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# A Comparative Study to Evaluate the Pharmacotherapy of Type II Diabetes in Patients Visiting Tertiary Care Teaching Hospital and Private Clinic

Kshirsagar Vinay Kumar*, Maulin Mehta

## Abstract

**Introduction:** Diabetes mellitus (DM) refers to a bunch of disorders of metabolism that share the phenotypic sign of hyperglycemia. Different variants of DM are caused due to the interaction of various genetic factors with environmental factors. Materials and Methods: This is prospective, comparative, and observational study. The study was conducted at SMBT Medical Institute and Research Centre Dhamangaon Nashik and private Diabetic clinic. Each center was 50 purposive sampling. **Inclusion Criteria:** All those patients who are diagnosed with Type II Diabetes and age of 18 years and above belonging to either gender were included in the study. **Exclusion Criteria:** Patients who are not willing to sign the informed consent were excluded from the study. Those individuals who are having Type I diabetes and suffering from co-morbid conditions such as hypertension, hyperthyroidism, and immune deficiency syndrome were excluded. **Results:** In our study, results revealed that mono and combination therapies for the treatment of type II DM. The present study revealed that most of the physicians initially prescribed mono therapy (25%) includes Metformin/Glibenclamide/Glimepiride/Gliclazide to control hyperglycemia followed by dual therapy (35%) FDC of Metformin + Pioglitazone/ Metformin + Glipizide/Metformin + Glimepiride/Metformin + Saxagliptin/Metformin + Voglibose and triple therapy (40%) includes Metformin + Glimepiride + Pioglitazone in group A. In Group B, mono therapy (35%) and triple therapy (35%) were used more commonly over dual therapy (30%) to control hyperglycemic. **Conclusion:** Hence, while comparing between tertiary care versus private care hospital, Group A: Biguanide: Metformin and Sulfonylureas: Glibenclamide, Glipizide, Gliclazide, and Glimepiride was most commonly prescribed drug. In Group B: Dapagliflozin (Sodium-glucose co-transport-2 inhibitors) and Teneligliptin: Dipeptidyl peptidase-4 inhibitors were most commonly used in private hospital.

**Keywords:** Diabetes mellitus, Hyperglycemia, Metformin, Sulfonylureas

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## Introduction

Diabetes mellitus (DM) refers to a bunch of disorders of metabolism that share the phenotypic sign of hyperglycemia. Different variants of DM are caused due to the interaction of various genetic factors with environmental factors. Depending on the pathogenic process leading to hyperglycemia DM is classified, as Type I, Type II, Gestational Diabetes, and Other specific types as maturity onset diabetes of youth, lipodystrophic diabetes, secondary diabetes due to pancreatitis, hemochromatosis, drug-induced, infectious, and insulin receptor antibodies.[1]

Type II DM (T2DM) is a chronic disease that develops due to defective insulin secretion and is frequently associated with insulin resistance.[2] It is also characterized by progressively decreasing beta-cell function over time.[3] It contributes to about 90–95% of all diagnosed cases of DM in adults and currently affects more than 61.3 million Indian people that are more than 8% of the adult population.[4,5] The age of onset of T2DM is 42.5 years on an average. Diabetes accounts to 1 million deaths in India every year.[6] The feature of chronic hyperglycemia is a forecaster of development of complications associated with diabetes. These can be divided into micro-vascular, macro-vascular, and other complications. Micro-vascular complications of diabetes include diabetic neuropathy, diabetic nephropathy, and diabetic retinopathy. The complications of DM categorized under macro-vascular complications include cardiovascular disease (CVD), cerebrovascular disease, and diseases related to peripheral vessels. Along with these complications, weight gain related with diabetes lead to further worsening of the disease. Other complications include acute metabolic complications and diabetic ketoacidosis.[7]

Drugs used in T2DM:

1. Sulfonylureas: Tolbutamide, Glibenclamide, Glipizide, Gliclazide, Glimepiride, etc.
2. Meglitinide analogues: Repaglinide, Nateglinide
3. Biguanides: Metformin
4. A Glucosidase inhibitors: Acarbose, Miglitol, Voglibose
5. Thiazolidinediones: Pioglitazone.

