, Cloke HR, Burrin JM, Schume B, Kohner EM; Serum immuno reactive insulin responses to a glucose load in Asian Indian

- and European type 2 (non-insulin-dependent) diabetic patients and control subjects. *Diabetologia*, 1986; 29(4): 235–237.
7. Ramachandran, A, Snehalatha C, Latha E, Satyavani K, Vijay V; Clustering of cardiovascular risk factors in urban Asian Indians. *Diabetes Care*, 1998; 21: 967–971.
 8. Baynes JW, Bunn HF, Goldstein D, Harris M, Martin DB, Peterson C *et al.*; National diabetes data group. Report of the expert committee on glycosylated hemoglobin. *Diabetes care*, 1984; 7(6):602-606.
 9. Melton LJ, Dyck PJ; Epidemiology. In: Dyck PJ, Thomas PK, Asbury A, Winegrad AI, Porte D, eds. *Diabetic neuropathy*, Philadelphia: W.B. Saunders, 1987:27-35.
 10. Lundbeck K; Introduction, In: Dyck PJ, Thomas PK, Asbury A, Winegrad A, Porte D, eds. *Diabetic neuropathy*. Philadelphia: W.B. Saunders, 1987:1-2.
 11. Klein R, Klein BEK, Moss SE, David MD, Demets DL; The Wisconsin epidemiological study of diabetic retinopathy, The prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmology*, 1984; 102:527-532.
 12. Klein R, Klein BEK, Moss SE, David MD, Demets DL; The Wisconsin epidemiological study of diabetic retinopathy, The prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmology*, 1984; 102:520-526.
 13. Klein R, Davis MD, Moss SE, Klein BEK, Demets DL; The Wisconsin epidemiologic study of diabetic retinopathy. A comparison of retinopathy in younger and older onset diabetic persons. *Adv Exp Med Biol*, 1985; 189: 321-325.
 14. Kahn HA, Bradley RF; Prevalence of diabetic retinopathy. *Br J Ophthalmology*, 1975; 85:28-34.
 15. Kahn HA, Liebowitz, Ganley JP; The Framingham eye study, I. outline and major prevalence findings. *Am J Epidemiol*, 1977; 106(1):769-776.
 16. Thomas MC, MacIsaac RJ, Tsalamandris C, Molyneaux L, Goubina I, Fulcher G *et al.*; The burden of anemia in type 2 diabetes and the role of nephropathy: A cross sectional audit. *Nephrol Dial Transplant*, 2004; 19(7): 1792-1797.
 17. Bonakdaran S, Gharebaghi M, Vahedian M; Prevalence of anemia in type 2 diabetes and role of renal involvement. *Saudi J Kidney Dis Transpl*, 2011; 22(2): 286-290.
 18. Cottone S, Lorito MC, Riccobene R, Nardi E, Mule G, Buscemi S *et al.*; Oxidative stress, inflammation and cardiovascular disease in chronic renal failure. *J Nephrol*, 2008; 21(2):175-179
 19. Ahmed AM, Hussein A, Ahmed NH; Diabetic autonomic neuropathy. *Saudi Med J*, 2000; 21(11): 1034-1037.
 20. Toyry JP, Niskanen LK, Mantyselä MJ, Lansimies EA, Uusitupa MI; Occurrence, predictors and clinical significance of autonomic neuropathy in NIDDM, Ten year follow-up from the diagnosis. *Diabetes*, 1996; 45(3): 308-315.
 21. Pirart J, Diabetic neuropathy: a metabolic or vascular disease? *Diabetes*, 1965; 14:1
 22. Pirart J; diabetic mellitus and its degerative complications: a prospective study of 4400 patients observed between 1947 and 1973. *Diabetes*, 1978; 1:168-188.
 23. Schuster SJ, Koury ST, Bohrer M; Cellular sites of extrarenal and renal erythropoietin production in anaemic rats. *Br J Haematol*, 1992; 81(2): 153-159.
 24. Andersson B, Marin P, Lissner L; Testosterone concentrations in women and men with NIDDM. *Diabetes Care*, 1994; 17: 405-411.