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

Human Journals
Research Article
August 2020 Vol.:19, Issue:1

Assessment of Complications in CKD Patients Undergoing Hemodialysis in a Tertiary Care Hospital in India

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

JENI JOSEPH[1]*, ANINA ANIL[2], RIA MARIA VARGHESE[3], STEPHY CHACKO[4], ABHILASH B[5], ELESSY ABRAHAM[6]

1,2,3,4 - 6th year Pharm D Students, Nazareth College Of Pharmacy, Othera, Thiruvalla. India

5-Assistant Professor, Department Of Pharmacy practice, Nazareth College of Pharmacy, Othera, Thiruvalla India

6-Principal and professor, Nazareth College of Pharmacy, Othera, Thiruvalla. India

Submission: 24 July 2020
Accepted: 30 July 2020
Published: 30 August 2020

Keywords: Chronic kidney disease; Haemodialysis; complications; anaemia; fluid overload; hyperphosphatemia; hyperkalemia

ABSTRACT

Chronic Kidney Disease (CKD) has emerged as a major public health hazard worldwide accounting for 98.02% increase in death over the last 27 years. All stages of CKD are associated with increased risks of cardiovascular morbidity, premature mortality, and/or decreased quality of life. 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[1]. When chronic kidney disease is detected, an attempt should be made to identify and treat the underlying conditions as well as the secondary abnormalities. These goals include slowing disease progression, detecting and treating complications and managing cardiovascular risk factors[2]. The most frequent complications of CKD include fluid and electrolyte abnormalities, anaemia, hypertension and hyperlipidemia, metabolic acidosis, abnormalities in calcium, phosphorus and mineral-regulating hormone and parathyroid hormone and abnormalities in sodium, potassium, water and acid-base homeostasis[3]and miscellaneous complications resulting from the effects of CKD on other organ systems, including malnutrition, pruritis and uremic bleeding[4]. **Objective**: The aim of this study was to assess various complications in chronic kidney disease patients undergoing haemodialysis in a tertiary care hospital in India. **Methods**: This prospective observational study was carried out with 135 patients who had undergoing hemodialysis in the Nephrology Department of Muthoot Healthcare hospital Pvt. Ltd., Kozhencherry, for a period of 6 months to assess various complications in chronic kidney disease patients. **Conclusion**: In our study, a total of 135 patients were included in which 73% were males and 27% were females. We assess various complications like anaemia, fluid overload, hyperphosphatemia and hyperkalemia. It was found that anaemia (31.3%) was the most common complication seen among the patients followed by fluid overload (26.6%), hyperphosphatemia (21.4%) and hyperkalemia (20.7). Most common complication found in this study was anemia in both males and females, followed by others and the frequency of complications were more prevalent in the age group of 61-80.

INTRODUCTION

Chronic kidney disease is also defined as a reduction in the glomerular filtration rate (GFR) and/or urinary abnormalities or structural abnormalities of the renal tract, present for 3 months or longer with implications for health; the structural abnormalities include albuminuria of more than 30mg/day, presence of hematuria and electrolyte disturbances. It is an irreversible progressive condition responsible for high morbidity and mortality rates[4]. When chronic kidney disease is detected, an attempt should be made to identify and treat the underlying conditions as well as the secondary abnormalities. These goals include slowing disease progression, detecting and treating complications, and managing cardiovascular risk factors. Suitable treatment also includes attention to the influence of various complications that follow. These complications occurs in the process of accumulation; decreased urinary excretion plays a crucial role and leads to retention of metabolites in the organism (e.g., creatinine, urea, electrolytes, water)[2].

Stages 1 and 2 CKD are usually not associated with any complication arising from the decrement in GFR. However, there may be symptoms from the underlying renal disease itself, such as edema, hypertension. If the decline in GFR progresses to stages 3 and 4, virtually all organ systems are affected[3]. The most common complications of stages 4 and 5 CKD include anemia, abnormalities in calcium, phosphorus, secondary hyperparathyroidism, fluid and electrolyte abnormalities, metabolic acidosis and malnutrition. Cardiovascular complications are also prevalent in the CKD population and are the leading cause of mortality in patients with ESRD. The management of CKD and the associated secondary complications should be initiated prior to development of ESRD. Patient education plays a critical role in the appropriate management of patients with stage 4 or 5 CKD and related complications[4].

