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Study On Prevalence Of Microvascular Complications Of Newly Diagnosed Type 2 Diabetes Mellitus

[1]Dr Anamika Das, [2] Dr Anirban Bhowmik, [3] Dr Soma Saha, [4] Dr Mukut Roy, [5] Dr Debaprasad Chakrabarti

[1] Senior Resident, Department of Medicine, Tripura Medical College & Dr BRAM Teaching Hospital.
[2] Assistant Professor, Department of Medicine, Tripura Medical College & Dr BRAM Teaching Hospital.
[3] Professor, Department of Medicine, Tripura Medical College & Dr BRAM Teaching Hospital.
[4] Professor, Department of Medicine, Tripura Medical College & Dr BRAM Teaching Hospital.
[5] Professor, Department of Medicine, Tripura Medical College & Dr BRAM Teaching Hospital.

Correspondence:
Dr Anirban Bhowmik

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is often asymptomatic for years, leading to delayed diagnosis and early development of microvascular complications such as retinopathy, nephropathy, and neuropathy. A significant proportion of patients already have complications at the time of diagnosis, particularly in resource-limited settings. Early detection is crucial to prevent long-term morbidity including blindness, end-stage renal disease, and diabetic foot complications. ***Aim:*** To estimate the prevalence of microvascular complications and identify associated risk factors among newly diagnosed T2DM patients. ***Methods:*** This cross-sectional study was conducted at TMC & Dr. BRAM Teaching Hospital from February 2021 to October 2022. A total of 81 newly diagnosed T2DM patients (aged 18–65 years) were enrolled as per ADA 2020 criteria. Participants underwent clinical, biochemical, and ophthalmological evaluation to detect retinopathy, nephropathy (urine albumin–creatinine ratio), and neuropathy (clinical examination and monofilament testing). Statistical analysis was performed using SPSS version 21. Chi-square test, Student's t-test, and logistic regression were applied, with $p < 0.05$ considered significant. ***Results:*** Microvascular complications were present in 34.57% of patients at diagnosis. Retinopathy was most common (32.09%), followed by nephropathy (17.28%) and neuropathy (13.58%). Among affected patients, 46.43% had two complications and 17.86% had three. Age, BMI, total cholesterol, HbA1c, fasting blood sugar, and postprandial blood sugar were significantly associated with complications ($p < 0.05$). Logistic regression identified age and HbA1c as independent predictors. ***Conclusion:*** A substantial proportion of newly diagnosed T2DM patients already have microvascular complications. Older age and poor glycemic control significantly increase risk, highlighting the importance of early screening and strict glycemic management at diagnosis.

Keywords: Diabetes Mellitus, Newly Diagnosed, Microvascular Complications

INTRODUCTION

Diabetes mellitus (DM) has routinely been described as a metabolic disorder characterized by hyperglycaemia that develops as a consequence of defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus (T2DM) encompasses individuals who have insulin resistance (IR) and usually relative insulin deficiency [1]. India is the second largest country in terms of DM burden with 65.1 million diagnosed cases. 193 million diabetics remain undiagnosed worldwide predisposing to the development of several long-term complications of untreated chronic hyperglycaemia at the initial presentation [2].

The pathologic hallmark of diabetes mellitus involves the vasculature leading to both microvascular and macrovascular complications. The asymptomatic phase of hyperglycaemia accounts for the relatively high prevalence of complications at initial presentation [3]. If left untreated it is characterized by chronic hyperglycemia and disordered carbohydrate, lipid and protein metabolism and is associated with the development of specific microvascular complications and of non-specific macrovascular disease. Microvascular complication includes the disease of eye, kidney and variety of clinical neuropathies [4]. Around 20% to 25% of type 2 diabetic people already have retinopathy at the time of diagnosis [5].

Diabetic retinopathy may be the most common microvascular complication of diabetes.4 Retinopathy may begin to develop as early as 7years before the diagnosis of diabetes in patients with type 2 diabetes [5]. Although intensive glycemic control lowers the incidence and progression of microvascular

complications, the morbidity associated with these complications is still increasing [6]. The gravity of the situation can be assessed by the fact that patients with diabetes mellitus are 25 times more likely to cause blindness in people compared to nondiabetics [7].

Whereas, diabetic nephropathy forms the leading cause of chronic kidney disease, end stage renal disease and CKD requiring renal replacement therapy. 7% of patients with type2 diabetes may already have microalbuminuria at the time they are diagnosed with diabetes [7]. Older age and higher BMI at diagnosis of diabetes are the risk markers for development of diabetic nephropathy [8]. It is seen that 20% of patients with T2DM already have diabetic nephropathy when they are diagnosed with diabetes [9].