Hence, the study has been planned out to compare and to evaluate the pharmacotherapy of Type II Diabetes in patients visiting tertiary care teaching hospital and private clinics.

[1]Phd Scholar, Department of Pharmacology, SBKS Medical Institute and Research Centre, Vadodara, Gujarat, India, [2]Head of Department, Department of Pharmacology, SBKS Medical Institute and Research Centre, Vadodara, Gujarat, India

**Corresponding Author:** Kshirsagar Vinay Kumar, Department of Pharmacology, SBKS Medical Institute and Research Centre, Vadodara, Gujarat, India. E-mail: kshirvinay@gmail.com

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### Aim

The aim of the study was to compare the pharmacotherapy of Type II diabetes and its associated complications at tertiary care hospital and the private clinic.

## Materials And Methods

### Place of Study

The study was conducted at SMBT Medical Institute and Research Centre Dhamangaon Nashik and private Diabetic clinic.

### Type of Study

It was comparative, prospective, and cohort study.

### Sample Description

This study was 100 (50 from each center) Purposive sampling.

### Inclusion Criteria

All those patients who are diagnosed with Type II diabetes and age of 18 years and above belonging to either gender were included in the study.

### Exclusion Criteria

Patients who are not willing to sign the informed consent were excluded from the study. Those individuals who are having Type I diabetes and suffering from co-morbid conditions such as hypertension, hyperthyroidism, and immune deficiency syndrome were excluded from the study.

- Group A: SMBT Medical Institute and Research Centre Dhamangaon Nashik
- Group B: Private Diabetic clinic.

## Results

Both groups had 50 subjects each.

The table reflects that in both groups maximum number of patients belonged to age group of 51–70 years. The age group (31–50) years had 19 patients in Group A and 21 patients in Group B, and least patients were in <30 years of age group as shown in Table 1.

Of the total 100 diabetic patients, distribution of tertiary care hospital patients on the basis of gender revealed that 29 (58%) were male and 21 (42%) were female patients. Similarly, out of 50 patients' private clinic consists of 31 (62%) were males and 19 (38%) were female patients as shown in Table 2.

As shown in Table 3, study patients in health facilities were distributed on the basis of area of living into urban or rural. Of 50 subjects of tertiary care hospital and private clinic each, it was observed that maximum percentage of study population was rural constituting 72% and 44% were urban. Percentage of tertiary care hospital study subjects living in urban areas was 28% whereas private clinic each was 56%.

Distribution of study subjects on the basis of family history of Type 2 Diabetes. Family history of Type 2 Diabetes was recorded in the enrolled population at both the health facilities. It was observed that 31 (62%) patients presented a positive family history out of 50 recruited from tertiary care hospital. Similarly, study population at private clinic reported positive family history in 34 (68%) patients as shown in Table 4.

In Table 5, study results revealed that total 118 drugs were prescribed in 50 patients enrolled at tertiary care hospital. Average number of drugs per prescription was 2.36. The minimum and maximum number of drugs per prescription was 1 and 5, respectively, used of branded and generic drugs in Group A patients and Group B patients with T2DM. In private clinic 50 patients enrolled, total 98 drugs were prescribed. Average number of drugs per prescription was 1.96. The minimum and maximum number of drugs per prescription was 1 and 6, respectively. Maximum drugs were prescribed by their brand names.

1. Sulfonylureas: Tolbutamide, Glibenclamide, Glipizide, Gliclazide, Glimepiride, etc.
2. Meglitinide analogues: Repaglinide, Nateglinide
3. Biguanides: Metformin
4. A Glucosidase inhibitors: Acarbose, Miglitol, Voglibose
5. Thiazolidinediones: Pioglitazone.

