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Research Article

# STUDY ON PRESCRIBING PATTERN OF ANTI-DIABETIC DRUGS AMONG TYPE 2 DIABETES PATIENTS WITH COMPLICATION IN SOUTH INDIAN TEACHING HOSPITAL

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**ABSTRACT**

**Objective:** To evaluate the drug utilization pattern of anti-diabetic agents with respect to glycosylated hemoglobin A1c (HbA1c) level in a Type 2 diabetes patient with complication.

**Methods:** This retrospective observational study was conducted as per the protocol approved by the Institutional Ethics Committee. The patients diagnosed with Type 2 diabetes mellitus with complication were identified, and those who had measured HbA1c level during previous follow ups were included in the study. All demographic, drug prescriptions, and clinical data of patients were collected and documented in a suitably designed case report form. Descriptive analyses were performed using Statistical Package for the Social Sciences Version 20.

**Results:** Based on the study criteria, 644 patients were selected and enrolled for the study. The majority of study subjects 494 (76.7%) were male and 415 (64.4%) were belonged to the age group 45-64 years. 252 (39.1%) of the patient, had normal weight followed by 234 (36.3%) were overweight, and 142 (22.1%) patients were obese. The prescription pattern showed the majority of patients 509 (79%) patients had 1-2 anti-diabetic medication followed 133 (20.7%) patient prescribed with 3-4 anti-diabetic drug. An insulin was prescribed in 507 (63.4%) patients and among oral anti-diabetic drugs, metformin 283 (43.9%), glimepiride 140 (21.7%), and voglibose 88 (13.7%) was most commonly prescribed.

**Conclusion:** Among all the anti-diabetic drugs, the insulin was highly preferred over oral hypoglycemic agents (OHAs) to control the glycemic level, and metformin accounted for the most commonly prescribed OHAs. In the second generation of sulfonylureas class, glimepiride and glipizide were most prescribed.

**Keywords:** Anti-diabetic agents, Diabetes mellitus, Prescription pattern.

## INTRODUCTION

Diabetes mellitus (DM) is a chronic illness along with disturbance of carbohydrate, protein, and fat metabolism due to defects in insulin secretion and/or insulin response that requires life-long medical care and ongoing patient self-management and support to prevent acute complications and to reduce the risk of morbidity and mortality [1,2].

The level of morbidity and mortality because of diabetes and its possible microvascular or macrovascular complications are tremendous and lead to considerable health care issues on both families and society. Optimal glycemic control will delay or prevent the progression of diabetes complication and improve the patient quality of life [3,4].

DM is reaching likely epidemic levels in India [5]. It is estimated that the number of people with diabetes in India was about 69.2 million in 2015 and will increase to 123.5 million in 2040 [6].

Optimal glycemic control still is the best strategy to manage the diabetes disorder. The currently anti-diabetic drugs are effective, but a lot of factors such as patient adherence, education related to diabetes, lifestyle modification, and cost and type of medication has an association with glycemic control [7-9].

Glycosylated hemoglobin A1c (HbA1c) is most commonly measured as an indicator of glycemic control during the preceding 2-3 months because it comprises the majority of HbAlc and is the least affected by recent fluctuations in blood glucose [10].

Medication costs, regimen complexity, and irrational prescribing are the challenges for patient compliance and therapy adherence that consequences will lead to poor glycemic control and increase the morbidity and mortality [9,11].

Study on anti-diabetic prescribing pattern provides useful insights into the current prescribing evaluation, and it eventually leads to achieve rational drug therapy, optimal glycemic control and reduce health-care cost for patients and society in large scale.

## METHODS

This retrospective observational study was conducted as per the protocol approved by the Institutional Ethics Committee: 561/2015. A study conducted based on in-patient and out-patient medical records of patients admitted in Kasturba Hospital, Manipal, during the 6-month period of study from October 2015 to March 2016.

The patients diagnosed with Type 2 DM with complication were identified and those who had measured HbA1c level during previous follow ups were included in the study. All demographic, drug prescriptions, and clinical data of patients were collected and documented in a suitably designed case report form. Descriptive analyses were performed using Statistical Package for the Social Sciences Version 20.

## RESULTS

Based on the study criteria, 644 patients were selected and enrolled for the study. The majority of study subjects 494 (76.7%) were male and 415 (64.4%) were belonged to the age group 45-64 years and 180 (28%) were in the age group of 65-79 years.

