Research Article

# Assessment of Drug Prescrbing Pattern in Patient of CKD along with CVD in Tertiary care Hospital

**Sindhura.P*[1], Balaiah Sandyapakula[2], B.Silvya Grace[2], Dr. Charan Tej.K[3]**
1. Pharm.D student, Nirmala College of pharmacy, Mangalagiri, Guntur, A.P, India.
2. Assit.Professor, Nirmala College of pharmacy, Mangalagiri, Guntur, A.P, India.
3. Deputy Medical Superintendent, Manipal Hospitals, Vijayawada, A.P, India.
***Corresponding author's E-mail:** balu.slns@gmail.com

**Received:** 04-03-2018; **Revised:** 28-03-2018; **Accepted:** 11-04-2018.

**ABSTRACT**

The background of this study is Chronic kidney disease (CKD) patients with hypertension are highly prevalent and are a major determinant of progression of renal disease. The Most important, high blood pressure (BP) is an undisputed risk factor for cardiovascular (CV) disease this point is critical taking into consideration that for these patients, CV risk is significantly high and greater than the risk for reaching end-stage renal disease. Aim of the study is to perform prescription analysis in chronic kidney disease patients with hypertension. The main objective of our study is to analyze the prescribing patterns in the management of hypertension in CKD patients by performing prescription analysis. Methodology: Selection of study site: Private hospitals in Guntur district specialized with nephrology department. Study design: This prospective, cross-sectional, observational study was conducted in nephrology department of super speciality hospitals, The Study was accepted by institutional ethics committee. Study period: 6months over 6-months period from December to April 2017. Inclusion criteria and exclusion criteria was followed. Results and Discussion: Demographic characteristics of patients. The total number of prescribed medications was 311. Out of 60 prescriptions analyzed, average number of drugs per prescription was 5.18. the evaluation is based on anatomical level of ATC classification, most commonly prescribed medications were drugs for gastrointestinal tract and metabolism (28.93%) followed by drugs for cardiovascular system (23.47%) and those for treatment of disorders of blood and blood forming organs (18.96%) . represents utilization pattern of Hypertensive's. Out of total prescriptions CCBs were prescribed in 45%. Some prescriptions had more than one CCBs. Most commonly prescribed CCBs was Amlodipine (6.43%), followed by diltiazem (4.8%) and verapamil (3.2%).Conclusion: To conclude, this study identified a wide variety of drug classes prescribed in a cohort of CKD patients with Hypertension indicative of prevailing morbidity. It provides a scaffold for incessant prescription assessment in clinical setting and suggests potential improvement in prescribing practices in patients of CKD with Hypertension

**Keywords:** CKD, Dialysis, Hypertension.

## INTRODUCTION

Chronic kidney disease is the progressive, longstanding and irreversible impairment of renal functions. It is a general term for heterogeneous disorders affecting kidney structure and function.[1]

Chronic kidney disease (CKD) with hypertension is highly prevalent and is a major determinant of progression of renal ailments. More important, high blood pressure (BP) is an undisputed risk factor for cardiovascular (CV) disease this point is critical considering that for these patients, CV risk is dramatically high and greater than the risk for reaching end-stage renal disease .conversely, intensive antihypertensive treatment prevents the development of CV events during the predialytic phase and ameliorates survival in the subsequent dialyticstage .therefore, strict control of BP to less than 130/80 mm hg is now considered a main goal for the care of patients with CKD. Most patients with moderate CKD are managed wholly by primary care (PC) physicians.[1,2,3]

In the future, this approach will stand for an obligation for nephrologists and a prospect for patients if one considers that the exponential increase in prevalence of CKD will make nephrology manpower inadequate. However, recent studies have emphasized that the Lack of nephrology referral in patients with CKD is coupled with a 2-fold greater risk for fatality. Therefore, comparative analysis of BP control in Primary care and tertiary care becomes mandatory. [4, 5]

Knowledge of clinical description of patients With CKD and evaluation of therapeutic intervention in primary care, the first step to correctly plan a shared program for the treatment of patients with CKD. To date, no study has provided a systematic comparison on the control of hypertension between family physicians and Nephrologists.[6] Hypertension is a numerous finding in both acute and chronic kidney disease, particularly with glomerular or vascular disorders. [7]

### Prevalence in CKD

More than 400,000 Americans have end-stage renal disease, and over 300,000 of these patients require maintenance dialysis. Mortality rates remain 20 percent per year with the use of dialysis, with more than half of the deaths related to cardiovascular disease with hypertension. The annual direct medical costs for end stage renal disease are nearly $23 billion.[4, 5]

**Pathogenesis of hypertension in kidney disease**

The pathogenesis of hypertension varies with the type of disease (eg, glomerular versus vascular) and with the duration of disease (acute versus chronic).

