Analysis of Prevalence and Course of Diabetic Retinopathy and other Microvascular Complications in Diabetic Patients

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ABSTRACT

Introduction: Diabetes mellitus(DM) has emerged as the leading cause of adult blindness, end stage renal disease and non traumatic lower extremity amputations. Current research aimed to study the impact of microvascular complications with the duration of diabetes.

Material and Methods: Observational study considered on 100 Type 2 diabetic patients of age group 18-65 yrs, for a period of 1 year. Variables used to assess are History and duration of Type 2 Diabetes mellitus, Glycosylated haemoglobin(HbA1c) , Fasting blood sugar, Fundus evaluation, Diabetic Neuropathy Symptom score, Kidney function tests, Urine analysis and lipid profile.

Results: The prevalence and severity of diabetic retinopathy increased with increase in duration of Type 2 Diabetes mellitus. 92 % patients of the patients had diabetic retinopathy with duration of diabetes of 30 years. Majority of the patients had dyslipidemia. Diabetic neuropathy was assessed by Diabetic Neuropathy symptom(DNS) score showed mainly the scores of DNS 2 and 3. Lower scores were present among patients with Diabetes mellitus with duration $\leq$10 years. Higher levels of DNS scores were present among patients with HbA1c $\geq$ 6.5% compared to HbA1c < 6.5%. Diabetic Nephropathy (Microalbuminuria as well as Macroalbuminuria) was correlated with Diabetic Retinopathy. This relation revealed Macroalbuminuria became apparent in severe Non proliferative diabetic retinopathy.

Conclusion: Risk of microvascular complications is directly proportional to the duration of disease and develop in the sequence of Retinopathy, Neuropathy, and then Nephropathy in this study.

Keywords: Diabetes mellitus, Diabetic Retinopathy, Diabetic Neuropathy, Diabetic Nephropathy

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease characterized by an increased level of plasma glucose. Insulin, released from beta cells of pancreas has a key role in maintaining the plasma equilibrium of glucose. Insulin deficiency is responsible for type 1 and its resistance defines type 2. Diabetes affects all the parts of the body.

According to diabetes atlas (7th edition) the worldwide prevalence of diabetes is projected at 415 million (8.8%), which will rise to 642 million in the next 25 year[1]. In India, there are nearly 69.2 million people living with DM & it is predicted that number crosses 123.5 million by 2040[1]. Furthermore, globally around 193 million DM stay undiagnosed affecting them to the development of numerous long-term complications of untreated chronic hyperglycemia[1].

HbA1c had been currently recommended for the diagnosis of type 2 DM by leading diabetes organizations & by WHO[2]. Keeping the HbA1c level < 6.5% is crucial for decreasing the incidence of diabetic complications[2].

The complications are categorized into 2 main groups:- microvascular (Neuropathy, Nephropathy, and Retinopathy) macrovascular (Cardiovascular, Peripheral Arterial Disease, and Cerebrovascular) with long-term uncontrolled hyperglycemia.

The microvascular complications are important risk factor for developing disabilities.DM has emerged as the leading cause of adult blindness, end stage renal disease and non traumatic lower extremity amputations. Retinopathy and nephropathy are both related to endothelial dysfunction mediated microvascular complications of DM.

Objective of the study was to study the impact of microvascular complications with the duration of diabetes.

MATERIAL AND METHODS

This study is a cross sectional observational study considered on Type 2 diabetes mellitus patients. Patients were diagnosed as diabetes mellitus based on World Health Organization as follows[3] :

1. Fasting Plasma Glucose of 126 mg/dl or higher,
2. A 2- hour Post Prandial glucose of 200 mg/dl or higher during a 75 gram oral glucose tolerance test,
3. Random Blood Sugar of 200 mg/dl or higher
4. Glycosylated Hemoglobin (HbA1c) level of 6.5% or higher.

100 diabetc patients who attended the OPD and IPD of age group 18-65 yrs were included in the study. Variable that were assessed included History and duration of type 2 DM as well as Hypertension(if present), Random as well as Fasting blood sugar, HbA1c, Dilated fundus examination, Diabetic Neuropathy Symptom score, Urine analysis, Kidney function tests and Lipid profile. The microvascular

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complications were examined and managed by the Physician as well as Ophthalmologist. The patients were followed for the duration of 1 year.

