IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
March 2020 Vol.:17, Issue:4

Assessment of Adverse Drug Reactions in CKD Patients Undergoing Hemodialysis in a Tertiary Care Hospital in India

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Submission: 23 February 2020
Accepted: 29 February 2020
Published: 30 March 2020

Keywords: Chronic kidney disease, Haemodialysis; Adverse drug reactions

ABSTRACT

Rational drug prescription is a difficult task in CKD patients. These patients are at higher risk of drug-related problems since they need complex therapeutic regimens that require frequent monitoring and dosage adjustments. Also, they usually have other co-morbidities· inappropriate use of medications can increase adverse drug effects, which can be reflected by excessive length of hospital stays, excessive health care utilization, and costs. As CKD progresses, the drugs that are given for these patients also increases and the prevalence of drug-related problems also increases. Appropriate drug selection for patients with chronic kidney disease (CKD) is important to avoid unwanted drug effects and to ensure optimal patient outcomes. This study aimed to assess the adverse drug reactions in chronic kidney disease patients undergoing hemodialysis in a tertiary care hospital in India. This prospective observational study was carried out with 135 patients who had undergone hemodialysis in the Nephrology Department of Muthoot Healthcare hospital Pvt Ltd, Kozhencherry, for 6 months study to assess the adverse drug reactions in chronic kidney disease patients. The incidence of potential adverse drug reactions including hyponatremia, hypokalemia, hypotension, hypoglycemia, nausea, vomiting, muscle pain, headache, and weakness was also determined. Hyponatremia (28 %) was found to be the most common ADR followed by hypokalemia (13.8%) and hypotension (13.8%), vomiting (11.6%), hypoglycemia (11%), although it can be attributed to the disease condition, hemodialysis procedure and/or other factors other than drug use.

INTRODUCTION

Chronic kidney disease (CKD), also called chronic renal insufficiency (CRI), is defined as a progressive loss of kidney function occurring over several months to years, and is characterized by the gradual replacement of normal kidney architecture with interstitial fibrosis[1], is an increasing public health issue[2]. The prevalence of CKD is estimated to be 8-16% worldwide. The prevalence of CKD increases with age and will continue to rise, reflecting the growing elderly population. As the prevalence of CKD increases, they are at a higher risk for progression into End-Stage Renal Disease (ESRD) requiring dialysis to maintain the patients' long term survival.

Rational drug prescription is a difficult task in CKD patients. These patients are at higher risk of drug-related problems since they need complex therapeutic regimens that require frequent monitoring and dosage adjustments[4,5,6]. Inappropriate use of medications can increase adverse drug effects, which can be reflected by excessive length of hospital stays, excessive health care utilization, and costs. As CKD progresses, the drugs that are given for these patients also increases and the prevalence of drug-related problems also increases. Patients with CKD and on maintenance hemodialysis are prescribed with an average of 12 medications per patient and are at a higher risk of developing drug-related problems thus leading to untoward effects. Dialysis patients require special consideration regarding the drugs used because of their altered pharmacokinetic and pharmacodynamic profiles and have increased potential for adverse reactions. Therefore appropriate drug selection for patients with chronic kidney disease (CKD) is important to avoid unwanted drug effects and to ensure optimal patient outcomes[3].

The incidence of adverse drug events is higher among patients with CKD compared with those without CKD because of impaired renal function and inappropriate medication use which can be associated with increased mortality [7,8,9]. Furthermore, older adults are at a greater risk for adverse drug events due to age-related kidney function changes[10]. Also, due to the nephrotoxic effects of medications, patients with CKD are susceptible to other adverse effects with agents routinely used in the management of CKD and comorbid conditions[11].

Diuretics like thiazide and loop diuretics are commonly used for natriuresis and BP control with a reduced GFR. This is especially important in advanced CKD, where extracellular volume excess is a concern and BP becomes more salt-sensitive [51]. Injudicious diuretic use

is associated with a range of electrolyte disturbances, including hypokalemia, hypomagnesemia, and hypochloremic metabolic alkalosis[12,13].

Treatment and prevention of hypokalemia include a reduction in diuretic use, sodium restriction, and liberalization of the patient's diet to include potassium-rich foods[11]. Consideration of potassium-sparing diuretics and RAAS blockers, where appropriate, under strict supervision[14].

