International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

ORIGINAL ARTICLE

# Comparing the Effect of a 40-Day Diet of Animal-based and Vegetable-based Protein in Patients with Chronic Kidney Disease under Hemodialysis; a Randomized Clinical Trial

Zohreh Mazloom[1*], Marzieh Mahmoodi[2], Najmeh Hejazi[1]

1. Nutrition Research Center, Department of Clinical Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
2. Student Research Committee, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

ARTICLE INFO

*Keywords:*
Chronic kidney disease
Proteins
Diet

*Corresponding author:
Zohreh Mazloom,
Nutrition Research Center,
Department of Clinical Nutrition,
School of Nutrition and Food Sciences,
Shiraz University of Medical Sciences,
Shiraz, Iran
**Tel:** +98-71-37251004
**Email:** zohreh.mazloom@gmail.com
**Received:** 1 January 2017
**Revised:** 8 March 2017
**Accepted:** 8 April 2017

ABSTRACT

**Background:** Chronic kidney disease (CKD) is an important health issue that will ultimately require routine dialysis or renal transplantation. Studies on dietary intervention comparing animal and or vegetable protein have not yet validated a suitable protein diet for patients on dialysis. We aimed to compare renal outcomes of patients on dialysis after animal- and vegetable-based protein dietary interventions to be able to designate an appropriate protein diet for patients on dialysis.

**Methods:** In this randomized clinical trial, patients referred to Nemazee Hospital dialysis center, in Shiraz Iran, were randomly divided into two groups of 30 patients: Group A received diet containing 60% animal protein and 40% vegetable protein and group B, 60% vegetable protein and 40% animal protein. Serum level of blood urea nitrogen (BUN), creatinine, serum albumin and total protein were measured. Patients' weight and blood pressure were also recorded before and after dialysis and compared with values after 40 days of dietary interventions.

**Results:** In group A, creatinine and serum total protein significantly reduced after dietary intervention (P=0.03, and 0.001, respectively). Mediating the effect of dialysis, there was a significant increase in serum total protein (P=0.002), and a significant decrease in serum creatinine (P=0.05) level in group A, while no significant changes were seen in the serum concentration of BUN (P>0.05).

**Conclusion:** 40-day animal- or vegetable-based protein dietary intervention could not significantly change the renal outcome, blood pressure, or body weight of patients with CKD undergoing hemodialysis.

Please cite this article as: Mazloom Z, Mahmoodi M, Hejazi N. Comparing the Effect of a 40-Day Diet of Animal-based and Vegetable-based Protein in Patients with Chronic Kidney Disease under Hemodialysis; A Randomized Clinical Trial. Int J Nutr Sci 2017;2(1):43-50.

## Introduction

Chronic kidney disease (CKD) is a major health issue worldwide, and is associated with increased risk of mortality and morbidity (1). In Iran, the prevalence of CKD is estimated over 700,000 in 2004 with an incidence of 173.5:100,000 population (2). Moreover, there are more than 24,000 people with end-stage renal disease (ESRD) in Iran (3) and over 12,500 patients on hemodialysis treatment with a 12% increasing rate over the past 10 years (4).

Considering the great expenses and time spent for hemodialysis, it is necessary to pay more attention to factors that play a role in the health status of the affected patients. Diet is proposed as an important factor that can lengthen the

interval between dialysis sessions and postpone the need for transplantation (5). One important component of diet that affects renal function is the amount and type of protein eaten by these patients (6). Studies suggest that high intake proteins regardless of the type accelerates the underlying disease process, while very low protein intake may cause malnutrition (7). Although the amount of protein intake in patients undergoing hemodialysis is suggested to be about 1-1.2 g/kg/day, whether this protein should be mainly animal-based or vegetable -based is still controversial (8).