CLASSIFICATION OF CKD

STAGE	GFR(ml/min/1.73m^2)	DESCRIPTION
STAGE 1	>90	Kidney damage with normal or increased GFR
STAGE 2	60-89	Kidney damage with mild Decreased GFR
STAGE 3a STAGE 3b	45–59 30–44	Moderately decreased GFR
STAGE 4	15-29	Severely decreased GFR
STAGE 5	<15	Kidney failure

Anaemia was defined according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines as hemoglobin <12 g/dL in women and <13.5 g/dL in men[5]. It is primarily caused by a deficiency in the production of endogenous erythropoietin by the kidney, is a common complication observed in patients with stages 4 and 5 CKD and contributes to cardiovascular disease. Management of anemia includes administration of erythropoietin- stimulating agents (ESAs) (epoetin alfa and darbepoetin alfa) and regular iron supplementation (oral or intravenous administration) to achieve target hemoglobin of at least 11 g/dl[4].

Fluid and electrolyte abnormalities, In persons with normal kidney function, sodium balance is maintained at a sodium intake of 120 to 150mEq/day. The fractional excretion of sodium (FeNa) is approximately 1% to 3%. Water balance is also maintained, with a normal range of urinary osmolality of 50 to 1,200mOsm/kg. An osmotic diuresis occurs with an increase in FeNa leading to obligatory water losses and impairment in the kidney's ability to dilute or concentrate urine. In patients with severe CKD (stages 4 and 5), serum sodium concentration is generally maintained as the result of an increase in FeNa by as much as 30%, but results in a volume-expanded state. Total renal sodium excretion decreases despite an increase in sodium excretion by remaining nephrons. Volume overload with pulmonary edema can result, but the most common manifestation of increased intravascular volume is systemic hypertension[4].

Hyperphosphatemia is defined as serum phosphate ≥4.5 mg/dL,[5]. The changes in calcium homeostasis and secondary hyperparathyroidism are common in patients with CKD and contribute to extravascular calcifications and an increased risk of cardiovascular mortality. Management of hyperphosphatemia, calcium balance, and secondary hyperparathyroidism includes dietary phosphorus restriction, prudent use of phosphate binding agents, vitamin D, and calcimimetic therapy [4].

Hyperkalemia is one of the most common and life threatening electrolyte disorders in CKD and ESRD. It becomes increasingly prevalent as CKD advances. Hyperkalemia has been classified into mild (5.1–<6 mmol/l), moderate (6–<7 mmol/l) and severe (≥ 7 mmol/l)[6].

Serum potassium is freely filtered at the glomerulus, reabsorbed in the proximal tubule and loop of Henle, and actively secreted into the urine at the cortical collecting duct. The kidneys normally excrete 90% to 95% of the daily potassium dietary load. Normally only 5% to 10% of ingested potassium is excreted through the gut.

Potassium homeostasis is also maintained by shifting extracellular potassium intracellularly immediately following ingestion of a potassium load. In patients with CKD, potassium balance is maintained by an increase in distal tubular potassium secretion in which aldosterone plays an important role. Thus the serum potassium concentration is usually maintained in the normal range until the GFR is less than 20 mL/min per 1.73 m2 body surface area, at which point mild hyperkalemia is likely to develop[3].

MANAGEMENT OF COMPLICATIONS ANAEMIA

Erythropoietin-stimulating agents (ESAs) are FDA-approved in CKD for goal hemoglobin of 10–11 g/dL. ESAs (epoetin and darbepoetin) are effective in correcting anemia of CKD. The starting dose of epoetin is 50 units/kg (3000–4000 units/dose) once or twice a week. Darbepoetin is started at 0.45mcg/kg and can be administered every 2 to 4 weeks. Iron therapy is an important component of anemia management. Iron supplementation is usually essential to ensure an optimal response to ESAs in patients with CKD because the demand for iron by the marrow frequently exceeds the amount of iron that is immediately available for erythropoiesis as well as the amount in iron stores (serum ferritin). Red cell transfusion can also be used to treat anemia in CKD patients [3].