Although CKD itself can precipitate hyponatremia due to impaired water homeostasis, it is more likely to be the result of the injudicious use of diuretics[15]. In a US population-based study, the point prevalence of hyponatremia was 13.5% and it was similar in ESRD patients[16]. Hyponatremia increases mortality in nondialysis-dependent, hemodialysis-dependent, and peritoneal dialysis-dependent CKD patients. The high incidence emphasizes the importance of the judicious selection of diuretic dose and regular monitoring[15].

Iron supplementation (oral or intravenous) is usually the first step in anemia management. However, oral iron use is often limited because of suboptimal efficacy and GI intolerance[17,18].

Poorly controlled type 2 diabetes mellitus(T2DM) can lead to microvascular complications, including nephropathy, as 40% of patients with T2DM have CKD [56]. Slowing the progression of nephropathy through glycemic control is of paramount importance in clinical management. [51,55]. Patients with T2DM on insulin or other oral hypoglycaemic agents are at an increased risk for hypoglycemia, due to decreased insulin elimination as kidney function declines hence the patients should be monitored and the insulin requirements should be tailored to meet the individual needs [19,20].

Gastrointestinal disturbances are the most common adverse effect of phosphate binders[21]. Long term use of sevelamer can precipitate symptoms like dyspepsia, nausea, vomiting, diarrhea [22].

Calcium channel blockers and beta-blockers may produce hypotension and headache in CKD patients[23,24]. Other medications like diuretics, antibacterials, hypoglycaemic agents, mineral supplements can cause adverse events like electrolyte disturbances, hypotension, hypoglycemia, muscle pain, diarrhea, vomiting, epigastric pain, weakness, and drowsiness.

The ADEs commonly affect the metabolic, endocrine, cardiovascular, gastrointestinal and hematological systems [25].

Here in this study, various adverse events like hyponatremia, hypokalemia, hypotension, hypoglycemia, nausea, vomiting, headache, weakness, muscle pain are being assessed.

MATERIALS AND METHODS

This is a prospective observational study conducted for 6 months in the Nephrology department of Muthoot Healthcare Hospital Pvt Ltd, Kozhencherry, Kerala, India after obtaining approval from the Institutional Ethics Committee of the hospital. A sample size of 135 patients of both genders diagnosed to have chronic kidney disease undergoing hemodialysis in the Nephrology unit between the age of 20-80 years were included in the study. Patients who were pregnant were excluded from the study. All subjects were provided with a brief introduction regarding the study and the confidentiality of the data. A written Informed Consent printed in their understandable language was obtained from the patient or caregiver if the subject was unable to give the same. Relevant information was collected according to the approved pre-designed data collection form. Data required as per the data collection proforma (Annexure 3) were collected prospectively from the patients' medical chart in the Nephrology department and the hospital records. To determine the adverse drug reactions, the objective data and direct patient interviews were done. The data collected were entered in Microsoft excel -2010 version and results were analyzed. Results were presented in tabular form and presented as frequency and percentages.

RESULTS AND DISCUSSION

RESULTS

Table No. 1: Distribution of Patients based on Age Group

SI.NO	Age Group	Frequency	Percentage (%)
1	20-40	7	5.1
2	41-60	53	39.3
3	61-80	75	55.6
	Total	135	100