Studies conducted in Asian countries reported variability in the prevalence rate of microalbuminuria ranging from 14.2% in Iran, 24.2% in Pakistan, to 36.3% in India [10]. In various studies in world incidence of neuropathy was tried to be accessed & it is seen that DPN in 46.4% of their newly diagnosed diabetic patients [11]. In India current data indicates neuropathy was found to be a second most common microvascular complication effecting about 33% newly diagnosed T2DM patients [11]. Diabetic neuropathy affects almost around half of the diabetic population [12]. It has a significant impact on the patient's functional ability and daily life activities. More than 80% of amputations occur after foot ulceration or injury, which can result from diabetic neuropathy [13].

It is already mentioned that a patient of T2DM may remain asymptomatic for a certain longer period which may lead to presentation with spectrum of symptoms associated with different microvascular complications. This also warrants for the early diagnosis and treatment of these complications associated with even newly diagnosed T2DM patients to improve the further progression of disease. Scarcity of research exists in the local population with the similar concept. Therefore, this study has been taken up to estimate the prevalence of microvascular complications in newly diagnosed T2DM patients attending department of Medicine, TMC & DR. BRAM Teaching Hospital.

MATERIALS AND METHODS

The present cross-sectional study was carried out in TMC & DR. BRAM Teaching Hospital from February 2021 to October 2022 (1.5 years). Sample size was calculated to be 81 considering 20% drop outs. Every subject who fits the criteria, was selected till the sample size was reached. All the adult subjects with newly diagnosed T2DM as per American Diabetes Association (ADA), were screened for their biochemical parameters, presenting in outpatient (OPD) of TMC & DR. BRAM Teaching Hospital with a raised blood sugar level and HBA1c for the diagnosis of T2DM as laid by ADA and who agreed to sign a written consent of all related aspect and outcomes were taken.

Inclusion criteria

1. Newly diagnosed type 2 diabetes mellitus.
2. Age greater than 18 years and less than 65 years.
3. Laboratory diagnosis of DM was confirmed by latest criteria laid by American Diabetic Association 2020.

Exclusion Criteria

1. Type 1 DM.
2. Pregnancy.
3. Known diagnosed DM under treatment.
4. Patient having history of chronic kidney disease, urinary tract infection, cataract, glaucoma, suffering from psychiatric disease or any psychiatric treatment. Cerebro-vascular accident.
5. Patient unwilling to give consent.

Methods: A questionnaire was phrased for obtaining the information about socio demographic status, age, gender, occupation, educational qualification, socio economic status, addiction history, past history, family history and complications. The presence of complications was evaluated by relevant investigations. Anthropometric measurements including weight, height (using stadiometer), body mass index (BMI; kg/m2), and waist circumference (using inelastic and flexible tape at the midpoint between the lower margin of the least palpable rib and top of the iliac crest nearest to 0.1 cm) were carried out at the time of recruitment.

Information about socioeconomic and lifestyle characteristics (smoking and alcohol consumption) was obtained through patient interview at the time of recruitment. BJ Prasad scale was used for assessing the socioeconomic status of the patients. Clinical systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels were recording using sphygmomanometer. Serum lipids, blood glucose and glycated haemoglobin (HbA1c), and hepatic and renal function levels were checked and recorded. Blood pressure was measured in the sitting position in right arm to the nearest 2mmHg with a mercury sphygmomanometer and the participants were considered to be hypertensive if they were taking antihypertensive medication (as documented in clinic records) or SBP $\geq$ 140mmHg or DBP $\geq$ 90mmHg. HbA1c was measured using the Variant machine (Bio-Rad Laboratories, Hercules, CA, USA).

Serum cholesterol (cholesterol oxidase-peroxidase method), high-density lipoprotein cholesterol (direct method polyethylene glycol- CHOD PAP method), serum triglycerides (enzymatic calorimetric method), and were measured using Erba XL 300 autoanalyzer, Serum LDL was calculated using Fried Wald's formula. LDL-C= Total Cholesterol-HDL-C-TGL/5. Retinopathy will be diagnosed by detailed fundus examination in a

dilated eye. The diagnosis of retinopathy was confirmed from clinical records (if already documented) or sent for extensive ophthalmological examination that included fundoscopy or retinal photography and measurement of visual acuity, performed by an ophthalmologist. They were classified into proliferative diabetic retinopathy (PDR) or non-proliferative diabetic retinopathy (NPDR) accordingly. Nephropathy was estimated by level of serum creatinine, blood urea & Urine Albumin Creatinine ratio and routine urine examination. Albuminuria is further classified into:

a. Normal<30 micrograms
b. Micro albuminuria- 30-229 micrograms
c. Macro albuminuria > 300 micrograms

