International Journal of Health Care and Biological Sciences

Research Article Open Access

A prospective observational study on drug-drug interactions in chronic kidney disease patients

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Article History

Received on: 06-02-2021
Revised On : 15-02-2021
Accepted on : 22-04-2022

***Keywords*:** Chronic Kidney Disease, Drug-Drug interactions.

DOI:
https://doi.org/10.46795/ijhcbs.v3i2.307

Abstract

Aim: To review Drug-Drug interactions among CKD patients.

Methodology: A concurrent conciliation study was performed on CKD patients with drug-drug interactions admitted in and around tertiary government and corporate hospitals, Visakhapatnam, Andhra Pradesh, India. Information regarding gender, and variety of drug interactions as mild, moderate, and major were recorded in the standard questionnaire.

Result: Overall 150 prescriptions were included after excluding missing data. The impact of concomitant disease in causing drug-drug interactions in 150 prescriptions them were Hypertension -35%, Diabetes Mellitus-19%, Hyperlipidemia-8%, Asthma- 7%, Seizures- 6%, Thyroid -5%, Congestive Heart Failure- 1%. Total of 201 interactions were revealed of which 15 were major interactions, 139 were moderate interactions, 47 were minor interactions.

Conclusion: By assessing the above data it absolutely was concluded that the patient should possess sound knowledge of drug interactions before employing a selected drug or two or more drugs at the identical time so as to possess identical medication.

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Introduction

Chronic kidney disease is a slow and progressive loss of kidney function over a period of several years. Eventually, people may develop permanent Nephropathy. It's far more widespread than people realize. It often goes undetected and undiagnosed until the disease is well advanced. It's commonplace for people to realize they have chronic kidney failure only When their kidney function is all the way down to 25 percent of normal. As the renal disorder advances and therefore the organ's function is severely impaired, dangerous levels of waste and fluid can rapidly build up within the body. Treatment is aimed at stopping or slowing down the progression of the disease; this is often usually done by controlling its underlying cause.

Stages

Changes within the GFR rate can assess how advanced the nephrosis is. In the UK, and plenty of other countries, uropathy stages are classified as follows:

Stage 1

GFR rate is normal. However, evidence of renal disorder has been detected.

Stage 2

GFR rate is not up to 90 milliliters, and evidence of nephrosis has been detected.

Stage 3

GFR rate is under 60 milliliters, regardless of whether evidence of renal disorder has been detected.

Stage 4

GFR rate is under 30 milliliters, irrespective of whether evidence of renal disorder has been detected.

Etiology

- Diabetes
- Specific kidney diseases, which incorporate polycystic uropathy.

Symptoms

The most common signs and symptoms of chronic uropathy include:

- Anemia
- Blood in urine
- Dark urine
- Decreased mental alertness
- Decreased urine output
- Edema - swollen feet, hands, and ankles (face if edema is severe)
- Fatigue (tiredness)
- Hypertension (high blood pressure)
- Insomnia
- Itchy skin, can become persistent
- Loss of appetite
- Male inability to get or maintain an erection (erectile dysfunction)
- More frequent urination, especially at night
- Muscle cramps
- Muscle twitches
- Nausea
- Pain on the side or mid to lower back
- Panting (shortness of breath)
- Protein in urine
- Sudden change in body weight

Drug-Drug Interaction

The phenomenon of drug interaction is defined as when the consequences of one drug are changed by the presence of another drug, food, or environmental agent. Drug interaction refers to the modification of response to at least one drug by another once they are administered simultaneously. The modification is generally quantitative, but sometimes it's qualitative. With the increasing availability of complex therapeutic agents and widespread polypharmacy, the potential for drug interaction is big.

Types of drugs most presumably to be involved in clinically important drug interactions

- Drug with a narrow margin of error, e.g. aminoglycoside antibiotics, digoxin, lithium.
- Drugs affecting closely regulated body functions, e.g. antihypertensive, antidiabetics, anticoagulants.
- Highly protein-bound drugs NSAIDs, oral anticoagulants, sulfonylureas.
- Drugs are metabolized by saturation kinetics, e.g. phenytoin, theophylline.

Types of Drug Interactions

Depending on the sort of the effect produced

Inhibiting drug interaction

An inhibiting interaction partially or completely prevents a drug from excreting its action thus diminishing its effect on the patient. E.g. Amphetamine and barbiturates Morphine and naloxone Adrenaline and propranolol

Potentiating drug interaction

A potentiating interaction enhances the toxic or therapeutic effect of a drug in patients.

