



## Chronic kidney disease and its complete scenario, management of chronic kidney disease by clinical pharmacists - a prospective interventional study

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### Abstract

Chronic kidney disease is a growing epidemic worldwide. Nearly two-thirds of CKD patients have diabetes mellitus, hypertension, and both comorbid conditions. Several disease management programs are developed and they implement with help of physicians, and highly trained clinical pharmacists to improve disease management and improve clinical outcomes. The goals of clinical pharmacist in the management of CKD patients by focusing on Four key areas: To obtain information about medication non-adherence, To assess the patient complications for dialysis, to assess the prevalence of chronic kidney disease patients, To evaluate the clinical pharmacist's role in improving patient medication adherence, To identify the correlation between CKD and other comorbidities, To observe the drug interactions in prescribed drugs. Lack of patient knowledge on CKD disease conditions, and limited reimbursement, lack of primary care by physicians and health care professionals are all barriers that must be overcome with help of the clinical pharmacist role in the management of CKD.

**Keywords:** Chronic kidney disease, diabetes mellitus, hypertension, clinical pharmacists, medication adherence, drug interactions, complications of dialysis.


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### Introduction

**Renal System: Kidney:** The paired kidneys are reddish, bean-shaped organs located just above the waist between the peritoneum and the posterior wall of the abdomen. Because their position is posterior to the peritoneum of the abdominal cavity, they are said to be retroperitoneal. The kidneys are located between the levels of the last thoracic and third lumbar vertebrae, a position where they are partially protected by the eleventh and twelfth pairs of ribs. The right kidney is slightly lower than the left because the

liver occupies considerable space on the right side superior to the kidney [1].

**Renal Failure/Kidney Failure:** Renal failure is a decrease or cessation of glomerular filtration. It is of two types. In **acute renal failure (ARF)**, the kidneys abruptly stop working entirely (or almost entirely). The main feature of ARF is the suppression of urine flow, usually characterized either by oliguria (daily urine output between 50 mL and 250 mL), or by anuria (daily urine output less than 50 mL).

**Chronic renal failure (CRF)** refers to a progressive and usually irreversible decline in glomerular filtration rate (GFR). CRF may result from chronic glomerulonephritis, pyelonephritis, polycystic kidney disease, or traumatic loss of kidney tissue. CRF develops in three stages. In the first stage, diminished renal reserve; nephrons are destroyed until about 75% of the functioning nephrons are lost. At this stage, a person may have no signs or symptoms because the

remaining nephrons enlarge and take over the function of those that have been lost.

#### **Definition of Chronic Kidney Disease (CKD) [2, 3]**

Chronic kidney disease is defined as an estimated or measured glomerular filtration rate (GFR) less than 60 ml/min/1.73m<sup>2</sup> that is present for  $\geq$  three months with or without evidence of kidney damage.

OR

Evidence of kidney damage with or without decreased GFR that is present for  $\geq$ three months as evidenced by the following, irrespective of the underlying causes:

- Albuminuria (Albumin Excretion Rate (AER)  $\geq$  30mg/24hrs; Albumin to Creatinine Ratio (ACR)  $\geq$  30mg/g)
- Haematuria after exclusion of urological causes
- Structural abnormalities (e.g., on kidney imaging tests)
- Pathological abnormalities (e.g., renal biopsy)
- Urine sedimentation abnormalities
- Electrolyte and other abnormalities due to tubular disorders.
- History of kidney transplantation

#### **End-Stage Renal Disease (ESRD)**

- Chronic kidney disease is a progressive disease that eventually leads to renal failure and, end-stage renal disease.<sup>4</sup>
- The number of patients with chronic kidney disease is increasing, and it is expected that the number of patients with the end-stage renal disease will double by 2020.<sup>5</sup>

#### **Signs and Symptoms**

Signs and symptoms of chronic kidney disease may develop over time if kidney damage progresses slowly. Loss of kidney of function can cause [6]

- Nausea
- Vomiting
- Fatigue and weakness
- Urinating more or less
- Muscle cramps

#### **Renal Dialysis**

End-stage renal disease (ESRD) occurs when there is progressive loss of kidney function over a period of months to years to the point where the kidneys can no longer remove wastes, concentrate urine, maintain acid–base homeostasis, and regulate fluid and electrolytes and other important body functions. ESRD is classified under stage 5 chronic kidney disease (CKD), which refers to patients with an estimated glomerular filtration rate (eGFR) less than 15 mL/minute/1.73 m<sup>2</sup>, or those requiring dialysis or transplantation.

