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Research Article

Cardiovascular risk factors and determinants of clinical outcomes in type 2 diabetic patients at a tertiary-care centre

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ABSTRACT

Background: The prevalence of type 2 diabetes mellitus (T2DM) is growing rapidly worldwide. The global burden of T2DM in 2013 was 382 million and projected to 592 million by 2035, accounting for 7.8% of the adult population. The objective of this study was to record treatments, risk factor control, determinants of glycaemic control and cardiovascular outcomes in type 2 diabetes (T2DM).
Methods: We included adult T2DM patients and followed up for 6 months. Patients were categorised into good (HbA1c <7%), moderate (7 to 8.5%) and poor control (>8.5%). We used multiple logistic regression to identify determinants of glycaemic control and outcomes.
Results: We recruited 785 patients with a mean age of 55.43 (±11.1) years, and 43.8% were women. At baseline, patients with poor control (45%) were younger and from lower socioeconomic strata (73.5%). At 6 months, the American Diabetes Association (ADA) targets of HbA1c was met only in 27.52%, systolic blood pressure (SBP) in 81.47% and low density lipoprotein (LDL) cholesterol in 48.86% patients. Patients with sedentary or low physical activity (Odds ratio 11.51, 95% confidence interval 3.48, 37.98; p<0.001) and with diabetes for a longer duration (OR 1.14 [1.07-1.22], p<0.001) were more likely to be in poor glucose control. Patients having sedentary or low physical activity (OR 6.66 [1.730-25.63] p = 0.006) and higher LDL cholesterol (OR 1.04 [1.01-1.07], p = 0.008) were more likely to get microvascular complications.
Conclusions: Management of modifiable risk factors and early control of hyperglycaemia should be given more importance.

Keywords: T2DM, Cardiovascular risk factors, India

INTRODUCTION

The prevalence of type 2 diabetes mellitus (T2DM) is growing rapidly worldwide. The global burden of T2DM in 2013 was 382 million and projected to 592 million by 2035, accounting for 7.8% of the adult population.[1] The International Diabetes Federation (IDF), estimates that 63 million people in India had T2DM in 2012 which is projected to rise to 101.2 million by 2030, an increase of 60.6%.[1] Among diabetic patients, cardiovascular disease (CVD) accounts for about 80% of all mortality and 75% of all hospitalizations.[2,3] Diabetics without prior coronary artery disease (CAD) have a similar risk as non-diabetics with prior CAD and a poorer prognosis.[4] Although T2DM alone is an independent risk factor, most patients have additional risk factors for macrovascular complications. Hypertension is prevalent in approximately 75% and dyslipidemia in approximately 70% of T2DM patients.[5] Thus hypertension and hyperlipidemia are important targets of therapy in addition to hyperglycaemia in diabetic patients.[6] The American diabetes association (ADA) guidelines

recommend the reduction of vascular complications through control of blood glucose, blood pressure, blood lipids, smoking cessation and intensified treatment for primary prevention of CAD.[7] In the Groningen Initiative to analyse Type 2 diabetes Treatment (GIANTT) registry in the Netherlands, over 4 years found that over half the patients were insufficiently controlled and medications were not promptly adjusted.[8] In the Chennai Urban Population Study (CUPS), CAD prevalence was 21.4% among T2DM compared to 9.1% in normoglycemic subjects.[9] In Indians, CAD occurs about one decade earlier than in the West.[10] We searched (PubMed Jan 1960 to June 2013; key words: type 2 diabetes mellitus, cardiovascular risk factors, complications, outcomes, India) and found no Indian studies on risk factor management and determinants of clinical outcomes in T2DM. Sensing an urgent need for studies on CAD in diabetic subjects in India, we aimed to record risk factor control, determine the reasons for poor glycaemic control and estimate determinants of cardiovascular outcomes among T2DM patients at 6 months.

