



METHODOLOGY IN EVALUATION OF DRUG UTILIZATION AND ANALYSIS OF DRUG RELATED PROBLEMS IN TYPE 2 DIABETIC IN PATIENTS AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT:

Diabetes mellitus has been traditionally classified into insulin-dependent diabetes mellitus and non-insulin-dependent diabetes Mellitus. The number of people affected with diabetes is projected to increase from 172 million in 2000 to 366 million in 2030. This is a prospective and observational study. During the hospital stay of 148 patients, prescriptions with insulin are documented more than prescription with various OHAs. In the current study metformin (41.17%) was the most common prescribed OHD followed by glimepiride(30.39%) and 45.76% of OHDs were prescribed as monotherapy whereas 35.59% & 18.64% as two drug combination and three drug respectively. There were 40 DRPs have seen in subjects. Insulin was mostly prescribed compared to other antidiabetic agents as monotherapy and three drug combinations are prescribed more among polytherapy. Three drug regimens were prescribed more among other multiple drug regimen. ADRs, DDIs , Sub therapeutic dose and Overdose were the DRPs found.

Key Words: Diabetes Mellitus, Oral Hypoglycaemic Agents, ADR, DRP.

Introduction:

Diabetes mellitus has been traditionally classified into insulin-dependent diabetes mellitus (IDDM), also known as type I (formerly called juvenile-onset diabetes mellitus), and non-insulin-dependent diabetes Mellitus (NIDDM), also known as type II (formerly referred to as adult-onset diabetes mellitus.) It is a heterogeneous group of disorders characterized by abnormalities in carbohydrate, proteins and lipid metabolism. The central disturbance in diabetes mellitus is an abnormality in insulin production or action or both, although other factors can be involved. Hyperglycemia is a common end point for all types of diabetes mellitus and is the parameter that measured to evaluate and manage the efficacy of diabetes therapy¹. The prevalence of this disease across the world was estimated to be 2.8% in 2000 and 4.4% in 2030. The number of people affected with diabetes is projected to increase from 172 million in 2000 to 366 million in 2030²

The prevalence of diabetes among adults has reached approximately 20% in urban and approximately 10% in rural populations in India.³

DRP is a worldwide health problem that compromises the quality of life, increase hospitalization; increase overall health care cost and mortality. Patients with T2DM are at risk of drug-related problems (DRP), which can happen at any step during the treatment process and it affects the therapeutic outcome

Study Plan and Methodology:

Study design: This is a prospective and observational study.

Study location:

This study was conducted in Department of Medicine of SN Medical College and HSK Hospital, Bagalkot

Inclusion criteria

Newly diagnosed and known cases of type 2 Diabetes Mellitus with other comorbidities who were receiving oral antidiabetic medicines and admitted as inpatients were included. Inpatients of either sex or age groups of 40 years and above were included

Exclusion criteria

- Type 2 diabetes patients of outpatient department.
- Type 1 diabetes patients
- Gestational diabetes were excluded.
- Those who were not willing to participate

Study duration:

- The study was carried out for 6 months, August 2019 to January 2020

Sources of data:

- Patient case notes.
- Patient treatment chart.
- Patient laboratory data.
- Patient interview.

Results:

Age group and gender wise categorization of diabetic patients

During the hospital stay of 148 patients, we found that out of 83 male patients 2(2.40%) belongs to above 80 age group followed by 14(16.86%) under 70-79 years age group, 28 (33.73%) under 60-69 years age group, 27 (32.53%) under 50-59 years age group and 12(14.45%) under 40-49 years age group. Out of 65 female patients 2(3.07%) belongs to above 80 years age group followed by 19(29.23%) under 70-79 years age group, 24 (36.92%) under 60-69 years age group, 11 (16.92%) under 50-59 years age group, 9(13.84%) under 40-49yrs