**Table 1:** Distribution of age group between tertiary care hospital and Private clinic

| *Age group* | *Group A (Tertiary care hospital)* | *Group B (Private clinic)* |
|---|---|---|
| <30 years | 8 | 6 |
| 31–50 years | 18 | 20 |
| 51–70 years | 24 | 24 |
| Total | 50 (100%) | 21 (100%) |

**Table 2:** Distribution of sex between two groups Tertiary care hospital and Private clinic

| *Gender* | *Group A (Tertiary care hospital) (%)* | *Group B (Private clinic) (%)* |
|---|---|---|
| Male | 29 (58) | 31 (62) |
| Female | 21 (42) | 19 (38) |
| Total | 50 (100) | 50 (100) |

**Table 3:** Distribution of sex between two groups Tertiary care hospital and Private clinic

| *Area of living* | *Group A (Tertiary care hospital) (%)* | *Group B (Private clinic) (%)* |
|---|---|---|
| Rural | 36 (72) | 22 (44) |
| Urban | 14 (28) | 28 (56) |
| Total | 50 (100) | 50 (100) |

**Table 4:** Distribution of Diabetic patients in both Health Facilities on the basis of Family History of Diabetes

| *Family history of diabetes* | | | *Group A (Tertiary care hospital) (%)* | *Group B (Private clinic) (%)* |
|---|---|---|---|---|
| Family History | Positive | Mother | 3 (6) | 5 (10) |
| | | Father | 6 (12) | 7 (14) |
| | | Sibling | 8 (16) | 9 (18) |
| | | Grandparent | 14 (28) | 13 (26) |
| | Negative | | 19 (38) | 16 (32) |
| | Total | | 50 (100) | 50 (100) |

**Table 5:** Comparing branded versus generic between two groups

| *Parameters* | *Group A (Tertiary care hospital)* | *Group B (Private clinic)* |
|---|---|---|
| Total number of prescriptions | 50 | 50 |
| Total no. of drugs prescribed | 118 | 98 |
| Average drugs per prescriptions | 2.36 | 1.96 |
| Encounter with Branded | 31 (62%) | 43 (86%) |
| Encounter with Generic | 19 (38%) | 7 (14%) |

Table 6 shows that mono and combination therapies for the treatment of T2DM. The present study revealed that most of the physician's initially prescribed mono therapy (25%) includes Metformin/Glibenclamide/Glimepiride/Gliclazide to control hyperglycemia followed by dual therapy (35%) FDC of Metformin + Pioglitazone/Metformin + Glipizide/Metformin + Glimepiride/Metformin + Saxagliptin/Metformin +Voglibose and triple therapy (40%) includes Metformin + Glimepiride + Pioglitazone in Group A. In Group B, mono therapy (35%) and triple therapy (35%) were used more commonly over dual therapy (30%) to control hyperglycemic.

In Table 7, while comparing between tertiary care (Group A) versus private clinic (Group B). In Group A: Metformin (Biguanide) and Sulfonylureas: Glibenclamide, Glipizide, Gliclazide, Glimepiride was most commonly prescribed drug and in Group B: Dapagliflozin (Sodium-glucose co-transport-2 [SGLT-2] inhibitors), and Teneligliptin dipeptidyl peptidase-4 (DPP-4) inhibitors were most in private hospital.

In Table 8, study results revealed that differences of statistical significance in fasting blood glucose (FBG) and postprandial blood glucose (PPBG) and hemoglobin A1 (HbA1c) levels between Group A and Group B study ($P < 0.001$ for all); in Group A patients with T2DM had higher FBG, PPBG, and HbA1c levels than those with group patients.

### Distribution of Study Subjects on the Basis of Control of Bronchial Asthma Type 2 Diabetes

Among the enrolled cases of Type 2 Diabetes from Tertiary care hospital, diabetes in maximum, that is, 29 (58%) patients were well controlled. In 18 (36%) Type 2 Diabetes patients were partly controlled whereas 3 (6%) were uncontrolled cases. On the other hand, in private clinic patients, 34 (68%) patients presented well controlled, and 14 (28%) patients presented partly controlled, followed by 14 (28%) with uncontrolled Type 2 diabetes as shown in Table 9.