**Treatment of hypertension slows the progression of CKD[8, 12]**

Hypertensive people with CKD stages 1-4 should be treated with an ACE inhibitor or an ARB, usually in combination with a diuretic. Target blood pressure in CKD stages 1-4 should be < 130/80 mm Hg.[7]

Generally in CKD treatment is based on the patient pathological condition and serum creatinine level, GFR.

| Stages of CKD | Glomerular filtration rate | Serum creatinine levels | Standard treatment |
|---|---|---|---|
| **Stage 1** | ≥90ml/min/1.73m² | <1.5mg/Dl | Observation, control of blood pressure |
| **Stage 2** | 60-89ml/min/1.73m² | >1.5mg/dL - <2.0mg/dL | Treating complications, control HTN,DM & slowing progression |
| **Stage 3** | 30-59ml/min/1.73m² | >2.0mg/dL - <5.0mg/dL | Evaluating& treating complications &slowing progression |
| **Stage 4** | 15-29ml/min/1.73m² | >5.0mg/dL - <8.0mg/dL | Preparation for dialysis or transplant |
| **Stage 5** | <15ml/min/1.73m² | >8.0mg/dL | Dialysis necessary. kidney transplant possible |

ACE inhibitors are more effective than other antihypertensive classes in slowing progression of kidney disease characterized by macro albuminuria in hypertensive patients. The beneficial effect of ACE inhibitors was greater in patients with decreased GFR at baseline, possibly because the end point, a doubling of baseline serum creatinine level, is achieved more quickly in patients with reduced GFR. [7,8,9,10,11]

In the opinion of the Work Group, ARBs can be used as an alternative class of agents CCBs to treat CKD in hypertensive people if ACE inhibitors cannot be used. ACE inhibitors, ARBs, and calcium channel blockers have a greater anti protein uric effect than other antihypertensive classes in hypertensive patients with CKD.[12, 13, 14, 15, 16]

High BP can be either a cause or a consequence of CKD. High BP may develop early in the course of CKD and can be associated with adverse outcomes such as worsening renal function and development of cardiovascular disease. Hypertension is a major promoter of the decline in GFR in both diabetic and non-diabetic kidney disease. [11, 16, 17]

## METHODOLOGY

**Aim**

The main aim of our study is to perform prescription analysis in chronic kidney disease patients with hypertension.

**Objective**

The main objective of our study is to analyze the prescribing patterns in the management of hypertension in CKD patients by performing prescription analysis.

**Selection of study site**

Private hospitals in Guntur district specialized with nephrology department.

**Study period**

6months (December 2016 to April 2017).

**Study design**

The study is prospective, cross-sectional, observational study was conducted in nephrology department of a super speciality hospital. The Study was approved by institutional ethics committee.

**Inclusion criteria**

1. The patients age in between 18-65years
2. Patients suffering with chronic kidney disease and hypertension
3. Outpatient and inpatient included.

**Exclusion criteria**

1. Patient above 65 years and below 18years
2. Patient suffering from chronic kidney disease with HTN.
3. Patient with other commorbidites
4. Pregnancy and lactation women

Phase 1- collection of case along with prescriptions

Phase 2- pooling of data from the prescriptions

Phase 3- results and discussions

## RESULTS AND DISCUSSION

**Table 1:** Demographic characteristics of patients suffering from chronic kidney disease (n=60)

| Characteristics | No of patients (%) |
|---|---|
| Gender | |
| Men | 44 (73.3%) |
| Women | 16 (26.6%) |
| Stages of CKD | |
| 5th stage (GFR <15ml/Min) | 28 (46%) |
| 4th stage (GFR 15-20 ml/min) | 18 (30%) |
| 3rd stage (GFR 30 – 50 mi/min) | 14 (23%) |
| Comorbidities | |
| Diabetes mellitus | 18 (30%) |
| Anaemia | 7 (11.6%) |
| Patients on haemodialysis | 12 (20%) |
| Patients on peritoneal dialysis | 6 (10%) |
| Note: CKD-Chronic Kidney Disease, GFR – Glomelular Filtration Rate | |

