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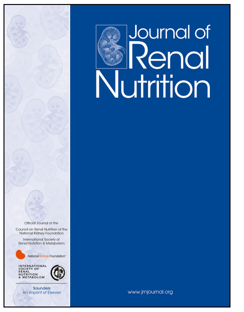

NUTRITIONAL ADEQUACY OF ESSENTIAL NUTRIENTS IN LOW PROTEN ANIMAL- AND PLANT-BASED DIETS IN THE UNITED STATES FOR CHRONIC KIDNEY DISEASE PATIENTS

Dina A. Tallman, PhD, RD, Ban-Hock Khor, PhD, Tilakavati Karupaiah, PhD, RnD, Pramod Khosla, PhD, Maria Chan, PhD, RD, Joel D. Kopple, MD

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Abstract

Objectives: The nutritional adequacy of both animal-based and plant-based low protein diets (LPDs) and moderate protein diets (MPDs) that are recommended for patients with chronic kidney disease (CKD) have not been well examined. We therefore analyzed the nutrient content of three representative LPDs and MPDs (lacto-ovo vegetarian, omnivorous, and vegan) containing foods that are likely to be prescribed for non-dialyzed CKD or chronic dialysis patients in the United States to determine the nutritional adequacy at different levels of protein intake.

Methods: Theoretical three-day menus were developed according to current renal dietary guidelines to model each diet at seven different levels of protein intake (0.5–1.2 grams/kilograms body weight/day [g/kg/d]). The diets were analyzed for their content of essential amino acids (EAAs) and other essential nutrients.

Results: At an *a priori* recognized inadequate dietary protein level of 0.5 g/kg/d, all three diets failed to meet the Recommended Dietary Allowances (RDAs) for the following EAAs: histidine, leucine, lysine, and threonine. The omnivorous LPD met both the RDA and Estimated Average Requirement (EAR) at levels of 0.6 g protein/kg/d or greater. The lacto-ovo and vegan diets at 0.6 and 0.8 g protein/kg/d, respectively, were below the RDA for lysine. The amounts of several other vitamins and minerals were not uncommonly reduced below the RDA or Adequate Intake (AI) with all three LPDs.

Conclusion: In comparison to omnivorous LPDs, both vegan and lacto-ovo LPDs are more likely to be deficient in several EAAs and other essential nutrients. In order of provide sufficient amounts of all EAA, vegan and lacto-ovo LPDs must be carefully planned to include adequate

amounts of appropriate dietary sources. Supplements of some other essential nutrients may be necessary with all three LPDs.

Keywords: Chronic Kidney Disease, CKD, Maintenance Dialysis, Low Protein Diets, LPDs, Nutrition, Essential Amino Acids, EAA, Vitamins, Trace Elements

Introduction

Low protein diets (LPDs) have historically been prescribed to patients with chronic kidney disease (CKD), especially in its advanced stages. The 2020 Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines for metabolically stable adult patients not on dialysis and without diabetes with CKD stages 3–5 recommend restricting protein intake [1]. The recommended LPDs are generally either (A) a LPD (0.55–0.60 grams protein/kilogram body weight/day [g/kg/d]) or (B) a very low protein diet (VLPD), providing 0.28–0.43 g/kg/d, which is supplemented with sufficient ketoacid analogs (KA) of certain essential amino acids (EAAs) plus other EAAs to meet the 0.55–0.60 g/kg/d requirement. The KDOQI guidelines for CKD patients stages 3–5 not on dialysis and with diabetes suggest a higher protein intake of 0.6–0.8 g/kg/d [1]. KDOQI protein recommendations for maintenance dialysis patients, both with and without diabetes, is 1.0–1.2 g/kg/d [1]. Due to a lack of adequate evidence, the KDOQI nutritional guidelines do not recommend that CKD patients stages 1–5D consume any particular type of protein-containing foods [1].

Over the last two decades, there has been a steady surge in publications related to the use of plant-based diets for people with chronic disease. A PubMed® search using the term "plant-based diet" revealed a 434% increase in the annual rate of publications from the years 2000 to 2021. In 2018, the Plant Based Foods Association commissioned a Nielsen report that revealed a

20% growth in dollar sales of plant-based foods from the previous year in the United States [2]. Notwithstanding the increased popularity of *plant-based* food intake, there is a lack of consensus regarding the meaning of the term plant-based. According to the Merriam-Webster Dictionary, there is no agreement as to the formal definition of this term [3]. Plant-based diets may take several forms, ranging from plant-rich omnivorous (includes both animal products and plants) to vegetarian (excludes meat and seafood, but may contain eggs and dairy products) to vegan (excludes all animal products).

Although the potential health and environmental benefits of plant-based diets have been discussed in a number of publications [4-6], the question of whether lacto-ovo vegetarian diets, and particularly vegan LPDs, are likely to be nutritionally adequate has not been well examined. Moreover, there are few studies of whether omnivorous, lacto-ovo vegetarian, or vegetarian diets provide adequate amounts of all essential nutrients, especially when the protein content of the diets is restricted [7].

Barsotti et al., in Italy, reported that an appropriate cereal-legume mixture supplied adequate EAAs at 0.7 g protein/kg/day [8]; however, the methods for assessing nutritional status were imprecise, and their findings were based on Recommended Dietary Allowances (RDA) that were over three decades old and which have since been updated. When consuming a vegan diet, meeting EAA requirements often necessitates the consumption of a variety of plant foods [9]. Unlike animal-derived proteins, which contain EAAs in roughly similar proportions to human skeletal muscle protein, plant proteins are more limited in certain EAAs, especially methionine in legumes and lysine in most other plant foods [10, 11]. The restricted variety and amounts of foods available with LPDs may also lead to marginal or deficient levels of some vitamins and minerals.

In people with CKD, skeletal muscle protein turnover appears to adapt to the restricted protein intake of a 0.55–0.6 g protein/kg/d LPD [12-14] and of a 0.45 g/kg/d VLPD supplemented with KAs/EAAs under medically supervised conditions [15]. Furthermore, KA-supplemented vegetarian VLPDs and conventional LPDs "seem nutritionally safe" [16, 17]. However, these short-term studies did not rule out the possibility that macromineral or micronutrient deficiencies may engender adverse nutritional or clinical outcomes over the long term in these CKD patients. The purpose of the present study was to examine whether the omnivorous, lacto-ovo vegetarian, and vegan LPDs that are likely to be prescribed for CKD patients are prone to be deficient in any essential macronutrients or micronutrients.

