ORIGINAL ARTICLE

Factors Associated With Adherence to Low Protein Diet Among Patients With Stage III-V of Chronic Kidney Disease in an Outpatient Clinic at Hospital Pakar Sultanah Fatimah

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ABSTRACT

Introduction: Although the benefit of low protein diet (LPD) on chronic kidney disease (CKD) progression is well documented, patients' adherence remains as the main challenge. Therefore, this study sought to identify adherence towards LPD among CKD patients and determine possible associating factors. **Methods:** This cross-sectional study was done at the Hospital Pakar Sultanah Fatimah in Muar, Johor, among stage III to V CKD patients. Three-day dietary recalls were used to quantify dietary energy (DEI) and protein intake (DPI). Factors investigated include socio-demographic characteristics, medical history, anthropometry and body composition measurements, dietary knowledge, appetite level, handgrip strength, perceived stress, and health locus of control. Associating variables were analysed with logistic regression analysis. **Results:** The final analysis included 113 patients (54% male) with a mean estimated glomerular filtration rate of 17.5±11.2mL/min/1.73m^2 and the average age of 56.3±12.8 years. Mean DEI and DPI were 22.4±5.9kcal/kg/day and 0.83±0.28g/kg/day, respectively. Only 34.5% of patients adhere to the LPD diet with 59% exceeding the DPI recommendation. Poorer LPD adherence was associated with longer duration of hospitalization (OR 0.707, 95%CI 0.50-1.00, p=0.048), higher energy intake (OR 0.744, 95%CI 0.65-0.85, p<0.001), advance CKD stage (OR 0.318, 95%CI 0.13-0.77, p=0.012) and having better dietary knowledge (OR 0.380, 95%CI 0.17-0.85, p=0.018). **Conclusion:** LPD adherence of CKD patients in our institution is very poor signifying the need for engagement at the earlier stage of CKD to identify and stratify the patients for a targeted dietary intervention.

Keywords: Chronic kidney disease, Low protein diet, Adherence, Energy intake, Protein intake

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INTRODUCTION

Chronic kidney disease (CKD) has emerged as one of the major public health issues worldwide (1). Accelerated by an increasing prevalence of hypertension (HPT), diabetes, obesity, and the progressively ageing global population, it is estimated that one in eight adults globally is diagnosed with CKD (2). Prescription of low protein diet (LPD) as a treatment to reduce uraemia and decrease mortality among advance CKD patients was first suggested in the 1960s (3). It was later found that LPD reduces the intraglomerular pressure and proinflammatory gene expressions which helps in conserving kidney functions (4). In terms of safety, recent data have shown that CKD patients prescribed with LPD did not suffer from nutrition deficiencies or develop protein-energy wasting (5).

However, poor dietary adherence among CKD patients remains the main challenge in dietary interventions particularly LPD implementation (6). This high prevalence of non-adherence has led to the debate on the clinical usability of LPD (7). Studies investigating dietary adherence among CKD patients are often focused on dialysed patients who require higher protein intake that is conversely detrimental in non-dialysed CKD (NDCKD) patients. Furthermore, there is a scarcity of literature reporting factors associated with LPD adherence among NDCKD. The Modification of Diet in Renal Disease (MDRD) published nearly two decades ago remained the reference for LPD adherence factors until today (8).

With the increasing burden of medical cost for RRT coupled with reports suggesting that earlier initiation of RRT may not be appropriate among CKD patients (9,10), there is a renewed interest in LPD intervention (3,5,11). Currently, it is established that both non-dialysed and dialysed CKD patients have poor dietary adherence, however there is little evidence on LPD adherence among NDCKD patients, highlighting the gap in the literature (8,12). In fact, the gap is wider in the local context where there is no published report up to date on the dietary adherence pertaining to LPD in this population. Information specific to our local NDCKD may provide important key points to improve the implementation of LPD either as a mean to delay the progression of CKD or as a conservative approach in CKD treatment. Therefore, we sought to investigate the LPD adherence rate and identify the factors that affect adherence in non-dialysed CKD (stage III to V) adults at Hospital Pakar Sultanah Fatimah, Muar, Johor. Identification of these factors may help physicians and dietitians in identification and stratification of the patients to improve the LPD adherence and enhance patients' health condition and quality of life (6).