Diabetic Neuropathy is assessed by DNS (Diabetic neuropathy symptom score)[4]. It is a four item validated score with high predictive value to screen for peripheral polyneuropathy in Diabetes mellitus.

Symptoms of –

1. Unsteadiness in walking
2. Numbness
3. Burning, aching pain or tenderness in legs /feet
4. Prickling sensations

The prescence of 1 symptom is scored as 1 point. Therefore Maximum scores are 4 points.

≥1 score → Positive for Polyneuropathy.

Diabetic Nephropathy is diagnosed by Prescence of Persistent Proteinuria > 0.5g/24 hours.

RESULTS

Distribution of patients: 100 patients were recruited for the study. 57 % were females and 43 % were males. Patients were also classified according to their Body Mass Index (BMI) [5]. Figure 2 reveals that majority (i.e, 56%) of the patients were overweight (BMI of 25.0 to <30). 41% patients were obese (BMI of 30 or higher) whereas only 3 % had BMI within normal range (18.5 to <25). 81% of type 2 diabetic patients were on Oral hypoglycaemic agents (OHA), and 16% were on Insulin injections, as evidenced in figure 3.

Lipid parameters of the patients were assessed according to the NCEP ATP III guidelines [6]. This study showed that dyslipidemia is very common in diabetic patients. 72 % patients had elevated Serum total Cholesterol(>200 mg/dl), 71 % had elevated Serum triglycerides (> 150 mg/dl), 25 % had low Serum HDL Cholesterol(<40 mg/dl) and 75 % had high Serum LDL Cholesterol (> 159 mg/dl).

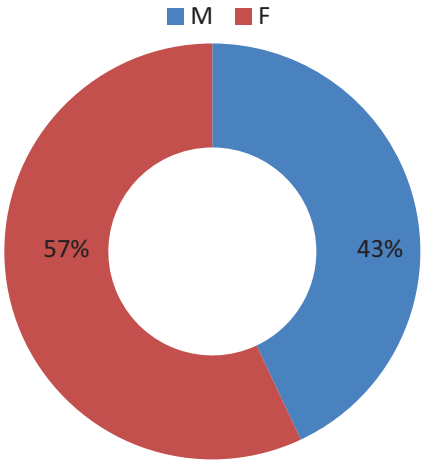


Figure-1: Distribution of patients based on sex

Retinopathy

Prevalence of Diabetic Retinopathy (DR) among Diabetics : As tabulated in Table 1, Diabetic retinopathy was present in 39 % of patients with Type 2 diabetes mellitus, of which 20 % patients developed diabetic retinopathy within 10 years whereas 92 % patients had diabetic retinopathy with duration

