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2013

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ORIGINAL ARTICLE

# Prescribing pattern of antidiabetic drugs and achievement of glycemic control in T2DM patients tertiary care hospital in North India

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Received: 22 May 2011 / Accepted: 16 April 2013 / Published online: 12 July 2013 © Research Society for Study of Diabetes in India 2013

Abstract Study was undertaken to identify patterns of antidiabetic drugs prescribing in established type 2 diabetes mellitus. Patients with established T2DM who attended the endocrinology Outpatient Clinic in Postgraduate Institute of Medical Education and Research, Chandigarh, India were evaluated for social, demographical and clinical variables and medications. 1185 established T2DM patients were assessed. Metformin was the most commonly prescribed drug [827 (70 %)], followed by insulin [627 (53 %)], sulfonylureas [520 (44 %)], and pioglitazone [329 (28 %)]. The most frequently prescribed monotherapy was insulin [214 (62 %)], followed by metformin in 81 (23 %), sulfonylurea in 49 (14 %) and pioglitazone in 4 (1 %) patients. 704 (59 %) treated patients had uncontrolled hyperglycemia. Family history (OR 1.76, 95%CI 1.18, 2.64), diabetes duration (OR 2.62, 95 % CI 2.05, 3.36), HbA1c (OR 1.25, 95%CI 1.01, 1.50), neuropathy(OR 1.57, 95 % CI, 1.14, 2.2), nephropathy(OR 1.77, 95 % CI 1.40, 2.24), retinopathy (OR 1.97, 95 % CI 1.63, 2.40), coronary arterial disease (CAD) (OR 1.57, 95 % CI, 1.14, 2.2) and diabetic foot (OR 1.62, 95 % CI 1.12, 2.40) were all significantly associated

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Department of Endocrinology, Post Graduate Institute of Medical Education and Research, Chandigarh, India with insulin therapy. Obese and overweight patients were prescribed oral antidiabetic drugs. Medication use was consistent with practice guidelines in T2DM, even though the outcome did not reach the goal.

Keywords Antidiabetic drug  $\cdot$  Glycemic control  $\cdot$  Tertiary care hospital  $\cdot$  T2DM  $\cdot$  India

#### Introduction

Diabetes mellitus is a chronic incurable disease with rising prevalence. Much of the burden of diabetes is due to the development of vascular complications [1]. Type 2 Diabetes Mellitus (T2DM) is a progressive disorder that is difficult to treat effectively over the long term [2]. It is also associated with other risk factors such as hypertension, adverse lipid profiles and obesity. Even after correcting these risk factors, CVD rates are still higher in patients with diabetes, implying that hyperglycemia per se may amplify the underlying risk of CVD. Optimal control of elevated blood glucose levels will reduce the symptoms of hyperglycemia and help to prevent the development of complications. Interventional studies have established chronic high blood glucose level as a cardiovascular disease (CVD) risk factor [3, 4].

Landmark trials have demonstrated that, intensive drug therapy can improve glycemic control, reduce risk of microvascular and other diabetes related complications [5–8]. Antidiabetic drugs play a major role not only in control of blood glucose but also in prevention or reduction of metabolic and cardiovascular risk associated with the disease.

The current treatment goals focus on adequate and aggressive treatment of blood glucose, blood pressure and cholesterol levels. Several guidelines [American Diabetes Association (ADA) [9], National Institute of Clinical Excellence (NICE) [10] and Indian Diabetes Management [11]] recommend aggressive management to avoid complications. Despite these guidelines, treatment gaps exist, whereby the actual patterns of practice do not meet clinical practice guideline recommendations. It is recognized that new guidelines or insights are not always implemented in daily practice [12, 13]. Studies are scanty in South Asian regions regarding practioners' choices of antidiabetic therapies for patients with established T2DM. The aims of this study were to identify patterns of antidiabetic drug prescribing in established type 2 diabetes mellitus patients and to evaluate determinants of the choice of antidiabetic therapy.

