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Nutritional Status of Patients with Chronic Kidney Disease in Iran: A Narrative Review

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ABSTRACT

Background: Chronic kidney disease (CKD) is a progressive condition that affects many aspects of patient's life with adverse outcomes of kidney failure, cardiovascular disease (CVD), and premature death. Malnutrition is a relatively common problem in these patients that may be the result of inadequate intake, increased catabolism, or loss of nutrients in the dialysis. The aim of this study was to review the nutritional status and requirements of CKD patients in Iran using previous studies. **Methods**: Search engines including PubMed, Scopus, Embase, Science Direct, Google scholar, Magiran, and scientific information database (SID) were applied with keywords such as chronic kidney disease, malnutrition, renal disease, end stage renal disease, nutritional deficiency, malnutrition, quality of life, vitamin deficiency, wasting, and Iran to find related articles published up to 2016**. Results**: The persistence of malnutrition increases susceptibility to infectious and cardiovascular diseases, delays wound healing, and finally increases morbidity and mortality. **Conclusion:** Considering the importance of nutritional status in patients with chronic kidney disease, it is necessary to design and development of more effective strategies to optimize nutritional status of these patients.

Key words: *Chronic kidney diseases; Renal disease; Chronic renal insufficiency; Malnutrition; Nutritional deficiency.*

Introduction

Chronic kidney disease (CKD) as a progressive disease is defined as the decreased kidney function—glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2 for 3 months or more (Levey *et al.*, 2005). It is a public health problem that is rapidly increasing, particularly in developing countries (Khajehdehi *et al.*, 2014, Levey *et al.*, 2007). Hypertension and diabetes are main reasons for developing kidney disease in adults (Chobanian *et al.*, 2003, Stevens *et al.*, 2008). Prevalence, mortality rate, and cost of care for patients on dialysis, kidney transplant, and end stage renal disease (ESRD) have increased during the last two decades (Hamer and El Nahas, 2006, USRDS, 1999). The prevalence of CKD varies in different nations based on the age of study population and

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among men and women (Zhang and Rothenbacher, 2008). A study in the United Stated of America (USA) reported that CKD prevalence was 1.5% in adult population (mean age 43.9 years) in 2005 (Kramer *et al.*, 2005). In another study the prevalence was reported 43.3% among people aged over 45 years (McClellan *et al.*, 2006). In a systematic review of 26 studies, the median prevalence of CKD in persons over 30 years of age was 7.2% (Zhang and Rothenbacher, 2008). A number of studies have investigated the prevalence of CKD in Iran. A study reported the prevalence of 18.9% among people aged over 20 years (Hosseinpanah *et al.*, 2009). Another study reported 19.5% for the prevalence for CKD among Iranian adults (Najafi *et al.*, 2012). In a study conducted by Safarnejad et al. the prevalence of chronic renal insufficiency (defined as GFR of 15-59 ml/min per 1.73 m2) was 8.1% among Iranian adult population (Safarinejad, 2009). The prevalence of this disease in our country is higher than countries such as USA, Australia, and Norway based on the previous studies (Hamer and El Nahas, 2006, Kopple, 2001b). The possible reason can be that the risk factors of CKD including diabetes and dyslipidemia in Iranian population are more than other countries (Najafi *et al.*, 2012, Safarinejad, 2009). Furthermore, the elderly population in Iran is growing and it might be contributed to the increasing prevalence of patients with CKD (Cibulka and Racek, 2007).

CKD has a major impact on health; it not only leads to kidney failure but also is associated with increased levels of inflammatory markers and plasma homocysteine (Shlipak *et al.*, 2003), anemia (Hsu, 2002), increased vascular calcification (Raggi *et al.*, 2002), abnormal levels of apo lipoproteins (Shlipak *et al.*, 2003), endothelial dysfunction and arterial stiffness (London *et al.*, 2003), as well as premature mortality. In 2003, American heart association (AHA) declared that patients with CKD are considered as people at high risk for cardiovascular diseases (Sarnak *et al.*, 2003).