According to the body mass index, 252 (39.1%) of the patient had normal weight followed by 234 (36.3%) were overweight and

142 (22.1%) patients was obese. The majority of study subjects were married, 642 (99.7%) and most of the patients were employed 421 (65.4%) (Table 1).

Out of 644 patients, 346 (53.7%) were suffering from DM more than 10 years. Remaining 157 (24.4%) and 141 (21.9%) had Type 2 DM for 5-10 years and <5 years, respectively. 179 (27.8%) of patients, had good glycemic control (HbA1c <7%) and 291 (45.2%) had HbA1c level greater 8.5% (Table 2).

Patients were suffering from different type of diabetes complication. 505 (78.4%) had one diabetic complication and majority of patients were suffering from diabetic peripheral and diabetic retinopathy, 174 (27%) and 154 (23.9%), respectively. In this study, 298 (46.3%) of patients had cardiovascular disorders including hypertension (HTN) and dyslipidemia and 179 (27.8%) did not have any comorbidity (Table 2).

In this study, 271 (42%) of patients received insulin as monotherapy followed by 236 (36.6%) insulin with oral hypoglycemic agents (OHAs) as combination therapy to control their blood glucose level (Fig. 1).

The prescription pattern showed the majority of patients 509 (79%) patients had 1-2 anti-diabetic medication followed 133 (20.7%) patient prescribed with 3-4 anti-diabetic drug as shown in Table 3. The insulin was prescribed in 507 (63.4%) patients and among them 369 (57.3%) patients received insulin mixtard (30/70) and 92 (14.3%) patients were on rapid acting insulin.

Among oral anti-diabetic drugs, metformin 283 (43.9%), glimepiride 140 (21.7%), and voglibose 88 (13.7%) were most commonly prescribed. 20 (3%) of patients had dipeptidyl peptidase 4 inhibitor agents as add on therapy in their prescription to control the blood-glucose level (Table 3).

## DISCUSSION

Studies on anti-diabetics drug prescription and analysis the medication can lead to the promotion of rational drug therapy and effective treatment tailoring that eventually can help to achieve optimal glycemic control and therapy adherence, which reduce the morbidity and mortality in diabetic patients.

A total of 644 patients were included in these study male patients were predominance, which is similar to result of other studies done in India [12-14]. The mean age of patients was 59.6 (standard deviation [SD] = 9.6) years, and the majority of patients 415 (64.4%) were belonged to the age group of 45-64 years, a study from Nepal was reported an average age of 56.9 (SD=12.6) years [15].

In our study, most of the patients had poor glycemic control as the mean HbA1c was found to be 8.6% (SD=2.2) and the mean duration of diabetes illness was 12.7 (SD=7.8) years. In study done by Satpathy *et al*. reported, the mean duration of diabetes was 9.52±6.5 years [16].

Most of the patient suffering from peripheral and retinopathy complication and 298 (46.3%) of study subject had cardiovascular disorders, including HTN and dyslipidemia, similar to studies reported

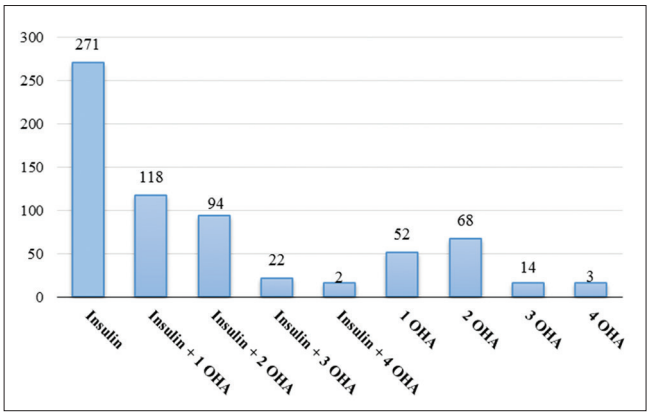


**Fig. 1: Pattern of anti-diabetic drug prescribed in diabetes patients (n=644)**

**Table 1: Demographic characteristics of diabetic patients (n=644)**

| Variable | Total patient n (%) |
|---|---|
| Gender | |
| Male | 494 (76.7) |
| Female | 150 (23.3) |
| Age (years) | |
| ≤44 | 34 (5.3) |
| 45-64 | 415 (64.4) |
| 65-79 | 180 (28) |
| ≥80 | 15 (2.3) |
| BMI (kg/m$^2$) | |
| Underweight | 16 (2.5) |
| Normal range | 252 (39.1) |
| Overweight | 234 (36.3) |
| Obese | 142 (22.1) |
| Marital status | |
| Single | 2 (0.3) |
| Married | 642 (99.7) |
| Employment status | |
| Employed | 421 (65.4) |
| Unemployed | 176 (27.3) |
| Retired | 47 (7.3 ) |