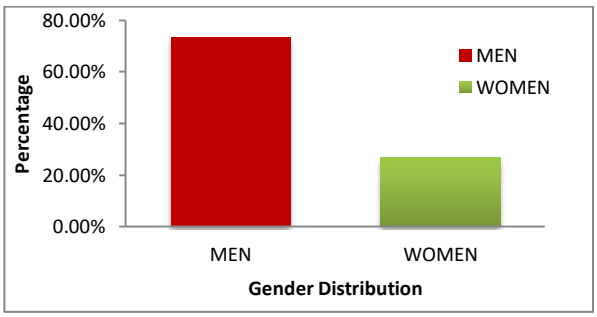


**Figure 1:** Gender distribution

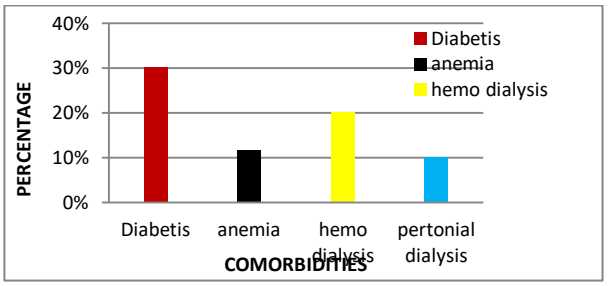


**Figure 2:** Comorbidities

**Table 2:** Analysis of Prescriptions in Chronic Kidney Disease- *WHO – drug core indicators*

| Prescribing indicators | Frequency |
|---|---|
| Prescription analysed | 60 |
| Total number of drugs prescribed | 311 |
| Average number of drugs per prescription | 5.18 |
| Number of drugs prescribed by generic names | 6 |
| Number of drugs from WHO essential drug list Out of total number of drugs prescribed | 112 (36.01%) |

Total 60 prescriptions of patients with age 18-70 years suffering from CKD were included in the study. Demographic characteristics of patients are shown in [Table 1]. The results of analysis of prescriptions for rationality are mentioned in [Table 2]. A total number of drugs prescribed were 311. Out of 60 prescriptions analyzed, average number of drugs per prescription was 5.18. On the basis of first anatomical level of ATC classification most commonly prescribed were drugs for gastrointestinal tract and metabolism (28.93%) followed by drugs for cardiovascular system (23.47%) and those for treatment of disorders of blood and blood forming organs (18.96%) [Table 3]. Vitamins and minerals were the most frequently prescribed drugs (4.18%), followed by cardiovascular drugs (16.72%), hematopoietic agents (7.71 %), and PBs (1.28 %.) [Table 4]. The five most commonly prescribed drugs were multivitamins (2.89%), iron (5.14%), folic acid (2.25%), and calcium carbonate (3.85%) Calcitriol(1.60%). [Figure 2] represents utilization pattern of Hypertensive's. Out of total prescriptions CCBs were prescribed in 45%. Some prescriptions had more than one CCBs. Most commonly prescribed CCBs was Amlodipine (6.43%), followed by diltiazem (4.8%) and verapamil(3.2%).

**Table 3:** Distribution of drugs prescribed for chronic kidney disease in different categories according to Anatomic Therapeutic Chemical classification

| Drug classes ( based on ATC classification) | Total no. of Drugs prescribed (%) |
|---|---|
| **A** - Drugs for gastrointestinal tract and metabolism | 90 (28.93%) |
| **B** – Drugs for treatment of disorders of blood and blood forming organs | 59 (18.96%) |
| **C** – Drugs for cardiovascular system | 73 (23.47%) |
| **D** – Dermatological drugs | 5 (1.06%) |
| **G** – Drugs for genitourinary system and sex hormones | 7 (2.25%) |
| **H** – Hormones for systemic use except sex hormones | 12 (3.85%) |
| **J** – Anti infectious drugs for systemic use | 3 (0.96%) |
| **L** – Antineoplastic and immunomodulating agents | 2 (0.64%) |
| **M** – Drugs for musculoskeletal systems | 6 (1.92%) |
| **N** – Drugs acting on nervous system | 9 (2.89%) |
| **P** – Drugs against parasites and insecticides | 1 (0.32%) |
| **R** – Drugs for respiratory system | 7 (2.25%) |
| **S**– Drugs for eye and ear | 00 |
| **V** - Various others | 37 (11.89%) |

