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Morbidity Profile and Causes of Mortality in Type 2 Diabetes Patients: Data from a Tertiary Teaching Hospital from Eastern India

Soumya Ranjan Behera[1], Manoranjan Behera[2*], Sidhartha Das[2], Bhabani Prasad Panda[3], Saroj Kumar Tripathy[2], Purna Chandra Dash[2]

[1]Department of Medicine, VSS Institute of Medical Sciences and Research, Burla, Sambalpur, Odisha, India
[2]PG Department of Medicine, Faculty of Medicine, Sriram Chandra Bhanja Medical College, Cuttack, Odisha, India
[3]PG Department of Medicine, Sriram Chandra Bhanja Medical College, Cuttack, Odisha, India
Email: *doctor_manoranjan@rediffmail.com

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Abstract

Background: Data regarding the prevalence of morbidity and mortality in patients of Type 2 Diabetes Mellitus (T2DM) is scanty in India. **Objectives**: To determine the prevalence of micro and macro vascular complications, acute metabolic complications, infections, Non Alcoholic Fatty Liver Disease (NAFLD) and cause of mortality in T2DM patients admitted to a tertiary care teaching hospital in Eastern India. **Material and Methods:** This was a hospital-based prospective study evaluating 150 T2DM patients admitted to a tertiary care institution in Eastern India. Diagnosis of micro and macro vascular complications, infections and NAFLD was made using standard protocols. In case of death, the most probable cause was noted. **Results:** Out of 150 patients, 14.7% of patients were newly diagnosed T2DM and out of them 41% of patients had vascular complications and 54.5% had infections. Of the total patients, 56% had nephropathy, 20% neuropathy, 17.3% retinopathy, 31.3% CVD, 11.3% CAD, 4.6% acute metabolic complications, 44% infections and 16.6% had NAFLD respectively. Macrovascular events occured earlier than microvascular complications. Multiple logistic regression analysis showed strong association of age, duration of diabetes, serum cholesterol, triglyceride, LDL-C with retinopathy (Regression coefficient β: −0.1086807, 0.4127152, −0.0513393, 0.0146429, 0.0587475; $p < 0.05$, < 0.001, < 0.05, < 0.05, < 0.05 respectively), while only duration of diabetes was strongly associated with nephropathy and neuropathy (Regression coefficient β: 0.2538751, 0.2261636; $p < 0.001$ for each). Increasing age was associated with CAD (Regression coefficient β: 0.055392; $p < 0.05$) and FBG was a risk factor for CVD (Regression coefficient β: 0.0055014; $p < 0.05$). 18.6% patients died due to diabetes related complications. Cardiovascular (CV)-related deaths (CVD+CAD) were most common

cause (51.5%: CVD 36.4%, CAD 15.1%) to be followed by infections (27.3%) and then chronic kidney disease (12.1%). **Conclusions:** This study highlights the high prevalence of vascular complications and infections in T2DM patients of Eastern India. CV-related deaths were principal causes of death, similar to that in developed world.

Keywords

Type 2 Diabetes Mellitus, Vascular Complications, Infections, NAFLD, Mortality

1. Introduction

Prevalence of diabetes mellitus (DM) is on an increase in India and Type 2 DM (T2DM) is the most prevalent form of DM seen in India, which constitutes more than 95% of the diabetes population. It has been observed in many studies that over 50% of patients with DM in India have a poor glycemic control and a substantial proportion amongst these also have diabetes-related complications [1]. According to the Chennai Urban Population Study (CUPS), the prevalence of coronary artery disease (CAD) was 21.4% (CUPS No 5) [2] and peripheral vascular disease (PVD) was 6.3% among patients of DM in South India [3]. Another study from North Delhi Diabetes centre comprising 720 T2DM patients, retinopathy was found in 21.2%, microalbuminuria in 41%, peripheral neuropathy in 15.3%, CAD in 7% and PVD in 7.4% of patients [1].

T2DM patients are susceptible to develop many acute and chronic infections primarily due to altered host immunity [4]. Urinary tract infection (UTI) is the most common infection and is a common cause for hospital admission in subjects of T2DM. Subjects with T2DM are at a three-fold higher risk of developing tuberculosis (TB) and it accounts for 15% of all TB and 21% of smear positive TB Worldwide [5].