BMI: Body mass index

**Table 2: Clinical characteristics of diabetic patients (n=644)**

| Variable | Total patient n (%) |
|---|---|
| Duration of diabetes illness (year) | |
| <5 | 141 (21.9) |
| 5-10 | 157 (24.4) |
| >10 | 346 (53.7) |
| HbA1c level (%) | |
| ≤7 | 179 (27.8) |
| 7.1-8.5 | 174 (27) |
| >8.5 | 291 (45.2) |
| Type of complication | |
| Ketoacidosis | 23 (3.6) |
| Nephropathy | 66 (10.2) |
| Retinopathy | 154 (23.9) |
| Neuropathy | 88 (13.7) |
| Peripheral | 174 (27) |
| Nephropathy+Neuropathy | 7 (1.1) |
| Neuropathy+Peripheral | 4 (0.6) |
| Neuropathy+Retionapthy | 10 (1.6) |
| Nephropathy+Peripheral | 18 (2.8) |
| Nephropathy+Retionapthy | 95 (14.8) |
| Peripheral+Retionapthy | 5 (0.8) |
| Co-existing illness | |
| No comorbidity | 179 (27.8) |
| Cardiovascular disorder* | 298 (46.3) |
| Respiratory disorder | 13 (2.0) |
| Neurological disorder | 12 (1.9) |
| Psychiatric disorder | 5 (0.8) |
| Dermatological disorder | 3 (0.5) |
| Thyroid disorder | 8 (1.2) |
| Rheumatic disorder | 16 (2.5) |
| Infectious diseases | 84 (13.0) |
| Cancer | 6 (0.9) |
| Liver disorder | 12 (1.9) |
| Iron deficiency anemia | 8 (1.2) |

*Including HTN and dyslipidemia, HbA1c: Glycosylated hemoglobin A1c, HTN: Hypertension

**Table 3: Distribution of anti-diabetic drug according to HbA1c value (n=644)**

| HbA1c (%) | n (%) | | | |
|---|---|---|---|---|
| | **Total patient** | **≤7** | **7.1-8.5** | **>8.5** |
| Number of anti-diabetic drug per prescription | | | | |
| 1-2 | 509 (79) | 150 (23.3) | 147 (22.8) | 212 (32.9) |
| 3-4 | 133 (20.7) | 29 (4.6) | 26 (4) | 78 (12.1) |
| >4 | 2 (0.3) | 0 | 1 (0.15) | 1 (0.15) |
| Type of anti-diabetic drug prescribed | | | | |
| OHA | 137 (21.3) | 53 (8.2) | 42 (6.5) | 42 (6.5) |
| Insulin | 271 (42.1) | 74 (11.5) | 72 (11.2) | 125 (19.4) |
| Insulin+OHA | 236 (36.6) | 52 (8) | 60 (9.3) | 124 (19.3) |
| Insulin | | | | |
| Rapid acting | 92 (14.3) | 32 (5) | 24 (3.7) | 36 (5.6) |
| Mixtard* (30/70) | 369 (57.3) | 87 (13.5) | 96 (14.9) | 186 (28.9) |
| Long acting | 8 (1.2) | 2 (0.3) | 0 | 6 (0.9) |
| Mixtard* (30/70)+Long acting | 3 (0.5) | 1 (0.15) | 1 (0.15) | 1 (0.15) |
| Mixtard (30/70)+Rapid acting | 16 (2.5) | 1 (0.15) | 4 (0.6) | 11 (1.7) |
| Rapid acting+Long acting | 19 (2.9) | 3 (0.5) | 7 (1) | 9 (1.4) |
| Sulfonylureas | | | | |
| Glibenclamide | 26 (4) | 6 (0.9) | 7 (1) | 13 (2) |
| Glimepiride | 140 (21.7) | 33 (5.1) | 37 (5.7) | 70 (10.9) |
| Gliclazide | 18 (2.8) | 6 (0.9) | 5 (0.8) | 7 (1) |
| Glipizide | 50 (7.8) | 15 (2.3) | 19 (3) | 16 (2.5) |
| Biguanide | | | | |
| Metformin | 283 (43.9) | 80 (12.4) | 71 (11) | 132 (20.5) |
| Thiazolidinediones | | | | |
| Pioglitazone | 2 (0.3) | 0 | 1 (0.15) | 1 (0.15) |
| Rosiglitazone | 1 (0.15) | 0 | 0 | 1 (0.15) |
| DPP-IV inhibitors | | | | |
| Sitagliptin | 10 (1.6) | 0 | 5 (0.8) | 5 (0.8) |
| Vildagliptin | 8 (1.2) | 3 (0.5) | 0 | 5 (0.8) |
| Saxagliptin | 2 (0.3) | 0 | 1 (0.15) | 1 (0.15) |
| Alpha glucosidase inhibitors | | | | |
| Voglibose | 88 (13.7) | 18 (2.8) | 22 (3.4) | 48 (7.5) |
| Non-sulfonylurea insulin secretagogues | | | | |
| Repaglinide | 1 (0.15) | 1 (0.15) | 0 | 0 |

