ORIGINAL RESEARCH

To Study Microvascular Complications and Its Correlation with Duration of Diabetes in Type 2 Diabetes Mellitus Patients in SN Medical College & Hospital, Jodhpur

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ABSTRACT

Background: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Most of the burden of T2DM is related to its micro and macro vascular complications.So this study is conducted for timely intervention to prevent these complications and to prevent further deterioration by applying measures to control chronic hyperglycemia.**Materials& Methods:** A hospital based cross sectional study done on 210 cases of type 2 diabetes mellitus in Upgraded department of medicine, SN Medical College & Hospital, Jodhpur during one year period. The T2DM group was divided into Group I (0-5 years), Group II (6-10 years) & Group III (>10 years) according to the duration of DM type2. Medical histories were obtained for all patients, including details of height, weight, and waist circumference. We also obtained fasting blood glucose (FBG), 2 hour post prandial blood sugar glycosylated hemoglobin (HbAlc), cholesterol lipid (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL),microalbuminurea, nerve conduction study and fundoscopy. Logistic regression would be done to predict microvascular complications on the basis of various independent predictors. The level of significance will be kept at 95% for all statistical analysis. **Results:** The mean age of study subjects was 58.38 years ranging from 35 to 86 years. The duration of Diabetes ranged from 1 to 22 years with a mean of 10.04 years. The proportion of Microvascular complications increased with increasing age and was highest in >70 years subjects. Patients in the 61-70 years age group had 95.4, 71.6 & 50.8 times higher risk of nephropathy, neuropathy & retinopathy respectively as compared to those under 40 years. The risk of microvascular complications was highest in patients with >10 years of DM. Microvascular complications were more common in patients with HbA1C ≥10% and gradually decreased in lower HbA1C values. Significant association of microvascular complications were seen only with age group and Duration of Diabetes ($P<0.05$ each). The risk of microvascular complications increased significantly with increasing Duration of DM. Though the proportion of microvascular complications increased with age, but it was not found to be an independent predictor.**Conclusion:**We concluded that early detection and treatment of these complications therefore plays a crucial role than glycemic control. Detecting these risk factors helps in correcting these at an early stage. Correlation between the various microvascular complications helps in better understanding of their pathogenesis and early control.

Keywords: Microvascular Complication, Duration of Diabetes, HbA1C, Type 2 DM

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INTRODUCTION

Diabetes is a syndrome characterized by chronic hyperglycemia and disturbance of carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretion and/or insulin action. The World Health Organisation (WHO) defines diabetes mellitus (DM) as: "a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Long term complications that affect retina, kidney and nervous system are termed as micro vascular complications.[1]

Type 2 diabetes mellitus (T2DM) is a global epidemic with an estimated worldwide prevalence of 6.4% (285 million) in 2010 that is forecast to rise to 7.7% (438 million) in 2030.[1] In addition 344 million people have

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impaired glucose tolerance (IGT) that is forecast to increase to 472 million by 2030.[2]

The health, social, and economic burden of T2DM is significant; patients with diabetes have a reduced life expectancy by 10-15 year[3] and the cost of diabetes was estimated to be 12% of the world's health expenditure in 2010.[2] Because of its increasing prevalence, T2DM (which accounts for 90% of all diabetes) presents a massive challenge to healthcare systems around the world.

The development of chronic complications is related to the duration of Diabetes Mellitus;however it may not reflect the true duration of disease, rather it reflects the time since diagnosis.[4]

Most of the burden of T2DM is related to its micro and macro vascular complications. Microvascular complications have a significant impact on morbidity, mortality and patients' quality of life. Diabetic retinopathy (DR) is one of the leading causes of blindness in the Western world. Diabetic nephropathy can lead to end-stage renal disease, which requires dialysis and/or renal transplantation and increases the risk of vascular disease. Diabetic neuropathy (DN) results in the development of foot ulcers that can result in amputations, sexual dysfunction and many other unpleasant symptoms in addition to increased mortality. The presence of microvascular complications has been shown to have a negative impact on patient's quality of life.[5-7] As a result, it is not surprising that there is great interest in improving understanding of the microvascular complications in patients with diabetes in order to develop effective strategies to treat, and ideally prevent, the development of such complications.