According to the CUPS-16, the overall mortality was nearly 2-fold higher in diabetic subjects compared to non-diabetic cohorts (18.9 vs. 5.3 per thousand person years, $P = 0.004$) [6]. The study also reported that the prevalence of mortality due to cardio vascular disease (diabetic subjects: 52.9%, non-diabetic subjects: 24.2%, $P = 0.042$) followed by renal disease (diabetic subjects: 23.5%, non-diabetic subjects: 6.1%, $P = 0.072$) was higher among diabetic subjects compared to non-diabetic counterparts [6]. A study from a tertiary care hospital of Odisha in 1991 had revealed the mortality pattern in DM patients as follows: chronic kidney disease (CKD) 35%, infection 33.7%, cerebrovascular disease (CVD) 32.5%, CAD 30% and diabetic coma 20.2% respectively [7].

Since then, there has been no systematic study on burden of morbidity and mortality in T2 DM patients in this part of the country. Hence, the present study was undertaken to determine the prevalence of microvascular complications, macrovascular complications, acute metabolic complications, other complications like infection, Non-Alcoholic Fatty Liver Disease (NAFLD) and to evaluate

the causes of mortality in patients of T2DM in this part of the country.

2. Material and Methods

This study was a prospective hospital based study conducted in the postgraduate department of Medicine, S.C.B. Medical College and Hospital, Cuttack, Odisha, India. One hundred and fifty cases of T2 DM patients admitted consecutively to the first unit of this department from August 2014 to November 2015 of both gender and age group ≥30 year were enrolled for the study. Patients with other forms of DM, history of chronic alcoholism or smoking, HIV/AIDS, those on immunosuppressive therapy or on chronic use of drugs known to cause vascular or neurological complications were excluded from this study. Institutional ethical committee clearance was duly obtained.

Each patient underwent complete clinical examination with detailed history obtained during the examination. Details regarding age, sex, urban or rural, socio-economic status, duration of diabetes and treatment history of diabetes were recorded for all the patients. DM was diagnosed according to WHO criteria [8]. Blood glucose level estimation was done by glucose oxidase method using a standard kit supplied by Acutex Biochemical Pvt. Ltd. (Mumbai, India). Glycosylated haemoglobin (HbA_1C) was measured by ion-exchange chromatography method. Lipid profile, liver function test, blood urea, serum creatinine, and serum electrolytes were done by auto analyser (TBA 120 FR, TOSHIBA) using specific kits. Serum cholesterol was estimated using a standard kit (Enzokit) supplied by Ranbaxy Fine Chemicals Ltd. Diagnostic Centre; serum triglyceride (TG) was estimated using a standard kit supplied by Chemelex SA, Barcelona; serum low-density lipoprotein cholesterol (LDL-C) was estimated using a standard kit supplied by Agappe Diagnostics Ltd. (Kerala, India); serum high-density lipoprotein cholesterol (HDL-C) was estimated using a standard kit supplied by Transasia Biomedicals Ltd. (Daman, India) and the Boehringer Mannheim photometer 5010 (Birkenfeld, Germany). Very low-density lipoprotein cholesterol (VLDL-C) was estimated by dividing the TG by 5.

The selected patients were evaluated for the presence of microvascular complications (retinopathy, nephropathy, and neuropathy), macrovascular complications (CAD, CVD, and PVD), acute metabolic complications, infections and NAFLD by clinical examination and relevant investigations as enumerated below. The cause of mortality of those patients who died inpatient was also recorded.

Direct and indirect fundoscopy was used to make the diagnosis and grading of retinopathy [9]. Nephropathy was diagnosed based on 24 hour urine albumin excretion rate (AER), done by immunoturbidimetry method. Incipient nephropathy was diagnosed by microalbuminuria (30 - 300 mg/24 hours) and overt nephropathy was established by macroalbuminuria (>300 mg/24 hours), abnormality in renal function, raised serum creatinine and estimation of glomerular filtration rate (GFR: >60 mL/min, CKD stage 1 + 2; 30 - 60 mL/min, CKD stage

3; < 30 mL/min, CKD stage 4 + 5) [10]. Neuropathy was diagnosed by history of paresthesia, numbness and tingling sensation and confirmed by touch sensation with 10-g monofilament pressure sensation at the distal plantar aspect of both great toes and metatarsal points, vibration sensation with 128 Hz tuning fork, ankle reflexes and nerve conduction studies [11].

CAD was diagnosed from history of angina or myocardial infarction documented by previous medical records or by ECG changes of ST-segment, Q-wave, or T-wave (Minnesota code) suggestive of CAD [2] as well as 2D-echocardiography. CVD was diagnosed from the history of neurological deficit, clinical examination and CT scan/MRI of brain. Diabetic keto acidosis (DKA) and hyperglycemic hyperosmolar state (HHS) were diagnosed by standard diagnostic criteria. NAFLD was diagnosed by ultrasonography showing evidences of fatty liver [12].

