DOI: 10.7860/JCDR/2016/16044.7063

Original Article

Internal Medicine Section

# Prescribing Pattern of Oral Antihyperglycaemic Drugs, Rationality and Adherence to American Diabetes Association (ADA) Treatment Guidelines among Type 2 Diabetes Mellitus (T2DM) Postmenopausal Women

SUDHAA SHARMA[1], VISHAL R. TANDON[2], ROSHI[3], ANNIL MAHAJAN[4]

## ABSTRACT

**Introduction:** Oral antihyperglycaemic prescription trends keep on changing and thus the drug prescription trend study may prove to be powerful exploratory tool for health care providers.

**Aim:** To investigate trends in prescriptions of oral antihyperglycaemic drugs (OHDs) among postmenopausal women suffering from T2DM in India and evaluate the rationality and adherence to ADA treatment guidelines.

**Materials and Methods:** An observational, cross-sectional descriptive prescription audit (n=500) was carried. Postmenopausal women were interviewed in their local language using pre-tested pre validated questionnaire after verbal informed consent at a teaching tertiary care hospital of north India. Oral antihyperglycaemic drugs (OHDs) drugs were categorized as per the pharmacological classification. Adherence to available clinical practice guidelines/recommendations issued under American Diabetes Association (ADA) 2015 Guidelines as well as rationality of these prescriptions were assessed using WHO Guide to Good Prescribing.

**Results:** Mean age of the study population was 58.14±12.86. Mean duration since menopause was 5.3 years and of T2DM was 9.5 years. A 93.4% of the prescriptions had only OHDs whereas 6.6% of the prescriptions had various insulin preprations + OHDs (p<0.0001). Biguanides followed by sulfonylureas, thiazolidinediones, DPP-inhibitors and alpha-glucosidases inhibitor were prescribed in 85.6%, 59.8%, 26.6%, 26% and 12.2% respectively as monotherapy or in combination. Among biguanides, metformin was the most frequently prescribed OHDs. In spite of black box warning on pioglitazone, it was prescribed in 26.6% as FDC. However, clear increase use of vidagliptine was noticed upto 26%. Among combinations most frequent was metformin plus glimipride followed by voglibose plus metformin, whereas, among FDC, metformin plus glimipride followed by metformin plus vidagliptine were most frequently prescribed.

**Conclusion:** Metformin was the most common OHDs to be prescribed followed by glimepiride. Although pioglitazone still continues to be prescribed after safety alert but apparently it appears that the share of pioglitazone has been shifted to vidagliptin or combinations like metformin plus glimipride. Polypharmacy, high use of FDC, & prescription by brand names were some of the irrationalities. Relatively low adherence to ADA treatment guidelines was observed.

**Keywords:** Oral antihyperglycaemic, Prescription trends, Type 2 Diabetes Mellitus

## INTRODUCTION

Drug prescription trend studies of oral antihyperglycaemic may be a powerful exploratory tool to establish treatment guidelines/rationality for type 2 diabetes mellitus and have an insight about common prescribing errors by the health care providers. Oral antihyperglycaemic prescription trends have shown many swings over a period of decade in view of various restrictions and ban imposed on one or other class of oral antihyperglycaemic drug over a period of time [1-5].

Ban was imposed on pioglitazone by French agency and German federal institute in view of increase risk of this drug to cause bladder cancer and worsening of Congestive Heart Failure (CHF). US FDA advices followed thereafter against the use of this drug in NYHA Class III and IV CHF patients.

As a knee jerk reaction, India drug regulatory authorities on 18th June, 2013 imposed ban on manufacturing and sale of pioglitazone and all formulations containing it in India. Indian government revoked this ban after the advice of the Drug Technical Advisory Board (DTAB) on 31st July 2013 with a condition on pharmaceutical companies to carry a box warning indicating the possible risk of bladder cancer. Furthermore, the media storm of this news created a great sense of insecurity among users and prescribers for the use of this drug [1].

The safety alerts have a clear impact on prescribing behavior as reported after rosiglitazone & sulfonylureas safety alert [2-4].

Although there is a study after pioglitazone safety alert [5] but it was from Netherlands, but no study has appeared from India after issue of the recent pioglitazone safety alert.

Menopause (surgical or natural) has an unfavorable effect on glucose metabolism and thus is likely to be responsible for increased incidence of Type 2 diabetes with advancing age after 40 years [6]. The reasons postulated for this are obesity, metabolic syndrome, inactivity, poor dietary habits, besides hormonal and metabolic changes [7,8]. Thus, diabetes is an important health issue among postmenopausal women [8].