E.g. Levodopa and carbidopa Sulphonamide and trimethoprim, Isoniazid and rifampicin

Causes of Drug Interactions

1. **Drug explosion, administration of two or more drugs simultaneously**
   It is a standard practice to prescribe more drugs at a time, which is referred to as "therapeutic jungle" or "polypharmacy"
2. **Patients may refer many doctors**
   Sometimes a patient isn't satisfied with the treatment of one doctor and will consult another doctor without informing about the consultation of the primary doctor.
3. **Irrational polypharmacy, concurrent use of prescribed and non-prescribed drugs**
   A patient may take drugs like Aspirin, and antacid which is available without a physician's prescription. If such patients are on other drugs prescribed by a physician for example digoxin or tetracycline, the drug interaction may occur.
4. **Patients' noncompliance**
   Sometimes patients don't adjust to the instructions given by the physician and may take food material that is being prohibited. For example, cheese with

monoamine oxidase inhibitors might lead to a severe hypertension crisis.

Factors Chargeable For Drug Interaction

- Insufficient knowledge: Inadequate understanding of pharmacokinetics and pharmacodynamics of the drug may result in drug interaction.
- Dietary factors: Constituents of an individual's diet include foodstuff- vegetables which can interact with certain drugs.
- Physiology of the individual: Factors like age, sex, weight, and genetic abnormalities influence the occurrence of drug interactions.
- Presence of disease states: Pathological conditions like liver disease, kidney damage, or altered enzyme systems may affect the handling of medicine by the body and lead cause adverse drug interaction.

Mechanism of Drug Interaction

- Pharmacokinetic interaction
- Pharmacodynamics interaction
- Synergistic interaction
- Antagonistic interaction

Materials of Methodology

Study site: The study was performed in and around tertiary government and corporate hospitals of Visakhapatnam.

Study period: The study was conducted for a period of 5months.

Study design: Observational and methodological design.

Sample size: A total of 150 prescriptions will be included in this study.

Study criteria

Inclusion criteria

- Male and female aged 18-70 years.
- Patients who are willing to sign the consent form.

