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Research Article

TO IDENTIFY, EVALUATE, AND ANALYZE THE POSSIBLE DRUG-DRUG INTERACTIONS IN PATIENTS DIAGNOSED AS TYPE 2 DIABETES MELLITUS WITH HYPERTENSION IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Objective: To identify, evaluate, and analyze the possible drug-drug interactions (DDIs) in patients diagnosed as Type 2 diabetes mellitus with hypertension in a tertiary care teaching hospital Davangere.

Methods: This prospective interventional study was conducted for a period of 6 months. Data were collected from patients who were prescribed with at least one antidiabetic drug and at least one antihypertensive drug at the same time. Data were analyzed for DDIs by using software Micromedex and other resources. Results were notified to the physicians for modification or alteration in the drug therapy.

Results: A total of 150 patients were analyzed out of which, 60.67% were male, and the rest 39.33% were female. In terms of interactions present, 95 (63.33%) prescriptions had one or more interactions. Antihypertensive drugs most frequently seen in prescriptions were diuretics (24.44%). Antidiabetic drugs seen frequently prescribed are biguanides (34.36%). A total of 167 possible DDIs were obtained. Angiotensin-converting enzyme inhibitors were most frequently involved antihypertensive drug in DDIs, with 60 of all possible DDIs identified. Insulin and biguanides were most frequently involved antidiabetic drugs in DDIs, with 58 each of all possible DDIs identified. Most frequently interacting drug pair was insulin + metformin (n=19).

Conclusion: For every possible DDIs found in the prescription, the appropriate intervention was advised from the investigator's part as well as provision for a physician to review and initiate modification of his choice.

Keywords: Hypertension, Possible drug-drug interaction, Type 2 diabetes mellitus.

INTRODUCTION

The root of many diseases is in the poisonous interactions arising from medications, given wrongly by the physicians in the first place to affect a cure. As per World Health Organization, "a drug-drug interaction (DDI) is a situation in which a substance (usually another drug) affects the activity of a drug when both are administered together." It can also be defined as "the modification of the effects of one drug (i.e., the object drug) by the prior or concomitant administration of another drug" [1]. DIs are a wide source of medication error. About 6-30% of all adverse drug reactions are a result of DI. Adverse DIs in hospitalized patients have been estimated to be between 2.2% and 30.0% and for ambulatory patients it is between 9.2% and 70.3% [2].

Drug therapy is growing more complex, thus making an appropriate decision on drug therapy increasingly challenging. DIs are most important in this context for DDIs as it may prevent harmful events [15]. Due to the complexity of the pharmacotherapy involved in the simultaneous use of several drugs and various therapeutic classes, critically ill patients are at an increased risk for DIs [23].

Based on the profile of medications prescribed, the DDIs are identified and classified. According to severity, potential DDIs are classified as:

1. Major: The effects are potentially life-threatening or capable of causing permanent damage.
2. Moderate: The effects may cause deterioration in patients' clinical status and additional treatment or extension of hospital stay.
3. Minor: The effects are usually mild [19].

Hypertension (HTN) is an extremely common co-morbidity of diabetes, affecting 20-60% of people with diabetes mellitus. The prevalence of HTN in the diabetes population is 1.5-3 times higher than that of non-diabetic age-matched groups.

Little is known about whether, and what extend, co-prescribing drugs from different antihypertensive and diabetic drug classes can result in DDIs that might alter the intended effects of individual agents. To date, there has been a lack of studies conducted locally and globally to investigate and document possible DDIs in Type 2 diabetes mellitus (T2DM) patients with HTN. There are no studies reporting the actual incidence of possible DDIs in T2DM patients with HTN in the Indian setting [15].

The aim of our study was to provide baseline data regarding possible DDIs to allow the implementation of more effective management and to reduce the mortality and morbidity associated with DDIs.

Objectives

1. To identify, evaluate, and analyze the possible DDIs in patients diagnosed as T2DM with HTN in a tertiary care teaching hospital
2. To identify the effect of age and gender in DDIs
3. To categorize and classify drugs according to the disease
4. To identify, evaluate, and analyze DDIs as harmful or beneficial
5. To immediately notify the physicians about the results of the DDIs
6. To find out the most frequently involved class of drugs in DDIs.

