A Study On Assessement Of Prescripion For Polypharmacy And Drug Interactions Among Hypertion And Diabetes Mellitus In Gereriatic Patients.

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ABSTRACT
Elderly persons were considered individuals aged 60 or older, as proposed by WHO. In elderly people, a drug prescription should always be written with utmost care keeping in mind the possibility of adverse drug reactions[1].

Methodology: A prospective observational study will be conducted in department of medicine for six months in basaweshwar teaching and general hospital on patient of above 60 years of age with the prior permission from HOD department of medicine and with prior approval of institutional ethics committee. The geriatric patients will enrolled into the study by confiding study criteria. The prescription of enrolled patients will be analysed as per study criteria. The data will be collected in a suitably designed from patient data collection form.

Results:A total of 103 patients were enrolled into the study, and their prescription have been analysed. Among 103 cases 61 were found with drug interactions with a total of 156 drug interactions and 5 contra-indicated drugs. There were 54(52.42%) males and 49(47.57%) females. Age distribution of patients showed that among 103 patients 46(44.60%) patients were in age group of 60-70years followed by 24(23.30%) patients in the age group of 66- 70years.12(11.65%) patients were in the age groups of 71-75years, 9(8.73%) patient were in the age group of 81- 85years. Then finally 01(0.97%)patient was in the age group of 86-90years.

Among 103 cases, the cases with interactions were 61(59.22%) and without interaction were 42(40.77%). Among 103 cases, the patient with hypertensive cases were 51(49.51%) and patients with diabetic cases were 25(24.27%) and the patients with both hypertensive and diabetic cases were 27(26.21%). Among 25 diabetics patients, their were 14(56%) male patients and 11(44%) female patients. Among 51 hypertensive patients, there were 30(58.82%) male patients and 21(41.17%) female patients.

Anti-hypertensive drugs showed that among 105 ant-hypertensive drugs, there were 38(36.1%) drugs prescribed from the class of angiotensin antagonist, 28(26.6%) drugs of class diuretics, 24(22.8%) drugs of class calcium channel blockers, 13(12.3%) drugs of class beta-blockers, and 02(1.9%) drugs of class ACE inhibitors. Among 54 anti-diabetic drugs, there were 10(18.5%) drugs of class biguanides, 36(66.6%) drugs of class insulin, and 8(14.8%) drugs of class sulfonylureas.

Out of 61 cases containing the drug drug interactions the cases with 1 drug-drug interactions were 21(34.42%). There were 18(29.50%)cases with 2 drug-drug interactions followed by 08(13.11%) containing 3 drug-drug interactions and 4 number of cases containing 7(11.47%) and >5 drug-drug interactions having 7(11.47%). Out of hypertensive and diabetic cases, the hypertensive cases containing drug-drug interactions were 17(43.58%).

Conclusion: we conclude that there were highest number of drug interactions found at the study site, hence there is need to conduct educational program to the physician in order to reduce the drug- drug interactions. In this regard the clinical pharmacist may play a key role.

Key words: Drug-Drug interactions, physician, clinical pharmacist.

I. INTRODUCTION

Diabetes mellitus: Diabetes mellitus (DM) is a group of metabolic disorder, resulting in hyperglycemia. It occurs due to lack of insulin hormone or insensitivity of cells to insulin, causing increased blood sugar level.

There are two types of DM: Type 1 caused by absolute insulin deficiency and Type 2 caused by insulin resistance due to defective responsiveness of insulin receptors. Long-term damage of vital organs such as kidney, heart, nerves, blood vessels, and eyes results from chronic effect of diabetes.[4]

Hypertension: High blood pressure (BP), or arterial hypertension, i.e., systolic BP (sBP) ≥ 140 mmHgand/or diastolic BP (dBP) ≥ 90 mmHg, is the main modifiable cardiovascular risk factor for ischemic heart disease and stroke, end-stage kidney disease, premature death and disability and overall, for mortality of any cause.

