



## Original Research Article

# Assessment of prescription pattern and cost effective analysis of oral hypoglycemic agents used in treatment of type 2 diabetes mellitus

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## ARTICLE INFO

## Article history:

Received 03-05-2024

Accepted 08-06-2024

Available online 08-08-2024

## Keywords:

Diabetes mellitus

Oral hypoglycaemic agents

Prescribing patterns

Cost effective analysis

## ABSTRACT

**Objectives:** Diabetes mellitus treatment that is cost-effective not only ensures rational drug use but also lowers patient costs. When a cost-effectiveness tool is used correctly in therapeutic decision making, the disease's complications are reduced, and the patients' quality of life is improved. This study aims to evaluate the prescribing patterns and to carry out cost effective analysis for Oral Hypoglycaemic agents used in the treatment of Type 2 Diabetes Mellitus.

**Materials and Methods:** A Prospective, observational study was carried out in the out-patient department of a Diabetes Specialty Centre-Bangalore for a period of 9 months. Individuals aged 18 and above and clinically diagnosed with T2DM with or without HTN and dyslipidaemia were considered eligible for the study. Individuals who were on Insulin for management and those with other types of Diabetes were excluded from the study.

**Results:** A total of 274 prescriptions were evaluated. The majority of the patients belonged to the age group of 60 years and older (55%). Prevalence of Diabetes were found to be more in men (53%) when compared to women (47%). Most of the study subjects were diagnosed with HTN + T2DM (35%) followed by T2DM+HTN+ Dyslipidaemia (27%). The average number of drugs per prescription were 2.04. It was observed that Sulphonylureas, Biguanides, Alphaglucoisidase inhibitors, DPP-4 inhibitors, Thiazolidinediones and SGLT2 inhibitors were the numerous drugs prescribed to the study population. Incremental Cost Effectiveness Ratio (ICER) was calculated and it was found that DPP-4 inhibitors are cost effective in monotherapy while DPP-4 inhibitors+ Biguanides for double combination therapy and DPP-4 inhibitors+SGLT2 inhibitors + Biguanides in three combination was found to be cost effective.

**Conclusion:** In our study, it was observed that Metformin was most commonly prescribed among the OHA and DPP-4 inhibitors are cost effective. Polypharmacy is a big issue, especially for the elderly population. This study provides the baseline data for carrying out further researches on prescription patterns as well as cost effective analysis including all costs in health care settings.

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## 1. Introduction

Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar levels and disruptions in carbohydrate, lipid, and protein metabolism, caused by issues with insulin secretion or action. Insulin is a hormone the pancreas produces that allows glucose to enter cells and

provide energy. There are four types of diabetes: type 1, type 2, gestational diabetes (which occurs during pregnancy), and others such as pre-diabetes and latent auto-immune diabetes.

In Type 1 diabetes, the pancreas does not produce enough insulin, leading to high blood sugar levels. This type is more common in children, teenagers, and young adults and was previously known as insulin-dependent and

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otherwise juvenile diabetes. Symptoms may include weight loss, nausea, excessive thirst, and impaired vision.<sup>1</sup>

Type 2 diabetes, also known as insulin-resistant diabetes, occurs when the pancreas produces insulin, but the body either doesn't use it effectively or doesn't produce enough. This type is most common in individuals over the age of 45, but is now increasingly seen in younger age groups. Symptoms may include increased thirst, frequent urination, fatigue, blurred vision, and slow-healing wounds.<sup>2</sup>

Gestational diabetes occurs during pregnancy and is caused by a combination of insufficient insulin secretion and response. Most cases do not present with symptoms, but some women may experience extreme hunger, thirst, or exhaustion. During pregnancy, hormonal changes can lead to insulin resistance, causing the body's cells to use insulin less effectively. Throughout pregnancy, a maternal body creates additional hormones and passes through some other changes, also including weight growth. These adaptations lead the body's cells on using insulin less appropriately, a condition known as insulin resistance. The body then requires more insulin in cases of insulin resistance. In late pregnancy, insulin resistance is a common occurrence in pregnant women. However, some females already have insulin resistance before conception. They require more insulin at the beginning of pregnancy and are therefore more likely to develop gestational diabetes.