Studies from different centres agreed that microalbuminuria is a strong predictor of subsequent development of overt diabetic nephropathy.[3] Diabetic nephropathy is a clinical hall mark of microangiopathy.[8] The most Common form of diabetic neuropathy is distal symmetric polyneuropathy involving sensory, motor and autonomic nerve fibres.[9,10] Diabetic retinopathy is leading cause of blindness in developing country.[11]It can be broadly categorized in to Non Proliferative and Proliferative Diabetic Retinopathy.[12]So this study is conducted for timely intervention to prevent these complications and to prevent further deterioration by applying measures to control chronic hyperglycemia.

MATERIALS & METHODS

A hospital based cross sectional study done on 210 cases of type 2 diabetes mellitus in Upgraded department of medicine, SN Medical College & Hospital, Jodhpur during one year period.

Inclusion Criteria

- All diagnosed cases of T2DM defined by ADA as FPG $\geq$126 mg/dl and 2HPG$\geq$200 mg/dl.
- Patients who taking specific medication for T2DM.

Exclusion Criteria

- Patients with malignancy, liver disease, HBV, HCV and HIV.
- Type 1 Diabetes Mellitus and Gestational Diabetes.
- Patient who had nephropathy before being diagnosed with Diabetes.
- Patients having neuropathy due to other systemic causes eg. vitamin deficiency, drug exposure, connective tissue disorders,thyroid disorder etc. or local causes like radiculopathies / plexopathies.
- Patients who do not provide consent.

Method

The diagnosis of diabetes adopts the World Health Organization's 2006 criteria:[13] (1) typical symptoms, random blood glucose ≥11.1 mmol/L; (2) fasting blood glucose ≥7.0 mmol/L; (3) oral glucose tolerance test, 2-hour blood glucose ≥11.1 mmol/L. Participants without typical symptoms should repeat the blood glucose test on another day. Patients meeting any one of the above criteria were diagnosed with diabetes.

Diagnostic Criteria of Diabetic Microvascular Complications

All the participants were diagnosed at the time of hospital discharge.

Diabetic peripheral vascular disease (DPV)[14]was diagnosed by color Doppler ultrasonography of bilateral lower extremity vessels or neck and brain vessels. In addition, there are symptoms of lower extremity pain, cool skin, intermittent claudication, dizziness, and headache.

The diagnosis of diabetic peripheral neuropathy (DPN)[15]was based on the following: 1) History of diabetes. 2) For those with clinical symptoms (pain, numbness, and paresthesia), any one of the following five items (ankle reflex, acupuncture pain, vibration, pressure, and temperature) is abnormal. 3) For those without clinical symptoms, any two of the following five items (ankle reflex, pinprick pain, vibration, pressure, and temperature) are abnormal. Neuropathy caused by other factors was excluded when DPN was diagnosed.

Diabetic kidney disease (DKD)[16] was diagnosed by urine albumin/creatinine ratio (UACR) and serum creatinine levels. All patients were asked to provide urine samples 3 times. DKD was diagnosed if the UACR was twice above 30 mg/g, or if an abnormally elevated serum creatinine level was detected. At the same time, CKD caused by hypertension or other diseases was excluded.

The T2DM group was divided into Group I (0-5 years), Group II (6-10 years) & Group III (>10 years) according to the duration of DM type2.

Medical histories were obtained for all patients, including details of height, weight, and waist circumference. We also obtained fasting blood glucose (FBG), 2 hour post prandial blood sugar glycosylated hemoglobin (HbAlc), cholesterol lipid

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(TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL),microalbuminuria, nerve conduction study and fundoscopy.

Statistical Analysis

Significance of difference in proportion will be inferred by Chi-square test. Significance of difference in means will be inferred by un-paired 't'-test. Association between microvascular complications and factors (duration and glycemic indices) will be inferred by Chi-square test. Logistic regression would be done to predict microvascular complications on the basis of various independent predictors. The level of significance will be kept at 95% for all statistical analysis.