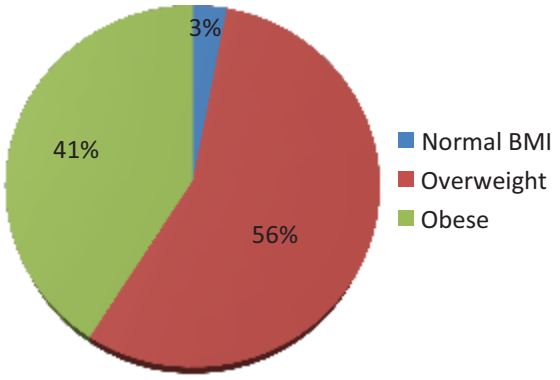


Figure-2: Distribution of patients based on BMI

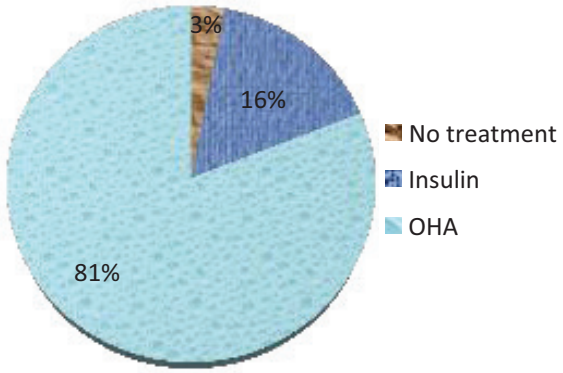


Figure-3: Distribution of patients based on type of treatment

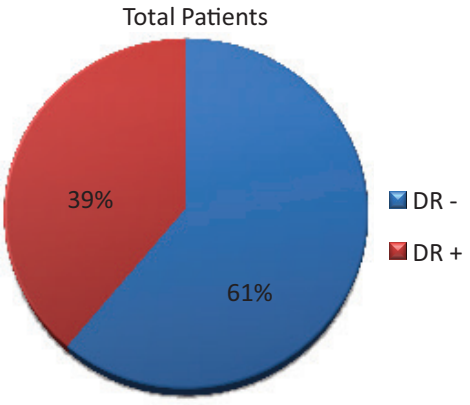


Figure-4: Prevalence Of Diabetic Retinopathy among Diabetics

DR +/-	Duration of DM				
	5 years	10 years	20 years	30 years	Total
DR -	8(100%)	36 (80%)	16 (47%)	1 (7%)	61
DR +	0 (0%)	9 (20%)	18 (53%)	12 (92%)	39
Total	8	45	34	13	100

Table-1: Distribution of cases according to duration of DM

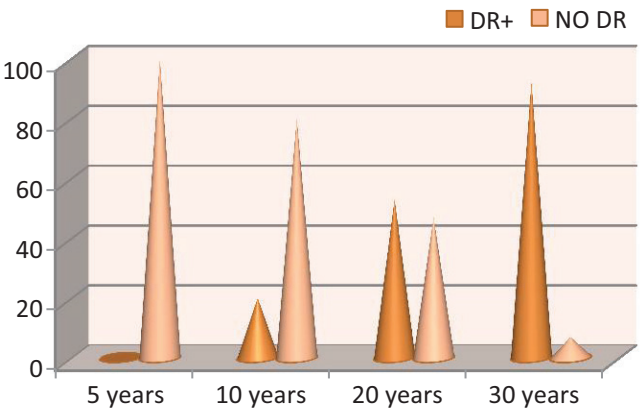


Figure-5: Prevalence Of Diabetic Retinopathy among Diabetics

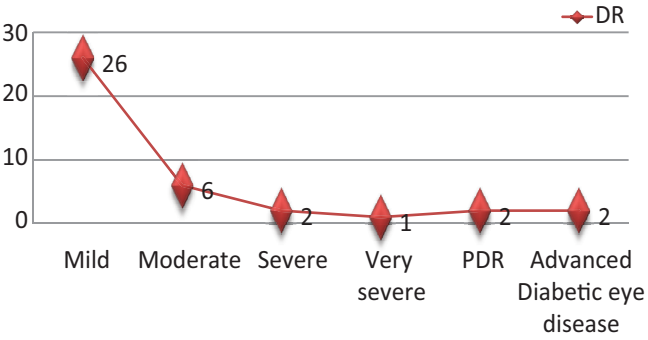


Figure-6: Prevalence Of Diabetic Retinopathy among Diabetics

of diabetes of 30 years. According to ETDRS staging[7] most patients had mild stage of diabetic retinopathy. Uncontrolled hyperglycaemic status leads to progression of diabetic retinopathy. Moderate Non Progressive Diabetic retinopathy has 26 % risk to develop Proliferative diabetic retinopathy within 1 year ,whereas Severe Non Progressive diabetic retinopathy has 50 to 75 % risk to develop Proliferative diabetic retinopathy during the course of 1 year. Sight threatening retinopathy (in the form of clinically significant macular edema) was present in 40 % of patients, Most of the eyes with diabetic macular edema had moderate NPDR-39.5% , followed by PDR(34.9%) and Severe NPDR

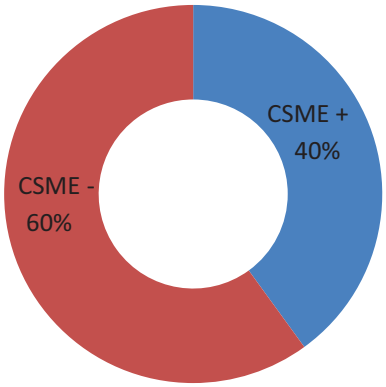


Figure-7: Prevalence Of "Vision affecting Diabetic Retinopathy"

