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Research Article

MANAGEMENT OF COMORBIDITIES IN CHRONIC KIDNEY DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Objective: The study was aimed to manage the comorbidities in chronic kidney disease (CKD) in multi-super specialty hospital. This is a prospective observational study done for a period of nine months from January to September 2012 at the inpatient block of Global hospital at Lakdi-ka-pool in Hyderabad.

Methods: Demographic details of patient, present disease condition, drugs prescribed was collected from case report and their care takers were interviewed for their past medication history, family history.

Results: Out of 150 cases, 108 were males (72 %), 42 were females (28 %). Of them age difference in the range 54-62 are (22%) than other age groups.114 (76%) patients were at stage V whereas, 27(18%) and 9(6%) were at IV and III stage respectively. Patients with highest percentage of co morbidity were 26% of hypertension (HTN)+diabetes mellitus (DM), only HTN 23.3% and 15.3% of HTN+DM+CAD. Out of 119 HTN patients combination therapy of drugs was prescribed in 62(52.1%), individual drug therapy of Calcium channel blocker in highest number 72(60.5%), Beta blockers 66(55.4%). For management of DM insulin therapy was prescribed. For patients with coronary artery disease (CAD) Anti-platelet therapy were given in 34(54.8%) patients. To treat anemia erythropoietin was given in 70(47.2%), for dyslipidemia, atorvastatin was prescribed in 46(90.1%).

Conclusion: CKD is comorbid with HTN, DM and CAD and for the management of this it require a standard guidelines.

Keywords: Comorbidities, Coronary artery disease, Diabetes mellitus, Hypertension.

INTRODUCTION

Renal failure or kidney failure is a medical condition in which the kidneys fail to adequately filter toxins and waste products from the blood. Chronic Kidney Disease (CKD) is a term used to describe a permanent loss of kidney function or kidney injury. Renal failure is described as a decrease in glomerular filtration rate (GFR). Two forms of kidney failure are acute (acute kidney injury) and chronic (chronic kidney disease); a number of other diseases or health problems may cause either form of renal failure to occur. A recent study from 1999 to 2000 evaluated the prevalence of diabetes, metabolic risk factors and other indicators of renal disease in the broad Australian community, and the results have provided an increased understanding of the burden of kidney disease within the community, and applicable worldwide [1].

Approximately 30% of patients with diabetic nephropathy eventually progress to end-stage renal failure and the rest usually die from cardiovascular disease before reaching end stage. The combination of diabetes, hypertension, and chronic kidney disease is now the most common cause of end-stage kidney failure worldwide. There are now over 1 million dialysis patients worldwide, with an incidence of about a quarter of a million new patients each year [2]. Over 1 million people worldwide are alive on dialysis or with a functioning graft. Incidence of CKD has doubled in the last 15 years. In USA, >30 million people suffer from CKD. Chronic kidney disease is the slow loss of kidney function over time. CKD slowly gets worse over time. In the early stages, there may be no symptoms. The loss of function usually takes months or years to occur. It may be so slow that symptoms do not appear until kidney function is less than one-tenth of normal. The final stage of chronic kidney disease is called end-stage renal disease (ESRD). At this stage, the kidneys are no longer able to remove enough wastes and excess fluids from the body. The patient needs dialysis or a kidney transplant. CKD and ESRD affect more than 2 out of every 1,000 people in the United States.

Diabetes and high blood pressure are the two most common causes and account for most CKD cases [3]. When advanced, it causes a higher risk of mortality. The risk of developing CKD increases with increasing age, and some conditions that coexist with CKD. There is evidence that treatment can prevent or delay the progression of CKD, reduce or prevent the development of complications and reduce the risk of cardiovascular disease (CVD). Because of a lack of specific symptoms people with CKD are often not diagnosed, or diagnosed late when CKD is at an advanced stage [4]. Renal failure is typically detected by an elevated serum creatinine level. Problems observed in kidney failure include abnormal fluid levels in the body, increased acid levels, abnormal levels of potassium, calcium, phosphate, and (in the longer term) anemia as well as delayed healing in broken bones [5]. CKD is classified based on glomerular filtration levels (GFL) and is shown in table 1.