We employed a food modeling approach to evaluate three different diets (lacto-ovo vegetarian, omnivorous, and vegan) providing seven different levels of protein intake (0.5–0.8 g/kg/day and 1.0–1.2 g/kg/day) to determine their adequacy for essential macro- and micronutrients. We also compared these diets to previously published plant dominant LPDs (referred to as PLADO diets) for dietary protein intakes of 0.5–0.8 g/kg/d. The PLADO diet is defined as comprising at least 50% of its protein from plant-based sources, preferably unprocessed, and provides 30 calories/kg/d, 25–30 g/d of dietary fiber, and no more than 3 g sodium/d [18]. Since the food composition and methods of preparation of protein-restrictive diets for CKD patients vary according to the food customs of a country and geographical region [19], we have limited the analysis to foods that are likely to be prescribed and consumed in the United States (U.S.) by CKD patients [20].

Materials and Methods

Menu Reference and Design

Menus were developed based on renal dietary guidelines from the Nutrition Care Manual (NCM) of the Academy of Nutrition and Dietetics in the U.S. and analyzed for nutrient content. The NCM section references renal diets and provides one-day sample menus for omnivorous, lacto-ovo vegetarian, and vegan diets for CKD stage 3–5 patients [21]. Additionally, the U.S. National Kidney Foundation (NKF) website provides recipes designed for specific clinical conditions, such as the stage of CKD, special dietary needs, and the meal type [22]. Incorporating both sample menu items from the NCM and selected recipes from the NKF website, three-day meal plans providing a range of protein intakes (from an *a priori* nutritionally inadequate 0.5 g protein/kg/d through 1.2 g protein/kg/d) were developed for the three different diet versions (lacto-ovo vegetarian, omnivorous, and vegan). Additionally, two versions of PLADO diets, one with 70% protein from plant sources, (termed "Higher PLADO" or HPL) and one with 52–53% protein from plant sources (termed "Lower PLADO" or LPL) were planned for protein intakes ranging from 0.5 to 0.8 g/kg/d [18]. The following criteria for selection of foods for menu planning were used:

(a) A complete profile of the EAAs of the food was available.

(b) Foods that were typically found in the U.S. Protein-free foods were omitted as these are not readily available in the U.S.

(c) Consideration for dietary restrictions of sodium, potassium, and phosphorus as relevant to CKD or chronic dialysis patients.

(d) An average of two servings each of whole, unprocessed fruits, vegetables, and grains (i.e., at least six servings of these three food categories), and one serving of nuts.

(e) Some preference was given to foods that allowed ease of meal preparation (Table S1).

The reference body weight for these diets was taken as 70 kg and menus for all diets provided 30 kcal/kg body weight/d [1]. Menus were designed to include at least 50% of high biological value protein for the omnivorous and lacto-ovo vegetarian diets [23, 24]. The meal plans varied only in the protein quantity and source, which depended on the type of diet, but the basic food items were very similar and usually identical between meal plans. Using each three-day plan as a template, minimal modifications were implemented to attain levels of dietary protein ranging from 0.5 g/kg/d to 1.2 g/kg/d. All meal plans were developed by a Registered Dietitian (DAT) experienced in menu development and analysis for CKD patients and were verified by an experienced practicing renal dietitian who has a university faculty appointment (MC).

Defining Reference Values

The 2005 Dietary Reference Intakes (DRIs) by the Institute of Medicine (IOM) were used to determine nutritional adequacy for the EAAs [25], and the following sources were employed to assess nutritional adequacy for macronutrients and micronutrients: 1997 Reference Intakes for Magnesium [26], 1998 Reference Intakes for Thiamin, Riboflavin, Niacin, Folate, Vitamin B12, Biotin, and Choline [27], 2000 Reference Intakes for Selenium [28], 2001 Dietary Reference Intakes for Vitamin A, Vitamin K, Chromium, Copper, Iron, Manganese, and Zinc [29] and higher B6 requirements in CKD [30, 31]. The DRIs, which have been determined for normal people and stratified for age, sex, and body weight, include both the Estimated Average Requirement (EAR) and the RDA. The EAR is the average daily nutrient intake level estimated to meet the daily dietary requirement of half the normal population; the RDA, which is set at the EAR plus twice the standard deviation, is designed to meet the nutrient requirement of nearly all (97–98%) of the general population [25]. The Adequate Intake (AI) is the average daily intake of a nutrient by a group or groups of people who are apparently healthy, and that is therefore assumed to be adequate. The AI is usually developed when an RDA cannot be determined for a nutrient [32].

A separate DRI was used for vitamin B6 (pyridoxine) because of evidence that advanced CKD and chronic dialysis patients have greater dietary vitamin B6 requirements [30, 31].

Nutrient Analyses

The nutrient content of foods was calculated using the Food Processor SQL software package (version 11.7, 2019, ESHA Research, Salem, OR, USA) [33, 34], which contains data collected from over 1,900 reputable sources, including the latest United States Department of Agriculture (USDA) Nutrient Database for Standard Reference. Only those foods having a complete amino acid profile were chosen from the Food Processor program to be included in the nutrient analysis. Because cysteine reduces the amount of methionine required in the diet and tyrosine reduces the dietary requirement for phenylalanine, the dietary content is reported together for both methionine plus cysteine and also for both phenylalanine plus tyrosine.

Substitution Analysis

As previously described, the original vegan menu was developed using sample menus and readily available foods typical of those consumed by vegans in the U.S. However, to evaluate if a different combination of less commonly consumed plant proteins and grains would change the EAA profile substantially, a substitution analysis (Table 3) was conducted. To increase the lysine and methionine + cysteine content for the vegan diet providing both 0.70 g and 0.80 g protein/kg/d, equal amounts of lentils were exchanged for garbanzo beans, Brazil nuts were substituted for almonds, sunflower seed butter for peanut butter, and quinoa for oatmeal.

Tempeh was increased by 0.5 ounce and tofu was decreased by 2 ounces, and one tablespoon dried spirulina (a protein rich dietary supplement usually obtained from blue-green algae) was added.

Statistical Methods

To show deviation from reference standards, mean values are described for each menu. Data analyses were conducted in R [35], and figures were produced using the package ggplot2 [36].

Results

The amount of HBV protein (i.e., animal derived protein) in the omnivorous and lacto-ovo vegetarian diets ranged from 63–66% and did not differ between diets. As shown in Figure 1 and Table 1a, at a dietary protein level of 0.5 g/kg/d, all five diets (lacto-ovo vegetarian, omnivorous, and vegan, HPL, and LPL) failed to meet the RDAs for the following EAAs: histidine, leucine, lysine, and threonine. Additionally, all diets failed to meet the EAR for lysine at 0.5 g protein/kg/d. At dietary protein intakes of 0.6 g/kg/d and greater for the omnivorous diet (Figure 2 and Table 1a), 0.7 g/kg/d and greater for the lacto-ovo and LPL diets, and 0.8 g/kg/d and greater for the HPL diet (Table 1b), the RDAs for all EAAs were attained. However, with the vegan diet, the quantity of protein required to achieve the RDAs for all EAAs was 0.8 g/kg/d (Table S3) after making several menu revisions.