METHODS

Study site

The study was conducted in the general medicine wards of a tertiary teaching care hospital in Davangere.

Study period

The study was conducted for a period of 6 months.

Study design
It is a prospective interventional study.

Study criteria

Inclusion criteria

The patients diagnosed with T2DM and HTN and patients who received at least one antidiabetic drug (oral antidiabetic drug or insulin) and at least one antihypertensive agent.

Exclusion criteria

Pediatrics and pregnant patients and patients with missing data.

Source of data
The data were collected from in-patient case sheets of a tertiary care hospital that were prescribed with at least one antidiabetic drug and not less than one antihypertensive drug at the same time.

Ethical approval
The Institutional Ethical Committee had approved the conduction of the study.

Phases of study

Identification

This involves the identification of the patients as per inclusion and exclusion criteria.

Data collection

Data of the identified patients was collected from the wards during the daily ward rounds.

Evaluation

The data were evaluated and analyzed for possible DDIs by using software Micromedex and other tertiary resources, e.g., Stockley's DIs. Any possible DDIs were notified to the physician as soon as possible.

Analysis

The secondary objectives such as the prevalence of DIs in each age category and gender. Beneficiality or harmfulness of the interaction was analyzed.

Study procedure
The investigators in their daily ward rounds collected the relevant patient data in a suitably structured data collection form. Data were collected only from patients who were prescribed with at least one antidiabetic drug and at least one antihypertensive drug at the same time. Investigators collected patient details, diagnosis and drugs prescribed with their doses and frequency of administration. The drugs were then categorized as antidiabetic drugs or antihypertensive drugs. The data were analyzed for DDIs by using Micromedex® which was available through the college library. The result of the analysis was notified to the physicians immediately. The prevalence of any possible DDIs in different age groups and based on gender will be identified. Beneficiality or harmfulness of the interactions will be determined using laboratory data obtained.

Development of documentation forms
Three types of forms were used in the study namely:

1. Informed consent form: Prepared in both English and regional language, Kannada
2. Patient profile form: Provisions for entering patient demographics and drugs prescribed along with separate columns for identified interactions
3. Interaction notification and therapy modification form: Form for the physician with provisions for severity of interaction and proposed recommendations/changes as well as physician's therapy modification apart from proposed recommendations.

RESULTS

Details of the patients enrolled
The prospective interventional study was conducted for a period of 6 months to identify and analyze possible DDIs in the medication charts of a tertiary care teaching hospital in Davangere. The total of 150 patients were enrolled in the study who were prescribed with at least one antidiabetic drug and not less than one antihypertensive drug at the same time.

The total of 150 patients were analyzed during the study period out of which, 60.67% were male, and the rest 39.33% were female.

In terms of interactions present, 95 (63.33%) prescriptions had one or more possible interactions while 55 (36.67%) prescriptions had no interactions.

The majority of possible DDIs were found in the age group of 50-60 years (36.53%).

In terms of types of drugs received, 46 different drugs were given, out of which 31 were antihypertensive drugs, and 15 drugs were antidiabetics. The antihypertensive drugs most frequently seen in prescriptions were diuretics (24.44%) followed by calcium channel blockers (CCBs) (22.56%) and angiotensin converting enzyme (ACE) inhibitors (19.92%).

The antidiabetic drugs seen frequently prescribed are biguanides (34.36%) followed by insulin (29.52%) and sulfonylureas (28.63%).

The identified possible DDIs were analyzed as major, moderate, and minor. The total of 167 possible DDIs were obtained from 95 cases. From these 8 (4.79%) were of major severity, 145 (86.83%) were of moderate severity, and 14 (8.38%) of minor severity. The majority of the identified possible DDIs were of moderate severity.

In the present study conducted, ACE inhibitors was the most frequently involved antihypertensive drug in DDIs, with 60 of all possible DDIs identified, followed by beta-blockers (n=42) and diuretics (n=39).