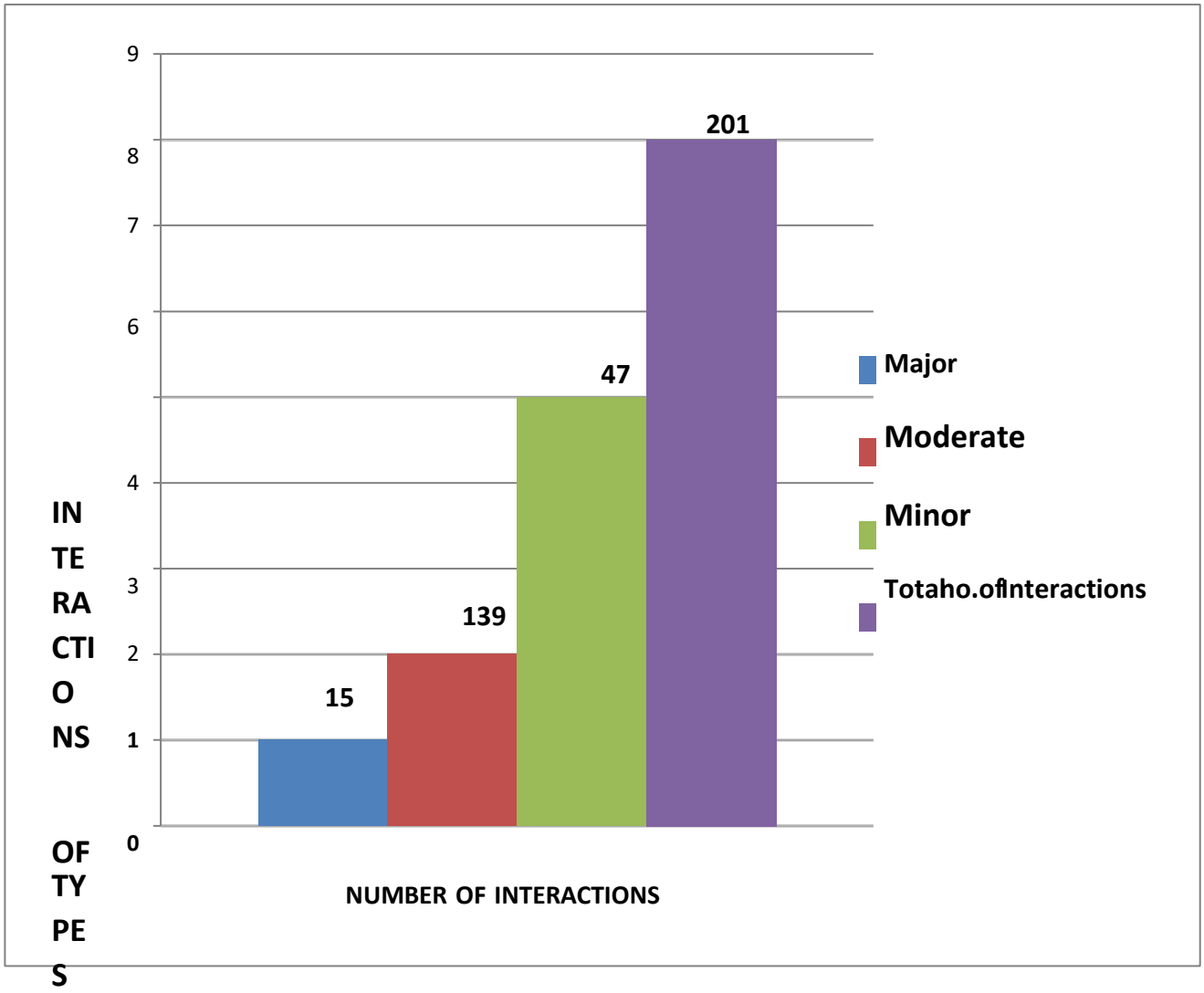
Exclusion criteria

- Male and female aged above 70 years. Pregnant women.
- Male and female aged below 18 years.
- Patients who are not willing to sign the consent form.

Results

Categorization of DDI According To Severity

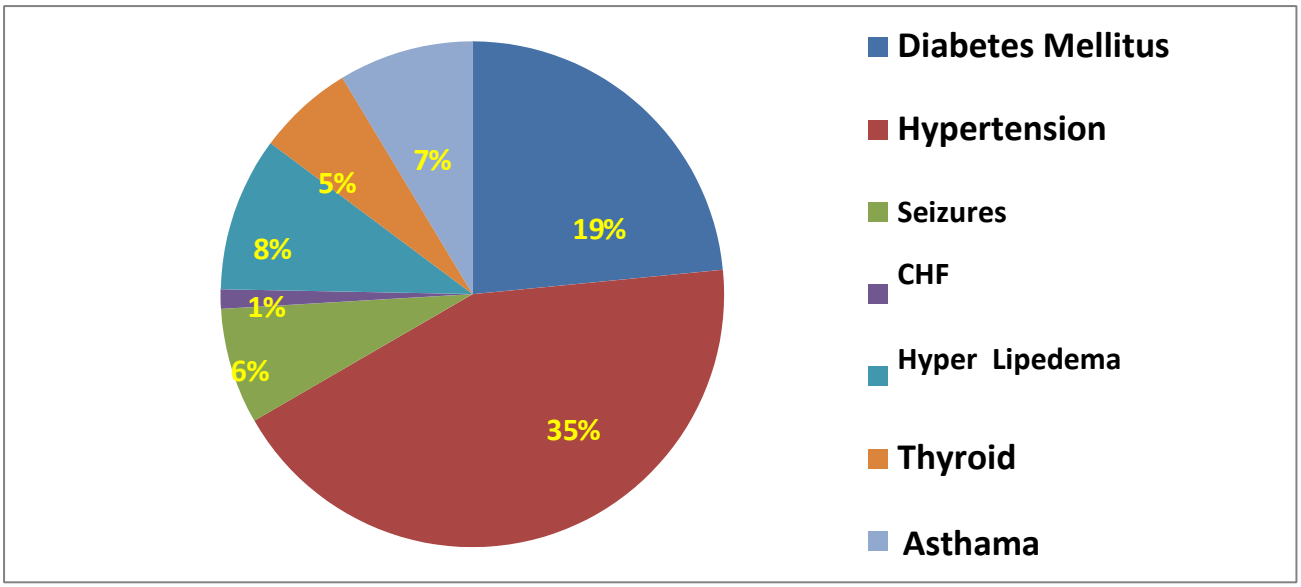
Total no. of prescriptions	Major Interactions	Moderate interactions	Minor interactions	Total no. of interactions
150	15	139	47	201



A Graph was plotted against no. of interactions on Y-Axis and types of interactions on X-axis. In which 201 are total interactions and out of which 15 are major interactions, 139 are moderate interactions, 47 are minor interactions.