Other relevant tests done were total leucocyte count, differential count, hemoglobin, urine routine and microscopic examination. Urine for ketone bodies/culture and sensitivity test, blood culture and sensitivity test, arterial blood gas analysis (ABG), and chest X-Ray (postero-anterior view) were done whenever required.

Statistical analysis was done using SPSS statistical package version 20.0. Quantitative variables were described as mean +/−standard deviation (SD) unless otherwise indicated. Qualitative variables were described by percentage. Multiple logistic regression analysis with stepwise additions of variables was performed to assess their association with each of the complication studied. For all statistical tests, p value < 0.05 was considered significant.

3. Results

Our study is a hospital based study and reflects the prevalence of diabetic complications in the in-patient setting.

Of the total 150 recruited patients with T2DM, majority were male (68%, n = 102), female (32%, n = 48), M: F (2.1:1). The age of the patients studied ranged between 30 - 90 years with a mean age of 60.46 (±12.6) years. The importance of age on prevalence of diabetes shows that majority of patients were from age group of 50 - 70 years (53.3%). Family history of diabetes was present in one third of patients (33.3%). The patients on antidiabetic medication were 85.3%. 14.7% (n = 22) patients were newly diagnosed with T2 DM out of which 40.9% (n = 09) patients were diagnosed to have vascular complications (nephropathy, retinopathy and CAD in 09% (n = 02) each, neuropathy in 4.5% (n = 01) cases, CVD in 31.8% (n = 07) cases and 54.5% (n = 12) had infections as complications mandating hospitalisation.

The prevalence of diabetes specific microvascular and macrovascular complications are shown in **Table 1**. Prevalence of microvascular complications was more than macrovascular complications. Among the microvascular complications, nephropathy was the most common form followed by neuropathy and retinopathy. In patients having diabetic retinopathy, majority (96%) were having nonproliferative diabetic retinopathy (NPDR). CVD was the most common ma-

crovascular complication to be followed by CAD and there were no case with evidence of PVD. Amongst CVD, 81% had cerebral infarction and 19% had intracerebral haemorrhage (ICH). Out of 150 patients, 24 patients (16%) did not have any vascular complications. The relationship of mean duration of diabetes and different vascular complications were as follows: retinopathy 10.23 (±6.34) years, neuropathy 9.36 (±7.11) years, nephropathy 7.89 (±5.2) years, CAD 7.88 (±5.21) years, and CVD 5.87 (±5.06) years as shown in Table 2. It signifies that macrovascular events occured earlier than microvascular complications. The prevalence of risk factors for macrovascular disease was as follows; Hypertension 46.6%, obesity 44%, and dyslipidemia in 25.3% of cases.

Relationship of different risk factors with all vascular complications is shown in Table 2. Blood pressure, total cholesterol and LDL-C were higher in patients having CVD, where as age and TG were higher in patients of CAD than patients

Table 1. Prevalence of vascular complications in Type 2 DM.

Complications	Male (%)	Female (%)	Overall (%) (N:150)
Microvascular			
Nephropathy	53.9 (N:55)	60.4 (N:29)	56 (N:84)
Neuropathy	17.6 (N:18)	25 (N:12)	20 (N:30)
Retinopathy	11.7 (N:12)	29.1 (N:14)	17.3 (N:26)
Macrovascular			
Cerebrovascular Disease (CVD)	30.39 (N:31)	33.33 (N:16)	31.33 (N:47)
Coronary Artery Disease (CAD)	13.72 (N:14)	6.25 (N:03)	11.33 (N:17)

Table 2. Relationship of different risk factors with complications.

PARAMETERS	Retinopathy	Neuropathy	Nephropathy	CAD	CVD
Age (Years)	58.92 ± 14.07	60.93 ± 14.60	62.12 ± 12.17	66.94 ± 11.80	61.91 ± 11.71
Duration of DM (Years)	10.23 ± 6.34	9.36 ± 7.11	7.89 ± 5.2	7.88 ± 5.21	5.87 ± 5.06
SBP (mm Hg)	141.69 ± 26.63	141.13 ± 35.30	144.55 ± 31.42	138.2 ± 30.2	166.85 ± 33.28
DBP (mm Hg)	81.15 ± 7.4	79.4 ± 8.5	81.01 ± 10.02	78.23 ± 9.1	88.38 ± 5.3
BMI (kg/m^2)	24.01 ± 2.96	24.44 ± 4.19	23.97 ± 3.07	24.616 ± 2.25	24.22 ± 2.87
HbA1c (%)	8.74 ± 1.93	8.40 ± 1.61	8.27 ± 1.79	8.386 ± 1.32	8.46 ± 1.78
Total cholesterol (mg/dL)	149.38 ± 57.01	168.67 ± 66.18	151.15 ± 57.39	159.24 ± 66.1	178.40 ± 60.18
HDL-C (mg/dL)	38.31 ± 12.18	38.60 ± 11.29	36.49 ± 10.59	40.71 ± 11.29	42.57 ± 11.21
LDL-C (mg/dL)	90.15 ± 37.76	91.67 ± 47.57	84.49 ± 40.77	90.71 ± 42.81	105.30 ± 48.40
TG (mg/dL)	140.03 ± 13.2	134.46 ± 11.3	128.24 ± 12.3	146.11 ± 11.4	135.85 ± 10.3