Metabolic conditions and several other factors affect nutritional status of patients with CKD. Factors such as poor appetite, inadequate nutrient intake, insulin resistance, infection, and oxidative stress are associated with nutritional depletion (Chung *et al.*, 2012). Furthermore, protein-energy wasting (PEW) usually observed in these patients, especially in the end stages of the disease (Ikizler *et al.*, 2013). Because malnutrition is associated with increased morbidity and mortality and also according to the increasing incidence of this disease in Iran, it is important to recognize nutrition status to manage and improve the quality of life in these patients. Hence, in this narrative review we aimed to assess nutritional status in Iranian CKD patients for the first time.

Materials and Methods

This narrative review manuscript was extracted by searching the creditable databases, including PubMed, Scopus, Embase, Science Direct, Google scholar, Magiran, and scientific information database (SID) using keywords such as chronic kidney disease, malnutrition, renal disease, end stage renal disease, nutritional deficiency, malnutrition, quality of life, vitamin deficiency, wasting, and Iran from the published literature (English and Persian language). In this regard, a variety of studies including prospective cohort, retrospective, case-control, clinical guidelines, and review articles were studied up to 2016.

Results

Protein-energy wasting (PEW) in patients with CKD: In spite of the advancements in medical science, mortality rates are still high in CKD patients (Kalantar-Zadeh *et al.*, 2006). These patients especially the ESRD ones suffer from catabolic conditions. Weight loss, reduced fat and muscle mass (Su *et al.*, 2013), increased inflammatory markers (den Hoedt *et al.*, 2014), decreased levels of serum albumin (that is affected by both inflammatory and nutritional conditions) (Kim *et al.*, 2013), metabolic acidosis (Kalantar-Zadeh *et al.*, 2004), altered intracellular insulin like growth factor 1(IGF-1) and insulin signaling (Bonanni *et al.*, 2011), as well as endocrine disorders (Ros and Carrero, 2013) are common in these patients. On the other hand, Anorexia

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resulting from uremia (Carrero *et al.*, 2007), restrictive diet that limits potassium, phosphorus, or sodium intake, loss of nutrients in the dialysis, and other factors affect food intake and thus disrupt the energy balance (Ikizler *et al.*, 1994). One of the main mechanisms that lead to muscle atrophy in patients with CKD is associated with increased catabolism of Ubiquitin-proteasome system (UPS) mediated protein (that reduces muscle proteins) and activation musculoskeletal myostatin (which inhibits cellular proliferation and muscle synthesis) in uremic situation (Mitch and Goldberg, 1996). In addition, the extensive tissue damage will increase the level of circulating actin that consumes gelsolin (the protein that assembles and disassembles actin) (Zhang *et al.*, 2011). Increased level of actin and reduced level of gelsolin are associated with increased risk of mortality (Gracia-Iguacel *et al.*, 2014). Another mechanism is related to insulin resistance. Insulin-like growth factor 1 can lead to an upregulation of myostatin and a declined proliferation of satellite muscle cell by activating the phosphoinositide 3-kinase pathway (Zhang *et al.*, 2010). This situation leads to loss of protein and energy in patients with CKD. In fact, PEW is a pathological condition associated with sustained reduction in protein and energy reserves due to inadequate intake and increased catabolism as a result of reasons already mentioned (Fouque *et al.*, 2008, Mak *et al.*). The prevalence of PEW in CKD patients have been reported 18-75% in various studies (Leinig *et al.*, 2011). This variety is due to different assessment methods and cut-off points (Gracia-Iguacel *et al.*, 2014). However, according to our review, only one study has been conducted on prevalence of PEW in Iran by Tabibi et al. They reported that the prevalence rates of mild-to-moderate and severe PEW were 60.5% and 1% in hemodialysis patients, respectively (Tabibi *et al.*, 2012). It seems that this prevalence is high in Iran. Protein-energy wasting in kidney disease patients can lead to events that affect different systems and organs (Kovesdy and Kalantar-Zadeh, 2009). In these patients, muscle catabolism increased due to inflammation, reduction of nutrients, metabolic acidosis, and other factors. Reduction of muscle mass can affect the arteries and heart function, it also might cause ventricular hypertrophy together with other factors such as water and sodium retention (Gracia-Iguacel *et al.*, 2014). Moreover, in PEW patients nutritional deficiency is associated with chronic immunodeficiency state (Vanholder and Ringoir, 1993), increased oxidative stress, delay in wound healing (Vanholder *et al.*, 1993), and susceptibility to infections (Dong *et al.*, 2011, Gracia-Iguacel *et al.*, 2013). These reasons are leading to an increase in overall mortality (Gracia-Iguacel *et al.*, 2014).