Studies suggest that vegetable based protein in patients with CKD is associated with lower mortality rate (9) and reduces serum lipid profile, and uric acid concentration in these patients (10). Differences in postprandial circulating hormones, sites of protein metabolism, and interaction with accompanying micronutrients are posited to play a role in this difference (7). Other studies have compared the effect of low animal-based diet with vegetable protein on renal function of patients with CKD. Although it has been suggested that 1-3 weeks of dietary soy protein delay the progression of CKD in rats (11), and review studies have posited that substitution of animal protein with soy protein result in favorable renal outcome in diabetic nephropathy (12, 13), the results of studies on humans with CKD are controversial still. Some studies suggest improved renal function by vegetable proteins in patients with late stage CKD (14, 15) and have suggested that vegetable protein can improve the patients' quality of life and psychological problems. They also stated that vegetable based protein diet provide greater variety and better palatability of food in patients with CKD (16), while others suggest no difference on renal function (17). The effect of animal and or vegetable-based protein on blood pressure and body mass index in patients with CKD is controversial (17).

Due to the controversies among studies, we aimed to compare renal function of patients on dialysis after animal- and vegetable-based protein dietary interventions.

## Materials and Methods

### *Study Design*

In the present randomized clinical trial, patients with CKD recruited from Nemazee Hospital dialysis center in Shiraz, Iran. The protocol of the study was approved by the Ethics Committee of Shiraz University of Medical Sciences. Written informed consent was obtained from participants after the design and objectives of the study were explained to them.

The sample size was calculated to be 56, considering previous studies and α=0.05 (95% CI) and 80% power using the following formula (18, 19):

$$n = \frac{2\delta^2\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2}{\left(\mu_1 - \mu_2\right)^2}$$

| | | |
|---|---|---|
| Z1-α/2=1.96 | 95% | δ=25 |
| Z1-β=0.84 | 80% | μ1-μ2=25 |

The ultimate sample size was considered at 60 (30 in each group). Adults aged 20-60 years who were not hospitalized in the last two weeks, were hemodialyzed at least one time a week, and did not have any other disease such as diabetes and CHD, also willing to participate were included in this study. We excluded patients who had undergone kidney transplantation and were hospitalized because of other diseases, or experienced any adverse changes such as digestive problems were excluded from this study.

At baseline, before group allocation, blood samples were drawn from patients before and after dialysis, blood then sent to the hospital's laboratory for assessment of serum concentration of blood urea nitrogen (BUN), creatinine, serum albumin and total protein. Patients' weight and blood pressure (BP) were also recorded before and after dialysis. After obtaining the laboratory results, nutritional intervention was planned for each patient according to the patient's blood parameters and anthropometric indices. Food habits, age, sex, and drugs used by patients were also considered. The required calorie and estimated required amount of protein (UFC) were calculated based on the number of dialysis per week and level of patients' BUN. For patients who were dialyzed two to three times a week, 1.2 g/kg of ideal body weight and for patients who were dialyzed once-daily, 0.9-1 g/kg of ideal body weight was considered. The

amount of dietary fat was considered 27% of total calories and the remaining calories were provided from carbohydrates.

Due to the elimination of water-soluble vitamins during dialysis, low-potassium fruits and vegetables which are good sources of vitamin C and folic acid were included in the patients' diet. The amount of fluid intake was calculated based on the daily urinary volume of the patients and according to their weight loss during dialysis. Patients then, were randomly divided into two groups by balanced block randomization method. This study had been single blind and the trial was planned in such a way that the participant did not know in which group he/she belonged to.

Group A (n=30) received diet containing 60% animal-based protein (meat, egg, and dairy products) and 40% vegetable-based protein (bread, vegetables, and cereal). Group B (n=30) received diet containing 60% vegetable-based protein and 40% animal-based protein. The designed diets then were explained to patients and checked after two weeks by a diet recall questionnaire and further explanations were given to them if needed.

At the end of the study, after 40 days, blood samples were taken before and after dialysis and blood indices were recorded, in addition patients' weight and BP that were also recorded and compared between groups. Patients' weight was evaluated by a scale and patients' height by a wall meter. Patients' weight and height was measured without shoes and with casual clothes. Table 1 shows the serum parameter. Difference in serum levels of BUN.I was considered as the primary outcome, which was calculated as follows:

$$BUNI = \frac{\text{BUN before diyalisis} - \text{BUN after diyalisis}}{\text{BUN before diyalisis}} \times 100$$

Number of patients excluded in each phase of the study is shown in figure 1.