Insulin and biguanides were the most frequently involved antidiabetic drugs in possible DDIs, with 58 each of all possible DDIs identified, followed by sulfonylureas (n=32).

The DIs are classified into three categories, namely interactions between antihypertensive drugs, interactions between antidiabetic drugs, and interactions between an antihypertensive and antidiabetic drug. The majority of the interactions (65.87%) were found between an antihypertensive and antidiabetic drug.

The most frequently interacting drug pairs were insulin + metformin (n=19), captopril + furosemide (n=9), insulin + ramipril (n=8), furosemide + metformin (n=8).

A total of 6 unique major possible interactions were identified which combinely occurred a total of 8 times.

A total of 67 possible DDIs were identified among the various drugs.

Among the possible DDIs, 5 (2.99%) were with excellent documentation status, 157 (94.02%) with good status, and 5 (2.99%) had fair status.

The distribution of possible DDIs presents per prescription. The majority of the patients had 1 possible DDIs (n=52) while the maximum concentration of possible DDIs (32.34%) were found in the patient group with 3 interactions (n=18).

For every possible DDIs found in the prescription, the appropriate intervention was advised from the investigator's part as well as provision for a physician to review and initiate modification of his choice.

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Table 1: Distribution of patients according to gender (n=150)

S. No.	Gender	Number of cases	Percentage
1	Male	91	60.67
2	Female	59	39.33
3	Total	150	100

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Table 2: Distribution of cases with respect to possible DDI (n=150)

Type of case	Number of cases	Percentage
Number of cases with possible DDIs	95	63.33
Number of cases without possible DDIs	55	36.67
Total number of cases	150	100

DDI: Drug-drug interactions

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Table 3: Distribution of patients with respect to age (n=150)

Age group	Number of patients	Number of possible DDIs	Percentage of DDIs
30-40	3	3	1.80
40-50	40	40	23.95
50-60	48	61	36.53
60-70	43	38	22.75
70-80	13	18	10.78
>80	3	7	4.19
Total	150	167	100

DDI: Drug-drug interactions

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Table 4: Distribution of frequency of antihypertensive drugs based on being found in prescriptions

S. No.	Drug classification	Frequency of being found in prescriptions	Percentage
1	Diuretics	65	24.44
2	CCBs	60	22.56
3	ACE inhibitors	53	19.92
4	ARBs	40	15.04
5	Beta-adrenergic blockers	28	10.53
6	Alpha-adrenergic blockers	9	3.38
7	Central sympatholytics	6	2.25
8	Alpha+beta blockers	5	1.88
9	Vasodilators	0	0
10	Total	266	100

CCB: Calcium channel blockers, ARB: Angiotensin receptor blockers, ACE: Angiotensin converting enzyme

DISCUSSION

Various studies have shown that possible DDIs are frequent when patients receive multiple prescriptions. This is true for patients with T2DM and HTN combined as most of such cases will be requiring to take more than 2 drugs simultaneously. In many cases, it causes unwanted effects and changes in therapeutic efficacies of the combined medicines, with consequent poor control of T2DM and HTN [1,22,27].

In this study, there had been an astonishing 67 types of possible DDIs identified; even though only the antihypertensive and antidiabetic drugs prescribed in the limited setup of a tertiary hospital were examined. To date, there has been no comparable study done specifically on possible DDIs in T2DM patients with HTN both locally and globally.

Among the study subjects, 91 patients (61%) were males, and 59 patients (39%) were females (Table 1). This study also revealed

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Table 5: Distribution of frequency of antidiabetic drugs based on being found in prescriptions

S. No.	Drug classification	Frequency of possible DDIs found in prescriptions	Percentage
1	Biguanides	78	34.36
2	Insulin	67	29.52
3	Sulfonylureas	65	28.63
4	Thiazolidinediones	6	2.65
5	Alpha-glucosidase inhibitors	4	1.76
6	DPPI-4 inhibitors	4	1.76
7	Meglitinide analogs	3	1.32
8	Total	227	100