Adult-onset autoimmune diabetes called latent autoimmune diabetes of adults (LADA) is a form of diabetes that does not initially require insulin for glycemic control for at least the first six months after diagnosis. LADA shares characteristics of both type 1 and type 2 diabetes in terms of genetics, immunology, and metabolism. It is also known as type 1.5 diabetes due to its similarities with these two types. In Japan, it is referred to as slowly progressing insulin-dependent type 1 diabetes mellitus (SPIDDM). The American Diabetes Association does not consider LADA as a distinct type of diabetes but rather a slower progression of type 1 diabetes. LADA is also known as slowly emerging immune-related diabetes according to the World Health Organization.<sup>3,4</sup>

Pre - diabetes, a condition where blood sugar levels are higher than normal but not yet classified as type 2 diabetes, is a significant health concern. An estimated 96 million people, or more than one in three American adults, have pre - diabetes, with over 80% being unaware of their condition. Pre - diabetes increases the risk of developing type 2 diabetes, heart disease, and stroke.<sup>5</sup>

Type 2 diabetes affects approximately 6.28% of the global population, totaling 462 million people. It was the ninth leading cause of death in 2017, causing over 1 million deaths. This is alarming considering that in 1990, it ranked 18th in terms of mortality. Type 2 diabetes is also the sixth most prevalent disease in terms of Disability Adjusted Life Years, which measure human suffering.<sup>6</sup> The prevalence of

the disease is slightly higher in males than in females, but the difference is not significant. Men tend to be diagnosed at a slightly younger age, and the incidence of the disease increases with age, peaking around 55 to 59 years old. Surprisingly, the highest rates of type 2 diabetes are found in island nations in the Pacific Ocean, such as Fiji, Mauritius, American Samoa, and Kiribati. Southeast Asian countries like Indonesia, Malaysia, Thailand, and Vietnam have also seen an increase in cases. However, China, India, and the US have the highest overall numbers of people affected due to their large populations.<sup>6</sup>

Globally and in emerging nations like India, the burden of diabetes is large and rising, primarily due to rising rates of overweight/obesity and unhealthy lifestyles. In India, 77 million people were estimated to have diabetes in 2019, and by 2045, that number is projected to reach over 134 million. About 57% of these people are still undiagnosed. The top three nations in terms of the number of people with diabetes in 2019 are China (116.4 million), India (77.0 million), and the United States of America (31.0 million). China (140.5 and 147.2 million people) and India (101.0 and 134.2 million people) are anticipated to continue to have the largest burden of diabetes in 2030 and 2045, respectively.<sup>7,8</sup>

Type 2 Diabetes Mellitus occurs when the body becomes less sensitive to insulin or is unable to properly utilize it. There are several common risk factors that increase the likelihood of developing this type of diabetes. These include consuming diets high in processed meats, consistently consuming alcohol, having low levels of physical activity, being exposed to occupational carcinogens, consuming diets low in whole grains, nuts, and seeds, having a high BMI, having a family history of diabetes, leading a sedentary lifestyle, belonging to certain ethnicities, and being influenced by environmental or genetic factors.<sup>9-11</sup>

Insulin is a hormone that is made by the pancreas and helps convert glucose from food into energy for the body's cells. In type 2 diabetes, the body produces insulin, but the cells don't use it effectively. This leads to the pancreas producing more insulin to try and get glucose into the cells, but eventually, it can't keep up and glucose levels in the blood become too high. Factors like genetics, weight, metabolic syndromes, liver glucose production, and problems with beta cells can contribute to developing diabetes.<sup>12</sup>

HbA1c is considered the most reliable test for diagnosing diabetes as it measures the average sugar levels over a 3-month period. It is suggested as an alternative to fasting glucose for diagnosis. HbA1c is important in understanding long-term glycemic control and is correlated with the likelihood of complications from diabetes. It is also recognized as a risk factor for developing heart disease and stroke. HbA1c reflects glucose levels over the past 6-8 weeks and is used to assess the effectiveness of diabetes treatment plans.<sup>13,14</sup>

Hemoglobin is the main protein found in red blood cells and is responsible for the red color of blood. Hemoglobin A is the most common type, accounting for about 90% of all hemoglobin. While 92% of Hemoglobin A is made up of a chemical substance, the remaining 8% contains slightly different elements. Minor components of Hemoglobin A include types A1c, A1b, A1a1, and A1a2. Hemoglobin A1c, also known as HbA1c, is a form of hemoglobin that binds to glucose. It is also referred to as glycated hemoglobin, glycosylated hemoglobin, or glycated hemoglobin.<sup>14</sup>

