

***Evaluating the prevalence and etiology of chronic renal failure***Ali Alidadi^{1,2}, ElhamTaheri Boroujeni³¹ Nephrology Department, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan , Iran² Clinical Immunology Research Center (CIRC) at Zahedan University of Medical Sciences (ZAUMS), Zahedan, Iran³ Student Research Committee, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran**ABSTRACT**

Introduction: Chronic renal failure is referred to as the progressive and irreversible loss of renal function, ultimately leading to the "end stage of renal disease" (ESRD), requiring one alternative treatment, including dialysis or grafting; in the final stage of renal disorders, kidney is unable to maintain metabolic function, fluid balance and electrolytes in the body; the ultimate consequence will be a dangerous and lethal condition called the uremia which, in turn, causes several serious complications in the body.

Methods: Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned.

Discussion: CKD can have a range of etiologic causes; however, diabetes and hypertension are two of the main causes of the disease .Diabetic nephropathy is the most common type of glomerulopathy; it is also the most common cause of ESRD in the United States and Europe. In fact, about 50% of ESRD patients are diabetic. Only about 30% of patients with type 1 diabetes and 35-40% of patients with type 2 diabetes show, despite glycemic control, diabetic nephropathy .Hypertension is the second major cause of ESRD. About 51-63% of all patients with CKD are hypertensive, and this number has reached 90% in patients over the age of 65.

KEY WORDS: prevalence, etiology, chronic renal failure

INTRODUCTION:

Chronic renal failure is referred to as the progressive and irreversible loss of renal function, ultimately leading to the "end stage of renal disease" (ESRD), requiring one alternative treatment, including dialysis or grafting; in the final stage of renal disorders, kidney is unable to maintain metabolic function, fluid balance and electrolytes in the body; the ultimate consequence will be a dangerous and lethal condition called the uremia which, in turn, causes several serious complications in the body (1,2).

Methods:

1.1. Search strategy

Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from

the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review search using the MESH terms and free terms according to the PRESS standard. After the MEDLINE strategy was finalized, it was adapted to search in other databases. Accordingly, PROSPERO was searched for ongoing or recently related completed systematic reviews. The key words used in the search strategy were prevalence, etiology, chronic renal failure which were combined with Boolean operators including AND, OR, and NOT.

1.2. Study selection

Results of the Literature review were exported to Endnote. Prior to the formal screening process, a calibration exercise was undertaken to pilot and refine the screening. Formal screening process of titles and abstracts were conducted by two researchers according to the eligibility criteria, and consensus method was used for solving controversies among the two researchers. The full text was obtained for all titles that met the inclusion criteria. Additional information was retrieved from the study authors in order to resolve queries regarding the eligibility criteria. The reasons for the exclusion criteria were recorded. Neither of the review authors was blinded to the journal titles, the study authors or institutions.

Prevalence

This disease has been quite progressive in recent years and its incidence has increased 10 times in the past 20 years in the United States (3). The annual growth rate of this disease in Iran, according to the reports issued by the Center for Transplant Management and Special Diseases of the Ministry of Health, was about 11%, reaching a number of 40000, in 2009. The annual incidence of this disease in Iran is 53 per 1 million people and its prevalence is 250 per 1 million people. In case of the United States, these figures are 200 and 975 per million, respectively. At the end of 2005, one million and 900,000 people were undergoing alternative therapies (4). The number of patients with end-stage renal disease in the world in 2006 exceeded 2 million and was 6% higher than world population growth (5). In Iran, with more than 13,000 dialysis patients, 150,000 dialysis sessions are conducted monthly (6).