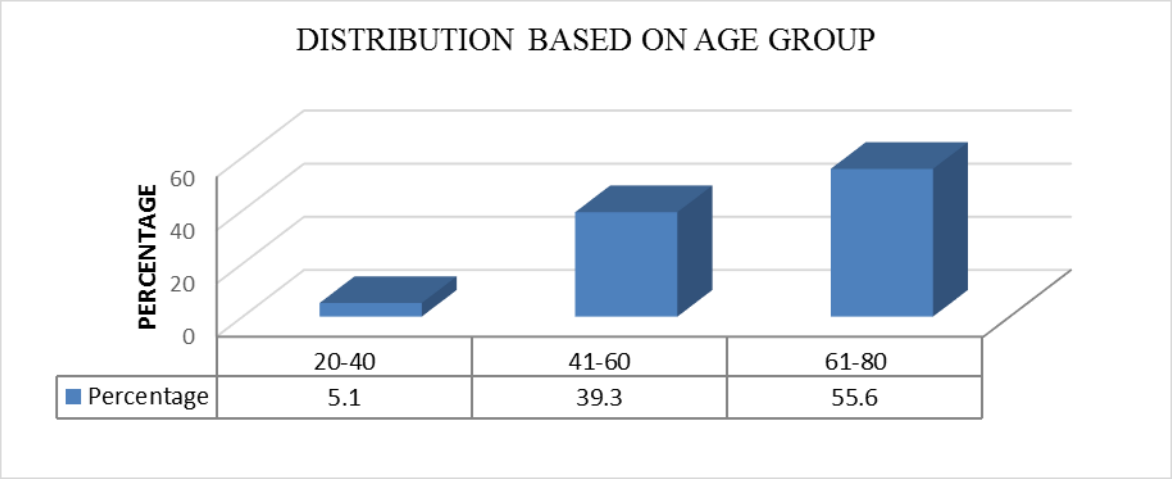

Figure No. 1: Distribution of Patients based on Age Group

In this study, the highest percentage of hemodialysis patients were found to be in the age group of 61-80(55.6%) followed by the age groups41-60(39.3%), and 20-40(5.1%).

Table No. 2: Distribution of Patients Based on Gender

SI.NO.	Gender	Frequency	Percentage (%)
1	Male	98	73
2	Female	37	27
	Total	135	100

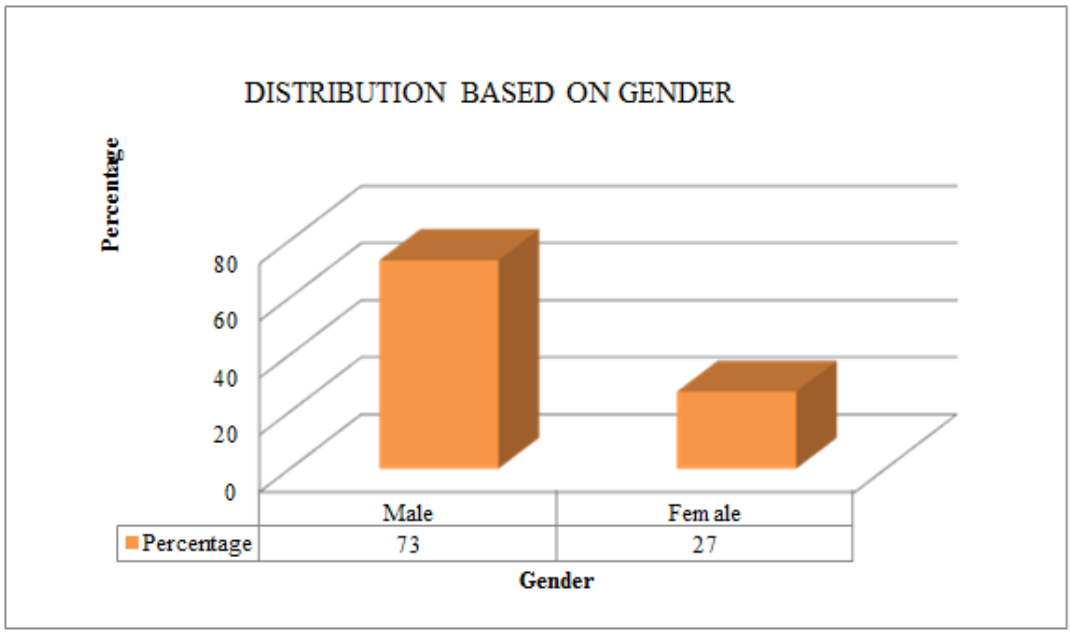

Figure No. 2: Distribution of Patients Based on Gender

In this study, 73% of the study population was constituted by males whereas 27% was constituted by females.

