

## COMPARISON OF LIPID PROFILE PATTERN IN OBESE AND NON OBESE TYPE 2 DIABETIC PATIENTS AND TO STUDY THE PRESCRIPTION PATTERN OF ANTIDIABETIC DRUGS.

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### ABSTRACT

The aim of study was to evaluate the prescribing pattern of antidiabetics and compare the serum lipid profile in diabetic patient. Prospective and observational study was conducted at Indira Gandhi memorial hospital Shirpur; Maharashtra India. 163 patients with type 2 diabetes were enrolled. Fasting serum lipid profile was analyzed. Antidiabetic's medications were evaluated in the selected study population for prescribing pattern of drugs and their cost evaluation. Altogether 163 patients, 90 females and 73 males were enrolled. The average number of drugs per prescription was 2.00. Among the various antidiabetics, Biguanides were mostly prescribed. The average cost per prescription was INR 116.85. (US \$ 2.63). Most of the study subjects had lipid abnormalities and there was statistically significant difference in the proportions of subjects with different BMI (Body Mass Index) category and lipid abnormalities. Significant increase in levels of serum cholesterol ( $P<0.01$ ) and serum LDL -C ( $P<0.0001$ ) and significant decrease HDL-C ( $P<0.0001$ ) in overweight subject was observed. Metformin was the most commonly prescribed antidiabetics. Elevated LDL-C and Serum cholesterol and Reduced HDL-C are the prevalent lipid abnormalities in our patients with DM.

**Keywords:** Type 2 Diabetes mellitus, Antidiabetics medication, prescribing patterns, body mass index, Dyslipidemia.

### INTRODUCTION

Diabetes is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia associated with abnormal carbohydrate, protein and lipid metabolism.<sup>1</sup>The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030.<sup>2</sup>India had 32 million diabetic subjects in the year 2000 and this number would increase to 80 million by the year 2030.<sup>3</sup>The macrovascular complications of diabetes account for more than 70% of all deaths in individuals with diabetes.<sup>4</sup> Lipid abnormalities in type 2 diabetes are characterized by High triglyceride concentrations, Low high density lipoprotein-cholesterol concentrations, normal total and low density lipoprotein cholesterol concentrations.<sup>5</sup>70–97% of individuals with diabetes have dyslipidemia.<sup>6</sup>Type 2 diabetes is an independent risk factor for coronary artery disease and risk of coronary disease is three to four fold increased in patients with Type 2 diabetes compared with non-diabetic population.<sup>7</sup>Irrational use of drugs is a common problem worldwide.<sup>8</sup> The impact of inappropriate use of medicine on the healthcare system is reduction of quality of medicine which leads to increased morbidity and mortality, increased cost of therapy.<sup>9</sup>The main aim of the study was to provide valuable information to the researchers, policy makers and the prescriber to determine the drug use pattern in diabetic dyslipidemia.

### MATERIALS AND METHODS

This is a The prospective and observational study that featured 163 subjects with type 2 DM from outpatient ward of Indira Gandhi Memorial Hospital Shirpur Maharashtra between 15<sup>th</sup> of July 2009 to 14<sup>th</sup> February 2010. All Study subject with DM were recruited for the

study after the study protocol was approved by Institutional Human Ethical Committee of R.C.Patel Institute of Pharmaceutical Education and Research. Type 2 diabetic patients with either sex, more than 18 years of age and prescribed with antidiabetic drug was included in the study. Patients who were admitted in internal medicine ward, all type 1 DM patients, and diabetic patients with pancreatitis, acromegaly, and patient with steroid or lipid lowering therapy were excluded from the study. Weight was recorded to the nearest kilogram with the subject standing on the weighing machine without shoes and using minimum of clothing. Height was recorded with the subject erect, bare footed feet together, back and heels against the upright bar of height scale and the body mass indices (BMI) were calculated. They were divided in to four groups under weight, normal weight, overweight and obese. Fasting total cholesterol, triglycerides and HDL was tested by "End point Biochemistry" method. The serum LDL cholesterol concentration was calculated from the serum concentrations of total cholesterol, HDL cholesterol and triglycerides using the formula,  $LDL-C = TC - (HDL-C + TG/5)$ (mg/dl). Parallel fasting and 2 hours post prandial blood glucose were performed. Lipid profile data were analyzed separately using unpaired student t- test and one way ANNOVA by the use of computer soft-ware program, Graph Pad Prism five. The prescribing pattern was assessed in term of individual drug use, their classes & their percentage value was calculated. Results were expressed as mean ( $\pm$  Standard Deviation (SD) or Standard Error Mean (S.E.M.) using Microsoft Excel 2003/2007 programme.



