

DRUG UTILIZATION EVALUATION OF ANTI DIABETIC THERAPY WITH TYPE-II DIABETES MELLITUS OF A TERTIARY CARE HOSPITAL IN CALICUT

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ABSTRACT

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from either insulin deficiency, insulin resistance or both. Type-II Diabetes Mellitus is a systemic disorder, potentially known to cause serious organ damage. Oral Anti-diabetic agents are the most commonly prescribed drugs for Type-II Diabetes Mellitus. But there are no accepted guidelines for treating Type-II Diabetes Mellitus in the Indian scenario because all are formulated in the western countries. Further, it is necessary to follow a treatment protocol in common comorbidities associated with Type-II Diabetes Mellitus. The present study will help in identifying the utilization of Anti-Diabetic drugs in Type-II Diabetes Mellitus. The study aims to determine the pattern of drug prescription among Type-II Diabetes Mellitus patients, so as to evaluate the prescribing pattern of the physician, Check the adherence of patients with Type-II Diabetes Mellitus to the prescribed drugs, Assess the drug related problems associated with the Type-II diabetes prescriptions. The study was conducted in PVS Hospital (P) Ltd, a 350 bedded multi-specialty care hospital, Calicut. The study found metformin as the most commonly prescribed oral anti-diabetic drug both in Monotherapy and combination therapy. Newer anti-diabetics were prescribed less frequently. The prescribing trend also appears to be moving towards combination therapy particularly two drug therapy.

INTRODUCTION

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from either insulin deficiency, insulin resistance or both [1]. The chronic hyperglycemia is associated with long term damage, leading to micro and macro vascular complications which degrade quality of life. Complications include altered metabolism of lipids, carbohydrates, proteins and an increased risk of vascular diseases [2].

Diabetes Mellitus is a complex syndrome that affects virtually every cell in the body and can lead to pathological changes in multiple organ systems. Type II Diabetes Mellitus is a systemic disorder, potentially known to cause serious organ damage involving eyes, heart, kidneys and limbs, which ultimately leads to blindness, heart attack, kidney failure and limb amputation. If diagnosed early and treated in time, with / without drugs, the damage of these organs can be completely prevented. Another important issue is that most complications cause clinical symptoms at a very late stage and thus for their early diagnosis, these complications have to be specifically looked for [3].

According to International Diabetes Federation (IDF), 65.1 million adults in India, had diabetes in the year 2013. It has been predicted that the prevalence of Diabetes in the Adult population in India will be increased 6% by the year 2025 [3]. The Indian Heart Association states that, India is the Diabetes Capital of the World with an estimated 109 million individuals with Diabetes by 2085. This high incidence of Diabetes in a developing country like India may be due to urbanization and lifestyle changes like consumption of high calorie food along with sedentary habits in pre disposed individuals who are generally susceptible [4-5].

Diabetes is a common and prevalent disease affecting the citizens of both developed and developing countries and is the most common endocrine disorder globally. Concurrent illness such as hypertension in diabetes makes it more difficult to avoid multiple drug use.

According to Intercontinental Marketing Service (IMS) data, the leading groups of drugs utilized World Wide are cardiovascular drugs which are usually co-prescribed along with Anti-diabetic drugs as a result of coexistence of the diseases.

Hence Diabetic patients are more prone to poly pharmacy and sometimes to irrational prescriptions [6]. Several problems in drug use patterns have been reported. This includes use of irrational combinations, excessive prescription of multivitamins, use of antibiotics in viral infections, etc. Often, the chronically ill patients like the diabetic patients suffer from multiple diseases and hence are prescribed with multiple drugs. Irrational prescriptions can increase the economic burden of the patients [7-10]. Moreover there are no accepted guidelines for treating Type II Diabetes Mellitus in the Indian scenario because all are formulated in the western countries.

It is necessary to follow a treatment protocol in common comorbidities associated with Type II Diabetes Mellitus. So we have aimed to study the utilization pattern of drugs used in Diabetes Mellitus in a tertiary care hospital. The present study will help in identifying the utilization of Anti-Diabetic drugs in Type II Diabetes Mellitus. It will give a view of the prescribing practices of physicians which can be modified if necessary to facilitate better health care delivery.

The study aims to determine the pattern of drug prescription among Type II Diabetes

Mellitus patients, so as to evaluate the prescribing pattern of the physician. Study the prescription pattern of Type II Diabetes Mellitus. 2. Check the adherence of patients with Type II Diabetes Mellitus to the prescribed drugs. Assess the drug related problems associated with the type II diabetes prescriptions.

MATERIAL AND METHOD

The study was conducted in PVS Hospital (P) Ltd, a 350 bedded multi-specialty care hospital, Calicut. After getting approval from Institutional Ethical Committee of hospital. The observational drug utilization study was conducted for a period of 6 months from November 2017 to April 2018. Patients having diabetes alone, receiving any type of anti-diabetes medication and with or without any other comorbidities or complications was included in the study.