The prevalence of hypertension increases with population aging, affecting more than half of all people aged 60–69 and more than three-fourths of all people over 70 years old. Moreover,approximately 90% of people aged 55–65 years who do not have hypertension will develop hypertension by the age of 80–85 years. In terms of sex, the prevalence of hypertension is generally higher in men (24%) than in women (20%[7].

Polypharmacy: Polypharmacy is most commonly defined as the use of five or more medications daily by an individual. In India, the prevalence of polypharmacy varies from 5.82 % to 93.14% in different states. Concerns about polypharmacy include increased adverse drug reactions, druginteractions, prescribing cascade, and higher costs. The present study is a non-interventional, observational, descriptive study carried out in 240 patients attending the medicine outpatient department of a tertiary care hospital, over one-and-a-half-year duration. The mean age of the study population was 53.97 ± 7.62 years, out of which 52.5% were male and 47.5% were female. 62% of the study population were from low socioeconomic status and 38 % were from the middle class. The mean duration in years for hypertension and diabetes was 7.1± 4.3years and 7.94+ 4.66 years respectively. Apart from various antihypertensive and antidiabetic medicines prescribed the study population was also prescribed Vitamins (51.6%), Hypolipidemics (42.5%), Miscellaneous (41.6%), Antiplatelets (40%), H2 blockers/PPI (35.8%), and Antibiotics (22.5%). Polypharmacy (5 or more than 5 drugs) was seen in 33.75% of the study population. Polypharmacy with is integral in patients suffering from hypertension with coexisting diabetes mellitus and other comorbidities. It is essential to practice judicious prescribing especially in patients with multiple conditions.[9]

Role of pharmacists in geriatric care Polypharmacy and adherence management role of pharmacists in providing geriatric care to reduce polypharmacy and clinical consequences of polypharmacy, including medication errors, nonadherence, adverse drug events, drug–drug interactions, urgent or emergent visits, and hospitalization.[11]

Relation of polypharmacy in diabetes mellitus
Polypharmacy indicates concomitant use of a number of drugs. In this complex scenario of therapeutics, especially for diseases such as diabetes, the exact burden and nature of polypharmacy on the society on different aspects including cost-effectiveness, is very important. The present study was a step to evaluate this complex scenario. The present study established the relation of age with comorbidity in diabetic patients. The mean comorbid conditions for the age group 31–40 years were 0.8 whereas of 71–80 years was 2. Another important information obtained from the present study highlighted the maximum level of polypharmacy (5.82) was prevalent in the geriatric age group of 61–70 years. However, astonishingly, it failed to support the correlation of smoking and drinking with diabetes. Therefore, reducing pill burden and yet providing maximum benefit to the patients is of utmost importance. More research on the pharmacokinetics and pharmacodynamics of appropriate and scientific fixed drug combinations is needed [5].

Drug interactions
A drug interaction is defined as the qualitative or quantitative modification of the effect of a drug by the simultaneous or successive administration of a different one. This may result in the alteration of therapeutic effect and safety of either or both drugs. Drug interactions can be due to pharmacokinetics(alteration in the delivery of drug to its site of action) or pharmacodynamics (modification of response of drug target) interactions[12].

Types of drug interaction;
A. Drug–disease interactions -The inter-individual variability in susceptibility to drugs is at least partly explained by differences in multi-morbidity. Diseases that affect the kidneys make the elderly patient more susceptible to ADR due to reduction in renal elimination.Liver diseases as well as cardiac diseases that affect hepatic blood flow may affect drug metabolism. In the same way,

diseases that affect other organ systems may make elderly patients even more susceptible to drugs.

B. Drug–food interactions - Drug food interaction adds variability to effects and adverse effects of drugs. For example, warfarin is known for its drug–food interactions. Warfarin has a narrow therapeutic interval and food with a high vitamin-k content counteract the effects of warfarin [14].