Etiology

CKD can have a range of etiologic causes; however, diabetes and hypertension are two of the main causes of the disease. Diabetic nephropathy is the most common type of glomerulopathy; it is also the most common cause of ESRD in the United States and Europe (7). In fact, about 50% of ESRD patients are diabetic (8). Only about 30% of patients with type 1 diabetes and 35-40% of patients with type 2 diabetes show, despite glycemic control, diabetic nephropathy (9). Hypertension is the second major cause of ESRD. About 51-63% of all patients with CKD are hypertensive, and this number has reached 90% in patients over the age of 65 (10). Hypertension causes nephrocyclopedicglomerulonephrosis, which is characterized by the following

characteristics: renal vasculopathy, which affects arterioles and glomerular plaque arteries, mainly due to atherosclerosis, endothelial dysfunction, fibrosis and thickening of the wall. 2. Microscopic node disease Glomerular tuft capillaries 3 - Distributed glomerulosclerosis and less commonly found focal and segmental glomerulosclerosis (FSGS) and 4 - Hyperthyroidism (11).

Staging

CKD is primarily staged in order to provide the most optimum management, including progression risk categorization and CKD complications. The classification of this disease is based on the GFR level, as shown in the followings (12):

G1 – GFR >90 mL/min per 1.73 m²

G2 – GFR 60 to 89 mL/min per 1.73 m²

G3a – GFR 45 to 59 mL/min per 1.73 m²

G3b – GFR 30 to 44 mL/min per 1.73 m²

G4 – GFR 15 to 29 mL/min per 1.73 m²

G5 – GFR <15 mL/min per 1.73 m² or treatment by dialysis

CKD complications and required treatments

Increase in volume: Sodium balance and intravascular volume are usually maintained by homeostatic mechanisms until the eGFR value reaches below 10 to 15. Patients with CKD and increased volume usually respond to combination therapy of diuretics and oral salt restriction. Some researchers have argued that limiting oral sodium can slow down the progression of CKD by lowering interglobulin pressure (13).

Metabolic acidosis: There is an increasing desire for hydrogen ion retention in patients with CKD. This can result in a progressive metabolic acidosis, so that the bicarbonate serum concentration usually stays between 12 and 20 and rarely reaches below 10. Metabolic acidosis can be treated by giving bicarbonate (14).

Hypertension: Hypertension is seen in approximately 80% to 85% of patients with CKD. Treatment of hypertension can also reduce the progression of protinuclear CKD and reduce cardiovascular complications. Treatment for hypertension in patients with CKD can be treated with an angiotensin converting enzyme (ACEI) inhibitor or an ARB and a diuretic (15).

Anemia: Anemia is one of the most important complications of chronic kidney failure (16); it is,

also, one of the predictors of mortality in patients with advanced chronic renal failure; this disorder, in turn, leads to several pathophysiologic disorders and problems such as decreased tissue oxygenation, left ventricular hypertrophy, angina pectoris and heart failure, as well as impairment of the immune system. The main cause of anemia in chronic renal failure is the reduction of erythropoietin production. This complication has experienced significant decrease in recent years due to the widespread use of human recombinant erythropoietin in the treatment of these patients; however, erythropoietin is expensive and increases the cost of treatment (17).

Erythropoietin hematopoiesis is the main hormone regulator in human body. From the embryonic, neonatal and puberty period, the hematopoietic continuity factor is the main source of hormones, and, the erythrocyte precursors proliferate, differentiate into soft blood and prolong the life of red blood cells through the control of apoptosis (18). Erythropoietin is a glycoprotein 400/30 Daltonium with 165 amino acids, containing 40% carbohydrates. This hormone is produced in the liver in the fetus and in renal peri-tubular cells and a very small amount in the liver in the adults. Initially, it was thought that erythropoietin is only cytokine that affects hematopoiesis, but now it has been proven that its receptors are very broad and it is quite effective in the development of endothelial cells in the digestive tract and human brain (19).

Following the use of rhEPO and increased hemoglobin in patients with CKD, patients' quality of life is significantly improved (20).

