Research Article

Cost-effectiveness Analysis of Oral Hypoglycemic Drugs for the Treatment of Type-II Diabetes Mellitus in a Tertiary Care Setup Karachi

Saira Shahnaz[1]*, Maqsood Ahmed Khan[2], Shazia Alam[2], Tauseef Ahmad[3], Zeb-un-Nisa[2], Syed Imran Ali[1], Mudassar Iqbal Arain[4]

1Department of Pharmacy Practice, Faculty of pharmacy, Ziauddin university Clifton Karachi, Pakistan.

2Department of Pharmaceutics, Faculty of pharmacy, Ziauddin university Clifton Karachi, Pakistan.

3Department of Medicine Diabetes and Endocrinology Ziauddin University, Pakistan.

4Department of pharmacy practice, Faculty of pharmacy, University of Sindh Jamshoro, Pakistan.

***Corresponding author's E-mail:** msairakhan1302@gmail.com

Received: 05-01-2020; **Revised:** 21-02-2020; **Accepted:** 28-02-2020.

ABSTRACT

The aim of the study was to analyze the current prescription pattern and compare the cost-effectiveness parameter of oral monotherapy and combination hypoglycemic drugs among type-II diabetes mellitus. A cross sectional study was conducted in a tertiary care hospital of Karachi Pakistan for a period of six months. A total of 377 diabetic type II patients were enrolled via purposive sampling method. Detailed sheets were prepared based on objectives of study for analysis of prescription and cost effective therapy. Out of total 377 enrolled type-II diabetes mellitus 70.8% (n=267and 29.2% (n=110) were females with mean age of 36.16±11.15, the prescription status showed that 18.30% (n=69) received monotherapy and 57.30% (n=216) of dual drug therapy and 24.40% (n=92) of triple therapy among combination therapy of oral antidiabetic drugs. The effectiveness of treatment is considered for the treatment obtaining lesser values for ICER hence the value of ICER among mono drug therapies for Glibenclamide 5mg was -720, with baseline value for HbA1C 7.6±0.99, and effectiveness of 0.5, with %E of 0.8.For glimepiride 2mg the ICER was calculated as -2160, with baseline of 7.2±1.5, IE -0.5and ΔE 0.3 of from class alpha glucose inhibitor for voglibose 0.3mg ICER was obtained-800, with baseline HbA1C of 7.5±2.1, IE 0.1, and ΔE 0.5% as shown in below table 4. The ICER for the add on therapy of Glibenclamide 2.5mg+Metforming 500mg with baseline value of 8.1±2.1 with ΔE of 0.3%, and incremental cost (IC) of -10087.2 was obtained 0. ICER was also 0 for sitagliptin 50mg +metformin 500mg with baseline 7.8±0.5, ΔE 0.6% and IE value of 0. ICER value of sitagliptin 50mg +metformin 850mg was obtained -648 with ΔE 0.1%, IE value -0.5. An ICER value of -2676 was obtained for metformin 850mg +pioglitazone 15mg with baseline of 7.6±1.7 and ΔE of 0.4% and IE of this therapy was 0.3. The outcome of drug utilization studies evaluates the current prescribing pattern of oral hypoglycemic agents and concomitant drugs with respect to the clinical efficacy of hypoglycemic drugs.

Keywords: Diabetes mellitus, cost-effectiveness, hypoglycemic drugs, therapy

INTRODUCTION

Diabetes mellitus is the most prevalent and chronic disease worldwide.[1] In year 2012, 9.3% of population from US suffered diabetes mellitus[2]. The numbers Patients prescription of antidiabetic drugs were estimated 211 million in 2015, which is a greater number compared to total 174 million prescriptions in 2011.[3] Metformin is considered a great consensus for oral antidiabetic first-line therapy for type-II diabetes mellitus[5-7]. While there is a huge argument over the best second-line therapeutic regimen[8]. The key point to treat the type-II diabetes mellitus is to control the glycemic levels among the patients with type 2 diabetes mellitus and complications that are linked with the diabetes related and extent of damage to the targeted organ. There are several oral hypoglycemic agents present in the market, each agent with its particular mechanism and site of action; hence the glucose lowering effects and costs of medication among patients is significant to be monitored[9]. Drugs utilization research (DUR) is an analytical descriptive collection of methods for the understanding and quantification of prescribing, dispensing, and medication consumption among patients, to enhance the quality and test the interventions of these processes.[10] The studies based on the cost-effectiveness analysis of drugs helps to promote the proper utilization of medication, and provide the more access to the affordable medications, such kind of studies promotes the policy makers to regulate the high cost of medication specifically among the developing countries like Pakistan. As the treatment regimen for diabetes mellitus protracts, it's a difficult to control the blood sugar level effectively among the patients with a single therapy. The combination therapies are required to support the optimal glycemic control in clinical practices. To this prospective several studies are evaluating the comparative efficacy of metformin (first-line therapy) and combination therapies with context to cost and their effectiveness[11-13]. In order to control the blood sugar level Majority of patients with type-II diabetes take one or more oral antidiabetic drugs in addition to the first line therapy i.e. Metformin. During the evaluation of prescription record two different treatment pathways was analyzed, started with metformin considering it first-line therapy or monotherapy. According to WHO (world health organization), the drug utilization research involves prescription, distribution, marketing and use of medication in the society which leads to the medical and

