Original Article

Dietary Protein Intake in a Multi-ethnic Asian Population of Healthy Participants and Chronic Kidney Disease Patients

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Abstract

Introduction: Clinical practice guidelines recommend different levels of dietary protein intake in predialysis chronic kidney disease (CKD) patients. It is unknown how effectively these recommendations perform in a multi-ethnic Asian population, with varied cultural beliefs and diets. We assess the profile of protein intake in a multi-ethnic Asian population, comparing healthy participants and CKD patients. Materials and Methods: We analysed the 24-hour urine collections of the Asian Kidney Disease Study (AKDS) and the Singapore Kidney Function Study (SKFS) to estimate total protein intake (TPI; g/day). We calculated ideal body weight (IDW; kg): 22.99 × height^2 (m). Standard statistical tests were applied where appropriate, and linear regression was used to assess associations of continuous variables with protein intake. Results: There were 232 CKD patients and 103 healthy participants with 35.5% diabetics. The mean TPI in healthy participants was 58.89 ± 18.42 and the mean TPI in CKD patients was 53.64 ± 19.39. By US National Kidney Foundation (NKF) guidelines, 29/232 (12.5%) of CKD patients with measured glomerular filtration rate (GFR) <25 (in mL/min/1.73 m^2) had a TPI-IDW of <0.6 g/kg/day. By Caring for Australasians with Renal Impairment (CARI) guidelines, 76.3% (177/232) of CKD patients had TPI-IDW >0.75g/kg/day. By American Dietetic Association (ADA) guidelines, 34.7% (44/127) of CKD patients with GFR <50 had TPI-IDW between 0.6 to 0.8 g/kg/day. Only 1/6 non-diabetic CKD patients with GFR <20 had a protein intake of between 0.3 to 0.5 g/kg/day. A total of 21.9% (25/114) of diabetic CKD patients had protein intake between 0.8 to 0.9 g/kg/day. Conclusion: On average, the protein intake of most CKD patients exceeds the recommendations of guidelines. Diabetic CKD patients should aim to have higher protein intakes.

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Key words: Asian continental ancestry group, Diet, Kidney failure, Malnutrition

Introduction

Clinical practice guidelines recommend different amounts of dietary protein intake for chronic kidney disease (CKD) patients.[1-3] The recommended daily protein intake varies according to the level of kidney function (glomerular filtration rate (GFR) in mL/min per 1.73 m^2 body surface area). It is unknown how effectively these recommendations perform in a multi-ethnic Asian population, with its cultural beliefs and different diets.[4,5] In this cross-sectional study, we compare dietary protein intake in a multi-ethnic Asian population of CKD patients versus a cohort of healthy participants.

Materials and Methods

This is a sub-study of data from the Singapore Kidney Function Study Phase 1 (SKFS1) and the Asian Kidney Disease Study (AKDS), approved by the institution review board.[6]

Participants

In SKFS1, we recruited 103 healthy volunteers presenting to the National University Hospital Singapore (NUHS). The inclusion criterion was non-pregnant adults (>21 years). Volunteers were excluded if they had any of the

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following: inability to consent, physical conditions that render phlebotomy for blood samples difficult, inability to collect urine samples successfully, use of regular medications, hypertension, diabetes, possible kidney dysfunction (by urinalysis, or on renal imaging), and any condition that potentially interferes with the accuracy of the measurement of GFR. Volunteers were screened with urine dipsticks for haematuria, leukocyturia, proteinuria and microalbuminuria.

In AKDS, we recruited 232 patients with CKD presenting to the outpatient nephrology clinics in NUHS. The inclusion criteria were non-pregnant adult (>21 years), serum creatinine with an estimated or measured GFR (MDRD, Cockroft-Gault[7] or creatinine clearance) of 10 mL/min to 90 mL/min, "stable CKD" defined as 2 serum creatinines measured >60 days apart of less than 20% difference, and the definition of CKD that followed the clinical practice guidelines.[8] Patients were excluded if they had any of the following: inability to consent, physical conditions that render phlebotomy for blood samples difficult, inability to collect urine samples successfully, acute kidney function deterioration, or any condition that potentially interferes with the accuracy of the measurement of GFR.