Table 1: Classification of CKD based on GFR level

Stage	GFR level	Symptom
Stage 1	Normal Renal Function (GFR ≥ 90 ml/min)	
Stage 2	Mild Impairment (GFR 60-89 ml/min)	Asymptomatic
Stage3a	Moderate Impairment	Asymptomatic
Stage3b	(GFR 45-59 ml/min) Moderate Impairment (GFR 30-44ml/min)	Anemia, Fatigue, Muscle cramps
Stage 4	Severe impairment (GFR 15-39 ml/min)	Anorexia, Nausea, Gout, Insomnia, Neuropathy
Stage 5	End Stage Renal Disease (GFR < 15 ml/min)	Itch, Headache, Cognitive Impairment, Death

Main risk factors for this CKD include diabetes, hypertension, blockages in the kidney, overuse of painkillers and allergic reactions to antibiotics, inflammation family history of kidney disease, premature birth, age and trauma/accident [6].

Co morbidity refers to any two or more diseases that occur in one person at the same time. In this report co morbidity refers to the presence of CVD, diabetes or CKD in combination with one or both of the other diseases. Cause of co morbidity can be summarized into two main groups: direct and indirect causal relationships between the diseases and shared risk factors. The direct and indirect causal

relationships between CVD, diabetes and CKD have been demonstrated by substantial evidence from pathological and epidemiological studies [7, 8].

Diabetes is a well known risk factor for CVD. One established explanation is that diabetes increases atherosclerosis (thickening of the wall of a blood vessel with deposits of plaque), which is the underlying cause of most CVD's. It is also established that people with diabetes tend to have higher levels of blood pressure and abnormal cholesterol level, both of which are factors that increase the risk of atherosclerosis and CVDs. Diabetes can also lead to kidney damage a complication known as diabetic nephropathy [9]. Moreover, diabetes also increases the risk of kidney damage and accelerates the reduction of kidney function by increasing the risk of hypertension.

CKD has been found to independently increase the risk of hypertension and other cardiovascular diseases, including heart attack, angina, coronary artery disease, stroke and heart failure. Some established risk factors of CVD, such as obesity, abnormal lipid levels and diabetes, are also common among people with CKD. In addition, CKD complications, such as anemia and disturbed mineral metabolism, also contribute to increased risk of CVD [10]. Shared risk factors of these diseases also promote co-occurrence of these diseases and strengthen the association between them. These risk factors do not just affect the onset of CVD, diabetes and CKD, but also affect their progression and increase the risk of complications. Because of these complex interactions, the risk of developing these diseases and their co morbidities is even greater among those with multiple risk factors.

Ageing is another factor that has a particularly strong association with many forms of co morbidity, including co morbidity of CVD, diabetes and CKD. All of these diseases are more likely to first arise among middle aged to old people. Complications of these diseases may develop over a considerable period (about 10–20 years) after the onset of the original disease. By the time co morbidity presents, most of these people are at an old or very old age. The period between onset of the disease and its co morbidity is extremely important for the prevention and management of co morbidity, as early detection and better management of the original disease can effectively reduce the risk of co morbidity and/or delay its occurrence.

Management of kidney failure can be done by treatment of hypertension in patients with chronic kidney disease, treatment of diabetes in patients with chronic kidney disease, treatment of dyslipidemia in patients with chronic kidney disease, lifestyle management for patients with chronic kidney disease, treatment of proteinuria in patients with chronic kidney disease, treatment of anemia in patients with stage 3-5 chronic kidney disease, assessment and treatment of mineral metabolism abnormalities in patients with chronic kidney disease and preparation for initiation of renal replacement therapy for patients with chronic kidney disease

MATERIALS AND METHODS

Study site: The proposed study was conducted at In-patient wards of Nephrology department of Global Hospital, Lakdi-ka-pool, and Hyderabad. Global hospitals group is one of India's leading healthcare institutions offering multi-super specialty tertiary care of international standards. Global hospital, Hyderabad situated at Lakdi-ka-pool has earned the reputation for being one of the best tertiary care multi-super specialty hospitals in India.

It is a 200-bedded hospital providing tertiary level multi-super specialty care and multi-organ transplantation services. It provides specialized services in Gastroenterology, Minimal Access Surgery, Cardiology and Cardio Thoracic Surgery, Nephrology, Urology, Neurology, Orthopedics, Joint Replacement, Spine surgery, Multi-organ transplantation.

Study design: Prospective Observational Studies

Study duration: The study was conducted for a period of Nine months from January 2012 to September 2012.

Study Population: In this study a total of 150 patients were enrolled.

Study criteria: The patients visiting the nephrology in patient departments were enrolled in to the study after taking their consent and by considering following inclusion and exclusion criteria.

