ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.gjmpbu.org

Global Journal of Medical, Pharmaceutical, and Biomedical Update

Original Article

Cost-effective Analysis of Prescribed Oral Hypoglycemic Agents amongst Pre-obese and Obese Diabetic Patients in a Tertiary Care Hospital in Odisha

Vartika Srivastava[1], MBBS, MD, Sougata Sarkar[2], DM, MD, MBBS, Ratikanta Tripathy[1], MD, MBBS, Chaitali Pattanayak[1], MD Pharmacology, Mangala Charana Das[1]

[1]Department of Pharmacology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, [2]Department of Clinical and Experimental Pharmacology, School of Tropical Medicine, Calcutta Medical College, Kolkata, West Bengal, India.

***Corresponding author:**
Vartika Srivastava,
Assistant Professor, Department of Pharmacology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India.

vartika.srivastava@kims.ac.in

Received : 20 February 2023
Accepted : 23 March 2023
Published : 04 July 2023

DOI
10.25259/GJMPBU_23_2023

Quick Response Code:

ABSTRACT

Objectives: Diabetes is more prevalent in middle- and higher-income groups and is spreading at an alarming rate. Drug therapy is compulsory because of the chronic and progressive nature of the disease. With such multifactorial background of high prevalence, progressive nature of the disease leading to various complications, increased healthcare cost, and availability of multiple therapeutic regimens prescribed, this study has been done to evaluate the cost-effective analysis of oral hypoglycemic agents.

Materials and Methods: This is a prospective, parallel group, and comparative observational study conducted by the Department of Pharmacology in collaboration with the Department of Endocrinology at Kalinga Institute of Medical Sciences, Bhubaneswar. The duration of the study was of 2 years. A total number of 220 patients were selected and based on body mass index, patients were categorized into preobese (new and old diabetic patients) and obese (new and old diabetic patients) categories. In this study, cost-effectiveness analysis (CEA) was done to evaluate the cost differences between two or more medication groups, with a similar clinical effect. Results of CEA are expressed as an average cost-effectiveness ratio or as an incremental cost-effectiveness ratio.

Results: From this study, it is observed that in terms of benefit, dual therapy of Metformin and Dapagliflozin was most efficacious followed by Metformin and Sitagliptin as well as Metformin and Glimepiride combinations. If cost is considered, Metformin montherapy and metformin and Glimepiride dual therapy was most cost-effective. In triple regimen, MET+VOG+GLIM combination was seen to be more cost effective than gliptin combination, both in terms of control of FBS as well as PPBS. The cost of treatment goes parallel with duration of disease, being higher in the old cases of long-standing duration.

Conclusion: The present study shows that SGLT2 inhibitors are better class of oral hypoglycemics in terms of long-term benefits and this group is prescribed as dual therapy more frequently but cost of therapy is the greatest barrier. Metformin and Sulfonylureas remain the most beneficial combination, both in terms of efficacy and cost. The cost of treatment was varying, depending on the duration of disease, being higher in old cases and lower in new cases.

Keywords: Cost-effective analysis, Pharmacoeconomics, Diabetes mellitus, Oral hypoglycemic agents, Metformin, Sulfonylureas, Dipeptidyl peptidase 4 inhibitors, Sodium-glucose transport protein 2 inhibitors

INTRODUCTION

Diabetes is the most common and prevalent non-communicable disease, which is generally associated with various comorbidities and complications such as coronary artery disease, hypertension, renal complication, retinal damage, neurological disorders, the incidence of

stroke at different sites, and generalized infections. There are many treatment options available for diabetes including oral hypoglycemic agents, insulin, and lifestyle modification. But whatever treatment is prescribed has to be continued for a lifetime.

Diabetes is more prevalent in middle- and higher-income groups and the cases are increasing at an alarming rate and soon it is projected that India shall become the capital of diabetes. Drug therapy is compulsory because of the chronic and progressive nature of the disease. The total cost of treatment in the uncomplicated case is Rupees 15,000/annum and four times more in complicated cases which leads to an increased financial burden to the individual and the healthcare system as well.[1]

With such multifactorial background of high prevalence, progressive nature of the disease leading to various complications, increase healthcare cost, and availability of multiple therapeutic regimens prescribed, this study has been conducted to evaluate the cost-effective analysis of oral hypoglycemic agents. It will be a pharmacoeconomic (PE) study[2] that will include the number of drugs prescribed, defined daily dose, duration of treatment in months and years, the total cost incurred, and overall benefits in the reduction of glycemic parameters.

MATERIAL AND METHODS

This is a prospective, parallel group, and comparative observational study conducted by the Department of Pharmacology in collaboration with the Department of Endocrinology at Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar. The study was approved by the Institutional Ethical Committee (KIMS/KIIT/IAEC/040/2014) and written informed consent from all patients participating in the study was obtained. The duration of the study was 2 years.