Impact of Concomitant Disease in Causing Drug-Drug Interactions

Type of concomitant disease	No. of prescriptions
Diabetes mellitus	19
Hypertension	35
Seizures	6
CHF	1
Hyperlipidemia	8
Thyroid I	5
Asthma	7

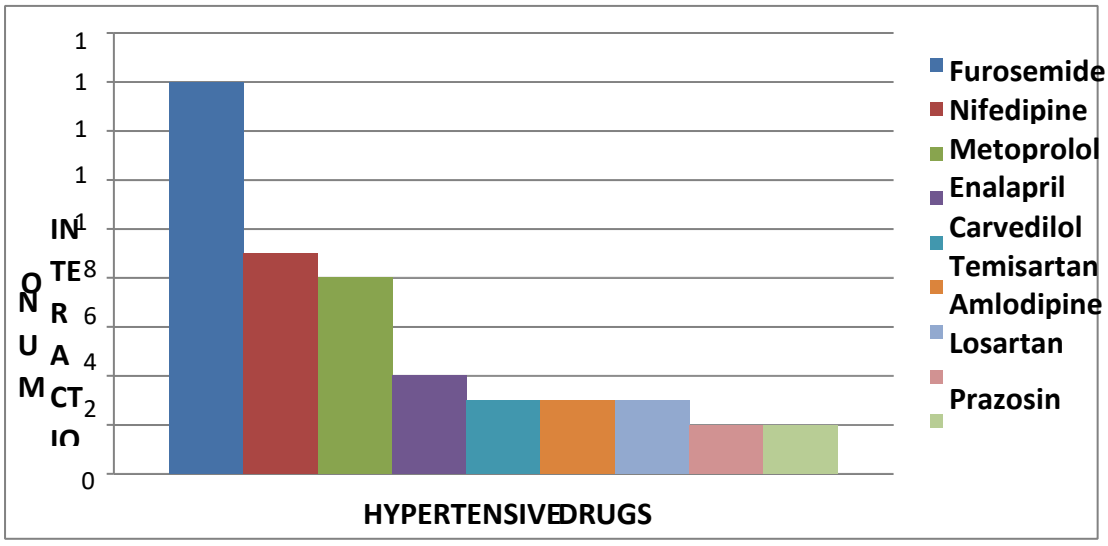


A pie chart was drawn on impact of concomitant disease in 150 prescriptions in which Hypertension was major concomitant disease in 131 prescriptions. And next to diabetes was found in 19 prescription.

3. Hypertensive Drugs Involved In Drug Interactions

Hypertensive drugs	No of interactions
Furosemide	16
Nifedipine	9
Metoprolol	8
Enalapril	4
Carvedilol	3
Telmisartan	3
Amlodipine	3
Losartan	2
Prazosin	2
Atenolol	2