Among the Diabetic patients enrolled at Tertiary care hospital, nonsteroidal anti-inflammatory drugs (NSAIDs) (28%) were the most commonly prescribed concomitant medication. Other frequently prescribed drugs were multivitamins and multimineral (18%), Pregabalin (22%), antihistamines (14%), and antibiotics (26%). In private clinic, among the diabetic patients that concomitant drugs were multivitamins and multimineral (22%), antihistamines (10%), and NSAIDs (34%), antibiotics (22%) were the prescribed concomitant medications as shown in Table 10.

For the management of diabetes in patients in tertiary care hospital, the average cost of drug was found to be Rs. 119.1 (SD = 17.43). The minimum and maximum cost of drug was 0.70 and 370, respectively. On the other hand, the average cost of drug administered in private clinic was observed as Rs. 133.2 (SD = 19.14). The minimum and maximum cost of drug was 0.90 and 390, respectively.

## Discussion

DM is a metabolic disorder as stated by the WHO which requires the chronic treatment.[8] Besides the lifestyle modifications and dietary changes, the pharmacological treatment an integral component in the management of diabetes.[9] We set out in this study to compare the quality of outpatient follow-up care offered to persons with T2DM at a Tertiary care center and private clinic. In our study, the prevalence of DM is more in male (64%) than females (36%) in both tertiary care and private center. The older-aged group people (51–70 years) are more prevalence to the DM followed by 31–50 years

**Table 6:** Distribution of drug therapy between two groups

| *Therapy* | *Group A (Tertiary care hospital) (% of Population) (%)* | *Group B (Private clinic) (% of Population) (%)* |
|---|---|---|
| Monotherapy | 25 | 35 |
| Dual therapy | 35 | 30 |
| Triple therapy | 40 | 35 |

**Table 7:** Distribution of oral antidiabetic drug therapy between two groups

| *Drugs* | *Group A (Tertiary care hospital) (%)* | *Group B (Private clinic) (%)* |
|---|---|---|
| Metformin, Glibenclamide, Glipizide, Gliclazide, Glimepiride | 78 | 33 |
| Dapagliflozin and Teneligliptin | 22 | 67 |

**Table 8:** Comparing glucose triad between two groups

| *Parameters* | *Group A (Tertiary care hospital) (Mean±SD)* | *Group B (Private clinic) (Mean±SD)* | *P-value* |
|---|---|---|---|
| Fasting Blood glucose, mg/dl | 151.21±23.22 | 136.54±21.43 | <0.001 |
| Postprandial blood glucose, mg/dl | 231.32±38.49 | 201.32±32.49 | <0.001 |
| HbA1c, % | 7.24±0.68 | 6.23±0.31 | <0.001 |

**Table 9:** Distribution of diabetic patients in both health facilities on the basis of control of Type 2 Diabetes

| *Severity of Type 2 Diabetes* | *Group A (Tertiary care hospital) (%)* | *Group B (Private clinic) (%)* |
|---|---|---|
| Well controlled | 29 (58) | 34 (68) |
| Partly controlled | 18 (36) | 14 (28) |
| Uncontrolled | 3 (6) | 2 (4) |
| Total | 50 (100) | 50 (100) |

**Table 10:** Distribution of concomitant drugs in Tertiary care hospital patients and Private clinic

| *Concomitant drug* | *Group A (Tertiary care hospital) (%)* | *Group B (Private clinic) (%)* |
|---|---|---|
| Ondansetron | 3 (6) | 4 (8) |
| Proton pump inhibitors | 4 (8) | 7 (14) |
| Pregabalin | 11 (22) | 9 (18) |
| Antihistamines | 7 (14) | 5 (10) |
| Antispasmodics | 3 (6) | 4 (8) |
| Antidiarrheal | 4 (8) | 6 (12) |
| Antibiotics | 13 (26) | 11 (22) |
| Calcium in combination with vitamin D3 and/or other drugs | 7 (14) | 6 (12) |
| Iron supplements | 6 (12) | 9 (18) |
| Multivitamin and Multimineral | 9 (18) | 11 (22) |
| NSAIDs | 14 (28) | 17 (34) |
| Vitamin D and analogs | 9 (18) | 11 (22) |
| Zinc supplements | 4 (8) | 6 (12) |