Inclusion criteria

The following criteria were included in the study:

- New cases of type 2 diabetic patients between 40 and 70 years of age
- Patients with body mass index (BMI) between 25 and 34.99 (preobese and obese) and a sedentary lifestyle
- Patients already on antidiabetic medications for <3 years
- Glycated hemoglobin (HbA1C) levels between 6% and 9%
- Diabetic patients with co-morbid conditions such as hypertension, obesity, and dyslipidemia
- Diabetic patients presenting with microvascular complications such as retinopathy, nephropathy (glomerular filtration rate [GFR] not less than 40 mL/min/1.73 m^2), and neuropathy.

Exclusion criteria

The following criteria were excluded from the study:

- Patients <40 and more than 70 years of age
- BMI <25, BMI ≥35, athletes or patients whose work involves heavy exercise
- Diabetic patients with advanced nephropathy whose GFR <40 mL/min/1.73 m^2
- Untreated hypo or hyperthyroidism patients
- Patients suffering from acute metabolic disorders such as diabetic ketoacidosis or hyperosmolar coma
- Patient on oral contraceptive pills
- Patients suffering from severe liver or kidney disease.

A total number of 230 patients attending endocrinology OPD, KIMS, were selected for the study out of which there were 10 dropouts due to loss of follow-up. Based on BMI, patients were categorized into preobese and obese categories. The enrolled patients were then divided into groups as follows:-

- Pre-obese - divided into - (a) new diabetic (First time diagnosed), (b) old diabetic (<3 years duration)
- Similarly, obese divided into – (a) new diabetic (First-time diagnosis), (b) old diabetic (<3 years duration).

Each category was further divided into four subgroups according to the treatment received:

- Monotherapy - Only Metformin
- Combination therapy - Metformin + another antidiabetic group, preferably sulfonylureas (SUs), dipeptidyl peptidase 4 (DPP4) inhibitors, sodium-glucose transport protein 2 (SGLT2) inhibitors or alpha-glucosidase inhibitors
- Triple therapy (Metformin + any of the two drugs given above)
- Insulin with other oral hypoglycemic drugs.

Based on the above criteria, the total patients were categorized as follows-

Treatment received	Preobese (*n*=168)		Obese (*n*=52)	
	New diabetic cases (*n*=52)	Old diabetic cases (*n*=116)	New diabetic cases (*n*=12)	Old diabetic cases (*n*=40)
Metformin	11	0	3	2
Dual therapy	41	86	9	27
Triple therapy	0	30	0	11

- Dual therapy includes Metformin + Glimepiride, Metformin + Dapagliflozin/any SGLT2 inhibitor, Metformin + Voglibose, Metformin + Sitagliptin/DPP 4 inhibitor
- Triple therapy includes Metformin + Glimepiride +

Sitagliptin, Metformin + Glimepiride + Dapagliflozin, Metformin + Glimepiride + Voglibose.

PE analysis comprises different methods of analysis such as: "cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), cost minimization analysis (CMA), cost-utility analysis (CUA), and cost of illness analysis (COI)."

In this study, CEA was done to evaluate the cost differences between two or more medication groups, with a similar clinical effect. Results of CEA are expressed as an average cost-effectiveness ratio (ACER) or as an incremental cost-effectiveness ratio (ICER).

ACER/ICER = Healthcare cost divided by clinical outcome/ Benefit

Hence, the aim of the present study was to investigate which therapy is most efficacious and has more cost benefit to the patient.

The collected data of the above-mentioned parameters were compiled, tabulated, and entered in Microsoft Excel and statistically analyzed using GraphPad Prism 7 (http://graphpad.com/quickcalcs/ttest1/?Format=C) for the determination of significance. The result of this analysis was used to provide the comparison of data to finalize the study results. The "*P*" value was determined based on the data related to drug efficacy using paired and unpaired T-tests. "*P*" < 0.05 was considered significant. The clinical relevance of the results in the light of statistical analysis was displayed (at a 95% confidence interval) and discussed.

RESULTS

All medications prescribed are branded products from a reputed multinational company. Metformin 500 and 1000 mg is found to be the cheapest among oral preparations. In the dual combination form, costs of metformin combination with SGLT2 inhibitors (Dapagliflozin) and metformin with DPP4 inhibitors (Sitagliptin) were on the higher side while in the triple combination, metformin 1000 mg + Sitagliptin 50 + Glimepiride 2 mg has the highest cost followed by same combination with Glimepiride 1 mg.