#### **Principles and Transport Process of Dialysis Techniques**

Hemodialysis (HD): Dialysis is a process that facilitates the removal of excess of water and toxins from the body, both of which accumulate as a result of inadequate kidney function. During HD, a patient's anti-coagulated blood and an electrolyte solution that stimulates plasma are simultaneously perfused through a dialyzer (artificial kidney) on the opposite side of a semi permeable membrane.<sup>6</sup>

- Solutes (e.g., metabolic waste products, toxins, potassium, and other electrolytes) are removed from the patient's blood by diffusing across concentration gradients into the dialysate.

#### **Blood and Dialysate Flow**

- Although small-molecule clearance is highly dependent on blood flow, the relationship is not strictly linear. Increased blood flow yields a less than proportional response in urea clearance.<sup>6</sup>
- This is likely because of an insufficient time for equilibration to occur between the blood and dialysate compartments as well as a greater membrane resistance to diffusion from an increased stagnant layer.

#### **Vascular Access [6]**

- Permanent vascular access site provides easy access to high blood flow, which cannot be achieved through routine venipuncture of superficial veins. Different types of vascular access are available: Arteriovenous fistula (AVF), Arteriovenous Graft (AVG).
- An AVF is created surgically by subcutaneous anastomosis of an artery to an adjacent vein. The AV fistula may not be suitable for patients with poor vasculature, such as elderly patients or those with diabetes, atherosclerosis, or small vessels.

#### **Hemoperfusion**

Hemoperfusion is a treatment technique in which large volumes of the patient's blood are passed over an adsorbent substance in order to remove toxic substances from the blood. Adsorption is a process in which molecules or particles of one substance are attracted to the surface of a solid material and held there

#### **Peritoneal Dialysis (PD) [6]**

Peritoneal dialysis utilizes similar principle; blood is exposed to a semi permeable membrane as like hemodialysis against which a physiologic solution is placed. In PD the semi permeable membrane is peritoneal membrane and a sterile dialysate instilled in to the peritoneal cavity.

#### **Management of Diabetes Mellitus**

Management of diabetes is also important. First, glycemic control may delay progression of CKD, with most guidelines recommending a goal hemoglobin A1c of  $\sim$  7.0% [7, 8, 9]. Second, dose adjustments in oral hypoglycemic agents

may be necessary. In general, drugs that are largely cleared by the kidneys (eg, glyburide) should be avoided, whereas drugs metabolized by the liver and/or partially excreted by the kidneys (eg, metformin and some dipeptidyl peptidase 4 [DPP-4] and sodium-glucose cotransporter-2 [SGLT-2] inhibitors) may require dose reduction or discontinuation, particularly when eGFR falls below 30 mL/min/1.73 m<sup>2</sup>.

#### **Management of Hypertension**

Many guidelines provide algorithms detailing which agents should be used to treat hypertension in people with CKD.10 [11].The presence and severity of albuminuria should be evaluated. Blockade of the renin-angiotensin-aldosterone system with either an angiotensin-converting enzyme inhibitor (ACE-I) or an angiotensin II receptor blocker (ARB) is recommended for adults with diabetes and a urine ACR of at least 30 mg per 24 hours or any adult with a urine ACR of at least 300 mg per 24 hours.

#### **Anaemia and the Role of Erythropoietin in CKD**

Anemia is among the most common complications of CKD. In a study that included 19 CKD cohorts from across the world, 41% of the 209 311 individuals had low levels of hemoglobin (defined as <13 g/dL in men and <12 g/dL in women) [12]. The initial workup of anaemia should include assessment of iron stores: those who are iron deficient may benefit from oral or intravenous iron repletion

#### **Dietary Management**

Dietary management to prevent CKD progression is controversial since large trials have had equivocal results [13, 14, 15]. For example, the MDRD study evaluated 2 levels of protein restriction in 840 patients, finding that a low-protein diet compared with usual protein intake resulted in slower GFR decline only after the initial 4 months and that a very low-protein diet compared with a low-protein diet was not significantly associated with slower GFR decline. Both levels of protein restriction appeared to have benefits in the subgroup with proteinuria greater than 3 g per day, although this group was small.

