Original Article

A Prospective Observational Study to Evaluate Co-Morbidities and Drug Related Problems Among Type 2 Diabetes Mellitus Patients in A Tertiary Care Teaching Hospital

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ABSTRACT

Background: Type 2 diabetes mellitus is most frequent disorder now in which co- morbidities and drug related problems (DRPs) are commonly among type 2 diabetes mellitus patients. The studies objective is to evaluate patients' co-morbidities and DRPs.

Methods: A prospective observational study to evaluate comorbidities and DRPs among T2DM patients conducted over period of six months at a tertiary care teaching hospital.

Results: A total of 80 patients was enrolled in our study in which male 68.75% and female 31.25%. %) Out of 77 patients 26 (33.76%) have diabetic comorbidities while 51 (66.24%) have non-diabetic comorbidities. The most common diabetic comorbidities is diabetic nephropathy 60.72% whereas diabetic non-comorbidities is hypertension about 20.60%. The most commonly prescribed anti diabetic drug is human regular insulin57.69% and metformin is 43.90%. The most frequent types of DRPs were potential drug-drug interactions (38.78%), followed by Adverse drug reaction (33.75%), Untreated indication (12.5%), overdose (6.25%), Subtherapeutic dose (5%), Improper drug selection (2.5%), and Failure to receive drug (1.25%). Out of 41 interventions 29 (70.74%) were accepted and 12 (29.26%) were not accepted. Change in therapy was done in27 (65.85%) and 14 (34.15%) drug therapies remain unchanged.

Conclusion: Early identification of DRPs and factors associated with them are essential to prevent and resolve DRPs in T2DM patients with co-morbidities. Identification and resolving DRPs is a serious and important health care tool in the provision of elderly pharmaceutical care.

Keywords: Diabetes mellitus, co-morbidities, observational study, drug related problems.

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by hyperglycaemia due to defects in insulin secretion its prevalence has been steadily increasing throughout the world in 2019. The international diabetes federation estimated 463 million adult people with diabetes worldwide. India has the second largest diabetic population in the world the chronic nature of the disease and high prevalence of co-existing chronic medical conditions or co morbidities.

Globally the burden of diabetes mellitus (DM) is a major public health concern according to the estimation about 371 million people have dm and about 80 live in low income countries the number of old people expected to have DM by 2030 is over 550 million co-morbid disease are common in diabetes such as hypertension ischemic heart disease nephropathy and retinopathy are considered concordant to diabetes such as depression rheumatologic disease chronic lung disease cardiovascular disease.[3]

Appropriate evaluation and treatment of concurrent conditions can lead to more effective disease management and in turn improve patient functioning quality of life and mortality risk drops are pharmacotherapy problems that actually or potentially have an impact on desired health outcome the diabetic patients are vulnerable in experiencing drug-related problems. Moreover type 2 diabetes mellitus often accompanied by various co-morbidities resulting in increased risk of drug related problems 831 of the type 2 diabetic patients had at least one drug related problems. The causes of DRPs were mainly in the prescribing section, including "drug selection" and "dose selection", while patients; poor adherence in the use of section was also an important cause of DRPs.[6]

Other factors such as renal impairment, poor lipid control, cardiovascular disease, and the duration of hospital stay also increase DRP risk. DRP is a worldwide health problem that compromises the quality of life, increase hospitalization, increase overall health care cost and mortality.[7] DRPs were highly prevalent among their geriatric population ranging from 63.3% to 95.4%.

Furthermore, a systemic review analysis indicated that drug related problems (DRPs) account for more than 15.4% of hospital admissions and 2.7% death rate, with individuals on multiple medications and older adults being at an elevated risk of hospitalization caused by DRPs.[8] Hence the current study is required.

MATERIALS AND METHODOLOGY

Study Design:

A Prospective Observational Study.

Study Location:

The study was conducted at the S.N. Medical College and H.S.K. Hospital and Research Centre, Bagalkote.

Study Setting:

At General medicine and surgery departments in S.N. Medical College H.S.K Hospital and Research Centre, Bagalkote.

Study Criteria:

Inclusion criteria

In – patients of both sex and age > 18 years.

All patients admitted in General medicine and Surgery departments suffering from Type 2 Diabetes mellitus.

Exclusion criteria

Patients who are not willing to participate in the study,

Outpatients,

Patients who were pregnant and lactating mothers.