#### Patients and methods

This cross-sectional study was carried out from June 2007 to March 2009 at the Nehru Hospital, Postgraduate Institute of Medical Education and Research, Chandigarh. Consecutive patients with T2DM, who attended the Endocrinology Outpatient Clinic in Nehru hospital, were evaluated. We included those patients who were diagnosed to have T2DM at least 6 months earlier and were on stable dose of antidiabetic drugs for the past 3 months. We excluded pregnant and lactating women as well as patients with type 1 diabetes. The study protocol was approved by the Institute's Ethics Committee. Informed and written consent was obtained from all the participants. The subjects were evaluated for social, demographical and clinical variables and medications.

Anthropometric characteristics Standing body height (to the nearest 0.5 cm) was measured with a commercial stadiometer. A digital scale, with an accuracy of  $\pm 100$  g, was used to measure body weight (BW). The waist circumference (WC) was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. Hip circumference (HC) was measured at the fullest point around the buttocks with a metallic tape. The measurements were taken thrice and the mean was taken in all cases. WC (cm) was divided by HC (cm) to calculate waist to hip ratio (WHR). Body mass index (BMI)  $(kg/m^2)$  was calculated by dividing weight (in kilograms) by the square of height (in meters), as a measure of total adiposity. Systolic and diastolic blood pressure (SBP & DBP) were measured twice at an interval of 3 min in the sitting position after a 15 min rest, and the mean was taken using Blood Pressure Instrument Table Model. Percent body fat (%BF) was evaluated by impedance plethysmography bioelectrical impedance meter (Omron BF 302, Tokyo).

*Biochemical and clinical parameters* Blood samples (3 ml) were drawn after 8-12hr overnight fasting for the measurement

of lipid profile [total cholesterol, high density lipoprotein (HDL) cholesterol, and triglycerides] and fasting plasma glucose levels. Plasma glucose was measured using the glucose oxidaseperoxidase method [14], serum total cholesterol [15] and triglycerides [16] by standard enzymatic procedures and HDL cholesterol by direct assay method.

We also assessed both microvasular complications (neuropathy, nephropathy retinopathy) and macrovascular complications (coronary heart disease, cerebrovascular disease, peripheral vascular disease). Neuropathy was evaluated by history of numbness, paraesthesias, tingling sensation, burning sensation and it was confirmed by touch sensation using 10 g monofilament, vibration sense by biothesiometer Vibrometer-VPT® (Diabetic Foot Care, Madras Engineering Service, India) (VPT at great toe >25 mV were considered significant) and ankle reflex. Incipient nephropathy was diagnosed by Micral test and it was presumed to be present if any two readings out of three of urinary albumin and creatinine ratio were ranging from 30 µg/mg to 300 µg/mg. Clinical nephropathy was evaluated by the estimation of 24 h urine protein more than 500 mg/total volume of urine. Ophthalmologist diagnosed retinopathy by detailed fundus examination and was classified according to Diabetic Retinopathy Study (DRS) and Early Treatment Diabetic Retinopathy Study (ETDRS) [17]. Coronary artery disease was diagnosed by history of angina or myocardial infarction or documented by previous treatment records. Interpretation of ECG was recorded as per Minnesota codes. Pathological Q wave (major Q wave abnormalities) in an ECG recording (Minnesota codes 1.1.1-1.2.7), ST segment depression (codes 4.1-4.2), T wave abnormalities (codes 5.1-5.4) and chest x-ray was done to assess cardiac size. Peripheral vascular disease (PVD) was diagnosed by history of intermittent claudication or if one or more peripheral pulses were absent in both feet. The grading was done according to ankle brachial pressure index (ABPI) by Doppler Study [Multi Duplex(R)-II (Huntleigh Diagnostics-UK)]. PVD was diagnosed when ankle brachial index was less than 0.9.