RESULTS

The mean age of study subjects was 58.38 years ranging from 35 to 86 years. The duration of Diabetes ranged from 1 to 22 years with a mean of 10.04 years. The Diabetes control in most subjects was poor as the mean HbA1C was 9.3% ranging from 5.4 to 36.95%. The mean 24 hr urinary protein was 0.41 g/dl. The most common micro vascular complication in DM-II patients was Nephropathy seen in 60% patients, followed by Neuropathy seen in 56.2% patients. Retinopathy was seen in only 29.5% of patients.

Microvascular complicationswere seen in only one patient under 40 years of age. The proportion of Microvascular complications increased with increasing age and was highest in >70 years subjects. Patients in the 61-70 years age group had 95.4, 71.6& 50.8times higher risk of nephropathy, neuropathy& retinopathy respectively as compared to those under 40 years. The proportion of nephropathy, neuropathy was more in females (64.4%& 60.2% respectively) as compared to males (56.9%& 55.3% respectively) but the proportion of Retinopathy was almost equal in females (29.9%) and males (29.3%). The risk of microvascular complications was highest in patients with >10 years of DM. Microvascular complications were more common in patients with HbA1C ≥10% and gradually decreased in lower HbA1C values. Significant association of microvascular complications were seen only with age group and Duration of Diabetes (P<0.05 each) (table 1).

Logistic regression analysis revealed that only Duration of Diabetes was the significant independent factor associated with microvascular complications.The risk of microvascular complications increased significantly with increasing Duration of DM. Though the proportion of microvascular complications increased with age, but it was not found to be an independent predictor (table 2).

Table 1: Association of various factors with nephropathy, neuropathy and Retinopathy among DM-II patients

	Sub-group	Nephropathy			Neuropathy			Retinopathy		
		Yes	No	P-value	Yes	No	P-value	Yes	No	P-value
Age group (years)	≤ 40	1 (5.3%)	18 (94.7%)	<0.001*	1 (5.3%)	18 (94.7%)	<0.001*	1 (5.3%)	18(94.7 %)	<0.001*
	41 – 50	6 (14.6%)	35 (85.4%)		3 (7.3%)	38 (92.7%)		0	41 (100%)	
	51 – 60	37 (63.8%)	21 (36.2%)		34(58.6 %)	24 (41.4%)		5 (8.6%)	53(91.4 %)	
	61 – 70	53 (84.1%)	10 (15.9%)		51 (81%)	12 (19%)		32 (50.8%)	31(49.2 %)	
	>70	29 (100%)	0		29 (100%)	0		24 (82.8%)	5 (17.2%)	
Sex	Femal e	56 (64.4%)	31 (35.6%)	0.345	50(60.2 %)	37 (39.8%)	0.345	26 (29.9%)	61(70.1 %)	0.955
	Male	70 (56.9%)	53 (43.1%)		68(55.3 %)	55 (44.7%)		36 (29.3%)	87(70.7 %)	
Duration of DM-II	≤ 5	5 (8.6%)	53 (91.4%)	<0.001*	1 (1.7%)	57 (98.3%)	<0.001*	1 (1.7%)	57(98.3 %)	<0.001*
	6 – 10	13 (43.3%)	17 (56.7%)		7 (23.3%)	23 (76.7%)		2 (6.7%)	28(93.3 %)	
	>10	108(88.5 %)	14 (11.5%)		110(90 %)	12 (9.8%)		59 (48.4%)	63(51.6 %)	
HbA1C (%)	< 8	42 (56.8%)	32 (43.2%)	0.537	39(52.7 %)	35 (47.3%)	0.393	21 (28.4%)	53(71.6 %)	0.923
	8 – 9.99	34 (57.6%)	25 (42.4%)		31(52.5 %)	28 (47.5%)		17 (28.8%)	42(71.2 %)	
	≥ 10	50 (64.9%)	27 (35.1%)		48(62.3 %)	29 (37.7%)		24(31.28 %)	53(68.8 %)	

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Table 2: Logistic regression analysis for independent predictors of Nephropathy neuropathy and Retinopathy among DM-II patients