METHODS

We conducted an observational study with a 6 months follow-up at St. John's Medical College, a tertiary care centre in Bangalore. We included T2DM patients from the endocrinology, medicine and cardiology outpatient departments, on pharmacotherapy. Patients in whom the 6 month follow up were not possible and pregnant women were excluded. Patient recruitment was done over 14 months. The study was approved by the institutional ethics committee and informed consent was obtained from all the participants prior to recruitment.

We estimated sample size, based on the annual cardiovascular event rate in diabetic patients under good and poor control.[11] Using a risk difference of 2.25% between the groups and a 95% confidence interval, sample size was 654 patients. Factoring for a 20% drop out, we recruited 785 patients. Patients were categorised by their HbA1c levels into good (<7%), moderate (between 7 to 8.5%) and poor control (>8.5%).[8] The target levels for good risk factor control are based on ADA guidelines.[7] The subdivision into classes of moderate and insufficient control was made because it can be expected that prescribers will react differently to levels closer to target compared to more elevated levels.[12]

We recorded demography, lifestyle, socio economic status (education, total family income, occupation, number of dependents), medical history (diabetes onset and duration, co-morbidities) and drug history. Blood pressure, height, weight and blood investigations done in last 3 months were recorded. All patients were followed up once between the first and third months and at 6 months. The data included drugs taken, investigations and clinical outcomes if any in last 6 months. Macrovascular complications included angina pectoris, myocardial infarction, heart failure, stroke, coronary revascularisation, peripheral vascular disease (PVD), amputations or death. Microvascular complication included microalbuminuria, end stage renal disease, retinopathy, and peripheral neuropathy and foot complications. Cardiovascular outcomes were assessed based on clinical, ECG, Echo and laboratory findings.

We summarized data of patients as mean, median and crude rates. Categorical variables were compared using Chi-squared tests. All continuous variables were checked for normality and compared using ANOVA. To assess the determinants of poor glycaemic control and macro vascular complications at 6 months, we used multivariable logistic regression analysis. We report the adjusted odds ratios (adjusted for age and gender) with their 95% confidence intervals. A p value<0.05 was considered significant for all tests. Statistical analyses were performed using commercially available software (SPSS version 17).

RESULTS

We recruited 785 T2DM patients and their characteristics are summarised in Table 1. Mean age was 55.4 (±11.1) years, median duration of diabetes was 6.0 years (IQR: 2, 12) and 43.8% were women. Majority were from lower middle (48.9%) and poor (24.6%) social classes. Over half the patients had hypertension (61.8%) and dyslipidemia (60.4%) and 45% had both. At baseline, 391 (49.8%) had either microvascular or macro vascular complications with neuropathy (20.4%) and ischemic heart disease (15.5%) being the commonest. Data on fasting (FBS), post prandial sugars (PPBS) and HbA1c levels were available for 84%, 77.3% and 56.1% patients respectively. The mean FBS, 2 hour PPBS and HbA1c were 157.5±72.9 mg/dL, 232.8±98.1 mg/dL and 8.7±2.2% respectively. Data on lipids were available for 53% patients. Micro albuminuria was present in 122 (15.5%) patients out of 31.9% in whom it was checked. Eye checks were done in 559 (71.2%) patients and diabetic retinopathy was present in 66 (8.4%) patients.

Table 2 depicts patient characteristics by levels of glucose control.

Patients were categorised by their HbA1c levels into good (<7%), moderate (between 7 to 8.5%) and poor control (>8.5%).[8] Patients in the poor control group were younger [53.14 ±11.9 years] than the patients in the good and moderate control [59.41±11.2, 56.17±10.4 years p<0.001]. The proportion of patients in poor control group from the lower middle class and poor backgrounds were higher (82.8% versus 17.2%, p = 0.017). The total cholesterol levels (185.1 mg/dL in poor control versus 174.0 mg/dL in moderate and 168.3 mg/dL in good control, p<0.05) and microvascular complications were higher in the poor control group compared to other groups (59.9% in poor control versus 24.3% in moderate and 15.8% in good control, p<0.01).

Table 1: Baseline characteristics of patients with T2DM.