(Abbreviations: CAD, coronary artery disease; CVD, cerebrovascular disease; DM, diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; HbA1c, glycosylated hemoglobin; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride).

having other complications. HDL-C level were either normal or higher in subjects suffering from CVD or CAD. Similarly mean HbA_1C was highest in the retinopathy group.

Table 3 shows the profile of other complications. Infection related complications were found in 44% cases. The profile of infections is shown in Table 4. UTI followed by pneumonia and septicemia were most common in these patients. *E. coli* was the most common (62%) pathogen isolated from the urine sample followed by *S. aureus* in 14.3% cases. No growth was found in 19.4% cases.

Considering the all cause mortality, 22% patients died due to different complications. CVD was the most common cause of death followed by infection, CAD, CKD and HHS in descending order. Hence, cardio-vascular (CV) related death (CVD and CAD) was the most common cause of death as shown in Table 5.

Table 6 shows the association of age, duration of DM, systolic and diastolic blood pressure, fasting blood glucose (FBG), HbA1C, BMI, serum cholesterol, serum TG, serum HDL-C, serum LDL-C and serum VLDL-C with microvascular complications. Among these factors age, duration of diabetes, serum cholesterol, serum TG and serum LDL-C showed strongest association with retinopa-

Table 3. Other complications.

Other complications	Overall (%) (N:150)
Hypoglycemia	5.3 (N:08)
Hyperglycemic Hyperosmolar State (HHS)	4.0 (N:06)
Diabetic Ketoacidosis (DKA)	0.6 (N:01)
Infections	44 (N:66)
Non Alcoholic Fatty Liver Disease	16.6 (N:25)

Table 4. Profile of infections in Type 2 DM.

Types of Infections	Overall % (N:66)
Urinary Tract Infection	31.8 (N:21)
Pneumonia	30.3 (N:20)
Septicemia	30.3 (N:20)
Malaria	06 (N:04)
Enteric fever	06 (N:04)
Diabetic Foot	4.5 (N:03)
Tuberculosis	4.5 (N:03)
Encephalitis	4.5 (N:03)
Dengue	03 (N:02)

Table 5. Causes of mortality (n = 33).

Causes	Percentage (No of patients)
CVD	36.4 (n = 12)
Infection	27.3 (n = 9)
CAD	15.16 (n = 5)
CKD	12.1 (n = 4)
HHS	9.0 (n = 3)

(Abbreviations: CVD, cerebrovascular disease; CAD. coronary artery disease; CKD, chronic kidney disease; HHS, hyperglycemic hyperosmolar state).

Table 6. Results of multiple logistic regression analysis showing association of various risk factors with microvascular complications. (a) Diabetic nephropathy; (b) Diabetic neuropathy; (c) Diabetic retinopathy.

(a)

Variable	Odds Ratio	95% Cl	Regression coefficient β	P value
Age (Years)	0.997489	0.9615452 - 1.034777	−0.0025141	0.893
Duration of DM (Years)	1.289011	1.151751 - 1.442628	0.2538751	0.000
SBP (mm Hg)	0.9981147	0.9712355 - 1.025738	−0.0018871	0.892
DBP (mm Hg)	0.9785502	0.9095401 - 1.052796	−0.0216832	0.561
BMI (Kg/m^2)	1.011192	0.8888238 - 1.150408	0.0111301	0.866
FBG (mg/dL)	1.000417	0.9958869 - 1.004968	0.0004168	0.857
HbA1c (%)	1.062085	0.835399 - 1.350238	0.0602341	0.623
Cholesterol (mg/dL)	1.004075	0.9860692 - 1.02241	0.0040668	0.660
Triglyceride (mg/dL)	0.9918294	0.9827685 - 1000974	−0.0082041	0.080
HDL-C (mg/dL)	0.9496184	0.900919 - 1.00095	−0.0516951	0.054
LDL-C (mg/dL)	0.9987817	0.9783527 - 1.019637	−0.0012191	0.908
VLDL-C (mg/dL)	1.04021	0.9797455 - 1.104405	0.0394223	0.197