Prescriptions were collected and evaluated for prescribing patterns in Type II Diabetes Mellitus using WHO Drug indicators like drug class, dosage form, dose, total number of drugs prescribed, average number of drugs per prescription, use of fixed dose combinations (FDCs), drugs prescribed by generic or brand names. Data Collection Forms records the mostly prescribed drug, drug class, dosage form, dose and frequency

of the drugs prescribed for Type II Diabetes Mellitus, associated comorbidities and drug interactions.

The collected data forms also records the drug related problems observed in the study subjects. The drug charts are assessed to identify the total number of drugs prescribed in the prescription, number of anti-diabetic drugs, anti-diabetic combinations, and drugs prescribed in generic names, and other WHO drug use indicators.

RESULT AND DISCUSSION

The data of 200 diabetic patients were collected and analyzed. The gender analysis showed that 122 (61%) patients were male and 78 (39%) patients were female. Male to female ratio was found to be 1.56:1.

Age and Gender:

The patients were categorized into four age groups to evaluate which groups were more prone to Type-II Diabetes Mellitus. The number of males and females of each group were also categorized. Majority of the patients (48%) were in the age group of 51-70 years. The mean age of the study population was found to be 64.24 years. 17 (8.5%) patients were below 45 years of age group indicating that Type II Diabetes is increasing in the younger age (Table-1).

In this study, the prevalence of Diabetes was found to be more common among male population with a male to female ratio of 1.56:1. This is comparable with a similar previous study done by Sekhar Mandal *et al*, where they found the ratio to be 1.58:1. This might be due to the reason that the prescribing pattern is being similar in different sites. Also due to reason that men require relatively lower Body Mass Index than women to acquire the disease [1].

In our study, it was found that the prevalence of Type II Diabetes Mellitus was higher in the age group 51-70 years of age. The predisposition in the middle age group has negative socio-economic and psychological outcomes which adversely affects the quality of life. Type II Diabetes is increasing in the younger age group with an incidence of 8.5%, warranting a strict lifestyle modification in those with family history of Diabetes from an early age [5].

Significant Family History:

Positive family history of diabetes in either one or both the parents was observed in 166 (83%) patients Table-2. This study showed that 166 (83%) patients suffered from Type II Diabetes Mellitus due to genetical reasons and the remaining due to unknown causes.

This was similar to previous studies conducted by Afroz Abidi *et al* and Kannan *et al* [5, 14]. This clearly emphasize the genetic relationship to the occurrence of Type II diabetes mellitus.

Significant Comorbidities:

Out of 200 patients, 178 (89%) patients had comorbid conditions and 22 (11%) patients were found to have no comorbidities. The four most common comorbidities observed in the study population with Type II Diabetes Mellitus were Hypertension (37%), Cardiovascular Diseases (20%), Dyslipidemia (18%) and Metabolic Disorders (14%). However other comorbid conditions (11%) were also analyzed.

The percentage distribution of comorbidities is given in figure-1. Hypertension was found to be the most common comorbid condition with Type II Diabetes Mellitus. This is similar to the study conducted by Sekhar Mandal *et al*, Bela Patel *et al*, Ratna Agarwal *et al* and Kannan *et al* [1,6,4].

In a similar drug utilization study conducted for Anti-Hypertensive, the most common comorbidity along with hypertension was found to be Type II Diabetes Mellitus.^[28] However, in a study conducted by Swapna

R. Nayaka *et al*, the most common comorbidity with Diabetes Mellitus was found to be respiratory diseases and in a study of Afroz Abidi *et al*, the most common comorbidity was found to be metabolic disorders [8,6].

The predominance of hypertension and cardiovascular diseases may be due to the fact that Diabetes Mellitus is a risk factor of Atherosclerosis and hypertension.

Significant Complications:

67 (33.5%) patients were found to have complications of Diabetes Mellitus. The most common complication observed was Cellulitis in 34 (41.5%) patients, followed by Diabetic Nephropathy in 28 (34.15%) patients. Diabetic Ketoacidosis in 2 (2.5%) patients showed the least distribution in the study population Figure-2.

The most common complication was Cellulitis (41.5%). The patients with Diabetes have a 12-25% risk of developing cellulitis due to slow healing of ulcers and wounds or infections. Soft-tissue infection often results from contiguous spread of microorganisms via skin ulcerations. In addition, occurrence of peripheral arterial

disease impairs blood flow and defence mechanism.

Diabetic ketoacidosis was the least common complication found in this study. This is in contrast to the study of Aseefa *et al* held in Ethiopia, where Diabetic ketoacidosis was the most frequent complication reported as there was an unaffordability of insulin, lack of self-monitoring of glucose level and low levels of education, all of which are much better in India [15].

Type of Therapy:

Most of the patients (66.5%) received more than one anti-diabetic drug. Only 67 patients received Monotherapy Table-3. Most of the patients received two or more drugs to achieve glycemic control. This was similar to the studies conducted by Vengurlekar S *et al* and Dhanaraja *et al*. [16, 17].

