

Management and treatment outcome of complications of chronic kidney disease patients in a South Indian tertiary care hospital

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ABSTRACT

Background: Chronic diseases are emerging as one of the leading cause of death nowadays. Among them, the prevalence of chronic kidney disease (CKD) is increasing because of the increased incidence of diabetes and hypertension which are the main cause of CKD. The rate of progression of CKD to end stage renal disease (ESRD) can be reduced by the early detection and management of risk factors and complications associated with it. The present study aims to study the complications, treatment pattern and associated outcome in hospitalized CKD patients.

Materials and Methods: A prospective observational study was conducted from October 2012 to March 2013 in the nephrology unit of Kasturba hospital, Manipal. Adult patients (> 18 years old) who were diagnosed with CKD were included. Patient demographics, clinical, pharmacological management and laboratory data were collected in a specially designed form for this study purpose. Demography of the patients, complications and medications used for the management etc. were documented and evaluated using SPSS version 16.0.

Results: 312 CKD patients were included in the study.. Maximum number of patients was in the age group of 46-60 years and study showed male predominance (77.6%). Anemia was the most observed complication in the study population (81.7 %). Monotherapy or combinations of drugs like nebulisation albuterol, insulin with glucose and sodium polystyrene sulfonate was used for the management of hyperkalemia. Anemia is managed by oral and parenteral iron products, erythropoietin and by blood transfusions. Average length of hospital stay was found to be 7.34 ± 4.89 days. Serum creatinine, creatinine clearance rate, serum urea, serum sodium and serum potassium had improved significantly ($p < 0.001$) from the base line. Total serum calcium was also improved after treatment.

Conclusion: Present study highlights the complications, treatment pattern and outcomes in CKD patients from a tertiary care hospital in South India which may help in targeting the major causes of CKD and treatment pattern for the renal failure population. Early identification of patients who are at risk and strategies to decrease the rate of progression of CKD will help to reduce the prevalence and mortality associated with CKD in future.

Key words: Chronic kidney disease, mortality, complications, treatment pattern, outcome.

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INTRODUCTION

Chronic Kidney Disease (CKD) is defined by National Kidney Foundation (NKF) as kidney damage for ≥ 3 months associated with structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR), manifested by either pathological abnormalities or markers of kidney

damage. The NKF has classified chronic kidney disease into 5 stages.^[1]

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CKD is a continually growing problem worldwide^[2] and imposing a substantial burden on the patients affected and on the health - care systems caring for them.^[3] According to SEEK study^[4] (Screening and Early Evaluation of Kidney Disease), the prevalence of CKD is 17.2 % in India with approximately 6% of patients have CKD stage 3 or worse. In 2009, the prevalence of CKD in India is approximately about 800 per million populations and the incidence of end stage renal disease is about 150-200 per million populations.^[5] For patients with stage 5 CKD the five-year survival rate was 38 percent, less than that of acquired immune deficiency syndrome (AIDS) and many cancers, the five year survival rate is only 18% for patients more than 65 years.^[6] The life expectancy of average 60-year old patient on dialysis is only 4.6 more years compared to 21 years of life expectancy of general population of same age level. The annual mortality rate of patients with stage 5 of CKD is approximately 16%.^[7] Even in developed country settings prevalence of CKD is reported to be higher.^[8,9]

There have been very few studies explaining the management of complication of CKD. For example, the Correction of Hemoglobin (Hb) and Outcomes in Renal Insufficiency (CHOIR) trial studied the outcomes of anemia treatment in CKD patients. But the study was terminated prematurely because of higher than targeted Hb levels^[10] that led to higher mortality rates and adverse events. There has only been one single-center open-label study examining the effect of bicarbonate level in CKD.^[11] More studies are needed to determine how CKD affects independent function and life expectancy in older patients and determine the appropriate agents required for the management of complications like secondary hyperparathyroidism.^[12-14]

The present study aimed to evaluate the effect of therapy on CKD patients condi-

tions by considering mortality rate, average length of hospital stay and laboratory values before and after the treatment; and to study the management of complications of CKD and study the outcomes associated with management.