Data was recorded in coding sheets and analyzed using SPSS software, version 16.0 for windows (SPSS Inc., Chicago, IL). The results of quantitative variables were reported as mean±standard deviation (SD) and the results of categorical variables were reported as frequency (percentage). Kolmogorov-Smirnov test was used to assess the normal distribution of data. Categorical variables were compared using chi-square test. Comparison of continuous variables before and after dialysis was performed by paired T test and comparison of continuous variables between groups was performed using Student's T test. For analysis, p values of 0.05 or less were considered statistically significant.

## Results

The mean±SD age of the participants in group A (60% animal-based protein) was 45.72±14.17 (range: 21-69) years, and 49.72±12.78 (range: 26-70) years in group B (60% vegetable-based protein) (P>0.05). In group A, 19 patients were male and 11 were female, where, in group B

**Table 1:** Comparison of mean difference (before and after dialysis) and standard deviation of serum parameters, blood pressure, and patients' weight before and after diet intervention between study groups

| Serum parameters | Group A | | Group B | | *p*-value |
|---|---|---|---|---|---|
| | Before intervention | After intervention | Before intervention | After intervention | |
| Albumin (g/dL) | -0.42±SD | -0.35±1.02 | -0.36±0.45 | -0.27±0.58 | NS |
| P value | NS | | NS | | |
| Blood pressure (mmHg) | 6.92±20.35 | 5.38±25.46 | 15.86±15.47 | 11.27±29.28 | NS |
| P value | NS | | NS | | |
| Blood urea nitrogen (mg/dL) | 35.27±13.60 | 34.73±14.30 | 31.82±13.20 | 36.82±17.50 | NS |
| P value | NS | | NS | | |
| Creatinine (mg/dL) | 6.82±3.60 | 5.38±2.65 | 5.33±1.92 | 5.52±2.8 | NS |
| P-value | 0.03 | | NS | | |
| Weight (kg) | 2.61±1.56 | 2.58±1.30 | 2.45±1.40 | 2.28±1.23 | NS |
| P value | NS | | NS | | |
| Serum protein (g/dL) | -1.25±1.13 | -0.12±1.11 | -0.91±0.78 | -0.77±1.37 | NS |
| P value | 0.001 | | NS | | |