**Table 4:** patterns of drug utilization in patients suffering from chronic kidney disease

| Drug classes | ATC code | Total No of prescription drugs (%) |
|---|---|---|
| Cardiovascular drugs | - | 52 (16.72%) |
| Calcium channel blockers | C08CA | 45 (14.46%) |
| Diuretics | C03CA | 12 (3.85%) |
| Alpha blockers | C02CA | 6 (1.92%) |
| ACE Inhibitors | C09AA | 12 (3.85%) |
| ARBs | C09CA | 7 (2.25%) |
| Beta blockers | C07AB | 5 (1.60%) |
| Drugs for GIT | - | 12 (3.85%) |
| PPI | A02BC | 9 (2.89%) |
| H2 blockers | A02BA | 5 (1.60%) |
| Anti diabetic drugs | - | 8 (2.57%) |
| Insulin | A10A | 4 (1.28%) |
| Oral hypoglycaemic agents | A10B | 2 (0.64%) |
| Heamopoitic agents | - | 24 (7.71%) |
| Iron | B03A | 16 (5.14%) |
| Folic acid | B03B | 7 (2.25%) |
| Erythopoietine | B03XA01 | 6 (1.92%) |
| PBs | - | 4 (1.28%) |
| Calcium carbonate | A02AA04 | 12 (3.85%) |
| Calcium acetate | A12AA12 | 3 (0.96%) |
| Sevelamer hydro chloride | V03AE02 | 2 (0.64%) |
| Vitamins and minerals | - | 13 (4.18%) |
| Vitamin D3 | A11HA | 7 (2.25%) |
| Calcitrol | A11CC04 | 5 (1.60%) |
| Antimicrobial agents | J01 | 16 (5.14%) |
| Multivitamins and minerals | A11AA | 9 (2.89%) |
| Herbal drugs | - | 5 (1.60%) |
| Miscellaneous | - | 3 (0.96%) |