Relation of DDIs in hypertension
Patients with hypertension are particularly vulnerable to DDIs due to their advanced age, gender, polypharmacy, increasing length of hospital stay, and the influence of heart disease on drug metabolism. The DDIs potential for a particular anti hypertensive drug varies with the individual, the disease being treated, and the extent of exposure to other drugs. There were less number of studies reported DDIs among hypertensive patients in the Indian setting. Hence, the present study was designed to assess the incidence and pattern of clinically significant DDIs in hospitalized hypertensive patients at a superspeciality hospital, with the assessment of reaction characteristics, outcome, and management [15].

Role of clinical pharmacist in management of hypertension
The role of a clinical pharmacist in community pharmacies is to identify and resolve medication problems, such as prescribing errors and problems that develop from patient behavior. Clinical pharmacists have the knowledge and skill base to contribute to improved medication safety and effectiveness through collaborative participation in patient- specific medication and disease management[16].

Roles of clinical pharmacist in management of diabetes mellitus
Optimizing the drug therapy for achieving the better therapeutic outcomes without causing drug related problems has been considered as the primary goal of therapy in the diabetes management. Well trained and readily accessible clinical pharmacists are the key healthcare professionals who can move closer towards achieving better medication therapy outcomes for the patients. Clinical pharmacist coordinates with the physician during drug therapy and applies his clinical expertise in identifying, resolving and preventing drug related problems by providing interventions which is of valuable aid in accurate, safe and cost effective use of drugs for the physicians[18].

II. METHODOLOGY
MATERIAL AND METHOD

1. Source of data:
Case sheet of In-patients admitted in Medicine Department

2. Method and collection of data:
- **Study site:** Study will be conducted at HKES Basaveshwar Teaching and General Hospital, Kalburgi
- **Study duration:** The study will be carried out for a period of 6 months.
- **Study design:** ―A Prospective observational study‖
- **Study Criteria:** Patients will be enrolled into the study by considering studycriteria.

Inclusion criteria:
- Geriatric Patients of either sex
- Geriatric patients above the age of 60
- Geriatric patient admitted to the medicine department
- Geriatric patients diagnosed with hypertension or diabetes mellitus or both
- Geriatric patient with or without co-morbidity.
- The patient willing to participate in the study.

Exclusion criteria
- Geriatric patient admitted to other departments
- Geriatric patients who are not willing to participate.
- Geriatric patients end stage complications.

CASE STUDY PROCEDURE:
A Prospective observational study as conducted in department of medicine for six months in basawaeshwar teaching and general hospital on patient of above 60 years of age with the prior permission from HOD department of medicine and with prior approval of institutional ethics committee. The geriatric patient will enrolled into the study by confiding study criteria. The prescription of enrolled patients will be analysed as per study criteria. The data will be collected in a suitably designed from patient data collection form.

III. RESULTS AND DISCUSSION

1. Gender Distribution of patients: Among 103 patients enrolled in the which 54(52.42%) Males and 49(47.57%) females.

Gender	Number of patients	Percentage(%)
Male	54	52.42
Female	49	47.57
Total	**103**	**100%**

2. Age distribution of the patient: Age distribution of the patients showed that among 103 patients. 46(44.60%) patients were in the age group of 60-65 years followed by 24(23.30%) patients were in the age group of 66- 70years. 12(11.65%) patient were in the age group of 71-75years, 9(8.73%) patient were in the age group of 76-80years and 11(10.67%) patient were in the age group of 81-85 years. Then finally 01(0.97%) in the age group of 86-90 years.

| Age group	Number of patients	Percentage(%)
60-65	46	44.60
66-70	24	23.30
71-75	12	11.65
76-80	09	8.73
81-85	11	10.67
>86	01	0.97
Total	**103**	**100%**

Diabetic And Hypertensive cases: Among 103 cases observed, The patients with Hypertensive cases were 51(49.51%) and patients with Diabetic cases were 25(24.27%) and the patients with both hypertensive and diabetic cases were 27(26.21%).