MATERIALS AND METHODS

Study Design and Patient Recruitment

This cross-sectional study recruited patients from the nephrology clinic at the Hospital Pakar Sultanah Fatimah (HPSF), Malaysia. This study was conducted from January 2018 to March 2018. Inclusion criteria were aged 18 years and above with glomerular filtration rate less than 60 mL/min/1.73m2, had previously consulted on LPD by health professionals either by medical officers or dietitians. Exclusion criteria included patients on dialysis treatment, presence of serious communication or intellectual impairment or terminal illnesses, pregnant or lactating mothers, and hospitalized patients. Before recruitment, informed consent was taken from eligible patients. Ethical approval was obtained from the Medical Research and Ethics Committee, Ministry of Health, Malaysia (ID: NMRR-18-27-39541).

Sample Size and Sampling Technique

G-power computer program application version 3.1.9.2 (13) was used to determine sample size with logistic regression as the primary model. The sample size was calculated as described by Erdfelder et al with significance level and power of the test set at 0.05 and 0.80, respectively (14). Possible predictors (i.e. sociodemographic factors: age, gender, and educational level and patient related factors: dietary knowledge, mental health and personal beliefs about current disease conditions) were pre-selected from previously published factors for dietary adherence in end-stage kidney disease (ESKD) patients (8,12,15). Additional possible predictors such as parameters of nutritional status was then added after consultation with clinical experts in nephrology as those factors were commonly encountered in the practice. The required sample size was 106 patients and an additional 30% of patients were approach given the high prevalence of dietary under-reporting (16).

Purposive sampling was used to recruit patients who fulfil the inclusion criteria. This selection of homogeneous cases reduces total variability thus simplifying analysis (17). CKD patients from the nephrology clinic was first screened according to inclusion and exclusion criteria via their medical records. Patients fulfilling the study criteria were then invited for study recruitment.

Socio-demographic Characteristics and Medical History

Information on age, gender, ethnicity, monthly income, educational and marital status, medical history including presence of comorbid disease, stage of kidney disease, recent hospitalization, and biochemical data were accessed retrospectively from patient's files.

Anthropometry Measurement

Patients' measurements were done by a single trained dietitian in accordance with the International Society of the Advancement of Kinanthropometry (18). A non-stretchable Luftkin tape was used to measure the circumference of the mid-arm (MAC) and waist (WC). Triceps skinfold (TSF) was measured with a Harpenden skin-fold calliper. Muscles circumference (MAMC) and area (MAMA) of the mid-arm were estimated with methods as described by Heymsfield and colleagues (19).

Body Composition

A body composition monitor (BCM) utilizing bioimpedance spectroscopy (Fresenius Medical Care, Germany) was used. Before body composition measurement, the patient was rested on their back for approximately 15 minutes. The electrodes were then attached to one hand and one foot of the patient and subsequently connected to the device as described by Passauer and colleagues (20).

Functional Status

Jamar dynamometer was used to measure handgrip strength (HGS) with the protocol as per recommendations by the American Society of Hand Therapists (ASHT) (21).

Dietary Assessment

Energy and protein intake was calculated based on dietary data collected using three days of dietary recalls (3DDR) (22). Dietary analysis was done using the Nutritionist Pro™ 2.2.16 (First Databank Inc., 2004) with reference to the Malaysian food composition database (23). Patients' ideal body weight (IBW) was used to interpret dietary energy intake (DEI) and dietary protein intake (DPI). The first question of the original 44-item appetite and diet assessment tool (ADAT) (24) was used to determine the appetite for the past week, and dietary knowledge was assessed using the questionnaire modified and adapted from previous ESKD studies (25,26). The assessment and scoring of dietary knowledge were performed as previously described by Gibson and colleagues (15).

Dietary misreporting (over- and under-) was identified based on the ratio of energy intake (EI) from 3DDR to basal metabolic rate (BMR) estimated using the Harris-

Benedict equation (27). The cut-offs for EI misreporting were derived using the equation as described by Black, 2000 (28). Low category of physical activity level (PAL) was applied to all patients regardless of the age group as suggested by previous reports that CKD patients have a lower PAL as compared to healthy sedentary adults (29). Each subject's EI: BMR was calculated and the ratios of <0.872 and >2.249 were classed as under and over-reporters for patients of this study, respectively. Under and over-reporters were then excluded from the final analysis.

Psychosocial Assessment

Patients perceived stress which was detected using the perceived stress scale questionnaire (30). The multidimensional health locus of control (MHLC) 18-item Form C (31) was used to determine patients' health beliefs as utilized in other studies (15).