Figure 3 illustrates the amounts of sodium, potassium, phosphorus, and calcium provided by each diet type across the ordinal protein thresholds. The omnivorous diet contributed the lowest content of potassium, phosphorus, and calcium, whereas comparatively, both the lacto-ovo vegetarian and vegan diets provided higher levels of both potassium and phosphorus, with the lacto-ovo vegetarian diet providing the highest amounts of calcium. It should be noted that the vegan LPD contained tofu, rice milk, and soy milk, all of which contained calcium added during processing. Sodium content did not differ between the diets, except for more sodium in the lacto-ovo vegetarian diet at the highest protein levels.

The calculated micronutrient content of the diets and their relation to the DRIs [37] are shown in Tables 2a, 2b, and S5. All LPDs failed to meet the RDA for choline and for the increased vitamin B6 (pyridoxine) requirements for CKD patients [30, 31]. The lacto-ovo LPD was also low in vitamins B3 (niacin), folate, and magnesium. Nutrient shortfalls for the omnivorous LPD included folate, biotin, zinc, and magnesium. The vegan LPD was low in vitamin B12 (cobalamin) and selenium compared to the RDAs. The polyunsaturated fatty acid eicosapentaenoic acid (EPA) was present in only negligible amounts in the vegan and lacto-ovo vegetarian diets, and the content of docosahexaenoic acid (DHA) was negligible in the vegan diet.

Additional nutrient shortfalls of the moderate protein diets (MPDs) that provide 1.0 to 1.2 g protein/kg/d are displayed in Table S5. Greater deficiencies were found for folate, biotin, and magnesium with the omnivorous and lacto-ovo vegetarian diets as compared to vegan diets. All diets failed to meet the higher B6 requirements for CKD patients [30, 31]. Only the lacto-ovo vegetarian diet met the RDA for choline.

Discussion

The findings from this study indicate that for a 70 kg person, LPDs ranging from 0.5–0.8 g protein/kg/d, which are commonly prescribed for CKD patients in the United States, and which provided 30 kcals/kg/d, were deficient in certain essential nutrients (Tables 2a and 2b).

Deficiency for one or more EAAs occurred with the omnivorous diet providing 0.5 g protein/kg/d, with the lacto-ovo vegetarian diet providing 0.6 g protein/kg/d or lower, and with vegan diet providing 0.8 g protein/kg/d or less. The omnivorous diet was found to be less deficient in EAAs than either the vegan diet or the lacto-ovo vegetarian diet. The LPL diet met the RDA for lysine at 0.7 g protein/kg/d, whereas the HPL required 0.8 g/protein/kg/d to meet the RDA. This difference may be attributed to the higher percentage of animal proteins in the LPL diet (47–48%) versus the HPL diet (30%). The vegan diet only achieved the RDAs for all EAAs with dietary protein intakes providing at least 0.8 g/kg/d, and even then, only with substitution of selected plant foods that provide greater amounts of lysine and methionine (Table 3). However, inclusive of this previously discussed vegan diet, all diet types, including the vegan diet and the HPL and LPL diets, met the RDA for EAAs at protein intakes of 0.8–1.2 g/kg/d.

Proteins in legumes are low in the sulfur-containing amino acids methionine and cysteine and are richer in lysine; whereas cereal proteins, such as rice and wheat, are low in lysine and richer in methionine. Therefore, cereal proteins are often mixed with legumes to provide a complete amino acid profile [38]. Lysine, threonine, tryptophan, and the sulfur-containing amino acids are often described as “limiting amino acids,” meaning protein synthesis is limited to the extent that these EAAs are available [39, 40]. Limiting amino acids refer to the EAAs most likely to be deficient in LPDs, especially when the biological quality of the protein is low. Additionally, if not inactivated by thermal processing, trypsin inhibitors in pulses and legumes can decrease protein quality [41].

Patients with advanced CKD are at increased risk for a number of nutritional and metabolic derangements, including protein-energy wasting (PEW) [42]. Both malnutrition and hypoalbuminemia have been associated with lower plasma levels of sulfur-containing amino acids [43]. Additionally, ingestion of amino acid mixtures containing lower amounts of such EAAs as lysine and the sulfur-containing amino acids has been associated with lower rates of muscle protein synthesis when compared to diets providing isonitrogenous amounts of animal protein that contain larger quantities of these amino acids [44, 45]. Lucas et al. reported that CKD patients placed on an EAA/KA-supplemented VLPD diet (consisting of predominantly vegetable protein) may slow the decline in renal function, but at the risk of loss in muscle mass [46].

At a LPD providing 0.55–0.6 g/protein/kg/d, which is the lowest dietary protein intake we studied that has been recommended by KDOQI for CKD patients [1], only the omnivorous diet met both the RDA and EAR for all EAAs (Table 1). Indeed, the nutritional adequacy of an omnivorous LPD providing adequate energy (≥30 kcals/kg/d) and 0.60 g protein/kg/d with approximately ≥50% high biological value protein derived from animals has been confirmed. Such diets will maintain neutral or positive nitrogen balance in clinically stable people with advanced CKD [12, 14].

Notwithstanding the data in this study indicating that vegan LPDs providing 0.5–0.7 g protein/kg/d and lacto-ovo vegetarian LPDs containing 0.5–0.6 g protein/kg/d are both deficient in certain EAAs, several reports indicate no increase in PEW in CKD patients who reportedly ingest plant dominant LPDs [47, 48]. The following possibilities might account for these findings. First, the actual EAA intake with the LPDs may be greater than reported. For example, the LPDs these CKD patients ingested, although plant dominant, may also have been omnivorous [48, 49] and such patients may ingest greater amounts of animal-based protein than they were prescribed [50]. Eggs, which contain very high biological value protein, may be included in the soy-based vegetarian diet [51]. Second, the CKD patients may have ingested more protein than was prescribed, a common occurrence with CKD patients assigned to LPDs [52]. Third, the methods for assessing protein-energy status in several studies were not very sensitive [51]. Fourth, in these studies, intakes of EAAs below the RDAs, or even the EARs, may still be nutritionally adequate for many people. [32]. Since the RDAs for EAAs are designed to provide an adequate EAA intake for about 97% of all normal people, it follows that for most normal people, an intake of an EAA that is somewhat below the RDA will still be nutritionally adequate. Nonetheless, CKD patients who adhere closely to their prescribed diets may be at greater risk for PEW if they are eating a vegan diet providing less than 0.8 g protein/kg/d or a lacto-ovo vegetarian or omnivorous diet containing less than 0.7 and 0.6 g protein/kg/d, respectively, unless these diets are supplemented with EAAs or ketoacid analogs. It may therefore be prudent to monitor the adequacy of the actual nutrient intake of people prescribed these low protein diets.