The possible reason for this is that Type II Diabetes is a chronic disease with a progressive deterioration in glycemic control due to the continuous loss of Beta cell function. Monotherapy for Type II Diabetes may therefore be not sufficient to maintain glycemic control over time.

Pattern of Distribution of Insulin Preparations:

In the overall utilization pattern of 200 patients, 102(51%) patients received insulin. Total number of insulin preparations was found to be 115. The most common insulin preparation prescribed for the study subjects was premixed insulin (88.69%), followed by short acting insulin (29.5%) and the least prescribed insulin was long acting insulin (2.60%) Table-4. In this study, insulin was found to be prescribed in 102 patients i.e. 51% of the total study sample.

It is quite high when compared to a study done in Bengal by Sekhar Mandal *et al* [¹¹]. This may be because insulin is required for patients of Type II Diabetes Mellitus when their blood glucose is not controlled with oral hypoglycemic, as stated in a study of Vipul P. Chaudhari *et al* [18]. Premixed insulin was the most commonly prescribed insulin which may be due to better control of post prandial glucose exertions than regular insulin, by premixed insulin.

Distribution of Oral Hypoglycemic Agents:

In the overall utilization pattern of 200 patients, 238 oral hypoglycemic agents were prescribed in which, biguanides followed by

sulphonyl ureas were the most commonly prescribed categories of drugs. Alpha Glucosidase Inhibitors takes the third place in the prescribed class of drugs. The overall distribution is given in Figure-3.

Biguanides:

More than a majority of patients, i.e. 148 (74%) patients were prescribed with biguanides (Metformin). Metformin was prescribed in different doses ranging from 500 mg to 1850 mg daily. Most commonly prescribed dose was 500 mg. Daily dose of 500 mg, 850 mg, 1000 mg, 1500 mg, and 1850 mg were prescribed to 112 (56%), 4 (2%), 29 (14.5%), 1 (0.5%) and 2 (1%) patients respectively out of 148 receivers Figure-4.

Distribution of other Oral Hypoglycemic Agents:

Among other Oral Hypoglycemic Agents, Sulphonyl Ureas 72 (25.4%), followed by Alpha Glucosidase inhibitors 28 (11.76%), and DPP-4 Inhibitors 25 (10.5%), were prescribed. The distribution of other oral hypoglycemic agents is summarized in the table 5. Among the Anti-diabetic medications, Metformin was the most commonly prescribed drug which was given

in 148 patients, followed by sulphonyl ureas in 72 (52.4%) patients.

This is similar to other studies conducted by Sekhar Mandal *et al*, Afroz Abidi *et al*, and Ratna Agarwal *et al* [1,4,5]. Metformin is usually preferred as the best choice due to its obvious advantages over other hypoglycemic like, increased safety profile, decrease LDL cholesterol, increase HDL cholesterol, reduce platelet aggregation, effective in individuals with insulin resistance and does not cause weight gain. Sulphonyl ureas is the second preferable class of oral hypoglycemic agents, as it reduces micro vascular risks, and promote increased systemic bioavailability of insulin.

The most commonly prescribed Sulphonyl Urea is Glimepiride. Among Sulphonyl Ureas, selection of Glimepiride has been recommended by Texas Diabetes council because of lower incidence of Hypoglycemia [12]. Alpha Glucosidase inhibitors (Voglibose) was prescribed to 14% of the study population, which is higher in comparison to a study conducted by Ratna Agarwal *et al*, where it had been prescribed to only 4.3%.^[4] The reason for higher prescription may be due to its

enhanced effect in controlling post prandial blood sugar.

The utilization pattern of Thiazolidinedione was relatively very low compared to previous study conducted by Sekhar Mandal *et al* [1]. This may be attributed to its side effects like weight gain, edema, and liver toxicity, in addition to its slow onset of action. Oral Hypoglycemic like Meglitinides and GLP-1 Agonists are least preferred in this study population which may be attributed to its high cost [14].

In this study, Bromocriptine, an ergotene derivative and a dopamine agonist, used generally in the treatment of Pituitary Tumours, Parkinson's disease, and Type II Diabetes Mellitus was prescribed to one patient. However, there is no clear evidence for its hypoglycemic mechanism of action [3].

Combination Therapy:

In this study, 61 anti-diabetic combinations were given to patients. 56 (91.8%) two drug combinations and 5 (8.19%) three drug combinations were prescribed to the subjects. The most frequently prescribed combination was that of Glimepiride and Metformin, followed by Metformin/Glibenclamide and Metformin/

Vildagliptin. Metformin, Voglibose and Glimepiride were the most common three drug combination prescribed. The distribution of different combinational therapy is given in Figure-5.