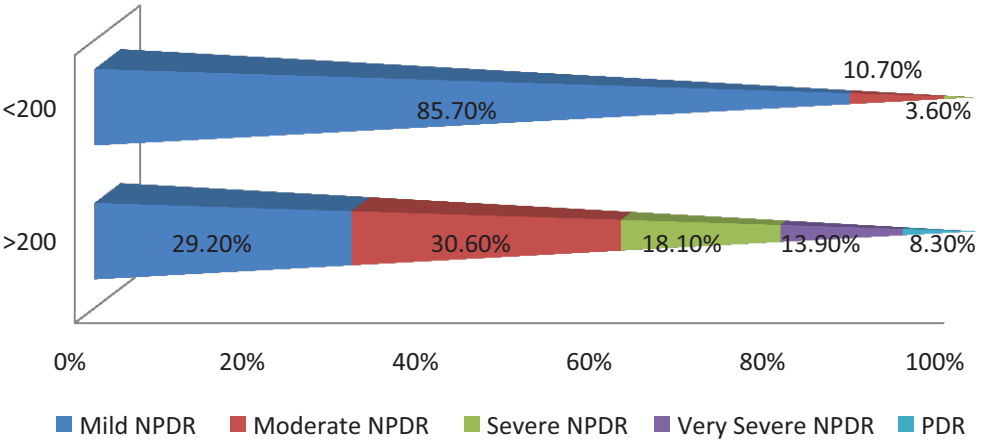


Figure-8: Correlation of DR staging and S. Cholesterol

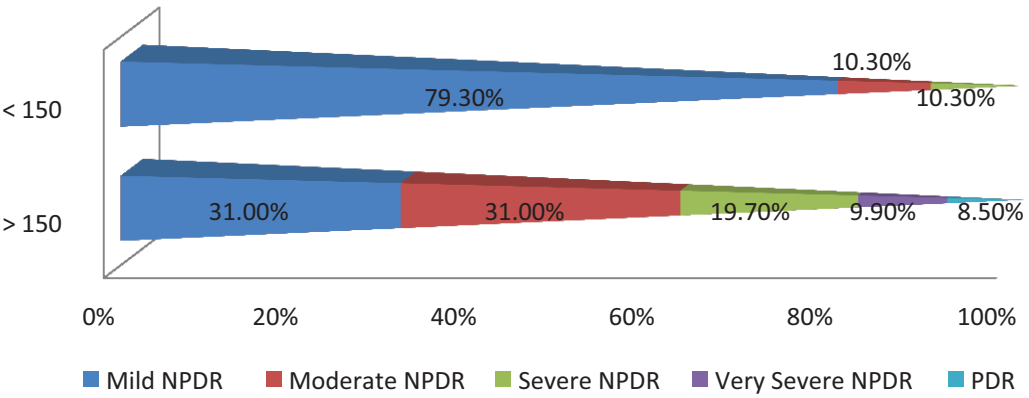


Figure-9: Correlation of DR staging and S. Triglycerides

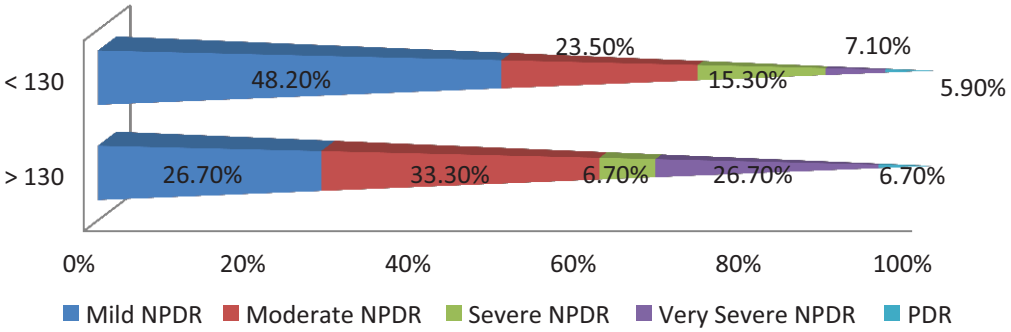


Figure-10: Correlation of DR staging and S. LDL

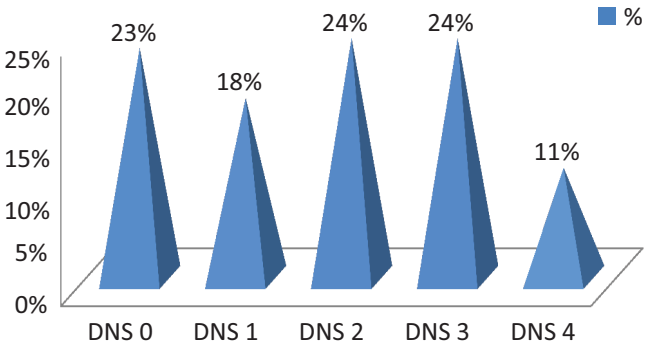
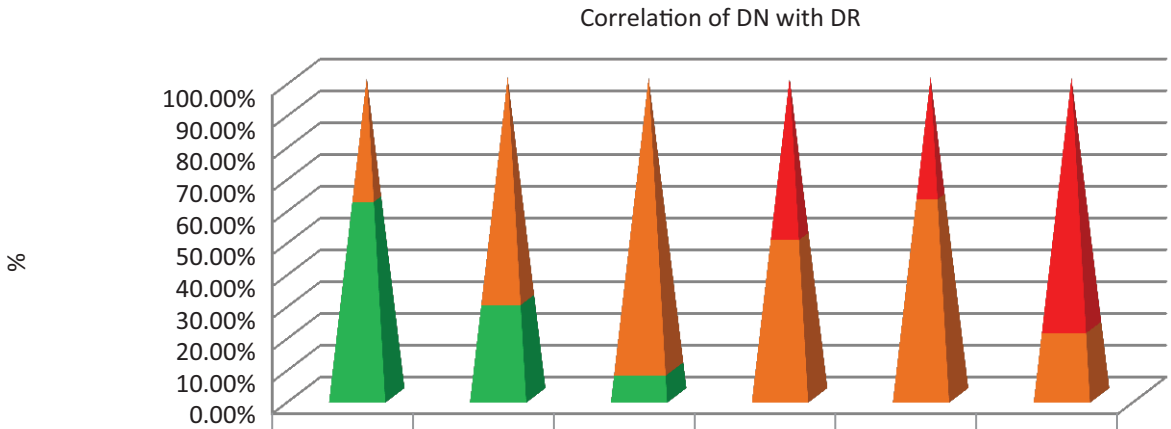


Figure-11: Prevalence Of Diabetic Neuropathy among Diabetics, assessed by DNS Scores



	DR -	mild NPDR	moderate NPDR	severe NPDR	Very severe NPDR	PDR
Macroalbuminuria	0%	0%	0%	50%	37.50%	78.60%
Microalbuminuria	38.30%	70%	91.70%	50%	62.50%	21.40%
Normal	61.70%	30%	8.30%	0%	0%	0%

Figure-12: Prevalence of Diabetic Nephropathy among Diabetics, and correlated with Diabetic retinopathy

(25.6%). This study showed the median duration of diabetes with CSME was 12 years with minimum duration of 4 years of diagnosis of diabetes. None of the patients with macular edema had mild diabetic retinopathy. This study showed the median duration of diabetes with CSME was 12 years with minimum duration of 4 years of diagnosis of diabetes mainly in moderate non proliferative diabetic retinopathy. Majority of the patients had dyslipidemia.

Correlation of lipid profile with diabetic retinopathy :

1. Serum Cholesterol (*Figure 8*) – 85.70% of diabetic patients with Normal serum cholesterol(<200mg/dl) had mild retinopathy, whereas 29.20% and 30.60% of diabetic patients with Elevated serum cholesterol(>200mg/dl) had mild and moderate diabetic retinopathy, respectively.
2. Serum Triglycerides (*Figure 9*) – 79.30% of diabetic patients with Normal serum triglycerides(<150mg/dl) had mild retinopathy, whereas 31.00% of diabetic

patients with Elevated serum triglycerides(>150mg/dl) had mild and moderate diabetic retinopathy.