From [Table 1], it can be observed that Metformin monotherapy and metformin-SU combination are highly cost-effective for the patients but in terms of glycemic benefit, a dual combination of metformin and dapagliflozin is most efficacious followed by a metformin-glimepiride combination. Alpha Glucosidase inhibitors were cost-effective but were noticed to reduce postprandial blood sugar (PPBS) more effectively than fasting blood sugar (FBS).

Dual or triple combination therapy is always required in this group of patients. From [Table 2] it is observed that in terms of benefit, dual therapy of Metformin and Dapagliflozin was most efficacious followed by Metformin and Sitagliptin as well as Metformin and Glimepiride combinations. If cost is considered, Metformin and Glimepiride dual therapy was the most cost-effective. In a triple regimen, the MET+VOG+GLIM combination was seen to be more cost-effective than the gliptin combination, both in terms of control of FBS as well as PPBS. The cost of treatment goes parallel with duration of the disease, being higher in the old cases of long-standing duration.

From [Table 3], it can be observed that Metformin monotherapy and metformin-SU combination are highly cost-effective for the patients but in terms of glycemic benefit, the dual combination of metformin and SGLT2 inhibitors are most efficacious followed by metformin-SU and metformin-DPP 4 inhibitors combination.

From [Table 4], it is observed that in terms of benefit, dual therapy of Metformin and Dapagliflozin was most efficacious followed by Metformin and Sitagliptin as well as Metformin and Glimepiride combinations. If cost is considered, Metformin and Glimepiride dual therapy was the most cost-effective. In the triple regimen, the MET+VOG+GLIM combination was seen to be more effective than the gliptin combination and was cost-effective too, both in terms of control of FBS and PPBS.

Table 1: The cost-effective analysis of diverse prescribed regimens considering FBS and PPBS as determinants of effectiveness.

Cost-effective analysis - Preobese new diabetic (*n*=52)							
Drug name	**ATDC**	**ATB (controlled FBS to near normal)**	**ACER/MONTH (FBS)**	**ACER/YEAR (FBS)**	**ATB (controlled PPBS to near normal)**	**ACER/ MONTH (PPBS)**	**ACER/ YEAR (PPBS)**
MET–MONO	1346.25	36.125	3.10	37.25	32	3.50	42.10
MET+VOG	6255.54	48.53	10.70	128.90	103.07	5.05	60.70
MET+GLIM	3212	70.41	3.80	45.60	174.5	1.50	18.40
MET+SITA	11680	51.44	18.90	227.10	151.11	12	144.00
MET+DAPA	10154	72.65	12.63	184.96	184.34	10.50	125.30

ATDC: Average total direct cost, ATB: Average total benefit, ACER/MONTH: Average cost-effective ratio of each drug per month and ACER/YEAR: Average cost-effective ratio of each drug per year. MET–MONO: Metformin monotherapy, MET+VOG: Metformin and voglibose, MET+GLIM: Metformin and glimepiride, MET+SITA: Metformin and sitagliptin, MET+DAPA: Metformin and Dapagliflozin combination, FBS: Fasting blood sugar, PPBS: Post prandial blood sugar

Table 2: The cost-effective analysis of diverse prescribed regimens considering FBS and PPBS as determinant of effectiveness.

Cost-effective analysis - Preobese old diabetic (*n*=116)							
DRUG NAME	**ATDC**	**ATB**	**ACER/MONTH**	**ACER/YEAR**	**ATB**	**ACER/MONTH**	**ACER/YEAR**
MET+GLIM	3447.60	29.20	9.80	118.10	41.75	6.85	82.55
MET+VOG	6357.35	20.21	26.20	314.45	22.17	22.20	286.70
MET+SITA	11680	31.5	30.10	370.80	40.5	24.00	288.40
MET+DAPA	10154	32.76	28.51	350.56	44.34	21.50	278.30
MET+GLIM+VOG	8537.20	28.37	25.10	301.00	48.16	14.75	177.30
MET+GLIM+SITA	34572.4	21.44	134.35	1612.50	30.10	75.60	907.15

ATDC: Average total direct cost, ATB: Average total benefit, ACER/MONTH: Average cost-effective ratio of each drug per month and ACER/YEAR: Average cost-effective ratio of each drug per year. MET+MONO: Metformin monotherapy, MET+VOG: Metformin and voglibose, MET+GLIM: Metformin and glimepiride, and MET+SITA: Metformin and sitagliptin MET+DAPA: Metformin and Dapagliflozin combination. The triple regimen includes MET+GLIM+VOG: Metformin, glimepiride and voglibose, MET+GLIM+SITA: Metformin, glimepiride and sitagliptin combination, FBS: Fasting blood sugar, PPBS: Post prandial blood sugar

Table 3: The cost-effective analysis of diverse prescribed regimens considering FBS and PPBS as determinant of effectiveness.