Medications used to treat diabetes include insulin, which can be given intravenously, and various oral drugs. These oral drugs belong to different classes, such as Biguanides (Metformin), Sulfonylureas (Gliclazide), Glitazones (Pioglitazone), Glinides, DPP-4 inhibitors (Sitagliptin), SGLT2 inhibitors (Dapagliflozin), and Alpha-Glucosidase inhibitors (Acarbose).<sup>15,16</sup> There are also newer drugs, like Semaglutide and Tirzepatide, which are incretin mimetic that act similarly to Glucagon-like peptide 1 (GLP-1). Trials have shown that Tirzepatide was superior to Semaglutide in reducing HbA1C levels and managing weight.<sup>17</sup>

The rising cost of healthcare has made it necessary to find solutions that provide high-quality care while considering affordability. The high prices of healthcare are a barrier for many people to access necessary treatments. One potential solution is to promote the use of generic pharmaceuticals instead of branded drugs, as this can reduce prescription costs and make expensive medications more affordable. Policy-makers have also shown interest in expanding the role of pharmacists in healthcare due to evidence that pharmaceutical services can lead to positive outcomes. However, there is a need for thorough economic evaluations to determine the economic impact of pharmacists on reducing overall health spending.<sup>18</sup> Pharmacoeconomics, a subfield of health economics, aims to maximize value for patients, healthcare payers, and society by weighing the pros and cons of interventions with limited resources. Health technology assessments can provide guidance for decision-making in implementing healthcare interventions, including those involving clinical pharmacy.<sup>19</sup>

Pharmacoeconomics can assist policymakers and healthcare professionals in determining the accessibility and affordability of reasonable drug usage. It focuses on efficiency and provides recommendations on maximizing the benefits of resource use. There are various evaluation techniques, such as cost-minimization analysis, cost-effectiveness analysis, cost-benefit analysis, and cost utilization analysis, which help identify and quantify the cost of drugs. These techniques differ in how they measure the value of health benefits and outcomes. Pharmacoeconomics evidence can support decisions related to pharmaceutical licensing, pricing, reimbursement, and formulary maintenance. It is suggested that India should

establish a Pharmacoeconomics platform with a validated methodology and necessary training for insurance firms to offer better services at a lower cost.<sup>20</sup>

Cost effective analysis is a method that compares different approaches to divert schemes and their associated costs in order to achieve additional benefits. It is commonly used to compare treatment alternatives for specific diseases, particularly in relation to health benefits. This analysis is a widely used Pharmacoeconomics method because it allows for easy identification and measurement of outcomes.<sup>21</sup>

In the healthcare industry, there is a need for new tools and approaches due to the changing healthcare environment and concerns about costs, access, and quality of care. Health economics has helped in developing specialized approaches to address the health needs of different populations. In the case of Type 2 Diabetes Mellitus (T2DM), it is a lifetime and costly disease, which places an economic burden on patients. The prevalence of non-communicable diseases like diabetes is increasing, and if not well managed, it can lead to various complications with clinical, social, and economic implications. Cost-effective diabetes therapy not only ensures rational drug use but also reduces patient costs and improves treatment outcomes, thus reducing complications and improving patients' quality of life when used appropriately in therapeutic decision making.

The objectives of the current study were to evaluate common prescribing patterns according to World Health Organization (WHO) indicators, and conduct a cost-effective analysis of oral hypoglycemic drugs for type 2 diabetes treatment.

## 2. Materials and Methods

### 2.1. Study design

Prospective observational cohort study

### 2.2. Study site

'Sudha' The Prevention Centre- Diabetes Specialty Management Centre, Bangalore, India

### 2.3. Study period

The study was carried out for a period of 9 months from January 2022 to September 2022.

### 2.4. Sample size

Considering the population of people visiting Sudha to be around 1000, sample size was estimated to be 286 with the error of margin kept at 95%  $\alpha=5$ .

### 2.5. Inclusion criteria

1. Patients who visited the outpatient department in Sudha

2. Patient aged above 18 years, who were clinically diagnosed with type 2 diabetes
3. Those who were taking oral anti - diabetic drugs, without any cognitive impairment, severe vision problems, or hearing problems
4. Patients with DM with or without HTN, dyslipidemia.
5. Those who were willing to participate in the study were considered eligible.