#### **Adherence to Medication**

Adherence to medication is defined as 'the extent to which the patient's behaviour matches agreed recommendations from the prescriber' 16. In chronic kidney disease (CKD), adherence to medication is a key component of effective disease management [17, 18]. The main goals of medication are to slow progression of the disease and monitor and correct disease-associated complications and comorbidities while treating the underlying etiology.

#### **Role of the Clinical Pharmacist in Improving Medication Adherence in CKD Patients**

In the patient care, the pharmacist plays an important role while dispensing the medication, he maintains patient care through counselling, medication therapy management (MTM), disease- state management and other means. In order to improve patients adherence and therapeutic outcomes, there are different opportunities in pharmacy practice. In particular, their will be reimbursement for such activities with the introduction of new health care reform laws – patient protection and affordable care act.

#### **The Role of Diabetes Mellitus and Hypertension in Chronic Kidney Disease Prevalence**

With interest, we read the article by Hernandez *et al.* about increasing awareness of chronic kidney disease [19]. We agree with the authors of the article that, diabetes mellitus and hypertension are the leading causes of chronic kidney disease (CKD). Over the last decade, different kinds of glomerulonephritis (GN) were the leading causes of CKD in the world, too. However, it is mainly due to lifestyle changes and increasing prevalence of obesity, diabetes and hypertension and because of more available aggressive treatment of GN, it is well well-known that diabetes and hypertension are now the primary causes of CKD in developed countries [20-24].

#### **Aims and Objectives**

##### **AIM**

To study about Chronic Kidney Disease and its complete scenario, management of chronic kidney disease by clinical pharmacists – A prospective interventional study.

##### **Objectives**

- To obtain information about medication nonadherence
- To observe the patient compliance with dialysis process
- To assess the patient's medication adherence status.
- To evaluate the clinical pharmacist's role in improving patient medication adherence
- To identify the co-relation between CKD and other comorbidities
- To observe the drug interactions in prescribed drugs.

##### **Methodology**

- The study was conducted in the department of nephrology of MIMS hospital, Nellimarla.
- The participants enrolled in the study involved inpatients and outpatients only after filling a properly written informed consent.

- The data was collected in a pre-designed data collection form (CASE REPORT FORM).

### Study Site

Maharaja Institute Of Medical Sciences (MIMS), Nellimarla, Vizianagaram

### Study Population

300 inpatients and outpatients attending the nephrology department.

### Study Duration

8 Months [November 2021 to June 2022].

### Study Design

Prospective interventional study approved by the hospital ethical committee.

### Study Criteria

#### Inclusion Criteria

- Patients of either sex of age between 20 – 80.
- Patients with comorbidities like hypertension & diabetes mellitus.
- Patients diagnosed with CKD.
- Patients who are willing to participate in the study by signing an informed consent form (ICF).

#### Exclusion Criteria

- Patients of age <20
- Children
- Patients who are not willing to participate in study by signing the ICF form.
- Pregnant women
- Lactating mothers

### Study Procedure

#### Phase I

- Obtaining consent from hospital authorities
- Literature survey
- Designing of the data collection form
- Data collection

#### Phase II

- Assessment of medication non-adherence of patients
- Assessment of drug interactions
- Assessment of patient compliance during dialysis
- Evaluating the role of clinical pharmacist in improving medication adherence
- Evaluating the role of clinical pharmacists in improving the overall condition of the patient.

#### Phase III

- Data analysis and evaluation

### Parameters Monitored in Study

- Medication Adherence

- Drug Interactions
- Comorbidities Like Hypertension ,Diabetes
- Dialysis Frequency
- Lab Values Such As Serum Creatinine, Blood Urea Nitrogen

### Out Comes of the Study

- Patient knowledge about drugs and disease condition was increased.
- Physician acceptance about alternation of drug increased by the continuous efforts of clinical pharmacists.

### Statistical Analysis

Drugs are classified based upon WHO-ATC classification, data collected was analyzed statistically using descriptive analysis, namely mean and standard deviation for quantitative variables and non-parametric tests for qualitative variables, whenever necessary results will be depicted in form of percentages, pie charts and graphs.

