Research Article

Potential drug interactions in chronic kidney disease patients - A cross sectional study

S Hegde[1], P Udaykumar[2*], M S Manjuprasad[3]

[1,3]PG Student, [2]Professor and HOD, Department of Pharmacology, Father Muller Medical College, Kankanady, Mangalore-575002, Karnataka, INDIA.

Email: shramikahegde@gmail.com, padmajaudaykumar@gmail.com, manjuprasadms@gmail.com

Abstract

Chronic kidney disease (CKD) is a major systemic condition whose prevalence is rising in India. Presence of comorbid conditions like hypertension, diabetes mellitus, metabolic bone disease and electrolyte disturbances along with the deteriorating renal function makes the management of CKD complex .The aim of this study was to assess the pattern of drug drug interactions in CKD patients. This was a prospective cross sectional study conducted in a tertiary care medical hospital in India. A total of 120 patients were enrolled and the list of drug interactions in them was analysed using drug interaction software. The mean age of the study group was 58.53±8.38 years. Hyperphosphataemia, hypertension and diabetes mellitus were among the frequently associated comorbid illnesses.146 potential drug drug interactions (PDDI) were found with an average of 2.39 interactions per patient. Of these 38.14% were mild, 45.36% were moderate and 16.41% were severe. Hypotension, hypertension, hyperkalemia, hypokalemia, anemia, hyperphosphatemia, hyperuricemia were among the commonest outcomes of interactions. Sodium bicarbonate, ferrous sulfate, calcium carbonate, aspirin, pantoprazole, allopurinol were the drugs commonly involved in PDDI. There was a positive correlation between the age and number of interactions (Karl Pearson correlation coefficient: 0.607; p value<0.001) and the number of tablets and number of interactions (karl pearson coefficient: 0.876; p value<0.001). The prevalence of PDDI among CKD patients in this study was high (80.83%). Hence, rational prescription, early detection of harmful drug combinations and careful monitoring of these patients can prevent the occurrence of drug interactions.

Keywords: Potential drug drug interactions, drug interactions, chronic kidney disease, end stage renal disease, polypharmacy.

***Address for Correspondence:**
Dr. Padmaja Udaykumar, Professor and HOD, Department of Pharmacology, Father Muller Medical College, Kankanady, Mangalore, 575002, Karnataka, INDIA.
Email: padmajaudaykumar@gmail.com

Received Date: 18/05/2015 Revised Date: 29/06/2015 Accepted Date: 01/08/2015

Access this article online	
Quick Response Code:	Website: www.statperson.com
	Volume 5 Issue 3

INTRODUCTION

Chronic kidney disease is emerging as a major health concern. The prevalence of chronic kidney disease (CKD) and end stage renal disease (ESRD) is increasing globally which may be attributed to the rising prevalence of diabetes mellitus, hypertension and ischemic heart disease.[1] Prevalence of CKD in India is approximately 800 per million population (pmp), and ESRD is 150-200 pmp.[2] According to the Kidney Disease Outcomes Quality Initiative (KDOQI) and Kidney Disease Improving Global Outcomes (KDIGO) guidelines, CKD is defined as the presence of kidney damage **or** decreased kidney function for three or more months, irrespective of the cause.[3] Kidney damage refers to pathologic abnormalities (reported by renal biopsy or imaging studies) or as indicated by markers such as urinary sediment abnormalities or increased rates of urinary albumin excretion. Decreased kidney function implies to a decreased glomerular filtration rate (GFR) estimated usually by serum creatinine levels. The management of CKD involves tackling the reversible causes of renal dysfunction and preventing or slowing down the progression of renal disease. The deteriorating renal function in these patients may lead to many complications like hyperkalemia, metabolic acidosis, volume overload and hyperphosphatemia accompanied by certain systemic and endocrine disturbances like anorexia, nausea,