Table No. 3: Distribution of Patients Based on Social Habits

SI.NO:	Social History	Frequency	Percentage (%)
1	Smoking	8	6
2	Alcohol	23	17
3	Smoking and Alcohol	37	27.4
4	No Social History	67	49.6
	Total	135	100

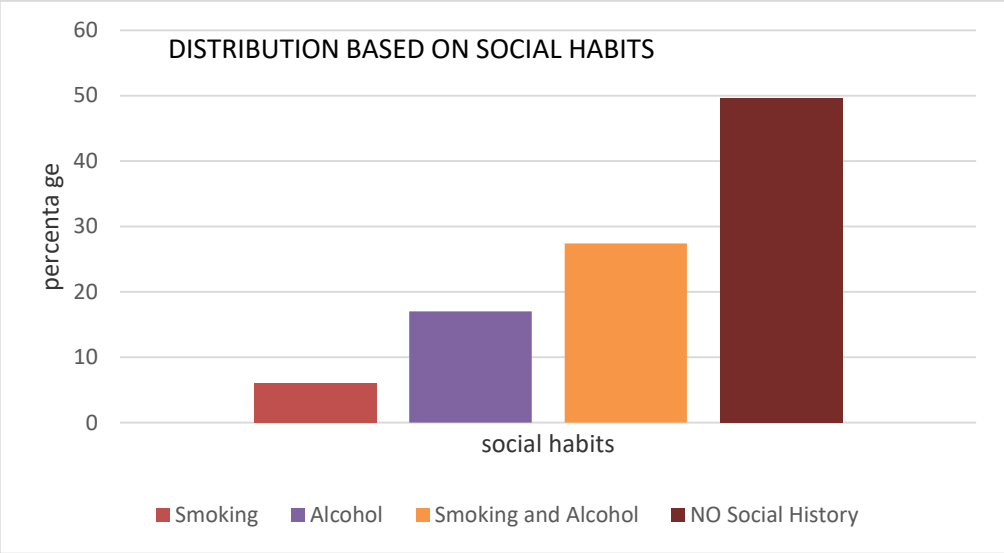

Figure No. 3: Distribution of Patients Based on Social Habits

Here, 49.6% of the study population had no history of alcoholism and smoking, 17% had a history of alcoholism, 6% had a history of smoking and 27.4% had a history of both alcoholism and smoking.

Table No. 4: Number of Dialysis Sessions Per Week

SI.No:	Duration of Dialysis per week	No. of Subjects	Percentage(%)
1	3 Times	82	60.7
2	2 Times	52	38.5
3	1 Time	1	0.8
	Total	135	100

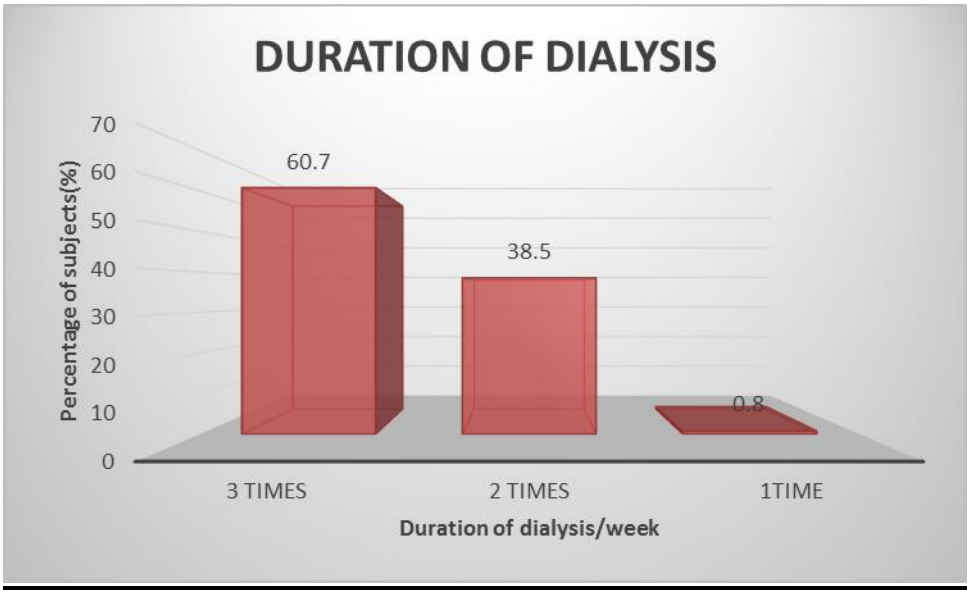

Figure No. 4: Number of Dialysis Sessions Per Week

In this study most of the patients (60.7%) have been undergoing dialysis 3 times a week, followed by 38.5% of patients undergoing 2 times a week and 0.8% of patients undergoing dialysis once in a week.