Study Duration:

The study will be carried out from 25th March 2024 to 25th September 2024.

Sources of Data:

Case sheet Patient interview Laboratory data

Patient treatment chart

Study Approval:

The protocol is submitted to the Institutional Human Ethics Committee of B. V. V. S. Hanagal Shri Kumareshwar College of Pharmacy, Bagalkote for approval.

Forms Used in the Study:

The forms given below are used for the collection of data for the study: Pharmacist intervention form (Annexure II)

Adverse drug reaction reporting and documentation form (Annexure III) Drug interaction and Documentation form (Annexure IV)

Study Procedure

The study will begin with the approval by the H S K Hospital's Institutional Ethics committee. The study will be conducted in accordance with the ethical principles of the ethics committee guidelines. The patients will be prospectively identified from a schedule and once included in the study a detailed review of their complete medication on day-1 is recorded. The medication chart will be chosen randomly and / or the details will be followed till discharge of the patients, until reaches the sample size of = 80. The data for present study will be collected by chart review method.

During the study, the case records of the patients who are admitted in the general medicine and surgery departments will be reviewed, which includes patients case history, diagnosis, physician medication order sheets, nurse medication administration records, progress chart, laboratory investigations and report of other diagnostic tests. This information will be documented in the patient profile form.

Whenever any pharmacist intervention is identified, then the data from patient profile form is transferred to the pharmacist intervention form. All the prescriptions will be checked for interactions, drug duplication, ADR, or any medication errors using CIMS website (cimsasia.com), and those will be confirmed by additional standard references (MICROMEDEX version 2), drug today handbook, and Drug digest website. All the data will be represented as percentages.

Analysis of the results:

The data collected will be analysed for the following parameters:

- ✓ Demographic profile of the patients.
- ✓ Age wise categorization of patient.
- ✓ Prevalence of drug related problems.
- ✓ Types of drug related problems identified.
- ✓ Causes of drug related problems.
- ✓ Drugs involved in drug related problems.

Collection of data

Collection of data was done by approaching patients admitted in Medicine and Surgery departments, collecting their demographic details, Case sheets, Laboratory data, Analysing treatment charts and pharmacist intervention forms.

Statistical Analysis

Data Analysis will be done using the Statistical Methods like Percentages, Proportion and Chi square Test and to arrive at a Conclusion for finding the significant differences.
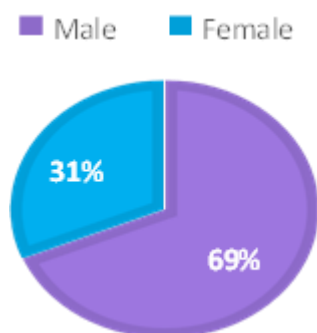
RESULTS

1. Age group and gender wise categorization of diabetic patients

During the hospital stay of 80 patients, we found out that out of 55 male patients, 24(43.64) % Belong to 60 years and above age group followed by 26 (47.27%) under 40-59 age group, 4 (7.27%) under 30-39 years age group, 1 (1.82%) under 19-29 years age group. Out of 25 female patients, 7 (28%) belong to 60 years and above group followed by 16 (64%) under 42-59 years age group,2 (8%) under 32-39 years age group and no patients under 19-29 years age group. (Results were summarised in Table 1 and Figure 1).

Table 1: Age group and gender wise categorisation of diabetic patients.

Age Groups (Years)	Male	Female	Total	Percentage (%)
19-29	1	0	1	1.25
30-39	4	2	6	7.5
40-59	26	16	42	52.5
60 and above	24	7	31	38.75
TOTAL	55	25	80	100

Figure 1: Gender wise categorisation of diabetic patients

2. Oral hypoglycaemic drugs prescribed among the study population

Four different classes of OHAs were prescribed in 80 patients. Among these, Metformin was mostly prescribed 18 (43.90%), second most was Glimepiride 11 (26.82%), followed by Gliclazide 4 (9.76%), and both Sitagliptin and Linagliptin 3 (7.32%), followed by Vildagliptin and Dapagliflozin 1 (2.44%). (Results were summarized in table 2).

3. Types of insulin used in study population

In present study among 80 patients, Regular Insulin 45 (57.69%) was mostly prescribed followed by Insulin glargine 27 (34.62%), and Isophane insulin 6 (7.69%). (Results were summarised in Figure 2).