### 2.6. Exclusion criteria

1. Patients with other immuno-suppressive conditions (cancer, AIDS, TB)
2. Patients with type 1 diabetes, Gestational diabetes and Latent autoimmune diabetes of adults
3. Patients who were on Insulin for Diabetic management
4. Patients prescribed with weight loss medications, steroids, oral contraceptives, antiviral drugs, antibiotics, immunosuppressant's
5. Those who have not given consent to participate were not enrolled in the study

### 2.7. Sample size

Considering the population of people visiting Sudha to be around 1000, sample size was estimated to be 286 with the error of margin kept at 95%  $\alpha=5$ .

### 3. IEC Approval

Approval was obtained from Sudha' The Prevention Centre-Diabetes Specialty Management Centre, Bangalore, India and from PES University, Bangalore India

#### 3.1. Source of data

Patient prescription, Patient Medical Record and Patient interview (whenever necessary).

#### 3.2. Statistical analysis

Descriptive analysis was carried out using Microsoft excel 2019

#### 3.3. Outcome measures

Medical condition of patients, their economic status, prescriptions pattern of anti diabetic agents, cost of drugs prescribed in study population, cost effective analysis of single, double and triple therapy was measured

This study was a prospective observational cohort study that followed participants for three months. The same group of participants were assessed before and after treatment. The study evaluated the participants' sugar values and prescriptions. The participants were recruited from a diabetic specialty center using convenience sampling and 286 patients gave their consent to participate. The inclusion

criteria were patients with type 2 diabetes who visited the outpatient department, were at least 18 years old, taking oral anti - diabetic drugs, without cognitive impairment, severe vision or hearing problems, and willing to participate. Patients with comorbid conditions, gestational diabetes, or latent autoimmune diabetes of adults were excluded, as well as those prescribed with certain medications. Patient information, including name, age, gender, phone number, clinical diagnosis, comorbid conditions, sugar values, and medication details, were documented. The study also evaluated the prescription pattern and cost effectiveness of different oral hypoglycemic agents. The effectiveness was measured by the average maintenance of sugar values and the patients were counseled by a physician and Diabetologist regarding medication adherence using a Patient Information Leaflet. Microsoft Excel 2019 was utilized to record and analyze data from the recruited subjects. Descriptive statistical analysis, such as calculating the mean, was used to analyze the data. The research received approval from the institutional ethics committees of 'Sudha' The Prevention Centre- Diabetes Management in Bangalore, India and PES University Bangalore, India.

### 4. Results and Discussion

Diabetes Mellitus is a significant healthcare issue in India, with the prevalence of the disease estimated to rise by 5.4% globally by 2025. In developed countries, it is more common in those aged 65 and older, but in India, it is prevalent in the age group of 45-64.<sup>22</sup>

As per Diabetic Atlas, which is published by the Indian Diabetic Federation (IDF), there exists an alarming rise of the disease from 40 million in 2007 to 70 million in 2025 in India. It has also expressed that every 5th person in the world with Diabetes will be an Indian.<sup>23</sup>

This recent study focused on the prescribing patterns and cost-effective analysis of various oral medications used to treat Type 2 Diabetes Mellitus in a Diabetes Specialty Centre over a period of 9 months.

Overall, 274 prescriptions were analyzed, with the majority(55%) of participants being 60 years and older, followed by 42% of those aged 35-60. Older individuals with diabetes are affected by factors such as decreased insulin secretion, increased insulin resistance, and changes in environmental factors related to obesity.<sup>24</sup>

1 demonstrates the demographic details with respect to the Distribution of Age, Gender, and Medical condition with Co-morbid conditions of the patients. The study found that men accounted for 57% of the patients, while women accounted for 42% which attributed the male-to-female ratio to be 1.12. The higher prevalence of the disease in older men may be attributed to a larger amount of visceral fat in men compared to women.<sup>25</sup>

In this study, the most common co-existing condition was hypertension (35%), followed by a combination of