MAINTENANCE OF FLUID BALANCE

It has been suggested to limit sodium intake for its effects on both fluid balance and blood pressure. In advanced CKD, the kidney is unable to adapt to large changes in sodium intake. Intake >3–4 g/day can lead to hypertension and volume overload, whereas intake of <1 g/day can lead to volume depletion and hypotension. A goal of 2g/day of sodium is reasonable for most patients. A daily intake of 2L of fluid maintains water balance [3].

MINERAL AND BONE DISORDER

In CKD, hypocalcemia results from inadequate production of calcitriol by the kidneys needed for calcium retention and resorption. Hyperphosphatemia is a consequence of reduced urinary phosphate excretion due to declining GFR. Phosphorus complexes with calcium, deposits in soft tissues and causes soft tissue calcification. Hypocalcemia, decreased calcitriol and hyperphosphatemia stimulates the parathyroid glands for secretion of excessive parathyroid hormone (PTH) resulting in secondary hyperparathyroidism.

Control of hyperphosphatemia is the first step in the treatment of CKD-MBD. This involves dietary phosphorus restriction (milk, cheese, eggs, nuts, peas, beans and dairy products) initially, followed by the administration of oral phosphorus binders, such as calcium carbonate/ gluconate (500 mg/tablet) or calcium acetate (667 mg/capsule) that block absorption of dietary phosphorus in the gut but may cause hypercalcemia. Hence, phosphorus-binding agents that do not contain calcium can be given, i.e., aluminium hydroxide, sevelamer and lanthanum. Sevelamer, 800–3200 mg and lanthanum carbonate, 500-1000 mg[3].

HYPERKALEMIA

Hyperkalemia often responds to dietary restriction of potassium, avoidance of potassium supplements as well as potassium-retaining medications (spironolactone, ACE inhibitors/ARBs).

a) Acute hyperkalemia: calcium chloride or gluconate intravenously, insulin administration with glucose intravenously, bicarbonate intravenously, and potassium-binding resin, cardiac monitoring.

b) Chronic hyperkalemia: dietary potassium restriction and sodium polystyrene, 15–30g once daily orally in juice or sorbitol[3].

MATERIALS AND METHODS

This is a prospective observational study conducted for a period of 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 haemodialysis 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 patient's medical chart in the Nephrology department and the hospital records. To determine the complications, objective data and direct patient interview 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