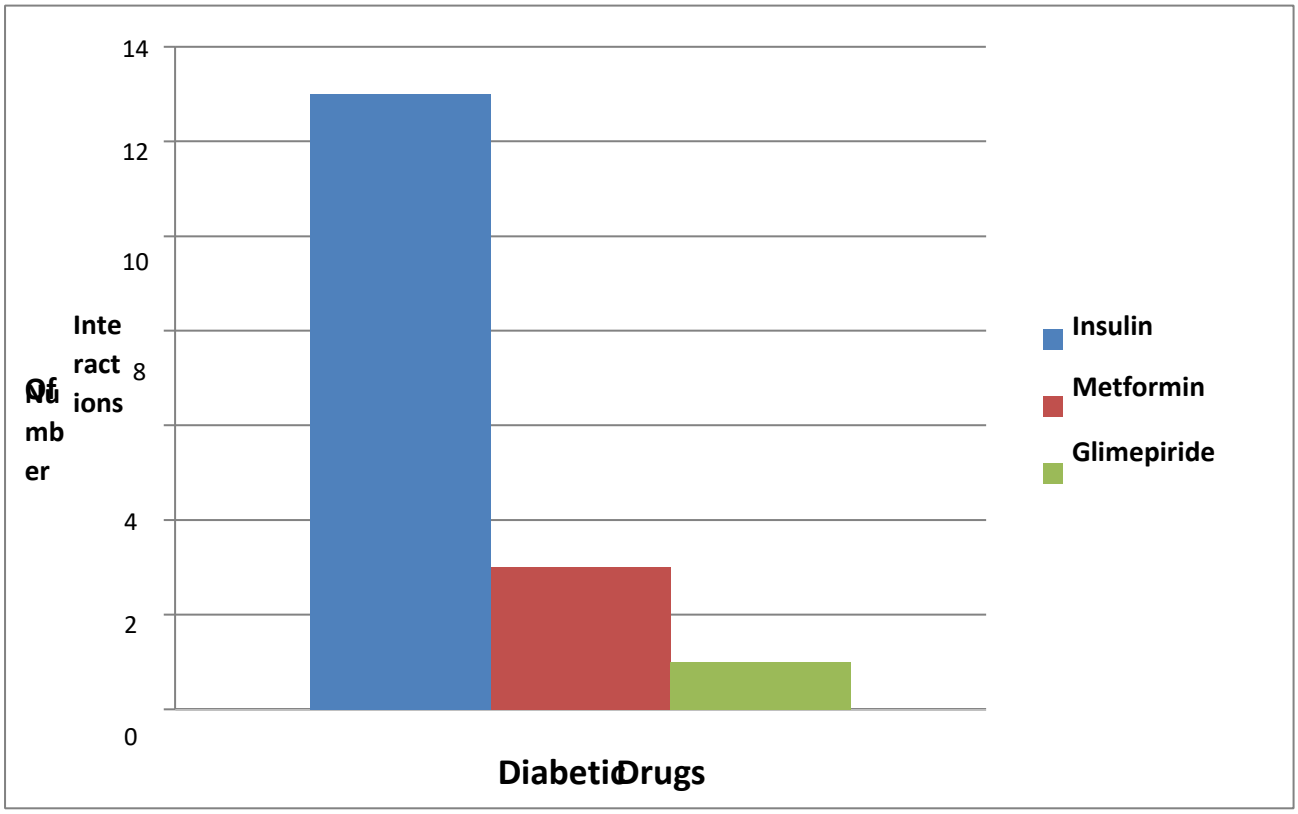
Graphical representation of Hypertensive drugs involved in drug interactions