**Table 11:** Descriptive statistics for price caps of drugs used in paediatric OPD at both Health facilities AQ3

| *Grouping* | *Total number of drugs prescribed (n)* | *Minimum cost of drug* | *Maximum cost of drug* | *Mean* | *SD* |
|---|---|---|---|---|---|
| Group A (Tertiary care hospital) | 118 | 0.70 | 370 | 119.1 | 17.43 |
| Group B (Private clinic) | 98 | 0.90 | 390 | 133.2 | 19.14 |

OPD: Outpatient department

and least were <30 years in both tertiary care and private center, which is same results were obtained in study the of drug utilization pattern and effectiveness analysis in DM conducted by Barlow.[10]

From our study, Metformin (Biguanides) and Glicazide, Glimepiride, Glibenclamide (Sulfonylureas) were found to be the most commonly used oral antidiabetic drugs among all drug groups in tertiary care and in private clinics Dapagliflozin SGLT-2 inhibitors and Teneligliptin DPP-4 inhibitors was most in private hospital. This complies with the study done by Rother.[11] Biguanides have the potential advantage of targeting insulin resistance, rather than increasing plasma insulin concentration which is an early feature of the disease.[12] Hence, it was found to be the most commonly used oral antidiabetic drug. In addition, biguanides do not cause weight gain and may reduce adipose tissue mass.[13] Thus, they may be preferred in obese and non-obese patients with insulin resistance. From the literature, biguanides cause less fasting hypoglycemia compared to sulfonylureas.[14] Besides, sulfonylureas can cause weight gain and induce severe hypoglycemia.[15] From this study, we found that biguanide has got more advantages compared to sulfonylurea.

In our study, the most commonly used drugs among the sulfonylurea group was glimepiride followed by gliclazide and glibenclamide in tertiary care. Our study results are similar to those of the study done by Kahn.[16] In his study, Glimepiride is a sulfonylurea that is pharmacologically distinct from other sulfonylureas because of differences in receptor-binding properties and potentially selective effects on ATP-sensitive K+ channels.[17] The pharmacokinetic profile of glimepiride makes it suitable for once-daily dosing and appears to be a useful option for patients with type 2 diabetes not controlled by diet and exercise alone and who want to achieve tight glucose control.[18]

Several combinations of oral antidiabetic agents like sulfonylurea and metformin, a sulfonylurea plus an alpha-glucosidase inhibitor; a sulfonylurea, metformin, and a thiazolidinedione have been shown to further improve glycemic control when compared to monotherapy. Thiazolidinediones, sulfonylureas, and metformin produced similar reductions in HbA1c levels when used as monotherapy. Combination therapies had additive effects, producing an absolute reduction in HbA1c levels of about 1% point more than monotherapy.[19]

The dual therapy of sulfonylureas + biguanides and triple therapies of sulfonylurea, thiazolidinediones and biguanides were found to reduce preprandial blood glucose by 26.5% and 27.1%, respectively, and post-prandial blood glucose by 30.5% and 32.6%, respectively. This result has been supported by the study conducted by Yoon *et al*.[20] In his study, high quality evidence showed that both therapy (dual and Triple) reduced blood glucose level to a similar degree. Metformin was more effective than other medications as monotherapy as well as when used in combination therapy with another agent for reducing blood glucose level according to Barnett.[21] Our study showed that dual therapy (sulfonylurea and biguanide) and triple therapy (sulfonylurea, thiazolidinedione, and biguanide) showed a similar reduction in pre-and post-prandial blood glucose levels.