4. Class of drugs prescribed other than Anti-diabetic drugs

13 different classes of drugs other than anti-diabetic were prescribed. Among 80 patients, Antihypertensives 95(20.60%) were mostly prescribed followed by Antacids 85 (18.44%), Antibiotics (15.61%), Antiemetics (9.3%). The least prescribed were Antidiarrheals and Antispasmodics (0.44%). (Results were summarised in Table 3).

Table 2: Oral hypoglycemic drugs prescribed among the study population.

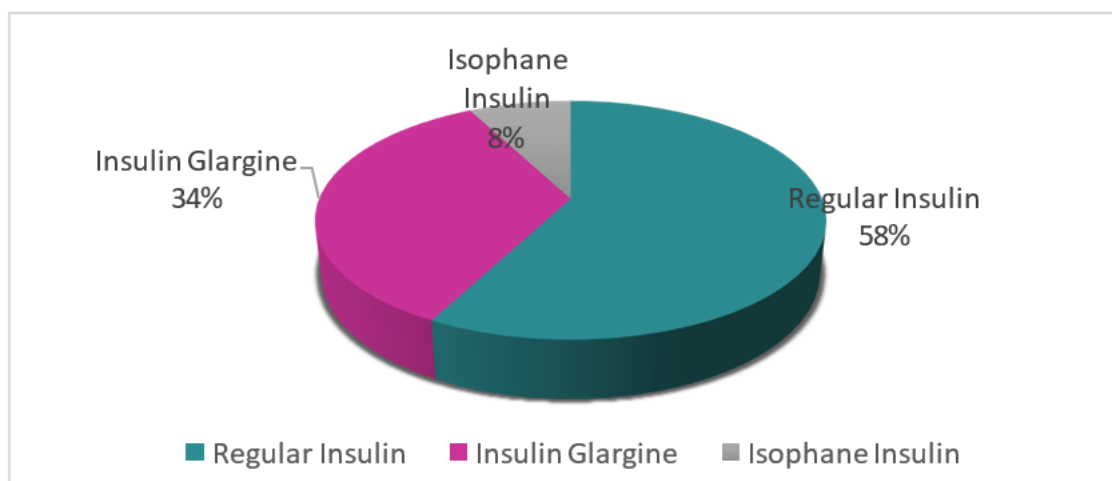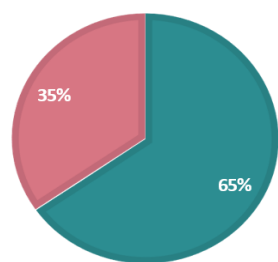| SL.NO	Class of OHA Prescribed	Drug Prescribed	Number of drugs Prescribed in individual patients	Percentage of Drug prescribed
1	**Enhances insulin secretion**			
(A)	Sulfonyl Ureas	Gliclazide Glimepiride	4 11	9.76 26.82
(B)	Dipeptidyl peptidase-4 (DDP-4) inhibitors	Sitagliptin Vildagliptin Linagliptin	3 1 3	7.32 2.44 7.32
2	**Overcome insulin Resistance** -Biguanides	Metformin	18	43.90
3.	**Miscellaneous Drugs** Sodium -glucose co-transport-2 inhibitor	Dapagliflozin	1	2.44
	Total		41	100

Figure 2: Types of insulin used in study population.

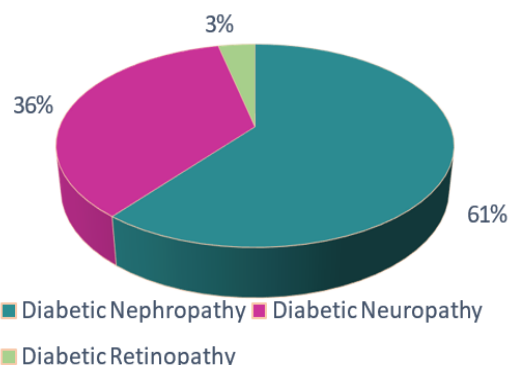**Table 3:** Drug prescribed other than anti-diabetics

Class of drugs	Number of Drugs	Percentage (%)
Antihypertensives	95	20.60
Antacids	85	18.44
Antibiotics	72	15.61
Antiemetics	43	9.33
Analgesics	42	9.11
Expectorants	28	6.07
Bronchodilators	25	5.43
Antiinflammatory	23	4.98
Diuretics	22	4.77
Laxatives	19	4.13
Anticoagulants	3	0.65
Antidiarrheal	2	0.44
Antispasmodics	2	0.44
Total	**461**	**100**

Figure 3: Monotherapy and polytherapy of oral hypoglycemic drugs prescribed in Type 2 Diabetic patients.