social consequences. [14] Controlling the cost of treatment is a major issue, as it affects the national budget, and situation is worse in the developing countries where resources are limited.[15] Evaluation of prescription pattern describes the local consumption, as it evaluates the therapeutic effects and resistance pattern of medications. Metformin has well established a long-term post marketing evidence for safety and effectiveness[16]. While metformin has general consent for first line therapy in the management of type-II diabetes mellitus.[17] there has been a dynamic debate for the second line therapy in the management of type-II diabetes mellitus[18] sulfonylureas are the commonly known for their fast onset in glucose lowering , hence considered as second line therapy for type-II diabetes mellitus,[19-20] however risk of hypoglycemia, weight gain, and safety related risk are concerned.[19-20] Where newer drugs of class dipeptidyl peptidase -4 inhibitors are costlier than sulfonylureas but comparative with lower risk of weight gain, hypoglycemia.[21] Increasing prevalence and emergence of diabetes related complications are the major consequences of early morbidities and mortalities, hence leading to enormous burden to health care services. The glycemic control is the key objective among type-II to prevent the complication's and co-morbidities arising from diabetes, the optimal glycemic control is difficult to achieves in a long-term management planning for a complicated disease like diabetes type-II. Poor glycemic control can be associated to the patients alone or may be linked with healthcare providers also.[22] The pharmaco-economic study highlights the need of compressive management for the patients of type-II diabetes mellitus that include the prevention of complications, comorbidities, diabetes related complications, life-style modifications events of hypoglycemia, and rational use of antidiabetic medication.

METHODOLOGY

A cross sectional observational study was conducted among the patients with confirmed diagnosis of type-II diabetes mellitus at three campuses of tertiary care hospital Karachi for the period of 6 months from June 2019- December 2019. Sample size was calculated based on the prevalence rate of diabetes. Total 377 participants attending the outpatient's department (OPD) of diabetology /endocrinology were enrolled in the study. Patients aged 35years and above were included while inpatients and patients diagnosed with type-I DM was excluded from the study. Good glycemic control was considered based on Glycemic status of Patients i.e. HbA1C <7%. While poor glycemic control of patients considered was HbA1C levels of >7%. All the treatment related records were obtained from the patients file/Prescription and analyzed statistically.

Ethical Approval

Ethical approval required for the study was obtained from the Ethical review committee of Ziauddin university Karachi. A written informed consent was obtained from the participant in English and Urdu (local language) was obtained from enrolled participants.

Statistical Analysis

Collected variables was entered in a predesigned MS (Microsoft) Excel spread sheet imported into the statistical software (SPSS) 20.0, Descriptive analysis included mean, median, standard deviation, proportion, percentages and range. The odds ratio (OR) with confidence interval (CI) of 95% was calculated for all therapies. All the statistical tests were applied at significant level of 5%, and value of p was considered ≤0.05.

RESULTS

Out of total 377 enrolled type-II diabetes mellitus 70.8% (n=267) were males with mean age of 39.14±9.30 and 29.2% (n=110) were females with mean age of 36.16±11.15. 13.5% (n=51) patients were single, 61.5% (n=232) were married while 24.9% (n=94) were found widowed/divorce. The BMI of 27.9% (n=105) enrolled patients was found between 18.5-23.