DPPI: Dipeptidyl peptidase inhibitors

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Table 6: Distribution of possible DDIs according to the degree of severity

Severity of possible DDIs	Number of possible DDIs	Percentage of possible DDIs
Major	8	4.79
Moderate	145	86.83
Minor	14	8.38
Total number of possible DDIs	167	100

DDI: Drug-drug interactions

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Table 7: Frequency of possible DDIs of antihypertensive drugs based on drug classification

S. No.	Drug classification	Frequency of involving in possible DDIs
1	ACE inhibitors	60
2	Beta blockers	42
3	Diuretics	39
4	CCBs	18
5	ARBs	17
6	Beta+alpha blockers	6
7	Alpha blockers	3
8	Central sympatholytics	2
9	Vasodilators	0

DDI: Drug-drug interactions, CCB: Calcium channel blockers, ARB: Angiotensin receptor blockers, ACE: Angiotensin converting enzyme

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Table 8: Frequency of possible DDIs of antidiabetic drugs based on drug classification

S. No.	Drug classification	Frequency of involving in possible DDIs
1	Insulin	58
2	Biguanides	58
3	Sulfonylureas	32
4	Thiazolidienediones	4
5	Alpha glucosidase inhibitors	3
6	DPPIs	2
7	Meglitinide analogs	0

DPPI: Dipeptidyl peptidase inhibitors

the male predominance over female as similar to a study conducted by Mahendra *et al*. In contrast more prevalence of DIs in women has been found in a study conducted by Neto *et al*. [18]. These differences in the distribution of gender are perhaps a consequence of the enrollment of more females in the latter study.

The total of 150 patients were selected for the study. Out of these, 95 patients (63.33%) had some kind of possible interactions while

55 patients (36.66%) did not have any kind of interactions (Table 2). A study conducted by Neto *et al*. done in a restricted population of elderly had found that 47.7% of the patients had one or more possible DDI. This frequency is lower than the figure reported in a Mexican study, where almost 80% of patients presented potential pharmacological interactions [8]. The comprehensive study here found that 1 possible DDI was found in the majority of the patients (n=52). A possible explanation for the lesser number of DIs is that the hospital in which this study was conducted uses the drugs that are highly involved in interactions less frequently due to the inaccessibility of these drugs to the hospital or fear of their adverse outcomes in the setup with limited infrastructures to monitor the patients or unfamiliarity of the physicians with these drugs.

In the present study, the age group 40-70 had the maximum number of interactions present. This is also same in the study by Chelkeba *et al*. [25] where maximum concentration of interactions was found in the age groups 37-47, 48-58, and 59-69 (Table 3).

The most frequently prescribed antihypertensive drug classes were diuretics, CCBs, and ACE inhibitors (Table 4). This showed a close association with the findings of a retrospective study conducted by Zaman Huri and Fun Wee [1] at a tertiary hospital in Malaysia, where CCBs, ACE inhibitors, and diuretics were found to be the most commonly prescribed antihypertensive drugs.

Biguanides were seen to be the most frequently prescribed antidiabetic drug followed by insulin (Table 5). This is contrary to the results of the study conducted by Zaman Huri and Fun Wee [1] where insulin was more widely than oral agents. A constrained sample size might have brought up the discrepancy in the study.

Identified possible DDIs were classified into major, moderate, and minor using the software Micromedex®. In the 167 possible DDIs, 8 were of major severity (4.79%), 145 were of moderate severity (86.82%), and 14 were of minor severity (8.38%) (Table 6). Of the total possible DDIs, the majority were of moderate severity in our study which is similar to a study conducted by Jimmy *et al*. [3]. Other studies confirming the same was by Neto *et al*. [8].where 93.2% of the interactions were found to be of moderate severity, Moura *et al*. [22] where 78% of the interactions were found to be of moderate severity, and Chelkeba *et al*. [25] in which 67.3% of the interactions were of moderate severity, compared to 29.6% major and 3.1% minor severity.