The most commonly prescribed drug combination was Metformin and Glimepiride (57.3%). Similar results were obtained in the studies done by Sekhar Mandal *et al*, Bela Patel *et al*, but in contrast to a study from Nigeria in which Metformin and Glibenclamide was the most common combination for Diabetes [1, 6]. Adding a second agent is usually better than increasing the dosage of an agent.

Glimepiride and Metformin combination has a rational basis of use i.e. both of these agents act through different mechanisms, the former as an insulin secretagogue and the latter as an insulin sensitizer [6]. Hence, this contributes to better control of blood sugar levels in the patients. Also, metformin is considered to be safer and cost-effective drug over others in terms of hypoglycemia. This could be a possible reason for the common Metformin + Sulphonyl urea combination.

Pattern of Distribution of Other Drugs:

Anti-hypertensive drugs was the most commonly prescribed drug for comorbid

conditions, as Hypertension was the most frequent associated comorbidity in the study samples. Among them, Angiotensin Receptor Blockers was the most frequently prescribed (15%), followed by Diuretics (14.8%), Beta Blockers and Calcium channel blockers comprising (10%) of the total study population.

The least prescribed anti-hypertensive drug was ACE Inhibitors (1.9%). Anti- Platelets comprised of 24.6% of the comorbid drugs, followed by HMG Co. A Reductase Inhibitors (17.3%) and Nitrates (5.6%) Figure-6. An estimation of other drugs like multivitamins, Proton Pump Inhibitors, Histamine 2 Receptor Blockers, Calcium Supplements and anti- emetics were also done. 198 Multivitamins were found to be the most prescribed drug in the study, followed by NSAIDs and proton pump inhibitors Figure-7.

The most commonly co-prescribed medications along with anti-diabetic drugs were antihypertensive drugs which is similar to a study conducted by Sekhar Mandal *et al* [1]. The high anti-hypertensive prescription reflects the high rate of comorbidity of hypertension and diabetes. Most commonly used drugs other than antihypertensive drugs were anti-platelets (Clopidogrel) and Statins

which suggest association of cardiovascular diseases. However, in this study, ACE Inhibitors were found to be the least prescribed anti-hypertensive drugs. This is dissimilar to other studies conducted by Sekhar Mandal *et al* [1]. Hence; the difference may be due to difference in the prescribing patterns of the places. Increased prescription of multivitamins was also observed. In the present study, vitamins accounted for 12% of the total drugs. This is high when compared to another study conducted by Kannan *et al* [14].

In a study conducted by Dr. Sandeep Ankham *et al*, increased prescription of multivitamins is attributed as one of the various problems associated to drug use patterns. NSAIDs accounted for 11.85% of the total drugs. The prescriber should be aware of the interaction of oral hypoglycemic and NSAIDs. Concurrent use of NSAIDs and sulphonyl ureas may result in an increased risk of hypoglycemia [13].

Key Prescribing Indicators:

A total of 1586 drugs were prescribed to the study population. Among this, 385 (24.27%) drugs were found to be anti-diabetic drugs. The total cost for anti-diabetic drugs was found to be 123138.045 INR. The mean cost of anti-diabetic drugs was found to be 615

INR. The various prescribing indicators were analysed Table 6. The average number of drugs per prescription was 7.93 which was high compared to a study conducted in UAE by Lisha Jenny John *et al.* This was high mainly because of comorbid illness of patients enrolled in the study, who would require more medications for their additional illness.

The high average number of drugs prescribed in this study is not surprising. It is recognized that patients with Diabetes Mellitus are generally prescribed more drugs than other patients. However the average number of anti-diabetic drugs were found to be 1.73 which is similar with the studies conducted by Kannan *et al* [14].

Cost of prescriptions is very important in a chronic disease like diabetes as it may be a major cause for non-adherence to treatment. In this study, the average cost for both insulin and oral antidiabetic agents was 615.7 INR which is dissimilar to a study conducted by Kannan *et al* [14]. This may be due to the inclusion of more number of inpatients and due to the prescription of two or more drugs, as in this study dual therapy is found to be higher. The reason for low cost in the study conducted by Kannan *et al*

is due to supply of drugs at low cost to below poverty line patients and prescription of cheapest brand of antidiabetic drugs as most of the patients belonged to low socioeconomic status [14]. High amount of drugs were given in injections as compared to earlier study by Khushali G. Acharya *et al.*

This finding can be explained as in this study more number of inpatients were included. In this study, drugs prescribed by generic names were found to be 6.36% which is less compared to a study conducted by Shewade D.G *et al.* Very few studies have been conducted focusing on this aspect of drug prescribing. These findings clearly indicate that there is a need to encourage prescribing by generic names, particularly in hospitals attached to medical colleges. Prescribing by generic names allows flexibility of stocking, and dispensing cheaper brands that indirectly affects the compliance of patients, as stated in a study by Bela Patel *et al* [6]. 46% of the patients received antibiotics.

A total number of 130 (8.2%) of antibiotics were prescribed. This may be due to the fact that the most common complication was cellulitis which require antibiotics to prevent and treat infections.