Table 1: Demographic of Enrolled Diabetic Patients

Parameters	**Male** 267(70.8%)	**Female** 10(29.2%)	**Total** 377(100%)
Mean Age (years)	39.14 ±9.30	36.16 ±11.15	-
Marital status of enrolled participants			
Single	36(9.5%)	15(3.9%)	51(13.5%)
Married	104(27.5%	128(33.9%)	232(61.5%)
Widow/Divorced	38(10%)	56(14.8%)	94(24.9%)
BMI levels of enrolled patients			
18.5-23	33(8.7%)	72(19%)	105(27.9%)
23-24.9	13(3.4%)	9(2.3%)	22(5.8%)
25-29.9	162(42.9%)	88(23.3%)	250(66.3%)
History with II-diabetes mellitus			
1-3 months	70(18.5%)	32(8.4%)	102(27.1%)
>3, <6 months	23(6.1%)	14(3.7%)	37(9.8%)
>6 months	138(36.6%)	239(63.3%)	238(63.1%)

Table 2: Prescribing Status of Antidiabetic Medications

	Status		Frequency	Percent	P-Value
Total (n=377)	Monotherapy		69	18.30%	0.001*
	Combinations Therapy (n=308)	Dual Therapy	216	57.30%	
		Triple Therapy	92	24.40%	

For most of the patient's high level of BMI were noted 66.3% (n=250). The history of patients with disease were obtained from patient's medical record and was found for 63.1% (n=238) more than 6 months. For 27.1% (n=102) was found between 1-3 months, while 9.8% (n=37) patients had history with disease for 3-6 months.

Table 2 shows the prescription status showed that 18.30% (n=69) received monotherapy among total of 377 patients. While 57.30% (n=216) of dual drug therapy and 24.40% (n=92) of triple therapy among combination therapy of oral antidiabetic drugs.

During prescription evaluation for monotherapy (n=69) of enrolled patients, 7.24% (n=5) patients were prescribed with metformin 1g, 8.70% (n=6) with metformin 500mg, 13.04% (n=9) with Glibenclamide 5mg, 4.35% (n=3), 10.15% (n=7) with Glimepiride 3mg, 10.15% (n=7) Glimepiride 4mg, 4.35% (n=3) were prescribed with gliclazide 30mg, and 8.70% (n=6) with gliclazide 60mg while 7.24% (n=5) were prescribed with pioglitazone 45mg .Among antidiabetic 377 diabetic patients, 18.30% (n=69) were prescribed with monotherapy of oral antidiabetic therapy. 15.94% (n=11) drugs from class Biguanides, 66.66% (n=46) with class Sulphonylureas, 7.24% (n=05) of drugs were prescribed from class Thiazolidinedione's, while 10.14% (n=7) of drugs from class DPP-4 Inhibitors as shown in table 3.

Table 3: Class of Antidiabetic Medications

Class of Antidiabetic Medications	Frequency	Percent
Biguanides	11	15.94%
Sulphonylureas	46	66.66%
Thiazolidinedione's	05	7.24%
DPP4 Inhibitors	7	10.14%
Total	69	100.0%

The significant objective of the current study was to compare the treatment cost for the period of 6 months and incremental cost-effectiveness ratio (ICER) analysis of monotherapy and add on therapy i.e. dual drug therapy oral anti-diabetic drugs among type-II diabetes mellitus. The cost-effectiveness analysis was calculated for both therapies based on effectiveness of oral anti-diabetic drugs and baseline HbA1C levels of patients by obtaining the effectiveness and average cost ΔC. The average cost ΔC was obtained by comparing two oral therapies i.e. drug A, and drug B. The effectiveness ΔE of drugs therapies was calculated by obtaining the differences between total number of blood glucose tests (HbA1C). The effectiveness of treatment is considered for the treatment obtaining lesser values for ICER hence the value of ICER among mono drug therapies for Glibenclamide 5mg was -720, with baseline value for HbA1C 7.6±0.99, and effectiveness of 0.5, with %E of 0.8. For glimepiride 2mg the ICER was calculated as -2160, with baseline of 7.2±1.5, IE -0.5and ΔE 0.3 of from class alpha glucose inhibitor for voglibose 0.3mg ICER was obtained-800,with baseline HbA1C of 7.5±2.1, IE 0.1, and ΔE 0.5% as shown in below table 4. The ICER for the add on therapy of Glibenclamide 2.5mg+Metforming 500mg with baseline value of 8.1±2.1 with ΔE of 0.3%, and incremental cost (IC) of -10087.2 was obtained 0. ICER was also 0 for sitagliptin 50mg +metformin 500mg with baseline 7.8±0.5, ΔE 0.6% and IE value of 0. ICER value of sitagliptin 50mg +metformin 850mg was obtained -648 with ΔE 0.1%, IE value -0.5. An ICER value of -2676 was obtained for metformin 850mg +pioglitazone 15mg with baseline of 7.6±1.7 and ΔE of 0.4% and IE of this therapy was 0.3. as shown in table no. 5.