Laboratory Tests

All participants performed a 24-hour urine collection and presented the following day for GFR measurement, and provided blood and urine samples. GFR was determined by 3-sample plasma clearance of an intravenous bolus of 99mTc-DTPA.[9] Body surface area is calculated using the du Bois equation.[10] Urine urea nitrogen (g/day) was measured in the 24-hour urine collections to estimate dietary protein intake using the following formulae: total protein intake (g/day) = 6.25 × urine urea nitrogen + 30 × weight (kg).

Statistics

Ideal body weight (IDW) for Asians was calculated as: weight (kg) = 22.99 × height^2 (m).[11] We expressed total protein intake per actual body weight and per IDW for comparisons. Data is presented as mean ± 1 SD, or median and interquartile range depending on distribution. We used standard statistical tests including t-test, analysis of variance (ANOVA), chi-square test, and linear regression where appropriate. Significance was taken at the 5% level. Analyses were performed on JMP (Cary, NC, USA).

Results

There were 335 participants (Table 1). Using a body mass index (BMI) of 22.99 as the normal upper limit in Asians, normal participants were on average 5.0 ± 10.4 kg overweight, and CKD patients were 11.8 ± 13.6 kg overweight. The average serum total protein was similar between normal and CKD participants but serum albumin was lower in CKD patients (-1.76 g/L, 95% CI, -2.46 to -1.06).

Table 1. Characteristics of Participants

	SKFS1 (n = 103)	AKDS (n = 232)	*P* Value
Age (years)	42.5 ± 14.3	58.4 ± 12.8	<0.001
Male (n, %)	51 (49.5)	120 (51.0)	0.72
Ethnicity (n, %)			<0.001
Chinese	35 (34.0)	94 (40.5)	
Malay	25 (24.3)	74 (31.9)	
Indian	23 (22.3)	56 (24.1)	
Others	20 (19.4)	8 (3.5)	
Smokers (n, %)	22 (21.4)	46 (20.0)	0.77
Diabetes (n, %)	0	119 (51.3)	<0.001
Hypertension (n, %)	0	192 (82.8)	<0.001
Height (m)	1.62 ± 0.10	1.59 ± 0.09	0.008
Weight (kg)	65.7 ± 12.8	70.3 ± 15.9	0.010
Body mass index (kg/m^2)	24.9 ± 4.03	27.6 ± 5.45	<0.001
Body surface area (m^2)	1.70 ± 0.20	1.73 ± 0.01	0.35
Ideal body weight (kg)	60.7 ± 7.2	58.5 ± 6.7	0.008
Measured glomerular filtration rate (mL/min/m^2)	101 ± 16	52 ± 27	<0.001
Serum creatinine (μmol/L)	70 ± 16	153 ± 92	<0.001
Serum carbon dioxide (mmol/L)	28.2 ± 2.7	25.8 ± 3.4	<0.001
Serum total protein (g/L)	72.7 ± 4.1	72.2 ± 5.7	0.36
Serum albumin (g/L)	43.5 ± 2.6	41.8 ± 3.2	<0.001
24-hr urine volume (L)	1.58 ± 0.70	1.76 ± 0.78	0.042
24-hr urine total protein (g)	0.07 (0 – 0.11)	0.6 (0.12 – 0.67)	<0.001
24-hr urine urea nitrogen (g/day)	7.45 ± 2.80	6.47 ± 2.92	0.004
Total protein intake (g/day)	58.9 ± 18.42	53.6 ± 19.39	0.021
Protein intake/actual body weight (g/kg/day)	0.91 ± 0.27	0.77 ± 0.26	<0.001
Protein intake/ideal body weight (g/kg/day)	0.97 ± 0.28	0.91 ± 0.30	0.102