Parameter	Overall (785)
Age (years) (SD)	55.43 (11.06)
Male gender [n (%)]	441 (56.2)
Socio- economic status [749 (95.4%)]	
Rich	40 (5.1)
Upper middle	124 (15.8)
Lower middle	384 (48.9)
Poor	201 (24.6)
BMI (kg/m2)	26.0 (3.95)
Diabetes duration [n (%)]	
<2 years	159 (20.3)
2-5 years	213 (27.1)
>5 years	413 (52.6)
Physical activity [n (%)]	
Sedentary/low	322 (41.0)
High/moderate	463 (59.0)
CV risk factors	
Smoking [Current] (%)	74 (9.4)
Hypertension [n (%)]	485 (61.8)
Dyslipidemia [n (%)]	474 (60.4)
HTN + Dyslipidemia [n (%)]	353 (45.0)
Blood investigations	
FBG (mg/dL) (SD)	157.54 (72.9)
2hPPBG (mg/dL) (SD)	232.84 (98.1)
Total cholesterolemia (mg/dL) (SD)	178.70 (48.8)
HDL (mg/dL) (SD)	39.67 (15.1)
LDL (mg/dL) (SD)	106.55 (36.6)
SBP (mmHg) (SD)	128.00 (17.2)
DBP (mmHg) (SD)	79.99 (8.3)
Any Microvascular complications [n (%)]	298 (38.0)
Retinopathy [n (%)]	86 (10.9)
Nephropathy [n (%)]	24 (3.1)
Neuropathy [n (%)]	160 (20.4)
Microalbuminuria [n (%)]	122 (15.5)
Any Macrovascular complications [n (%)]	161 (20.5)
MI [n (%)]	49 (6.2)
IHD [n (%)]	122 (15.5)
Stroke/TIA [n (%)]	36 (4.6)
PVD [n (%)]	11 (1.4)
Either macrovascular or microvascular complications [n (%)]	391 (49.8)

Treatments and outcomes

Dietary advice was given in 95.8% patients, among which 83.6% reported following it at 6 months. Exercise advice was given in 92.9% patients. At 6 months, majority reported moderate physical activity (50.7%), 33.9% reported low physical activity and 7.1% reported sedentary lifestyle. About half the patients (46.3%) were on 2 classes of antidiabetic agents. The most commonly prescribed was metformin (84.1%) followed by sulphonylureas (SU) (50.7%). Thiazolidinediones (TZD) were prescribed in 8.9% and alpha glucosidase inhibitors in 3.1% patients. Among newer agents, gliptins were prescribed in 71 (9%) and glucagon like peptide-1(GLP-1) analogues exenatide, liraglutide were prescribed in 5 (0.7%) patients. Insulin was prescribed in 317 (40.4%) patients and 253 (32.2) patients were on oral antidiabetic agents and insulin. At baseline, almost all (93.8%) patients reported taking over 80% of prescribed doses in the preceding month.

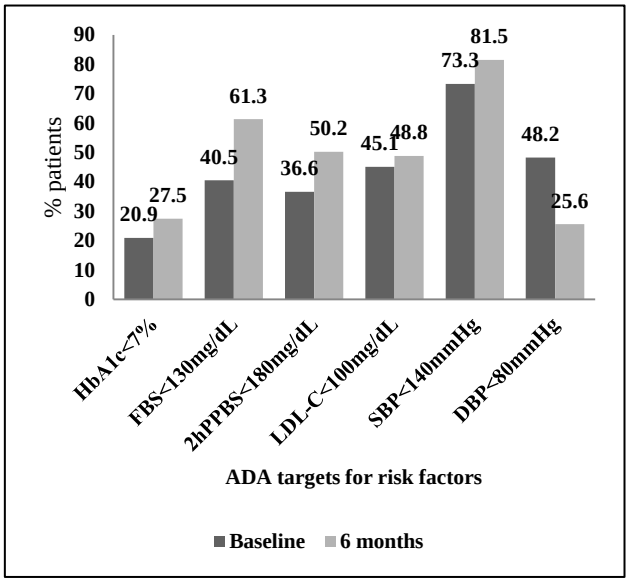

Figure 1: Patients who met ADA targets for risk factor control.