Drugs were grouped in four major classes of monotherapyinsulin, metformin, sulphonylureas, and thiazolidinedione. Combination therapy was analyzed separately. Monotherapy was defined as a prescription for one agent. Combination therapy was defined as a prescription for more than one agent from two classes. Uncontrolled hyperglycemia was defined as HbA1c (Glycosylated heamoglobin A1c) >7 % or FPG (Fasting Plasma Glucose) >110 mg/dl or PPG (Post Prandial Glucose) >140 mg/dl.

#### Statistical analysis

Results are reported as mean±SD or percentages, if not indicated otherwise. Differences in characteristics between

T2DM patients were tested with independent t tests for normal distributed variables, with the Wilcoxon rank sum test for skewed variables, and with the chi-square test for categorical variables. Data were validated after double entry. Logistic regression was used to find determinants for prescribing of particular drug. Possible determinants were taken as per recommendation in guidelines such as age, body mass index, fasting and post prandial glucose level, lipid levels, serum creatinine level, etcetera. Results are expressed as Odds Ratio (OR) at 95 % confidence intervals (CI). All statistical analyses were carried out using sigma stat (Version 2.03, USA).

#### Results

1185 T2DM [606 (51 %) male and 579 (49 %) female] patients were assessed. The mean (SD) age of patients was 55 (10) years. Patients had a mean duration of diagnosed diabetes (SD) of 10 (7) years. The characteristics of the T2DM patients are shown in Table 1.

Patterns of use of anti-diabetic drugs is shown in Table 2. Metformin was the most commonly prescribed antidiabetic drug [827 (70 %)] in general, followed by insulin [627 (53 %)], sulfonylureas [520 (44 %)], and thiazolidinedione [329 (28 %)]. Metformin was mainly used from biguanides and pioglitazone was mainly prescribed from thiazolidinedione. None of the patients was on alpha-glucosidase inhibitors.

Among the 1185 patients, 348 (29 %) patients received monotherapy and 837 (71 %) combination therapy. 570 (48 %) patients were on two drug combinations and 267 (22 %) on three or more . Among the monotherapy insulin was the most frequently prescribed drug [214 (62 %)], followed by metformin in 81 (23 %), sulfonylurea in 49 (14 %) and thiazolidinedione in 4 (1 %) patients. In the combination drug therapy, oral antidiabetic drug (OAD) combination was prescribed in 428 (36 %) patients and insulin-OAD combination in 409 (34 %) patients. 277 (65 %) patients received a combination of OADs metformin and sulfonylureas while 183 (45 %) patients received a combination of insulin and metformin.

The utilization of diabetes medication in controlled and uncontrolled hyperglycemic patients is in Table 3. 481 (41 %) patients had controlled hyperglycemia. 704 (59 %) treated patients had uncontrolled hyperglycemia. Among the patients with uncontrolled hyperglycemia, the monotherapy drug was prescribed in 239 (34 %), and the combination therapy was in 465 (66 %) patients. Insulin as a monotherapy was prescribed in 145 (61 %) patients, and as a combination with metformin was in 114 (46 %) patients. Among the OADs the highly prescribed combination was metformin and sulfonylureas 134 (62 %).

The utilization of diabetes medication in T2DM patients with complications is shown in Table 3. In patients with microvascular complications [936 (79 %)], the monotherapy prescribed was in 287 (31 %) while combination drug therapy was prescribed in 649 (69 %). Insulin was the most commonly prescribed monotherapy [176 (61 %)] in patients with microvascular complications. The most commonly prescribed OADs combination in patients with microvascular complication in patients with microvascular complication was metformin and sulfonylureas 207 (66 %). Insulin and metformin combination was prescribed in 151 (45 %) patients.