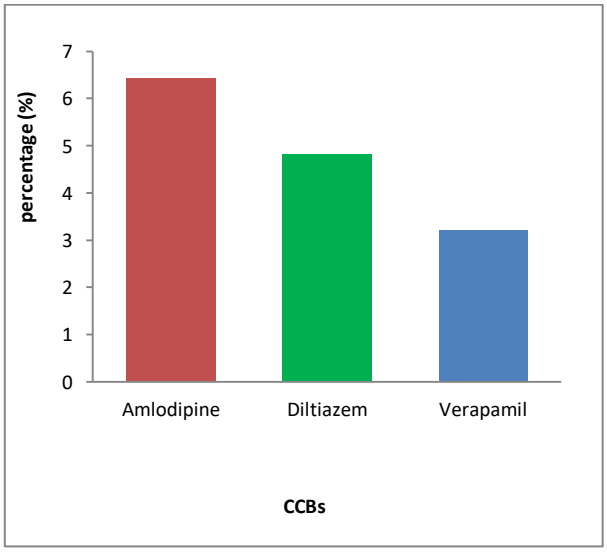


**Figure 3:** Utilisation pattern of calcium channel blockers in patients with chronic kidney disease

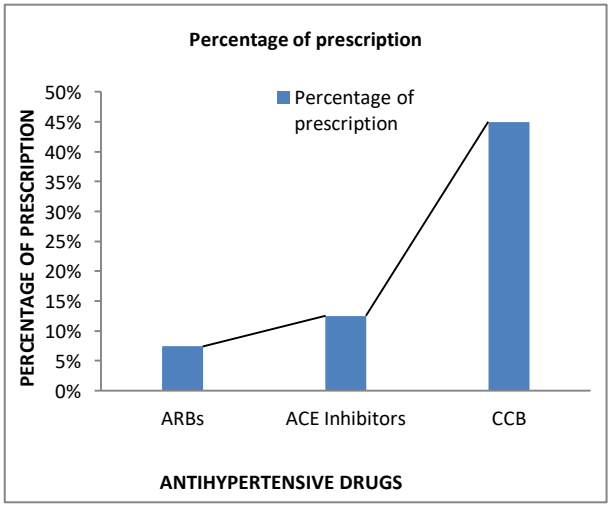


**Figure 4:** utilization pattern of anti hypertensive's in chronic kidney patients

## DISCUSSION

The gender distribution and mean age of patients in our study was Male 73.3% & Female was 26.7% and mean age will be 32 years. Average number of drugs per prescription was 5.18. Practice of poly pharmacy is a common finding in similar studies in CKD patients with average number of drugs per prescription varying from 4to 6.8. Poly pharmacy is defined as prescription of five or more medications to one patient at one time. However, considering the necessity of poly pharmacy in CKD, it may not be considered as poly pharmacy. Hence, some experts have even advised redefining poly pharmacy as nine or more medications, rather than five or more. In this study, only the prescribed medicines were considered. But it is well-known that over-the-counter use of medicines is common in this country. This further increases the chances of drug interactions and ADRs.

In our study, no drug was prescribed by its generic name, showing that prescribing by brand name is the norm, which needs to be discouraged. Encouraging prescription of drugs by generic names is always recommended by various national and international bodies to promote rational use of medicines. But implementation of this practice is never satisfactory and requires motivation of prescribers and strong regulatory interventions.

Only 36.01% of the prescribed drugs were from the WHO essential medicines list. So making these drugs freely available in public health facilities is less likely. Majority of the patients attending these facilities cannot afford to purchase these drugs from private pharmacies. Hence, whether the patients are actually consuming all the prescribed drugs or not is a matter of great concern.

Out of total prescribed drugs (311), most commonly prescribed were vitamins and minerals (4.18%), cardiovascular drugs, (16.72%), and hematopoietic agents (7.71%). Considering individual drugs, the five most commonly prescribed drugs were multivitamins (2.89%), iron (5.14%), folic acid (2.25%), calcium carbonate (3.85%), and calcitrioln (1.60%). These findings are similar to most of the earlier reported studies where calcium carbonate, multivitamin, folic acid, and ferrous sulphate were the most commonly prescribed drugs for CKD patients.

Out of all the drugs prescribed, 1.28% was PBs. Among PBs, calcium carbonate was the most frequently prescribed and sevelamer was the least prescribed. These findings are similar to those reported in an earlier study using data from contributors to the European practice database. But even in the said study which analyzed data from five different countries, higher use of sevelamer was reported in Greece. Similarly a study from Brazil also reported a large percentage of prescriptions of sevelamer among patients on maintenance haemodialysis despite the high cost of the medication and absence of contraindications for PB with calcium salts.

In contrast to previous study, wherein calcium channel blockers (CCBs) were most frequently prescribed antihypertensive drugs, in our study diuretics (3.85%) were found to be most frequently prescribed followed by CCBs (14.46%). In chronic renal failure or end stage renal disease, hyperkalemia is more likely to develop when Angiotensin converting enzyme (ACE) inhibitors or Angiotensin receptor blockers (ARBs) is prescribed. Also, unlike CCBs, most of the ACE inhibitors need dose modification in renal failure. So the choice of CCBs and diuretics seems to be logical.

Out of 18 patients suffering with diabetes mellitus, antidiabetics were prescribed in only 6 patients with preference for insulin (4) over oral hypoglycaemic drugs(2) . In diabetic patients, rigorous glycaemic control decreases the rate and progression of micro-albuminuria. However, during the phase of deteriorating renal function, insulin requirement falls because the kidney is a site of insulin degradation and this might be reason for the remarkable number of patients not receiving any antidiabetic agent, similar to previous study.

In contrast to previous studies, antimicrobials were less prescribed in this study in spite of high risk of infection seen in patients on haemodialysis and peritoneal dialysis a fact which needs to be noted. Most of the CKD patients are anemic. Underutilization of erythropoietin in the present study is surprising despite recommendations for its use. The high cost of erythropoietin may be the reason for its underuse since most patients visiting this government hospital are economically backward. The low prescription rate of erythropoietin indicates lacunae of current treatment practices and signals an opportunity for improvement in prescribing practices in CKD patients.