As previously mentioned, the most important reason for PEW in patients with CKD is inadequate dietary protein and energy intake and also additional nutrient loss during dialysis (Combarnous *et al.*, 2002, Kloppenburg *et al.*, 1999, Wang *et al.*, 2003). A study in Tehran showed that protein and energy intakes were less than the recommended rates in 86.1 and 94.1% of hemodialysis patients, respectively (Taghdir *et al.*, 2011). In another study conducted by Pasdar et al., lack of energy and protein intakes in hemodialysis patients were 66 and 30%, respectively (Pasdar Khoshknab and Keshavarz, 1996). These prevalence rates were reported as 88 and 84.5%, respectively in a study conducted by Ashabi study et al. (As habi *et al.*, 2011). These results were consistent with findings of a study conducted by Pourghaderi et al. (Pourghaderi *et al.*, 2015). Average rates of energy and protein intake were reported as 17.5 kcal/kg and 0.8 g/ kg of bodyweight per day in dialysis patients, that are lower than the recommended daily intakes (Mardani *et al.*, 2016). Several approaches can be used to avoid inadequate nutrition intake. Energy and protein intake in patients with stage 3-5 CKD who are clinically stable and not on dialysis, should be 30–35 kcal/ kg and 0.6–0.8 g/kg of ideal body weight per day, respectively to prevent loss of muscle protein (Cano *et al.*, 2009, Kopple, 2001a). It is therefore worth noting that in patients who have hyper catabolic conditions such as infection, these values should be adjusted. In patients with end-stage renal disease who are on

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dialysis, the minimum rate of protein and energy requirements should be 1.2 g/kg and 30–35 kcal/kg of ideal body weight per day, respectively according to the physical activity level (for both hemo- and peritoneal dialysis). Notably, at least 50% of protein should be of high biological value (Ikizler *et al.*, 2013).

Consumption of high-protein meals or supplements during dialysis is a strategy to meet the recommendation, especially in at-risk patients (Kalantar-Zadeh and Ikizler, 2013). The important issue in these patients is control of phosphorus intake. Studies have shown that increased protein intake and low serum phosphorous can get the best result in hemodialysis patients (Shinaberger *et al.*, 2008). So, when a protein is recommended, its phosphorus content should also be noted. Patients who received this recommendation are not able to prevent weight loss and muscle building, so, nutritional supplementation is the next step. Furthermore, in cases of patients who are unable to tolerate oral supplements (such as severe anorexia or dysphagia) tube feeding is used (Cano *et al.*, 2009).