Cost-effective analysis - Obese new diabetic (*n*=12)							
DRUG NAME	**ATDC**	**ATB (controlled FBS to near normal)**	**ACER/MONTH (FBS)**	**ACER/YEAR (FBS)**	**ATB (controlled PPBS to near normal)**	**ACER/ MONTH (PPBS)**	**ACER/ YEAR (PPBS)**
MET–MONO	1971	17.33	9.50	113.70	19	8.65	103.70
MET+VOG	6570	39	14.25	173.10	103.67	5.40	65.10
MET+GLIM	3285	59	4.60	55.70	213	1.30	15.40
MET+SITA	11680	41	23.75	284.90	189	8.45	101.55
MET+DAPA	10154	65	13.52	193.54	221.34	9.50	99.30

ATDC: Average total direct cost, ATB: Average total benefit, ACER/MONTH: Average cost-effective ratio of each drug per month and ACER/YEAR: Average cost-effective ratio of each drug per year. MET+MONO: Metformin monotherapy, MET+VOG: Metformin and voglibose, MET+GLIM: Metformin and glimepiride and MET+SITA: Metformin and sitagliptin MET+DAPA: Metformin and Dapagliflozin combination, FBS: Fasting blood sugar, PPBS: Post prandial blood sugar

Table 4: The cost-effective analysis of diverse prescribed regimens considering FBS and PPBS as determinants of effectiveness (*n*=116).

Cost-effective analysis - Obese old diabetic (*n*=40)							
DRUG NAME	**ATDC**	**ATB**	**ACER/MONTH**	**ACER/YEAR**	**ATB**	**ACER/MONTH**	**ACER/YEAR**
MET+GLIM	3481.50	34.92	8.30	99.70	59.70	4.85	58.30
MET+VOG	6351	30.66	17.25	207.15	29.66	17.85	214.10
MET+SITA	11680	29.8	32.65	391.95	39	24.95	299.50
MET+DAPA	10154	38.76	28.51	284.56	62.34	21.50	278.30
MET+GLIM+VOG	8796.5	47.5	15.40	185.20	94	7.80	93.60
MET+GLIM+SITA	34408.8	52	55.15	661.70	133.4	21.50	257.90
MET+GLIM+PIOZ	4380	34	10.70	128.80	163	2.25	26.90

ATDC: Average total direct cost, ATB: Average total benefit, ACER/MONTH: Average cost-effective ratio of each drug per month and ACER/YEAR: Average cost-effective ratio of each drug per year. MET+MONO: Metformin monotherapy, MET+VOG: Metformin and voglibose, MET+GLIM: Metformin and glimepiride and MET+SITA: Metformin and sitagliptin combination. Triple regimen includes MET+GLIM+VOG: Metformin, glimepiride and voglibose, MET+GLIM+SITA: Metformin, glimepiride, sitagliptin and MET+GLIM+PIOZ: Metformin, glimepiride and pioglitazone combination, FBS: Fasting blood sugar, PPBS: Post prandial blood sugar

A triple combination with pioglitazone was also cost-effective but was not prescribed much due to the previously reported cases of adverse events. Hence, it was seen that as the disease duration progresses, the cost of therapy further increases posing more financial burden to the patient.

Table 5: The analysis of variance comparing average cost-effective ratio of each drug per year in different groups (obese and preobese).

Parameters	Sum of squares	Degree of freedom	F statistic	*P*-value
ACER/YEAR (FBS)	508,331.7798	3	1.8071	0.1801
ACER/YEAR (PPBS)	251906.11	3	3.0806	0.0522

ACER/YEAR: Average cost-effective ratio of each drug per year, FBS: Fasting blood sugar, PPBS: Post prandial blood sugar

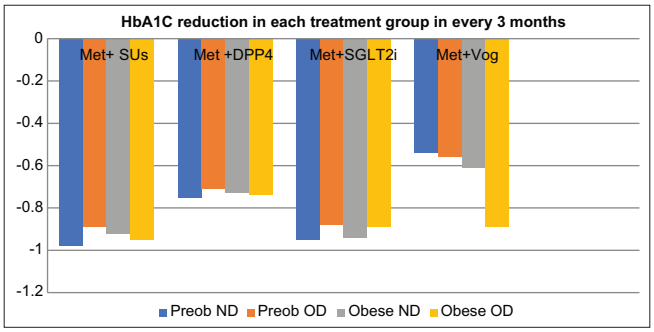

Figure 1: The overall reduction in HbA1c levels in each treatment group in every 3 month. Preob ND: Preobese new diabetic patient group, Preob OD: Preobese old diabetic patient group, Obese ND: Obese new diabetic patient group, Obese OD: Obese old diabetic patient group.