Diabetic Drugs Involved In Drug Interactions

Diabetic drugs	Insulin	Metformin	Glimepiride
no of interactions	13	3	1

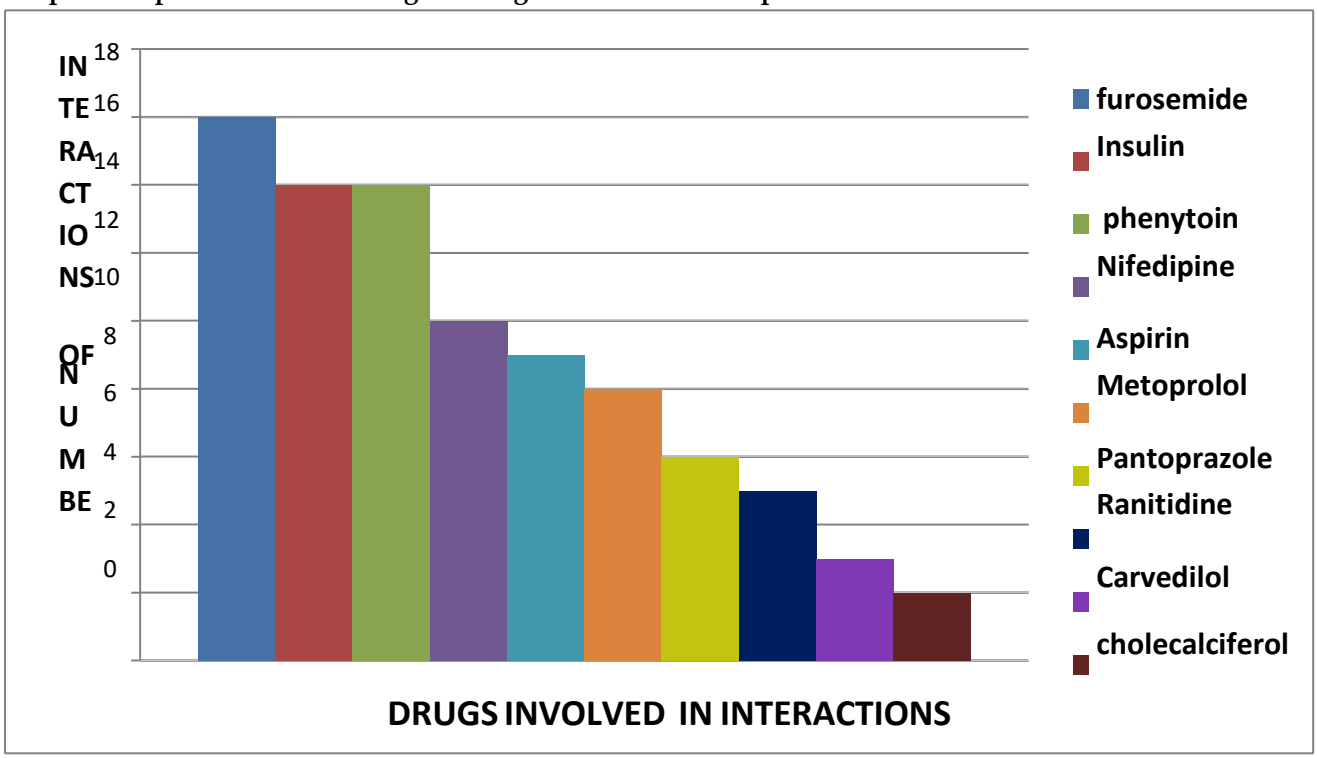
A Graph was plotted between no. of interactions on the Y-Axis and diabetic drugs on the X-axis in which Insulin was involved in 13 interactions out of 201 interactions.



Drugs Causing Major Number of Drug- Drug Interactions:

The dru involved in multiple interactions	No . of interactions
Furosemide	16
Aspirin	9 I
Insulin	14
Rantidine	5 I
Cholecalciferol	2
Carvedilol	3 I
Phenytoin	14
Pantoprazole	6 I

Graphical representation showing the drugs involved in multiple interactions



Percentage of drugs involved in multiple interactions

Drug involve in multiple interactions	No .of interactions	Percentage of Interactions
Furosemide	16	18.39%
Aspirin	9 I	10.34% I
Insulin	14	16.09%
Nifedipine	10 I	11.49% I
Metoprolol	8	9.19%
IRantidine	5 I	5.74% I
Cholecalciferol	2	2.29 %
Carvedilol	3 I	3.44% I
Phenytoin	14	16.09%
Pantoprazole	6 I	6.89% I

Discussion

The study included the prescription of 150 CKD patients. Potential drug interactions were detected in 148 patients. A grand total of 201 interactions were identified in which

Major Interactions- 15

Moderate Interactions- 139

Minor Interactions- 47

Inappropriate polypharmacy can lead to significant morbidities and mortality. Hypertension patients have a high risk of drug-drug interactions as it is observed that anti-hypertensives have been indicated with a high no. of DDI'S. The use of anti-diabetic drugs in CKD patients may cause serious hypoglycemia/ metabolic acidosis due to its precipitation. Our findings prove the optimization of the drug regimens offered to CKD patients in order to prevent the incidence of DDI.

Conclusion

The present review concludes that people should possess sound knowledge of drug interaction before using a particular drug or two or more drugs at the same time, in order to have safe medication.

The risk of DDI's in CKD patients is very high. They may need a dose adjustment or avoidance of some drug combinations. Physicians and clinical pharmacists should make use of available interaction software (Medscape, Drugs. com) in order to check for any potential drug interactions present. A cordial integrated relationship between healthcare professionals and pharmacists should be encouraged in order to optimize CKD patients' care and to reduce the occurrences of harmful drug-drug interactions in them. Reducing DDI saves lives and reduce mortality, morbidity, and healthcare cost. The prescription analysis is to be done on patients who are taking multiple drugs. Pharmacists should counsel the patient regarding the effects of drug-drug interactions for achieving safe drug therapy.

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