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

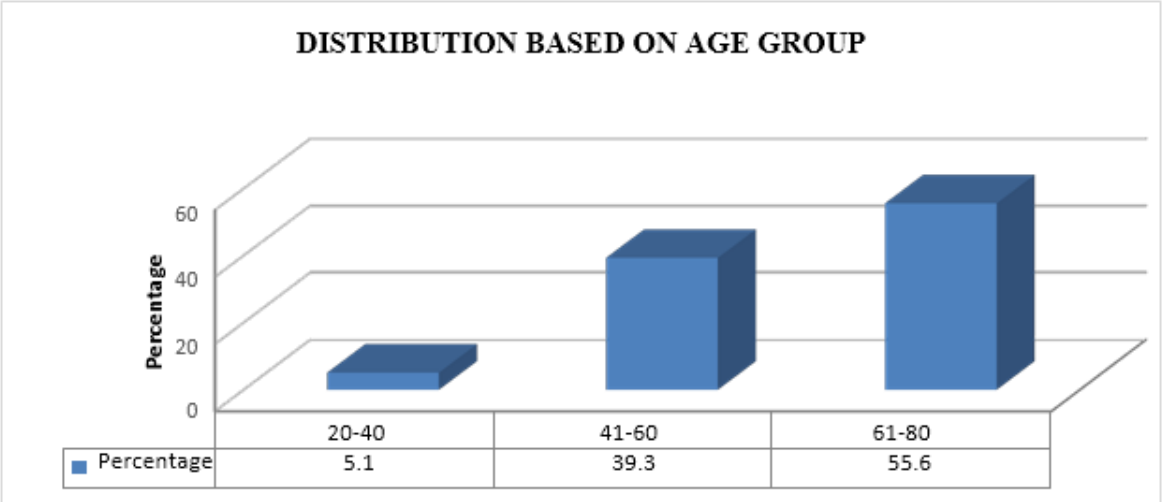

FIGURE NO. 1: DISTRIBUTION OF PATIENTS BASED ON AGE GROUP

In this study, the highest percentage of haemodialysis patients were found to be in the age group of 61-80(55.6%) followed by the age groups 41-60(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

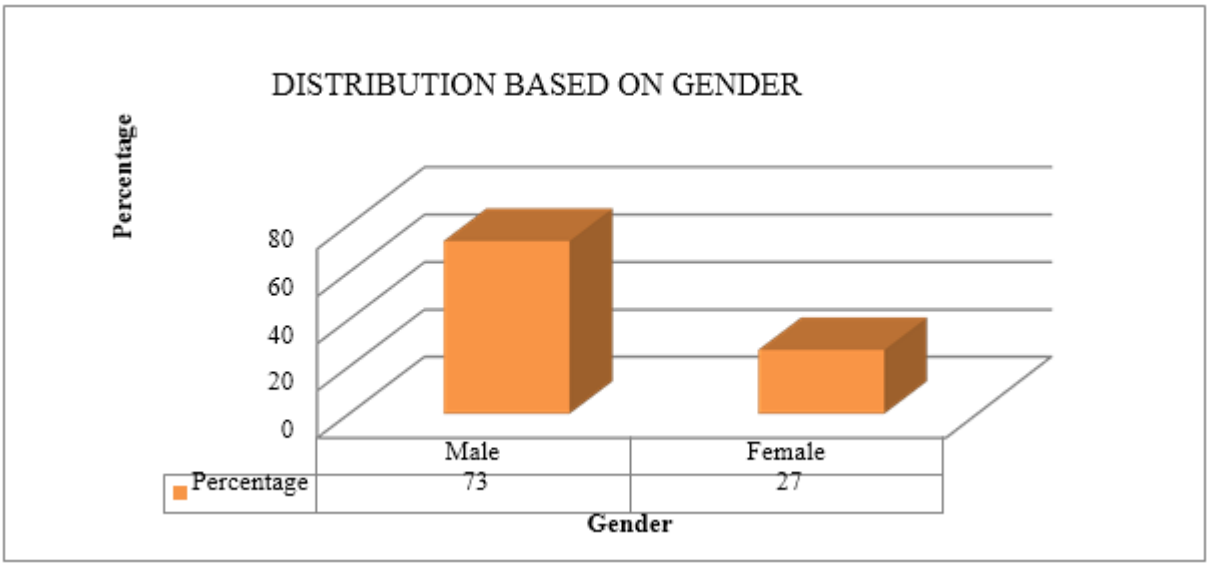

FIGURE NO. 2: DISTRIBUTION OF PATIENTS BASED ON GENDER

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

TABLE NO. 3: 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	1Time	1	0.8
	Total	135	100