**Table 1:** Demographics- Distribution of Age, Gender, Medical condition with Co-morbid conditions of the patients

Count of CEA NO.		18 - 35		36 - 60		MALE > 60		18 - 35		36 - 60		Male Total		Grand Total	
Female > 60															
Diabetic Complication															
T2 DM	1			2	3	2		1		3	6			9	
T2 DM +	1			6	7	3		2		3	8			15	
Dyslipidemia															
T2 DM + HTN	11			3	14	14				4	18			32	
T2 DM + HTN +	7			2	9	3				5	8			17	
Dyslipidemia															
Total	20			13	33	22		3		15	40			73	
DM + Cardiac Dysfunction															
T2 DM	1			1	2	1				2	3			5	
T2 DM + HTN	1			1	2	5				1	6			8	
T2 DM + HTN +						2				1	3			3	
Dyslipidemia															
Total	2			2	4	8				4	12			16	
DM + Psychiatric Disorder															
T2 DM	1				1									1	
T2 DM + HTN										1	1			1	
T2 DM + HTN +	1			1	2	1					1			3	
Dyslipidemia															
Total	2			1	3	1				1	2			5	
DM + Renal Dysfunction															
T2 DM						1					1			1	
T2 DM +				1	1	1				2	3			4	
Dyslipidemia															
T2 DM + HTN	1			2	3	1				2	3			6	
T2 DM + HTN +	1			1	2	2					2			4	
Dyslipidemia															
Total	2			4	6	5				4	9			15	
No Co - Morbidity															
T2 DM	9	2		8	19	4		1		17	22			41	
T2 DM +	2			10	12	3		2		11	16			28	
Dyslipidemia															
T2 DM + HTN	17			9	26	20				4	24			50	
T2 DM + HTN +	22			5	27	11				8	19			46	
Dyslipidemia															
Total	50	2		32	84	38		3		40	81			165	
Grand Total	76	2		52	130	74		6		64	144			274	

**Table 2:** Distribution of economic status of patients with Pie graph showing the distribution of economic status of patients

Economic status	Female	Male	Grand total	26, 9% 104, 38%		
<25K	22	4	26 (9%)	144, 53%		
>50K	48	96	144 (53%)			
25K-50K	60	44	104 (38%)	<25K	>50K	25K-50K
Total	130	144	274			

**Table 3:** Number of anti-diabetic drugs prescribed per prescription as per WHO guidelines.

Prescription pattern	No. of prescription (N=274)	Percentage (%)
Prescription with one antidiabetic agent	47	17.15
Prescription with two antidiabetic agents	88	32.12
Prescription with three antidiabetic agents	97	35.4
Prescription with four antidiabetic agents	25	9.12
Prescription with five antidiabetic agents	14	5.11
Prescription with six antidiabetic agents	3	1.09
Total	274	100.0

**Table 4:** Prescriptions with different class of drugs with number of prescriptions

Prescription with one antidiabetic agent	Prescription with two antidiabetic agents	Prescription with three antidiabetic agents	Prescription with four antidiabetic agents	Prescription with five antidiabetic agents	Prescription with six antidiabetic agents
Sulfonylureas -6	Sulfonylurea + biguanides -32	Sulfonylurea + biguanides + $\alpha$ -glucosidase inhibitors -20	Sulfonylurea + biguanide + DPP4 inhibitors + $\alpha$ -glucosidase inhibitors -6	Sulfonylurea + biguanide + DPP4 inhibitor + SGLT2 inhibitor + thiazolidinedione -8	SGLT2 inhibitor+ biguanide+ DPP4 inhibitor+ thiazolidinedione+ $\alpha$ -glucosidase inhibitor+ sulfonylurea -3
Biguanides -18	DPP4 inhibitors + biguanides -37	Sulfonylurea + biguanides + thiazolidinedione -7	Sulfonylurea + biguanide + SGLT2 in+ $\alpha$ -glucosidase inhibitors -7	SGLT2 inhibitor + biguanide+ DPP4 inhibitor+ thiazolidinedione+ $\alpha$ -glucosidase inhibitor -6	
$\alpha$ -glucosidase inhibitors -4	SGLT2 inhibitors + biguanides -4	SGLT 2 inhibitors + biguanide + DPP 4 inhibitors -25	SGLT2 inhibitors + biguanide + DPP4 inhibitors + $\alpha$ -glucosidase inhibitors -8		
DPP 4 inhibitors -10	$\alpha$ -glucosidase inhibitors + biguanides -15	Biguanide + DPP 4 inhibitors + $\alpha$ -glucosidase inhibitors -7	Sulfonylurea + SGLT2 inhibitors + DPP4 inhibitors + $\alpha$ -glucosidase inhibitors -4		
SGLT2 inhibitors -9		Biguanide + SGLT2 inhibitors + $\alpha$ -glucosidase inhibitors -11 Sulfonylurea + biguanides + DPP4 inhibitors -16 Sulfonylurea + biguanides + SGLT2 inhibitors -11			