The studies are available describing trends in the prescription of anti-diabetic medications among patients with type 2 diabetes [9-14] but to the best of our knowledge, no study exists that analyses such trends among postmenopausal women. Secondly,

such study trying to look at adherence with standard treatment guidelines recommendations issued under American Diabetes Association (ADA) 2015 Guidelines [15] as well as rationality of these prescriptions using WHO Guide to Good Prescribing [16] particularly after pioglitazone safety alert in India shall prove very useful to health care providers. Hence, the current study was undertaken to investigate trends in prescription of oral antihyperglycaemic drugs (OHDs) among postmenopausal women in India.

## MATERIALS AND METHODS

An observational, cross-sectional descriptive prescription audit study was carried over a period of one year in a teaching tertiary care hospital of north India, Government Medical College Jammu, after institutional ethics committee approval. A total of 500 prescriptions prescribed to postmenopausal women (with cessation of menstruation for one year) for diagnosed type 2 diabetes mellitus, were identified for one point analysis. Oral antihyperglycaemic drugs (OHDs) drugs were categorized as per the pharmacological classification.

Detailed epidemiological profile, common menopausal symptoms, presence or absence of any co-morbid conditions, OHDs drug prescription patterns/trends and their adherence to available clinical practice guidelines/recommendations issued under American Diabetes Association (ADA) 2015 Guidelines [15] as well as rationality of these prescriptions were assessed using WHO Guide to Good Prescribing [16]. The elements of assessment for the rationality and ADA treatment guidelines used in the current study are shown in [Table/Fig-1,2] respectively.

Data regarding OHDs drug monotherapy, dual combination and triple/four drug combination were recorded. Evaluation for rational drug therapy by evaluating average number of drugs per prescription, FDC prescription rate, prescription laying down importance of lifestyle management, prescription with defined goals, prescriptions with correct dose strength and dosage schedule were evaluated. Number generic and brand names used was also worked out. The prescriptions were collected by an independent person by clicking the picture by mobile of prescriptions mentioning duration of therapy, over-prescribing, banned drug formulations, outside the different medical/endocrinology/postmenopausal OPD and interviewing the postmenopausal women without the knowledge of prescriber to avoid any bias after due permission. Regarding some of the information regarding the disease, menopause and adherence to ADA guidelines postmenopausal women were interviewed in their local language using pre-tested pre-validated questionnaire after verbal informed consent.

## STATISTICAL ANALYSIS

All the analysis was carried out with the help of computer software SPSS Version 15 for windows. The data was expressed in n (%). Chi-square test was applied for some of the parameters to prove their statistical significance. The p-value < 0.05 was considered significant.

## RESULTS

Mean age of the study population was 58.14±12.86. Mean age at menopause was 54.56±2.76 years and mean number of menopausal symptoms was 3.70±0.76. Mean duration since menopause was 5.3 years and mean duration of T2DM was 9.5 years. Majority (91.2%) had natural menopause and were illiterate from rural area with sedentary lifestyle. Most common menopausal symptoms was urogenital (30%) followed by fatigue and lack of energy (25.6%) and vasomotor symptoms (24.6%). Old diagnosed T2DM accounted significantly p<0.0001 more (87.8%) then new diagnosed patients (12.2%).

Optimal glycaemic control was seen in case of 13.2% of the patients where as 26.8% had uncontrolled T2DM as indicated by HBA1c >6.5 and in case of 60%, information was not available about HBA1c. T2DM presented as isolated disease in 27.8% were as significantly (p<0.0001) high population (72.2%) presented with one or more co-morbid conditions. Acid peptic disease, obesity/ overweight, hypertension, dyslipidemia and metabolic syndrome

| Parameters | Variables | p-value (Chi-sq test) |
|---|---|---|
| Average number of drugs per prescription | 6.57 | |
| Prescription rate stressing vs not stressing importance of lifestyle / dietary management | 28(5.6%) Vs 472(94.4%) | Chi-square=788.544 DF=1 p < 0.0001 |
| Prescription rate with defined vs undefined anti-diabetic Goals | 47 (9.4%) Vs 453 (90.6%) | Chi-square = 659.344 DF=1 p < 0.0001 |
| Dose strength mentioned Vs Non Mentioned rate | 379(75.8%) Vs 121(24.2%) | Chi-square= 266.256 DF=1 p va<0.0001 |
| Dose Schedule mentioned Vs Non Mentioned rate | 488 (97.6%) Vs 12(2.4%) | Chi-square= 906.304 DF=1 p < 0.0001 |
| Ban drug formulation prescription rate | 0 | |
| Generic name Vs brand name prescription name | 123(24.6%) Vs 377 (75.4%) | Chi-square= 258.064 DF=1 p < 0.0001 |
| Prescription rate of fixed dose combination vs monotherapy rate/ drugs in combination | 230(46%) Vs 270(54%) | Chi-square= 6.400 DF=1 p = 0.0114 NS |
| Prescription rate of drug with box warning (Thiazolidinediones) Vs Other | 133 (26.6%) Vs 367(73.4%) | Chi-square= 219.024 DF=1 p <0.0001 |
| Prescription rate of newly introduced drugs (DPP-Inhibitors+GLP-1 analogs Vs Other | 130 (26%) Vs 370(74%) | Chi-square= 230.400 DF=1 p < 0.0001 |