How to cite this article: S Hegde, P Udaykumar, M S Manjuprasad. Potential drug interactions in chronic kidney disease patients- A cross sectional study. *International Journal of Recent Trends in Science and Technology* July to September 2015; 5(3): 56-60 http://www.statperson.com

vomiting, fatigue, hypertension, anemia, malnutrition, hyperlipidemia, and metabolic bone disease.[4] The presence of several co-morbid conditions makes the medical therapy of CKD patients complex.[5] Multiple medication use is commonly encountered in CKD patients due to the associated co-morbid conditions. Inevitably, CKD patients are at a higher risk for drug drug interactions (DDI). DDI are regarded as preventable medication related problems. It has been found that 11% of patients experience symptoms due to DDI and about 2.8% of hospital admissions occur as a result of DDI.[6] This study is conducted with an aim of finding the pattern of potential drug drug interactions in a patient with chronic kidney disease. With the sound knowledge of pharmacokinetic and pharmacodynamic properties of different medications, health care professionals can predict the potential drug drug interactions in a patient.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted in a tertiary care hospital in India. The study subjects were patients with a diagnosis of chronic kidney disease admitted in the nephrology ward of the hospital. The study was carried out over the duration of six months. It was approved by the Institutional Ethics Committee.

Selection Criteria

Inclusion Criteria

- Patients diagnosed with chronic kidney disease admitted for at least last 48 hrs.
- Patients above the age of 18 years of either sex.

Exclusion Criteria

- Patients diagnosed as acute renal failure.
- Patients on enteral feeds.
- Patients on herbal medications.
- Chronic alcoholics.

A written informed consent was taken from each patient enrolled in this study. Relevant data (patient demographic details, diagnosis, list of prescribed medications and duration of hospital stay) were documented in a case record form. The potential drug drug interactions were analyzed using Medscape Drug interaction checker tool (http://reference.medscape.com/drug-interactionchecker). The drug interactions detected by the software was documented. Data were analyzed using mean, frequency, percentage, Karl pearson coefficient correlation and Chi square test. SPSS software version 16.0 was used.

OBSERVATIONS AND RESULTS

A total of 120 patients were included in the study. Out of the total subjects, 97 (80.83%) patients showed potential drug drug interactions (Figure 1). The mean age of the subjects was 58.53±8.38 years. The study population consisted of 66 males (55%) and 54 females (45%) (Figure 1)

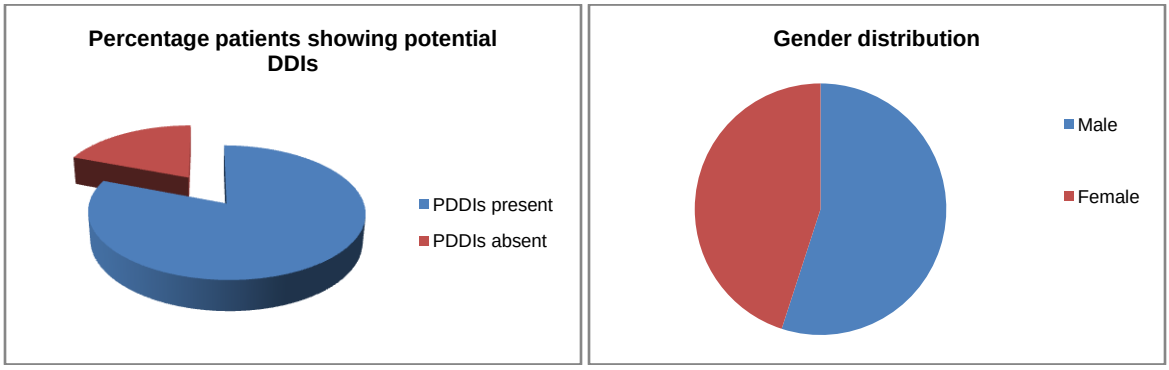

Figure 1: Percentage of PDDI and gender distribution

Co-morbid conditions: The following co-morbid conditions were seen in the study subjects. (Table 1)

Table 1: Comorbid conditions

Condition	Number of patients
Hyperphosphatemia	78
Hypertension (total)	48
Diabetes mellitus(total)	41
Hypertension +Diabetes	29
Congestive heart failure	16
Acute myocardial infarction	13
Hyperuricemia	8
Atrial fibrillation	4
Unstable angina	3

Characteristics of drug drug interactions

Among the 97 patients, 146 PDDI were found with an average of 2.39 interactions per patient. These interactions were categorized into mild (38.14%), moderate (45.36%) and severe (16.41%). Of the total 146 PDDI noted, majority were due to pharmacodynamic interactions (45.20%), 36.30% due to pharmacokinetic and the rest 18.49% were of unspecified nature. The pattern of PDDI in chronic kidney disease patients is shown in Table 2.