References

1. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Annals of internal medicine*. 2003 Jul 15;139(2):137-47.
2. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culeton B, Hamm LL, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P. 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*. 2003 Oct 28;108(17):2154-69.
3. Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA, Andress DL. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. *Kidney international*. 2007 Jan 1;71(1):31-8.
4. Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: systematic review. *BMC public health*. 2008 Dec;8(1):117.
5. Zhang L, Wang F, Wang L, Wang W, Liu B, Liu J, Chen M, He Q, Liao Y, Yu X, Chen N. Prevalence of chronic kidney disease in China: a cross-sectional survey. *The Lancet*. 2012 Mar 3;379(9818):815-22.
6. Hogg RJ, Furth S, Lemley KV, Portman R, Schwartz GJ, Coresh J, Balk E, Lau J, Levin A, Kausz AT, Eknoyan G. National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for chronic kidney disease in children and adolescents: evaluation, classification, and stratification. *Pediatrics*. 2003 Jun 1;111(6):1416-21.
7. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, Saran R, Wang AY, Yang CW. Chronic kidney disease: global dimension and perspectives. *The Lancet*. 2013 Jul 20;382(9888):260-72.
8. Moe S, Drüeke T, Cunningham J, Goodman W, Martin K, Olgaard K, Ott S, Sprague S, Lameire N, Eknoyan G. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney international*. 2006 Jun 1;69(11):1945-53.
9. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function—measured and estimated glomerular filtration rate. *New England Journal of Medicine*. 2006 Jun 8;354(23):2473-83.
10. Guaraldi G, Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, Berti A, Rossi E, Roverato A, Palella F. Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clinical Infectious Diseases*. 2011 Oct 13;53(11):1120-6.
11. Feldman HI, Appel LJ, Chertow GM, Cifelli D, Cizman B, Daugirdas J, Fink JC, Franklin-Becker ED, Go AS, Hamm LL, He J. The chronic renal insufficiency cohort (CRIC) study: design and methods. *Journal of the American Society of Nephrology*. 2003 Jul 1;14(suppl 2):S148-53.

12. Wen CP, Cheng TY, Tsai MK, Chang YC, Chan HT, Tsai SP, Chiang PH, Hsu CC, Sung PK, Hsu YH, Wen SF. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. *The Lancet*. 2008 Jun 28;371(9631):2173-82.
13. Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Annals of internal medicine*. 2013 Jun 4;158(11):825-30.
14. Gheissari A, Hemmatzadeh S, Merrikhi A, Tehrani SF, Madihi Y. Chronic kidney disease in children: A report from a tertiary care center over 11 years. *Journal of nephropathology*. 2012 Oct;1(3):177.
15. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJ, Mann JF, Matsushita K, Wen CP. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *The Lancet*. 2013 Jul 27;382(9889):339-52.
16. De Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. *Jama*. 2011 Jun 22;305(24):2532-9.
17. Muntner P, Hamm LL, Kusek JW, Chen J, Whelton PK, He J. The prevalence of nontraditional risk factors for coronary heart disease in patients with chronic kidney disease. *Annals of internal medicine*. 2004 Jan 6;140(1):9-17.
18. Stenvinkel P, Carrero JJ, Axelsson J, Lindholm B, Heimbürger O, Massy Z. Emerging biomarkers for evaluating cardiovascular risk in the chronic kidney disease patient: how do new pieces fit into the uremic puzzle?. *Clinical journal of the American Society of Nephrology*. 2008 Mar 1;3(2):505-21.
19. Muntner P, He J, Hamm L, Loria C, Whelton PK. Renal insufficiency and subsequent death resulting from cardiovascular disease in the United States. *Journal of the American Society of Nephrology*. 2002 Mar 1;13(3):745-53.
20. Forman DE, Butler J, Wang Y, Abraham WT, O'Connor CM, Gottlieb SS, Loh E, Massie BM, Rich MW, Stevenson LW, Young JB. Incidence, predictors at admission, and impact of worsening renal function among patients hospitalized with heart failure. *Journal of the American College of Cardiology*. 2004 Jan 7;43(1):61