Our results are similar to a recent study that we conducted of diets that might be prescribed for CKD patients using foods culturally typical for people living in the southern part of China or in India [53]. In this latter study, the omnivorous Asian diet was deficient in some EAAs, unless it provided at least 0.6 g protein/kg/d. However, only with a protein prescription of 0.7 g protein/kg/d did all the plant-based and vegan LPDs provide the RDAs for all EAAs.

We did not report on the taurine content of these diets, since the quantity of taurine in foods is not included in the USDA Nutrient Database [54]. Since some taurine is synthesized by the body from methionine and cysteine, taurine is normally considered to be a non-EAA. However, much data indicate that body taurine pools are not maintained with AIs of methionine if there is little or no taurine in the diet [55]. Although one of the two most abundant free (non-protein bound) intracellular amino acids in the human body, taurine is not incorporated into mammalian protein [56]. Animal tissue contains a high content of taurine in the cytosol; but, the taurine content of plant foods is almost undetectable [54, 57]. Vegetarians, and particularly vegans, consume little taurine and eat low sulfur amino acid diets; consequently they may have reduced levels of plasma and blood cell taurine and urinary taurine excretion [58]. Thus, it is possible that healthy people or CKD patients ingesting a low protein vegan or lacto-ovo vegetarian diet, which tend to be low in methionine + cysteine and in taurine, may also be at increased risk for taurine deficiency. Indeed, maintenance hemodialysis patients have been reported to be taurine depleted [59, 60], and placing these patients on a vegan or lacto-ovo vegetarian diet might place them at even greater risk of taurine deficiency.

All LPDs were low in a number of micronutrients, including some B vitamins, zinc, magnesium, and choline (Table 4). The omnivorous MPD was low in vitamin B6, folate, biotin, magnesium, and choline, whereas the vegan diet was low in vitamins B6 and B12 and in choline. At 1.1 g protein/kg/d, the lacto-ovo vegetarian MPD met the RDA for all micronutrients, which may be attributed to the three cups of milk and 3–4 whole eggs/egg whites provided daily with this diet. However, this diet was higher in potassium, phosphorus, and sodium than the omnivorous and vegan MPDs and there is usually a need to restrict the intake of these three minerals in CKD and chronic dialysis patients. The findings from this study provide a rationale for routine supplements of vitamins, other micronutrients, and possibly magnesium when CKD patients are prescribed LPDs. Supplemental vitamin D3 or D2 and calcitriol are often needed [1]. The recommended daily amount of vitamin B6 (pyridoxine) that we used for reference is substantially greater than the RDA for vitamin B6 for normal adults. The 2020 KDOQI guidelines arbitrarily did not review research papers published before 1986. The recommendation for this quantity of vitamin B6 is based on a number of studies prior to 1986 indicating that people with chronic kidney failure are often vitamin B6 deficient [30, 61]. One relatively small dose ranging study indicated that CKD and chronic peritoneal dialysis patients require a supplement of about 5 mg/d and maintenance hemodialysis patients require a supplement of 10 mg/d of pyridoxine HCl, respectively 4.1 and 8.2 mg/d of free pyridoxine, to correct vitamin B6 deficiency. More studies are needed in CKD patients to confirm and extend these findings using such modern methods for assessing vitamin B6 nutrition as the direct measurement of vitamin B6 compounds.

Several observational studies suggest that dietary patterns which include higher intakes of fruits, vegetables, and plant-based proteins are associated with a reduced incidence or rate of progression of CKD [62-65]. It is possible that the lower amounts of sodium, potassium, phosphorus, and calcium found at virtually all protein levels in the plant-rich omnivorous LPDs in this study, as compared to both the vegan and lacto-ovo vegetarian LPDs (Figure 1), may contribute to the lower rate of CKD progression [66]. Plant-rich omnivorous dietary patterns are also associated with a lower incidence of CKD and greater longevity [64, 67, 68].

Although it is not uncommon for healthcare workers to recommend plant-based LPDs for CKD patients [18, 69], the exact meaning of a plant-based diet is often unclear. Vegetables, and to a lesser extent fruits, have alkalizing effects, which may slow progression of CKD and also reduce net protein catabolism [41, 70, 71]. On the other hand, grain-based plant foods may actually provide an acid load [71]. But grains and nuts often contain large amounts of phytates [41] which, by binding to phosphate, may reduce intestinal phosphorus absorption [72]. The plant foods in the present study were primarily fruits and vegetables, with smaller quantities of whole grains and nuts.

It should be recognized that the actual sodium provided with all three of these diets will almost certainly be higher than reported here because sodium chloride is often added during cooking or at the dining table, and sodium is also commonly added to foods during processing. Dietary phosphorus is almost certainly underestimated in this study because of the common use of phosphorus-containing food additives in the manufacturing process [73-75]. The phosphorus content in food composition tables and electronic database programs substantially underestimates the actual measured amount of phosphorus present [76, 77]. On the other hand, phosphorus from plant and legume derived foods tends to be less accessible with a bioavailability of <40%, as compared to organic phosphorus from animal and dairy foods which are estimated to have a bioavailability of approximately 40–60% [78-81]. The inorganic phosphorus salts often added to foods have an even higher bioavailability. The lower bioavailability of phosphorus in plant foods, due to the phytate content, should confer a health advantage to vegan and plant-dominant diets with regard to mineral and bone disorders in CKD. It should be emphasized that the higher calcium content of the vegan LPDs was due to the inclusion of foods that had calcium added during processing. The high potassium content of the lacto-ovo vegetarian LPD is attributed to the relatively high potassium content of dairy products. The low dietary fiber content for both the lacto-ovo and omnivorous LPD may be attributed to fewer amounts of whole grains and vegetables, which can contribute a considerable quantity of protein. In order to provide the requisite egg, dairy, and meat to these diets, lower protein sources of carbohydrate were required.

The diets prepared by dietitians in this modeling study took considerable time, effort, and experience to maximize the nutritional value, including the EAA content of the diets. Unfortunately, at present, most CKD patients will not receive medical nutrition therapy (MNT) by a dietitian before initiation of dialysis [82, 83]. A patient following the same low protein plant-based diet would be unlikely to have the knowledge or perhaps the patience to devise a meal plan ensuring a balanced EAA intake. Patients also need to take caution when using many of the plant-based processed and ultra-processed foods currently on the market, which may be of poor nutritional quality [84]. The use of a skilled dietitian to conduct an individual nutritional assessment, plan the diet, counsel the patient and his/her family, and monitor the response to the dietary prescription is recommended and is consistent with KDOQI guidelines [1]. Approaches that may improve muscle protein anabolism when incorporating plant-based LPDs include (1) combining plant and animal proteins, (2) supplementing with essential AA or KA, and (3) combining several types of plant proteins to ensure adequate amounts of amino acids leucine, lysine, and methionine [85, 86].