Antidiabetic drugs at baseline were compared by levels of blood glucose control. In those with good control, 43.5% were using 2 drug classes and 37% were on monotherapy ($p<0.001$). In the poor control group, 13.1% were on monotherapy and 28.3% were on three or more drug classes ($p<0.001$). Also, 47.7% in poor control group were on OHAs alone.

Of 485 (61.8%) who had hypertension, 26 (5.4%) were not on any antihypertensive medication and 31.3% were on monotherapy. There were 34.6% on fixed dose combinations (supplementary file A; Table A.1). Angiotensin converting enzyme inhibitors (ACEIs) were prescribed in 23.9%, calcium channel blockers (CCBs) in 162 (33.4%) and beta blockers (BB) were prescribed in 142 (29.3%) patients. Among those prescribed BBs, 51 (35.9%) had CAD. Among those with good control of systolic blood pressure (SBP <140 mmHg), majority (69.7%) were on one or two drug combinations. (Supplementary file A; Table A.2). In 7.6% patients antihypertensive medications were changed or dose altered at 6 months.

Statins were used in 471 (60.0%) patients. Among 417 (53.1%) patients in whom LDL data were available, 229

(54.9%) had raised LDL-C at baseline (>100 mg/dL). In patients with raised LDL, 138 (60.3%) were on lipid lowering drugs and 91 (39.7%) were not any lipid lowering drugs. Anti-platelets were used in 49.7% patients (aspirin 313 [39.9%] and clopidogrel in 124 [15.8%]). Among them, 26.4% had history of CAD. At 6 months there was improvement in HbA1c, FBS and 2 hour PPBS levels. There was 8.1% reduction in HbA1c (p<0.001), 14.7% reduction in fasting sugar (p<0.001) and 14.6% reduction in post prandial sugars (p<0.001) over 6 months. The SBP, DBP and lipids (mean total cholesterol, LDL, HDL and triglyceride) did not differ significantly over 6 months.

Table 2: Baseline patient characteristics by levels of glucose control.