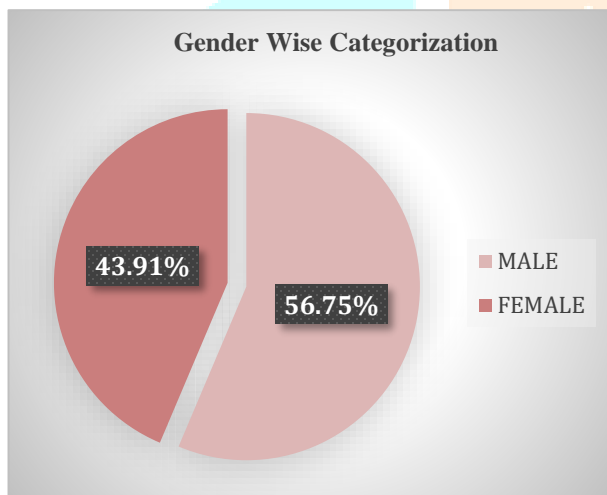


Fig 1: Gender wise categorization with percentage of diabetic patients

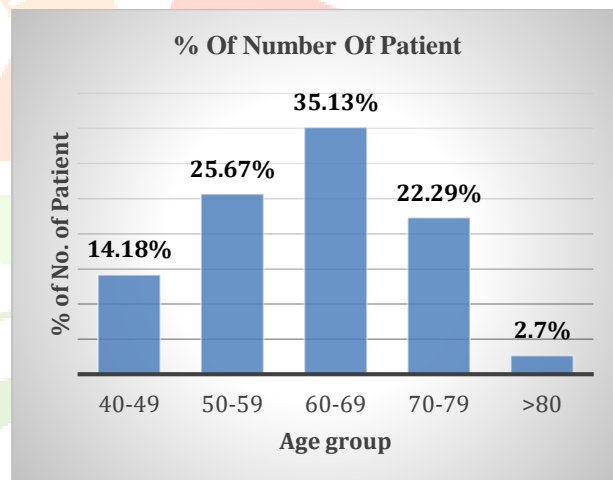


Fig 2: Age group categorization with percentage of diabetic patients

Oral Hypoglycaemic Agents prescribed in Diabetic patients

Five different classes of OHA's were prescribed in 102 patients. Among these Metformin was mostly prescribed 42 (41.17%), second most was Glimepiride 31(30.39%), followed by Teneligliptin 21(20.58%), Voglibose 3(2.94%), Gliclazide 2(1.96%), Pioglitazone 2 (1.96%), Sitagliptin 1(0.98%). Result were summarized in Fig.3.

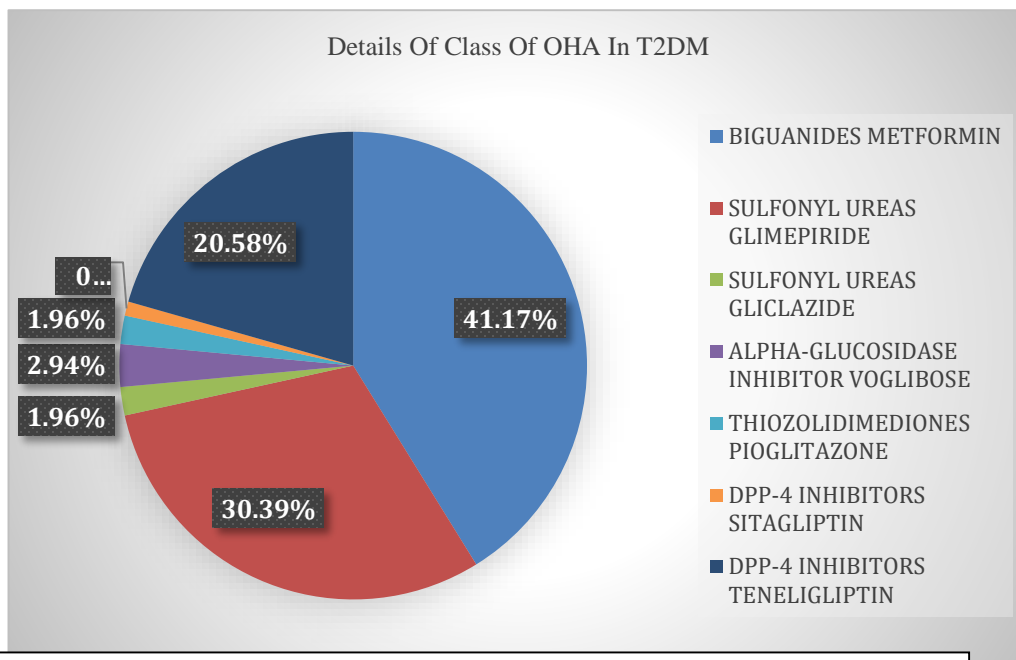


Fig 3: Details of class of OHA prescribed in T2DM among the study population.

Types of insulin prescribed in study population.

In present study, among 127 patients short acting insulin 101 (79.52%), long acting insulin 18 (14.17%), intermediate acting insulin 8 (6.29%) were used. Result were summarized in Fig.4.