**[Table/Fig-1]:** Evaluation of rational drug prescription of oral antihyperglycaemic drugs.

| Parameters | Variables | Chi-square test |
|---|---|---|
| Blood sugar checked by a laboratory Fasting Blood sugar: Meticulously/Regularly/Infrequently/ Rarely | 278(55.6%)/133(26.6%)/56(11.2) /33(6.6%) | p<0.0001 |
| Blood sugar checked by a laboratory Post Prandial: Meticulously/Regularly/Infrequently/ Rarely | 1479(29.4%)/109(21.8%)/99(19. 8%)/145(29%) | p<0.001 |
| HBA1c checked: Meticulously/ Regularly/ Infrequently/Rarely: | 33(6.6%)/57(11.4%)/167(33.4%) /243(48.6%) | p<0.0001 |
| Most patients should begin with lifestyle changes as per ADA guideline: Applicable/adhered /Non adhered | 107(21.4%)/23(4.6%)/ 84(16.8%) | p<0.0001 |
| Metformin monotherapy as initial therapy : applicable/adhered /Non adhered | 189(37.8%)/94(18.8%) /95(19%) | NS |
| A1C target is not achieved after approximately 3 months, considering a combination in step up approach as per ADA treatment guidelines: Applicable/adhered / Non adhered | 239(47.8%)/52(10.4%)/ 187(37.4%) | p<0.0001 |
| Exercise Protocol followed: Meticulously/Regularly/Infrequently/ Rarely | 45(9%)/55(11%)/155(31%)/24 5(49%) | p<0.0001 |
| Dietary restriction followed: Meticulously/ Regularly/Infrequently/ Rarely: | 56(11.2%) /35(7%)/167(33.4%)/242(48.4%) | p<0.0001 |
| Eye/CVS/Neurological check up: Meticulously/Regularly/Infrequently/ Rarely: | 17(3.4%)/23(4.6%)/57(11.4%)/4 03(80.6%) | p<0.0001 |
| Switch over to alternative/ herbal treatment Vs No Switch over | 23(4.6%) Vs 477(95.4%) | p<0.0001 |
| Switch over to other doctors vs No switch over | 137(27.4%) Vs 363(72.6 | p<0.0001 |
| Switch over of the ongoing treatment even if A1c control | 44 (8.8%) | |