From [Table 5], it can be concluded that there is no significant difference in ACER (average total direct cost per unit FBS and PPBS reduction) between different treatment groups for type-2 diabetes mellitus (DM).

From [Figure 1], it can be observed that HbA1C levels which show the long-term benefit of oral hypoglycemic agents are maximally reduced in two groups i.e. Metformin and SGLT2 inhibitors as well as Metformin and SUs combinations, followed by DPP4 inhibitors. Therefore, glycemic benefit was mostly observed in patients treated with SGLT2 inhibitors and SUs.

DISCUSSION

This study was conducted by the Department of Pharmacology in collaboration with Endocrinology at KIMS Hospital, Bhubaneswar. Patients were screened and selected based on BMI and divided into preobese and obese categories. Further, they were categorized into new diabetic and old diabetic groups based on the inclusion and exclusion criteria. The study was continued for 2 years and a cost-effective analysis was done.

An increase in comorbid non-communicable diseases like diabetes has further increased the healthcare cost and it is a foremost concern for developing nations. Patients generally get affected due to the high cost of drugs though their symptoms improve. A study was conducted to evaluate the cost associated with type-2 DM, in which it was revealed that the cost of diabetes treatment is enormous.[3] The economic assessment of therapy should be encouraged to ensure improved cost-effectiveness and efficiency in management. Similar studies are also available and are still being conducted every year.[4] Some studies demonstrated that treatment with new antidiabetic medications has increased the financial burden more in spite of better efficacy and fewer adverse effects.[5] A study was conducted in India to assess the cost of treatment of diabetic patients which showed that the cost was INR 14,508/out of which direct and indirect cost were approximately 68%, 28%, respectively, and the special cost was 2.8%.[6] In comparing all these costs, medication charges were found to be high, and it was concluded that diabetes is an expensive illness to manage which causes financial difficulties for the patients.[7] Therefore, to identify the best treatment option which is the least expensive with similar efficacy; there is a need for an analytical tool. PE analysis is an important tool to determine the optimized treatment in various alternatives available. It compares two or more medication options in terms of their cost, outcome, and benefit.[8] PE evaluation consists of various methods of analysis such as: "CBA, CEA, CMA, CUA, and COI." In this study, we have used CEA and evaluated the cost differences between two or more medications from one group and with a similar clinical effect. The result of CEA is expressed as an average cost-effectiveness ratio (ACER) or as an incremental cost-effectiveness ratio (ICER).[9]

ACER/ICER: Healthcare cost divided by clinical outcome benefit

Hence, the present study was aimed at finding out which model of therapy could be most cost-effective in type-2 DM without compromising its quality, so that the economic burden on the patient can be reduced.

By the above formula, the CBA of both FBS and PPBS was done in all four groups of patients. Patients were either prescribed metformin as monotherapy or metformin with various combinations such as alpha-glucosidase inhibitors, sulfonylureas, DPP4 inhibitors, or SGLT2 Inhibitors. All the medications prescribed were branded products from the same reputed pharmaceutical company. No generic drugs were prescribed. Different combinations with variable doses were given. The cost of each medication was calculated per prescription. The average total benefits in terms of FBS and

Table 6: The current cost of antidiabetic drugs including insulin, either single or in combination for 10 tabs (one strip) and per one tablet (all of same pharmaceutical company).

Drug/Combinations	Cost/*n* Tablets (Rs)	Cost/Tablet (Rs)
Metformin 500 mg	12.20/10 tabs	1.2
Metformin 1000 mg	27/10 tabs	2.7
Metformin 500+Glimepiride 1 mg	32.20/10 tabs	3.2
Metformin 500 mg+Glimepiride 2 mg	47.20/10 tabs	4.7
Metformin 1000+Glimepiride 1 mg	38/10 tabs	3.8
Metformin 1000 mg+Glimepiride 2 mg	52/10 tabs	5.2
Metformin 500 mg+Dapagliflozin 5 mg	82.50/10 tabs	8.2
Metformin 500 mg+Dapagliflozin 10 mg	105/10 tabs	10.5
Metformin 1000 mg+Dapagliflozin 10 mg	150/10 tabs	15
Metformin 1000 mg+Voglibose 0.2	85/10 tabs	8.5
Metformin 1000 mg+Voglibose 0.3	88/10 tabs	8.8
Metformin 1000 mg+Sitagliptin 50 mg	308/14 tabs	22
Metformin 1000 mg+Glimepiride 1 mg+/, Voglibose 0.2	98/10 tabs	9.8
Metformin 1000 mg+Glimepiride 2 mg+/, Voglibose 0.3	128/10 tabs	12.8
Metformin 500+Sitagliptin 50 mg, Glimepiride 1 mg	258/10 tabs	25.8
Metformin 500+Sitagliptin 50 mg, Glimepiride 2 mg	272/10 tabs	27.2
Metformin 850 mg+Glimepiride 2 mg+Pioglitazone 7.5 mg	60.4/10 tabs	6.04

PPBS were calculated per year along with the average total cost of the therapy. Then as per the above-stated formula, the average cost-effectiveness ratio was derived for a month and a year, per medication. Patients in whom the entire combination was changed were not included because the benefit changes with each drug and that would make this study biased.