MATERIALS AND METHODS

Study Setting

A prospective observational study was conducted in 1475 bedded tertiary care hospital in India. The study was carried out in the nephrology unit of Kasturba hospital, Manipal. Nephrology unit of Kasturba hospital consist of male ward, female ward and semi-special ward along with separate dialysis facility and kidney transplantation unit. The total number of bed in nephrology ward is 28. Ethical Committee approval was obtained from the Institutional Ethics Committee (IEC) of Kasturba hospital, Manipal.

Patients and data collection

The case records of CKD patients were reviewed prospectively during the period of October 2012 to March 2013 (6 month period) to evaluate the complications of disease, treatment pattern and associated outcomes. Patients (> 18 years old) who diagnosed to with CKD, according to the guideline given by The National Kidney Foundation - Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) admitted in nephrology units were included in this study.

Non CKD patients and Patients with diagnosis of cancer or who had received chemotherapy or radiotherapy for cancer were excluded. Data on patient demographic, clinical, pharmacological treatment management and outcomes were collected from patient case records using specially designed data collection forms which includes patient demographics, patient history notes, laboratory investigation report, drug treatment chart, report of outcomes of therapy etc.

Statistical Analysis

Data was analyzed using SPSS version 16.0. Demography and Clinical characteristics of the patients were analyzed by using descriptive statistics and outcome was analyzed using paired 't' test. P value < 0.001 was used as statistically significant in case of laboratory values like serum creatinine, creatinine clearance, serum urea, serum sodium, serum potassium and blood pressure. P value < 0.05 was taken as statistically significant in case of total iron binding capacity (TIBC), serum calcium and to compare the stages of CKD on admission and on discharge.

RESULTS

312 CKD patients were admitted during the study period (October 2012 to March 2013).

Demographic and clinical Characteristics of the study population

Of the 312 patients, 242 (77.6%) were males and 70 (22.4%) were females. Among the total patients maximum were in the age group of 46-60 years that is, 113 (36.22%) followed by other age groups. When the stage of the disease condition was analyzed stage 5 was more common with 74% followed by stage 4 with 14.4% of patients.

Out of 312 patients, weight and height of only 110 patients were available because most of the patients were bed ridden. The average body mass index of 110 patients was found to be 23.22 ± 4.22 kg/m². The average length of hospital stay of 312 patients was found to be 7.34 ± 4.89 days. The median number of drugs used was 8 with a range of 4 to 24 drugs in a single prescription.

The average number of drugs for a patient was found to be 13.62 ± 5.27 . Out of 312 patients, history of disease and history of hypertension was available for 143 patients. The average years of history of disease and hypertension was found to be 2.74 ± 2.73 years and 7.91 ± 6.54 years respectively. The average years of history

of diabetes mellitus of 118 patients was found to be 12.47 ± 7.29 . Out of total patients, 298 (95.51%) patients had hypertension as comorbidity and in 160 (51.3%) diabetes was the comorbidity. On admission 96 patients were on dialysis, among that 89 patients were on hemodialysis and 7 patients were on peritoneal dialysis. Out of 312 patients, 14 patients (4.5%) had undergone renal replacement therapy (Table 1).

Table 1: General characteristics of the chronic kidney disease patients

Characteristics	Mean \pm SD
Body mass index in kg/m ² (N=110)	23.22 \pm 4.22
Length of hospital stay in days (N=312)	7.34 \pm 4.89
History of disease in years (N=143)	2.74 \pm 2.73
History of diabetes in years (N=118)	12.47 \pm 7.29
History of hypertension in years (N=143)	7.91 \pm 6.54
No. of patients on dialysis on admission	96 (30.8%)
a) hemodialysis	a) 89 (28.5%)
b) peritoneal dialysis	b) 7 (2.2%)
No. of patients undergone renal replacement	14 (4.5%)
Average number of drugs for a patient	13.62 \pm 5.27

N - number of patients whose relevant data was available

Complications of CKD

Present study showed that out of 312 patients, majority of patients had more than one complications and maximum number of patients had two [74 (23.7%)] or four [72 (23.1%)] complications like anemia, hyponatremia, hyperparathyroidism, hypocalcemia and osteodystrophy. Out of 312 patients, majority of patients had anemia and hyponatremia as complications and that is 255 (81.7%) and 192 (61.5%) patients respectively (Table 2).