| Cases	Number of cases	Percentage (%)
Hypertensive cases	51	49.51
Diabetic cases	25	24.27
Both	27	26.21
Total	**103**	**100%**
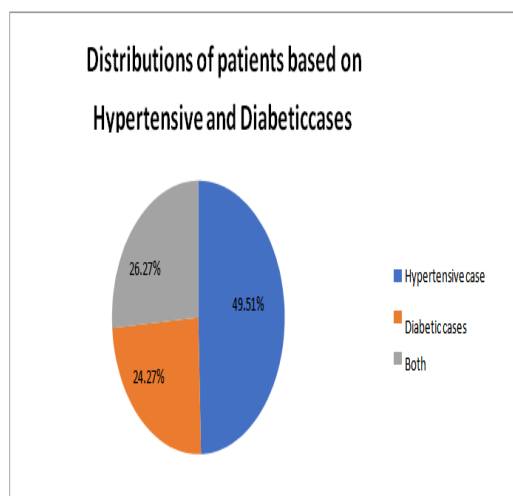
Anti-Hypertensive Drugs: Among 105 anti-hypertensive drugs, there were 38(36.1%) drugs of class Angiotensin antagonist,28(26.6%) drugs of class Diuretics, 24(22.8%) drugs of class Calcium channel blockers, 13(12.3%) drugs of class Beta-blockers, and 02(1.9%) drugs of class ACE inhibitors.

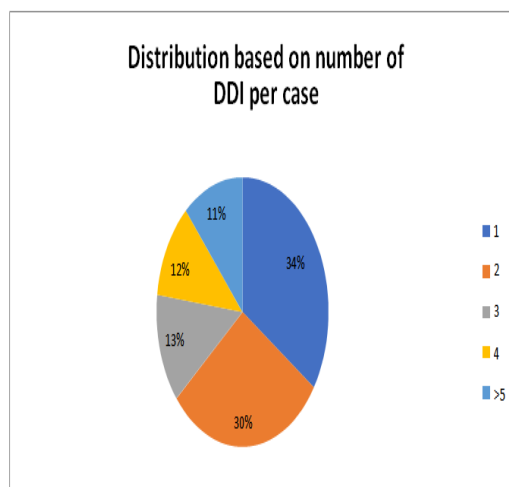| Class of drug	No. of Drugs	Percentage%
1)Angniotensin Antagonist	38	36.1
2)Diuretics	28	26.6
3)Calcium Channel Blockers	24	22.8
4)Beta-Blockers	13	12.3
5)ACE inhibitors	02	1.9
Total	**105**	**(99.7)100%**
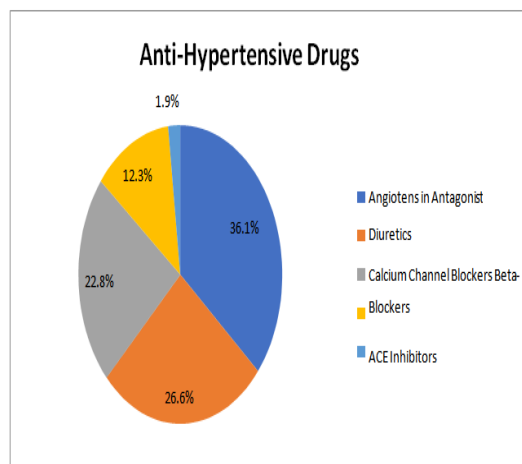
Anti Diabetic Drugs: Among 54 Anti-diabetic drugs, there were 10(18.5%) drugs of class Biguanide,36(66.6%) drugs of class insulin, and 8(14.8*%) drugs of class sulfonylureas

| Class of Drug	No. of Drugs	Percentage
1)Biguanides	10	18.5
2)Insulin	36	66.6
3)Sulfonylureas	8	14.8
Total	**54**	**(99.9)100%**