As expected, our results showed that both FBG and PPBG levels were significantly higher in Group A patients than Group B patients. An earlier study conducted in 2015 reported glucose levels to be significantly higher in patients with tertiary care center than private clinics ($P$ = 0.001).[22] Similarly, and as expected, the study findings further revealed that HbA1c was significantly higher in Group A and patients than Group B patients. However, we report that the level of glycemic control, as documented by HbA1c levels, is poor and comparable at Group B. An earlier study carried out in 2003 also reported Tertiary care center patients with T2DM having higher HbA1c levels than private clinics ($P$ = 0.002). HbA1c has also been suggested to be a highly specific and convenient screening and diagnostic tool for diabetes.[23] In another cross-sectional, descriptive study done at the University of Benin Teaching Hospital, Benin City, a tertiary health care center in Nigeria, between June and December 2004, it showed that many of the persons with DM in Benin city still had poor glycemic control similar to the previous reports.[24] Another study in China concluded that the overall status of glycemic control was unsatisfactory. Although, patients at tertiary hospitals appeared to have better control than those at primary or secondary hospitals.[25]

Oral hypoglycemic drugs were more frequently unavailable at the peripheral center. Direct costs incurred by patient were half to three quarter lower at the regional facility. Compared to tertiary facility patients, private clinic facility patients reported greater affordability and satisfactions with care offered and were less inclined to transfer care to other centers. In another study done in 1998 in KNH they found that Most patients (71 or 68 %) had very poor long-term glycemic control with an HbA1c level >10.0%, concluding that the majority of ambulatory diabetic patients attending the out-patient diabetic clinic had poor glycemic control.[26] A study in Finland concluded that the follow-up of most diabetic patients – including type 2 diabetes – can be organized in primary health care with the same quality as in secondary care units. The centralized primary care of type 2 diabetes is less, costly and requires fewer specialist consultations.[27]

In this study, all drugs were prescribed by brand name suggesting popularity of the brands among the physician and influence of pharmaceutical companies on the physician. It is advisable to prescribe by generic name for cost effective utilization. However, in this study, the percentage of drugs prescribed from national essential drug list was 67.1% which showed the awareness and selection of drugs from essential drug list for rational use of drugs.

About 41% patients on anti-diabetic drugs had controlled optimal glycemic levels, while 59% had inadequate/uncontrolled glycemic levels. Several studies have documented from 50% to 86%, which were higher than our studies. Although these variations across studies may be true, they may also be due to differences in populations surveyed, methods of data collection, measurements of blood-glucose/HbA1c, and definitions of blood-glucose/HbA1c cut-point for adequate glycemic control.[28]

As diabetes progresses, functional decline in beta cells is usually apparent, and the need for combination therapy is unavoidable. The basic rationale for combination therapy is to provide additive effects with different mechanisms of action and to allow lower doses for disease management. Consistent with the same, in the present study, majority (40%) of the patients were on triple therapy followed by dual and mono therapy. In a study conducted in rural areas of Tamil Nadu, monotherapy, and two drug combination therapies were prescribed in 21.7% and 78.3% patients, respectively. Metformin was more which is more utilized anti-diabetic drug than others and Glimepiride was more utilized drug in Sulfonylureas. Similar results were obtained in a study conducted by Cameron and Bennett on-Outpatient Utilization of Anti-Diabetic Drugs.[29]

### Limitation of the Study

It is hereby recommended that future studies should include larger population samples as well as inpatients in the hospitals concerned. Furthermore, study areas should include the rural, semi-urban and urban areas of the province as well as other parts of the country, thus allowing comparison of findings between urban and rural areas as well as different provinces in the country.

## Conclusion

Hence, while comparing between tertiary care versus private care hospital, Group A: Biguanide: Metformin and Sulfonylureas: Glibenclamide, Glipizide, Gliclazide, Glimepiride was most commonly prescribed drug. In Group B: Dapagliflozin SGLT-2 inhibitors and Teneligliptin: DPP-4 inhibitors were most commonly used in private hospital. Dapagliflozin helps lower blood glucose levels by helping the body to filter more excess glucose out of the blood and safe and beneficial in CVD including heart failure patients. Teneligliptin improved 24 h blood glucose levels by increasing active incretin levels and early-phase insulin secretion, reducing the postprandial insulin requirement, and reducing glucagon secretion.

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