Some of the most common drug classes involved in DDIs were ACE inhibitors (24%), insulin (24%), and biguanides (21%) (Table 7 and 8). A study by Chelkeba *et al*. [25] in 2011 showed that the drugs enalapril, furosemide, hydrochlorothiazide, and spironolactone were at the top of drugs with a high probability of causing DDIs at Jimma.

Interactions between antihypertensive drugs and antidiabetic drugs were seen more commonly (65.87%) compared to interactions between antihypertensive drugs (21.56%) and interactions between antidiabetic drugs (12.57%) (Table 9).

In our study, commonly interacting drug pairs were insulin-metformin (11.37%), captopril-furosemide (5.38%), followed by insulin-ramipril (4.79%), and furosemide-metformin (4.79%) (Table 10). The effects of these interactions were increased the effect of metformin in lowering

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Table 9: Categorization of possible DDIs between classes of drugs

S. No.	Interaction	Number of interactions	Percentage
1	Interaction between antihypertensive drugs	36	21.56
2	Interaction between antidiabetic drugs	21	12.57
3	Interaction between an antihypertensive and an antidiabetic drug	110	65.87
4	Total	167	100

DDI: Drug-drug interactions

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Table 10: Most prevalent DDIs

S. No.	Drug combination		Number of cases	Severity	Consequence
1	Insulin	Metformin	19	Moderate	Risk of hypoglycemia
2	Captopril	Furosemide	9	Moderate	Risk of postural hypotension (first dose)
3	Insulin	Ramipril	8	Moderate	Risk of hypoglycemia
4	Furosemide	Metformin	7	Moderate	Chance of lactic acidosis
5	Insulin	Captopril	7	Moderate	Increase effect of insulin by pharmacodynamic synergism
6	Nifedipine	Metformin	7	Minor	Concurrent use results in increased absorption of metformin
7	Glimepiride	Propranolol	5	Moderate	May result in hypoglycemia, hyperglycemis or HTN
8	Insulin	Telmisartan	5	Moderate	Risk of hypoglycemia
9	Insulin	Enalapril	4	Moderate	Risk of hypoglycemia
10	Atenolol	Glipizide	4	Moderate	Chance of hyperglycemia or hypoglycemia
11	Metformin	Hydrochlorothiazide	4	Moderate	Increase in blood sugar level and interference with diabetic control
12	Captopril	Metformin	4	Moderate	Risk of hypoglycemia

DDI: Drug-drug interactions

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Table 11: Identified major possible DDIs

S. No.	Drug combination		No. of cases	Consequence
1	Clonidine	Metoprolol	1	Lower blood pressure and bradycardia and exaggerated clonidine withdrawal symptoms
2	Ramipril	Telmisartan	1	Ramipril together with telmisartan may increase the risk of side effects such as low blood pressure and kidney function impairment
3	Nifedipine	Pioglitazone	1	Concurrent use of nifedipine and pioglitazone may result in decreased nifedipine exposure
4	Captopril	Telmisartan	2	Telmisartan – captopril either increases the toxicity of other by pharmacodynamic synergism. Possible life-threatening interaction
5	Captopril	Losartan	2	Captopril together with Losartan may increase the risk of side effects such as low blood pressure and kidney function impairment
6	Ramipril	Losartan	1	Ramipril together with Losartan may increase the risk of side effects such as low blood pressure and kidney function impairment

DDI: Drug-drug interactions

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Table 12: List of identified possible DDIs