AKDS: Asian Kidney Disease Study; SKFS1: Singapore Kidney Function Study Phase 1

Protein Intake and Metabolic Acidosis

Overall (n = 335), the total protein intake (TPI, g/day) is

lower in CKD patients ($P = 0.021$), women ($P < 0.001$), and diabetic patients ($P = 0.0038$) (Table 2). "Others" had the highest intake (65.9 ± 19.7 g/day), which is significantly more than in Malays (50.9 ± 17.7 g/day, $P < 0.001$), Indians (55.1 ± 18.9 g/day, $P = 0.00102$), and Chinese (56.3 ± 19.6 g/day, $P = 0.034$). TPI is positively correlated with height ($P < 0.001$), weight ($P < 0.001$), BMI ($P < 0.001$), serum albumin ($P = 0.0032$), and GFR (45.965 + 0.139 × GFR, $P < 0.001$).

When normalised to IDW, protein intake (TPI-IDW, g/kg/day) is similar in both normal kidney function and CKD patients. Distribution of TPI-IDW is shown in Figures 1a to 1d. Overall TPI-IDW was lower in women ($P = 0.019$), Indians (vs "Others", $P < 0.001$), and diabetics ($P = 0.015$). It is positively correlated with weight ($P < 0.001$), BMI ($P < 0.001$), serum albumin ($P = 0.0044$), and GFR (0.809 + 0.00181 × GFR, $P < 0.001$).

TPI-IDW in healthy participants was highest in the "Others" group ($P = 0.0262$) but did not vary with age or gender. It increases with weight ($P = 0.024$) and BMI ($P = 0.0076$) only. In CKD patients however, it was lower in women ($P = 0.0110$) and decreased with age ($P = 0.041$), but increased with weight ($P < 0.001$), BMI ($P < 0.001$), serum albumin ($P = 0.014$), and GFR (0.785 + 0.00248 × GFR, $P < 0.001$).

According to the National Kidney Foundation Kidney Disease Outcomes Quality Initiatives (NKF KDOQI) guidelines, amongst CKD patients with GFR <25 mL/min/1.73 m^2, only 2.2% (5/232) patients had a protein intake of about 0.6 g/kg/day (using the range of 0.55 to 0.65 for this analysis).[1] By the Caring for Australasians with Renal Impairment (CARI: http://www.cari.org.au/guidelines.php) guidelines, 76.3% (177/232) of CKD patients had protein intake >0.75 g/kg/day.[2] Using American Dietetic Association guidelines (now renamed Academy of Nutrition and Dietetics: www.eatright.org), 34.7% (44/127) of CKD patients with GFR <50 mL/min/1.73 m^2 had protein intake between 0.6 to 0.8 g/kg/day.[3] Only 1/6 non-diabetic CKD patients with GFR <20 mL/min/1.73 m^2 had a protein intake between 0.3 to 0.5 g/kg/day. For diabetic CKD patients, 21.9% (25/114) had protein intake between 0.8 to 0.9 g/kg/day. The distribution of protein intake (TPI-IDW) is shown in Figures 1a to 1d, showing lower protein intake in diabetic CKD patients.

Serum carbon dioxide decreased with declining GFR (CO_2 = 23.418 + 0.0467 × GFR, $P < 0.001$), and 16.4% (38/232) of CKD patients had levels <22 mmol/L. These patients had lower dietary protein intake (0.79 ± 0.26 vs 0.94 ± 0.30 g/kg/day, $P = 0.0074$).

Discussion

Existing literature suggests that a planned very low protein diet with adequate caloric intake can retard the progression of CKD and delay the need for renal replacement therapy.[1,12] But this has to be balanced against the risk of protein-energy malnutrition at the initiation of renal replacement therapy, which may be a risk for adverse outcomes.[1,2] Therefore, most guidelines recommend protein restriction to about 15% to 20% of daily energy intake.[1,2]

The NKF KDOQI guideline recommends protein restriction from 0.6 g/kg per day (preferred) to at least 0.75 g/kg per day in patients with GFR <25 mL/min.[1] The CARI guidelines also support restriction of dietary protein in predialysis CKD patients, but recommend a minimum daily protein intake (DPI) of 0.75g per kg of IDW per day to avoid protein malnutrition and a negative nitrogen balance.[2] It is notable that protein intake of our CKD patients is well in excess of guidelines, and the majority of patients did not achieve target ranges. Protein intake is however lower in diabetic CKD patients and in Indians. Therefore, in future studies, we need to explore the impact of cultural differences in dietary practices in a multi-ethnic population.