**[Table/Fig-2]:** Adherence to American Diabetes Association (ADA) treatment guidelines.

| Parameters (N=500) | Variables | Chi sq test |
|---|---|---|
| Mean age | 58.14±12.86 | |
| Mean age at menopause | 54.65 years ± 2.76 | |
| Mean number of menopausal symptoms | 3.70± 0.76 | |
| Mean duration since menopause | 5.3 years | |
| Mean duration of DM | 9.5 years | |
| Natural menopause Vs Surgical Menopause | 456(91.2%) Vs 44(8.8%) | p<0.0001 |
| Education status: Literate/ Illiterate | 228(45.6%)/272(54.4%) | p=0.0054 |
| Urban vs Rural | 212(42.4%)vs 288(57.6%) | p<0.0001 |
| Life style : Active / Hectic / Sedentary | 100(20%)/ 67(13.4%) 333(66.6%) | p<0.0001 |
| Dietary life style: Veg/ Non-veg/ Mixed | 389(77.8%)/67(13.4%)/44(8.8%) | p<0.0001 |
| **Common Menopausal Symptoms (more than I symptoms were noticed)** | | |
| Uro-genital symptoms | 150(30%) | |
| Vasomotor Symptoms/Hot Flushes | 123(24.6%) | |
| Fatigue, lack of energy | 128(25.6%) | |
| Cold hand and feet, rheumatic pain | 55(11%) | |
| Cold sweats, weight gain, irritability & nervousness | 69(13.8%) | |
| Palpitation of heart, excitable/ anxiety | 83(16.6%) | |
| Old diagnosed T2DM Vs New Diagnosed T2DM | 439(87.8%) Vs 61(12.2%) | p< 0.0001 |
| On OHDs Vs On Insulin +OHDs | 467 (93.4%) Vs 33(6.6%) | p<0.0001 |
| On mono-therapy | 166 (33.2%) | |
| Combination | 104 (20.8%) | |
| Fixed Drug Combination | 121(24.2%) | |
| FDC + Mono-therapy | 109 (21.8%) | |
| Optimal glycaemic Controlled Vs Uncontrolled T2DM by HBA1c <6.5 Vs Information not available | 66(13.2%) Vs 134(26.8%) Vs 300(60%) | p<0.0001 |
| Isolated disease with co-morbid condition | 139(27.8%) Vs 361(72.2%) | p<0.0001 |
| Most common co-morbid condition: Obesity & Overweight/ APD/Hypertension/ Dyslipidemia/ Metabolic syndrome/ OA/ Rheumatological Disorder/ Hypothyroidism/ Hyperuricaemia/ CHF/ COPD/ Asthma/ /IHD/ / Anxiety | 97(19.4%)/78(15.6%)/ 112(22.4%) 27(5.4%)/22(4.4%)/44(8.8%)/18(3.6%)/27(5.4%)/22(4.4%)/5(1%)/8(1.6%)/5(1%)/9(1.8%)/32(6.4%) | |
| With complication vs without complication | 30(6%) Vs 470(94%) | p<0.0001 |
| Most Common Complication of DM: Retinopathy/Gastropathy/ Neuropathy/nephropathy/ Tripathy | 5(1%)/12(2.4%)/40(8%)/7(1.4%) /2(0.4%) | |

**[Table/Fig-3]:** Demographic profile of study population

| | |
|---|---|
| **Mono-therapy (n=166)** | |
| Metformin 500 mg -2g BD | 94(18.8%) |
| Glimepiride 1- 4 mg BD | 52(10.4%) |
| Vidagliptine 50-100 mg BD | 11(2.2%) |
| Pioglitazone-15mg-30 mg BD | 2(0.4%) |
| Gliclazide 40mg- 80mg BD | 8(1.6%) |
| Sitagliptin | 1(0.2%) |
| **Combinations (n=104)** | |
| Metformin 500mg-1g + Glimepiride 1/2 mg BD | 29(5.8%) |
| Metformin 1g-2g + Glimepiride 1/2mg BD | 18(3.6%) |
| Glibenclamide 5mg+Metformin 500mg BD | 05(1%) |
| Voglibose 0.2mg TDS+ Metformin 500mg BD | 16(3.2%) |
| Voglibose 0.3mg TDS+Metformin 500mg BD | 12(2.4%) |
| Acarbose 50mg TDS + Metformin 500mg BD | 04(0.8%) |
| Vidagliptin 50mg BD +Metformin 500mg BD | 16(3.2%) |
| Sitagliptin+Metformin 500mg BD | 4(0.8%) |
| **FDC (n=121)** | |
| Metformin 500mg/1g + Glimepiride 1/2mg BD | 36(7.2%) |
| Metformin 1g + Glimepiride 1mg BD | 12(2.4%) |
| Metformin 1g + Glimepride 2mg BD | 11(2.2%) |
| Metformin 500mg+Pioglitazone15mg BD | 4(0.8%) |
| Metformin 500mg + Glimepiride 1mg+ Pioglitazone 15mg BD | 09(1.8%) |
| Metformin 500mg + Glimepiride 2mg+ Pioglitazone 15mg BD | 7(1.4%) |
| Metformin 1g + Glimepiride 1mg+ Pioglitazone 15mg BD | 5(1%) |
| Glibenclamide 5mg+Metformin 500mg BD | 3(0.6%) |
| Voglibose 0.2mg+ Metformin 500mg BD | 8(1.6%) |
| Voglibose 0.3mg+Metformin 500mg BD | 6(1.2%) |
| Vidagliptin 50mg +Metformin 500mg | 19(3.8%) |
| Sitagliptin +Metformin | 1(0.2%) |
| **Four drug combination (n=109) FDC + Mono-therapy** | |
| FDC(Metformin 500mg + Glimepiride 1mg+ Pioglitazone 15mg) + Vidagliptin 50mg BD | 23(4.6%) |
| FDC(Metformin 500mg + Glimepiride 2mg+ Pioglitazone 15mg) + Vidagliptin 50mg BD | 06(1.2%) |
| FDC (Metformin 1g + Glimepiride 1mg+ Pioglitazone 15mg) + Vidagliptin 50mg BD | 13(2.6%) |
| FDC(Metformin 500mg + Glimepiride 1mg+ Pioglitazone) 15mg + Sitagliptin BD | 2(0.4%) |
| FDC(Metformin 500mg + Glimepiride 1mg+ Pioglitazone 15mg) TDS+ Voglibose 0.3mg BD | 19(3.8%) |
| FDC (Metformin 1g + Glimepiride 1mg+ Pioglitazone 15mg) BD+ Voglibose 0.3mg TDS | 7(1.4%) |
| FDC(Metformin 500mg + Glimepiride 1mg) BD + Voglibose 0.3mg TDS | 5(1%) |
| FDC (Metformin 500mg + Glimepiride 2mg) BD+ Vidagliptin 50mg BD | 3(0.6%) |
| FDC(Metformin 1g + Glimepiride 1mg) + Vidagliptin 50mg BD | 18(3.6%) |
| FDC(Metformin 1g + Glimepiride 2mg) + Vidagliptin 50mg BD | 13(2.6%) |