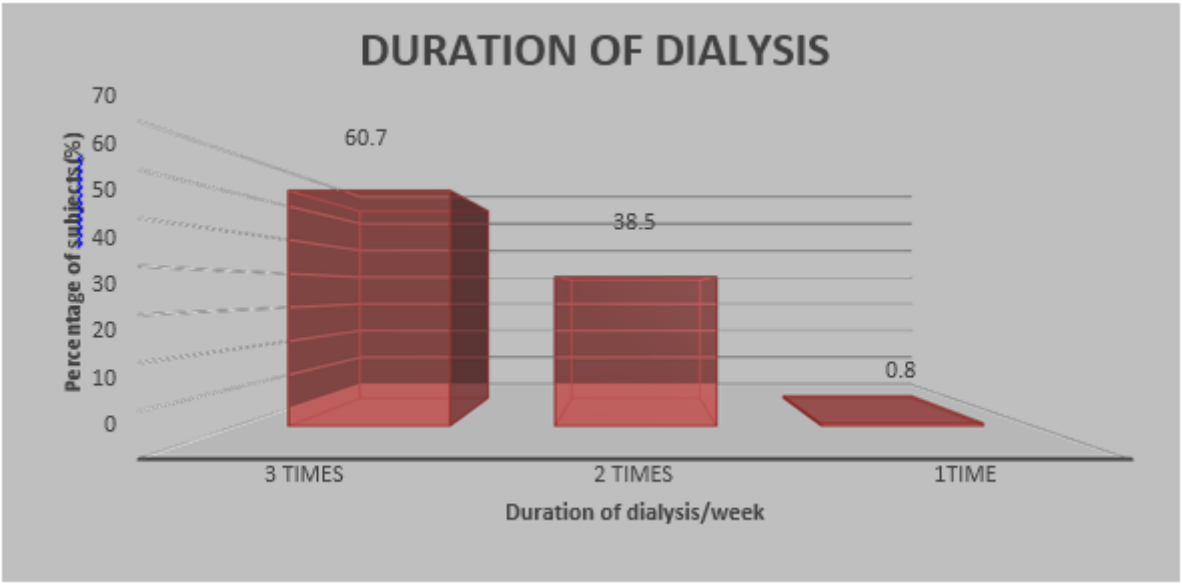

FIGURE NO. 3: NUMBER OF DIALYSIS SESSIONS PER WEEK

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. 4: DISTRIBUTION OF COMPLICATIONS IN CKD

Sl.no	Complications	Frequency	Percentage (%)
1	Anaemia	135	31.3
2	Hyperkalemia	89	20.7
3	Hyperphosphatemia	92	21.4
4	Fluid Overload	114	26.6
	Total	430	100

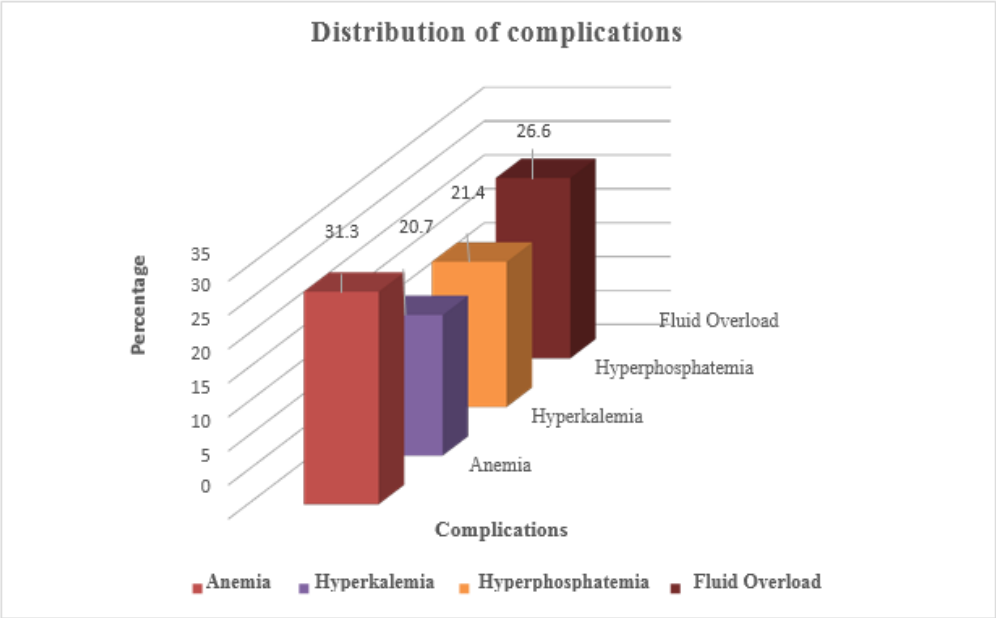

FIGURE NO. 4: DISTRIBUTION OF COMPLICATIONS IN CKD

In this study, most common complication was anaemia (31.3%) followed by fluid overload (26.6%).