Vitamins and minerals status in patients with CKD: Vitamin deficiency is common in CKD patients who do not take supplements (Piper, 1985). The reasons for this deficiency can be due to the low dietary intake caused by anorexia, loss through dialysis, kidney functional limitations, and limited foods because of their high potassium or phosphorus contents. Moreover, some drugs interfere with nutrients that can lead to deficiency (Piper, 1985, Steiber and Kopple, 2011). According to our review, a limited number of studies have been conducted on the micronutrient intake in Iranian CKD patients. In a study carried out by Ashoupour et al., 96.8 and 97.9% of hemodialysis patients had low intakes of vitamin A and E, respectively. In addition, this study showed that in 50-100% of patients, thiamine, riboflavin, niacin, pyridoxine, cobalamin, folate, and vitamin C intakes were lower than the recommended levels. In addition, in 36-99% of patients calcium, iron, magnesium, and zinc intake rates were lower than the recommendation (Ashourpour *et al.*, 2012). Mardani et al. carried out an investigation in Khorramabad and showed that the intake of calcium, magnesium, zinc, sodium, and potassium in more than 90% of the patients was lower than the recommended level. Furthermore, this study found that 5-50% of the patients were not taking the recommended amounts of riboflavin, pyridoxine, B12, folate, and vitamin C. However, 98% and 60% of these patients had deficient amounts of fat soluble vitamins E and A, respectively (Mardani *et al.*, 2016). The results of these studies in Iran are consistent with findings of most other studies (Cho *et al.*, 2008, Kalantar-Zadeh *et al.*, 2002, Raimundo *et al.*, 2006, Wang *et al.*, 2007).

Some studies expressed that vitamin C deficiency in dialysis patients is due to restrictions in the consumption of fruit and vegetables in order to reduce hyperkalemia. Dietary vegetables restriction might also lead to folic acid deficiency. In addition, cooking vegetables to reduce their potassium content causes inactivation of vitamin C (Chazot and Kopple, 1997, Wang *et al.*, 2001). While meat, beans, and dairy products are rich in vitamin B groups, they have a high phosphorus content; so, consumption of these foods are limited by patients (Sprenger *et al.*, 1983). In addition, consumption of protein-rich foods (meats and sea foods) is limited because of anorexia in these patients, which can lead to zinc and iron deficiency (Pollock *et al.*, 1997).

Lack of nutrients in patients with CKD has devastating effects on the endothelial dysfunction, antioxidant capacity, and increases vascular calcification and mortality (Wen *et al.*, 2008). Some studies suggested that patients need dietary supplements for water soluble vitamins and minerals (Mardani *et al.*, 2016). More studies are therefore needed for better illustration.

Quality of life in patients with CKD: One of the important aspects of patients with CKD, which is usually neglected, is the quality of life (QoL). Studies have indicated that kidney disease is associated with reduced QoL and increased mortality (Feroze *et al.*, 2011). In addition, poor

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values in QoL are associated with worse situation in malnutrition markers (such as Low levels of albumin, creatinine, and decreased muscle mass) (Mazairac *et al.*, 2011). Moreover, poor QoL in mental aspect is common in dialysis patients (Allen *et al.*, 2002). These patients are facing with problems such as hospitalization, dietary restrictions, loss of appetite due to uremia, complications such as cardiovascular disease, depression, fear of failure, and memory loss and all these factors can affect daily activities of their life (Gracia-Iguacel *et al.*, 2014, Pakpour *et al.*, 2010). A study conducted by Pakpour and et al., on Iranian patients showed that the QoL scores in all scales in patients undergoing hemodialysis were significantly lower than those of the general population (Pakpour *et al.*, 2010), which is consistent with most of other studies (Ahari *et al.*, 2007, Vos *et al.*, 2006). Further studies are required to determine and control factors affecting the quality of life in these patients.

According to the authors' knowledge, this is the first review article over nutritional status of CKD patients in Iran. Although the data presented in this review are not conclusive, it seems that nutritional status in these patients is not desirable. This manuscript can encourage researchers to develop new strategies to improve these patients' life conditions. Finally, through this study, we hope to shed some light on this issue.

Conclusions

Paying attention to the nutritional status of CKD patients is very important. According to the previous studies most Iranian CKD patients suffer from lack of protein, energy, and some micronutrients. Nutrition education programs are suggested for patients, their families, and health professionals. Furthermore, using nutritional supplementation in these patients appears to be useful in order to decreased morbidity and mortality. In addition, more widespread research should be performed on the causes of malnutrition to find appropriate strategies for the patients.

Authors' contributions

Abdollahi SH wrote the manuscript. Razmpoosh E and Toupchian O provided critical revision of the manuscript. Salehi-Abargouei A edited the manuscript. All of the authors approved the content of the manuscript and agreed on all aspects of the work.

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