DISCUSSION

The demographic detail of patients represents that 70.8% (n=267) were males with mean age of 39.14±9.30 and 29.2% (n=110) were females with mean age of 36.16±11.15 along with detail of 13.5% (n=51) patients were single, 61.5% (n=232) were married while 24.9%(n=94) were found widowed/divorce as a study conducted in Ogun State of Nigeria.[23] The BMI of enrolled patients for 27.9% (n=105) was found between 18.5-23. For most of the patient's high level of BMI were noted 66.3% (n=250).[24] Accordance in similar study, the prescription evaluation for 377 enrolled patients was made, and found the prescribed drugs 15.94 % (n=11) biguanides, 66.66%(n=46%), 7.24%(n=5) while 10.14% (n=7) of drugs were prescribed from class DPP4 inhibitors[25-26].

Table 4: Cost effective Monotherapy

Prescribed Medicines (Generic)	Average Cost/06 Months	Mean ±SD HbA1C		ΔE%	IC	ICER
		Baseline	Post treatment			
Metformin 1g	1080	7.3±0.99	7±1.57	0.3	-	-
Glibenclamide5mg	720	7.6±1.82	6.8±1.2	0.8	-360	-720
Glimepiride 2mg	1800	7.2±1.5	6.9±1.6*	0.3	1080	-2160
Glimepiride 3mg	2700	7.7±1.6	7.2±2.1	0.5	900	4500
Metformin 500mg	1080	6.9±1.5	6.8±1.8*	0.1	-1620	4050
Glipizide	4140	7.5±2.2	7.3±1.3	0.2	3060	30600
Glimepiride 4mg	5580	7.9±2.5	7.1±1.1	0.8	1440	2400
Sitagliptin 50mg	3150	7.3±1.2	7.1±1.5*	0.2	-2430	4050
Vildagliptin 50mg	2980	7.2±1.4	7.1±1.9	0.1	-170	1700
Voglibose 0.2mg	2900	7.5±2.1	7.3±1.6	0.2	-80	-800
Voglibose 0.3mg	2890	7.7±1.6	7.2±1.3	0.5	-10	-33.3
Gliclazide 30mg	2520	7.8±1.9	7.5±1.9*	0.3	-370	1850
Gliclazide 60mg	3600	7.5±2.4	7±1.1	0.5	1080	5400
Pioglitazone 45mg	4050	7.1±1.3	6.8±1.8	0.3	450	2250

Table 5: Cost effective Dual therapy

Prescribed Medicines (Generic)	Average Cost/06 Months	Mean ±SD HbA1C		ΔE%	IC	ICER
		Baseline	HbA1c			
Vildagliptin+ Metformin 50/1000mg	11293.2	8.1±2.1	7.8±1.7	0.3	-	-
Glibenclamide 2.5mg, Metformin 500mg	1152	7.8±0.2	7.5±1.5*	0.3	-10087.2	0
Glibenclamide 5mg, Metformin 500mg	1306.8	7.5±0.1	6.9±1.01	0.6	154.8	516
Sitagliptin, Metformin 50/1000mg	9936	7.8±0.5	7.2±1.2	0.6	8629.2	0
Sitagliptin 50mg, Metformin 850mg	10260	7.2±0.2	7.1±1.1	0.1	324	-648
Vildagliptin + Metformin 50/850mg	11286	7.4±0.2	6.7±1.01	0.7	1026	1710
Glimepiride:1mg, Metformin (HCl):500mg	4453.2	6.9±0.82	6.8±1.5**	0.1	-6832.8	11388
Metformin (HCl):850mg, Pioglitazone:15mg	3650.4	7.6±1.7	7.2±1.1	0.4	-802.8	-2676

Ic-incremental cost, IE- incremental effects, ICER- incremental cost effectiveness ratio