The cost of each antidiabetic drug, either as monotherapy or combination therapy which may or may not be fixed-dose combinations is shown in [Table 6].

Amongst preobese new diabetic 52 patients [Table 1], 8 were on metformin monotherapy, out of which 4 were on metformin 500 mg initially whose one tablet cost was Rs. 1.2 and the rest 4 were on metformin 1000 mg whose one tablet cost was Rs. 2.7. In some patients the dose was increased from 500 mg to 1000 or 1500 mg. Similarly, 12 patients were on metformin and glimepiride combination, out of which 1 patient was on 500 mg + 1 mg combination, 4 on 500 + 2 mg therapy, 4 on 1000 + 1 mg combination, and 3 on 1000 + 2 mg combination. Each tablet of 500 + 1 mg combination costs Rs. 3.2, 500 + 2 mg costs Rs. 4.7, and 1000 + 1 mg costs Rs. 3.8 while 1000 + 2 costs Rs. 5.2. Dosage was modified at some intervals depending on the requirement. Around 4 patients were on metformin and voglibose combination either 500 mg + 0.2 (n = 10) or 500 + 0.3 (n = 3) where each unit tablet of 500 + 0.2 combination costs Rs. 8.5 and 500 + 0.3 costs Rs. 8.8. About 8 patients were on metformin and sitagliptin combination, 500 mg + 50 mg dose, where each tablet costs Rs. 16, and 10 patients were on metformin and dapaflozin combinations, 5 + 500, 5 + 1000, where each tablet costs Rs. 8.5 and 10, respectively. After analysing the average total benefit and average direct cost, the average cost-effectiveness was calculated for each group for both FBS and PPBS [Table 1]. Hence, by comparing each group, Metformin remains the most preferred initial therapy and metformin and glimepiride was the most cost-effective treatment in type 2 diabetes but in terms of efficacy SGLT 2 inhibitors were more potent followed by SUs and DPP4 inhibitors. The physicians are preferring SGLT2 inhibitors in patients who can afford the treatment. Similar findings are seen in another study involving multicenter patients.[10]

In the obese new diabetic [Table 3], there were 12 patients in total, out of which 3 were on metformin monotherapy, 3 on metformin and glimepiride, 1 on metformin and voglibose, 1 on metformin and gliptin and 3 were on metformin and gliflozins combinations. Three patients on metformin monotherapy were on 1000 mg dosage (Rs. 2.7/tablet) while among 3 patients were on metformin and glimepiride combination,2 on 1000 + 1 mg (Rs. 3.8/tablet) and 2 were on 1000 + 2 mg (Rs. 5.2/tablet). Similarly, 1 patient was on metformin and voglibose 1000 + 0.2 mg combination (Rs. 9.3/tablet), and 1 patient of the DPP 4 inhibitor group was on 1000 + 50 mg therapy (Rs. 22/tablet). Further, 3 patients of the gliflozin group were on 1000 + 5 mg therapy (Rs. 10/tablet) and 1000 + 10 mg therapy (Rs. 15/tablet). The cost per prescription was analyzed according to the average benefit per year as stated above. It was again concluded that SUs with metformin were the most cost-effective combination and were prescribed to patients who were financially low but SGLT2 inhibitors were more efficacious and were preferred in patients who could bear the cost. Studies have shown that SGLT2 inhibitors also reduce weight in addition to lowering blood glucose levels. Therefore, physicians preferred this combination more in obese patients. A study done in northern India on

antidiabetic drugs concluded that metformin still remains the drug of choice but new drugs such as SGLT2 inhibitors and DPP 4 inhibitors are gradually catching up with the market, which coincides with the findings of our study.[11]

In old diabetic patient groups, both in obese and preobese, patients were generally given dual and triple therapy. A dual combination of metformin-dapagliflozin and metformin-glimiperide was most preferred followed by metformin-sitagliptin and metformin-voglibose. On assessing the benefit and costs, it was observed that the metformin and glimepiride combination was the most cost-effective combination but the metformin and Dapagliflozin combinations were better in terms of benefits (FBS and PPBS reduction) when compared with other combinations. Amongst triple regimens, MET+GLIM+VOG was seen to be the most cost-effective, efficiently reducing the PPBS more than FBS. Sitagliptin available both as a dual or triple regimen was effective in controlling the glycemic parameter but was found to be very expensive when compared with other medications, thus posing a financial burden to the patient. Pioglitazone was used in just one patient but effectively controlled FBS and PPBS. In the present study, it was concluded that as the disease duration progresses, the economic burden of the individual patient increases.