Inclusion Criteria

- Inpatients
- Age > 18 yrs
- Patients of either sex
- Patients diagnosed as CKD

Exclusion criteria

- Outpatients
- Age < 18 yrs, pediatrics
- Pregnant women
- Patients who are not diagnosed as CK

Data collection

The data was collected from the patients who met the inclusion criteria. To study the management of CKD, relevant details of every in-patient with CKD were collected in suitably designed form. The relevant data of each patient was collected from the in-patient record. The demographic data (age, sex), the diagnosis by the treating Nephrologists was obtained from the in-patient case records of each patient. Also, associated co-morbid conditions, risk factors identified for developing CKD were noted from the medical records. The laboratory parameters which were monitored during the treatment were also recorded. Any other relevant data required which could not be obtained from case records were obtained by interviewing the patients, their caretakers or health care providers. The details of the data collected were transferred into MS Office excel work sheet.

Study procedure

All patients admitted in the ward were reviewed on daily basis and patients were enquired about their previous history of CKD. Patients with known complaint were interviewed for their past medication history and who met the study criteria were enrolled and their demographic details such as name, age, sex, weight, residential address, date of admission, reasons for admission, history of previous illness, family history, social history were collected. Information of vitals (blood pressure, temperature, pulse rate and respiratory rate) laboratory data (hematology, chest x-ray and etc.), provisional diagnosis, current drug regimen, final diagnosis and discharge medication is collected from case sheets of patients. All the above mentioned data is entered in the patient profile form. Patients or their care takers are interviewed for source of treatment given previously. Results were analyzed manually and percentages were calculated.

RESULTS AND DISCUSSION

Table 2: Age wise distribution of patients

S. No	Age Group	No. of patients (n =150)	Percentage (%)
1	18-26	6	4
2	27-35	22	14.66
3	36-44	18	12
4	45-53	31	20.66
5	54-62	33	22
6	63-71	27	18
7	72-80	11	7.33
8	81-89	2	1.33

During the study period total of 150 patients were reviewed in nephrology department in multi-super specialty hospital. Out of 150 patients, 108 were male, 42 were female patients.

Age is a factor which causes CKD. Older people are at higher risk, so patients with CKD were distributed according to age (Table 2) and according to the stage of CKD (Table 3).

Table 3: Distribution of patients according to stage of CKD

S. No.	Stage of CKD	GFR Level (ml/min)	No. of patients (n=150)	Percentage (%)
1	Stage III	30-60	9	6
2	Stage IV	15-30	27	18
3	Stage V	<15	114	76

Several co morbidities were observed in CKD patients and the list is shown in table 4

Table 4: List of co-morbidities in CKD patients

S. No	Co morbidity	No. of Patients (n=150)	Percentage (%)
1	HTN+DM	40	26.6
2	HTN	38	25.3
3	HTN+DM+CAD	23	15.3
4	Anemia	15	10
5	HTN+ Hypothyroidism	7	4.66
6	DM	5	3.33
7	HTN+ DM+ Hypothyroid	4	2.66
8	HTN+CAD	3	2
9	HTN+ Anemia	3	2
10	Anemia+ Hypothyroid	2	1.33
11	Others	6	4

HTN = Hypertension, DM = Diabetes Mellitus, CAD = Coronary Artery Disease

A Total of 119 patients are Hypertensive among 150 Chronic Kidney Disease patients. Class of Anti-Hypertensive drugs mostly prescribed at the stage III, IV and V are Calcium channel blocker in 72 patients. Table 5 shows the different anti-hypertensive agents prescribed in CKD patients with hypertension. Prescription of combination (63 patients) of anti-hypertensives is shown in table 6.

Table 5: Anti-Hypertensive Drugs prescribed in CKD patients

S. No.	Category	No.of Patients (n=119)	Percentage (%)
1	Calcium channel blockers	72	60.5
2	Beta blockers	66	55.4
3	Diuretics	51	42.8
4	Angiotensin adrenergic blockers	31	26
5	Angiotensin receptors blockers	12	10
6	Angiotensin converting enzyme inhibitors	4	3.3

A study was conducted by Qiu-Li Zhang and Dietrich Rothen bacher on "Prevalence of chronic kidney disease in population-based studies: Systematic review". This article reviewed the published evidence of prevalence of CKD in population-based study samples. The article reviewed 26 studies which were conducted in different populations, and the number of study participants ranged from 237 to 65181. They observed that median prevalence of CKD was 7.2% in persons aged 30 years or older and in persons aged 64 years or older prevalence of CKD varied from 23.4% to 35.8% [11].

In the present study a total of 150 patients are enrolled. People at age difference 54-62 are 33(22%) are in large number, 45-53 are 31(20.66%), 63-71 are 27(18%), 27-35 are 22(14.66%), 36-44 are 18(12%). Whereas low no. of people i.e., 11(7.33%) and, 6(4%) are in the age difference 72-80 and 18-26 respectively suffering from CKD.