Some of the nutrient deficiencies found in the diets in this study may be due to the food choices in the three-day diet plans. The conclusions in this report are driven by the analysis of one diet plan, potentially biasing the analysis. However, it should be noted that the purpose of this modeling study is to demonstrate that, without careful menu planning with concomitant nutrient analysis, standard American fare for low protein vegan and lacto-ovo vegetarian diets may be deficient in one or more EAAs. Both of these LPDs, as well as omnivorous LPDs, may also be low in a number of vitamins and minerals.

Conclusions

In the United States, any LPD providing ≤0.5 g protein/kg/d may be deficient in several EAAs and other essential nutrients. Although any EAA deficiency in a LPD could be eliminated with EAA or KA supplements, these supplements currently are not readily available or commonly prescribed in the United States. Therefore, based on the type of diet (e.g., omnivorous, lacto-ovo vegetarian, or vegan) and quantity of protein prescribed, it may be necessary to carefully plan the LPD to ensure that adequate amounts all essential nutrients are provided. For example, for both vegan and lacto-ovo vegetarian diets containing less than 0.8 g protein/kg/d, it is recommended that efforts be made to ensure that the diets include adequate amounts of lysine- and methionine-rich foods. These latter diets can still contain substantial amounts of fruits and vegetables. CKD patients prescribed LPDs should also have their intake of calcium and magnesium monitored. Additionally, to preclude the possibility of deficiency in vitamins or trace elements, offering nutritional supplements, most importantly vitamin B6, folate, zinc, calcitriol, and calcium, should be considered for all CKD patients prescribed diets providing 0.8 g protein/kg/day or less. Unless further research provides evidence to the contrary, all advanced CKD and chronic dialysis patients should receive supplements of vitamin B6 (pyridoxine HCl).

Practical Applications

Patients with advanced chronic kidney disease (CKD) are often prescribed low protein diets (LPDs). Our analyses indicate that all LPDs designed for CKD patients using food patterns likely to be consumed in the United States may be deficient in some essential nutrients. Recently, some researchers have advocated plant-based LPDs for CKD patients. When LPDs for CKD patients in the United States are further limited to exclude meat or any animal protein, the diet is particularly likely to be deficient in certain essential amino acids and other essential nutrients. These nutritional deficiencies are especially likely to occur when the diets provide 0.6 g protein/kg body weight per day or less. Our results indicate that patients following these types of LPDs may benefit from both nutritional supplements and meal planning carried out with a dietitian.

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Table 1a. Essential amino acids supplied at lower protein intakes according to diet type

Essential amino acid	EAR	RDA	0.5 g protein/kg/d					0.6 g protein/kg/d				
			LO	OM	VE	HPL	LPL	LO	OM	VE	HPL	LPL
Histidine (mg)	**770**	**980**	790	860	730†	710†	780	990	1070	920	850	960
Isoleucine (mg)	**1050**	**1330**	1490	1420	1190	1130	1270	1880	1770	1490	1340	1530
Leucine (mg)	**2380**	**2940**	2540	2430	2160†	1960	2200†	3200	3030	2730	2320	2650
Lysine (mg)	**2170**	**2660**	1870†	2120†	1360†	1580†	1890†	2430	2730	1750†	1960	2270
Methionine + cysteine (mg)	**1050**	**1330**	1340	1190	940†	970†	1110	1660	1460	1090	1150	1320
Phenylalanine + tyrosine (mg)	**1890**	**2310**	2790	2400	2370	2030	2250	3510	2980	3020	2360	2720
Threonine (mg)	**1120**	**1400**	1210	1240	1060†	990†	1140	1530	1540	1330	1180	1370
Tryptophan (mg)	**280**	**350**	380	350	370	310	330	470	430	460	360	410
Valine (mg)	**1330**	**1680**	1850	1650	1430	1330	1510	2350	2050	1760	1560	1800

Note: Based on 19 years of age or older and 70 kg body weight; shaded values indicate values are below the RDA. †Does not meet EAR (Estimated Average Requirement).

Abbreviations: EAR: Estimated Average Requirement (nutrient intake value that is estimated to meet the requirement of half the healthy individuals in a group). RDA: Recommended Dietary Allowance (average daily level of intake sufficient to meet the nutrient requirements of nearly all [97%-98%] healthy people). LO: lacto-ovo vegetarian; OM: omnivorous; VE: vegan; HPL: PLADO with higher % of plant protein (70% protein from plant sources); LPL: PLADO with lower % of plant protein (52-53% protein from plant sources)

Table 1b. Essential amino acids supplied at lower protein intakes according to diet type

Essential amino acid	EAR	RDA	0.7 g protein/kg/d					0.8 g protein/kg/d				
			LO	OM	VE	HPL	LPL	LO	OM	VE	HPL	LPL
Histidine (mg)	**770**	**980**	1170	1270	1080	1090	1150	1220	1470	1230	1280	1280
Isoleucine (mg)	**1050**	**1330**	2240	2080	1760	1740	1820	2140	2440	2000	2030	2010
Leucine (mg)	**2380**	**2940**	3810	3540	3210	3000	3130	3810	4150	3650	3490	3470
Lysine (mg)	**2170**	**2660**	2940	3290	2100†	2550	2710	2870	3870	2390	3000	3030
Methionine + cysteine (mg)	**1050**	**1330**	1990	1720	1210	1470	1540	1730	2040	1350	1700	1700
Phenylalanine + tyrosine (mg)	**1890**	**2310**	4170	3440	3550	3050	3190	4150	4040	4050	3540	3520
Threonine (mg)	**1120**	**1400**	1810	1810	1580	1520	1610	1810	2100	1800	1770	1770
Tryptophan (mg)	**280**	**350**	550	490	530	460	480	560	550	610	530	530
Valine (mg)	**1330**	**1680**	2800	2370	2040	2010	2110	2650	2790	2310	2320	2330

Note: Based on 19 years of age or older and 70 kg body weight; shaded values indicate values are below the RDA. †Does not meet EAR (Estimated Average Requirement).

Abbreviations: EAR: Estimated Average Requirement (nutrient intake value that is estimated to meet the requirement of half the healthy individuals in a group). RDA: Recommended Dietary Allowance (average daily level of intake sufficient to meet the nutrient requirements of nearly all [97%-98%] healthy people). LO: lacto-ovo vegetarian; OM: omnivorous; VE: vegan; HPL: PLADO with higher % of plant protein (70% protein from plant sources); LPL: PLADO with lower % of plant protein (52-53% protein from plant sources).