 Table 1 Differentiating characteristics of the established T2DM patients

Characteristics	All (N=1185)	Male (N=606)	Female (N=579)	P value
Age (Yrs)	55.4±10.4	56.7±10.4	54.6±10	< 0.001
BMI (Kg/m <sup>2</sup> )	26.2±4.7	25.3±11.8	27.3±5.2	< 0.001
Duration of DM (Yrs)	9.6±7.4	$10.1 \pm 7.8$	9.4±7.1	0.0037
Duration of HTN(Yrs)	6.67±6.4	6.82±6.4	6.5±6.5	0.320
Waistline (cm)	93.6±11.7	95.1±8.96	94.3±11.4	0.012
SBP (mm Hg)	$138.8 \pm 18.6$	138.1±17.9	139.6±19.2	0.302
DBP (mm Hg)	85.9±10.9	84.7±10.8	85.7±11.0	0.890
FPG (mg/dl)	146.3±62.2	$142.9 \pm 59.9$	149.9±64.5	0.169
PPG (mg/dl)	$203.5 {\pm} 80.8$	196.2±77.2	210.9±64.5	0.023
HbA1c(%)	7.9±1.9	7.7±1.7	8.1±2.1	0.025
Scr (mg/dl)	1.13±0.7	$1.21 \pm 0.7$	$1.05 \pm 0.6$	< 0.001
TCh (mg/dl)	179.1±48.6	174.2±47.6	184.9±48.5	0.001
LDL (mg/dl)	90.9±41.1	87.9±38.7	94.1±43.3	0.079
HDL-C (mg/dl)	58.9±31.4	56.8±29.6	61.2±32.9	< 0.001
TG (mg/dl)	157.6±83.1	153.6±88.7	161.9±76.3	0.002

Drug classes N (%)	Overall	Monotherapy	Polytherapy				
			Overall	2 Drugs	3 Drugs or more		
Antidiabetics	1185(100)	348(29)	837(71)	570(48)	267(22)		
Insulin	627(53)	214(62)	409(49)	240(42)	169(63)		
Metformin	827(70)	81(23)	745(89)	484(85)	261(98)		
SUs	520(44)	49(14)	475(49)	319(56)	156(58)		
TZD (Pio)	328(28)	4(1)	325(39)	99(17)	226(85)		

Table 2 Patterns of use of anti-diabetic drugs in established T2DM patients

Percentages of individual drug classes are given within columns: overall, and by number of drugs in regimen

SUs Sulphonylureas, TZD (Pio) Thiazolidinedione pioglitazone

Patients with macrovascular complications [233 (20 %)], had the monotherapy prescription in 74 (32 %) and combination therapy prescription in 159 (68 %). The commonly prescribed monotherapy, OADs combination, insulin and OADs combination in patients with macrovascular complications were insulin 57 (77 %), metformin and sulfonylureas 55 (72 %), insulin metformin and pioglitazone 30 (36 %), respectively.

Choice of antidiabetic drug therapy and influencing factors

Table 4 shows odds ratio for exploratory variables in logistic regression for diabetic drug therapy. In this univariate analysis, family history, diabetes duration, HbA1c, neuropathy, nephropathy, retinopathy, coronary artery disease (CAD) and diabetic foot complications were all significantly associated with insulin. Patients with the family history of diabetes (OR 1.76, 95 %