## RESULTS AND DISCUSSION

### Results

Altogether 163 patients were enrolled in the study. Females were 90(55.21%), males were 73 (44.79%) and among these patients, the greatest number were in the age group of 41-50years [53 (32.51%)], followed by 51-60 years [52(31.90%)], 61-70 years [33 (20.24%)], 31-40 years [17 (10.42%)], 71-80 years [6 (3.71%)], 18-30 years[2 (1.22%)]. The mean  $\pm$  SD age of the patients was  $52.66 \pm 10.04$  years. In this study population 48 (29.44 %) subject were secondary educated followed by 45 (27.6%) were primary educated, 37 (22.7 %) were graduates and 28 (17.17%) were illiterates and 5 (3.06 %) were post graduate. Out of 163 patients, 75 (46.1%) female was housewives followed by 31(19.01%), patients as a serviceman, 27 (16.56 %) were farmer, 16(9.81%) were businessman, 14 (8.58%) were ex-service man. It was found that out of 163 patient, 66 (40.49%) was non vegetarian, 23 (14.11%) was Smoker, 22(13.49%) was alcoholics.

Among the study population, 38 (23.31%) had positive family history and 125 (76.68%) has negative family history of DM. 127 patients (77.91 %) had a diabetic history of less than 5 years, followed by 6-10 years in 21 patients (12.88 %), 11-15 years in 10 patients (6.13 %), 16-20 years in 4 patients (2.42 %) and more than 20 years in one patient (0.61%).

One, Two, three and four antidiabetic drugs were prescribed in 49 (30.06 %), 72 (44.17%), 34 (20.85%) and 8 (4.90 %) patients, respectively. The average number of drugs per prescription was 2.00. Among the various

antidiabetics, biguanides were the common class of drugs accounting for 152 (93.25%) of the total antidiabetics, followed by Sulphonylurea's 143 (87.73%), Thiazolidinediones 25 (15.33%), insulin 20 (12.26%) and  $\alpha$ -glucosidase inhibitors 7 (4.29%). Table 1.

**Table 1:** Class of Antidiabetics prescribed.

Class Of Antidiabetic Drugs	No Of Time Prescribed
<b>Sulphonylureas</b>	
Glibenclamide	18
Glimepiride	75
Gliclazide	6
Glipizide	44
<b>Biguanides</b>	
Metformin	152
<b>Thiazolidinedions</b>	
Pioglitazone	25
Insulin	20
<b>Alpha glucosidase inhibitor</b>	
Acarbose	1
Voglibose	6

In the present study 49 prescriptions contains monotherapy. Metformin accounts for greatest 28 (58.33%) prescription as monotherapy followed by Glipizide 8 (16.66%), Glibenclamide 7 (14.58%), Glimepiride and Insulin 2 (4.16%), Pioglitazone 1 (2.08%). Table 2.

**Table 3:** Distribution of combination therapy

No of drug in combination	Class of Drugs in Combination	No. of Time Prescribed	% of Total antidiabetic drug Prescribed
2	Biguanides + Sulphonyl urea's	64	56.14
	Biguanides + Thiazolidinedions	2	1.75
	SulphonylUrea's+ Thiazolidinedions	1	0.87
	Insulin + Biguanides	2	1.75
	Insulin +Sulphonylureas	3	2.63
3	Biguanides + SulphonylUrea's+ Insulin	7	6.14
	Biguanides + SulphonylUrea's+ Thiazolidinedions	16	14.03
	Biguanides + SulphonylUrea's+ $\alpha$ glucosidase inhibitor	3	2.63
	Biguanides + sulphonylureas	8	7.07
4	Biguanides +SulphonylUrea's+Thiazolidinedions + $\alpha$ glucosidase inhibitor	2	1.75
	Biguanides +SulphonylUrea's+ $\alpha$ glucosidase inhibitor + Insulin	1	0.87
	Biguanides +SulphonylUrea's + Insulin	2	1.75
	Biguanides +SulphonylUrea's+ $\alpha$ glucosidase inhibitor	1	0.87
	Biguanides +SulphonylUrea's+Thiazolidinedions	1	0.87
	Biguanides +SulphonylUrea's+Thiazolidinedions + Insulin	1	0.87



**Table 2:** Distribution of monotherapy

Name of drug	Dosage form	No of time prescribed	% of total antidiabetic drug prescribed
Glibencamide	Tablet ( 5 mg,2.5 mg)	7	14.58
Glimepiride	Tablet ( 1 mg, 2 mg )	2	4.16
Glipizide	Tablet 5 mg	8	16.66
Metformin	Tablet (500mg,1000mg)	28	58.33
Pioglitazone	Tablet (15mg,30mg)	1	2.08
Insulin	-	2	4.16

**Table 5:** Comparison of t-values between males and females

Category	BMI ( $kg/m^2$ )	Serum Cholesterol ( $mg/dl$ )	TG ( $mg/dl$ )	HDL-C ( $mg/dl$ )	LDL-C ( $mg/dl$ )
Underweight	0.78	2.86*	1.09	0.90	1.29
Normal	0.38	2.32*	0.41	2.81**	1.10
Overweight	0.16	2.66*	2.71**	0.10	3.11**
Obese	1.65	2.58*	2.34*	0.79	2.40*

p value less than 0.05 is considered as significant, method = Unpaired student - t test.