### Material and Methods

#### Phase -1 Obtaining Consent from Hospital Authority

- The study was carried out in hospital by the department of pharmacy practice. So it has to be approved by the Medical Superintendent (MS) and same should be informed to all physicians and surgeons of the hospital.
- For obtaining the consent, a study protocol has prepared which include proposed title, study site, inclusion and exclusion criteria, objective and methodology about the work to be carried out.
- Then the protocol of the study was submitted to Medical Superintendent (MS), permitted to perform the study by ward round and utilize the hospital facilities through a letter.

#### Obtaining ICF from Individuals

- The study was carried on each individual patient. So it needs approval from every individual. For this cause informed consent form (ICF) should be obtained from individuals also.

#### Data Entry Format

- A separate data entry format for incorporating inpatient details was designed it includes demographic details, family history, medical history, diagnosis and they are designed as questionnaires using different tools.

#### Phase-2

#### Collection of Data

- The study was planned to investigate 300 patient records to increase the precision of the Parameters.

Patient records from inpatient and outpatient wards of nephrology department were obtained. Each selected Chronic Kidney Disease patient was questioned regarding their condition by the help of designed data collection form.

### Phase -3

#### Analysis of Data

The data from the selected patients were collected from both inpatient and outpatient medical departments, paying attention to inclusion and exclusion criteria.

#### Data Evlution

- The data collected from all the selected patients were evaluated using SPSS software and information regarding the Chronic Kidney Disease and its complete scenario, management of chronic kidney disease by clinical pharmacists – A prospective interventional study.

## RESULTS

### Comorbidities

The maximum number of patients who were under our study suffered not just from CKD but also with some comorbidities, hypertension (HTN), Diabetes mellitus (DM), urosepsis, pulmonary edema, anemia, urinary tract infections, pyelonephritis. Among them high number of patients about CKD With Diabetes Mellitus - 123 (41%) cases followed by CKD With Hypertension -65 (21%) cases, followed by CKD With Both Hypertension AND DIABETES MELLITUS - 35 (11.6%) cases followed by CKD With Pulmonary Edema – 18 (6%) cases followed by CKD With Anemia - 22 (7.2%) cases followed by CKD WITH UTI- 14 (4.6%) cases followed by Ckd With Urosepsis - 12 (4%) cases followed by CKD With Pyelonephrities - 11 (3.6%) cases.

### Stages of CKD

To interpret the state of disease condition, stage of CKD is necessary. The number of patients who are among CKD Stage (III) were 46(15.3%). For stage IV CKD, stage V CKD, Stage V+ (ESRD) are 129 members (43%), 108 members (36%), 17 members (5.6%) respectively.

### Dialysis

The number of patients undergoing dialysis were of course more in number due to their chronic illness of kidney, who were 219 in number & (73%), patients about 81 members were not dialysed (27%).

### Dialysis Type

The common dialysis recommended is hemo dialysis unless their are heart problems for those patients. The hemo dialysis patients are 1155 (70.7%), peritoneal dialysis patients are 22 (10.4%), both 24(10.9%), and nill 18 (8.21%).

### Complications of Dialysis

Out of 300 patients 219 were dialysed and the complications observed are vomiting among 72(32.8%), hypotension among 33(15.0%), headache among 26(11.8%), muscle cramps among 23 (10.5%), epigastric pain among 21(9.58%), hotness among 19(8.67%), chest pain among 14(6.39%), backache among 11 (5.02%).

### Reason for Non-Adherence to Medication in CKD Patients

Among 300 patients, 154 patients were not adherent to medication. The reason for non medication adherence in those patients are due to forgetfulness 44(28.5%), difficulty to take large number of pills 18 (11.6%), fear of ADR 32 (20.7%), missed appointments 20 (12.9%), poor access to medication 19 (11.2%), depression 6 (3.8%), other illness 15 (9.7%).

### Anti-Hypertensive Drugs Prescribed In CKD Patients

A total of 100 patients are hypertensive among 300 chronic kidney disease patients. class of antihypertensive mostly prescribed at stage III, IV, and v are diuretics in 43 patients (43%), calcium channel blockers in 28 (28%), angiotensin converting enzyme inhibitors in 19(19%), and beta blockers in 10 (10%).