Drug Related Problems:

The drug interactions found were moderate type of interactions, and majority of them were pharmacodynamics interactions. The most common interaction was found to be between Metformin and ranitidine, which is known to cause decreased effect of Metformin. 23 adverse reactions were found among 200 patients which were moderate type of reactions.

The most frequent adverse drug reaction was hypoglycemia induced due to drug interactions or co administration of oral hypoglycemic. A brief list of the different adverse reactions found are as given in Table 7. The adverse drug reactions observed in this study were mild-moderate in severity. Such reactions were observed in a similar manner, in a study conducted by Sekhar Mandal *et al* [1]. These reactions were not found to be causing any worsening in the condition of the patient and was curable.

Index of patient adherence:

The patient adherence to the prescribed drugs were analysed using Morisky Green Level (MGL) scale. According to MGL scale, patient scoring 0 is categorized as highly adherent, 1-2 as moderately adherent and 3-4 as poorly adherent. In this study 56

(28%) patients were found to be highly adherent, 122 (61%) patients were found to be moderately adherent and 22 (11%) patients were found to be poorly adherent. Morisky Green Levine Adherence Scale (MGL) was used to study patient medication adherence. Phei Ching LIM *et al*, Nicole Rae Yurgin *et al* and Shaimol T. *et al* conducted studies using a similar four point scale, MMA (Morisky Medication Adherence) scale.

The tool contains four questions to test the attitude of patients towards drug therapy and accordingly patients are scored 1 or 0, depending on their responses. Out of 200 patients, majority of them showed medium adherence towards Anti-diabetic drugs. 61% of patients showed medium adherence and only 11% showed low adherence. As per a study conducted by Shaimol. T *et al*,

There was significant relation between age, and medication adherence. As age increases, the number of comorbid conditions increase, hence the adherence of patients is affected. Similarly, adherence to medications and type of therapy (Mono, Dual, Triple) can be related. Adherence of the patient is affected with the number of drugs and frequency of the medications.

CONCLUSION

The study showed that Type II Diabetes Mellitus is more prevalent in men than in women. Elderly patients were at higher risk of developing Type II Diabetes Mellitus. Among various comorbidities, cardiovascular complications caused major threat and among cardiovascular complications, hypertension was the major one.

The study showed that cause of Type II Diabetes Mellitus in most of the patients is hereditary. This emphasizes the genetic relationship of the disease and occurrence of disease. The study found metformin as the most commonly prescribed oral anti-diabetic drug both in Monotherapy and combination therapy. Newer anti-diabetics were prescribed less frequently. The prescribing trend also appears to be moving towards combination therapy particularly two drug therapy.

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EXPERIMENTAL RESULT TABLE AND FIGURE**Table -1 Age-Gender Distribution of Type II Diabetic patients**

S.No	Age Groups (in years)	Female		Male		Total
		Number	Percentage	Number	Percentage	
1	31-50	15	53.57	18	14.75	33
2	51-70	37	47.43	59	48.37	96
3	71-90	25	32.05	44	36.06	69
4	>90	1	1.28	1	0.81	2

Table-2 Family History of Patients

S.No	Number	Number	Percentage
1	One Parent	73	36.5
2	Both Parents	95	47.5
3	None	32	16

Table-3: Type of Therapy

S.No	Type of Therapy	Number	Percentage
1.	Monotherapy	67	33.5
2.	Dual Therapy	80	40
3.	Triple Therapy	40	20
4.	Quadruple Therapy	13	6.5

Table-4: Distribution of Insulin

S.No	Type of Insulin	Number	Percentage
1.	Premixed Insulin	60	52.14
2.	Rapid Acting Insulin	13	11.3
3.	Short Acting Insulin	34	29.5
4.	Intermediate Acting Insulin	5	4.34
5.	Long Acting Insulin	3	2.6

Table 5: Distribution of Other Anti-Diabetic Drugs

DRUG CLASS	DISTRIBUTION
<i>Sulphonyl Ureas</i>	72 (25.4%)
Glimepiride	52
Glibenclamide	8
Glicazide	11
Glipizide	1
<i>Alpha Glucosidase Inhibitors</i> (Voglibose)	28 (11.76%)
<i>DPP-4 Inhibitors</i>	25 (10.5%)
Linagliptin	3
Teneligliptin	15
Vildagliptin	6
<i>Thiazolidinediones</i> (Pioglitazone)	3
<i>Meglitinides</i> (Repaglinide)	4
<i>GLP-1 Agonists</i> (Liraglutide)	1
<i>Others</i> (Bromocriptine)	1

Table 6: WHO Prescribing Indicators

Average Number of drugs per prescription	7.93
Average Number of Antidiabetic drugs	1.73
Average Cost of Anti-Diabetic Drugs	615.7 INR
Percentage of Encounters prescribed with injections	65%
Percentage of Encounters prescribed with antibiotics	46%
Percentage of drugs prescribed in generics	6.36%