NS: Non-significant

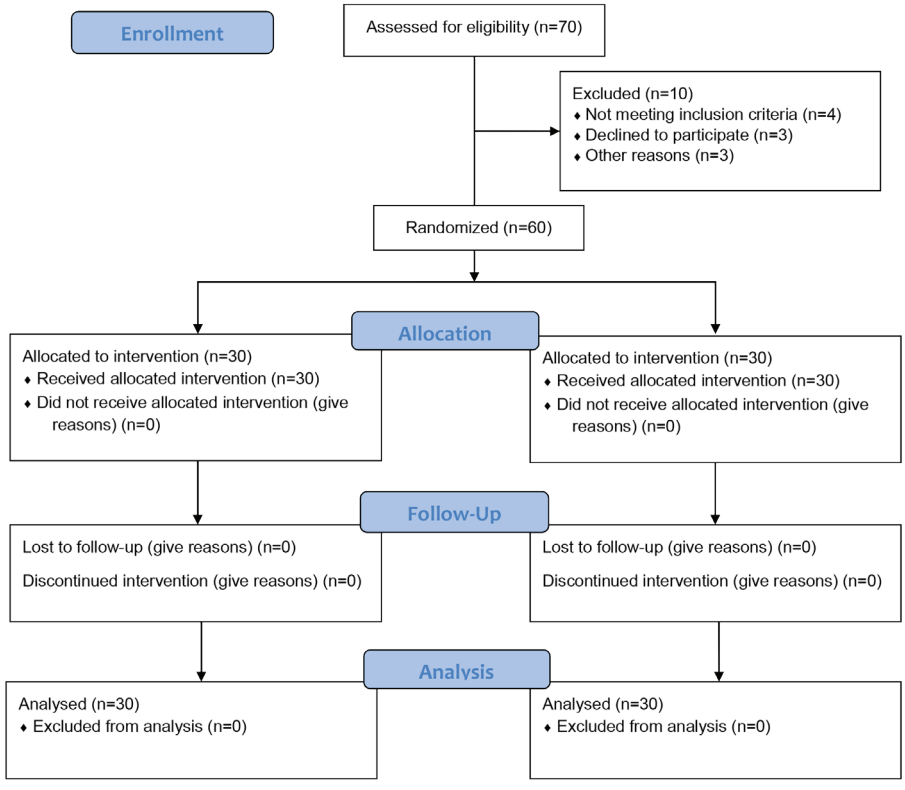


**Figure 1:** Flow diagram for participants' enrollment

18 patients were male and 12 were female (P>0.05). The mean height of patients in group A was 164.53±9.30 (149-179) cm and in group B, 158.22±10.26 (138-185) cm (P>0.05). Number of dialysis per week was once a week in 8 patients, twice a week in 18, and three times a week in 4 patients in group A, while it was once, twice, and three times a week in 10, 18, and 2 patients, respectively, in group B (P>0.05).

The mean difference in serum parameters, weight, and BP of the two groups before and after dietary intervention are demonstrated in table 1 and figures 2-4. As observed, creatinine and serum protein significantly reduced in group A (P=0.03, and 0.001, respectively), while the changes were not statistically significant in group B.

For the possible effect of dialysis, we compared the parameters before hemodialysis (table 2). There was a significant increase in serum protein (P=0.002), and a significant decrease in serum creatinine (P=0.05) in group A, while there was a significant increase in serum albumin and protein (P=0.03, and 0.01, respectively). BUN also decreased in group A and increased in group B, but the changes were not statistically significant (P>0.05).

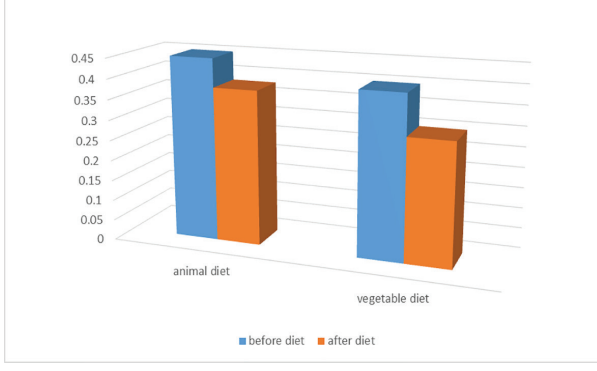


**Figure 2:** Variation of serum albumin level before and after animal versus vegetable protein diet in patietns undergoing hemodialysis (mean differences before and after hemodialysis)

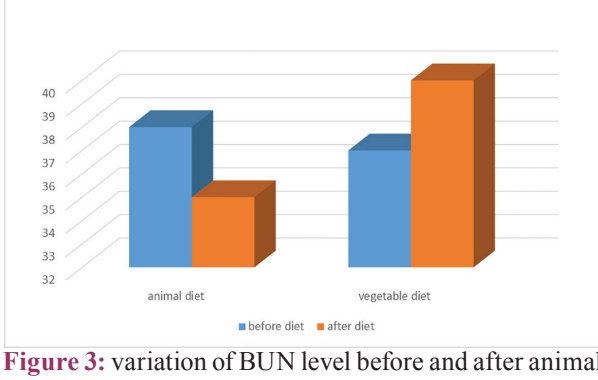


**Figure 3:** variation of BUN level before and after animal versus vegetable protein diet in hemodialysis patients (mean differences before and after hemodialysis)

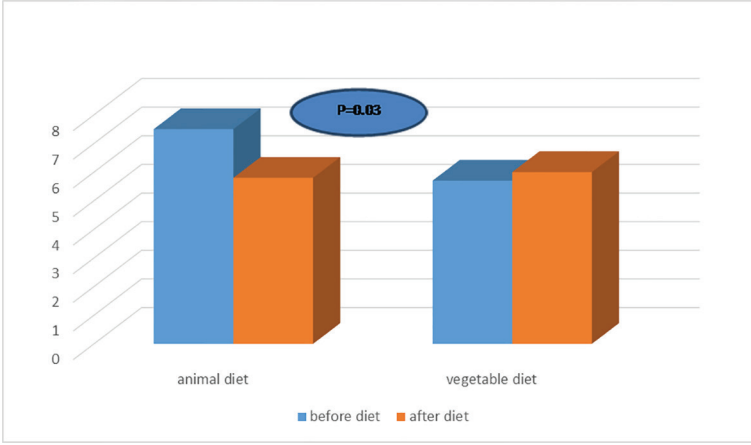


**Figure 4:** Variation of serum creatinine level before and after animal versus vegetable protein diet in hemodialysis patients (mean differences before and after hemodialysis)