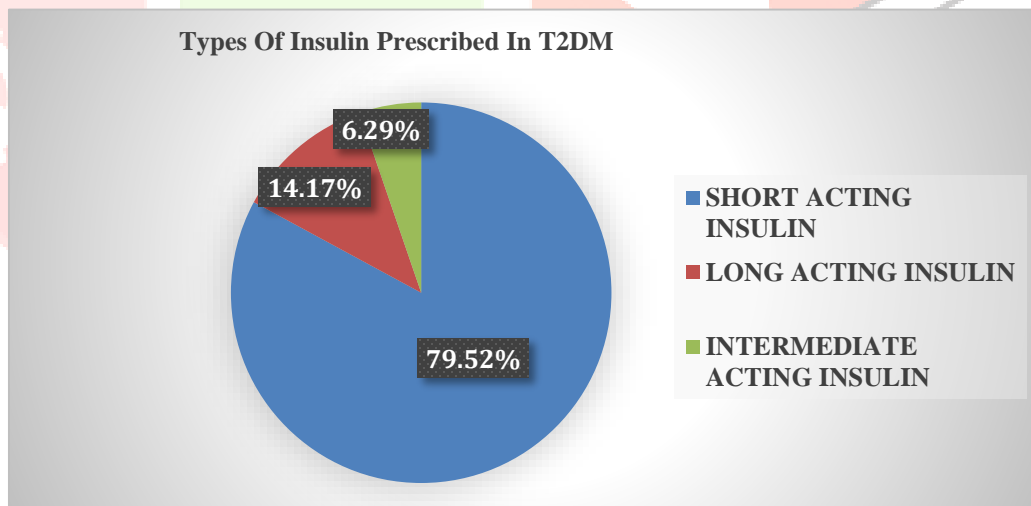


Fig 4: Details of class of OHA prescribed in T2DM among the study population.

Drug utilization of antidiabetic agents

During the 6 months of study, among 148 patients, drugs were given as monotherapy 110 (74.3%), two drug combination 11(8.76%), three drug combination 22 (14.8%), four drug combination 3 (2.02%).Result were summarized in and Fig.5.

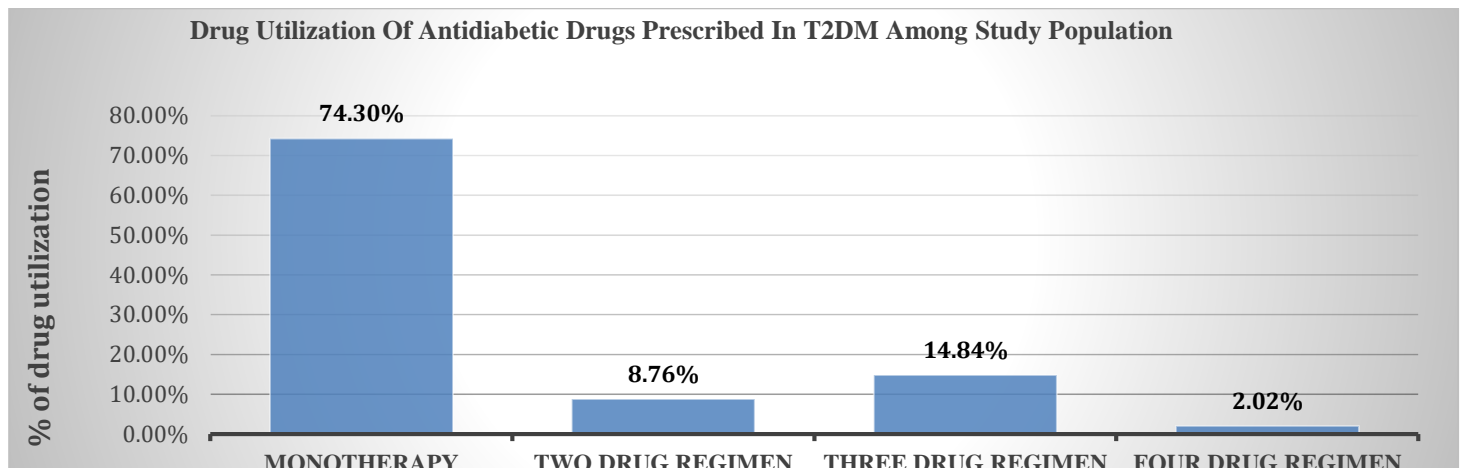


Fig 5: Drug utilization of antidiabetic drugs prescribed in T2DM among study population.

Percentage of oral hypoglycaemic agents and insulin preparations prescribed in diabetic patients

While assessing the antidiabetic treatment, it was found that insulin was used in 65.49% of patients and oral hypoglycaemic agents in 34.50% patients. Results were summarized in fig 6.