Table No. 5: Distribution of ADR in Haemodialysis Patients

Sl.no:	ADR	Frequency	Percentage(%)
1	Hypokalemia	25	13.8
2	Hypoglycemia	20	11
3	Hyponatremia	50	28
4	Weakness	11	6
5	Nausea	11	6
6	Vomiting	21	11.6
7	Muscle pain	11	6
8	Headache	7	3.8
9	Hypotension	25	13.8
	Total	181	100

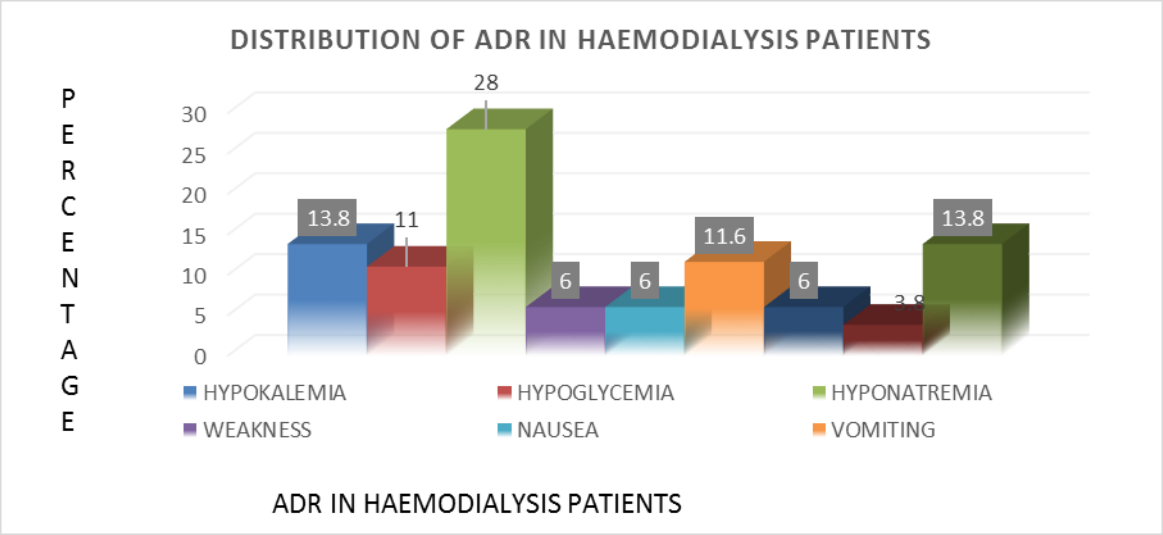

Figure No. 5: Distribution of ADR in Haemodialysis Patients

In this study, the most common ADR was found to be hyponatremia(28%) , hypokalemia(13.8%), hypotension(13.8%)followed by vomiting (11.6%), hypoglycaemia (11%),nausea (6%) ,weakness (6%), muscle pain (6%), headache (3.8%).

DISCUSSION

In our study conducted using 135 hemodialysis patients, we found that there was a large proportion of male patients (73%) and females (27%) and they were distributed over an age group of 21-40 (5.1%), 41-60(39.2%), and 61-80 (55.7%). CKD is more prevalent in males owing to their unhealthy lifestyles and the damaging effects of testosterone[27]. A large proportion of CKD patients were seen in the age group of 61-80 and lowest among 21-40 years as age progression may deteriorate the kidney function. In a study by **Narayana Murthy B. V et. al.**[3](2014); they reported the male dominance78.84% and 21 % in the female population among patients undergoing hemodialysis. In a study by **Chakraborty et.al**[15] (2016)**;** the average age with the highest frequency was reported to be more than 50 years and the lowest frequency of patients reported among 24 years.