Table 2: Pattern of PDDI

DDI	Number
sodium bicarbonate + ferrous sulfate	13
calcium carbonate + ferrous sulfate	8
aspirin + carvedilol	8
sodium bicarbonate + allopurinol	8
pantoprazole + ferrous sulphate	7
aspirin + prazosin	6
aspirin + torsemide	6
aspirin + atenolol	5
aspirin + amlodipine	5
calcium carbonate + amlodipine	5
atorvastatin + digoxin	5
calcium acetate + amlodipine	4
aspirin + losartan	4
carvedilol + digoxin	4
sodium bicarbonate + digoxin	4
sodium bicarbonate + atenolol	4
ofloxacin+sodium bicarbonate	4
losartan + atenolol	3
torsemide + digoxin	3
aspirin + digoxin	3
digoxin + torsemide	3
prazosin + amlodipine	3
clonidine + prazosin	2
calcium carbonate + atenolol	2
calcium acetate + atenolol	2
carvedilol + torsemide	2
insulin +metoprolol	2
aspirin + glimepiride	2
spironolactone + aspirin	2
ferrous sulfate + methyldopa	2
calcium carbonate + carvedilol	2
pantoprazole + digoxin	2
ferrous sulfate + levodopa	2
sodium bicarbonate + carvedilol	1
spironolactone + atorvastatin	1
losartan + spironolactone	1
calcium carbonate + nicardipine	1
carvedilol + nicardipine	1
hydralazine + carvedilol	1
prazosin + atenolol	1
calcium acetate + ibandronate	1
ofloxacin+ferrous sulphate	1

List of the most frequent PDDI is shown in the below table **(table 3)**

Table 3: List of the most frequent PDDI

Sodium bicarbonate + ferrous sulphate	13	sodium bicarbonate will decrease the level or effect of ferrous sulfate by increasing gastric pH.
Calcium carbonate + ferrous sulphate	8	calcium carbonate will decrease the level or effect of ferrous sulfate by increasing gastric pH.
Aspirin + carvedilol	8	aspirin decreases effects of carvedilol by pharmacodynamic antagonism.
Sodium bicarbonate + allopurinol	8	sodium bicarbonate decreases levels of allopurinol by inhibition of GI absorption.
Pantoprazole + ferrous sulphate	7	pantoprazole will decrease the level or effect of ferrous sulfate by increasing gastric pH.
Aspirin + prazosin	6	Prazosin absorption is reduced by aspirin
Aspirin + torsemide	6	aspirin increases and torsemide decreases serum potassium. Careful monitoring of serum potassium required.

Aspirin + atenolol	5	aspirin decreases effects of atenolol
Aspirin + amlodipine	5	Additive antihypertensive effect may be seen .
Calcium carbonate + amlodipine	5	calcium carbonate decreases effects of amlodipine by pharmacodynamic antagonism.
Atorvastatin + digoxin	5	atorvastatin will increase the level or effect of digoxin by P-glycoprotein (MDR1) efflux transporter.

The correlation between age of the patient, number of tablets prescribed/day and the number of drug interactions is shown in the table 4, figure 2 and figure 3.