We found that prescribing herbal drugs was a routine practice. This has not been reported in any previous study. Obtaining details about the contents of these preparations was, however, beyond the scope of ourstudy. There are several limitations to this study. First, the sample size may not be adequate to reflect the exact picture of prescribing patterns in general and PB in particular. Similarly, data from multiple centres need to be collected to get a broader yet more comprehensive idea of use of PB and to analyze the reasons for underuse of these drugs. Another shortcoming of the study is the point prevalence nature of the medication-related data. It cannot be assumed that the prescription characteristic of a particular medication for a given patient remains unchanged over the course of follow-up of these patients. In spite of these lacunae, this study certainly provides an insight into the problems associated with the use of drugs in CKD patients.

## CONCLUSION

To conclude, this study identified a wide variety of drug classes prescribed in a cohort of CKD patients with Hypertension indicative of prevailing morbidity. It

provides a framework for continuous prescription audit in a hospital setting and suggests possible improvement in prescription practices in patients suffering from CKD with Hypertension

## REFERENCES


1. National Kidney Foundation: K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, classification, and stratification. Am J Kidney Dis 39:S1- S266, 2002 (suppl 1)
2. Jafar TH, Stark PC, Schmid CH, et al: Progression of chronic kidney disease: The role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition. Apatient-level meta-analysis. Ann Intern Med 139, 244-252, 2003
3. BakrisGL,Weir MR, Shanifar S, et al: Effects of blood pressure level on progression of diabetic nephropathy. Results from the RENAAL Study. Arch Intern Med 163, 2003, 1555- 1565.
4. Sarnak MJ, Levey AS, Schoolwerth AC, et al: Kidney disease as a risk factor for development of cardiovascular disease. A statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 108, 2154-2169, 2003
5. 5. Keith DS, Nichols GA, Gullion CM, Brown JB, Smith Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch Intern Med 164:659-663, 2004
6. Go SA, Chertow GM, Fan D, McCulloch CE, Hsu C: Chronic kidney disease and the risks of death, cardiovascular events and hospitalization. N Engl J Med 351, 2004, 1296-1305.
7. Pahor M, Shorr RI, Somes GW, et al: Diuretic-based treatment and cardiovascular events in patients with mild renal dysfunction enrolled in the Systolic Hypertension in the Elderly Program. Arch Intern Med 158, 1998, 1340-1345.
8. Shulman NB, Ford CE, Hall WD, et al: Prognostic value of serum creatinine and effect of treatment of hypertension on renal function. Results from the Hypertension Detection and Follow-up Program. Hypertension 13, 1989, I180-I193.
9. Lucas MF, Quereda C, Teruel JL, Orte L, Marcen R, Ortuno J: Effect of hypertension before beginning dialysis on survival of hemodialysis patients. Am J Kidney Dis 41, 2003, 814-821.
10. Nissensson AR, Collins AJ, Hurley J, Petersen H, Pereira BJG, Steinberg EP: Opportunities for improving the care of patients with chronic renal insufficiency: Current practice patterns. JAmSocNephrol 12, 2001, 1713-1720.
11. Xue JL, Ma JZ, Louis TA, Collins AJ: Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. J Am SocNephrol 12, 2001, 2735- 2738.
12. National Kidney Foundation. KDOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 39, 2002, S1-266. [PUBMED]
13. Noordzij M, Korevaar JC, Boeschoten EW, Dekker FW, Bos WJ, Krediet RT, Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) Study Group. The Kidney Disease Outcomes Quality Initiative (K/DOQI) Guideline for bone metabolism and disease in CKD: Association with mortality in dialysis patients. Am J Kidney Dis 46, 2005, 925-32.
14. Savica V, Calo LA, Monardo P, Santoro D, Bellinghieri G. Phosphate binders and management of hyperphosphataemia in end-stage renal disease. Nephrol Dial Transplant 21, 2006, 2065-8.
15. Bailie GR, Eisele G, Liu L, Roys E, Kiser M, Finkelstein F, et al Patterns of medication use in the RRI-CKD study: Focus on medication with cardiovascular effect. Nephrol Dial Transplant 20, 2005, 1110-5.
16. Kinsella K, Wan H: U.S. Census Bureau, International Population Reports, P95/09-1, An Aging World: 2008, Washington, DC, US Government Printing Office, 2009.
17. Chobanian A, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Roccella Wright JT: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. *JAMA* 289, 2003, 2560–2572.


**Source of Support:** Nil, **Conflict of Interest:** None.