Variables N = 440	Good control HbA1c < 7% N = 92 (20.9%)	Moderate control HbA1c: 7-8.5% N = 150 (34.1%)	Poor control HbA1c >8.5% N = 198 (45%)	p value
Mean Age (years) (SD)	59.41 (11.1)	56.17 (10.4)	53.14 (11.9)	<0.001
Gender [n (%)]				
Male	61 (66.3)	66 (44.0)	102 (51.5)	0.003
Female	31 (33.7)	84 (56.0)	96 (48.5)	
BMI (Kg/m^2)	27.2 (4.7)	26.7 (3.9)	25.6 (3.5)	0.216
Socioeconomic status [n (%)]				
Rich	8 (29.6)	12 (44.4)	7 (25.9)	0.017
Upper middle	18 (26.1)	24 (34.8)	27 (39.1)	
Lower middle	54 (23.8)	73 (32.2)	100 (44.1)	
Poor	12 (10.3)	41 (35.0)	64 (54.7)	
Diabetes duration [n (%)]				
<2 years	16 (17.0)	31 (33.0)	47 (50.0)	0.074
2-5 years	32 (24.6)	53 (40.8)	45 (34.6)	
>5 years	44 (20.4)	66 (30.6)	106 (49.1)	
Physical activity [n (%)]				
Sedentary/low	23 (25.0)	74 (49.3)	80 (45.2)	0.001
High/moderate	69 (75.0)	76 (50.7)	118 (59.6)	
CV risk factors				
Smoking [current] (%)	9 (19.1)	16 (34.0)	22 (46.8)	0.030
Hypertension [n (%)]	63 (24.2)	94 (36.2)	103 (39.6)	0.016
Dyslipidemia [n (%)]	72 (25.5)	98 (34.8)	112 (39.7)	0.002
Blood investigations				
FBS (mg/dL) (SD)	115.2 (27.1)	134.5 (32.7)	188.1 (69.2)	<0.001
2hPPBG (mg/dL) (SD)	172.4 (57.8)	192.3 (57.0)	287.6 (91.4)	<0.001
Total cholesterolemia (mg/dL) (SD)	168.3 (56.9)	174.0 (38.0)	185.1 (50.5)	0.041
HDL (mg/dL) (SD)	44.4 (12.9)	39.2 (16.7)	38.5 (17.0)	0.060
LDL (mg/dL) (SD)	89.3 (38.2)	109.3 (36.3)	108.7 (32.7)	0.001
SBP (mmHg) (SD)	130.4 (19.5)	130.4 (18.5)	128.2 (16.1)	0.432
DBP (mmHg) (SD)	79.7 (8.9)	80.6 (7.6)	81.7 (9.4)	0.175
Any Microvascular complications [n (%)]	28 (15.8)	43 (24.3)	106 (59.9)	<0.001
Retinopathy [n (%)]	8 (20.5)	7 (17.9)	24 (61.5)	0.053
Nephropathy [n (%)]	0 (0.0)	1 (20.0)	4 (80.0)	0.256
Neuropathy [n (%)]	10 (11.1)	23 (25.6)	57 (63.3)	<0.001
Diabetic foot (%)	5 (23.8)	3 (14.3)	13 (61.9)	0.134
Any macrovascular complications (%)	15 (20.0)	37 (49.3)	23 (30.7)	0.006
MI (%)	8 (33.3)	11 (45.8)	5 (20.8)	0.045
IHD (%)	5 (12.5)	22 (55.0)	13 (32.5)	0.013
Stroke/TIA (%)	3 (13.6)	12 (54.5)	7 (31.8)	0.115
PVD (%)	0 (0.0)	1 (33.3)	2 (66.7)	0.623

HbA1c values were available only for 440 patients at baseline

Table 3: Treatment of T2DM at baseline with mean duration of DM and HbA1c levels.

Therapy	N (%) (785)	Mean duration of DM (years)	Mean HbA1c*
OHA alone	459 (58.5)	5.5	8.2
OHA + Insulin	253 (32.2)	12.1	9.9
Insulin alone	61 (7.8)	12.8	10.2
Monotherapy			
Metformin alone	128 (16.3)	3.7	7.4
Sulphonylurea alone	38 (4.8)	3.7	8.3
Gliptins alone	5 (0.6)	6.4	6.7
Insulin alone	61 (7.8)	12.8	10.2
Dual therapy			`
Sulphonylurea + Insulin	13 (1.7)	12.6	10.6
Metformin + Insulin	136 (17.3)	11.9	9.9
Metformin + alphaglucosidase (-)	4 (0.5)	6.8	8.4
Sulphonylurea + Metformin	187 (23.8)	7.7	8.6
Sulphonylurea + Gliptin	1 (0.1)	8.9	8.2
Sulphonylurea + Glitazone	3 (0.4)	9.8	8.7
Metformin + Glitazone	5 (0.6)	10.2	8.8
Metformin + Gliptin	12 (1.5)	9.4	8.2
Insulin + alphaglucosidase (-)	3 (0.4)	14.8	9.0
Triple therapy			
Metformin + Sulphonylureas + Insulin	72 (9.2)	12.8	10.7
Metformin + Sulphonylureas + Glitazone	33 (4.2)	10.2	8.8
Metformin + Sulphonylureas + Gliptins	32 (4.1)	8.9	8.9
Number of drug classes used			
1 drug class	232 (29.6)		
2 drug class	364 (46.3)		
≥ 3 drug class	189 (24.1)		
Statins	471 (60.0)		
Anti-platelets	390 (49.7)		

*HbA1c values were available only for 440 patients at baseline

Table 4: Drug therapy at baseline by levels of glucose control.