In the study the clinical parameters were considered as effectiveness of oral anti diabetic drugs was obtained by evaluating the baseline levels of HbA1c tests with mean and standard deviation for monotherapy and dual drugs therapy. The findings of current study are in agreement with previous study as, most commonly prescribed glimepiride 2mg and lesser values of ICER (-2160) was obtained among monotherapy.[27] The ICER values for mono drug therapies for Glibenclamide 5mg was -720, with baseline value for HbA1C 7.6±0.99, and effectiveness of 0.5, with %E of 0.8.For glimepiride 2mg the ICER was calculated as -2160, with baseline of 7.2±1.5, IE -0.5 and ΔE 0.3 of from class alpha glucose inhibitor for voglibose 0.3mg ICER was obtained-800,with baseline HbA1C of 7.5±2.1, IE 0.1, and ΔE 0.5% in agreement to similar conducted study.[28-29] The ICER for the add on therapy of Glibenclamide 2.5mg+Metforming 500mg with baseline value of 8.1±2.1 with ΔE of 0.3%, and incremental cost (IC) of -10087.2 which is similar to a study conducted for the evaluation of cost-effectiveness in add on i.e. dual therapy[30]. The ICER was obtained 0 for dual therapy of sitagliptin 50mg +metformin 500mg with baseline 7.8±0.5, ΔE 0.6% and IE value of 0. ICER value of sitagliptin 50mg +metformin 850mg was obtained -648 with ΔE 0.1%, IE value -0.5.[31] The cost-effectiveness analysis of oral hypoglycemic medications encourages the rational use of medication with maximum effectiveness and influences the patients to monitor HbA1C levels regularly

CONCLUSION

The outcome of drug utilization studies evaluates the current prescribing pattern of oral hypoglycemic agents and concomitant drugs with respect to the clinical efficacy of hypoglycemic drugs.

Acknowledgement: Author declare no conflicts of interest in the study. Patient's details were used for research purpose.

REFERENCES

1. Centers for Disease Control and Prevention. National diabetes statistics report: estimates of diabetes and its burden in the United States, Atlanta: Department of Health and Human Services; 2014.
2. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 36(4), 2013, 1033–46.
3. IMS Institute for Healthcare Informatics. Medicines use and spending in the U.S. A review of 2015 and outlook to 2020. IMS Parsippany: Institute for Healthcare Informatics; 2016.
4. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of diabetes. Diabetes Care. 38(1), 2015, 140–9.
5. Garber AJ, Abrahamson MJ, Barzilay JI, et al. AACE/ACE comprehensive diabetes management algorithm 2015. Endocr Pract. 21(4), 2015, 438–47.
6. Bennett WL, Maruthur NM, Singh S, et al. Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. Ann Intern Med. 154(9), 2011; 602–13.
7. Zhang Y, McCoy RG, Mason JE, Smith SA, Shah ND, Denton BT. Second-line agents for glycemic control for type 2 diabetes: are newer agents better? Diabetes Care. 37(5), 2014, 1338-45.
8. Shuyangu, zhiliu tang, lizhengshi, monikasawhney, huimeihu, hengjin dong. Cost-minimization analysis of metformin and acarbose in treatment of type 2 diabetes value in the health regional issues 6c (2015) 84 – 8 8
9. Das P, Das BP, Rauniar GP, Roy RK, Sharma SK. Drug utilization pattern and effectiveness analysis in diabetes mellitus at a tertiary care centre in eastern Nepal. Indian J PhysiolPharmacol. 55, 2011, 272-280.
10. Wang JY. Cost-effectiveness analysis of commonly used hypoglycemic drug combination regimens for the treatment of type 2 diabetes. For All Health 07, 2013, 14.
11. XueX, GaoJR, XiaLZ, et al., Cost-effectiveness analysis of glimepiride combined with different drugs in treatment of type 2 diabetes mellitus. AnHui MedPharmJ 18, 2014, 441–3.
12. Sun K. Comparison of the efficacy and costs of different treatments of type 2diabetes.HealthMust-ReadMagazine 11, 2012, 209–10.
13. Yurgin N, Lage MJ. Antidiabetic prescription and glycemic control in German patients with type 2 diabetes mellitus: a retrospective database study. Clin Ther. 29, 2007, 316-325.
14. Adedapo ADA, Amwe JV, Cost Effectiveness and Prescription Pattern of Antidiabetic Drugs in Patients with Diabetes Attending a Tertiary Health Facility in South West Nigeria. J Pharmacol Clin Toxicol, 5(3), 2017, 1078.
15. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of diabetes. Diabetes Care. 38(1), 2015, 140–9.
16. Garber AJ, Abrahamson MJ, Barzilay JI, et al. AACE/ACE comprehensive diabetes management algorithm. EndocrPract. 21(4), 2015, 438–47.
17. Zhang Y, McCoy RG, Mason JE, Smith SA, Shah ND, Denton BT. Second-line agents for glycemic control for type 2 diabetes: are newer agents better? Diabetes Care. 37(5), 2014, 1338–45.
18. Goke B, Gallwitz B, Eriksson J, Hellqvist A, Gause-Nilsson I. D1680C00001 investigators. Saxagliptin is non-inferior to glipizide in patients with type 2 diabetes mellitus inadequately controlled on metformin alone: a 52-week randomised controlled trial. Int J Clin Pract. 64(12), 2010, 1619–31.
19. Nathan DM, Buse JB, Davidson MB, et al. Medical management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of diabetes. Diabetologia. 52(1), 2009, 17–30.
20. Gitt AK, Bramlage P, Binz C, Krekler M, Deeg E, Tschope D. Prognostic implications of DPP-4 inhibitor vs. sulfonylurea use on top of metformin in a real-world setting - results of the 1 year follow-up of the prospective DiaRegis registry. Int J Clin Pract. 67(10), 2013, 1005–14.
21. Koro CE, Bowlin SJ, Bourgeois N, Fedder DO. Glycemic control from 1988 to 2000 among U.S. adults diagnosed with type 2 diabetes: a preliminary report. Diabetes Care, 27(1), 2004 Jan, 17–20.
22. I. A. Suleiman, 2O. F. Fadeke and 3O. O. Okubanjo Pharmacoeconomic Evaluation of Anti-Diabetic Therapy in A Nigerian Tertiary Health Institution, Annals of African Medicine Vol. 5, No. 3, 2006, 132 – 137.
23. González-Ortiz, M., Guerrero-Romero, J.F., Violante-Ortiz, R., Wacher-Rodarte, N., Martínez-Abundis, E., Aguilar-Salinas, C., Islas-Andrade, S., Arechavaleta-Granell, R., González-Canudas, J., Rodríguez-Morán, M. and Zavala-Suárez, E., Efficacy of glimepiride/metformin combination versus