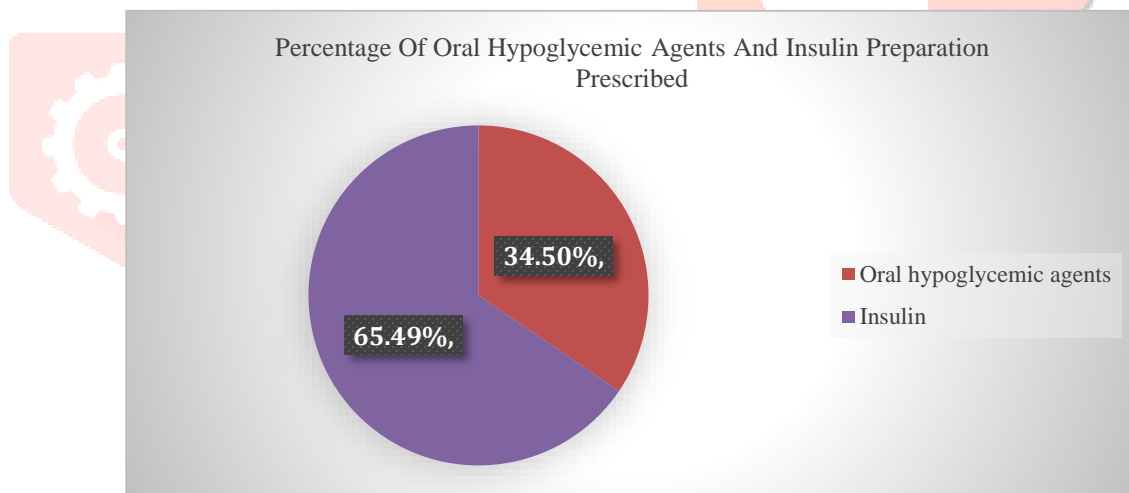


Fig 6: Percentage of oral hypoglycaemic agents and insulin preparation prescribed

Assessment of types and description of various DRP'S found in patients

Four drug related problems like adverse drug reactions, drug –drug interactions, sub therapeutic dose and overdose were assessed in patients. There were 9 (22.5%) adverse drug reactions like glimepiride, metformin, pioglitazone and insulin induced hypoglycaemia and insulin induced lipodystrophy 20(50%) clinically significant interaction which include insulin – ofloxacin,

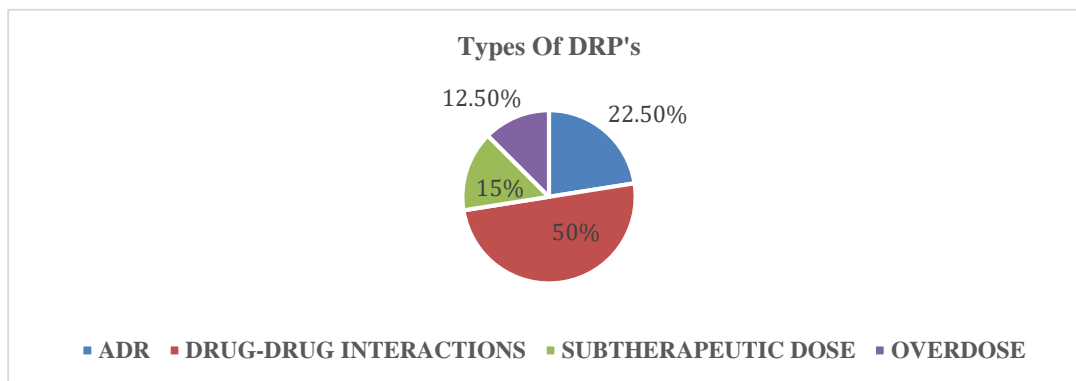


Fig 7: Types of DRP's found with antidiabetic drugs

metformin - ofloxacin induced hypoglycaemia, 6(15%) sub therapeutic dose of insulin and 5(12.5%) overdose of insulin also obtained. Results are summarized in fig 7.

Description and assessment of Adverse Drug Reactions found in antidiabetic prescriptions

During the study, 9 ADRs were found, out of which 2 (22.22%) are metformin-glimepiride induced 3 (33.33%) are insulin induced, 1 (11.11%) glimepiride induced & 1 (11.11%) metformin-glimepiride-pioglitazone induced hypoglycaemia along with 2 (22.22%) insulin induced lipodystrophy. Results were summarized in Fig 7a.