TABLE NO. 5: DISTRIBUTION OF COMPARISON OF COMPLICATIONS IN GENDER

Sl.no	Complications	Male	Percentage (%)	Female	Percentage (%)
1	Anaemia	98	31.1	37	32.1
2	Hyperphosphatemia	69	21.9	23	20
3	Hyperkalemia	63	20	26	22
4	Fluid overload	85	26.9	29	25.2
	Total	315	100	115	100

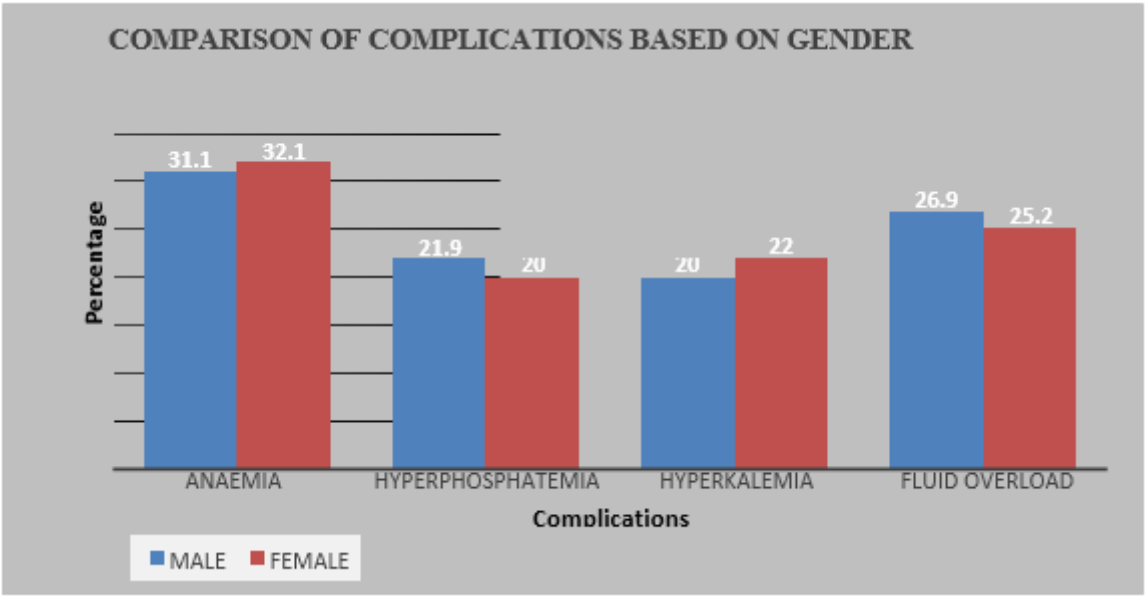

FIGURE NO. 5: DISTRIBUTION OF COMPARISON OF COMPLICATIONS IN GENDER

Most common complication found in this study was anemia in both males and females, followed by fluid overload, hyperkalemia and hyperphosphatemia.

TABLE NO. 6: DISTRIBUTION OF COMPLICATIONS ACCORDING TO AGE

Sl.no	Complications	20-40	41-60	61-80
1	Anaemia	8	53	74
2	Hyperphosphatemia	6	36	51
3	Hyperkalemia	6	39	43
4	Fluid overload	6	42	66