To summarize, the present study shows that SGLT2 inhibitors are a better class of oral hypoglycemics in terms of the long-term benefits and physicians are prescribing this group as dual therapy more frequently. The drugs in this category currently approved are dapagliflozin, Canagliflozin, and Empagliflozin. They reduce HbA1C levels by 0.5–0.8% as mono or dual therapy. There are additional non-glycemic benefits associated with SGLT2 inhibitors such as a decrease in the risk of cardiovascular (CV) adverse events in type 2 DM subjects, minimization of the risk of end-stage renal disease, a decrease in the rate of hospitalization for heart failure, and a decrease in serum creatinine in diabetic nephropathy and albuminuria.[12] Furthermore, there are studies showing the emerging role of this group of drugs in weight loss which in combination with diabetes and CV morbidity, leads to metabolic syndrome.[13] Due to all these reasons, currently, they are the first choice of drugs to be prescribed after metformin and this is in accordance with the international and national guidelines. SUs were the second most preferred drugs as dual and triple therapy due to their aggressive treatment and thus may be given to patients presenting with a higher HbA1c to facilitate a more rapid reduction in blood glucose levels. The combination of metformin and SU is one of the most commonly used combinations and can attain a greater reduction in HbA1c (0.8–1.5%) than either drug alone.[14,15] The dual and triple therapy with SUs was the most cost-effective combination and was prescribed to those patients who were financially weak. In another study also,[16] it was shown that metformin and glimepiride was the most cost-effective and most frequently prescribed drug which coincides with the the findings of the present study. Another study conducted in Bangalore concluded that a combination of metformin + glimipiride was found to be the most cost-effective drug for the treatment of type-2 diabetes mellitus when compared with other regimens.[8] This finding also corroborated the findings of the present study. The third most preferred group as an oral hypoglycemic agent was DPP 4 inhibitors. These include sitagliptin, vildagliptin, alogliptin, saxagliptin, linagliptin, and teneligliptin. Sitagliptin was the first of the DPP-4 inhibitors to be approved by the US Food and Drug Administration in 2006. This was followed by the approval of vildagliptin in February 2007. Saxagliptin (Onglyza®), vildagliptin (Galvus®), and sitagliptin (Januvia®) are currently available.[17] These drugs have modest efficacy, that is, reduce HbA1C levels by 0.5–0.8 mg/dL. Apart from antihyperglycemic effects, this class of drugs possesses antihypertensive effects, anti-inflammatory effects, antiapoptotic effects, and immunomodulatory effects on the heart, kidneys, and blood vessels. But the cost of therapy is expensive. Therefore, this group was preferred in those patients who were financially stable. And lastly, alpha-glucosidase inhibitors were preferred as the fourth drug of choice for dual and triple therapy. It was commonly given in those patients where PPBS was significantly higher and with HbA1C between 6.5 and 7.5. It possesses weight loss as an additional advantage.

As per the American Diabetes Association guidelines (2022), and RSSDI-ESI clinical practice recommendations 2021, Metformin still should be initiated early as an oral hypoglycemic agent. In case there is a risk of CV, renal, or hepatic morbidity, SGLT2 inhibitors should be initiated, followed by Glucagon-like peptide-1 analogues, SUs, and DPP4 inhibitors. If glucose is still not controlled with these agents, then alpha-glucosidase inhibitors and thiazolidinediones should be initiated.[18] Patients not achieving desired glucose levels even after triple therapy, should be switched over to insulin.[19] In the present study also, the same prescribing pattern has been followed where SGLT2 inhibitors were the preferred choice, and metformin and SUs were the choice for economically weak patients. Studies have also revealed that branded products were more prescribed than generic products, which justifies our study.[20]

CONCLUSION

From this study, it can be concluded that metformin remains the first preferred drug in the treatment of diabetes, both in the preobese and obese group and it is the most cost-effective option as well. In the case of dual therapy, SGLT2 combination with metformin was most efficacious but increased the financial burden while Metformin and SUs remain the most

beneficial combination, both in terms of efficacy and cost. In a triple regimen, metformin, SUs, and alpha-glucosidase inhibitors combination was seen to be more cost-effective, in terms of controlling both FBS and PPBS. The cost of treatment was varied, depending on the duration of the disease, being higher in old cases and lower in new cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Acknowledgment

The authors would like to thank the Department of Pharmacology and Department of Endocrinology, KIMS, Bhubaneswar, Odisha, India.