Variables	Nephropathy		Neuropathy		Retinopathy	
	Adjusted odd ratio	P- value	Adjusted odd ratio	P- value	Adjusted odd ratio	P- value
Female Sex	1.185 (0.502 - 2.797)	0.699 (NS)	0.516 (0.180 - 1.477)	0.218 (NS)	0.594 (0.233 - 1.517)	0.276 (NS)
Age(in years)	1.077 (0.998 - 1.163)	0.057 (NS)	1.026 (0.938 - 1.123)	0.570 (NS)	1.144 (1.049 - 1.247)	0.002 (S)
Duration of DM-II (in years)	1.442 (1.222 - 1.702)	<0.001 (S)	2.424 (1.741 - 3.376)	<0.001 (S)	1.609 (1.279 - 2.024)	<0.001 (S)
HBA1C (%)	1.134 (0.960 - 1.340)	0.139 (NS)	1.263 (0.965 - 1.652)	0.090 (NS)	1.055 (0.891 - 1.248)	0.534 (NS)

DISCUSSION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.[1]

Our study showed that the most common micro vascular complication in DM-II patients was Nephropathy seen in 60% patients, followed by Neuropathy seen in 56.2% patients. Retinopathy was seen in only 29.5% of patients.

Ramchandra et al found the prevalence of diabetic neuropathy in southern India 27.5.[17] while Shobha et al reported the prevalence of neuropathy as much as 70 %.[18]Knuiman et al found 14% prevalence of neuroapthy.[19] A study conducted at a Diabetic centre in south India the prevalence of Diabetic Retinopathy in Type -2 Diabetes mellitus in 34.1% and Duration of Diabetes and HbA1c Showed a positive association.[20]

A Study on prevalence of micro and macrovascular complications and their risk factors in type-2 Diabetes Mellitus was held in SP Medical College Bikaner, among 11157 Subjects retinopathy was diagnosed in 32.5 % Nephropathy was present in 30.2% and Peripheral neuropathy was present in 26.8%.Duration of Diabetes had significant association with neuropathy and nephropathy. Higher HbA1c increases the risk retinopathy, neuropathy and nephropathy. The Study highlights the high prevalence of vascular complications in Type 2 Diabetes Mellitus in Northwest India.[21]

In 2010, Omolase C O et al[22], in their study diabetic retinopathy in Nigerian community, this study suggest that the duration of DM significantly affect the development of diabetic retinopathy, our study support this study. Similar results were obtained in a study by Balasuriya et al reported a progressive rise in the number of retinopathy cases as the duration of diabetes increased.[23]Alwakeel et al also reported the progressors had a significantly higher prevalence of cataract, retinopathy, angina and neuropathy compared to non-progressors.[24] As reported by Rani et al, the prevalence of diabetic retinopathy was 17.6% in self reported rural population with diabetes.[25]

In March 2013 Jiji Inassi et al[26],in their study role of duration of diabetes in the development of nephropathy in type 2 diabetic patients, this study suggest that the duration of DM significantly affect the development of diabetic nephropathy, our study support this study.Balasuriya et al studied the prevalence of nephropathy (microalbuminuria) in a subset of Sri Lankan population in <1 year group was 18.8%, in 6-10 years group 21.2% and in over 20 years group 25.4%. [23] In related study, Alwakeel et al concluded that diabetic nephropathy among Saudis tends to be progressive with GFR decline at a rate of 3.3 mL/year with doubling of serum creatinine.[24]

In September 2010 OC Oguejiofor et al[27], in their study evaluation of the effect of duration of diabetes mellitus on PN using the UKST, Aesthesiometry, Bio-Thesiometry. This study suggests that the duration of DM significantly affects the development of diabetic neuropathy, our study also supports this study.

CONCLUSION

We concluded that early detection and treatment of these complications therefore plays a crucial role than glycemic control, there are no treatments for diabetic neuropathy, nephropathy and retinopathy. Thus, identifying potentially modifiable risk factors for microvascular complication is crucial. Detecting these risk factors helps in correcting these at an early stage. Correlation between the various microvascular complications helps in better understanding of their pathogenesis and early control.

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