Table 2a Nutrient content according to diet type and protein level of the LPDs

	RDA/AI		0.5 g protein/kg/d					0.6 g protein/kg/d				
	Males	Females	LO	OM	VE	HPL	LPL	LO	OM	VE	HPL	LPL
Vitamins												
Vitamin A (µg)	**3000**	**2333**	7991	7503	8108	7256	7282	8168	7590	7708	7260	7459
Vitamin B1 (mg)	**1.2**	**1.1**	0.9	1.0	1.2	1.2	1.1	0.9	1.0	1.3	1.3	1.2
Vitamin B2 (mg)	**1.3**	**1.1**	1.7	1.0	1.4	1.5	1.4	2.0	1.2	1.4	1.5	1.6
Vitamin B3 (mg)	**16**	**14**	9	14	12	15	16	9	16	14	16	17
Vitamin B6 (mg)^	**5.0^**		0.9	1.1	1.0	1.4	1.4	0.9	1.3	1.2	1.5	1.5
Vitamin B12 (mcg)	**2.4**	**2.4**	1.9	2.0	1.6	3.0	2.7	2.7	2.8	0.6	3.3	3.9
Folate (mcg)	**400**		247	223	312	329	305	260	227	380	337	290
Vitamin K (mcg)	120*	90*	133	158	153	223	229	131	157	145	223	227
Biotin (mcg)	30*		26	9	19	11	10	31	10	30	11	12
Minerals												
Copper (mg)	**0.9**		1.0	0.9	1.5	2.5	1.1	1.0	1.0	1.7	1.4	1.2
Iron (mg)	**8**	**8-18**	8	8.7	11	13	14	8	8.7	12	14	15
Manganese (mg)	2.3*	1.8*	2.9	2.9	5.4	4.7	3.3	3.1	2.9	6.1	4.8	4.2
Selenium (mcg)	**55**		54	51	40	49	48	67	60	42	55	55
Zinc (mg)	**11**	**8**	5	5	6	7	5	5	6	7	7	6
Magnesium (mg)	**400-420**	**310-320**	202	172	289	296	200	212	182	330	310	273
Polyunsaturated fatty acids												
20:5 – EPA (g)	ND		0.00	0.10	0.00	0.0	0.05	0.00	0.14	0.00	0.06	0.06
22:6 – DHA (g)	ND		0.02	0.34	0.00	0.20	0.18	0.04	0.48	0.00	0.22	0.22
Omega-3 Fatty Acid (g)	0.6-1.2*		1.5	2.8	1.8	2.0	2.7	1.4	3.1	1.6	2.1	2.8
Omega-6 Fatty Acid (g)	5-10*		17	19	21	17	15	17	18	20	18	17
Other nutrients												
Choline (mg)	550*	425*	253	123	160	191	230	352	138	181	204	268
Fiber (g)	30-38*	21-25*	21	18	28	32	26	20	18	30	27	27

Note: Recommended Dietary Allowances (RDAs) in bold type and Adequate Intakes (AIs) in ordinary type followed by an asterisk (*) for 19 years of age or older; shaded values indicate RDA/AI value is not met. ^Dietary vitamin B6 (mg) needs for CKD patients are greater than the DRI (25-27). LO: lacto-ovo vegetarian; OM: omnivorous; VE: vegan; PL: PLADO

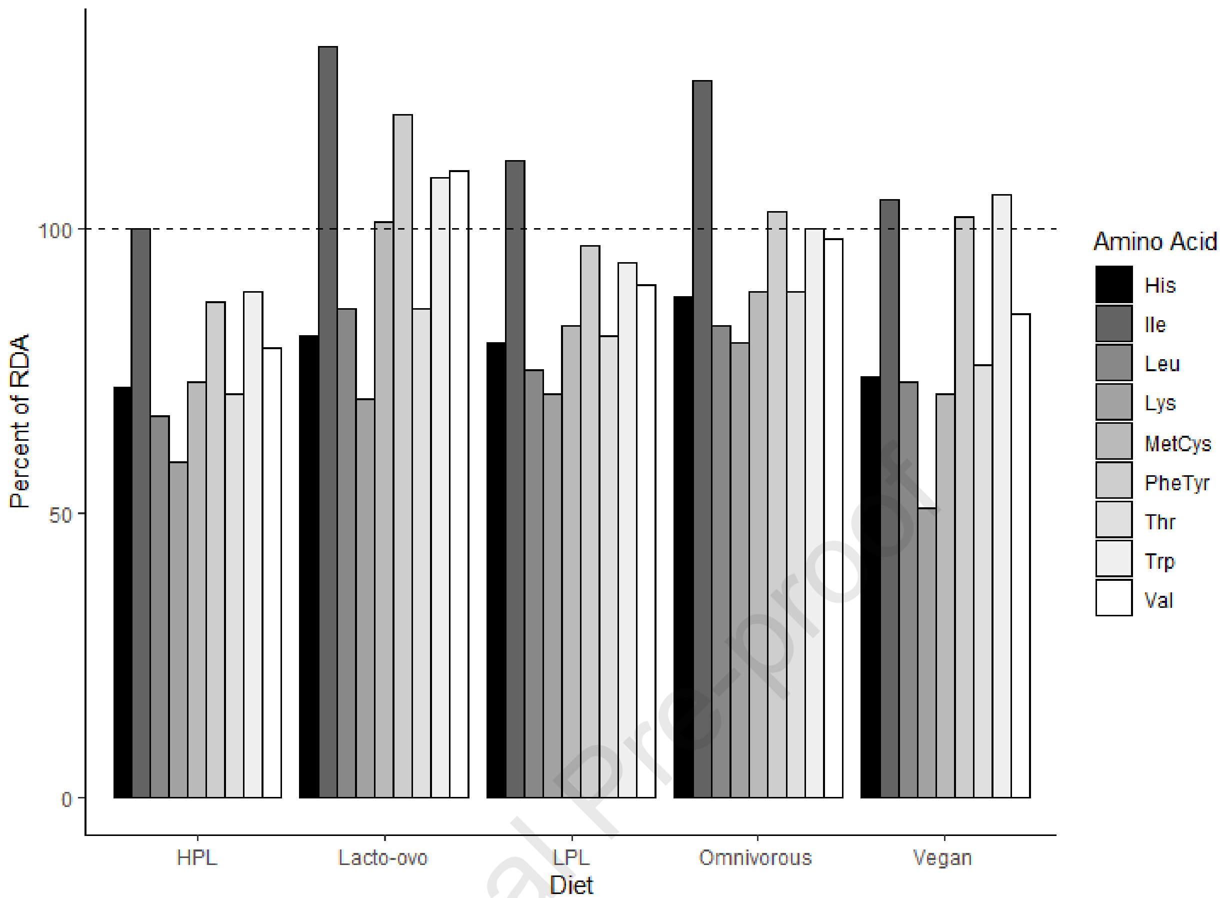
Abbreviations: µg: microgram; mg: milligram; g: gram; ND: not defined.