Neuropathy was diagnosed by history of numbness, tingling and burning sensation and confirmed by vibration test with tuning fork and monofilament test (clinical diabetic neuropathy score). Assessment of neuropathy was done using 10 gm Von Frey monofilament (VMF), pinprick sensations, ankle reflexes, and vibration perception threshold (VPT). 10 gm VMF was located perpendicular to the skin and pressure was applied until the filament just bends with a contact time of 2 seconds. Inability to comprehend the sensation at any site was considered abnormal. In addition, presence or absence of ankle reflex was checked using percussion hammer. Depending on above parameters, Neuropathy was classified as:

1. No neuropathy: 0 to 5
2. Mild neuropathy: 6 to 8
3. Moderate neuropathy: 9 to 11
4. Severe neuropathy: 12 to 19

Routine biochemical marker studies like fasting blood sugar, post prandial blood sugar, HBA1c, LDL cholesterol, triglyceride in relation to urine albumin creatinine ratio, retinopathy and neuropathy was recorded. Height, weight (BMI), abdominal circumference, Systolic blood pressure, diastolic blood pressure was measured in the subjects.

Statistical analysis: Entire data was entered in Excel 2007 spreadsheet by masking personal identity of each respondent. Mean and percentage was calculated for each suitable studied variable. Linear regression analysis was used to establish the association between diabetes complication and risk factor. SPSS version 21 software was used for statistical analysis. Chi square test, student t test was applied to find out any statistical significance. P value < 0.05 was taken as significant.

RESULTS

Out of total 81 cases who presented at our institute with newly diagnosed T2DM without any pharmacological/life style modifications 28 patients (34.57%) were having microvascular complication at the time of presentation whereas, 53 patients (65.43%) had no complication at presentation. 26 patients presented with diabetic retinopathy; 14 patients had diabetic nephropathy on presentation while 11 patients had diabetic neuropathy on presentation (table 1).

Table 1: Distribution of Microvascular Complications

Microvascular Complications	Frequency (N=81)	Percentage (%)
Absent	53	65.43%
Present	28	34.57%
Type		
Retinopathy	26	32.09%
Nephropathy	14	17.28%
Neuropathy	11	13.58%
No. of Complications	N=28	
One Complication	10	35.71%
Two Complications	13	46.43%
Three Complications	5	17.86%

Out of total 28 patients who presented with microvascular complications, 26 patients (92.86%) patients had retinopathy, 14 (50%) patients had nephropathy and 11 (39.28%) patients had neuropathy as a microvascular complication at the time of diagnosis. Out of 26 patients who presented with diabetic retinopathy at the time of diagnosis 18 had mild NPDR and 8 had moderate NPDR. Out of 11 patients who had neuropathy at presentation 6 patients presented with mild neuropathy and 5 had moderate neuropathy (table 2).

Chi square test has been done and it is seen that age group (p value=0.000), gender (p value= 0.001), addiction (p value =0.004) were found to be statistically significant (p value<0.05) in patients with microvascular complications among the newly diagnosed T2DM patients at the time of diagnosis (table 3).

Table 2: Distribution of retinopathy in patients with microvascular complications

Complications	Frequency (N=28)	Percentage (%)
Retinopathy		
Absent	2	7.14%
Present	26	92.86%
Nephropathy		
Absent	14	50%
Present	14	50%
Neuropathy		
Absent	17	60.72%
Present	11	39.28%

Table 3: Sociodemographic association with microvascular complications

Variables	Microvascular Complications Absent	Microvascular Complications Present	Test Value	p-value
Age groups (in years)				
<50	28 (52.83%)	3 (10.71%)	13.76	0.000
>50	25 (47.17%)	25 (89.29%)		
Gender				
Female	20	4	4.83	0.003
Male	33	24		
Religion				
Christian	2	0	1.76	0.414
Hindu	42	25		
Muslim	9	3		
Address				
Rural	17	13	1.61	0.202
Urban	36	15		
Educational qualification				
Graduate	18	9	2.73	0.433
Post graduate	6	1		
Primary	10	9		
Under graduate	19	9		
Socio-economic status				
Low middle	24	17	2.74	0.254
Lower class	13	7		
Upper middle	16	4		
Addiction				
No	33	8	8.32	0.004
Yes	20	20		

Parameters in association with microvascular complications having statistically significant differences ($p < 0.05$) are Age, BMI, Cholesterol, HbA1c, FBS and PPBS (table 4).