Anti Diabetic Drugs
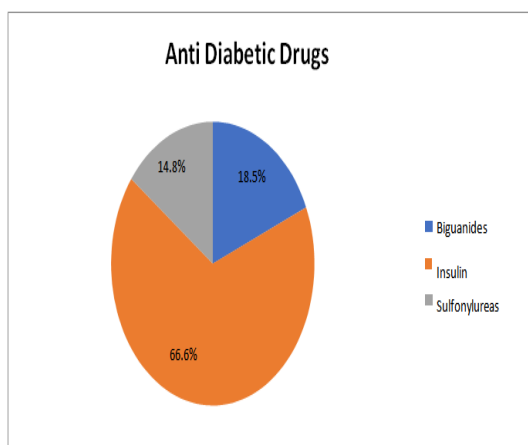
5. **Number of Drug-Drug Interactions per case:** Out of 61 cases containing the Drug-Drug interactions the cases with 1 Drug-Drug interactions were 21(34.42%). The next were 18(29.50%) with 2 Drug-Drug interactions followed by 08 (13.11%) containing 3 Drug-Drug interactions and 4 number of cases containing 7 (11.47%) and >5 Drug-Drug interactions having 7 (11.47%).

Number of Drug-Drug Interactions	Number of Drug-Drug Interactions per case	Percentage(%)
1	21	34.42
2	18	29.50
3	08	13.11
4	07	11.47
>5	07	11.47
Total	**61**	**100%**

Distribution based on number of DDI per case

5. **Drug-Drug Interactions in Diabetic and Hypertensive Cases:** Out of 39 Hypertensive and Diabetic cases, the Hypertensive cases containing Drug-Drug interactions were 22(56.41%) and Diabetic cases containing Drug-Drug interactions were 17(43.58%).

Cases	Number of Drug-Drug interactions	Percentage (%)
Hypertenstive cases	22	56.41
Diabetic Cases	17	43.58
Total	**39**	**100%**

Distribution based on Number of Drug-Drug interactions in hypertensive and Diabetic cases
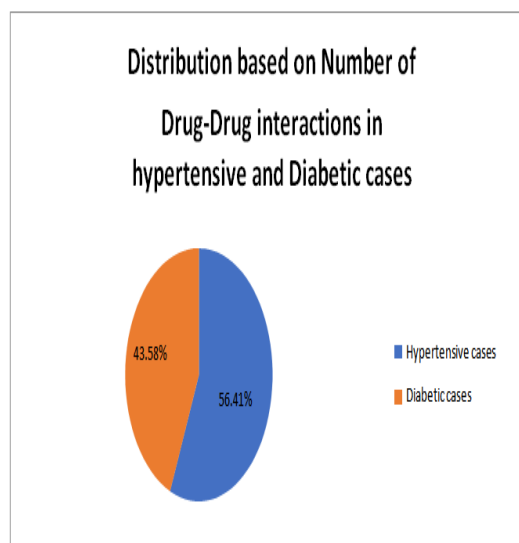
Ploypharmacy in prescription: Among the Polypharmacy cases 68(66.01%) were major and 28(27.18%) were moderate and 07(6.79%) were minor

Type of polypharmacy	Number of cases	Percentage
Major	68	66.70
Moderate	28	27.18
Minor	07	6.79
Total	**103**	**100%**

Poly pharmacy in prescriptions
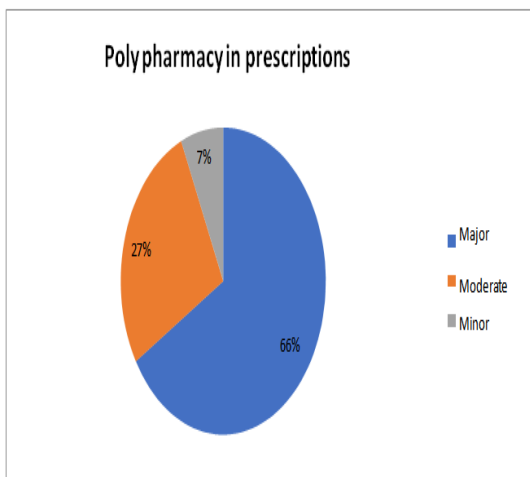
Co-Morbidities: :Among 103 cases enrolled in the study, patient having co-morbid conditions. The Patient with 1 co- morbid condtion were 40((38.83%). 2 co-morbid condition were 36(34.95%) and 3 co-morbid conditions were 15(14.56%) and co-morbid condition >4 were 9(8.73%) and least observed on the patients with 0 c0- morbid condition were 3(2.91%)