3. Serum LDL (*Figure 10*) – 48.20% and 23.50% of diabetic patients with Normal serum LDL(<130mg/dl) had mild and moderate retinopathy, respectively; whereas 26.70% and 33.30% of diabetic patients with Elevated serum triglycerides(>130mg/dl) had mild and moderate diabetic retinopathy, respectively.

Neuropathy

As evidenced by Figure 11, Diabetic neuropathy, assessed by Diabetic Neuropathy symptom score[4] showed mainly the scores of DNS 2 and 3. Mean values of DNS scores were lower among patients with DM duration $\leq$ 10 years (1.76 $\pm$ 1.4) compared to patients with DM >10 years (2 $\pm$ 1.08). Higher levels of DNS scores were + among patients with HbA1c $\geq$ 6.5% compared to HbA1c < 6.5%.

Nephropathy

Diabetic Nephropathy (Microalbuminuria as well as Macroalbuminuria) was correlated with Diabetic Retinopathy, as demonstrated in figure 12. This revealed that in the diabetic patients those had diabetic retinopathy, 38.30% patients had microalbuminuria but none (0%) had macroalbuminuria. Macroalbuminuria became apparent in severe Non proliferative diabetic retinopathy. In patients with Proliferative diabetic retinopathy, 78.60% patients had Macroalbuminuria and only 21.40% had microalbuminuria.

DISCUSSION

Risk of microvascular complications of DM is directly proportional to the duration of disease and develops in the sequence of Retinopathy, Neuropathy, and then Nephropathy in this study. Diabetic retinopathy was present in 51% of the cases in the normoalbuminuria group. The study also reported that the prevalence of diabetic retinopathy was more with macroalbuminuria (58%).

Addressing the Systemic Risk Factors for development of DIABETIC RETINOPATHY

A. Blood Sugar Control – According to *DCCT*[8] *& UKPDS*[9] trials, for a 10 to 11% reduction in HbA1C, DR reduces by nearly 30%.
B. Blood Pressure Control – Hypertension commonly co-exists in diabetics and is considered an important confounding factor in the vascular complications of diabetes. In the present study, 42.4% of the cases were hypertensives. The proportion of hypertensives who had co- existing diabetic retinopathy was 37.3%. The association between severity of diabetic retinopathy and the co existence of hypertension was significant (p = 0.006) .According to *UKPDS trial*[9], 10% reduction of systolic BP reduces r/o DR by 10%. It was found that Systolic BP>140 increases risk of DR by 3 fold.
C. Lipid Lowering agents :– Statins and fibrates both have a role in reducing DR.
D. Managing Nephropathy :– In accordane with the DCCT[8] study – intensive treatment of DM decrease the incidence of microabuminuria by 39%, whereas UKPDS study[9] states that there is reduction of risk for the development of microalbuminuria by 30%, observed in the group intensively treated for hyperglycemia.
E. Managing Anaemia :– Haemoglobin less than 12 g/dl is a risk factor for DR.

CONCLUSION

Diabetic Retinopathy is among the earliest microvascular complication that affects the patients suffering from Diabetes mellitus. The risk of development of microvascular complications is more in patients with uncontrolled blood sugar levels. Therefore patients suffering from diabetes mellitus must undergo periodic dilated fundus examination to look for retinal vasculature changes induced by chronic hyperglycemic levels and oxidative stress. According to ETDRS[7], Patients who had not yet developed retinopathy must be followed annually for the fundus examination. Patients with mild and moderate grades of Non proliferative diabetic retinopthy must undergo dilated fundus examination within 12 months and 6 months, respectively. Patients with severe grades of Non proliferative diabetic retinopathy require close follow up of 2 to 4 months, whereas those with Proliferative diabetic retinopathy require extensive treatment and monthly follow up. Controlling the blood sugar levels along with the elimination of modifiable risk factors is the only preventive strategy to limit the progression of the disease.

Glycosylated haemoglobin (HbA1c) provides a sign of chronic glycemia, rather than being a test of glycemia at a single point of time. It provides a combined index of glycemia over the entire 120 day life span of the RBC. It can be conducted at any time of the day and does not need any extraordinary preparation, such as fasting. Therefore, intensive treatment of glycaemia aiming at HbA1c < 7% should be pursued as early as possible to prevent the development of complications. Early and regular follow up with tight glycemic control can improve the outcomes and prevent the risk of disability.

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