**[Table/Fig-4]:** Frequency distribution of oral antihyperglycaemic drugs

accounted main co-morbid condition in the current study cohort. A 6% had the complication of diabetes whereas significantly larger number of population had no complications (p<0.0001) [Table/Fig-3].

A 93.4% of the prescriptions had only OHDs where as 6.6% of the prescription had various insulin preprations + OHDs (p<0.0001). 33.2% of the prescriptions had OHDs prescribed as monotherapy whereas 20.8%, 24.2% & 21.8% had OHDs in combination, as FDC and FDC along with monotherapy respectively. The detailed categorization of the OHDs is depicted in [Table/Fig-4].

Biguanides followed by sulfonylureas, thiazolidinediones, DPP-Inhibitors and glucosidase inhibitor were prescribed in 85.6%, 59.8%,26.6%, 26% and 12.2% respectively as monotherapy or in combination [Table/Fig-5].

Among Biguanides, metformin was the most frequently prescribed OHDs alone, in pure combination or as FDC as well as along with Insulin. Whereas, among sulfonylureas, glimepiride was the most frequently drug prescribed. Maximum daily dose reported was 2g for metformin and 4mg for glimipride in the current study. Among alpha- glucosidases inhibitor, voglibose remained most frequently prescribed not as monotherapy but as in combination or as co therapy along with FDC. In spite of the of black box warning on pioglitazone, it was found prescribed in 26.6% of the prescription mainly as FDC. However, clear increased use of vidagliptin as monotherapy and mainly as FDC or in combination was noticed as up to 26%, matching pioglitazone prescriptions.

Among combinations most frequent was metformin plus glimepiride followed by voglibose plus metformin, whereas, among FDC,

| Class of OHDs | Frequency distribution |
|---|---|
| Sulfonylureas | 299(59.8%) |
| Biguanides | 428(85.6%) |
| Alpha- Glucosidases inhibitor | 61(12.2%) |
| Thiazolidinediones | 133(26.6%) |
| DPP-Inhibitors | 130(26%) |
| GLP-1 analogs | 0(0%) |

**[Table/Fig-5]:** Frequency distribution of Oral antihyperglycaemic drugs as per pharmacological Classification

metformin plus glimepiride followed by metformin plus vidagliptine and metformin plus voglibose were most frequently prescribed FDC even taking preference over triple combination of metformin, glimepiride & pioglitazone in the current study. Most popular four drug combination was FDC (Metformin + Glimepiride + Pioglitazone) + Vidagliptine or voglibose [Table/Fig-4].

While evaluating the rationality of the prescription polypharmacy was reported as average number of drugs per prescription was recorded to be 6.57 which is relatively high. Significantly high p<0.0001 prescription failed to stress by documentation about life style/ dietary management and anti diabetic treatment goals. Significantly high p<0.0001 OHDs in prescription were prescribed by their brand names. FDC prescription rate was also very high in the current study. Whereas, there was no banned drug found to be prescribed in the current study and majority of prescriptions were found to prescribe in correct dose strength and schedule, pioglitazone in spite having black box warning still continue to be prescribed in substantial number of prescriptions but there was clear tendency of using new drug at first go in the form of vidagliptines in the current study [Table/Fig-1].

While evaluating the adherence to ADA standard treatment guidelines results depicted that 55.6% and 29.4% of prescriptions adhered to the practice of getting fasting/ post prandial blood sugar done meticulously. Whereas the HBA1c was significantly (p<0.0001) less got checked meticulously by only 6.6% of the study cohort. As per ADA guidelines most patients should begin with lifestyle changes as this was applicable in 21.4% of the population but was adhered significantly less (p<0.0001) in only 4.6% of the subjects.