Table 7: Drug Related Problems Observed in the Study Subjects

Hypoglycaemia	10(43.7%)
<i>Coadministration of Oral hypoglycemic agents or Insulin</i>	6 (60%)
<i>Drug Interaction Induced</i>	4(40%)
Drug Interaction (Metformin ↔ Ranitidine) induced Light Headedness and Nausea	2 (8.7%)
Diarrhoea induced by Voglibose	2(8.7%)
Metformin induced GI upset	5 (21.73%)
Drug Interaction induced Hyperglycemia	3 (13.04%)
Drug Interaction Lactic Acidosis	1(4.34%)

Figure 1: Distribution of comorbidities

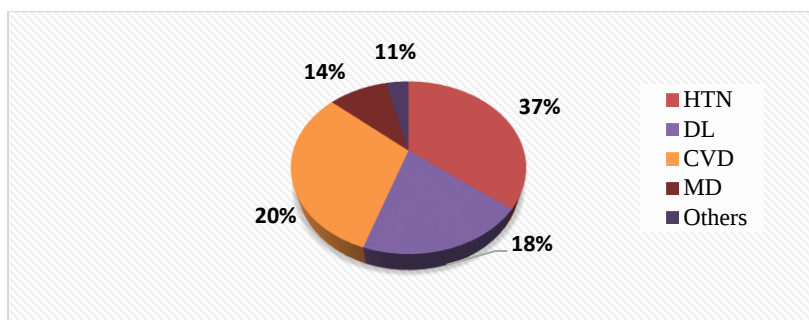


Figure 2: Distribution of Complications

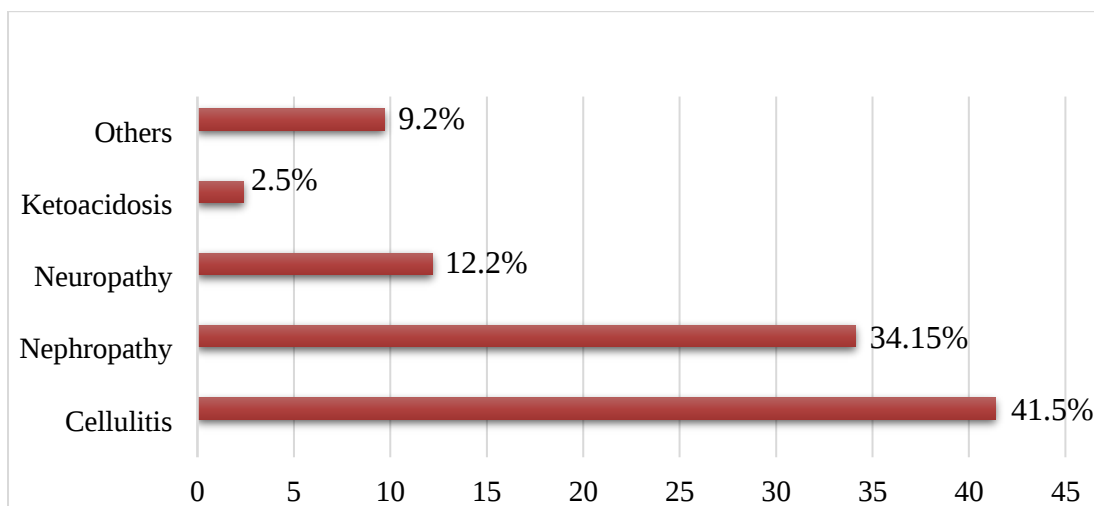


Figure 3: Pattern of anti-diabetic Drugs

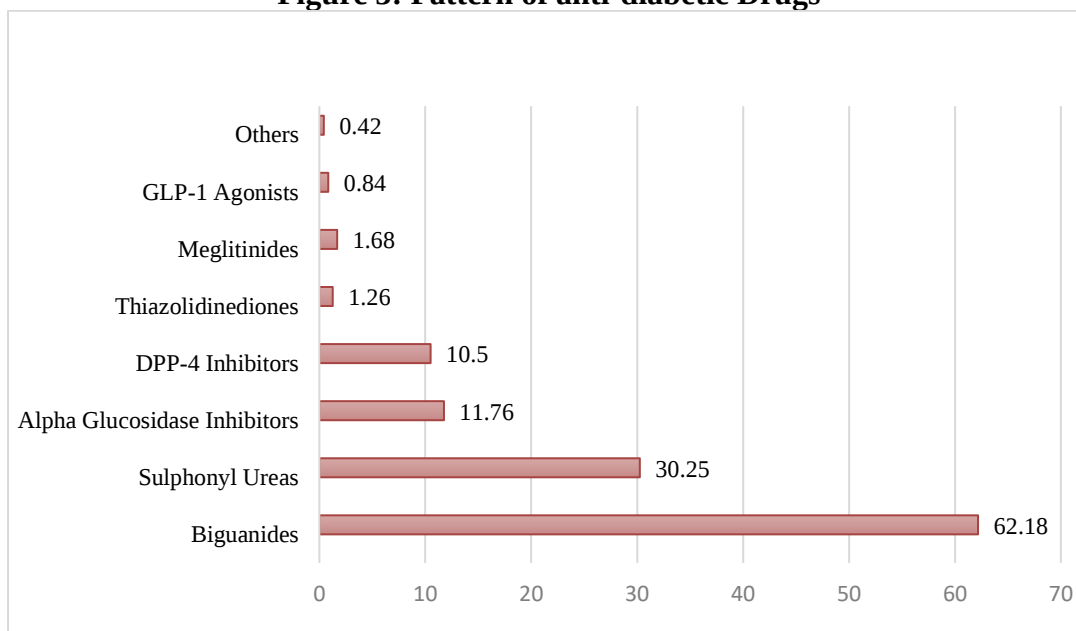


Figure 4: Distribution of Metformin in Different Doses