**Table 2:** Comparison of mean and standard deviation of serum parameters, blood pressure, and patients' weight before and after diet intervention between study groups (before dialysis for neglecting the impact of dialysis on results)

| Serum parameters | Group A | | Group B | | *p*-value |
|---|---|---|---|---|---|
| | Before intervention | After intervention | Before intervention | After intervention | |
| Albumin (g/dL) | 3.72±0.66 | 3.86±0.44 | 3.54±0.53 | 3.75±0.53 | NS |
| P value | NS | | 0.03 | | |
| Blood pressure (mmHg) | 150.70±21.35 | 144.62±24.37 | 156.21±23.96 | 145.86±31.34 | NS |
| P value | NS | | NS | | |
| Blood urea nitrogen (mg/dL) | 35.27±13.60 | 34.70±14.30 | 31.82±13.20 | 36.82±17.50 | NS |
| P value | NS | | NS | | |
| Creatinine (mg/dL) | 14.34±6.27 | 12.41±4.14 | 11.65±3.54 | 11.53±4.12 | NS |
| P-value | 0.05 | | NS | | |
| Weight (kg) | 65.78±8.70 | 64.50±9.07 | 57.22±10.18 | 55.74±10.51 | NS |
| P value | NS | | NS | | |
| Serum protein (g/dL) | 6.60±1.02 | 7.70±0.85 | 6.44±0.87 | 6.95±1.10 | NS |
| P value | 0.002 | | 0.01 | | |

NS: Not significant

**Table 3:** Mean±SD BUN in patients undergoing hemodialysis before and after receiving diets containing animal and vegetable protein

| Group | Blood urea nitrogen (mg/dL) | | *p*-value |
|---|---|---|---|
| | Before intervention | After Intervention | |
| Group A (n=30) | 49.45±11.76 | 47.25±13.70 | NS |
| Group B (n=30) | 48.07±18.35 | 49.58±13.20 | NS |

The BUN indexes were compared in patients undergoing hemodisalysis before and after receiving diets containing animal and vegetable protein but no significant changes were observed (P>0.05, table 3).

## Discussion

The present study compared the effect of vegetable based versus animal based protein diet on the renal function and anthropometric indices of hemodialysis patients. We found no significant differences in BUN level in group receiving vegetable protein when compared to animal protein group (P>0.05). However, serum creatinine and protein concentration significantly reduced after dietary intervention in vegetable protein group (P=0.03, and 0.001, respectively), needless to say that the changes were not statistically significant in group receiving animal protein. After mediating the

effect of dialysis, there was a significant increase in serum albumin and protein in vegetable protein group (P=0.03, and 0.01).

The favorable outcome of low-protein diet in patients with CKD has been previously suggested (20-24), whereas the impacts of vegetable or animal-based protein on renal function is still controversial. Although studies on individuals with normal kidney function (25) and diabetic nephropathy(12, 13) have suggested lower urine protein by vegetable base diets, the results of studies which have been focused on patients with CKD are not clear. The beneficial effects of vegetable protein versus animal protein on proteinurea in patients with proteinuric glomerulopathies were also not also determined (26).

Soroka and colleagues studied the effect of a 6-month vegetable and animal-based protein in patients with CKD in a randomized crossover trial and have reported higher caloric intake, and compliance in vegetarian-based protein when compared to animal protein (14). Similar anthropometric measurements, cholesterol and albumin concentration, total lymphocyte count, and 24-hour protein excretion were also reported, blood urea nitrogen, urine urea nitrogen, protein catabolic rate, and 24-hour urine creatinine and phosphate were lower in vegetable protein group (14). The results of their study is in line with the present study regarding no change in body weight and anthropometric indices, this result has been also confirmed by other studies, as well (9, 17). Soroka and colleagues reported changes in renal function in group receiving vegetable protein which is not consistent with the present study, as we could not show significant impact of diets on renal function. This difference could be due to the differences in details of the prescribed diet, the duration of study, and patients' adherence to diets. Lin and co-workers found no difference in serum creatinine and other renal parameters between vegetable and animal- protein fed diets, which is consistent with the results of the present study, although they reported lower systolic blood pressure, serum levels of BUN, sodium, glucose, cholesterol and urinary specific gravity in the vegetarian group (17). But in the present study, the decrease in BUN levels in vegetable-protein group and increase in BUN levels in animal- protein group were not statistically significant that may be due to the short-term administration of diets. In addition, the mixture of protein types in the present study could be another factor for lack of significant results, as studies have suggested favorable renal function outcomes after pure vegetarian diets (27, 28).