### Drug Interactions

Out of 300 patients, drug interaction were found in 195 cases. The major drug interaction were Furosemide + Pantoprazole in 43 Patients (22.0%), Furosemide + Ceftriaxone in 27 Patients (13.8%) Nifedipine + Calcium Carbonate In 19 Patients(9.7%),Furosemide + Insulin In 38 Patients (19.48%)Insulin + Enalapril In 17 Patients (8.71%),Metformin +Furosemide 51 Patients (26.1%).

### Prescription Errors

In 300 patients, 170 prescripational errors were found. The types of errors identified were incomplete Rx (35.2%), prior ADR (21.1%),high dose (14.1%), unnecessary drug (11.7%),inconvenient drug (6.4%), contra indication (4.7%), wrong dosage form (3.5%), low dose (1.7%), others (1.1%).

## Discussion

The results of the study revealed that majority of the patients of age 51-60(24.6%) were affected by the chronic kidney disease followed by 31-40 years patients of 19.3%,61-70 years with 18.3%,41-50 with 16.6%. Males are mostly affected by this condition when compared to the female's i.e 60.6% and 39.3% respectively. The risk factors included are smoking and alcohol drinking. We found that 157 patients of 52.3% are smokers and 142 patients of 47.3% are alcoholics. Most of the patients with CKD and comorbidities like hypertension and diabetes are having these risk factors (alcohol drinking and smoking). In a retrospective study it reported that the patients with a combination of smoking and hypertension

resulted into renal failure in short time when compared with non smoking hypertensive patients.

#### **CO-Morbidities**

In consideration of comorbidities of chronic kidney disease, it was observed that majority of 123 cases of 41% were seen with chronic kidney disease and diabetes mellitus, followed by 65 cases of 21.6% were with chronic kidney disease and hypertension, followed by both hypertension and diabetes mellitus with 35 case of 11.6%, anemia with 22 cases of 7.3%, followed by pulmonary edema with 18 cases of 6%. As an existing fact in accordance with the literature review, diabetes mellitus and hypertension are the major culprits for the prevalence of chronic kidney disease.

#### **Medication Non-Adherence**

In this study we conclude that reasons for non medication adherence is mainly due to forgetfulness(34.6%), followed by difficult to take large number of pills(14.5%), followed by fear of adverse drug reactions(13.7%). This work is in similar with work done by Varleta P, Akel C, Acevedo M et al. in Assessment of adherence to antihypertensive therapy who concluded that the reason for nonmedication adherence is forgetfulness in 67% patients using Morisky questionnaire.

#### **Management**

Diuretics were most commonly used in the patients(43%) in the patients followed by other anti-hypertensive drugs such as calcium channel blockers and ACE inhibitors (28%) and (19%). This was similar to the study Bajait et al reported that diuretics are mostly used than CCBs and ACE inhibitors. Diuretics are used to reduce blood pressure and to reduce overload. In diuretics, Furosemide is most commonly used.

#### **Conclusion**

Chronic kidney disease one of the major culprit for most number of deaths across the globe. After data analysis and statistical interpretation the following conclusions were drawn. Males were more prone to CKD when compared to females because of their habits and life styles. Chronic alcoholism and smoking act as triggers for the prevalence of CKD. Long-term complications like diabetes and hypertension could lead to kidney complications if they were not treated properly. CKD could be treated effectively if the diagnosis was done in early stages. Late stage diagnosis is the main reason for complete kidney failure and leading to dialysis. Patients were left with no choice except going for dialysis of which the procedure itself causing more inconvenience to the patients due to unavoidable complications.

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#### **Author Contribution**

All authors contributed equally.

#### **Conflict of Interest**

The authors declared no conflict of interest.