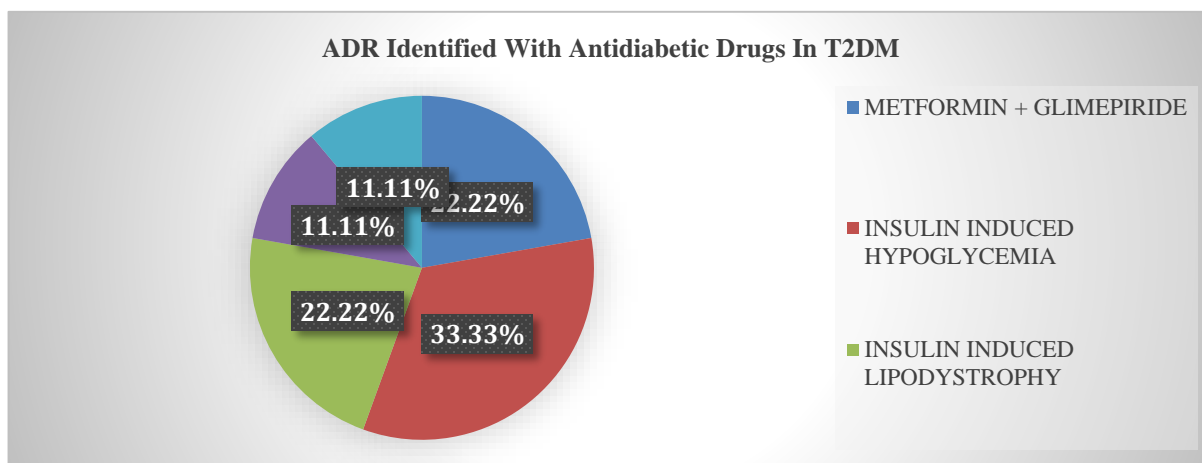


Fig 7a: ADR identified with antidiabetic drugs in T2DM patients

Description and assessment of drug interactions found in antidiabetic prescriptions

During the study, 40 DRPs were found, out of which 20 were drug interactions, 5(25%) were found as major drug interactions mentioned in table 1, Moderate 14(70%), Minor 1(5%). Results were summarized in Fig 7b.

Table-1 Major Drug Interactions

NUMBER OF INTERACTIONS	DRUG COMBINATION	NUMBER OF PATIENTS(n=20)	SEVERIETY	CONSEQUENCES OF DDI	TOTAL n (%)
1.	Insulin + Ofloxacin	2	MAJOR	Concurrent use of SELECTED FLUROQUINOLONES AND SELECTED ANTIDIABETIC AGENTS may result in changes in blood glucose and increased risk of hypoglycaemia or hyperglycemia.	5(25%)
2.	Ciprofloxacin + Insulin	1	MAJOR	Concurrent use of FLUROQUINOLONES AND ANTIDIABETIC AGENTS may result in changes in blood glucose	

				and increased risk of hypoglycaemia or hyperglycemia.
3.	Glimepiride + Isoniazid /Pyrazinamide /Rifampin	1	MAJOR	Concurrent use of GLIMEPIRIDE and ISONIAZID may result in increased glimepiride exposure and risk of hypoglycemia.
4.	Glimepiride + Ofloxacin	1	MAJOR	Concurrent use of SELECTED FLUROQUINOLONES AND ANTIDIABETIC AGENTS may result in changes in blood glucose e and increased risk of hypoglycaemia or hyperglycemia.