5. Monotherapy and polytherapy of oral hypoglycaemic drugs prescribed in Type 2 DM patients

Among 26 patients using OHA, Monotherapy therapy with OHA was most frequently prescribed 17 (65.38%) followed by two drug combination 9 (34.62%) (Results were summarised in Figure 3).

Figure 4: Diabetic comorbidities in study population

6. Comorbidities in study population

In present study among 80 patients, 77 patients had comorbidities with diabetes. Out of 77 patients 26 (33.76%) have diabetic comorbidities while 51 (66.24%) have non-diabetic comorbidities. Out of 51 non-diabetic comorbid patients 38 (71.69%) were found to be male and 31 (54.16%) were found to be female. Out of 26 diabetic comorbid patients 15 (28.31%) were male and 11 (45.84%) were female. (Results were summarised in Table 4 and Figure 4).

Table 4: Comorbidities in study population

Sl. No	Comorbidities	Number of patients		Percentage of patients (%)		Total
1	Diabetic	15	11	57.70	42.3	100
2	Non-Diabetic	38	13	74.50	25.50	100

Table 5: Non-diabetic comorbidities in study population

SL. NO	Non-diabetic Comorbidities	Number of Comorbidities	Percentage of Comorbidities
1	Cardiovascular disorder	40	28.16
2	Neurological disorder	33	23.23
3	Nephrological disorder	24	16.91
4	Respiratory disorder	22	15.49
5	Infectious diseases	8	5.63
6	Hepatological disorder	6	4.23
7	Gastrointestinal disorder	5	3.53
8	Hematological disorder	5	3.53
	TOTAL	**142**	**100**

Table 6: Prevalence and pattern of co-morbidity among Type-2 diabetics with age

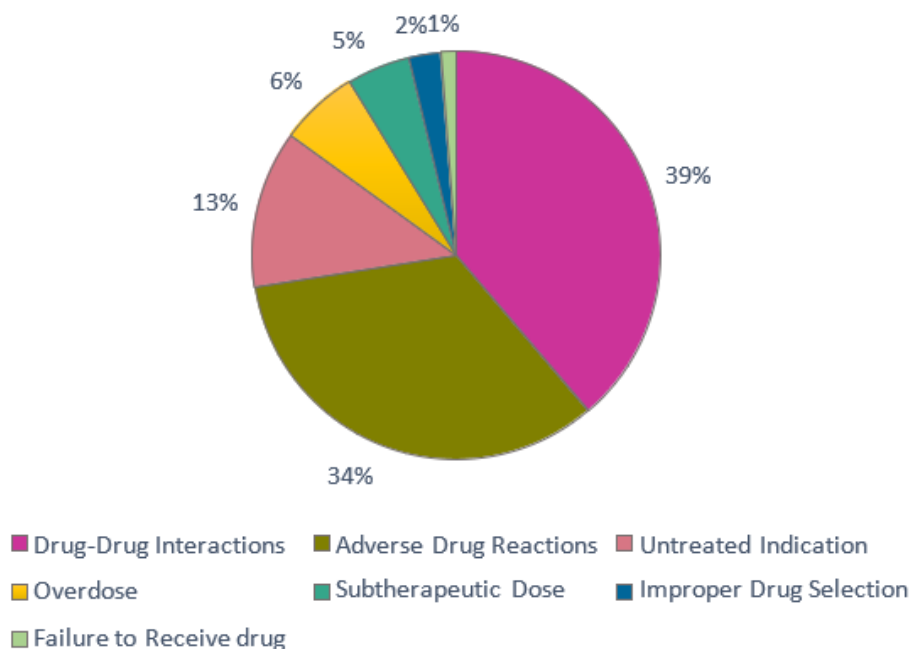| Age group (Years)	Co-morbidity	No co-morbidity	Total	t-value (N=80)	P value
19-29	1	0	1	0.04	<0.05
30-39	16	1	17		
40-59	36	0	36		
60 and above	24	2	26		