In our, the study population also showed several ADRs with hyponatremia (28%) to be the most prevalent one followed by both hypokalemia (13.8%) and hypotension (13.8%), vomiting (11.6%), hypoglycemia (11%), nausea (6%), weakness (6%), muscle pain (6%) and headache (3.8%). These findings closely converge with similar other relevant studies. However, the occurrence of these ADRs can be attributed to the patients' dosage regimen, disease condition and/or other factors. Hyponatremia and hypokalemia can be due to the use

of diuretics, hypoglycemia can be precipitated by insulin therapy, hypotension and headache can be attributed to antihypertensives. Gastrointestinal disturbances like nausea, vomiting can be due to iron supplements and phosphate binders.

In the study by **Chakraborty et. al.[15];** (2016) they reported the incidence of ADRs was hyponatremia (32%) being most common followed by hypoglycemia, (16%) and hypokalemia (10%) which is similar to our study.

In a study by **P. Ansuman Abhishek et. al.;[26]** (2017) they reported the frequently observed AEs as per the laboratory investigations. They concluded the following hyponatraemia (27.8%) hypokalemia (6.08%), hypoglycaemia (10.43%), hypotension (9.56%), weakness (19.3%), vomiting (20.86%), body ache and joint pain (35.65%). This is similar to our study were we noted hyponatremia to be the most common adverse drug event.

CONCLUSION

The study was conducted prospectively by using a sample size of 135 patients to assess the adverse drug reactions in chronic kidney disease patients undergoing hemodialysis admitted in the nephrology department for a study period of 6 months. 135 CKD patients undergoing HD were selected for the study and their demographic details and information relevant to the study were obtained from the patient medical records. As per our study hyponatremia (27.8%) was the most common adverse event seen in CKD patients followed by hypokalemia (13.8%), hypotension (13.8), vomiting (11.6%) and hypoglycemia (11%).

LIMITATIONS

While evaluating the ADR, we have considered any deviations from laboratory value outside the normal range as abnormal, which may have lead to the overestimation of adverse drug reactions. Furthermore, these symptoms can also occur due to the disease itself or due to the hemodialysis sessions. Due to the time constraints, we could not estimate correctly whether these symptoms are due to the disease or dialysis sessions or actual drug use.