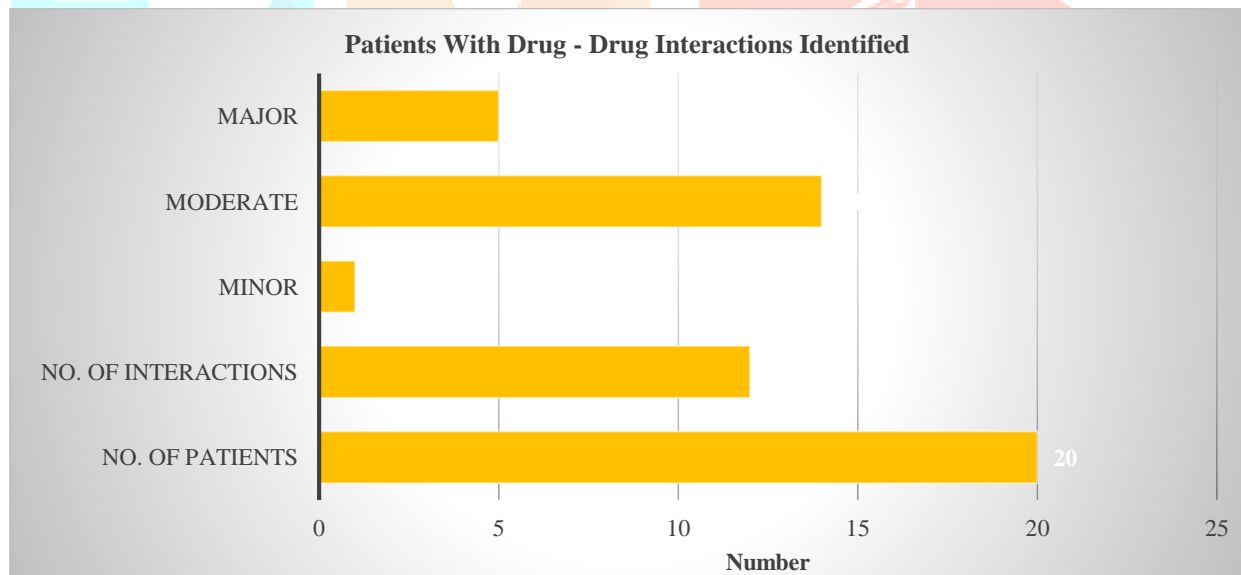
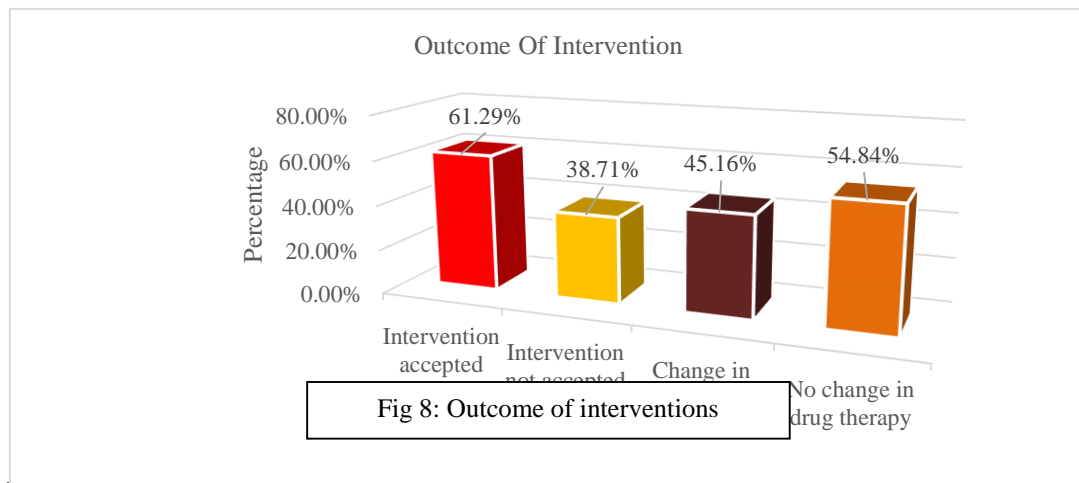


Fig 7b: Patients with drug - drug interactions identified

Assessment of the outcome of pharmacist interventions

The suggestions were evaluated by the physician and out of 31 interventions, 19(61.29%)were accepted and 12(38.709%) were not accepted. Change in drug therapy was done in 14(45.161%). 17(54.838%) drug therapies remained unchanged. Results are summarized in Fig 8