S. No.	Drugs prescribed		Number of cases	Severity
1	Amlodipine	Metoprolol	1	Moderate
2	Amlodipine	Pioglitazone	2	Moderate
3	Amlodipine	Ramipril	1	Minor
4	Atenolol	Amlodipine	1	Moderate
5	Atenolol	Chlorpropamide	2	Moderate
6	Atenolol	Glipizide	4	Moderate
7	Atenolol	Insulin	1	Moderate
8	Atenolol	Metformin	1	Moderate
9	Atenolol	Nifedipine	1	Moderate
10	Atenolol	Telmisartan	1	Moderate
11	Benzapril	Amiloride	1	Moderate
12	Benzapril	Insulin	3	Moderate
13	Captopril	Amlodipine	2	Minor
14	Captopril	Furosemide	9	Moderate
15	Captopril	Glipizide	3	Moderate
16	Captopril	Losartan	1	Major
17	Captopril	Metformin	4	Moderate
18	Carvedilol	Chlorpropamide	2	Moderate
19	Carvedilol	Clonidine	1	Moderate
20	Carvedilol	Insulin	2	Moderate
21	Carvedilol	Glimepiride	1	Moderate
22	Clonidine	Metoprolol	1	Major
23	Enalapril	Glimepiride	2	Moderate
24	Enalapril	Metformin	3	Moderate
25	Esmolol	Glipizide	2	Moderate
26	Furosemide	Enalapril	2	Moderate
27	Furosemide	Glimepiride	3	Moderate
28	Furosemide	Metformin	7	Moderate
29	Furosemide	Propranolol	2	Moderate
30	Glimepiride	Metoprolol	1	Moderate
31	Glimepiride	Nadolol	1	Moderate
32	Glimepiride	Propranolol	5	Moderate
33	Glipizide	Lisinopril	1	Moderate
34	Glipizide	Propranolol	2	Moderate
35	Hydrochlorothiazide	Glipizide	1	Moderate
36	Hydrochlorothiazide	Propranolol	1	Moderate
37	Insulin	Captopril	7	Moderate
38	Insulin	Enalapril	4	Moderate
39	Insulin	Glibenclamide	3	Minor
40	Insulin	Losartan	1	Moderate
41	Insulin	Metformin	19	Moderate
42	Insulin	Metoprolol	1	Moderate
43	Insulin	Propranolol	3	Moderate
44	Insulin	Ramipril	8	Moderate
45	Insulin	Telmisartan	5	Moderate
46	Insulin	Valsartan	1	Moderate
47	Lisinopril	Metformin	1	Moderate
48	Metformin	Hydrochlorothiazide	4	Moderate
49	Metformin	Propranolol	2	Moderate
50	Metformin	Torsemide	1	Moderate
51	Metoprolol	Metformin	2	Moderate
52	Metoprolol	Prazosin	1	Moderate
53	Nifedipine	Acarbose	1	Moderate
54	Nifedipine	Metformin	7	Minor
55	Nifedipine	Pioglitazone	1	Major
56	Prazosin	Hydrochlorothiazide	2	Moderate
57	Prazosin	Propranolol	2	Moderate
58	Ramipril	Losartan	1	Major
59	Ramipril	Metformin	2	Moderate
60	Ramipril	Telmisartan	1	Major
61	Spironolactone	Captopril	1	Major
62	Spironolactone	Metformin	1	Moderate
63	Spironolactone	Telmisartan	2	Moderate
64	Telmisartan	Captopril	2	Major
65	Vildagliptin	Gliclazide	1	Moderate
66	Vildagliptin	Glipizide	1	Moderate
67	Voglibose	Metformin	1	Minor

DDI: Drug-drug interactions

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Table 13: Distribution of possible DDIs according to documentation status

S. No.	Documentation status	Number of cases	Percentage
1	Fair	5	2.99
2	Good	157	94.02
3	Excellent	5	2.99
4	Total	167	100

DDI: Drug-drug interactions

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Table 14: Distribution of possible DDIs per prescription

S. No.	Number of possible DDIs per prescription	Number of patients	Percentage of DDIs
1	1	52	31.14
2	2	20	23.95
3	3	18	32.34
4	4	4	9.58
5	5	1	2.99
6	Total	95	100

DDI: Drug-drug interactions

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Table 15: Utilization of recommended therapy modification

S. No.	Initiated action	Number of cases	Percentage
1	Change in therapy (investigators recommendation applied)	85	50.90
2	Change in therapy (physician's modification applied)	12	7.19
3	No change in therapy	70	41.91
4	Total	167	100

blood sugar, hypotension, increased risk of hypoglycemia, and lactic acidosis, respectively. Interactions between enalapril-furosemide, captopril-spironolactone, captopril-furosemide, atenolol-amlodipine had already been well-established in literatures, and they were seen in the at hand study too.