(b)

Variable	Odds Ratio	95% Cl	Regression coefficient β	P value
Age (Years)	0.9662639	0.9220365 - 1.012613	−0.0343183	0.151
Duration of DM (Years)	1.253781	1.123073 - 1.399701	0.2261636	0.000
SBP (mm Hg)	0.9927321	0.9617348 - 1.024738	−0.0072944	0.652
DBP (mm Hg)	0.9937687	0.915065 - 1.079242	−0.0062508	0.882
BMI (kg/m^2)	1.043847	0.9090641 - 1.198614	0.0429131	0.543
FBG (mg/dL)	1.004511	0.9991358 - 1.009916	0.0045012	0.100
HbA1c (%)	0.9856609	0.7349496 - 1.321897	−0.0144429	0.923
Cholesterol (mg/dL)	1.00659	0.9882576 - 1.025262	0.0065683	0.484
Triglyceride (mg/dL)	0.9942332	0.9829178 - 1.005679	−0.0057835	0.322
HDL-C (mg/dL)	1.004526	0.9471536 - 1.065374	0.0045162	0.880
LDL-C (mg/dL)	0.9956035	0.9733089 - 1.018409	−0.0044062	0.703
VLDL-C (mg/dL)	1.033067	0.9600939 - 1.111587	0.0325322	0.384

(c)

Variable	Odds Ratio	95% Cl	Regression coefficient β	P value
Age (Years)	0.8970168	0.8401426 - .9577411	−0.1086807	0.001
Duration of DM (Years)	1.510915	1.284931 - 1.776642	0.4127152	0.000
SBP (mm Hg)	0.969123	0.9328745 - 1.006781	−0.0313633	0.107
DBP (mm Hg)	1.098773	0.9853866 - 1.225207	0.0941942	0.090
BMI (kg/m^2)	0.9680751	1.020503 - 1.10208	−0.0324456	0.741
FBG (mg/dL)	1.001163	0.994861 - 1.007506	0.0011627	0.718
HbA1c (%)	1.209262	0.8777259 - 1.037205	0.1900104	0.219
Cholesterol (mg/dL)	0.9499563	0.9852334 - 1.147663	−0.0513393	0.002
Triglyceride (mg/dL)	1.014751	1.002837 - 1.026806	0.0146429	0.015
HDL-C (mg/dL)	1.063351	0.9201851 - 0.9806906	0.0614255	0.115
LDL-C (mg/dL)	1.060507	0.798459 - 1.173723	0.0587475	0.003
VLDL-C (mg/dL)	0.9541392	0.8499264 - 1.72052	−0.0469457	0.270

(Abbreviations: CI, confidence interval; DM, diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; HDL-C high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; VLDL-C, very low density lipoprotein-cholesterol).

thy (P value of 0.001, 0.000, 0.002, 0.015, and 0.003). Regarding nephropathy and neuropathy, duration of diabetes was strongly associated with development of these complications (P value = 0.000 for each).

Table 7 shows that increasing age was a risk factor for developing CAD in patient with T2DM (P value 0.041). FBG was strongly associated for developing CVD in these patients (P value 0.042).

4. Discussion

About 30% - 45% of all patients of T2DM suffer from microvascular complications. People with DM have a four-fold greater risk of having a cardiovascular event, 2-to 4-fold greater risk of stroke and 15 times more likely to have lower limb amputation than people without DM [13].

In the present study, nephropathy was found in 56% of cases. Previous studies have reported prevalence of nephropathy in India as: 41% [1], 30.2% [14], 25.5% [15], 36.3% [16], and 23.0% [17], respectively. The WHO multicentric study of vascular disease in diabetics, reported a wide geographical variation in prevalence of diabetic nephropathy. It ranged from 2.4% (Hong Kong), 23% (Delhi), to 37% (Oklahoma, USA) respectively, [18] suggesting a visible variation in prevalence of nephropathy depending on ethnicity and population under study.

Higher prevalence of nephropathy (56%) in our study is both due to the fact that the Indian ethnicity and the study being a hospital based. On applying multiple logistic regression analysis, we found a significant association of duration of DM with diabetic nephropathy (Table 6). Significant association of duration of DM and nephropathy have also been reported in previous Indian population

Table 7. Results of multiple logistic regression analysis showing association of various risk factors with macrovascular complications. (a) Cerebro vascular disease; (b) Coronary artery disease.