Drugs (n = 440) #	Good control HbA1c<7% N = 92 (20.9%)	Moderate control HbA1c: 7-8.5% N = 150 (34.1%)	Poor control HbA1c>8.5% N = 198 (45%)	p value
Number of antidiabetic drug classes used				
1 drug class (n = 97)	34 (37.0)	37 (24.7)	26 (13.1)	
2 drug class (n = 230)	40 (43.5)	74 (49.3)	116 (58.6)	<0.001
≥3 drug class (n = 113)	18 (19.6)	39 (26.0)	56 (28.3)	
Treatment modality				
OHA alone	68 (75.6)	125 (84.5)	94 (47.7)	
OHA + Insulin	22 (24.4)	20 (13.5)	93 (47.2)	<0.001
Insulin alone	0 (0.0)	3 (2.0)	10 (5.1)	
Statins (n = 282)	72 (25.5)	98 (34.8)	112 (39.7)	0.001
Anti-platelets (n = 213)	61 (28.6)	70 (32.9)	82 (38.5)	0.047

HbA1c values were available only for 440 patients at baseline

At 6 months, the ADA recommended target levels for (HbA1c<7%) were met in 27.52%, FBS in 61.30%, PPBS in 50.25%, SBP in 81.47%, DBP in 25.61% and LDL cholesterol in 48.86% patients (Figure 1). Patients with sedentary or low physical activity (OR 11.51 [3.48-37.98] p<0.001), with diabetes for a longer duration (OR 1.14 [1.07-1.22], p<0.001), higher baseline HbA1c (OR 1.54 [1.04-2.27], p = 0.030), higher baseline FBS (OR 1.05 [1.02-1.07], p<0.001) and higher baseline PPBS (OR

1.02[1.01-1.03], p<0.001) are more likely to be in poor glucose control (supplementary file A; Table A.3).

We were able to follow up 623 (79.6%) patients at 6 months. At this time, 3 (0.4%) had died, 14 (2.2%) had macrovascular complications (myocardial infarction, heart failure, stroke, PVD) and 38 (6.1%) developed microvascular complications (peripheral neuropathy, microalbuminuria, retinopathy). Patients with sedentary or low physical activity (OR 6.658 [1.730-25.627] p = 0.006), prior CV event (OR 3.313 [1.068 - 10.278], p = 0.038) and higher LDL cholesterol (OR 1.041 [1.010-1.073], p = 0.008) were more likely to get macrovascular complications (supplementary file; Table A.3).

Supplementary file A

Table A (1): Treatment of hypertension in T2DM patients at baseline.

Therapy	N (%) (485)
None	26 (5.4)
1 drug class	152 (31.3)
2 drug classes	168 (34.6)
3 drug classes	105 (21.6)
>3 drug classes	34 (7.0)
Fixed dose combinations	162 (33.4)
Monotherapy	
ARBs	63 (13.0)
ACE inhibitors	44 (9.1)
CCBs	23 (4.7)
Diuretics	1 (0.2)
Beta blockers	20 (4.1)
Alpha + beta blocker	1 (0.2)
Dual therapy	
ARB + Diuretic	65 (13.4)
ARB + CCB	17 (3.5)
CCB + beta blocker	17 (3.5)
ACE inhibitor + diuretic	17(3.5)
ARB + beta blocker	15 (3.1)
ACEI + beta blocker	10 (2.1)
ACEI + alpha beta blocker	9 (1.9)
CCB + ACE inhibitors	6 (1.2)
Beta blocker + diuretic	5 (1.0)
CCB + Diuretic	3 (0.6)
ARB + alpha beta blocker	1 (0.2)