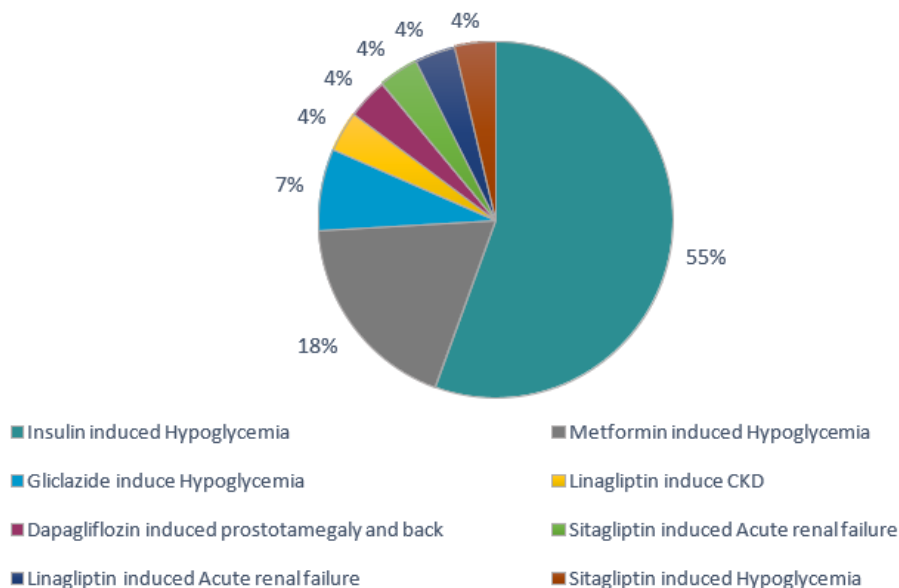**Figure 5:** Types of DRPs found in study population

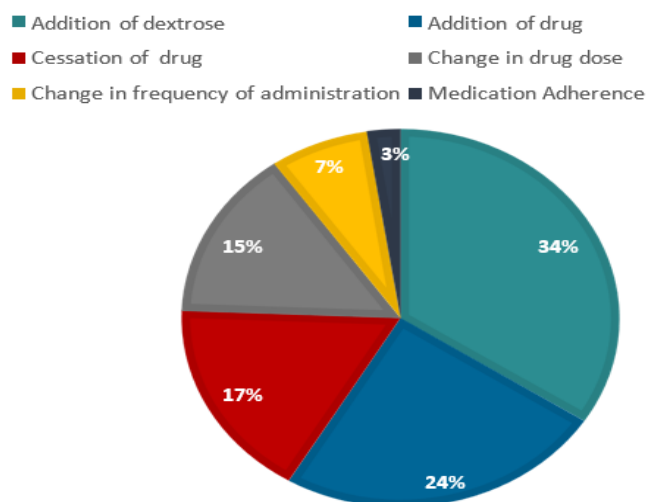**Figure 6:** Types of ADR found in anti-diabetic drugs

Figure 7: Intervention made by pharmacist

Table 7: Types of drug-drug interaction among anti-diabetic drugs

SL.NO	Severity of Drug-Drug Interaction	Number of Cases	Percentage of Cases (%)
1	Major	16	52
2	Moderate	15	48
	Total	31	100

Table 8: Outcome of pharmacist intervention

Types of Intervention	Number	Percentage (%)	Total
Intervention Accepted	29	70.74	41
Intervention not Accepted	12	29.26	
Change in Drug Therapy	27	65.85	41
No Change in Drug Therapy	14	34.15	

7. Diabetic comorbidities in study population

Out of 26 diabetic comorbid patients, 17 (60.72%) were found to have diabetic nephropathy followed by diabetic neuropathy 10 (35.71%) and diabetic retinopathy 1 (3.57%). (Results were summarised in Table 4).

8. Non-diabetic comorbidities in study population

A Total of 142 non-diabetic comorbidities were found in 51 patients. Among 142 non- diabetic comorbidities, Cardiovascular disorders 40 (28.16%) were mostly found followed by Neurological disorders 33 (23.23%) and Nephrological disorders 24 (16.91%). (Results were summarised in Table 5).

9. Prevalence and pattern of co-morbidity among Type 2 diabetes

For studying the prevalence and pattern of comorbidity among type 2 diabetic patients, we formulated a hypothesis that there is a significant difference in prevalence of comorbidities with respect to age. The t-value was found to be 0.04 which was less than significant level. The study accepts the hypothesis that there is a significant difference between the comorbidity and age. Older age group tends to increase comorbidity burden. (Results were summarised in Table 6).