*Mixtard (30/70): Soluble 30%+Isophane 70%, DPP-IV: Dipeptidyl peptidase 4. OHA: Oral hypoglycemic agents, HbA1c: Glycosylated hemoglobin A1c

by Iglay *et al*., which highest co-prevalence was for the combination of HTN and hyperlipidemia in patients with diabetes [17].

HbA1c is the gold standard for the monitoring and evaluation the optimal glycemic control. In this study, patients divided into three groups based on HbA1c levels, good control (≤7%), moderate control (7.1-8.5%), and poor control (>8.5%) [18]. Our study revealed that 323 (50.2%) of patients had one anti-diabetics drug on their prescription, and we observed that by increasing the HbA1c level they were received combination therapy with different classes of anti-diabetic medication.

A total of 1131 anti-diabetic drugs were prescribed, and the average number per prescription was 1.7 (SD=0.8) that indicating rational prescribing practices. A survey done by Agarwal *et al*. reported average number of 1.4 anti-diabetic drugs per prescription [19].

As indicated by Devi and George [20], Insulin was preferred over oral anti-diabetic medication in patients with diabetic nephropathy; we also observed that prescribing of insulin was highly preferred over OHAs. Insulin preparations alone and/or in combination, therapy accounted for 507 (78.7%) of the total patients, and the most common preparation 369 (57.3%) was insulin mixtard (30/70). Intensive glycemic control by insulin injection therapy may help to delay or prevent the progression of diabetic macrovascular and microvascular complication [21,22].

Combining metformin with insulin therapy has been shown to result in less weight gain and better glycemic control with lower insulin requirements [23]. In this study, we observed, Metformin was the most commonly prescribed drug among OHAs, the same result reported by study done by Khan, Hussain *et al*. and Adhikari and Pai [24-26] but a survey done by Sridevi and Ganesh. reported the sulfonylureas were the most common prescribed OHAs [27].

In this study, we found that among the sulfonylureas, glimepiride, and glipizide were most prescribed and combinations of sulfonylureas and metformin 154 (23.9%) was most frequently prescribed. A similar result reported in a survey by Abidi *et al*. and Yada *et al* [28,29].

As indicated by Talaviya *et al*., alpha-glucosidase inhibitors as an add-on therapy with metformin and sulfonylureas in uncontrolled obese/overweight Type 2 DM provides desired glycemic control, improves lipid parameters and reduces body weight [30]. As well as in our study, we observed that 88 (13.7%) Voglibose prescribed as add-on treatment to achieve the optimal glycemic control.

## CONCLUSION

Among all the anti-diabetic drugs, Insulin was highly preferred over OHAs to control the glycemic level, and metformin accounted for the most commonly prescribed OHAs. In the second generation of sulfonylureas class, glimepiride and glipizide were most prescribed. Our data indicating rational prescribing practices of anti-diabetics agents but factors like patient's compliance and education regarding diabetes and lifestyle modification are also important to achieve the optimal glycemic control that needs further investigation.

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