hypertension and dyslipidemia (27%). These conditions increase the risk of developing diabetes. 20 The majority (60.2%) of diabetic patients did not have any complications, but a significant portion (26.64%) had complications such as diabetic foot, peripheral neuropathy, and retinopathy. It's important to note that chronic high blood sugar levels can have negative effects on both nerves and vital organs in the body.

2 depicts the distribution of economic status of patients with Pie graph showing the distribution of economic status of patients. In this study, medications were prescribed using their brand names rather than their generic names. The study found that, on average, 2.9 drugs were prescribed per prescription, which is higher than the recommended number according to WHO guidelines. The WHO suggests that the average number of drugs prescribed per prescription should be between 1.6 and 1.8. Table 3 depicts the number of anti-diabetic drugs prescribed per prescription as per WHO

guidelines.

4 demonstrates the total prescriptions with different class of drugs with number of prescriptions. The most commonly prescribed oral hypoglycemic agent for the treatment of type 2 diabetes is Biguanides (38%), followed by Dipeptidyl Peptidase-4 inhibitors (DPP-4 inhibitors) (21.2%) in monotherapy. Unlike other classes of medications, such as Sulphonylureas and Thiazolidinediones, Metformin (a type of Biguanide) does not cause weight gain, making it a preferred choice for obese patients. Metformin also rarely leads to hypoglycemia (low blood sugar) when used alone because it decreases excess glucose production in the liver without increasing insulin levels. Therefore, it is widely considered as the ideal first-line treatment for type 2 diabetes. Additionally, Metformin is affordable, which makes it more accessible for patients in developing countries like India.<sup>26,27</sup>

**Table 5:** Cost-effectiveness analysis of single, double and triple combination drugs

Drugs class	No. of prescriptions	Unit cost /month (INR)	Average HbA1c (%)		Difference	Avg maintenance HbA1c (%)
			Before treatment	After treatment		
CEA of Monotherapy						
Biguanide	18	51	8.5	8.1	0.4	8.1
DPP 4 Inhibitors	10	246	8.2	7.8	0.4	7.8
SGLT 2 Inhibitors	9	345	8.4	8	0.4	8
CEA of Two combination therapy						
Sulfonylurea + biguanide	32	222	8.4	8	0.4	8
DPP 4 inhibitors + biguanide	37	270	8.3	7.8	0.5	7.8
$\alpha$ -glucosidase inhibitors + biguanide	15	267	8.3	7.9	0.4	7.9
CEA of Three combination therapy						
Sulfonylurea + biguanides+ $\alpha$ -glucosidase inhibitors	20 25	465 420	8.3 8.3	7.9 7.5	0.4 0.8	7.9 7.5
SGLT 2 inhibitors + biguanide + DPP 4 inhibitors						

The majority of patients in combination therapy for diabetes were prescribed with either DPP-4 inhibitors and Biguanides (42.04%) or Sulphonylureas and Biguanides (36.36%). Interestingly, the potential benefits of DPP-4 inhibitors include their complementary mechanism of action with other anti-diabetic medications, a favorable adverse effect profile, and a neutral effect on weight. With a low risk for hypoglycaemia, DPP-4 inhibitors are advantageous to patients that are close to their target HbA1c but continuously experience elevated glucose levels after meals.<sup>28</sup>

When compared to the combination of Sulphonylureas and Biguanides, using DPP-4 inhibitors with Biguanides was associated with a 38% decreased risk of cardiovascular complications due to diabetes progression.<sup>29</sup>

In triple combination therapy, a combination of SGLT2 inhibitors + DPP-4 inhibitors + Biguanides constituted for the majority of prescriptions (26.04%). The American Diabetes Association (ADA) and the European Association for the study of Diabetes (EASD) recommend for the initiation of dual combination therapy if the HbA1c targets are not achieved after 3 months of monotherapy and then proceed to triple combination therapy if HbA1c targets are not achieved after 3 months of dual therapy.<sup>30,31</sup>