A binomial logistic regression was performed to ascertain the effects of age, gender, religion, Addiction, FBS, PPBS, HBA1c, total cholesterol, HDL, LDL, BMI on the likelihood of development of microvascular complications. The logistic regression was statistically significant $x2(12) = 82.02$, p value=0001. The model explained 87.0% (Nagelkerke R^2) of the variance in developing microvascular complications. Out of 11 predictors only two variables (p value=<0.05) i.e. HBAIC and age were statistically significant. Males have 148 times higher Odds for developing microvascular complications. Increase in HBA1c increases likelihood for developing microvascular complications (table 5).

Table 4: Association of microvascular complications among newly diagnosed T2DM with various biochemical & anthropometric findings

Parameter	Microvascular Complications Absent (Mean ± SD)	Microvascular Complications Present (Mean ± SD)	p-value
Age	52.51 ± 10.40	61.12 ± 9.67	0.000
BMI	25.01 ± 3.13	26.79 ± 2.84	0.015
Chol	149.64 ± 49.61	179.00 ± 57.17	0.026
Tri	197.64 ± 97.44	239.89 ± 90.79	0.061
HDL	48.26 ± 16.84	46.82 ± 15.81	0.706
IDL	56.60 ± 38.15	95.14 ± 52.61	0.072
HbA1c	6.85 ± 0.49	7.86 ± 1.18	0.000
FBS	166.49 ± 38.22	200.29 ± 55.08	0.002
PPBS	252.37 ± 65.63	297.67 ± 89.58	0.001
SBP	137.24 ± 21.36	137.85 ± 19.92	0.901
DBP	81.66 ± 9.58	85.64 ± 11.81	0.105

Table 5: Binary logistic regression analysis of various predictor variables to develop microvascular complications

Variables	Crude OR With 95% CI	Adjusted OR With 95% CI	P Value
Age	1.0944 (1.033–1.15)	1.106 (1.026–1.19)	0.000
BMI	1.21 (1.03–1.42)	0.796 (0.46–1.37)	0.415
Cholesterol	1.0009 (1.0008–1.0172)	1.002 (0.991–1.013)	0.692
Triglyceride	1.01 (1.00–1.01)	1.01 (0.98–1.02)	0.602
LDL	1.01 (1.00–1.02)	0.950 (0.84–1.07)	0.452
HBA1C	7.184 (2.452–21.04)	9.997 (2.616–38.315)	0.000
GENDER			
Male	3.63 (1.003–1.2017)	2.053	0.3909
Female		(0.3969–10.62)	
RELIGION			
Christian	8.30	1	0.999
Hindu	1.00	1.17	0.999
Muslim			
ADDICTION			
No	1	1	0.657
Yes	4.12 (1.53–11.01)	1.980 (0.104–35.77)	
FBS	1.0011 (1.0046–1.0262)	1.0070 (0.9742–1.012)	0.906
PPBS	1.00760 (1.0046–1.026)	1.00090 (0.9861–1.0012)	0.6305

DISCUSSION

Harris et al [14] showed that the onset of newly diagnosed T2DMprobably occurs even earlier than 4–7 years before clinical diagnosis. This becomes more important due to limited resources. It has been seen that early detection of these microvascular complications like retinopathy, nephropathy or neuropathy may delay or prevent progression towards blindness, end stage renal diseases and diabetic foot ulcers. Hence this study has been conducted in TMC and DR BRAM Teaching Hospital for a period of one-half year among the patients who presented with T2DM for the first time at the OPD or IPD of the hospital & who are not under any pharmacological or lifestyle modifications to increase the awareness and prevent the lethality of microvascular complications by early diagnosis.

The mean age group of these patients was 61.12 ± 9.67years which is similar to the study conducted by wild S [15], Ramchandra A [16], where the age group for development of microvascular complication at the time of diagnosis was also more than 60 years. However, this is in contradiction with the studies conducted Wani FA et al [17] where the mean age of such patients was found to be 53 years & mean age group was found to be 56 years in the study conducted by Basal D [18].

Male predisposition of the complication has been established in the currenr study. In the current study, majority of the complications were seen in the males which was found to be 67.90% and females 32.10% which is alliance with the study conducted by Solace A et al [19] where majority of the cases with microvascular complications were males which is 67% in comparison to females which is 33%. Also, the study by Hussain M et al [20] males constituted 61.7% of the study sample and females were 38.3%. But the findings are in contradiction to the study conducted by Mitra V

[21], where 57% of the patients were males and 43% were females & Bansal D [18] where majority of study population were females. Among them were 46% were males and 54% were females.