Antidiabetic drugs	Overall 1185(100) N (%)	Microvascular complication(s)		Macrovascular complication(s)		Hyperglycemia	
		Present 936 (79)	Absent 249 (21)	Present 233 (20)	Absent 952 (80)	Controlled 481 (41)	Uncontrolled 704 (59)
Monotherapy	348(29)	287(31)	61(24)	74(32)	274(29)	109(23)	239(34)
Insulin	214(62)	176(61)	38(62)	57(77)	157(57)	69(63)	145(61)
Metformin	81(23)	78(27)	3(5)	4(5)	77(28)	19(17)	62(26)
SUs	49(14)	31(11)	18(30)	13(18)	36(13)	20(18)	29(12)
Pioglitazone	4(1)	2(0.7)	2(3)	0(0)	4(1)	1(1)	3(1)
OADs Combination	428(36)	314(34)	114(46)	76(33)	352(37)	212(44)	216(31)
Metformin+SUs	277(65)	207(66)	70(61)	55(72)	222(63)	143(67)	134(62)
Metformin+Pio	24(6)	17(5)	7(6)	3(4)	21(6)	10(5)	14(7)
SUs+Pio	30(7)	19(6)	11(10)	3(4)	27(8)	6(3)	24(11)
Metformin+SUs+Pio	97(23)	71(23)	26(23)	15(20)	82(23)	53(25)	44(20)
Insulin plus OADs	409(35)	335(35)	74(30)	83(35)	326(34)	160(33)	249(35)
Insulin+Metformin	183(45)	151(45)	32(43)	28(34)	155(48)	69(43)	114(46)
Insulin+SUs	12(3)	12(3)	0(0)	1(1)	11(3)	5(3)	7(3)
Insulin+Pio	45(11)	28(8)	17(23)	8(10)	37(11)	13(8)	32(13)
Insulin+Metformin+SUs	40(10)	39(12)	1(1)	14(17)	26(8)	29(18)	11(4)
Insulin+Metformin+Pio	110(27)	92(27)	18(24)	30(36)	80(25)	33(21)	77(31)
Insulin+SUs+Pio	5(1)	3(1)	2(3)	0(0)	5(2)	3(2)	2(1)
Insulin+Metformin+SUs+Pio	14(3)	10(3)	4(5)	2(2)	12(4)	8(5)	6(2)

Table 3 Prescribing pattern of anti-diabetic drugs in established T2DM patients with complications

OAD oral anti-diabetic drugs, SU sulphonylureas, Pio pioglitazone

Percentages are calculated within row for categories in column wise and within categories in each box

<b>Table 4</b> Odds ratio for explanatory variables in logistic regression for diabetic drug f
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Variables	Insulin		Sulphonylureas		Pioglitazone		Metformin	
	OR (95 % CI)	P-value	OR(95 % CI)	P-value	OR (95 % CI)	P-value	OR (95 % CI)	P-value
Age (>55 vs. ≤55 years)	1.00 (0.99–1.02)	0.540	1.00 (0.99–1.01)	0.221	0.99 (0.98–1.01)	0.930	0.99 (0.98–1.00)	0.063
Sex (Male vs. Female)	1.04 (0.83–1.31)	0.750	0.80 (0.51-1.37)	0.243	0.94 (0.73–1.22)	0.657	0.68 (0.53-0.87)	0.003
FH (Yes vs. No)	1.76 (1.18-2.64)	0.006	0.03 (0.03-0.04)	<0.001	0.75 (0.48–1.17)	0.210	1.10 (0.73–1.67)	0.647
DDM (>9 vs. ≤9 years)	2.62 (2.05-3.36)	0.001	0.54 (0.42-0.69)	<0.001	1.17 (0.90–1.50)	0.240	0.87 (0.79-0.96)	0.006
DHTN (>5 vs. ≤5 years)	0.88 (0.69–1.11)	0.275	1.05 (0.83-1.33)	0.711	0.99 (0.76–1.30)	0.950	1.16 (0.90–1.50)	0.255
BMI ( >25 vs. ≤25 kg/m <sup>2</sup> )	0.79 (0.63-0.99)	0.048	1.28 (1.01-1.61)	0.040	0.99 (0.76–1.28)	0.916	1.25 (1.15–1.35)	<0.001
Waistline*	0.96(0.68-1.36)	0.835	1.27(0.90-1.80)	0.172	0.92(0.63-1.35)	0.678	1.67(1.16-2.49)	0.005
SBP ( >130 vs. ≤130 mmHg)	1.10 (0.87–1.4)	0.410	1.04 (0.82–1.32)	0.682	1.05 (0.80-1.36)	0.748	0.99 (0.76–1.30)	0.922
DBP( >80 vs. ≤80 mmHg)	0.99 (0.79–1.25)	0.940	1.07 (0.85-1.36)	0.550	1.07 (0.84–1.38)	0.575	1.02 (0.79–1.30)	0.860
FPG(>110 vs. ≤110 mg/dl)	1.30 (0.90–1.87)	0.149	0.85 (0.57-1.172)	0.269	0.92 (0.63-1.9)	0.272	0.81 (0.54–1.20)	0.549
PPG (>140 vs. ≤140 mg/dl)	2.12 (1.47-3.1)	<0.001	0.59 (0.40-0.83)	0.003	0.87 (0.60-1.30)	0.489	0.79 (0.53-1.18)	0.969
HbA1c (>7 vs. ≤7 mg/dl)	1.25 (1.00-1.50)	0.017	0.42(0.30-0.60)	<0.001	1.37 (0.94–1.90)	0.105	1.07 (0.74–1.56)	0.700
Neuropathy (yes vs. no)	1.96 (1.52-2.50)	0.035	0.63 (0.49-0.82)	<0.001	0.98 (0.74–1.31)	0.921	0.78 (0.51-0.90)	0.008
Nephropathy (yes vs. no)	1.77 (1.40-2.24)	<0.001	0.57 (0.45-0.73)	<0.001	1.20 (0.95-1.60)	0.115	0.72 (0.56-0.90)	0.01
Retinopathy (yes vs. no)	1.97 (1.63-2.40)	<0.001	0.63 (0.52-0.76)	<0.001	1.13 (0.93–1.40)	0.214	0.72 (0.60-0.86)	<0.001
CAD (yes vs. no)	1.57 (1.14-2.20)	0.034	0.59 (0.43-0.83)	0.002	0.58 (0.39-0.85)	0.006	0.64 (0.46-0.88)	0.007
CVA (yes vs. no)	1.57(0.82-2.9)	0.172	0.45(0.23-0.91)	0.027	0.86(0.42-1.78)	0.16	0.68(0.36-1.29)	0.237
DF (yes vs. no)	1.62(1.12-2.4)	0.01	0.56(0.38-0.83)	0.004	0.65(0.41-1.01))	0.055	0.51(0.36-0.72)	<0.001
Scr(>1.2 vs. ≤1.2 mg/dl)	1.65(1.26-2.16)	<0.001	0.58 (0.44-0.76)	<0.001	0.86(0.64-1.16)	0.337	0.44(0.33-0.56)	<0.001