Low Protein Diet Adherence

Adherence to LPD was defined with patients achieving actual protein intake (g/day) equal to ±20% of the recommended intake. The DPI obtained from 3DDR was compared against the recommended intake/ prescriptions from K/DOQI, 2001 (32). Non-diabetic and diabetic patients were prescribed with DPI of 0.6 and 0.75 g/kg/day, respectively. This criterion was adapted from Paes-Barreto JG et al., 2013 (33), taking considerations on a few earlier studies addressing the adherence issue (34,35). DPI was then used to classify patients into two groups, adherer, and non-adherer.

- Non-adherer (NA) dictates DPI either less than recommendation (NA-L) or higher than recommendation (NA-H).
- Patients with DPI within the ±20% of recommended intake are considered as adherers (AD).

Statistical Analysis

The relationship between an independent variable and adherence status (AD with NA groups) was determined with statistical analysis. Mean ± standard deviation or median (interquartile range) or frequency (percentages) were used to present the variables as appropriate. Univariate analysis was done on all candidate predictors with predictors having $p>0.25$ are discarded (36). Variables were entered into separate multivariable models adjusted for age, gender and education level. $p<0.05$ was used for all statistical significance. Data analysis was done using the IBM SPSS statistics software version 22.0.

RESULTS

A total of 140 eligible patients were approached with seven patients refused recruitment resulting in a total of 133 eligible patients recruited. We identified 16 patients (11.4%) under-reported their energy intake as per the criteria described in the methodology. This resulted in the exclusion of 20 patients from the final analysis due to missing values (n=4) and energy under-reporters (n=16) (Fig. 1). Of the final 113 patients, 54% were male and mean ± SD age was 56.4 ± 12.8 years old. The mean estimated GFR (eGFR) was 17.5 ± 11.2mL/min/1.73m2 and nearly half (46%) of the patient population are at stage V CKD.

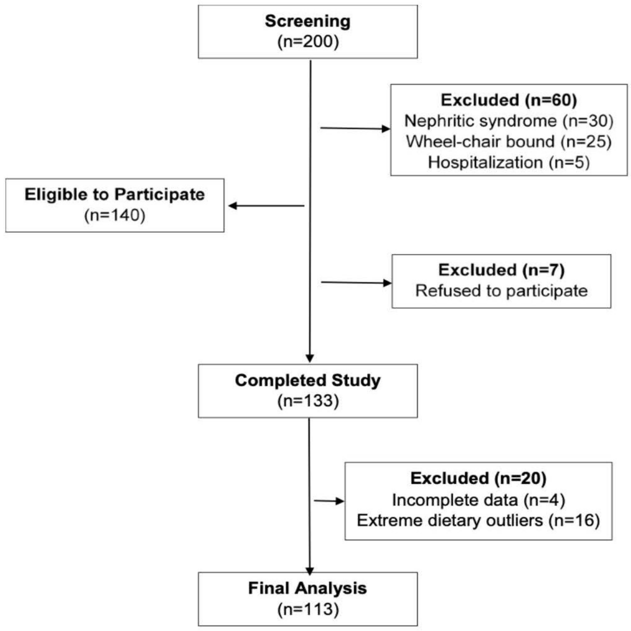

Figure 1: Flow chart of subjects' recruitment

For dietary intake assessment, it is revealed that mean EI was 1270 ± 387 kcal per day. When compared against IBW, the mean DEI was 22.4 ± 5.9 kcal/kg/day and way below the recommended 30 kcal/kg/day (32). Mean protein intake (PI) however was at 47.4 ± 17.6 g/day translating to 0.83 ± 0.28 g/kg/day which is slightly above the recommended range (32). The prevalence of LPD adherence in CKD patients was 34.5% with 59.3% of patients having DPI exceeding the recommended range as presented in Table I.