DISCUSSION

In our study, over half of the patients had hypertension and dyslipidemia as comorbidity and half of the patients had either macrovascular or microvascular complications at baseline. HbA1c target levels were not achieved in majority (79.1%) of patients. Those in poor control were younger and from lower socioeconomic backgrounds. Also among patients with diabetes duration less than 2 years, 50% were under poor control. There was an overall reduction in the HbA1c, FBS and PPBS levels over 6 months but the ADA targets were not met in many patients. Sedentary lifestyle and long disease duration were found to be important risk factors for poor control. Low levels of glycaemic control has been similarly shown in a cross-sectional study from Asian countries and other studies done in Thailand and Pakistan.[12-15] A systematic review by Sanal TS et al on studies done in India from 1980 to 2010, showed diabetes control was poor among younger adults (O.R.= 1.61, 95% C.I, 1.11, 2.33).[16] This poses serious implications on development of long term complications at a relatively young age. The 10 year follow up of the Chennai Urban Population Study (CUPS) showed a rapid reversal of socioeconomic gradient for diabetes and cardio metabolic risk factors and high prevalence in urban poor.[17] This trend could be because of rapid urbanisation, 'fast food' culture, life style changes and delay in timely treatment among the poor. High LDL levels and microvascular complications associated with poor control was seen in other studies also.[13,18] This highlights the importance of glycaemic control to prevent or delay micro vascular complications. A cross sectional study from India in 2005, demonstrates that a substantial proportion fail to meet ADA target levels for HbA1c and LDL cholesterol similar to our study.[19] Only 10% met target levels for all 3 risk factors at baseline in our study. In cross-sectional analysis of the prospective Diabetes Registry to Improve Vascular Events (DRIVE, 2005-2006) cohort, on 3002 patients, only 21% achieved the combined targets for SBP, A1c and LDL-C.[20]

Metformin, sulfonylureas and insulin were most prescribed in our study, due to their proven efficacy, known side effects and low cost. TZDs were commonly used in combination with SU and metformin in the subjects with relatively a longer duration of diabetes. Similar results were seen in study by Kosachunhanun N et al.[18] Patients with less duration of diabetes and lower mean HbA1c received OHAs alone while those with long standing diabetes and less favourable glycaemic control were on insulin with or without OHA. This indicates the stepwise approach to therapy is being followed in our hospital. Among patients in poor control, about half were on OHAs alone. This might reflect under usage or delay in starting insulin therapy which often leads to accumulation of glycaemic burden in patients before intensification of therapy. The ADA7 recommend initiation of insulin in patients with elevated HbA1c at the outset only if glycaemia target is not achieved by maximal tolerated dose of monotherapy in 3-6 months. An observational study on 66,726 T2DM patients in India also noted suboptimal use of insulin.[15] The delay in initiating insulin therapy may be probably due to worry about daily injections, fear of hypoglycaemia, modification of lifestyle due to insulin and dependence on insulin for life. An average patient accumulates 5 years of HbA1C more than 8%, and 10 years of HbA1C more than 7% before insulin therapy is initiated.[23] The early glycaemic control has beneficial effect on diabetic complications even if later returned to poorer metabolic control which is known as 'metabolic memory'.[24] So there

is an urgent need to change the clinical inertia in intensification of treatment early to reduce the glycaemia burden and prevent complications.

ARBs were most commonly prescribed antihypertensive, followed by diuretics and CCBs in our study in contrast to a study in North India where ACE inhibitors were prescribed most, followed by ARBs and CCBs.[24] The ADA prefers RAS blockers for initial therapy due to their superior cardiovascular and renal protective effects.[25] The use of ACE inhibitors in combination therapy was suboptimal in our study, possibly due to adverse effects like dry cough associated with ACE inhibitors. The 2014 hypertension guidelines recommend initiating antihypertensive treatment using thiazide diuretic, CCB or RAS blockers.[26] Major concern with the use of diuretic is the tendency to worsen hyperglycemia, but this effect was found to be small and did not produce more CV events compared with the other drug classes.[27] Majority (81.47%) achieved target SBP in our study at 6 months. The 2014 hypertension guidelines[26] and 2015 ADA guidelines[25] recommend target SBP below 140 mm Hg and DBP below 90 mm Hg. In our study, among patients with raised LDL cholesterol, 39.5% patients were not on any lipid lowering treatment. A meta-analysis on the effect of statins on LDL cholesterol, recommended using statins to lower LDL cholesterol and reduce CAD risk by almost 60%.[28] Among patients with increased cardiovascular risk (39.6%), anti-platelets were prescribed for primary prevention in 66.2% patients.