\*Waist (≤80 vs. >80 cm for male and ≤90 vs. >90 cm for female and sex adjusted odds ratio was calculated)

Odds ratio of >1.1 or <0.9 are in bold

*FH* family history, *DDM* duration of diabetes melietus, *DHTN* duration of hypertension, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *FPG* fasting plasma glucose, *PPG* post pradial glucose, *HbA1c* glycosylated heamoglobin A1C, *CAD* coronary artery disease, *CVA* cerebrovascular accidence, *DF* diabetic foot, *SCr* serum creatinin

CI 1.18, 2.64), and those with duration of diabetes more than 9 years (OR 2.62, 95 % CI 2.05, 3.36), were more likely to receive insulin. Patients with BMI >25 kg/m<sup>2</sup> were more likely to receive oral antidiabetic drugs vs. insulin, [metformin (OR 1.25, 95 % CI 1.15, 1.35), sulfonylurea (OR 1.28, 95 % CI 1.01, 1.61)] compared with those having BMI  $\leq$ 25 kg/m<sup>2</sup>.

Among controlled vs. uncontrolled BP patients, there were no differences in prescribing pattern of antidiabetic drugs. The uncontrolled hyperglycemia and choice of the treatment were mostly congruous; for example, patients with HbA1c >7 % were more likely to receive insulin therapy. Patients with post prandial glucose (PPG) >140 mg/dl were more likely to receive insulin vs. oral antidiabetic drugs, compared with those  $\leq$ 140 mg/dl PPG (OR 2.12, 95 % CI, 1.47, 3.10). The odds ratio of receiving sulfonylurea therapies according to the PPG >140 mg/dl vs.  $\leq$ 140 mg/dl was 0.59 (95 % CI 0.40, 0.83).