Table 4: Correlation between age of the patient, number of tablets prescribed/day and the number of drug interactions

	Karl pearson correlation coefficient	p value
Age- number of tablets	0.489	p<0.001
Age- number of interactions	0.607	p<0.001
Number of tablets- number of interactions	0.876	p<0.001

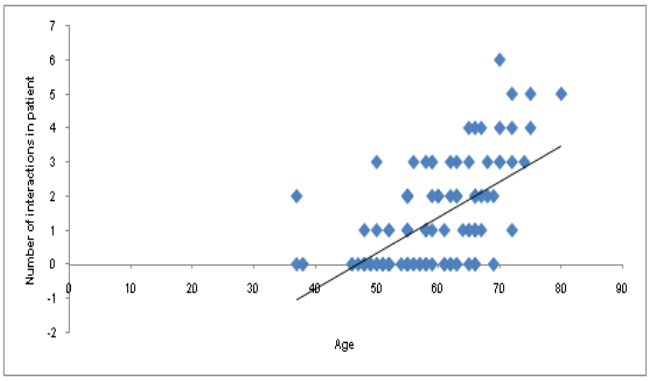

Figure 2

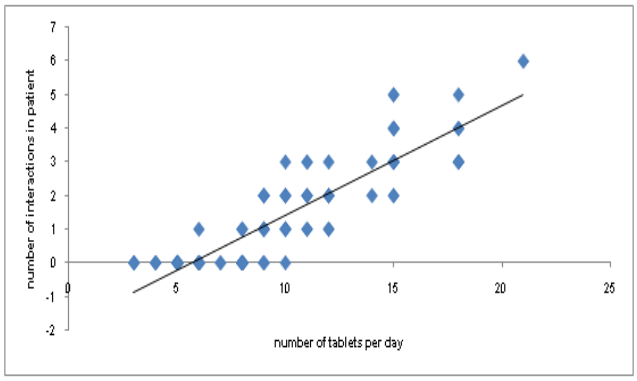

Figure 3

Legend

Figure 2: Scatter plot showing age and number of interaction

Figure 3: Scatter plot showing correlation between number of tablets/day and number of interactions in a patient

DISCUSSION

The present study was undertaken to see the pattern of drug drug interactions in chronic kidney disease patients. It was found that PDDI could occur in 80.83% of CKD patients which indicates that the frequency was high. An average of 2.39 interactions per patient was seen. In a study done by Dubova *et al* on ambulatory patients above 50 years of age, it was seen that the 80% of the patients had prescription with PDDI which was the same as seen in our study .[7] In another study by Marquito AB *et al* done in a similar setting as the present study on chronic kidney disease patients, the frequency was 74.9%.[8] Therefore it is seen that the prevalence of DDI is high in chronic kidney disease patients. In this study we see an increase in the number of interactions with the increase in age. There was a positive correlation between age and number of interactions (Karl Pearson correlation coefficient: 0.607; p value<0.001). Similar findings were documented in a study done by Chavda NB *et al* to assess PDDI on Indian patients attending medicine outpatient department.[9] The study by Marquito AB *et al* also confirms the correlation between age and number of interactions. The number of tablets prescribed per patient per day in our study ranged from 3-21. The average was 9.38±3.89 tablets/day. This was less compared to the figures stated by M Rama *et al* in their study conducted in a tertiary care hospital where the average number of tablets per day was 12.08±6.30 with 3-27 medicines/day.[10] There was a positive correlation seen between the number of tablets prescribed per day and the number of interactions (karl pearson coefficient: 0.876; p value<0.001). In the current study, the drugs prescribed for comorbid conditions like hyperphosphatemia, hypertension and nutritional deficiency contributed the most for the PDDI. Majority of the drug interactions were of moderate severity which was a common finding in the previous studies also.[8,10] The commonest interactions were that of ferrous sulfate with sodium bicarbonate and with calcium carbonate where the level or effect of ferrous sulphate would be decreased due to the raised intragastric pH by the latter agents. However these were minor interactions. Most of the PDDI seen were due to pharmacodynamic interactions. The outcome of these drug interactions were reduced drug levels (leading to diminished therapeutic efficacy and precipitation or worsening of the treating condition), increased drug