Number of co-morbidities	Number of cases	Percentage (%)
0	03	2.91
1	40	38.83
2	36	34.95
3	15	14.56
>4	09	8.73
Total	**103**	**100%**

Distribution of patient based on number of co-morbid conditions
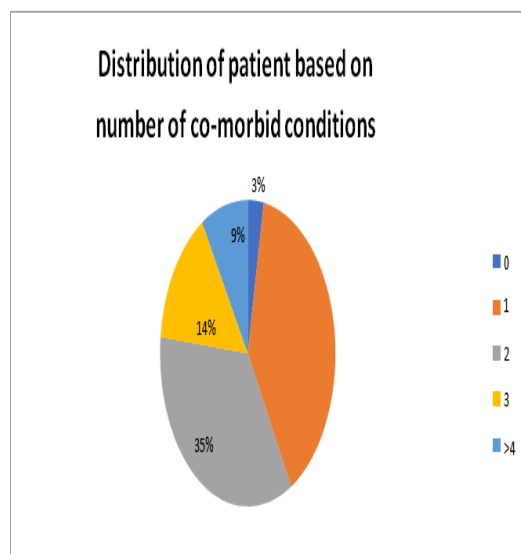
Severity using Micromedex: Among 161 drugs interactions observed were major 80(49.68%), Moderate DDIs were 74(45.96%), Contea-indication were 5(3.10%) and minor were 02(1.24%)

Severity level	Number of cases	Percentage (%)
Major	80	49.68
Moderate	74	45.96
Minor	02	1.24
Contra indications	05	3.10
Total	**161**	**100%**

Distribution of DDI According to severity
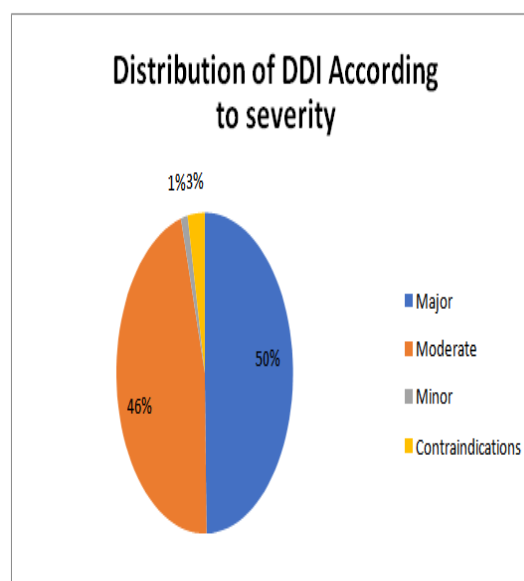
IV. DISCUSSION

Among 103 patients enrolled, the gender distribution of the patients showed that DDIs were more in (52.42%) Males than the (47.57%) Females. Our findings were found to be similar to studies carried out by (61.25% Males and 38.75% females) Mangi AA et al[22], (56.6% Males and 43.4% females) Annie Mariya Joseph et al[5], (47% Males and 53% females) Shailesh Nagpure et al[30], shown that the rate of DDIs are more in Males than females.

Age distribution of patients:

Among 103 patients enrolled, the age distributions of the patients reveals that the rate of DDIswere more, (44.60%) in the age group of 60-65 years and (23.30%) in the rage of 66-70 years.The studies conducted by (41.6%) Ansha Subramanian et al[12], were found to be similar. Whereas the study conducted by (44.76%) Manjusha S et al[31], shown the rate of DDI more in the range of 60-65 years and 66-70 years respectively.

Polypharmacy Prescriptions:

For 103 patients enrolled in this study the results showed that the average number of drugs prescribed per prescription is 9.8, Whereas the study conducted by Annie Mariya Joseph et al[5], showed 8.7 as the average number of drugs prescribed per prescription which is almost similar to our study.