(a)

Variable	Odds Ratio	95% Cl	Regression coefficient β	P value
Age (Years)	1.023978	0.9832345 - 1.066409	0.0236948	0.253
Duration of DM (Years)	0.9692579	0.8830328 - 1.063903	−0.0312245	0.511
SBP (mm Hg)	1.0266	0.9971288 - 1.056941	0.026252	0.077
DBP (mm Hg)	1.017734	0.9385662 - 1.103579	0.0175782	0.671
BMI (Kg/m^2)	1.001836	0.8681151 - 1.156154	0.0018339	0.980
FBG (mg/dL)	1.005517	1.000208 - 1.010854	0.0055014	0.042
HbA1c (%)	1.063118	0.8078992 - 1.398963	0.0612065	0.662
Cholesterol (mg/dL)	1.007109	0.9872851 - 1.027331	0.0070838	0.485
Triglyceride (mg/dL)	1.003872	0.9945877 - 1.013244	0.003865	0.415
HDL-C (mg/dL)	1.037312	0.9830227 - 1.094599	0.0366324	0.182
LDL-C (mg/dL)	0.9981724	0.9755718 - 1.021297	−0.0018293	0.876
VLDL-C (mg/dL)	0.9649452	0.9044688 - 1.029465	−0.035684	0.280

(b)

Variable	Odds Ratio	95% Cl	Regression coefficient β	P value
Age (Years)	1.056582	1.002316 - 1.113786	0.055392	0.041
Duration of DM (Years)	1.033227	0.9264394 - 1.152323	0.0326868	0.557
SBP (mm Hg)	0.992804	0.9564622 - 1030527	−0.007333	0.704
DBP (mm Hg)	0.9767028	0.8890805 - 1.07296	−0.0235729	0.623
BMI (Kg/m^2)	1.144335	0.9517975 - 1.37582	0.1348233	0.151
FBG (mg/dL)	0.9973596	0.9894435 - 1.005339	−0.0026439	0.516
HbA1c	1.140005	0.7764706 - 1.673742	0.1310326	0.504
Cholesterol (mg/dL)	0.9977098	0.9736308 - 1.022384	−0.0022928	0.854
Triglyceride (mg/dL)	1.006625	0.9954544 - 1.017922	0.0066035	0.246
HDL-C (mg/dL)	1.040883	0.9727079 - 1.113837	0.0400696	0.246
LDL-C (mg/dL)	1.002423	0.972505 - 1.033262	0.0024205	0.876
VLDL-C (mg/dL)	0.9721942	0.8987329 - 1.05166	−0.0281997	0.482

(Abbreviations: CI, confidence interval; DM, diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; VLDL-C, very low density lipoprotein-cholesterol).

studies [14] [16].

Diabetic neuropathy is one of the most common long-term microvascular complication of DM. In our study, neuropathy was present in 20% patients. Similar prevalence was also reported from South India *i.e.* 19.5% [19]. The prevalence of neuropathy in earlier studies from India are 15.3% [01], 26.8% [14], and

33.1% [15] respectively. This variation may be due to glycemic control, genetic susceptibility to develop neuropathy and environmental factors. Statistical evaluation applying multiple logistic regression analysis for diabetic neuropathy, a positive association was found for duration of diabetes (**Table 6**). Agrawal *et al.* have published similar observation in their study [14].

In the present study retinopathy was found in 17.3% cases which is on par with the observations of earlier Indian studies *i.e.* 18% [20], and 21.2% [01] respectively. On the contrary, few other studies reported higher prevalences *i.e.* 32.5% [14] and 37.9% [15] respectively, probably due to clinic based studies. Multiple logistic regression analysis for diabetic retinopathy revealed a positive association for age of patients, duration of diabetes, serum cholesterol, serum TG and serum LDL-C level (**Table 6**). Agarwal *et al.* found a positive association for age of patients, duration of diabetes, blood pressure, FBG, and HbA_1C with diabetic retinopathy [14].

The prevalence of cerebrovascular disease was 31.3% in the present study. The prevalence of CVD as reported in earlier studies varies from 0.5% to 9.2% amongst T2DM subjects in India [21]. Our own study from Cuttack in 2011 showed the prevalence of DM was 38.7% among stroke patients [22]. Similar observation was reported by Nagaraja D *et al.* from Bangalore *i.e.* 23.1% [23]. This present study found that cerebral infarction was more common than haemorrhage (25% vs. 06% of total patients) which is at par with observation by Padma MV *et al.* (cerebral infaction 21.1%, cerebral haemorrhage 6.35%) [24].