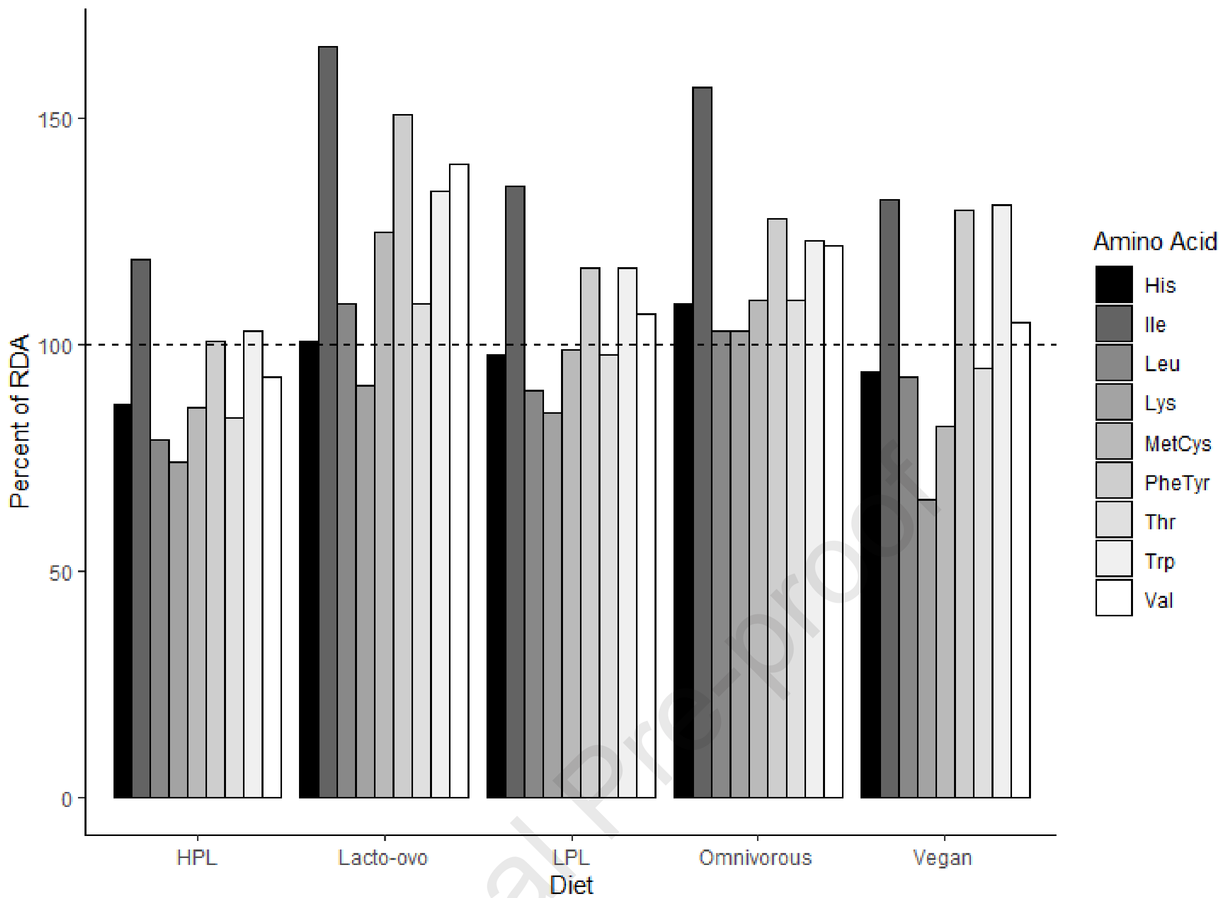
Table 2b Nutrient content according to diet type and protein level of the LPDs