In the current study the prevalence of microvascular complications is 34.57% which is similar to the cross-sectional study over 6958 subjects conducted by Gedeberg A et al [22] where microvascular complications were found in about 34% cases at the time of diagnosis. Also allies with the findings depicted by Faith et al [23] & Huyen Dieu [24] et al where prevalence of microvascular complications was seen in 30% & 40% respectively at the time of the diagnosis.

But in contradiction with other studies like Bansal D et al [18] where prevalence of such complications was detected only in 18% of the studied cases. Study conducted by Solace A et al [19] where prevalence was seen only in 20% of the total cases is different from the findings in the present study. This is again different to the result observed by Hussein M et al [20] where the prevalence of microvascular complication is 45.9%. and the prevalence was as high as 51% in the study conducted by Mitra V et al [21].

The prevalence of diabetic retinopathy was similar to the study conducted by Ali A et al [25] where prevalence of retinopathy was found to be 31%, Mitra V et al [21], where prevalence of retinopathy was 29% and Jain SK96 where prevalence of retinopathy was also 30%. It is supported by the findings given in the study conducted by Abera Ejigu et al [26] and Mengsitu et al [27]. But the results are dissimilar to findings pointed out by Chang et al [28] where the prevalence retinopathy was only 10% at presentation & Bansal D et al88 where the prevalence was 9.5%.

The prevalence of nephropathy in this study was 17% in the current study which is similar to the findings of study conducted by Vinik AI et al [9], where prevalence of nephropathy was 20%. The study conducted by Sosale et al [29] and Wang DD et al [30] showed the prevalence of diabetic nephropathy to be 13% & 19% is almost similar to the findings of our current study. But however, the prevalence of diabetic polyneuropathy is different in other studies conducted by Pfannkuche et al [31] & Al-Mahroos F et al [32] & where the prevalence was depicted to be 40.3% & 36.6% respectively.

The mean BMI of the patients with microvascular complications in our recent study was 26.79±2.84 which is similar to the study conducted by Bansal D et al [18] & Jain SK [33] where mean BMI was 27. There is almost a linear relationship between the value of HBA1C value and occurrence of microvascular complications. Mean HBA1C in the current study was found to be 7.9±1.2 g% amongst the patients who were found to have complications at presentation which was similar to the result shown by Hussein M et al [20], Mittal M et al [34] &Raman R et al [35] where the findings showed higher the HBA1C higher is the predilection for development of microvascular complication on presentation mean value being 7%.

In our recent study, the mean value of total cholesterol 179 ± 57.17mg/dl which is significantly related to the presence of microvascular complications in the study population. Kumar M et al [36] depicted that their study cohort had a mean cholesterol value of 168.71±34.88 mg/dl and pictured a significant association with hypercholesteremia with the development of microvascular complication. In the study conducted by Singh Y et al [37] pointed out that dyslipidaemia in the form of increased triglyceride, high total cholesterol, high LDL & low HDL level are responsible for the development of microvascular & macrovascular complications of diabetes. Their study elaborated the dyslipidaemia profile as total cholesterol of cases was 232.13±145.9 mg /dl, triglyceride198.32±59.8, LDL 156.86 ±39.3 mg/dl.

In current study the mean value of fasting blood sugar level of cases with complications is 200.286± 55.08 whereas, mean postprandial blood sugar is 297.67±89.577. Many of the studies shows linear degree of association with blood sugar levels and development of microvascular complications [36].

Also, the study Kumar M et al [36] found the 194.50± 53.71mg/dl and the post prandial value to be 331.28±92.38mg/dl. K Vani et al [38] in their study found the mean fasting blood sugar value 171.67±89 mg/dl whereas, mean postprandial sugar values to be 255±112.78 mg/dl Hence early detection & tight glycaemic control is highly recommended to prevent such complications.

Limitations

1. The study size is small and is a cross sectional study. Large scale analytical study with adequate follow up period is required as microvascular complication is dynamic process.
2. Nerve conduction velocity is more accurate way of diagnosis of diabetic neuropathy could not be done.

CONCLUSION

Microvascular complications were seen in 34% of the study cohort. Out of which 10 persons (35.71%) of them has at least one complication at presentation whereas, 13 (46.43%) had two complications and 5 persons (17.86%) had three complications at presentation. 26 persons (32.09%) had diabetic retinopathy, 14 (17.28%) had nephropathy & only 11(13.58%) had neuropathy at the time of diagnosis. Majority of the study population were hypertensive and had history of addiction. Microvascular complications were more common in older age, males and patients with an increased BMI. Significant correlation was also

seen between microvascular complications and age, total cholesterol level, fasting blood sugar at presentation as well postprandial blood sugar and HBA1C.

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