REFERENCES

1. International Diabetes Federation. Atlas. 6th ed. Belgium: International Diabetes Federation; 2013. Available from: https://www.idf.orgen_6e_atlas_full [Last accessed 2013 on Dec 30].
2. Tonin FS, Aznar-Lou I, Pontinha VM, Pontarolo R, Fernandez-Llimos F. Principles of pharmacoeconomic analysis: The case of pharmacist-led interventions. Pharm Pract (Granada) 2021;19:2302.
3. Suleiman IA, Fadeke OF, Okubangjo O. Pharmacoeconomic evaluation of anti-diabetic therapy in Nigerian tertiary health institution. Ann Afr Med 2006;5:132-7.
4. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, *et al.* Management of hyperglycemia in Type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2022;45:2753-86.
5. Davies MJ, Chubb BD, Smith IC, Valentine WJ. Cost-utility analysis of liraglutide compared with sulphonylurea or sitagliptin, all as added-on to metformin monotherapy in Type 2 diabetes. Diabet Med 2011;10:1464-5491.
6. Yesudian CA, Grepstad M, Visintin E, Ferrario A. The economic burden of diabetes in India: A review of the literature. Global Health 2014;10:80.
7. Grover S, Avasthi A, Bhansali A, Schkarabarti S, Kulhara P. Cost of ambulatory care of diabetes mellitus a study from north India. Postgrad Med J 2005;81:391-5.
8. Kulkarni U, Dalvi K, Moghe VV, Deshmukh YA. Pharmacoeconomics: An emerging branch in heath science for decision making. Afr J Pharm Pharmacol 2009;3:362-8.
9. Abdelaziz MS, Rani HS. Pharmacoeconomic evaluation of oral-hypoglycemic agents at hospital in Bangalore. IOSR J Pharm Biol Sci 2015;10:46-50.
10. Liu G, Huang Z, Xin Q. Cost-effectiveness of oral antidiabetic drugs: A prospective multicenter study of real-world patients. Evid Based Complement Alternat Med 2021;2021:9972386.
11. Singla R, Bindra J, Singla A, Gupta Y, Kalra S. Drug prescription patterns and cost analysis of diabetes therapy in India: Audit of an endocrine practice. Indian J Endocrinol Metab 2019;23:40-5.
12. Padda IS, Mahtani AU, Parmar M. Sodium-glucose transport Protein 2 (SGLT2) inhibitors. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/nbk576405 [Last accessed on 2022 Sep 23].
13. Xu L, Ota T. Emerging roles of SGLT2 inhibitors in obesity and insulin resistance: Focus on fat browning and macrophage polarization. Adipocyte 2018;7:121-8.
14. Charbonnel B, Schernthaner G, Brunetti P, Matthews DR, Urquhart R, Tan MH, *et al.* Long-term efficacy and tolerability of add-on pioglitazone therapy to failing monotherapy compared with addition of gliclazide or metformin in patients with Type 2 diabetes. Diabetologia 2005;48:1093-104.
15. Hanefeld M, Brunetti P, Schhernthaner GH. One year glycemic control with sulphonylurea plus pioglitazone versus sulphonylurea plus metformin in patients with Type 2 diabetes. Diabetes Care 2004;27:141-7.
16. Sarumathy S, Ravichandiran V. A study on drug use pattern and cost impact of antidiabetic drugs in Type 2 diabetic patients in a secondary care hospital. World J Pharm Pharm Sci 2013;2:5913-9.
17. Scheen AJ. Dipeptidylpeptidase-4 inhibitors (gliptins): Focus on drug-drug interactions. Clin Pharmacokinet 2010;49:573-88.
18. American Diabetes Association. Standards of medical care in diabetes-2022 abridged for primary care providers. Clin Diabetes 2022;40:10-38.
19. Available from: https://www.rssdi.in/newwebsite/pdfdata/chawla2020_article_rssdi-esiclinicalpracticerecom.pdf [Last accessed on 2022 Oct 24].
20. Abdulganiyu G, Fola T. Cost-cost analysis of anti-diabetic therapy in a tertiary healthcare institution, north-eastern Nigeria. Int J Pharm Pharm Sci 2014;6:281-6.

How to cite this article: Srivastava V, Sarkar S, Tripathy R, Pattanayak C, Das MC. Cost-effective Analysis of Prescribed Oral Hypoglycemic Agents amongst Pre-obese and Obese Diabetic Patients in a Tertiary Care Hospital in Odisha. Glob J Med Pharm Biomed Update 2023;18:13.