Table 2: Complications observed in the chronic kidney disease study population

Complications	No. of patients (%)
Anemia	255 (81.7)
Hyponatremia	192 (61.5)
Metabolic acidosis	166 (53.21)
Hyperphosphatemia	144 (46.2)
Hypocalcaemia	119 (38.1)
Hyperkalemia	105 (33.7)
Hyperuricemia	83 (26.6)
Secondary hyperparathyroidism	52 (16.67)

Management of Complications of CKD

Management of anemia

Among 312 patients, 255 (81.7%) patients had anemia as complication, of that 220 (86.27%) patients were on drugs and 35 (13.73 %) patients were not on any medication. Out of 220 patients who were on drugs, 97 (58.43%) patients were on ferrous fumarate and folic acid for the management of iron deficiency anemia. Oral folate was used by 33 (12.94%) patients for the management of folic acid deficiency anemia. Erythropoietin was used by 101 patients for the management of anemia in chronic disease.

Management of Hyperkalemia

Among 312 patients, 105 (33.7%) patients had hyperkalemia as complication. Majority of patients (85.71%) were on more than one drug. 17 (16.19%) patients were on monotherapy with nebulisation albuterol or calcium gluconate or Insulin with glucose. 22 (20.95%) patients were on two drugs for the management of hyperkalemia and maximum number of patients 44 (42%) were on three drug combinations like albuterol nebulization, Insulin with glucose and sodium polystyrene sulphonate.

Management of electrolyte and mineral abnormalities

The electrolytes and mineral abnormalities like hyperphosphatemia, hyponatremia, secondary hyperparathyroidism and hypocalcaemia were treated with monotherapy or combination therapy (Table 3).

Management of Metabolic Acidosis

Among 312 patients, 166 (53.21%) patients had metabolic acidosis as one of the complication of CKD and all patients were treated with sodium bicarbonate.

Management of Hyperuricemia

Among 312 patients, 83 (26.6%) patients had hyperuricemia as one of the complication

Table 3: Electrolyte and mineral abnormalities and management

Complication, No. of patients (%)	Management
Hyperphosphatemia, 144 (46.2%)	Calcium acetate or Calcium carbonate or Sevelamer Carbonate
Hyponatremia, 192 (61.5%)	Normal saline
Secondary hyperparathyroidism, 52 (16.6%)	Alfacalcidol and calcium carbonate monotherapy or combination
Hypocalcemia, 119 (38.1%)	Calcium carbonate and Calcium gluconate as monotherapy or in combination

of CKD and 72 (86.75%) patients were on drug. Majority of patients were on monotherapy. Allopurinol was used by 57 (81.43%), followed by 13 (18.57%) patients with febuxostat.

Assessment of outcome of therapy in study population

Outcome of therapy was assessed by considering mortality rate, average length of hospital stay and by comparing the laboratory values before treatment and after treatment.

Out of 312 patients included in the study, 3 patients passed away during the study period and the remaining patients were managing well with the therapy. The average length of hospital stay of 312 patients was found to be 7.34 ± 4.89 days (Table 4).

DISCUSSION

Chronic Kidney Disease and its complications were the main focus of the study as this condition results in lot of cost and adversely impacts the quality of life of patients.