There were indications of selective prescribing. Patients with microvascular complications neuropathy, nephropathy and retinopathy were more likely to receive insulin vs. oral antidiabetic drugs compared with those without neuropathy (OR 1.96, 95 % CI 1.52, 2.50), nephropathy (OR 1.77, 95 % CI 1.40, 2.24) and retinopathy (OR 1.97, 95 % CI 1.63, 2.40). Patients with CAD

and diabetic foot were more likely to receive insulin vs. oral antidiabetic drugs, compared with those with macrovascular complications CAD (OR 1.57, 95 % CI, 1.14, 2.2) and diabetic foot (OR 1.62, 95 % CI 1.12, 2.40).

#### Discussion

We evaluated patterns of antidiabetic drugs prescribed among established T2DM patients at PGIMER, Chandigarh. Metformin was the most common antidiabetic medication prescribed in T2DM obese patients. This pattern is consistent with practice recommendations [18–20]. Post United Kingdom Prospective Diabetes Study (UKPDS) metformin use increased after 1997 [21–24]. The anti-atherogenic effects of metformin contributes to reduction in atherothrombotic risk [25], decreases weight gain, and is regarded as a useful adjunct in insulin-requiring patients with type 2 diabetes [26].

Insulin was the most frequently prescribed monotherapy and also in those with microvascular and macrovascular complications, longer duration of diabetes and general hyperglycemia. This is in line with consensus in use of insulin could be justifiable for following evidences; recent meta-analysis suggesting the benefit of intensive glycemic control by reduction cardiovascular risk in intensive treatment group [27]. The studies, The Diabetes Control and Complications Trial - Epidemiology of Diabetes Interventions and Complications (DCCT-EDIC) [28] and the UKPDS [29] suggested that intensive glycemic control initiated soon after diagnosis of diabetes in those with a lower level of CVD risk might impart long-term protection from CVD events. Long-term follow-up of the DCCT and UKPDS cohorts suggested that treatment to  $A1_C$  targets below or around 7 % in the years soon after the diagnosis of diabetes was associated with long-term reduction in macrovascular complications.

About 70 % of T2DM patients were on combination therapy. Majority of the T2DM patients received two drug combinations metformin and sulfonylurea or metformin and insulin. Patients with microvascular and macrovascular complications were on combination therapy metformin and sulfonylurea followed by metformin and insulin with the rationale being to enhance insulin action. Metformin, added to insulin improved body weight, glycemic control, insulin requirements, and reduce the risk of macrovascular disease [30]. Sulfonylurea-metformin combination therapy was associated with a lower all-cause mortality; cardiovascular disease related mortality rates were lower in metformin users, compared with users of sulfonylurea monotherapy [31]. The treat to target algorithms of recent studies combining OADs plus insulin analogs have demonstrated that patients can reach glycemic treatment targets with low risk of hypoglycemia, greater convenience and with some analogs limited weight gain versus conventional insulin. Further, in a study of bedtime isophane insulin in combination with metformin, better glycemic control was achieved with less weight gain and lower rates of hypoglycemia than either insulin monotherapy or insulin in combination with sulfonylurea [32]. The use of metformin or glitazones in combination with insulin has insulin-sparing properties [33].

This pilot study has several limitations also. The choice of antidiabetic depends on the type of patients, their concurrent illness, the potential risks and benefits, the profile of adverse events, cost factors, as well as the availability of medicines. The discordance between recommendations and actual practice can be partially attributed to "clinical inertia," a phrase used to described as the recognition of a problem with a patient's management but failure to act [34]. The study has not taken into account above variables for prescribing pattern.

In conclusion, this study finding indicates that medication use was mostly consistent with evidence based practice guidelines in T2DM however, more than half of the patients had uncontrolled hyperglycemia. There was scope for improvement in prescribing, especially in the T2DM patients with complications.

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#### Conflicts of interest None

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