levels (leading to enhanced therapeutic effect or toxicity) and serum electrolyte disturbances. Hypotension, hypertension, hyperkalemia, hypokalemia, anemia, hyperphosphatemia, hyperuricemia were among the common manifestations. Previous studies have shown that polypharmacy is one of the major causes of drug interactions.[11,12,13] In patients with chronic kidney disease, multiple medication use cannot be avoided in most of the situations for the welfare of the patient. A study by Manley HJ *et al* showed that factors like subtherapeutic dosage, overdosage of a drug, prescription of two or more medications from the same class of drugs frequently lead to polypharmacy.[14] These factors are well within the control of the prescribing physician and hence must be avoided. Careful monitoring of these patients is a must in view of the potential drug drug interactions that could occur in them. The medical case record of the patient should have the details of all the drugs prescribed to the patient so that there is no duplication of the drugs when the patient is referred to another doctor. It is also a good practice to have a clinical pharmacologist in a hospital who can go through all the prescriptions of the patients to detect any interactions and notify the physician. In the present study specific to chronic kidney disease patients, we find the increased necessity to rationally prescribe the drugs for the comorbid conditions and to continuously monitor them for any drug interactions.

CONCLUSION

Chronic kidney disease patients are a vulnerable group for drug interactions. Rational prescription, early detection of harmful drug combinations and careful monitoring of these patients can prevent the occurrence of drug interactions.

REFERENCE

1. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, *et al*. Chronic kidney disease: Global dimension and perspectives. Lancet. 2013; 382:260–72.
2. Modi GK, Jha V. Incidence of End stage renal disease in India: a population based study. Kidney Int. 2006 Dec; 70(12):2131-3.
3. KDIGO. Chapter 1: Definition and classification of CKD. Kidney Int Suppl 2013; 3:19. http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf (last accessed on July 25, 2015).
4. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. Prim Care. 2008; 35:329–344.
5. Olyaei AJ, Bennett WM. Drug dosing in the elderly patients with chronic kidney disease. Clin Geriatr Med. 2009 Aug; 25(3):459-527. doi:10.1016/j.cger.2009.04.004. Review.
6. Mahmood M, Malone DC, Skrepnek GH, Abarka J, Armstrong EP, Murphy JE, *et al*. Potential drug-drug interactions within veterans affairs medical centers. Am J Health Syst Pharm. 2007; 64:1500–5.
7. Doubova Dubova SV, Reyes-Morales H, Torres-Arreola Ldel P, Suárez-Ortega M. Potential drug-drug and drug-disease interactions in prescriptions for ambulatory patients over 50 years of age in family medicine clinics in Mexico City. BMC Health Serv Res. 2007 Sep 19; 7:147.
8. Marquito AB, Fernandes NM, Colugnati FA, de Paula RB. [Identifying potential drug interactions in chronic kidney disease patients]. J Bras Nefrol. 2014 Jan-Mar; 36(1):26-34.
9. Chavda NB, Solanky PP, Baria H, Naik R, Bharti K. Study of potential drug–drug interaction between prescribed drugs in patients attending outpatient department of medicine at tertiary-care hospital in south Gujarat region. Natl J Physiol Pharm Pharmacol. 2015; 5(3): 236-242. doi:10.5455/njppp.2015.5.0508201428.
10. Rama M, Viswanathan G, Acharya LD, Attur RP, Reddy PN, Raghavan SV. Assessment of Drug-Drug Interactions among Renal Failure Patients of Nephrology Ward in a South Indian Tertiary Care Hospital. Indian J Pharm Sci. 2012 Jan; 74(1):63-8.doi: 10.4103/0250-474X.102545.
11. Vyas A, Pan X, Sambamoorthi U. Chronic Condition Clusters and Polypharmacy among Adults. Int J Family Med 2012; 2012:193168.
12. Venturini CD, Engroff P, Ely LS, Zago LF, Schroeter G, Gomes I, *et al*. Gender differences, polypharmacy, and potential pharmacological interactions in the elderly. Clinics (São Paulo) 2011; 66: 1867-72.
13. Weir MR, Fink JC. Safety of medical therapy in patients with chronic kidney disease and end-stage renal disease. Curr Opin Nephrol Hypertens. 2014 May; 23(3):306-13. doi: 10.1097/01.mnh.0000444912.40418.45. Review.
14. Manley HJ, Cannella CA, Bailie GR, St Peter WL. Medication-related problems in ambulatory hemodialysis patients: a pooled analysis. Am J Kidney Dis 2005; 46:669-80.

Source of Support: None Declared
Conflict of Interest: None Declared