Table I: Dietary intake characteristic of the subjects according to adherence status (n=113)

Characteristics	Total Intake	Adherence Status		
		AD (n=39)	NA	
			NA-L (n=7)	NA-H (n=67)
Energy Intake (kcal)	1270 ± 387	1051 ± 219	1009 ± 234	1424 ± 403
Dietary Energy Intake (kcal/kg/day)	22.4 ± 5.9	18.7 ± 3.2	17.4 ± 1.5	25.0 ± 6.0
Protein Intake (g)	47.4 ± 17.6	34.4 ± 5.2	22.6 ± 6.1	57.6 ± 15.5
Dietary Protein Intake (g/kg/day)	0.83 ± 0.28	0.61 ± 0.07	0.39 ± 0.07	1.01 ± 0.23

SD: standard deviation;
DEI and DPI were adjusted to Ideal Body Weight (31)although there are several clinical practice guidelines on nutritional issues for patients with advanced chronic renal failure (CRF
Data were presented as mean ± SD

Table II shows the mean difference of continuous variables of patients' characteristics with LPD adherence. There is no significant difference in terms of anthropometry and body composition measurements, blood pressure, handgrip strength, biochemical data, perceived stress and health locus of control between LPD adherence groups (AD vs ND). The variables which are found to be significantly different ($p<0.05$) are the eGFR, duration of hospitalization and EI.

Table II: Mean difference between age, hospitalization data, dietary knowledge, blood pressure, handgrip strength, nutritional status parameters, psychosocial factors, and LPD adherence

Variables	Adherence Status		p-value
	AD (n=39) Mean ± SD	NA (n=74) Mean ± SD	
Age (years)	56.2 ± 12.0	56.6 ± 13.3	0.871
Estimated GFR[†] (mL/min/1.73 m^2)	14.4 ± 9.4	19.0 ± 11.8	0.037*
Frequency of hospitalization in the past 3 months	1.2 ± 0.4	1.4 ± 0.8	0.481
Duration of hospitalization (days)	3.1 ± 2.2	8.4 ± 6.4	0.003*
Total dietary knowledge score	7.6 ± 7.4	8.8 ± 7.9	0.416
Systolic Blood Pressure (mmHg)	146 ± 23	146 ± 24	0.963
Diastolic Blood Pressure (mmHg)	69 ± 13	75 ± 14	0.063
Mean Arterial Pressure (mmHg)	95 ± 13	98 ± 15	0.227
Handgrip strength (kg)	21.3 ± 6.6	22.6 ± 9.3	0.377
Anthropometry Measurements			
Body Mass Index (kg/m^2)	26.3 ± 5.4	27.6 ± 5.2	0.245
Middle Arm Circumference (cm)	29.7 ± 5.5	30.9 ± 4.8	0.202
Triceps skinfold (cm)	18.3 ± 9.3	19.0 ± 7.9	0.656
Waist circumference (cm)	89.6 ± 14.0	91.8 ± 12.6	0.401
Mid Arm Muscle Circumference (cm)	23.9 ± 3.8	25.0 ± 3.4	0.135
Mid Arm Muscle Area (cm^2)	45.9 ± 15.5	49.8 ± 13.5	0.166
Body Composition Measurements			
Overhydration (L)	+ 2.9 ± 3.8	+ 2.7 ± 2.6	0.764
Total Body Water (L)	35.7 ± 8.0	36.2 ± 7.8	0.739
Extracellular Fluid (L)	17.7 ± 4.4	17.7 ± 4.0	0.921
Intracellular Fluid (L)	18.0 ± 4.1	18.2 ± 4.8	0.783
E/I Ratio	1.0 ± 0.1	1.0 ± 0.1	0.563
Lean Tissue Index (kg/m^2)	14.2 ± 3.0	14.9 ± 3.6	0.328
Fat Tissue Index (kg/m^2)	10.8 ± 5.2	11.4 ± 5.2	0.552
Lean Tissue Mass (kg)	36.7 ± 9.3	38.1 ± 10.9	0.492
Lean Tissue Percentage (%)	54.9 ± 11.8	55.0 ± 13.3	0.975
Fat Tissue Mass (kg)	20.3 ± 9.7	21.1 ± 9.1	0.653
Fat Tissue Percentage (%)	29.0 ± 10.1	29.7 ± 10.5	0.736
Adipose Tissue Mass (kg)	27.6 ± 13.2	28.6 ± 12.5	0.693
Body Cell Mass (kg)	20.7 ± 6.4	21.9 ± 7.3	0.377
Biochemical Data			
Urea (mmol/L)	20.5 ± 7.4	18.5 ± 7.9	0.186
Creatinine (µmol/L)	490 ± 184	421 ± 225	0.100
Sodium (mmol/L)	140 ± 8	138 ± 3	0.068
Potassium (mmol/L)	4.4 ± 0.8	4.4 ± 0.7	0.824
Phosphate (mmol/L)	1.6 ± 0.4	1.6 ± 0.7	0.935
Corrected Calcium (mmol/L)	2.2 ± 0.2	2.2 ± 0.2	0.497
Total Cholesterol (mmol/L)	4.5 ± 1.0	4.9 ± 1.5	0.119
HDL-C (mmol/L)	1.1 ± 0.3	1.2 ± 0.4	0.588
LDL-C (mmol/L)	2.6 ± 0.9	2.9 ± 1.3	0.123
Triglyceride (mmol/L)	1.7 ± 0.8	1.9 ± 1.4	0.459
Total Protein	77.1 ± 6.5	75.3 ± 6.7	0.170
Serum albumin level (g/L)	38.5 ± 4.9	37.2 ± 5.1	0.167
TWBC (x10^3/µL)	8.3 ± 2.3	8.8 ± 2.3	0.285
Haemoglobin level (g/dL)	10.1 ± 2.1	10.5 ± 2.2	0.342
Fasting blood glucose (mmol/L)	5.7 ± 1.6	6.5 ± 3.3	0.159
Dietary Intake			
Energy Intake (kcal/day)	1051 ± 219	1385 ± 219	<0.001*
Dietary Energy Intake (kcal/kg/day)	18.7 ± 3.2	24.3 ± 6.1	<0.001*
Psychosocial Factor			
Perceived Stress Score	12 ± 5	12 ± 5	0.674
Multidimensional Health Locus of Control			
Internal	29 ± 3	29 ± 4	0.465
Chance	25 ± 7	24 ± 7	0.388
Doctor	15 ± 2	16 ± 2	0.193
Other People	15 ± 2	14 ± 3	0.161