**Table 6:** Prevalence of Dyslipidemia in the groups

Lipid Profile	Underweight (n=10)	Normal (n=73)	Overweight (n=48)	Obese (n=32)	Total n=163
Increased serum cholesterol	6 (60%)	44(60.23%)	41(85.41%)	21(65.25%)	68.71%
Increased TG	0 (0%)	18(24.65%)	12(25%)	15(46.87)	27.60%
Decreased HDL	4 (40%)	35(47.94%)	37(77.08%)	21(65.62%)	64.41%
Increased LDL	6 (60%)	52(71.1%)	46(95%)	29(90.62%)	81.59%

**Table 7:** Comparison of lipid profile pattern in four categories

Lipid Profile	Underweight Mean±SD	Normal Mean±SD	Overweight Mean±SD	Obese Mean±SD	P -value
Serum cholesterol	207.3±45.98	218.4±54.03	247.9±47.98	233.5±52.37	0.0110*
TG	105.8±30.31	125±79.68	135.2±53.95	154.6±64.70	0.1177
HDL-C	70.21±31.03	56.14±19.12	42.53±13.04	45.52±13.60	0.0001***
LDL-C	116.0±50.97	137.5±53.44	178.3±48.87	160.2±57.18	0.0001***

p value less than 0.05 is considered as significant, method=one way ANNOVA.

In this study 114 prescriptions contains combination of 2 or more drug. Biguanides and Sulphonylureas was found to be most frequently used Two drug combination in 64 (56.14 %) prescriptions, followed by Biguanides, Sulphonylureas and Thiazolidinedions a three drug combination in 16 (14.03 %). A four drug combination was also prescribed. Insulin with OHA is prescribed in 16 (14.03%) patients. Table 3.

Among the various insulin preparations, Insulin (30/70) was prescribed in 14 (70%) patients, Insulin Actrapid in 4 (20%), Insulin Human Mixtard in 2 (10%) patient.

The average cost per prescription was INR 116.85. (US \$ 2.63). The details regarding the cost of prescriptions are listed in Table 4.

Out of 163 diabetic patients 98(60.12%) had at least one coexisting illness during the study period. There were total of 106 illnesses in these 98 patients. Hypertension was found in 69(65.09%) patients.



**Table 4:** Cost of therapy

Cost In Rupees	No of prescriptions	%
<100	92	56.44
101-200	42	25.76
201-300	14	8.58
301-400	10	6.13
401-500	2	1.22
>500	3	1.84

Out of 163 patients 10 (6.13%) (3 males and 7 females) was underweight, 73 (44.80%) (39 males and 34 females) was normal weight, 48 (29.44%) (23 males and 25 females) was overweight, 32 (19.63%) (8 males and 24 females) was obese.

When comparisons was made on the distribution of BMI and four lipid components between males and females, statistically significant differences ( $p < 0.05$ ) were found for serum cholesterol in all categories ( $t=2.86, t=2.32, t=2.66$  and  $t=2.58$  for underweight, normal, overweight and obese respectively). Statistically significant differences ( $p < 0.05$ ) were found in serum triglycerides and LDL-C in overweight and obese. ( $t=2.71, t=2.34$  and  $t=3.11, t=2.40$  for overweight and obese respectively), For HDL-C statistically significant differences ( $p < 0.01$ ) were found only in normal weight category. Unpaired student- t test was used to compare the data in males and females. Table 5.

More than 50% of patients in all the groups showed hypercholesterolemia. Overweight patients had a higher percentage 41(85.41%) with hypercholesterolemia. 27.60 % had high serum triglyceride, obese patients, 21(65.25%) found high incidence of hypertriglyceridemia. 64.41 % of the total subjects were found to have low HDL cholesterol levels. Overweight patients had a high incidence 37(77.08%) of low HDL cholesterol. 81.59 % were found to have increased levels of serum LDL Cholesterol, 46(95%) in overweight subjects had high LDL-C. The prevalence of dyslipidemia is listed in Table 6.