Regarding treatment depending A1C target giving three months treatment and then, considering a combination in step up approach as per ADA treatment guidelines was applicable in 47.8% but only 10.4% adhered whereas significantly high (p<0.0001) number amounting up to 37.4% did not adhere to such protocol.

Significantly high (p<0.0001) 49%, 48.4%, 80.6% of the patients rarely adhered to follow exercise, dietary and eye/CVS/neurological check up protocol as advised and recommended by ADA guidelines. Similarly switch over to intermittent alternative treatment/doctors and even to ongoing treatment in spite of controlled A1C was observed in significantly high (p<0.0001) of the population [Table/Fig-2].

## DISCUSSION

In the current study the mean age was 58.14±12.86 & mean duration since menopause was 5.3 years and of T2DM was 9.5 years. Most common menopausal symptoms were urogenital followed by fatigue and lack of energy. Optimal glycaemic control was seen only in 13.2% of the patients and majority presented with one or more co-morbid conditions. Only 6% had the complications of diabetes. This clearly suggests that DM is a major health issue among postmenopausal women which is in accordance to the study of van Dijk et al., [8].

Further, management of T2DM is very complex in this particular group and shall depend on various co-morbid conditions, duration of diabetes, presence of complications and surely affects the menopausal symptoms and related problems. Lejsková et al., in their study showed that compared with natural menopause, surgical menopause may have significantly more adverse effect on glucose metabolism [6]. Larsen et al., concluded that in older women, obesity is inversely associated with type II diabetes, although obesity /overweight was very common co-morbid condition and natural menopause was more common in our study subjects [7].

The study documented 93.4% of OHDs prescribed and only 6.6% of the prescription had various insulin preparations + OHDs (p<0.0001). The results are in contradiction to the study of Agarwal et al., as 43.6% of the prescription in their study contained insulin preparation in T2DM patients [17]. This discrepancy might be due to varied disease duration and less number of prescriptions (100) studied by them.

In the current study 33.2% of OHDs were prescribed as monotherapy where as 20.8%, 24.2% & 21.8% had OHDs in combination, as FDC and FDC along with monotherapy respectively. Biguanides followed by sulfonylureas, thiazolidinediones, DPP-inhibitors and glucosidase inhibitor were prescribed in 85.6%, 59.8%, 26.6%, 26% and 12.2% respectively. The results are in contradiction to the results of previous studies [10,11,17] wherein sulfonylureas were the most commonly prescribed class of OHDs followed by biguanides and then FDC. In the current study metformin was the most common prescribed individual OHDs followed by glimepiride which is similar to several previous studies [9,13,14].

The reasons why metformin was most preferred choice in the current study is probably because of the fact that it has many advantages like it does not cause hypoglycaemia and weight gain due to its peculiar mechanism of action beside having many non-glycaemic advantages like its utility to prevent insulin resistance, metabolic syndrome, fatty liver helping as an adjuvant in keeping check over dyslipidemia and hypertension [18]. The results are in accordance to the ADA 2015 standard treatment guidelines which recommend metformin to be used as initial therapy in most of the patients in view of long-standing evidence base for efficacy and safety, also because it is inexpensive, and may reduce risk of cardiovascular events [15].

Metformin may be contraindicated as per ADA guidelines in elderly patients with age more than 65 years with renal insufficiency or significant heart failure [15]. However, in our study it was the most frequently prescribed drug both alone or in combination. The possible reasons for it may be that mean age of the patients was 58.14 years and there were only two patients of nephropathy and five patients presented with congestive heart failure.

Among sulfonylureas, glimepiride was the most frequent by prescribed drug. The choice was possibly because of its efficacy to achieve glycaemic control as monotherapy or in combination. However, as per ADA guidelines [15] it is recommended only as dual combination after failure with metformin to achieve gylcaemic control as initial therapy. Thus, results reflect that biguanides and sulfonylureas are still the choice of most physicians in the treatment of type 2 diabetes even for postmenopausal women. Among alpha-glucosidases inhibitor, voglibose remained most frequently prescribed not as monotherapy but as combination or as co-therapy along with FDC in the current study. But the number was far less (12.2%) probably reflecting that the post meal blood sugar control is given low priority in Indian setup. This is further observed in the current study that only 29.4% of the population recorded post meal blood sugar meticulously, whereas post meal hyperglycaemia is more prevalent problem among Asian population [19].