Earlier studies by us from this centre (Cuttack) and Chennai had shown that at any given age subjects with DM had higher value of carotid intimal-medial thickness than non DM counterparts where the difference reached statistical significance after the age of 50 years [22] [25]. This is significant as the mean age of the patients suffering from CVD was 61.9 years in this study which can be extrapolated into corroborating the mean age of the patients with high prevalence of CVD. Multiple logistic regression analysis showed a positive association between FBG and CVD. Acute hyperglycemia could be one of the precipitating factor for CVD.

Coronary artery disease was found in 11.3% cases in our series. Prevalence of CAD was not uniform in different studies from India where earlier observations from Chennai revealed 11.4% [26], but the prevalence reported from North Delhi was 07% [01], where as a higher prevalence was reported from North West India *i.e.* 25.8% [14] and recent studies from Chennai *i.e.* 21.4% [2]. Prevalence of CAD in patients with DM was reported to be lower in this part of the country [27]. Multiple logistic regression analysis showed a definite association between age and CAD. Mohan V *et al.* have reported age and LDL-C as the risk factor for CAD [2].

Previous studies from this institute by us have shown, atherosclerosis to be more prevalent in subjects with DM and the quantum of involvement of vascular channels (coronary artery segments) were more profound as compared to the non-DM patients with CAD [28]. Such association suggests that uncontrolled

hyperglycemia is an independent and important determinant for developing atherosclerotic vascular disease (ASVD) in subjects with DM [28] [29].

In one of our recent publication, it was shown that a significant inflammatory state was prevalent in patients with T2DM as compared to healthy individuals. Type 2 diabetes with macrovascular disease (MVD) had significantly higher high-sensitivity C-reactive protein (hs-CRP) as opposed to T2DM subjects without MVD. Further NF-kB expression was significantly higher where as adiponectin level was lower in patients of DM with MVD. Such proinflammatory state could be an independent determinant of atherosclerosis in this population. Further, this study has shown that persons with DM had significantly higher cholesterol and TG levels than non-DM counterparts [30].

Amongst acute metabolic complications, hyperglycemic hyperosmolar state (HHS) was found in 4% and DKA in 0.6% of cases respectively. Kitabchi AE *et al.* reported a prevalence of HHS to be less than 1% of all diabetes related hospital admissions and Faich GA *et al.* reported the prevalence of DKA to be 1.6% in Rhode Island [31] [32]. The high prevalence of HHS in our study could be due to hospital-based study.

In our study, it is observed that 44% patients have suffered from one or multiple infections. Most common infection was UTI (31.8%). Most common pathogens isolated were *E. coli* (61.9%) to be followed by *S. aureus* (14%). Sterile culture was found in 19.4% of cases. Sridhar CB *et al.* reported symptomatic UTI to be 14% in mostly menopausal women with DM, which is significantly lower than our observation, which may be due to the fact that our study is hospital based and most of the hospital admissions are due to infections that encompass UTI mostly [33]. Our observation is comparable with that of Bettegowda S *et al.* who reported prevalence of UTI to be 26.8% and *E.* coli was the most common pathogen isolated followed by *Candida albicans* and Jenifer J *et al.* from South India who reported prevalence of UTI to be 42.8% and *E.* coli as the most common pathogen isolated where as sterile culture was found in 24.3% cases [34] [35].

Pneumonia was found in 30.3% cases in our study which is higher than that reported by previous Indian studies *i.e.* 11.6% [33] and 4.4% [34] possibly because of a referral tertiary care hospital and emphasizes the importance of non-tubercular pulmonary infection in subjects with T2DM.

Tuberculosis (TB) was found in 4.5% cases in our series. Earlier study by Patel JC from India had reported TB to be the most common associated illness (5.9%) with DM [36]. Other studies done much earlier by Bhatia (1975), Bahulkar (1975), Nanda and Tripathy (1968) had reported the prevalence of TB in DM to be 14%, 4.5% and 12% respectively [37]. The low prevalence in our study could be due to awareness and early detection of Pulmonary TB with wide availability of anti-tubercular drug therapy.

Diabetic foot was found to be present in 4.5% cases in our study. Viswanathan V *et al.* in a multicentric study from India reported the prevalence of diabetic foot infection to be 6% - 11% [38]. Our observation is at par with the observation of Pendsey SP, who found the point prevalence of foot ulcers in patients of

diabetes in clinic population to be 3% [39].

NAFLD was found in 16.6% patients. Recent studies from India have reported the prevalence of NAFLD as 56.5% [40] and 57.2% [41] respectively in T2DM patients. The low prevalence in our series compared to those published from metro cities may be likely due to lower prevalence of obesity in our population.