The average age of the study population was found to be 51.29 ± 14.62 years which is comparable with the NEOERICA (New Opportunities for Early Renal Intervention by Computerized Assessment) project results (58.1 ± 18.1 years), SEEK (Screening and Early Evaluation of Kidney Disease) study in India^[3,4] (52.27 ± 14.78 years) and KEEP^[8] (Kidney

Table 4: Assessment of therapy outcome by lab value comparison on admission and discharge

Biochemical tests (units), No. of patients data available	On admission (Mean \pm SD)	On discharge (Mean \pm SD)	Mean difference	95 % C.I	p value
S. Creatinine (mg/dL), 233	7.39 \pm 4.08	6.56 \pm 3.53	0.83	0.49, 1.17	0.001
Clcr (mL/min), 233	13.32 \pm 10.33	15.44 \pm 13.47	-2.11	-3.27, -0.95	0.001
S. Urea (mg/dL), 215	120.07 \pm 54.95	107.15 \pm 48.36	12.92	6.54, 19.29	0.001
S. Sodium (mEq/L), 221	130.60 \pm 7.41	133.22 \pm 5.76	-2.62	-3.53, -1.72	0.001
S. Potassium (mEq/L), 234	4.70 \pm 0.98	4.26 \pm 0.69	0.44	0.31, 0.57	0.001
S. Calcium (mg/dL), 29	7.27 \pm 2.32	7.84 \pm 1.37	-0.57	-1.21, 0.08	0.081
Hemoglobin (g/dL), 119	8.44 \pm 2.03	8.24 \pm 1.67	0.21	-0.09, 0.51	0.177
S. Phosphorus (mg/dL), 9	6.52 \pm 1.95	5.99 \pm 2.62	0.53	-1.37, 2.43	0.535

S= serum, Clcr- Creatinine Clearance

Early Evaluation Program) study. The maximum number of patients was in the age group of 46-60 years. And the number of patients in age more than 75 years was less. But other studies such as KEEP study [24% of participants were 65 yr or older] and Third National Health and Nutrition Examination Survey^[15] (NHANES III, 1999-2000) showed the increasing prevalence of CKD as age increases.

Study showed male predominance (77.56%) which is similar to study conducted by S.K. Agarwal and R.K. Srivastava^[5] where 70% of study population were males and in SEEK study 61% of study population were males. In other study, KEEP study (68% of females) and NHANES III^[15] (1999 - 2000) survey showed female predominance in their study population. The average BMI of the study population was found to be 23.22 ± 4.22 kg/m² which is comparable with SEEK study^[4] where BMI of study population was 25.12 ± 5.67 kg/m² and study by Wei-Hung Kuo et al^[16] where average BMI was 24.5 ± 4.2 kg/m². But NEOERICA project results^[3] showed little higher range that is 27.1 ± 5.5 kg/m².

For the management of CKD and its complication along with risk factors, it requires multiple drug therapy. The average number of drugs per patient was found to be 13.62 ± 5.27 ,

which is higher than studies by Rowa Al-Ramahi^[17] (in the first phase of the study 9.38 ± 3.63 medications on an average and in the second phase of study 9.94 ± 3.78 medication on an average) and Bailie et al^[18] (8.00 ± 4.00 medications on an average).

Kidney is an organ with multiple functions so decline in kidney function will lead to the development of several complications. In the present study, anemia was the most common complication seen in CKD patients that is 255 (81.7%) patients, which is comparable to PAERI (Prevalence of Anemia in Early Renal Insufficiency) survey.^[19] PAERI survey shows the increasing prevalence of anemia from 26.7% to 76% when CKD stage change from 3 to 5. Compared to SEEK study^[4] (40.7%) the percentage of patients with anemia is higher in present study.

Metabolic acidosis is also a complication of CKD and it was observed in 166 (53.21%) patients. A study by Miriam Moviat and Anniek M et al^[20] showed the presence of metabolic acidosis in kidney failure patients. In the present study, hyperuricemia was observed in 83 (26.6%) patients. 105 (33.7%) patients in the present study had hyperkalemia as one of the complication of CKD. A study by Sarafidis et al^[21] showed the prevalence of hyperkalemia in pre-dialysis patients with CKD that is about 54.2%.