Major possible DDIs such as Clonidine - Metaprolol, Ramipril -Telmisartan are also found in the study [Table 11].

During the study 67 unique interactions were found amounting to a total of 167 interactions [Table 12].

The documentation status of most of the possible DDIs was good (94.02%), suggesting that these possible DDIs may be prevented by an evidence-based approach [Table 13]. Perhaps, better approaches are to obtain data on drugs from drug information center or information on drugs from clinical pharmacists during prescribing, thus ideally avoiding DDIs. The results here are slightly higher than a study done by Chelkeba *et al*. [25] on the assessment of potential DDIs among outpatients receiving cardiovascular drugs. The reasons for better documentation could be due to better awareness of prescribers about major DDIs and presence of drug information center and clinical pharmacists.

The majority of the patients had 1 possible DDIs (n=52) while the maximum concentration of possible DDIs (32.34%) were found in the patient group with 3 interactions (n=18) (Table 14).

Regarding the interventions applied, 52% of the time the physician made appropriate changes to the therapy while 48% of the time, the therapy was continued (Table 15).

The identified possible DDIs related problems were notified to the physician and assured that they will take possible safety measures to minimize the DDIs in future.

The recognition of DIs by general practitioners will help to improve the patient safety and therapeutic outcome. We are also recommending developing a collaborative, patient centered approach to the education of pharmacy professionals to deliver effective drug therapy, so the incidence of drug therapy problems will be minimized.

In this study, most possible DDIs were moderate. These possible DDIs suggest that there is a need for modification or alteration of therapy such as dosage adjustment. To prevent these DDIs, health care providers should have adequate information about DDIs not only via drug information center which can provide evidence-based information to healthcare professionals but also through encouraging the empowerment of clinical pharmacists that can provide the evidence-based approach to drugs and thereby prevent drug therapy problems which DDIs are one.

CONCLUSION

The possible DDIs are frequent among the hospitalized patients who were prescribed with at least one antidiabetic drug and not less than one antihypertensive drug at the same time. According to gender, out of 150 cases, 91 patients (60.67%) were males and 59 (39.33%) were females. The possible DDIs were found in 95 (63.33%) cases out of 150 cases. The patients in the age group of 50-60 years had most of the possible DDIs. Most frequently used antihypertensive drugs are diuretics (24.44%). Biguanides are the most frequently used antidiabetic drugs (34.36%).Total 167 possible DDIs were identified from 95 cases. The majority of the possible DDIs identified were of moderate sevierty (86.83%). In antihypertensive drugs, ACE inhibitors were found to be like the most frequently involving interacting drug class. Insulin (n=58) and biguanides (n=58) were found to be the most frequently involved interacting drug classes in antidiabetic drugs. Interactions between an antidiabetic drug and antihypertensive drug were found to be 110 (65.87%) out of 95 cases. The interaction between antidiabetic drugs were found to be (36, 21.56%) more compare to the interaction between antihypertensive drugs (21, 12.57%). Most interacting drug pairs were insulin-metformin, captopril-furosemide, insulin-ramipril followed by furosemide-metformin. In the distribution of possible DDIs present per prescription, the majority of the patients had 1 possible DDIs (n=52) while the maximum concentration of possible DDIs (32.34%) were found in the patient group with 3 interactions (n=18). In our study, out of 167 cases investigators therapeutic recommendations were applied for 85 cases (50.60%), Physician's modifications were applied for 12 cases (7.19%), and no change for rest of the 70 cases (41.91%). From this study, it has been concluded that possible DDIs in patients taking antihypertensive and antidiabetic drugs has been on the higher margin. Therefore, future studies are needed to assess possible DDIs and other drug related problems that may appear clinically.

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Author Queries???

AQ1: Kindly provide department

AQ2: Kindly cite references 4-7, 9-14, 16, 17, 20, 21, 24, 26-32 in text part. Kindly cite all references in chronological order

AQ3: Kindly cite Tables 1-15 in text part