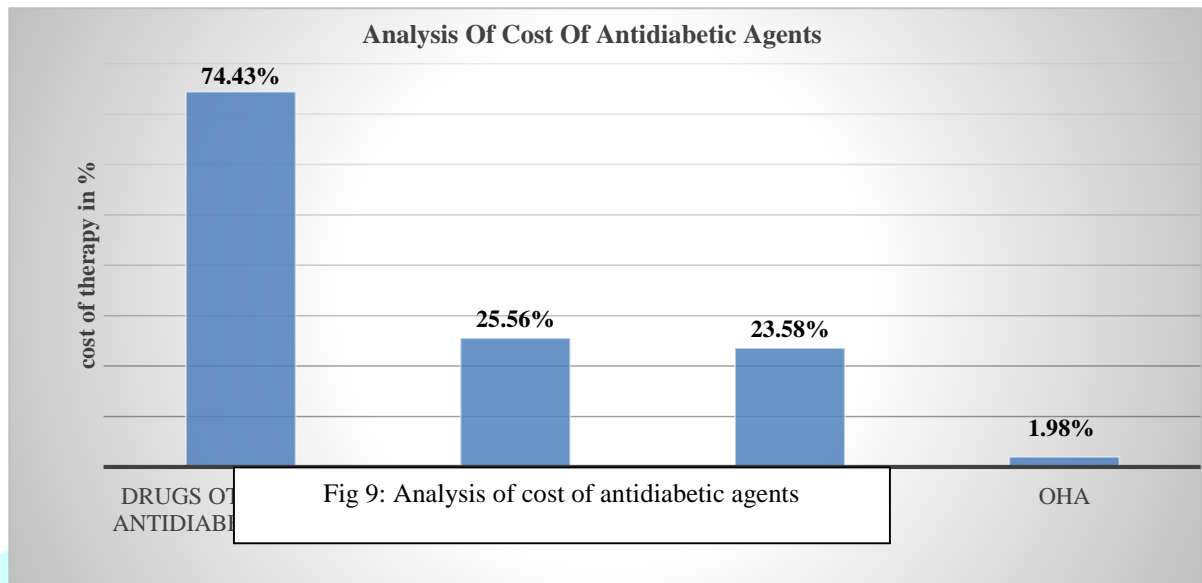


References consulted for retrieving proper evidence

References used for finding evidence for the 40 DRP's were obtained from the three resources. Out of the 3 resources, secondary resources like Micromedex, was used more 20(68.962%). Primary resources like ADA guidelines were also referred 6(20.683%). The tertiary resource were also used in 3(10.344%) interventions.

Analysis of cost for antidiabetic agents

Cost of drugs used by 148 patients during their hospital stay is found to be 2, 05,052.96 rupees. Among this, 48364.3 (23.588%) rupees were spent for Insulin therapy and 4065.5 (1.98%) rupees for oral hypoglycaemic agents. Results are summarized in Fig 9 .



Discussion and conclusion:

Diabetes mellitus is a major public health problem worldwide. Its prevalence is rising in many parts of the developing world, and India is no exception to this. It will become diabetes capital in near future. Individuals with Type 2 DM are considered on high priority, as they are potential candidates for rapid evaluation to prevent and halt the progression of complications.

Drug utilization studies provide useful insights into the current prescribing practices and identify irrational prescribing. The consequences of irrational prescribing include non-adherence to medications, which can result in complications due to uncontrolled blood glucose levels and escalate drug costs and health care costs. In view of this, the present study was designed to evaluate the prescribing pattern of anti-diabetic drugs among diabetic inpatients in a tertiary care teaching hospital.

Out of 148 prescription of antidiabetics, 83 were men and 65 were women indicating that men predominated over women similar to other reports from India and in contrast with studies from UAE¹³. Maximum patients with Diabetes Mellitus were of age group of 60-69 years followed by the age group of 50-59 years. Greater prevalence in this age group may be due to change in life style, lack of exercise and stress. In this study, hypertension was the commonest comorbidity observed similar to Patel B et al 2013 study. Different

studies also reported similar observation with regard to the co-morbidity in patients with diabetes. The proportion of diabetic patients found to have co-morbid hypertension is high which is not surprising since it reflects what obtains globally²¹.

Type 2 diabetes mellitus is a chronic disease and most of the patients (38.51%) in the present study had observed with a diabetic history of 10-15 years followed by history of 5-10 years.

The study documented 65.496% of prescriptions with insulin and only 34.504% of the prescription had various OHAs. The result are in contradiction to the study conducted by Diabetology and Medicine Department of a Tertiary Care Hospital in Navi Mumbai. As 43.6% of their prescription in their study contained insulin preparation in T2DM patients and more prescriptions are with OHDs.¹⁴ Among the total insulin prescribed, short acting insulin were prescribed more in the patients due to its sudden onset and longer duration.

In the present study, the most commonly used antidiabetic medicine (monotherapy) was insulin during hospital stay. Total 89 (79.4%) patients were prescribed insulin as monotherapy during hospital stay. In majority of the patients, the reason for prescribing insulin was stated as presence of various co-morbid conditions (e.g., hypertension, nephropathy, infections, etc.) or resistance to oral hypoglycaemic drugs in the patients' case note. During hospital stay percentage of patients receiving monotherapy as insulin in this study (79.4%) is in accordance with the result of Sayed Aliul et al study. Among Oral hypoglycaemic agents teneligliptin (63.15%) was more prescribed.