glibenclamide/metformin in patients with uncontrolled type 2 diabetes mellitus. *Journal of Diabetes and its Complications*, *23*(6), 2009, pp.376-379.

24. T. Tamilselvan, T. Kumutha, Amrita Lekshmi V., Anju C. James, Juliya S. Reji and NamithaCheriyan Pharmacoeconomical Evaluation of Oral Hypoglycemic Agents for Type-2 Diabetes Mellitus in a Multispeciality Hospital, IJPSR, Vol. 8(5), 2017, 2243-2248
25. Charpentier, G., Fleury, F., Kabir, M., Vaur, L., & Halimi, S. Improved glycemic control by addition of glimepiride to metformin monotherapy in type 2 diabetic patients. Diabetic Medicine, 18, 2001, 828–834.
26. Amandeep Singh, Shakti Bala Dutta, Amit Varma, Mirza Atif Beg, Hitender Kumar, Amanjot Kaur, A drug utilization and pharmacoeconomic study of anti-diabetic drugs prescribed to type 2 diabetes mellitus patients visiting the medicine outpatient department of a tertiary care hospital of north India International Journal of Basic & Clinical Pharmacology, Vol 5 (Issue 4), July-August 2016, Page 1220-1227
27. Holstein A, Plaschke A, Egberts EH. Lower incidence of severe hypoglycemia in type 2 diabetic patients treated with glimepiride versus glibenclamide. Diabetologia, 157, 2000, A40.
28. Hermann L, Schersten B, Bitzen PO, Kjellstrom T, Lindgarde F, Melander A. Therapeutic comparison of metformin and sulfonylurea, alone and in various combinations. Diabetes Care, 17, 1994, 1100-1109.
29. Aduragbenro DA Adedapo, Jerry Vincent Amwe, Cost-effectiveness and prescription pattern of antidiabetic drugs in patients with diabetes attending a tertiary health facility in south west Nigeria, journal of pharmacology & clinical toxicology, 5(3), 2017, 1078.
30. FirmanPribadi, Iman Permana, analysis of the cost-effectiveness of antidiabetic drugs among self-paid participants of the Indonesia national security service with type II diabetes mellitus, 8(3), 2018, 108-111.

Source of Support: Nil, **Conflict of Interest:** None.