10. Types of DRPs found in study population

During the hospital stay, a total of 80 DRPs were found among 80 patients. Among 80 DRPs, Drug-Drug Interactions were 31(38.78%) followed by Adverse drug reactions 27 (33.75%), Untreated indication 10 (12.5%), Overdose 5 (6.25%), Subtherapeutic dose 4 (5%), Improper drug selection 2 (2.5%) and Failure to receive drug 1 (1.25%). (Results were summarised in Figure 5).

11. Types of ADR found in anti-diabetic drugs

27 ADRs were found to be due to anti-diabetic medications. 15 (55.55%) of 27 ADR were found to be Insulin induced hypoglycemia followed by metformin induced hypoglycemia 5 (18.55%), Gliclazide induced hypoglycemia 2 (7.4.%), Linagliptin induced CKD 1 (3.70%), Dapagliflozin induced Prostatomegaly and back pain 1 (3.70%), Sitagliptin induced hypoglycemia 1 (3.70%), Sitagliptin induced AKI 1 (3.70%), and Linagliptin induced AKI 1 (3.70%). (Results were summarised in Figure 6).

12. Types of drug-drug interaction among anti-diabetic drugs

Out of 31 drug-drug interactions, majority were major drug interactions 16 (51.62%) followed by 15 (48.38%) moderate drug-drug interactions. (Results were summarised in Table 7).

13. Description of pharmacist intervention found in study population

During the hospital stay, the suggestion like addition of dextrose (34.14%) for example in case of Adverse drug reactions like insulin induced hypoglycemia, Addition of drug (24.40%) in case of untreated indication. Cessation of drug (17.07%) in case of adverse drug reactions like Linagliptin induced CKD, AKI followed by Change in drug dose (14.63%) in case of overdose and subtherapeutic dose and promoting medication adherence (2.44%). (Results were summarised in Table 8 and Figure 7).

14. Assessment of outcome of pharmacist intervention

The suggestions were evaluated by the physician and out of 41 interventions 29 (70.74%) were accepted and 12 (29.26%) were not accepted. Change in therapy was done in27 (65.85%) and 14 (34.15%) drug therapies remain unchanged. (Results were summarised in Table 8 and Figure 7).

DISCUSSION AND CONCLUSION

Diabetes Mellitus is a major public health problem in the worldwide. Its prevalence is rising in many parts of the developing world, no exception to this. It will become a diabetes capital of the world 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.[20]

This study provides an insight and relationship between various diabetic and non-diabetic complications which had led to an increased number of prescribed drug and the

associated risks of DRPs. The present study evaluates the number of comorbidities and DRPs among the type 2 DM patients.

Comparing to gender proportionality, male patients were (n=55) and female patients were (n=25). This was similar to the study conducted by Rajesh Hadia et.al.[13] It was observed that the highest number of patients were 40-59 years age group (25%) which was similar to the study conducted by Rajesh Hadia et.al. and Pati S et.al.[1314] Greater prevalence in this age group may be due to the changes in their lifestyle or lack of exercise and stress.

In the present study, the most commonly used anti-diabetic medicine was insulin during the hospital stay. Total 78 patients were prescribed insulins. 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.) During hospital stay percentage of patients receiving monotherapy as in this study (79.4%) is in accordance with the result of Sayed Aliul et al study[18]

In the current study Metformin (43.90%) was the most common prescribed OHD followed by Glimepiride (26.82%) which is in line with findings of Sayed A et al.[18] 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 cause 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 dyslipidaemia 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 based for efficacy and safety, also because it is inexpensive, and may reduce risk of cardiovascular events.[19] Among sulfonylureas, glimepiride (26.82%) 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 glycaemic control as initial therapy. Thus, results reflect that biguanides and sulfonylureas are still the choice of most physicians in the treatment of type 2 DM. It is accordance to the study conducted in tertiary care hospital, In Ahmedabad, monotherapy of OHAs were used frequently followed by dual therapy and triple therapy.[20]

The maximum prescribed class of drugs other than Anti-diabetics were Anti-Hypertensive drugs (20.60%) followed by Antacids (18.44%) and Antibiotics (15.61%). Result of a study conducted by Mable Babu et.al shared a similar report, were Anti-Hypertensive drugs in (14.14%) followed by antacids (10.17%) and antibiotics (11.95%).[17] In this study, hypertension was commonest comorbidity observed similar to Patel B et.al 2013 study. Different studies also reported similar observation with regard to the comorbidities in patients with diabetes. The proportion of

diabetics found to have comorbid hypertension is high which is not surprising since it reflects what obtains globally.[21]