In addition to the issues raised above, the differences in the results of the study can be attributed to the cultural differences of the study population's country that not only affect the demographic characteristics of the participants, but also affect the type of food they consume for protein supply. For example, most Iranians do not use soy protein conventionally (29) and recent studies have suggested addition of soy protein to Iranian diets, especially for patients with metabolic syndrome (30, 31). Considering the fact that Iranian dietary patterns have been considered to be associated with several diseases (32, 33), it is necessary to pay greater attention to the Iranian diet, especially in patients with CKD. As far as the authors are concerned, future Iranian studies should address the details of diet on CKD patients.

Considering the fact that a long-term vegetarian diet can induce favorable renal outcomes in patients with CKD (7, 34), it is essential that physicians and researchers pay greater attention to this matter.

The present study had some limitations, including short-term dietary interventions. In addition, data collection tool for adherence of participants to the diets were self-report of participants that could have caused bias in the results. Moreover, the results of the study might have been affected by possible confounders affecting outcomes, such as physical activity.

## Conclusion

A 40-day animal- or vegetable-based protein dietary intervention could not significantly change the renal function, blood pressure, or body weight of patients on hemodialysis.

## Acknowledgment

We are grateful of those who participated in this study.

## Conflict of Interest

None declared.

## References

1 Coresh J, Astor BC, Greene T, et al. Prevalence of chronic kidney disease and

decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis*. 2003;41:1-12.
2 Nafar M, Mousavi SM, Mahdavi M, et al. Burden of Chronic Kidney Disease in Iran. *Iran J Kidney Dis*. 2008;2:183-92.
3 Ghods AJ. Governed financial incentives as an alternative to altruistic organ donation. *Exp Clin Transplant*. 2004;2:221-8.
4 Aghighi M, Heidary Rouchi A, Zamyadi M, et al. Dialysis in iran. *Iran J Kidney Dis*. 2008;2:11-5.
5 Hunsicker LG, Adler S, Caggiula A, et al. Predictors of the progression of renal disease in the Modification of Diet in Renal Disease Study. *Kidney Int*. 1997;51:1908-19.
6 Knight EL, Stampfer MJ, Hankinson SE, et al. The impact of protein intake on renal function decline in women with normal renal function or mild renal insufficiency. *Ann Intern Med*. 2003;138:460-7.
7 Bernstein AM, Treyzon L, Li Z. Are high-protein, vegetable-based diets safe for kidney function? A review of the literature. *J Am Diet Assoc*. 2007;107:644-50.
8 Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med*. 2003;139:137-47.
9 Chen X, Wei G, Jalili T, et al. The associations of plant protein intake with all-cause mortality in CKD. *Am J Kidney Dis*. 2016;67:423-30.
10 Jenkins DJ, Kendall CW, Vidgen E, et al. High-protein diets in hyperlipidemia: effect of wheat gluten on serum lipids, uric acid, and renal function. *Am J Clin Nutr*. 2001;74:57-63.
11 Fair DE, Ogborn MR, Weiler HA, et al. Dietary soy protein attenuates renal disease progression after 1 and 3 weeks in Han: SPRD-cy weanling rats. *J Nutr*. 2004;134:1504-7.
12 Anderson JW. Beneficial effects of soy protein consumption for renal function. *Asia Pac J Clin Nutr*. 2008;17:324-8.
13 de Mello VD, Zelmanovitz T, Perassolo MS, et al. Withdrawal of red meat from the usual diet reduces albuminuria and improves serum fatty acid profile in type 2 diabetes patients with macroalbuminuria. *Am J Clin Nutr*. 2006;83:1032-8.