Anemia is the one of the most common complication in CKD which is caused by decrease in production of the hormone erythropoietin (EPO) by kidney, decreased life span of RBC in presence of uremia, iron deficiency etc. Anemia can be managed by iron preparations, erythropoietin, blood transfusions etc. Iron preparations were used by 157 (50.32%) patients out of 312 patients for the management of anemia. It is higher compared to study by George Bailie et al (13%).^[18] Hundred and one (32.37%) patients were on erythropoietin in the present study, which is higher than the study by George Bailie et al. (20%).^[18]

Uremic toxins and protein - energy malnutrition can lead to the development of impaired cell mediated immunity and absolute lymphopenia,^[22] so CKD patients are more prone to infections. Fifty percent of patients (157 patients) were using antibiotics during hospital stay for the management of different infections. It is comparable to the study by Rowa Al-Ramahi.^[17]

Majority of patients were on monotherapy for the management of hyperphosphatemia and associated effects. Calcium acetate was the most frequently used calcium phosphate binder which is comparable to the study by Manley et al.^[23] But non-calcium containing phosphate binder, sevelamer used by less patients compared to Manley et al. study (31.1 %).^[23]

Since main route of excretion of potassium is kidney, decrease in kidney function is associated with hyperkalemia. In the present study 33.7% of patients had hyperkalemia as one of the complication of CKD and majority of patients were on more than one drug which is supported by the study by Michael allon et al ^[24] in hemodialysis patients.

Hypocalcemia was seen in 119 (38.1%) patients in the study population. Calcium carbonate was used by 83 (69.74 %) patients in the study either alone or in combination with

other drugs which are used to elevate calcium levels, which is supported by the study by Rowa Al-Ramahi^[17] (65.7% in first phase and 67 % in second phase). Hyponatremia is the one of the most important electrolyte abnormality seen in CKD patients. In the present study, 192 (61.5%) patients had hyponatremia as complication. Diuretics especially furosemide and normal saline were the most common used drugs in the present study for the management of hyponatremia. Study by Kian peng goh^[25] supports the use of diuretics and isotonic saline for the management of hyponatremia.

Duration of hospital stay was one of the measures used to assess the outcome of therapy. The average length of hospital stay of 312 CKD patients was found to be 7.34 ± 4.89 days, which is less than the study conducted by the Chan et al.^[2] That study showed that the early referred patients had a mean hospital stay of 13.5 ± 2.2 days and late referred patients had a mean hospital stay of 25.3 ± 3.8 days.

Laboratory values were also analyzed to assess the outcome of therapy. Lab values like serum Creatinine, serum urea, serum potassium and blood pressure had decreased and Creatinine clearance and serum sodium had increased at the end of study period. Change in laboratory values before and after treatment were statistically significant ($p < 0.001$).

Reduction in serum Creatinine (7.39 ± 4.09 at the time of admission vs 6.56 ± 3.55 at the time of discharge, $P < 0.001$) was comparable to study by Wei-Hung Kuo et al^[16] (3.2 ± 2.0 at baseline vs 4.3 ± 3.4 after 2 years of multidisciplinary care, $P < 0.001$). There was no significant improvement in the level of hemoglobin before and after treatment which is comparable to study by Wei-Hung Kuo et al.^[16] Serum calcium of all 29 patients was also improved after treatment, but it was statistically not significant.

During the data collection it was found that outcome related data was not available in all the cases making difficult to follow the improvement. Drug utilization studies can be carried out for patients who are on poly pharmacy. There is also a need to study the drug related problems in the dialysis patients. The present study gives an idea about the drug use pattern and extend of disease and its complications and management.

The present study showed that CKD patients have various long term complications. The most common complication was anemia and hyponatremia. Most of the complications were managed well and lab parameters of the patients improved significantly during the discharge. Appropriate management of the complications might reduce the rate of progression and increase the life expectancy of CKD patients.

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