Table 6: Combination of Anti-Hypertensive Drugs in CKD Patients

S. No.	Combination of Anti-Hypertensive Drugs	No. of patients
1	Calcium channel blockers + Beta blockers	13
2	Calcium channel blockers + Diuretics	10
3	Angiotensin adrenergic blockers + Beta blockers + Calcium channel blockers	8
4	Diuretics + Angiotensin adrenergic blockers + Beta blockers + Calcium channel blockers	6
5	Diuretics + Beta blockers + Calcium channel blockers	5
6	Diuretics + Beta blockers	6
7	Angiotensin receptors blockers + Calcium channel blockers	3
8	Angiotensin receptors blockers + Calcium channel blockers + Angiotensin adrenergic blockers + Beta blockers	2
9	Calcium channel blockers + Angiotensin adrenergic blockers	2
11	Others	8

In 150 patients a total of 53 patients are diabetic. CKD patients with diabetes are mostly treated with insulin during the hospital stay. Numbers of units prescribed in diabetic patients are shown in table 7.

Table 7: Usage of Human Insulin Act rapid for diabetic patients

S. No.	Random Blood Sugar (RBS) Level	Insulin Units	Route	No. of Patients(53)
1	100 -150 mg/dl	4U	S/C	9
2	150-200 mg/dl	6U	S/C	5
3	200-250 mg/dl	8U	S/C	17
4	250 -300 mg/dl	10U	S/C	8
5	>300 mg/dl	12U	S/C	14

Out of 150 patients, 62 patients are with Coronary artery disease (CAD). It also causes CKD and in the management of CAD following category of drugs are prescribed (Table 8).

Table 8: Drugs used in CAD in CKD Patients

S. No.	Category	No. of Patients (62)	Percentage (%)
1	Anti-Platelet	34	54.8
2	Nitrates	25	40
3	Anti- Arrhythmic	3	4.8

Out of 150 patients a total of 51 are with high cholesterol levels. Cholesterol levels are increased in CKD patients. So for the management of cholesterol in CKD, statins are prescribed (Table 9).

Table 9: Statins used in CKD Patients

S. No.	Category	No.of Patients (51)	Percentage (%)
1	Atorvastatin	46	90.1
2	Rosuvastatin	5	9.8

Management of anemia and dietary supplements used in CKD patients are shown in table 10.

Table 10: Drugs used for Anemic and Dietary supplement in CKD

S. No	Category	No. of Patients	Percentage (%)
1	Calcium carbonate	38	82.6
2	Erythropoietin	70	47.2
3	Levocarnitine	43	29
4	Ferric carboxy maltose	29	19.5
5	Sodium Bicarbonate	8	17.3
6	Iron sucrose	6	4

A study conducted by Robert D. Toto on "Management of Hypertensive Chronic Kidney Disease: Role of Calcium Channel Blockers" has demonstrated that systolic BP is a strong predictor for development of ESRD. Epidemiologic and clinical trial suggests that lowering BP and slows progression of CKD lower CV death risk. CCBs are safe and effective at reducing risk of both CKD progression and CV events and are used as first-line antihypertensive agents in CKD patients if there is a contraindication (e.g., hyperkalemia) to an ACE inhibitor or an ARB. Also, in hypertensive proteinuric patients not treated with an ACE inhibitor or an ARB, nondihydropyridine CCBs significantly reduce proteinuria whereas dihydropyridine CCBs do not [12]. In the present study a total of 119 patients are Hypertensive.Class of Anti-Hypertensive drugs prescribed are Calcium channel blocker in 72(60.5%) patients, Beta Blockers in 66 (55.4%) patients, Diuretics are prescribed in 51(42.8%) patients. Finally Angiotensin Receptor Blockers (ARBs) and Angiotensin Converting Enzyme Inhibitors (ACEIs) are prescribed in 12(10%) and 4(3.3%) patients respectively. CCBs are mostly prescribed to treat HTN, when ACEIs and ARBs are contraindicated.

A study conducted by Walter C. Coats, Sara Z. Baig, on "Management of Coronary Artery Disease in Patient with Chronic Kidney Disease". They stated that aspirin is safe and effective in patients with CKD for primary prevention of ischemic events and management of acute coronary syndromes and clopidogrel to treat acute coronary Disease. Recently, a sub study of the CREDO (Clopidogrel for the Reduction of Events During Observation) trial revealed that clopidogrel may have decreased effectiveness in patients with mild-to moderate CKD. There finding was not associated with increased bleeding in particular subgroup. Low molecular weight heparins such as enoxaparin are associated with increased bleeding in patients with CKD largely because of decreased renal excretion and difficulty in using factor Xa levels [13].