14 Soroka N, Silverberg D, Greemland M, et al. Comparison of a vegetable-based (soya) and an animal-based low-protein diet in predialysis chronic renal failure patients. *Nephron*. 1998;79:173-80.
15 Moorthi RN, Armstrong CL, Janda K,et al. The effect of a diet containing 70% protein from plants on mineral metabolism and musculoskeletal health in chronic kidney disease. *Am J Nephrol*. 2015;40:582-91.
16 Cupisti A, Morelli E, Meola M, et al. Vegetarian diet alternated with conventional low-protein diet for patients with chronic renal failure. *J Ren Nutr*. 2002;12:32-7.
17 Lin CK, Lin DJ, Yen CH, et al. Comparison of renal function and other health outcomes in vegetarians versus omnivores in Taiwan. *J Health Popul Nutr*. 2010:470-5.
18 Caria S, Cupisti A, Sau G,et al. The incremental treatment of ESRD: a low-protein diet combined with weekly hemodialysis may be beneficial for selected patients. *Bio Med Central*. 2014;15:172.
19 Wiliams B, Hattersley J, Layward E, et al. Metabolic acidosis and skeletal muscle adaptation to low protein diets in chronic uremia. *Kidney Int*. 1991,40:500-6
20 Fouque D, Wang P, Laville M,et al. Low protein diets for chronic kidney disease in non diabetic adults. *Cochrane Database Syst Rev*. 2001;(2):CD001892.
21 Cianciaruso B, Pota A, Pisani A,et al . Metabolic effects of two low protein diets in chronic kidney disease stage 4-5--a randomized controlled trial. *Nephrol Dial Transplant*. 2008;23:636-44.
22 Brunori G, Viola BF, Parrinello G,et al. Efficacy and safety of a very-low-protein diet when postponing dialysis in the elderly: a prospective randomized multicenter controlled study. *Am J Kidney Dis*. 2007;49:569-80.
23 Carrero JJ, Cozzolino M. Nutritional therapy, phosphate control and renal protection. *Nephron Clin Pract*. 2014;126:1-7.
24 Garneata L, Mircescu G. Effect of low-protein diet supplemented with keto acids on progression of chronic kidney disease. *J Ren Nutr*. 2013;23:210-3.
25 Wiwanitkit V. Renal function parameters of Thai vegans compared with non-vegans. *Ren Fail*. 2007;29:219-20.

26 Ahmed MS, Calabria AC, Kirsztajn GM. Short-term effects of soy protein diet in patients with proteinuric glomerulopathies. *J Bras Nephrol*. 2011;33:150-9.
27 Mircescu G, Gârneaţă L, Stancu S, et al. Effects of a supplemented hypoproteic diet in chronic kidney disease. *J Ren Nutr*. 2007;17:179-88.
28 Piccoli GB, Attini R, Vasario E, et al. Vegetarian supplemented low-protein diets. A safe option for pregnant Patients with CKD: report of 12 pregnancies in 11 patients. *Nephrol Dial Transplant*. 2011;26:196-205.
29 Sadeghian M, Hajishafiee M, Izadi V, et al. Soy product consumption and association with health characteristics and dietary quality indices in Isfahan, Iran. *ARYA Atheroscler*. 2015;11:94.
30 Azadbakht L, Kimiagar M, Mehrabi Y, et al. Soy inclusion in the diet improves features of the metabolic syndrome: a randomized crossover study in postmenopausal women. *Am J Clin Nutr*. 2007;85:735-41.
31 Mirmiran P, Esmaillzadeh A, Azizi F. Diet composition and body mass index in Tehranian adults. *Asia Pac J Clin Nutr*. 2006;15:224.
32 Esfarjani F, Roustaee R, Mohammadi-Nasrabadi F, et al. Major dietary patterns in relation to stunting among children in Tehran, Iran. *J Health Popul Nutr*. 2013;31:202-10.
33 Azadbakht L, Esmaillzadeh A. Dietary patterns and attention deficit hyperactivity disorder among Iranian children. *Nutrition*. 2012;28:242-9.
34 Garneata L, Stancu A, Dragomir D, et al. Ketoanalogue-Supplemented Vegetarian Very Low-Protein Diet and CKD Progression. *J Am Soc Nephrol*. 2016;27:2164-76.