AREAS OF CONFLICT: NIL

REFERENCES

1. Melanie S Joy, Abhijit Kshirsagar, Nora Franceschini; Chronic Kidney Disease: Progression-Modifying Therapies; Joseph T. Dipiro, Robert L.Talbert, Gary C.Yee, Barbara G.Wells, Pharmacotherapy, A Pathophysiological Approach, 7th edition, Page no:745-847.
2. Prof. Vivekanand Jha DM; CKD: global dimensions and perspectives; the lancet, 2013; 382 (9888), 260-272.
3. Narayana Murthy B. V, Satyanarayana V; Prescribing pattern of drugs in chronic kidney disease patients on hemodialysis at a tertiary care hospital, International Journal of Basic & Clinical Pharmacology, April 2017, 4,(6), Page 928-932.
4. Perico N, Remuzzi G; Chronic kidney disease: a research and public health priority, Nephrol Dial Transplant; 2012;27(iii); 19-26.
5. R Funfstuck, Ott U, Naber KG; The interaction of urinary tract infection and renal insufficiency; International Journal of Antimicrobial Agents; 2006; 72-77.
6. Manley HJ, Cannella CA, Bailie GR, Pater WL; Medication-related problems in ambulatory hemodialysis patients: A pooled analysis; Am J Kidney Dis; 2005; 46; 669-80.
7. Janelle GuirguisBlakea, Gina A Keppelb, John Holmes, RexW Forces, William Kriegsmand and Laura-Mae Baldwin; Prescription of high-risk medications among patients with chronic kidney disease: a cross-sectional study from the Washington, Wyoming Alaska, Montana and Idaho region Practice and Research Network, Family Practice; 2018; 1–6
8. Seliger SL, Zhan M, Hsu VD, Walker LD, Fink JC; Chronic kidney disease adversely influences patient safety; J Am Soc Nephrol 2008; 19(10); 2414–19.
9. Chapin E, Zhan M, Hsu VD; Adverse safety events in chronic kidney disease: the frequency of 'multiple hits'; Clin J Am Soc Nephrol 2010; 5 (11); 95–101.
10. Breton G, Froissart M, Janus N; Inappropriate drug use and mortality in community-dwelling elderly with impaired kidney function the three cities population-based study; Nephrol Dial Transplant 2011; 26; 2852–9.
11. Chanel F. Whittaker, Margaret A. Miklich, Roshni S. Patel, Jeffrey C. Fink; A Medication Safety Principles and Practice in CKD, Clin J Am Soc Nephrol 2018;13: 1738–1746
12. Wilcox CS; Metabolic and adverse effects of diuretics; Semin Nephrol 1999; 19; 557–568
13. Palmer BF; Metabolic complications associated with use of diuretics; Semin Nephrol; 2011; 31: 542–552
14. Kovesdy CP, Appel LJ, Grams ME, Gutekunst L, McCullough PA, Palmer BF, Pitt B, Sica DA, Townsend RR; Potassium homeostasis in health and disease: A scientific workshop co-sponsored by the National Kidney Foundation and the American Society of Hypertension; J Am Soc Hypertens 2017;11: 783–800.
15. Sourav Chakraborty, Saugata Ghosh, Avishek Banerjea, Radha Raman De, Avijit Hazra, Swapan Kumar Mandal; Prescribing patterns of medicines in chronic kidney disease patients on maintenance hemodialysis, Indian Journal of Pharmacology,2016, (5); 586-590
16. Kovesdy CP, Lott EH, Lu JL, Malakauskas SM, Ma JZ, Molnar MZ; Hyponatremia, hypernatremia, and mortality in patients with chronic kidney disease with and without congestive heart failure; Circulation 2012;125:677‑84.
17. Macdougall IC, Bock AH, Carrera F, Eckardt KU, Gaillard C, Van Wyck D, Robert B, Nolen JG, Roger SD; FIND-CKD: A randomized trial of intravenous ferric carboxymaltose versus oral iron in patients with chronic kidney disease and iron deficiency anemia; Nephrol Dial Transplant 2014,29: 2075–2084.
18. Macdougall I C; Iron supplementation in the nondialysis chronic kidney disease (ND-CKD) patient: Oral or intravenous? CurrMed Res Opin 2010;26: 473–482
19. BaileyRA, WangY, ZhuV, RupnowMF; Chronic kidney disease in US adults with type 2 diabetes: An updated national estimate of prevalence based on Kidney Disease: Improving Global Outcomes (KDIGO) staging; BMC Res Notes; 2014;7; 415
20. Hahr AJ, Molitch ME; Management of diabetes mellitus in patients with chronic kidney disease; Clin Diabetes Endocrinol 2015; 1-2.
21. Veronica Legg; Complications of Chronic Kidney Disease, AJN 2005,105 (6); 40-49
22. Reena Popat; Chronic kidney disease managing the complication; Clinical pharmacist Journal,2011; 3;20-24

23. Andrea Coorsonello, Claudio Pedone, Francesco, Bruno Mazzei, Angel Di Iorio, Pieurgo carbon in, Rafflale Antonelli inealzi; Concealed renal failure and adverse drug reactions in older patients with type 2 diabetes mellitus; Journal of Gerontology, Medical sciences;2005; 60(9);1147-1151.
24. Zachry A, Marcum, Linda F.Fried; Aging and antihypertensive medication-related complications in the chronic kidney disease patient, Curr Opin Hypertens, 2011;20(5);449-456
25. Y. Hassan1, R.J. Al-Ramahi, N.A. Aziz, R. Ghazali; Adverse drug events in hospitalized patients with chronic kidney disease, International Journal of Clinical Pharmacology and Therapeutics; 2010; 48 (9); 571-576.
26. P. Ansuman Abhisek, Rajendra PA, Rajashree Sama, Namita Mohapatra, Srikanta Mohanty; Drug Utilisation Pattern and Adverse Events in Patients with Chronic Kidney Disease Undergoing Maintenance Haemodialysis at a Tertiary Care Hospital of Odisha, Journal of Clinical and Diagnostic Research; 2017; 11(10): 11-16.
27. Juan Jesus Carrero, Manfred Hecking, Nicholas C. Chesnaye, Kitty J. Jager; Sex and gender disparities in the epidemiology and outcomes of chronic kidney disease, Springer Nature Reviews Nephrology, 2018;1-14