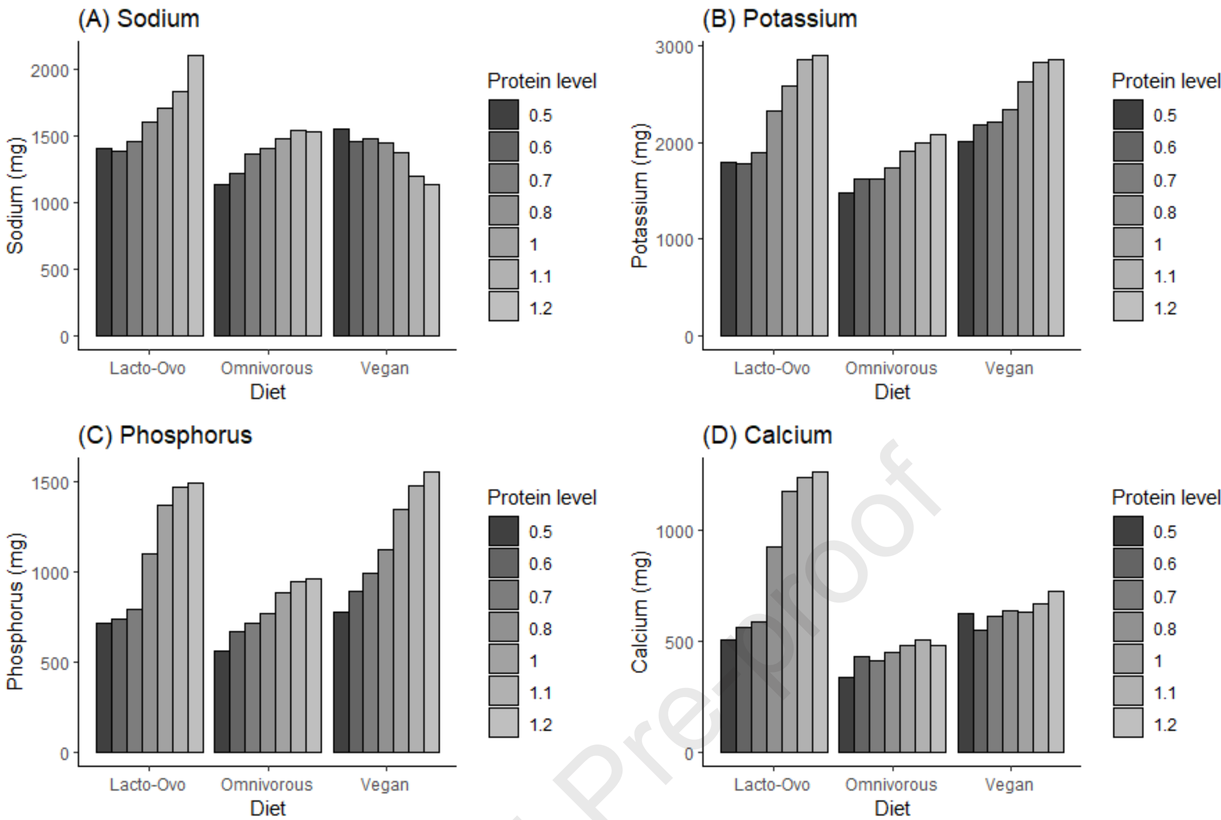
	RDA/AI		0.7 g protein/kg/d					0.8 g protein/kg/d				
	Males	**Females**	LO	OM	VE	HPL	LPL	LO	OM	VE	HPL	LPL
Vitamins												
Vitamin A (µg)	**3000**	**2333**	8327	7565	7561	7462	7462	8185	7507	7417	7314	7315
Vitamin B1 (mg)	**1.2**	**1.1**	1.0	1.0	1.3	1.3	1.3	1.4	1.1	1.3	1.3	1.3
Vitamin B2 (mg)	**1.3**	**1.1**	2.3	1.3	1.4	1.8	1.8	2.1	1.4	1.5	1.9	1.9
Vitamin B3 (mg)	**16**	**14**	9	18	14	18	18	12	19	15	20	20
Vitamin B6 (mg)^	**5.0^**		1.0	1.4	1.2	1.7	1.7	1.1	1.5	1.2	1.7	1.7
Vitamin B12 (mcg)	**2.4**	**2.4**	3.2	3.2	0.6	4.1	4.1	3.9	3.7	0.6	4.4	4.4
Folate (mcg)	**400**		271	230	432	306	307	351	229	475	338	338
Vitamin K (mcg)	120*	90*	132	154	143	224	224	116	153	142	221	221
Biotin (mcg)	30*		36	10	32	17	17	41	12	32	19	19
Minerals												
Copper (mg)	**0.9**		1.0	0.9	1.9	1.4	1.4	1.2	1.0	2.0	1.5	1.5
Iron (mg)	**8**	8.4	8.4	9.0	13	16	16	10.8	9.1	14	17	17
Manganese (mg)	2.3*	3.0	3.0	2.9	6.6	4.5	4.5	4.2	2.9	7.0	4.5	4.5
Selenium (mcg)	**55**		78	68	45	68	68	70	78	46	75	75
Zinc (mg)	**11**	**6**	6	6	7	7	7	8	7	8	8	8
Magnesium (mg)	**400-420**	**310-320**	233	188	360	326	326	264	195	415	354	354
Polyunsaturated fatty acids												
20:5 – EPA (g)	ND		0.00	0.18	0.00	0.08	0.08	0.00	0.20	0.00	0.10	0.10
22:6 – DHA (g)	ND		0.05	0.61	0.00	0.29	0.29	0.03	0.68	0.00	0.36	0.36
Omega-3 Fatty Acid (g)	0.6-1.2*		1.5	3.3	1.7	3.0	3.0	1.1	3.4	1.7	3.6	3.6
Omega-6 Fatty Acid (g)	5-10*		18	19	21	17	17	13	18	20	17	17
Other nutrients												
Choline (mg)	550*	425*	409	150	194	306	310	370	166	203	322	322
Fiber (g)	30-38*	21-25*	21	17	31	29	29	21	17	32	32	32

Note: Recommended Dietary Allowances (RDAs) in bold type and Adequate Intakes (AIs) in ordinary type followed by an asterisk (*) for 19 years of age or older; shaded values indicate RDA/AI value is not met. ^Dietary vitamin B6 (mg) needs for CKD patients are greater than the DRI (25-27). LO: lacto-ovo vegetarian; OM: omnivorous; VE: vegan; PL: PLADO

Abbreviations: µg: microgram; mg: milligram; g: gram; ND: not defined.


Percent of RDA
100
50
0
HPL
Lacto-ovo
LPL
Omnivorous
Vegan
Diet
Amino Acid
His
Ile
Leu
Lys
MetCys
PheTyr
Thr
Trp
Val


150
100
50
0
Percent of RDA
HPL
Lacto-ovo
LPL
Omnivorous
Vegan
Diet
Amino Acid
His
Ile
Leu
Lys
MetCys
PheTyr
Thr
Trp
Val


(A) Sodium
Sodium (mg)
0
500
1000
1500
2000
Lacto-Ovo
Omnivorous
Vegan
Diet
Protein level
0.5
0.6
0.7
0.8
1
1.1
1.2
(B) Potassium
Potassium (mg)
0
1000
2000
3000
(C) Phosphorus
Phosphorus (mg)
1500
(D) Calcium
Calcium (mg)

NUTRITIONAL ADEQUACY OF ESSENTIAL NUTRIENTS IN LOW PROTEN ANIMAL- AND PLANT-BASED DIETS IN THE UNITED STATES FOR CHRONIC KIDNEY DISEASE PATIENTS

Dina A. Tallman, PhD, RD[1], Ban-Hock Khor, PhD[2], Tilakavati Karupaiah, PhD, RnD[3], Pramod Khosla, PhD[1], Maria Chan, PhD, RD[4], Joel D. Kopple, MD[5]*

[1]Department of Nutrition and Food Science, Wayne State University, Detroit, MI 48202, USA.*

[2]Faculty of Food Science and Nutrition, Universiti Malaysia Sabah, Kota Kinabalu, Sabah 56000, Malaysia.

[3]School of Biosciences, Faculty of Health Sciences, Taylors University, 47500 Subang Jaya, Malaysia.

[4]Department of Nutrition and Dietetics, The St. George Hospital, Kogarah, Australia.

[5]Division of Nephrology and Hypertension and the Lundquist Institute at Harbor-UCLA Medical Center, Torrance, California; David Geffen School of Medicine at UCLA and UCLA Fielding School of Public Health, Los Angeles, California.

[*]Current address: US Food and Drug Administration, Detroit, MI, USA

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Address correspondence *to Joel D. Kopple, MD Division of Nephrology and Hypertension and the Lundquist Institute at Harbor-UCLA Medical Center, 1124 West Carson Street, Torrance, California 90502* jkopple@lundquist.org

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Dina Tallman: Writing – Original draft, Methodology, Formal analysis, Investigation. Ban Hock Khor: Writing – review and editing, Formal analysis, Investigation. Tilakavati Karupaiah: Conceptualization, Methodology, Writing – review and editing. Pramod Khosla: Methodology, Writing – review and editing. Maria Chan: Writing – review and editing. Joel D. Kopple: Conceptualization, Supervision, Methodology, Writing – review and editing.