In the current study metformin (41.17%) was the most common prescribed OHD followed by glimepiride(30.39%) which is in line with findings of Sayed A et al²². The reasons why metformin was most choice in the current study is probably because of the fact that it has many advantages like it will not cause hypoglycaemia and weight gain due to its peculiar mechanism of action besides having many non-glycaemic advantages like its utility to prevent insulin resistance, metabolic syndrome, fatty liver helping as an adjuvant in keeping check over dyslipidemia and hypertension. The results are in accordance to the ADA 2015 standard treatment guidelines which recommend metformin to be used as initial therapy in most of the patients in view of long- standing evidence base for efficacy and safety, also because it is inexpensive, and may reduce risk of cardiovascular events²³. Among sulfonylureas, glimepiride (30.39%) was the most frequent prescribed drug. The

choice was possibly because of its efficacy to achieve glycaemic control as monotherapy or in combination. However, as per ADA guidelines it is recommended only as two drug combination after failure with metformin to achieve glycemia control as initial therapy. Thus, results reflect that biguanides and sulfonylureas are still the choice of most physicians in the treatment of type 2 diabetes. Among DPP-4 inhibitors teneligliptin remained most frequently prescribed as monotherapy as well as combination in the current study.²⁴

In the current study 45.76% of OHDs were prescribed as monotherapy whereas 35.59% & 18.64% as two drug combination and three drug respectively. It is accordance to the study conducted in medicine outpatient clinic of tertiary care hospital, Ahmedabad where monotherapy of OHAs used frequently followed by dual therapy and tripletherapy.¹³

In the study done by Kumar et al, insulin+metformin was the most prescribed antidiabetic combination followed by glimepiride + metformin. But as per the present study the result was just vice versa to the above statement. However, the most prescribed three drug regimen was insulin+ glimepiride+ metformin which is consistent with our results.²⁵ Four drug regimen was prescribed rarely when the glycemic control hadn't attained even with three drug regimen. In current study the use of combinations of OHA like metformin + gliclazide were recorded which is in contrast to the study from Nigeria in which Metformin + glibenclamide was most common combination for diabetes.¹⁴

In spite of the black box warning on pioglitazone, it was found prescribed in combination with glimepiride and metformin in 1 patient and observed hypoglycaemia as ADR. Although it will be difficult to comment that the pioglitazone use has decreased or remained same after safety alert in India as no attempt was made to compare before and after safety alert prescription trend of pioglitazone.²²

There were 40 DRPs have seen in subjects. The drug class that was most likely to cause DDIs were aspirin and fluoroquinolones. Examples of other medications include as albuterol, budesonide and rifampin. 9 ADRs were reported during the study. Hypoglycemia was the most common ADR observed, which is consistent with Alex et al 2015 study at Amrita Institute of Medical Sciences and Research Centre.¹⁶ 6 subtherapeutic dosage and 5 overdosage were observed with insulin treatment.

The net cost consumed by insulin therapy is huge when comparing with the cost of OHA. Antidiabetic drugs costs around 25.568% of total drug cost of 148 patients.

Significant drug-drug interactions and adverse drug reactions to equally involve with the physicians to improve the patient understanding and care. A preliminary interest of pharmacist was to analyze, identify, categorize, minimize and prevent the DRPs.

Pharmacist interventions were evaluated by the physicians to develop an effective prescription pattern. Pharmacist intervention suggestion in the present study was found to be effective, most of the interventions were accepted (61.29%) and 38.709% drug therapy were changed including change in therapy, change in frequency, change in dose of prescribed drugs and management of DRPs.

DM is an important issue in middle aged and elderly people. Among all patients males are more in number when compared to females. The middle aged group people (50-70 years) are more prone to the diabetes mellitus. The most associated comorbidity with diabetes is Hypertension. Insulin dominates the prescription patterns as monotherapy as well as in combination with OHA. Metformin was most commonly utilized OHA than others and Glimpiride was most utilized drug in Sulfonylureas. Metformin alone and Metformin combinations (with other antidiabetic drugs) were commonly prescribed to diabetic patients in current scenario. Combination therapy is preferred more in current setting in order to control the FBS of the patients, in which 2-drug combination is more in use, and in 2 drug combination Metformin+ Glimpiride and Metformin+ Insulin were the most commonly prescribed than other combinations. We have found drug related problems like ADRs, DDIs, subtherapeutic dose and overdose in prescription.

The study can be concluded as, Insulin was mostly prescribed compared to other antidiabetic agents as monotherapy and three drug combinations are prescribed more among polytherapy. Three drug regimens were prescribed more among other multiple drug regimen. ADRs, DDIs, Subtherapeutic dose and Overdose were the DRPs found in the current study. Among total expenditure of antidiabetic drugs, the cost for Insulin is more compared to OHA.

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