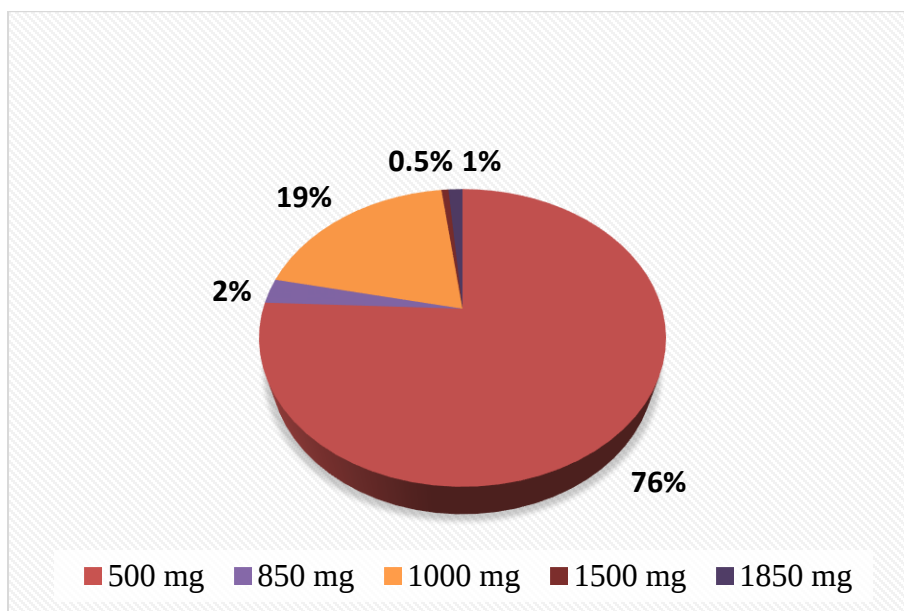


Figure 5: Distribution of Anti-diabetic Combinations

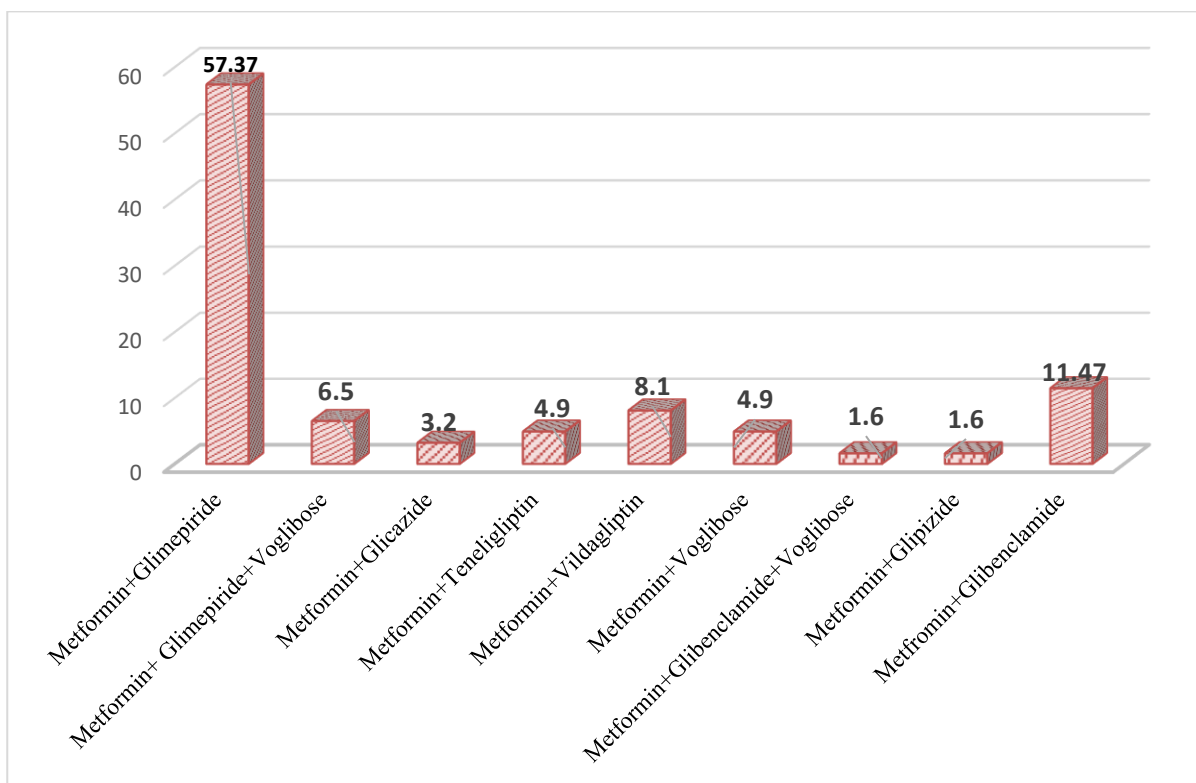


Figure 6: Drug Distribution in Comorbid Conditions

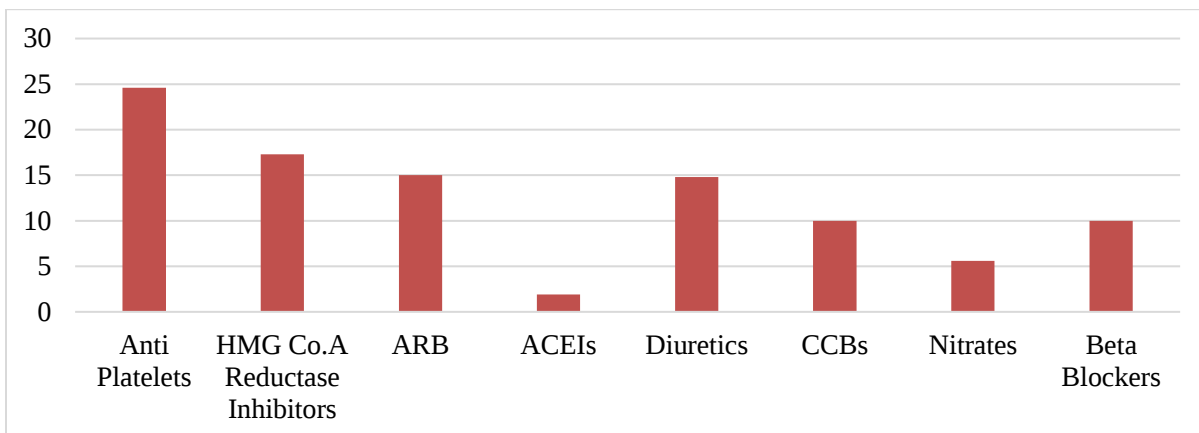


Figure 7: Distribution of Other Drugs

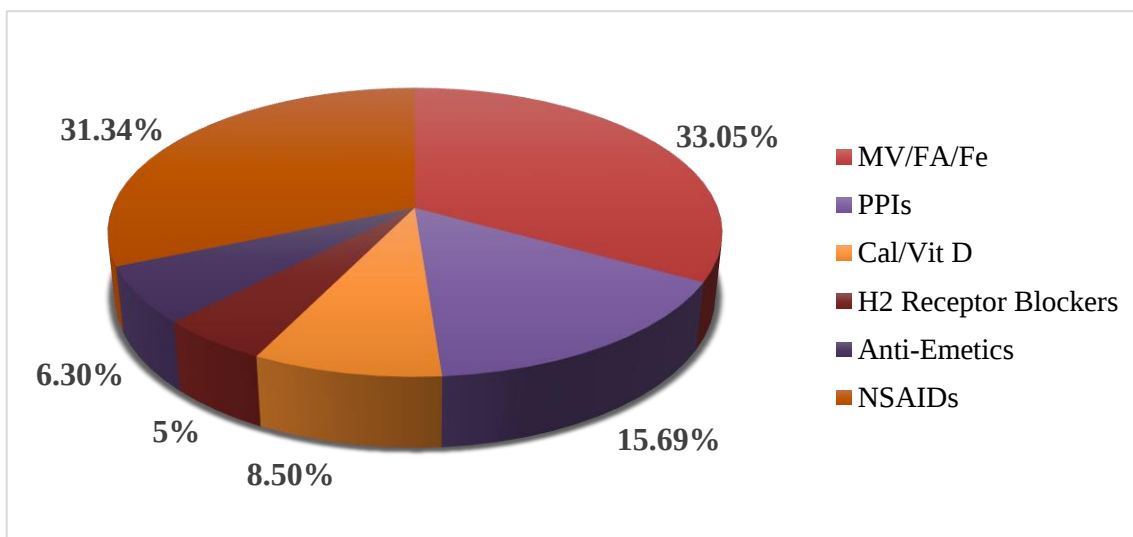


Figure 8: Index of Patient adherence