SGLT2 inhibitors work differently than other diabetes medications by lowering glucose levels independently of the beta cell function. This improves insulin sensitivity. When added to DPP-4 inhibitors and Biguanides, this combination has been effective in reducing HbA1c levels and slowing the progression of the disease.<sup>32,33</sup>

5 depicts the cost-effective analysis carried out for single, double and triple combination drugs. Cost-effectiveness analysis was conducted separately for single

and combination drug therapy. The cost for each drug class was calculated in INR and the average maintenance HbA1c levels after treatment was calculated using the incremental cost ratio using the formula,  $ICER = (\text{cost of A} - \text{cost of B}) \div (\text{effect of A} - \text{effect of B})$ , where A is most cost effective drug and B is second most cost effective drug. In our study, cost effectiveness of monotherapy was calculated and found that DPP 4 inhibitors was cost effective followed by SGLT2 inhibitors with an incremental cost ratio of 495. A study conducted by Tamilselvan T et.al.,<sup>34</sup> showed contrasting result that sulfonylurea was cost effective followed by DPP4 inhibitors, because the study considered generic drug and dose for cost calculation and FBS was considered for blood sugar monitoring.

In our study among combination therapy, cost effectiveness analysis of two drug combination therapy showed that DPP4 inhibitors + biguanide is cost effective followed by  $\alpha$ -glucosidase inhibitors + biguanide with an ICER of 30. A study conducted by Divya Singh et.al.,<sup>35</sup> showed that in combination therapy DPP 4 inhibitors + biguanide was cost effective combination.

Among triple combination therapy, our study found that SGLT2 inhibitors + biguanide + DPP 4 inhibitor was cost effective combination followed by sulfonylurea + biguanide +  $\alpha$ -glucosidase inhibitors with an incremental cost ratio of 112.5.

The results reveal that the anti-diabetic prescribing trend has moved away from monotherapy and seems to be moving towards combination therapies to achieve better glycaemic control and slowing down the progression of the disease. The Medical council of India have called upon doctors practising medicine to prescribe drugs with generic names,

as far as possible. In spite of these regulations, prescribing by brand names is a matter of concern.

The findings of this study have to be seen in light of some potential limitations. It was conducted at a single center for a short period of time and included a small number of participants. Additionally, patients on insulin management were not included, which could have provided better insights into cost effectiveness as diabetes is a chronic condition. The study also did not consider indirect and intangible medical costs. Lastly, the study was limited to a single site in South Bangalore, Karnataka, and would have had a greater impact if it had access to multiple centers within India to analyze usage trends more extensively.

## 5. Conclusion

This study reports that combination therapy of oral hypoglycaemic agents was more widely prescribed than monotherapy. Furthermore, it was also reported to be more cost-effective than monotherapy in the maintenance of Glycosylated hemoglobin. This finding indicates that medication use was mostly consistent with evidence-based practice guidelines. This study has certain limitations constraining to a single centre, short duration, and exclusion of insulin in the management of DM for the study. However, it provides baseline data for carrying out further studies about prescribing patterns and cost-effective analysis for treatments used in the management of Type 2 diabetes mellitus. Polypharmacy is a concerning issue, especially for the elderly. This study also necessitates the need to develop and use a standardized ideal format for all prescriptions so as to reduce the chance of medication errors and to provide clearer information to pharmacists and patients. Inadequate oral instructions regarding the use of medications are prone to a decrease in medication adherence, so there exists a need for proper guidance with respect to medications as well as lifestyle modifications to attain better outcomes.

## 6. Ethical Approval

Ethical approval was obtained from the Institutional Ethics Committee from PES College of Pharmacy and Sudha- The Prevention Centre. Hereby attesting the same.

## 7. Availability of Data and Materials

Microsoft Office was used for data collection and analysis.

## 8. Source of Funding

No funding was received.

## 9. Conflict of Interest

The authors declared that they have no conflict of interest.


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**Cite this article:** Manapurthu MG, Deepashree C, Pradeep R, Nivedha M. Assessment of prescription pattern and cost effective analysis of oral hypoglycemic agents used in treatment of type 2 diabetes mellitus. *J Pharm Biol Sci* 2024;12(1):68-76.