Table A (2): Number of drugs for hypertension by SBP control at baseline.

Antihypertensive medications (472)*	Good control SBP <140 mmHg N = 287 (60.8%)	Moderate control SBP: 140-160 mmHg N = 130 (27.5%)	Poor control SBP>160 mmHg N = 55 (11.7 %)	p value
None (n = 22)	15 (5.2)	7 (5.4)	0 (0.0)	
1 drug class (n = 148)	101 (35.2)	40 (30.8)	7 (12.7)	
2 drug classes ((n = 166)	99 (34.5)	48 (36.9)	19 (34.5)	
3 drug classes (n = 102)	57 (19.9)	24 (18.5)	21 (38.2)	0.002
>3 drug classes (n = 34)	15 (5.2)	11 (8.5)	8 (14.5)	

*Among hypertensive patients (n=485), SBP measurements were available for 472 patients (97.3%)

Table A (3): Risk for poor glucose control* and macro-vascular complications at 6 months.

	Poor control of blood glucose		Macrovascular complications	
Variables	**Adjusted OR (95% CI)#**	**p value**	**Adjusted OR (95% CI)#**	**p value**
Baseline HbA1c	1.54 (1.04-2.28)	0.030	-	-
Baseline FBS	1.05 (1.03-1.08)	<0.001	-	-
Baseline PPBS	1.02 (1.01-1.03)	<0.001	-	-
OHA alone	1	-	-	-
OHA + Insulin	2.97 (0.56–15.74)	0.918	-	-
Insulin alone	2.60 (1.17–5.79)	0.002	-	-
No use of statins	1.40 (0.67-2.94)	0.376	-	-
Sedentary/low physical activity (versus moderate/high)	11.51 (3.49-37.98)	<0.001	6.66 (1.73 -25.63)	0.006
Diabetes duration	1.15 (1.07-1.22)	<0.001	1.05 (0.99-1.12)	0.123
Prior CV event	--	--	3.31 (1.07 -10.28)	0.038
Total cholesterol	--	--	1.01 (0.99 -1.02)	0.279
LDL - C	--	--	1.04 (1.01 - 1.07)	0.008

*poor control of glucose defined as HbA1c> 7%; # Adjusted for age and gender; Baseline HbA1c, FBS, Antidiabetic medications, No use of statins was not significant for macrovascular complications in univariate analysis

HbA1c data were available in 28.5% whereas FBS and PPBS data were available in more than 60% in our study. This may be because of high cost of HbA1c testing that may not be affordable to many coming to our hospital. The fasting and post prandial sugar values may not reveal the true glycaemic status of the patient. Sedentary or low physical activity was found to be highest modifiable predictor for insufficient glycaemic control. Among treatment related factors, compared to patients who were on OHAs alone, those on insulin alone or in combination with OHA were associated with increased odds of insufficient glycaemic control. The study by Khattab[18] showed longer diabetes duration and non-adherence to lifestyle as risk factors for poor glycaemic control. We

found sedentary lifestyle, increased LDL cholesterol and prior CV event as significant predictors for macro-vascular complications whereas Ciardullo found smoking as a significant predictor for macro-vascular complications.[29]

This study gives an overview of the cardiovascular risk factors, prescription patterns and determinants of clinical outcomes in T2DM at a tertiary care hospital. The study has several limitations. First, this was a single centre study and patterns of drug usage may be different in different health care settings. Follow up data were obtained in 79.6%. Due to the short follow up period we are unable to comment on long term clinical outcomes.

The potentially modifiable risk factors like sedentary life style and high LDL cholesterol should be addressed more aggressively. Individualizing therapeutic goals and treatments to meet targets safely and without delay remains the key factor in improving patient outcomes.

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