In the present study a total of 62 people with CAD. Clopidogerl was prescribed in large no 34(54.8%) whereas Nitrates (Isosorbide mononitrate) and Anti-Arrhythmic (Amidarone) are given in 25 (40%) and 3 (4.8%) respectively. Low molecular weight Heparin (Enoxaparin) prescribed in 22(35.4%) when renal excretion is decreased. A study was conducted by Anthony J. Pinevich on "Erythropoietin Therapy in Patients With Chronic Renal Failure". Recombinant human erythropoietin (epoetin alfa was approved in 1989 for use in treating the anemia of chronic renal failure. Several studies have reported the effect of the use of epoetin in patients with progressive kidney failure. Administering epoetin was successful in raising the hematocrit in virtually all patients. The quality of life is improved as anemia is corrected in patients before the progression to end-stage disease and concluded that the use of epoetin is beneficial and well tolerated [14]. In the present study out of 150 patients erythropoietin was used in 70(47.2%) which reduced the progression of kidney failure to ESRD and increase in hematocrit levels.

A Retrospective observational study was conducted by Eric D. Weinhandl, Madhumati Rao on "Protective effect of intravenous levocarnitine on subsequent-month hospitalization among prevalent hemodialysis patients" stated that use of levocarnitine is helpful in the reduction of length of hospitalization stay [15].

In the present study levocarnitine was prescribed in 43(29%) which reduced the length of stay.

A study was conducted by Seliger et al on "Statin treatment for dyslipidaemia in chronic kidney disease and renal transplantation: a review of the evidence". They found better survival in a small subgroup of statin users (n=362) compared with non-statin users (n=3,354) (39). Patients using statins had a reduced risk of total mortality (RR=0.68; 95% CI, 0.54-0.87) as well as CV-specific mortality (RR=0.64; 95% CI, 0.45-0.91) compared with non-statin users in the study. Statins have been extensively studied in a large variety of patient populations, with proven efficacy in the treatment of dyslipidaemia, reduction of CV mortality and regression of coronary calcification in the non-CKD setting [16, 17]. In the present study atorvastatin was used in 46(90.1%) and Rosuvastatin 5(9.8%) to lower the cholesterol level and reduce the mortality rate.

A study was conducted by Sanjay Kalra, Bharti Kalra and Navneet Agrawal on "Combination therapy in hypertension: An update". More recent clinical trials suggest that using monotherapy for the control of hypertension is not likely to be successful. Thiazide diuretics and CCBs are effective, as well as combinations that include rennin-angiotensin-aldosterone system (RAAS) blockers, in reducing BP. β-blockers showed increased risk for stroke, cardiovascular events and mortality in majority of the studies as compared to other anti-hypertensive's. BBs have more restricted place in cardiovascular therapy and can be possibly indicated in hypertensive's with anxiety and fast heart rate. The combination of a RAAS blocker and a low dose thiazide is useful if treatment with a CCB cannot control BP in patients with hypertension. The results of these studies confirm that diuretic/ACEI or diuretic/ ARB combinations reduce BP further than monotherapies in hypertensive diabetic subject [18].

In the present study combination of calcium channel blocker and Beta blocker are given in 13 patients, Calcium channel blocker and Diuretics are given to 10 people. Angiotensin Converting Enzyme Inhibitors (ACEIs)/ Angiotensin Receptor Blockers (ARBs) are used in combination with Calcium channel blockers (CCBs) in 8 and 3 patients respectively.

CONCLUSION

During the study we found that CKD is caused by many risk factors. With respect to age the patient with age in the range 54-62 are more prone to CKD than other age groups. The stage of the CKD is observed from the GFR levels. The people at stage V are in large number than at stage III and IV. Different comorbid conditions are responsible for the progression of the disease. In the study mostly people with hypertension and diabetes mellitus are in large number than other co morbidities. To manage HTN mostly CCB's and BB's are used in more number of people. Diabetes is managed by insulin therapy. Combination therapies for treatment of HTN, the drugs used mostly are CCB's along with BB's. In some patients CCB's with Diuretics are also used to treat HTN. Combination therapy is safe and effective for the management of HTN. CAD is treated by using Anti-platelet therapy in highest number than other category of drugs. Statins like atorvastatin and rosuvastatin are given for dyslipidemia. In them atorvastatin is used mostly. To treat anemia erythropoietin is prescribed and to treat thyroid disease, thyroxin was prescribed. Standard guidelines are needed for the management of CKD.

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