Out of 150 patients studied, 33 patients (18.6% of total, male: 75.7%, female: 24.3%) died due to various diabetes related complications. The mean age at death was 62.2 years (male: 62.6 years, female: 61.2 years). Das *et al.* reported the age at the time of death for people with DM to be 55 - 61 years and that mortality among hospitalized patients with non-insulin-dependent DM was nearly 20%, which is comparable with the findings of present study [7]. A recent population based study from South India by Mohan *et al.* reported the mean age of death to be 66 years and mortality related to diabetic complications to be 11.9% [6]. Analysing the causes of mortality in our cohort it was found that CVD (36.4%) was the most common cause of death followed by infection (27.3%), CAD (15.1%), CKD (12.1%), and HHS (9.0%). Cardiovascular (CV) related death (which includes CAD and CVD) was by far the most common cause of death in our series accounting for more than half (51.5%) of total death which could be due to the fact that macrovascular complications occured earlier than microvascular complications. Mohan *et al.* also had similar observations from South India, reported CV related deaths was the most common etiology, accounting for mortality in nearly 53% cases [6]. Das *et al.* also had similar observation from this institution 25 years ago reporting CV related death to be 62.5% cases [7]. Bhansali *et al.* from a tertiary care hospital in North India reported CV related death as second most common cause of death (23.4%) following infections [42]. Infections, which accounted for 27.3% cases of death was the second most common cause of death in our study. Das *et al.* also reported infection as the leading cause of death (33.7%) in their study [7]. Bhansali *et al.* also observed infection as the most common cause of death (46.5%) in their series [42]. The continued prevalence of infections in causing mortality in our patients may be attributed to overall high incidence of infections in this part of the country and poor glycemic control in these patients. Analysing the above figures of prevalence of infection and CV related death in T2DM patients in this part of the country, it seems that there is a shift in pattern of death from infection to CV related death possibly due to increased awareness among patients of DM regarding infection, seeking health service at right time, as well as availability of better health care facilities including ICU care. Chronic kidney disease (CKD) was the third most common cause of death in our study (12.1%). Bhansali *et al.* also reported a prevalence of 9.4% of CKD related death [42]. Mohan *et al.* from South India reported CKD related death to be 23.5% [6]. This could be due to poor glycemic control, inadequate facility for renal replacement therapy (RRT) like dialysis/transplant, and lack of affordability to RRT.

5. Limitations of the Study

As this was a tertiary hospital based study and may not be real reflection of the population. The work was a prospective cross-sectional study, it is not possible to determine whether levels of variables showing association with complications actually preceded the development of the complications. Hence, the clinical and laboratory variables showing association with the complications in this study may only be interpreted as potential risk factors. As this study was a part of Post Graduate thesis and so was time limited. More prolonged study is required in future.

6. Conclusions

This study highlights the high prevalence of vascular complications and infections in T2DM patients of this part of India. Nephropathy was the most common microvascular complication and cerebrovascular disease was the most common macrovascular complication. Macrovascular complications occurred earlier than microvascular complications. CV-related death was the most common cause of death (CVD more than CAD) followed by infections and CKD. CVD occurred earlier and was the most common cause of mortality in our patients of T2DM.

This study emphasizes the need for screening of all T2DM patients for complications at the time of diagnosis for early detection. The higher prevalence of cerebrovascular disease and nephropathy as observed by us may be similar to a few Indian studies but a visibly different from world literature. This suggests further work on etiopathogenesis of T2DM as well as its complications in our population group.

Conflict of Interest

This study was neither funded nor sponsored by any agency or pharmaceutical firm. This original research work is part of the regular postgraduate research thesis work of the Postgraduate Department of Medicine. The authors undertake that there is no conflict of interest, whatsoever with anyone.

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Abbreviations

AER: Albumin excretion rate
BMI: Body Mass Index
CAD : Caronary Artery Disease
CKD: Chronic Kidney Disease
CUPS: Chennai Urban Population Study
CV: Cardio Vascular
CVD: Cerebro Vascular Disease
DM: Diabetes Mellitus
DKA: Diabetic Keto Acidosis
HbAIC: Glycosylated Haemoglobin
HDL-C: High-density Lipoprotein-Cholesterol
HHS: Hyperglycemic Hyperosmolar State
ICH: Intracerebral Haemorrhage
LDL-C: Low-density Lipoprotein Cholesterol
MVD: Macro Vascular Disease
NF-kB: Nuclear factor-kappa B
NPDR: Non-Proliferative Diabetic Retinopathy
NAFLD: Non Alcoholic Fatty Liver Disease
PVD: Peripheral Vascular Disease
TB: Tuberculosis
T2DM: Type 2 Diabetes Mellitus
TG: Triglyceride
UTI: Urinary Tract Infection