Table 2. Distribution of Daily Total Protein Intake by Ethnicity

		Chinese	Malay	Indian	Others
Total protein intake* (g/day)	Normal	55.7 ± 15.0	55.8 ± 20.1	57.7 ± 17.1	69.7 ± 20.4
	CKD	56.6 ± 21.1	49.3 ± 16.6	54.1 ± 19.6	56.3 ± 15.1
Total protein intake per actual body weight† (g/kg/day)	Normal	0.90 ± 0.26	0.84 ± 0.27	0.89 ± 0.24	1.03 ± 0.28
	CKD	0.86 ± 0.29	0.66 ± 0.20	0.77 ± 0.24	0.83 ± 0.31
Protein intake per ideal body weight‡ (TPI-IDW, g/kg/day)	Normal	0.93 ± 0.24	0.92 ± 0.29	0.94 ± 0.24	1.14 ± 0.34
	CKD	0.95 ± 0.33	0.85 ± 0.26	0.92 ± 0.30	0.94 ± 0.25

CKD: Chronic kidney disease; TPI-IDW: Total protein intake-ideal body weight

*Normal participants: Others > Chinese ($P = 0.0064$), Others > Malay ($P = 0.011$), Others > Indian ($P = 0.031$); CKD patients: Others > Malay ($P = 0.16$).

†Normal participants: Others > Malay ($P = 0.014$); CKD patients: Chinese > Malay ($P < 0.001$), Chinese > Indian ($P = 0.032$), Indian > Malay ($P = 0.019$).

‡Normal participants: Others > Chinese ($P = 0.0065$), Others > Malay ($P = 0.0091$), Others > Indian ($P = 0.19$); CKD patients: Chinese > Malay ($P = 0.029$).

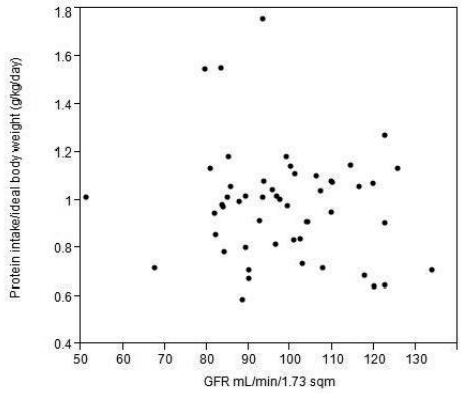

Fig. 1a. Protein intake per ideal body weight against measured GFR for healthy men.

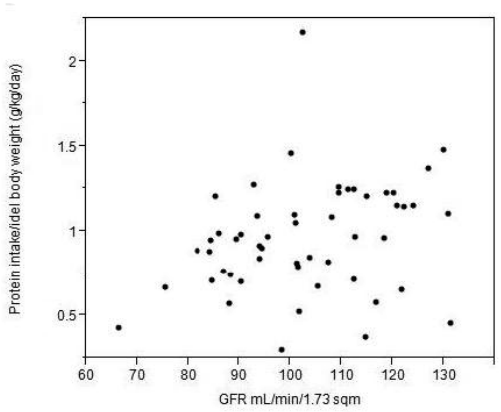

Fig. 1b. Protein intake per ideal body weight against measured GFR for healthy women.