#### **References**

1. Gerard J. Tortora, Bryan Derickson. Chapter: 26 The Urinary system, Principles of Anatomy and Physiology. John Wiley & Sons, Inc. 12th Edi. - 2009; 1020,56.
2. Tim Mathew. Chronic kidney disease management in general practice Hand book.3rd Edi.-2015; 13.
3. Jennifer RL, Van Harrison R. UMHS Chronic Kidney Disease Guideline: Guidelines on clinical care ambulatory. University of Michigan.2014; 3, 4.
4. Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, Rotschafer JC, Dipiro JT, Section 4: Chapter 23.Chronic and ESRD. Pharmacotherapy Principles & Practice-2008:373-401.
5. Joseph TD, Robert LT, Gary CY, Gary RM, Barbara GW, Michael LP et.al. Chapter 47, Renal disorders, Pharmacotherapy: A Pathophysiologic Approach. Mc Graw Hill Medical, 7th Edition-2008; 765.
6. Chronic kidney disease - Symptoms and causes - Mayo Clinic
7. Pathophysiology and Classification of Kidney Diseases - PMC (nih.gov)
8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013; 3 (1):1–150. [Google Scholar]
9. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. *Am J Kidney Dis.* 2014; 63 (5):713–735. doi: 10.1053/j.ajkd.2014.01.416 [PubMed] [CrossRef] [Google Scholar]
10. Zinman B, Wanner C, Lachin JM, et al.; EMPA-REG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med.* 2015;373(22):2117–2128. doi: 10.1056/NEJMoa1504720 [PubMed] [CrossRef] [Google Scholar].

11. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507–520. doi: 10.1001/jama.2013.284427 [PubMed] [CrossRef] [Google Scholar]
12. Williams B, MacDonald TM, Morant S, et al.; British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. *Lancet*. 2015;386(10008):2059–2068. doi: 10.1016/S0140-6736(15)00257-3 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
13. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney Int Suppl*. 2012;2(4):279–335. [Google Scholar]
14. Klahr S, Levey AS, Beck GJ, et al.; Modification of Diet in Renal Disease Study Group. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. *N Engl J Med*. 1994;330(13):877–884. doi: 10.1056/NEJM199403313301301 [PubMed] [CrossRef] [Google Scholar]
15. Menon V, Kopple JD, Wang X, et al. Effect of a very low-protein diet on outcomes: long-term follow-up of the Modification of Diet in Renal Disease (MDRD) study. *Am J Kidney Dis*. 2009;53 (2):208–217. doi: 10.1053/j.ajkd.2008.08.009 [PubMed] [CrossRef] [Google Scholar]
16. Banerjee T, Crews DC, Wesson DE, et al.; Centers for Disease Control and Prevention Chronic Kidney Disease Surveillance Team. High dietary acid load predicts ESRD among adults with CKD. *J Am Soc Nephrol*. 2015;26(7):1693–1700. doi: 10.1681/ASN.2014040332 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
17. Inker LA, Grams ME, Levey AS, et al.; CKD Prognosis Consortium. Relationship of estimated GFR and albuminuria to concurrent laboratory abnormalities: an individual participant data meta-analysis in a global consortium. *Am J Kidney Dis*. 2019;73(2):206–217. doi: 10.1053/j.ajkd.2018.08.013 [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]
18. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney Int Suppl*. 2012;2(4):279–335. [Google Scholar].
19. Hernandez GT, Nasri H. World Kidney Day 2014: increasing awareness of chronic kidney disease and aging. *J Renal Inj Prev*. 2014;3(1):3–4. [PMC free article] [PubMed] [Google Scholar]
20. Ritz E, Rychlik I, Locatelli F, Halimi S. End-stage renal failure in type 2 diabetes: A medical catastrophe of worldwide dimensions. *Am J Kidney Dis*. 1999;34:795–808. [PubMed] [Google Scholar]
21. Perneger TV, Brancati FL, Whelton PK, Klag MJ. End-stage renal disease attributable to diabetes mellitus. *Ann Intern Med*. 1994;121:912. [PubMed] [Google Scholar]
22. USRDS: The United States Renal Data System. Excerpts from the USRDS 2009 annual data report: Atlas of end-stage renal disease in the United States. *Am J Kidney Dis*. 2010;55(Suppl 1):S1. [Google Scholar]
23. Van Dijk PC, Jager KJ, Stengel B, Grönhagen-Riska C, Feest TG, Briggs JD. Renal replacement therapy for diabetic end-stage renal disease: Data from 10 registries in Europe (1991-2000) *Kidney Int*. 2005;67:1489. [PubMed] [Google Scholar]
24. Robert C. Atkins. The epidemiology of chronic kidney disease. *Kidney Int*. 2005;67:14–18. [PubMed] [Google Scholar]