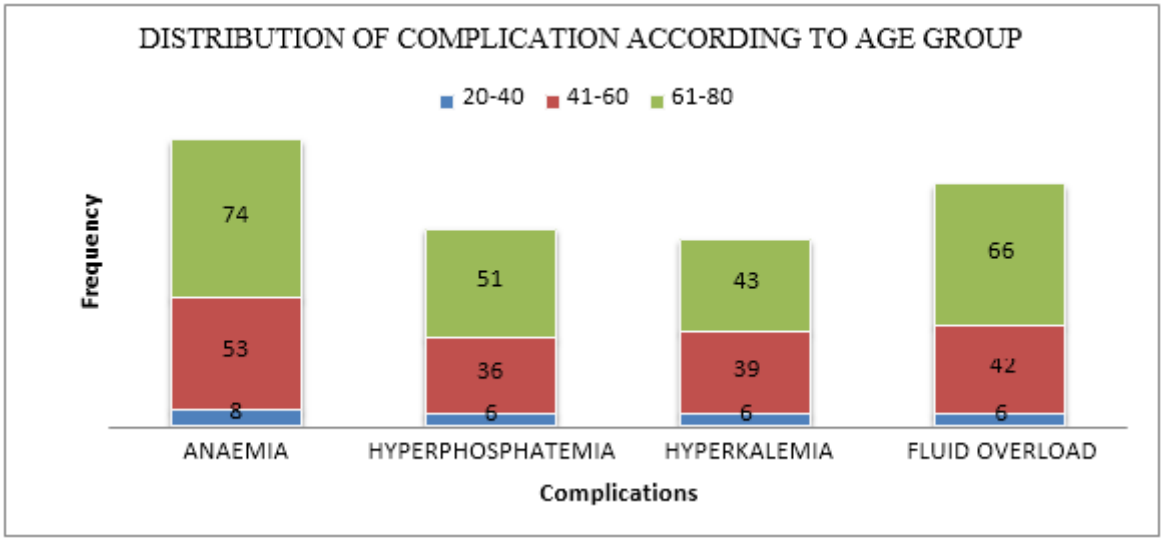

FIGURE NO. 6: DISTRIBUTION OF COMPLICATIONS ACCORDING TO AGE

In this study, the frequency of complications were more prevalent in the age group of 61-80.

DISCUSSION

In our study conducted using 135 haemodialysis patients, we found that there was a large proportion of male patients (73%) and females(27%) and they were distributed over an age groups 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[7]. 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 study by **Narayana Murthy B. V et. al**[4](2014); they reported the male dominance78.84% and 21 % in the female population among patients undergoing haemodialysis. In study by **Chakraborty et. al**[8]

(2016)**;** the average age with highest frequency was reported to be more than 50 years and lowest frequency of patients reported among 24 years.

The 135 haemodialysis patients were also analysed to evaluate complications including anaemia, fluid overload, hyperkalemia and hyperphosphatemia distributed as per gender and age groups. 31.3% showed anaemia followed by 26.6% with fluid overload, 21.4% with hyperphosphatemia and 20.7% with hyperkalemia. Because the kidneys secrete 90% of the endogenous hormone erythropoietin, necessary for erythropoiesis, declining kidney function can lead to erythropoietin deficiency and anaemia. A significant proportion of the subjects also showed fluid overload. Progressive loss of renal function causes reduced sodium filtration and inappropriate suppression of tubular reabsorption that ultimately lead to volume expansion. Fluid overload frequently manifests in patients with moderate to particularly late stages of CKD.

The patients in the age group of 61-80 were found to be the most affected and patients in the age group of 20-40 were found to be least affected, furthermore, showcasing the relevance of age as a significant risk factor in the development of CKD. These findings are supported by similar other relevant studies on the progressive impact of the condition [9,10,11].

In study by **Gautham Viswanathan et. al**[12] (2013) they reported the prevalence of anaemia, followed by hyperphosphatemia as 43%, 16% respectively. There was a graded increase in the prevalence of the complications which is similar to our study.

In study by **Richard Kobina Dadzie Ephraim et. al**[13](2010) they reported various complications where hyperphosphatemia (74.00%), was common followed by anemia (53.40%) and hyperkalemia (38.35%).

In a study by **Eriksen BO et. al**[14] (2006) they reported about CKD and its effects on gender and age. From their study, these authors found a slower rate of GFR decline and better renal survival in female patients. The male patients showed more decline in GFR and are at an increased risk of renal failure and death. They also reported that the prognosis of CKD depended strongly on gender. This is similar to our study where there is an increase dominance of complication in male patients.