Number of Co- Morbidties:

Among 103 cases enrolled in the study patient having co-morbid conditions. The patient with 1 co- morbid condition were 40(38.9%), 2 co-morbid conditions were 36 (34.95%) and >3 co-morbid condition were 15(14.56%). Our findings were found to be similar to studies carried by 1 co - morbid conditions were (27.9%), 2 co- morbid conditions were (16%) and >3 co- morbid conditions were(5.6%) Juhwan Noh MD et al[35].

Category and Class of Anti-Hypertensive and Anti-Diabetic medications:

Among 105 anti-hypertensive drugs prescribed, the results showed that angiotensin antagonist class of drugs were more (36.1%) than the other class of anti-hypertensive drugs. The studies conducted by (34.9%) Supratim Datta et al[32], were found to be similar.

Among 54 anti-diabetic drugs prescribed, the results showed that the class of Insulin drugs were more (66.6%) than the other class of anti-diabetic drugs. The studies conducted by(52%) Abdul Hannan et al[33], were found to be similar.

Number Drug-Drug Interactions:

Among 103 patients enrolled 61 prescriptions contained total of 155 DDIs with an average of per prescriptions is 9.8. The results showed that 21(34.2%) patients were with 1 DDI, followed by 18(29.5%) patients were with 2 DDIs ,8 (13.11%) patients were with 3 DDIs. Our findings were found to be similar with studies conducted by Lujaw RT et al[34], which reports the rate of DDIs was 48(37.8%), 6(4.7%) and 1(0.8%) in 1,2 and 3 DDIs respectively.

Distribution based on Severity (Using Micromedex):

Among the 161 DDIs, the rate of major DDIs was 80(49.68%) followed by moderate DDIs 74(35.96%) and minor DDIs 02(1.24%) and contra-indications were 5(3.1%). Our findings were found to be Similar with Rajat KA et al[24], 32(7.94%) major DDIs, followed by 204(50.62%) of Moderate DDIs and 35(8.64%) minor DDIs.

V. CONCLUSION

Our study concludes that among 103 geriatric patients enrolled, majority of the patients were males and majority of them belongs to the age group of (60-65 years).

When Drug-Drug interaction were assessed majority of the prescription (59.2%) were with drug-drug interactions, these are of more concern.

Among 103 patients, there are more number of hypertension cases when compared to diabetesmellitus.

Among 51 hypertension patients the major class of drug used was angiotensin antagonist. Theminimal use ACE inhibitors was observed. Among 25 geriatric diabetic patients Biguanides were the drug of choice when compared to sulfonylureas.

When the drug-drug interactions analysed among geriatrics, a total of 61 drug- drug interactions were noticed, among 61 interactions 22 prescriptions contained drug interactions more than 3 per prescriptions. These need to be addressed by informing the physicians in regard to these in order to reduce the drug-drug interactions.

The increased number of drug interactions among geriatric need to specially addressed as it may increase the hospital readmission and pharmacoeconomic burden.

The distribution of drug- drug interactions based on severity reveals that about 50% of the drug interactions were major drug interaction, these may lead to morbidity and mortality among the geriatrics.

Finally, we conclude that there were highest number of drug interactions found at the study site, hence there is need to conduct educational program to the physician in order to reduce the drug- drug interactions. In this regard the clinical pharmacist may play a key role.

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AUTHOR'S CONTRIBUTION
All the authors have contributed equally.

CONFLICT OF INTEREST
All the authors declare no conflict of interest.

ETHICS DECLARATION
The protocol was verified by the Institutional Ethic Committee of Rajiv Gandhi college of pharmacy Kalaburgi.
Informed consent was obtained from the BTGH hospital kalaburgi.

CONSENT FOR PUBLICATION
All authors have given their consent for publication

COMPETING INTERESTS
The authors declare that they have no competing interests.

AUTHORS FUNDING

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