In spite of the of black box warning on pioglitazone, it was found prescribed in 26.6% of the prescriptions mainly as FDC. Although it will be difficult to comment that the pioglitazone use has decreased or remained same after safety alert in India as no attempt was made to compare before and after safety alert prescription trend of pioglitazone. But apparently it appears that the share of pioglitazone has been shifted to other treatment options. The clear increase use of vidagliptin as monotherapy and mainly as FDC or in combination

was noticed as upto 26% in the current study matching pioglitazone prescriptions. Similar increase in use of combinations like metformin plus glimipride followed by voglibose plus metformin and FDC of metformin plus glimipride followed by metformin plus vidagliptine and metformin plus voglibose were recorded. This might be the effect of safety alerts issued recently by Indian regulatory agencies over pioglitazone.

The results are thus in accordance to the study of Hurren et al., who recorded approximately 23% of patients to discontinue rosiglitazone and switched over to pioglitazone and also recorded an increase in sitagliptin prescribing in patients who discontinued TZDs after rosiglitazone safety alert [2]. Leal et al., also recorded the increased use of pioglitazone surpassing rosiglitazone from April 2008 onwards and the incidence of rosiglitazone use decreased sharply after May 2007 (0.8/1000 person-years) after the safety alert [3]. Sato et al., recorded glimepiride dose reduction trend after hypoglycaemia safety alert with the drug. In our study also maximum dose of glimepiride used was 4mg per day and of metformin was 2 g per day [4].

The results of current study are also in accordance to the Ruiter et al., who recorded decreased prescribing of rosiglitazone and pioglitazone following safety signals in the Netherlands from 1998 to 2008 after drug safety alerts [5]. Irrationalities in the prescriptions documented in the form of polypharmacy, use of FDC, brand names, drugs having black box warning as in case of pioglitazone and clear tendency to use new drug at first go in the form of vidagliptins were noticed in the current study. The results are in accordance to our previous similar study undertaken among postmenopausal women in regards to anti-hypertensive drug prescription trends [20].

While evaluating the adherence to ADA standard treatment guidelines [15] results depicted that poor adherence to the practice of getting post meal blood sugar and get HBA1c checked meticulously were prevalent. Regarding treatment depending HBA1c target giving three months treatment and then, considering a combination in step up approach as per ADA treatment guidelines was also poorly adhered in the current study. Significantly high number of the patients rarely adhered to follow exercise, dietary and eye/CVS/neurological check up protocol as advised and recommended by ADA guidelines. Similarly switch over to intermittent alternative treatment/doctors and even to ongoing treatment in spite of controlled HBAIC was observed in significantly high number of subjects. The results clearly stress that there is need to create awareness at the level of patients and prescribing doctors regarding the most widely referred and used treatment guidelines in the form of ADA guidelines [15] for diagnosis and treatment of T2DM.

## LIMITATIONS

The current study has some limitations like no attempt was made to correlate the study parameters with menopausal parameters. No attempt was made to compare prescription before and after safety alerts on pioglitazone in India.

## CONCLUSION

DM is an important health issue among postmenopausal women. Metformin was the most common individual OHDs to be prescribed followed by glimepiride. Although pioglitazone still continues to be prescribed after safety alert but apparently it appears the share of pioglitazone has been shifted to other treatment options like vidagliptine or combinations like metformin plus glimipride, voglibose plus metformin, metformin plus vidagliptine. Polypharmacy, high use of FDC, & prescription by brand names were some of the irrationalities. Relatively low adherence to ADA treatment guidelines was observed in the current study.

**Conflict of Interest:** The current study is just a prescription trend study undertaken on 500 prescriptions. The result of the current study do not endorse/ recommend or refute use of any OHDs.