In this study we observed that among 80 patients of type 2 DM 77 Patients were having at least one comorbid condition similar to the study conducted in Gujarat.[13 14] A high prevalence of comorbidities was observed in males (68.75%) than in female (31.25%) which is similar to the study conducted by Rana R et.al were males were 69.6% and females were 30.4%.[15] It is observed that 40-59 age group were maximum but in older patients, its existence was high. This represents that a strong association with increasing age with comorbidity also reported by few authors earlier.[16 17]

These comorbid conditions were further divided into diabetic comorbidities and non- diabetic comorbidities. The patients with only diabetic comorbidities were 33.76% which was higher to the study carried out in Gujarat (19.05%). The non-diabetic comorbidities were 66.24% which was relatively lower than the study carried out in Gujarat (87.27%) and higher than the study done in Bijapur (74.80%). The non-diabetic comorbidities were found to be more than the diabetic comorbidities similar to the studies conducted in the earlier.[13, 16, 17] In the earlier studies done, cardiovascular disorders were the most common when compared to any other disorders in non-diabetic comorbidities similar to that of our study.[22, 13 17]

DRPs are considered as serious, expensive and complicated to the health-care system. They are common among people living with chronic illness like diabetic patients.[23]

If drug therapy problems are not addressed, they can lead to clinical complications. Detecting and resolving DRP is important to ensure, whether the patients will achieve the optimal therapeutic goals.[24]

Overall, the current study showed that 90% of study participants had at least one DRP. This result is similar to previously conducted studies done by Argaw A et.al(80%).[25] However, it is higher than the findings of another study previously conducted in Ethiopia which reported 64.2% of DRPs among diabetic patients and study conducted by Javedh S et.al where 71.1% of patients had at least one DRP.[26] In our study, DRPs were mainly classified into ADR, DDI, Subtherapeutic dose, Untreated indication, Improper drug selection, Failure to receive drug, Overdose. 31 DDIs were theoretically identified which contributes 38.78% of the total DRPs similar to the study done by Rajesh Hadia et.al (88%)[13] and results were in contrast to the study carried out by Zazuli Z et.al were the DDI identified was 18. %[27] These identified DDI were further classified into moderate (48.38%) and major (51.62%). During the study period, 27 ADR were identified and reported among the study participants. Hypoglycemia was the most common observed ADR, which is consistent with Alex et al 2015 study at Amrita institute of Medical Science and Research Centre.[28] Significant drug-drug interactions and Adverse drug reactions equally involve with the physicians to improve the patient understanding and care. A preliminary interest of

pharmacist was to analyze, identify, categorize, minimise and prevent the DRPs.

Pharmacist intervention was evaluated by the physician. Pharmacist intervention suggestion in the present study was found to effective, most of the intervention were accepted70.74% and 65.85% drug therapy were changed.

DM is an important issue in middle aged and elderly people. Among all patients' male 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 pattern. Metformin was most commonly utilized OHA than others and Glimepiride was most utilized drug in sulfonylureas. Metformin alone and metformin combinations (with other antidiabetic drugs) were commonly prescribed to diabetic patients in current scenario. We have found drug related problems like ADRs, DDIs, subtherapeutic dose, overdose, untreated indication, failure to receive drug in our study.

The study can be concluded as; a high frequency of comorbidity and drug related problems was identified in our study population. Majority of recommendations made by the clinical pharmacist were accepted. Early identification and management of DRPs would augment the efficacy and outcome of the health care. Identification and resolving DRPs is a serious and important health care tool in the provision of elderly pharmaceutical care, and vigilant practice to curb drug related menace causing severe risk for failure of drug therapy and over all clinical outcome. The study shows evidence of physician and pharmacist collaboration in hospital setting to identify and resolve clinically significant DRPs.

In terms of decreasing morbidity and mortality, comorbidities should be one of the major focus of clinicians rather than only focusing on anti-diabetic treatment

The rate of drug related problems in type 2 diabetes patients is high. Patients with longer duration of diabetes and co-morbidities had a higher chance of developing DRPs. Clinical pharmacist plays a major role in identifying and resolving DRPs and therefore it is important to strengthen clinical pharmacist services in health care system.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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