In study by **Chakraborty et. al[8];**(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 study by **P. Ansuman Abhisek et. al;[3]**(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

Chronic kidney disease is becoming a major public health care problem worldwide and is responsible for high morbidity and mortality rates and the number of CKD patients is increasing in the current scenario. In comparison to the previous decades, currently the prevalence of chronic kidney disease in human population is continued to rise worldwide and similar situations prevail in India and Kerala as well. Along with the advancement in age, there is an increased chance of CKD progression to ESRD stage due to renal failure resulted in hemodialysis and disease associated complications. The multiple effects of CKD associated complications, coexisting diseases, frequent dialysis, increased number of drug administration including polypharmacy further affect the overall treatment outcome and quality of life of the afflicted patient populations.

The study was conducted prospectively by using a sample size of 135 patients with the aim of assessing the complications in chronic kidney disease patients undergoing haemodialysis 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 informations relevant to the study were obtained from the patient medical records. As per our study anaemia (31.3%) was the most common complication seen among the patients followed by fluid overload (26.6%), hyperphosphatemia (21.4%) and hyperkalemia (20.7%).

AREAS OF CONFLICT: NIL

REFERENCES

1. Soumya Santra, Divya Agrawal, Sanjay Kumar, Sudhanshu Sekhar; A Study on the Drug Utilization Pattern in Patients with Chronic Kidney Disease with Emphasis on Antibiotics Journal of Integrative Nephrology and Andrology 2015; 2(3),85-89

2. Roman Cibulka, Jaroslav Racek; Metabolic Complications of Chronic Kidney Failure and Hemodialysis, Special Problems in Hemodialysis Patients, Prof. Maria Goretti Penido (Ed.), (2011), (ISBN: 978-953- 307-396-5); 155-164

3. Sheikh Salahuddin Ahmed. Aminul Haque Khan, Tarafdar Runa Laila; Treatment and Prevention of Common Complications of Chronic Kidney Disease, Journal of Enam Medical College 2014; 4(1);45-55

4. 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

5. Aghogho Okparavero, Meredith C. Foster, Hocine Tighiouart, Vilmundur Gudnason, Olafur Indridason, Hrefna Gudmundsdottir, Gudny Eiriksdottir, Elias F.Gudmundsson, Lesley A. Inker Andrew S. Levey; Prevalence and complications of chronic kidney disease in a representative elderly population in Iceland Nephrol Dial Transplant (2016) 31: 439–447

6. Tsering Dhondup, Qi Qian; Electrolyte and Acid–Base Disorders in Chronic Kidney Disease and End-Stage Kidney Failure, Blood Purif Review – Advances in CKD 2017;43;179–188

7. 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

8. 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.

9. Macdougall IC, Bock AH, Carrera F, Eckardt KU, Gaillard C, Van Wyck D, Roubert 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 anaemia; Nephrol Dial Transplant 2014,29: 2075–2084.

10. 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.

11. Bellazzi, R. Sacchi L, Caffi. E, De Vincenzi, A. Nai, M. Manicone, F and Bellazi R.; Implementation of an automated system for monitoring adherence to haemodialysis treatment: a report of seven years of experience, International Journal of Medical Informatics, 2012 81(5),320-331.

12. Gautham Viswanathan, Mark J. Sarnak, Hocine Tighiouart, Paul Muntner, Lesley A. Inker; The association of chronic kidney disease complications by albuminuria and glomerular filtration rate: a cross-sectional analysis, Clinical Nephrology;2013; 80 (1); 29-39.

13. Richard Kobina Dadzie Ephraim, W.K.B.A. Owiredu, Ben Eghan, E. F. Laing; Predictive equations, oxidative and metabolic risk factors among ghanaian patients presenting with chronic kidney disease; 2010;102-107

14. BO Eriksen, OC Ingebretsen; The progression of chronic kidney disease: A 10-year population-based study of the effects of gender and age; Kidney International (2006) 69; 375–382.