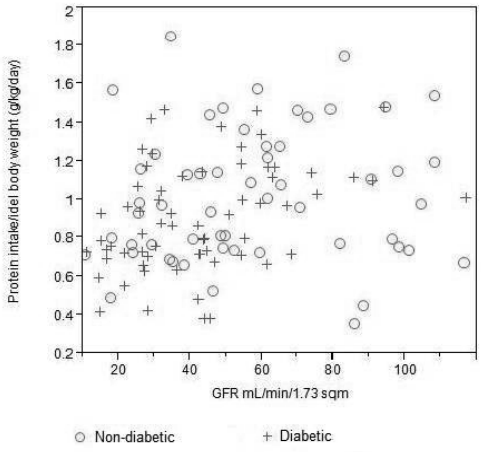

Fig. 1c. Protein intake per ideal body weight against measured GFR for men with chronic kidney disease.

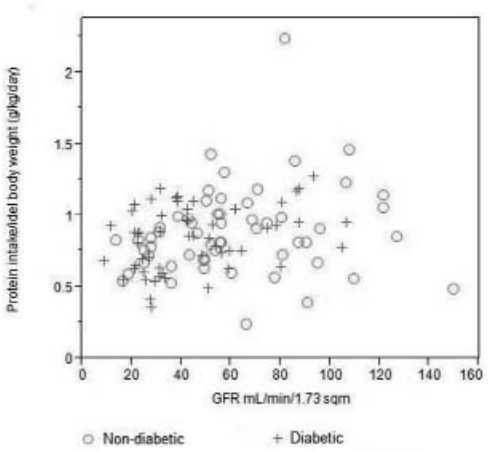

Fig. 1d. Protein intake per ideal body weight against measured GFR for women with chronic kidney disease.

One of the difficult and potentially contentious issues of protein assessment is the method of normalising (or standardising) intake values in predialysis Asian CKD patients. US NKF KDOQI guideline recommends referencing to standard body weight from second US Health and Nutrition Examination Survey (NHANES II) data.[1] The CARI guidelines recommend normalising to ideal body weight.[2] Therefore, what should be the "ideal" body weight for referencing Asians? Do separate standards apply for Chinese, Indian, and Malay ethnicities? The goal of adequate protein intake is to ensure protein balance and prevent skeletal muscle atrophy. In Asian CKD patients, the assessment may be confounded by 1) CKD-associated edema, and 2) higher body fat composition per body weight.[13] Therefore, we believe that a better indicator is derived when protein intake is normalised to IDW obtained from healthy BMI for Asians.[11] Protein intake has to be at least that needed to sustain lean body mass balance for an Asian at the upper limit of ideal BMI. Nonetheless, this attracts the problem of inadequate clinical outcomes data supporting such an evaluation method. There is currently no clear scientific base to support a consensus guideline on the most appropriate method of standardising protein intake in predialysis CKD patients.

Some of our CKD patients did not have adequate correction of metabolic acidosis, which may have a negative impact on protein intake and utilisation. The CARI guidelines recommend correction of metabolic acidosis in CKD patients, to avoid skeletal muscle breakdown and urinary nitrogen loss, before enforcing a protein-restricted diet.[2] Therefore, metabolic acidosis needs to be corrected before recommending increased protein intake, especially in CKD patients with diabetes.

Our normal participants appear to have slightly higher daily protein intake than the 10th percentile of the general population in the Report of the National Nutrition Survey 2010 published by the Health Promotion Board, Singapore.[14] It should be noted that the survey estimated protein intake through the use of dietary practices and food frequency questionnaires. Our healthy subjects may have been healthier than the general population because we excluded participants with diabetes and hypertension. The CKD patients in our study however, have a daily protein intake that is slightly lower than the 10th percentile of the general population. It is unclear how much of this is due to the effect of dietary interventions, and a future study should quantify their effect size.

The strengths of our prospective study include the fairly large study size for patients with reference GFR measurements and systematic urine collections for objective urea nitrogen assay, which were consistently performed by the same research personnel. Recruitment was strategised to ensure a spread of healthy and CKD patients over the GFR range with adequate numbers of participants' representative of ethnicity and gender. We are limited by the lack of information on previous formal dietetic assessment and intervention by a dietitian, although most patients would have received dietary advice during follow-up.

Conclusion

Protein intake of most CKD patients exceeds recommendations of guidelines. Diabetic CKD patients should aim to have higher protein intakes.

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