## REFERENCES


[1] Bhaumik S. Flip flop policy over pioglitazone licence causes media storm in India. *BMJ*. 2013;347:f4937.
[2] Hurren KM, Taylor TN, Jaber LA. Antidiabetic prescribing trends and predictors of thiazolidinedione discontinuation following the 2007 rosiglitazone safety alert. *Diabetes Res Clin Pract*. 2011;93(1):49-55.
[3] Leal I, Romio SA, Schuemie M, Oteri A, Sturkenboom M, Trifirò G. Prescribing pattern of glucose lowering drugs in the United Kingdom in the last decade: a focus on the effects of safety warnings about rosiglitazone. *Br J Clin Pharmacol*. 2013;75(3):861-68.
[4] Sato D, Sato Y, Masuda S, Kimura H. Impact of the sitagliptin alert on prescription of oral antihyperglycaemic drugs in Japan. *Int J Clin Pharm*. 2012;34(6):917-24.
[5] Ruiter R, Visser LE, van Herk-Sukel MP, Geelhoed-Duijvestijn PH, de Bie S, Straus SM, et al. Prescribing of rosiglitazone and pioglitazone following safety signals: analysis of trends in dispensing patterns in the Netherlands from 1998 to 2008. *Drug Saf*. 2012;35(6):471-80.
[6] Lejsková M, Pitha J, Adámková S, Auzký O, Adámek T, Babková E, et al. Bilateral oophorectomy may have an unfavorable effect on glucose metabolism compared with natural menopause. *Physiol Res*. 2014;63(Suppl 3):S395-402.
[7] Larsen BA, Allison MA, Laughlin GA, Araneta MR, Barrett-Connor E, Wooten WJ, et al. The association between abdominal muscle and type II diabetes across weight categories in diverse post-menopausal women. *J Clin Endocrinol Metab*. 2015;100(1):E105-09.
[8] van Dijk GM, Kavousi M, Troup J, Franco OH. Health issues for menopausal women: the top 11 conditions have common solutions. *Maturitas*. 2015;80(1):24-30.
[9] Adibe MO, Aguwa CN, Ukwe CV, Okonta JM, Udeogaranya PO. Outpatient utilization of anti-diabetic drugs in the South Eastern Nigeria. *Int J Drug Dev Res*. 2009;1:27-36.
[10] Hasamnis A, Patil S. Prescription pattern study in type 2 diabetes mellitus in an Indian referral hospital. *Internet J Pharmacol*. 2009;7:1. Available at : http://ispub.com/IJPHARM/7/1/11216
[11] Rajeshwari S, Adikhari P, Pai MR. Drug utilisation study in geriatric type 2 diabetic patients. *J Clin Diagn Res*. 2007;1:440-43.
[12] Sutharson L, Hariharan RS, Vamsadhara C. Drug utilization study in diabetology outpatient setting of a tertiary hospital. *Indian J Pharmacol.* 2003;35:237-40.
[13] Sultana G, Kapur P, Aqil M, Alam MS, Pillai KK. Drug utilization of oral hypoglycaemic agents in a university teaching hospital in India. *J Clin Pharm Ther*. 2010;35:267-77.
[14] Hassan Y, Mathialagan A, Awaisu A, Aziz NA, Yahaya R, Salhani A. Trend in the use of oral hypoglycaemic agents in an outpatient pharmacy department of a tertiary hospital in Malaysia (2003-2006). *Asian J Pharm Clin Res*. 2009;2:40-46.
[15] Cefalu WT. American Diabetes Association. Standards of Medical Care in Diabetes 2015. *Diabetes Care*. 2015;38(Suppl 1):S1-S90.
[16] de Vries TPGM, Henning RH, Hogerzeil HV, Fresle DA. Guide to good prescribing: a practical manual. Geneva; World health Organization, Action Programme on Essential Drugs, 1995:14-31.
[17] Agarwal AA, Jadhav PR, Deshmukh YA. Prescribing pattern and efficacy of anti-diabetic drugs in maintaining optimal glycaemic levels in diabetic patients. *J Basic Clin Pharma*. 2014;5:79-83.
[18] Tandon VR. Metformin Therapy: Benefits beyond glycaemic Control. *International Journal of Diabetes in Developing Countries*. 2007;27(1):1-4.
[19] Shrivastava U, Misra A. Need for ethnic-specific guidelines for prevention, diagnosis, and management of type 2 diabetes in South Asians. *Diabetes Technol Ther*. 2015;17(6):435-39.
[20] Tandon VR, Sharma S, Mahajan S, Mahajan A, Khajuria V, Mahajan V, et al. Antihypertensive drug prescription patterns, rationality, and adherence to Joint National Committee-7 hypertension treatment guidelines among Indian postmenopausal women. *J Midlife Health*. 2014;5(2):78-83.



**PARTICULARS OF CONTRIBUTORS:**
1. Post Graduate Student, Department of Obstetrics and Gyanecology, Government Medical College Jammu- J&K, India.
2. Post Graduate Student, Department of Pharmacology, Government Medical College Jammu- J&K, India.
3. Post Graduate Student, Department of Pharmacology, Government Medical College Jammu- J&K, India.
4. Professor and Head, Department of General Medicine, Government Medical College Jammu- J&K, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Annil Mahajan,
Professor and Head, Department of General Medicine, Government Medical College Jammu- J&K-180001, India.
E-mail: annil_mahajan@rediffmail.com



**FINANCIAL OR OTHER COMPETING INTERESTS:** None.

Date of Submission: **Aug 02, 2015**
Date of Peer Review: **Sep 21, 2015**
Date of Acceptance: **Oct 20, 2015**
Date of Publishing: **Jan 01, 2016**