It was observed that the significant increase in levels of serum cholesterol ( $P < 0.01$ ) and serum LDL -C ( $P < 0.0001$ ) in overweight patient. There is a significant decrease in HDL-C ( $P < 0.0001$ ) in overweight as compare to normal weight, underweight and obese patient. The increased level of serum triglyceride was found in obese patient but the difference is not statistically significant. Table 7.

## DISCUSSION

Prescribing practice studies, aggregate data or health facility indicators may indicate that there is over or under-consumption of medicines and qualitative studies may indicates why certain health staff and patients behave the way they do. The type of lipoprotein abnormality in diabetes depends upon many factors such as type of diabetes, endogenous insulin reserve, degree and

distribution of obesity, degree of glycemic control, type of therapy and the presence or absence of Nephropathy. Majority of selected patients were females this is contradictory to previous studies that is study from Nepal and Indore.<sup>10,11</sup>

In this study, we found a higher incidence of diabetes among elderly patients, in the age group between 41-50 years. This study reported a lower age of patients as compared to other studies<sup>10,11</sup> Women of high socioeconomic status tend to be more concerned about their fitness, consume healthy food, and practice regular exercise as found in servicing woman, but this correlation between health practices and economic status does not exist in male subjects with service as a occupation, the finding of this study correlates with Spanish study.<sup>12</sup>

In the present study, nearly two-thirds (77.91%) of the patients had a diabetic history of less than 5 years. Patients with a long duration of diabetes are at a higher risk of developing complications. Among the various complications, cardiovascular complications create burden on patients regarding treatment.

The average number of drugs per prescription was found to be 2.00. Previous study from Nepal reported it as 3.76 drugs per prescription.<sup>10</sup> Our study shows 2 drug combination therapy was most prescribed similar as in study from Indore.<sup>11</sup> This study shows that biguanides are the most commonly prescribed antidiabetic class of drug followed by sulfonylureas. A study from Malaysia and Taiwan reported sulfonylurea's as the most common drug class followed by biguanides.<sup>13,14</sup> The present study shows that Metformin and Glimepiride was most frequently used combination. In previous studies Sulfonylurea + Metformin, was most often prescribed two drug fixed dose combination.<sup>15</sup> In our study 20 (12.26%) patients received insulin therapy. Another study from Diabetic Clinic in Ibadan Nigeria, found 26.4% of patients received insulin.<sup>16</sup>

In our study, average cost per prescription was found to be INR 116.85. Approx US \$ 2.63). Study from India shows the average estimate of direct annual expenditure on ambulatory care of diabetes was Rs. 6000 (US\$ 150).<sup>17</sup> There is a huge scope in reducing the prescription cost by prescribing cheaper alternatives. However, while choosing cheaper brands, one should keep in mind the quality of the brands.

In present study, hypertension accounted for highest of the total co-morbidities seen in the diabetic patients. According to study from Orissa, India<sup>18</sup> most common disease associated with diabetes was found to be hypertension. Evidence suggest that the possible cause of increased rate of hypertension in diabetic patient is due to possible mechanism of Insulin resistance leading to abnormalities in renal tubular ion exchange, rennin angiotensin system, prostaglandin kallikrein/kinin system., diabetic nephropathy.<sup>19</sup>



The major cause of mortality in type 2 diabetes mellitus is coronary heart disease.<sup>20</sup> The most characteristic lipid abnormality in diabetes is hypertriglyceridemia, with or without associated increase in plasma cholesterol. Studies from various parts of India reveal differences in the prevalence of lipid abnormalities in diabetes. In this study majority of the subjects were found to higher LDL-C levels, which is comparable to study from Hazara division. The higher number overweight patients are prevalent of high LDL cholesterol. Another prevalent lipid abnormalities includes increased serum cholesterol, low HDL-C as complimentary to study from northern India.<sup>22,23</sup>

In current study we compare the lipid profile pattern of underweight, normal weight; overweight and obese diabetic patients. Study shows overweight individual had statically significant difference in serum cholesterol, LDL-C and HDL-C levels as compare to normal weight and obese patient. More than half of the overweight and obese patient had increased serum cholesterol and increased LDL-C level and decreased HDL-C levels as compare to normal weight and underweight patients. This study comparable to study from Nigeria<sup>24</sup> which shows that half of the study subjects with dyslipidemia were overweight.

## CONCLUSION

This study had provided a baseline data regarding the prescribing pattern of antidiabetic drugs in diabetes patients. Metformin was the most commonly prescribed antidiabetics. We hope that our data will helpful to sensitize health care practitioners on screening of medications and treating dyslipidemia. Elevated LDL-C and reduced HDL-C should be the primary targets of treatment in our patients with dyslipidemia.

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