AD, LPD adherer; NA, LPD non-adherer; GFR, glomerular filtration rate; E/I ratio, extracellular to intracellular fluid ratio; lean tissue and fat tissue index are adjusted with IBW; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TWBC, total white blood cells; DEI, dietary energy intake adjusted to IBW; [†]GFR is calculated from MDRD equation (35)controlled trial.

*$p<0.05$

Table III shows the association of categorical variables of patients' characteristics with LPD adherence. No significant difference was found in socio-demographic factors and dietary aspects with LPD adherence. Variables that are found to be significantly associated are the stage of CKD and dietary knowledge score category.

Based on findings of univariate analysis, significant variables including duration of hospitalization, EI, stage of CKD and knowledge category were entered into the multivariate logistic regression analysis and presented in Table IV. According to the multivariate logistic regression, CKD patients were 30% less likely to adhere to LPD with each additional day of hospitalization (OR 0.707, 95%CI 0.50-1.00, p=0.048). Patients with higher DEI were 26% less like to adhere to LPD (OR 0.744, 95%CI 0.65-0.85, p<0.001). Patients who were at stage IV of CKD were approximately 70% less likely to adhere to LPD as compared to stage V CKD patients (OR 0.318, 95%CI 0.13-0.77, p=0.012). CKD patients having good dietary knowledge scores were 62% less likely to adhere to LPD as compared to patients with poor dietary knowledge (OR 0.380, 95%CI 0.17-0.85, p=0.018). The value of Nagelkerke R square was 0.665. Hosmer and Lemeshow test indicated that this model was fit (p=0.739). Based on the classification table, 89.7% of cases were classified correctly.

Table III: Association between sociodemographic characteristic, stage of CKD, diabetes status, dietary aspects, dietary knowledge, and LPD adherence

Variables	Adherence Status		X^2	p-value
	AD (n=39) n (%)	NA (n=74) n (%)		
Sociodemographic characteristic				
Sex				
Male	20 (32.8)	41 (67.2)	0.175	0.676
Female	19 (36.5)	33 (63.5)		
Ethnicity				
Malay	30 (35.7)	54 (64.3)	0.209	0.821
Non-Malay	9 (31.0)	20 (69.0)		
Marital Status				
Single	2 (40.0)	3 (60.0)	0.068	0.794
Married	37 (34.3)	71 (65.7)		
Educational Level				
Primary	16 (34.0)	31 (66.0)	0.008	0.929
Secondary	23 (34.8)	43 (65.2)		
Household income				
≤RM2000	26 (34.2)	50 (65.8)	0.009	0.923
>RM2000	13 (35.1)	24 (64.9)		
CKD Stage				
III	4 (23.5)	13 (76.5)	7.844	0.020*
IV	10 (22.7)	34 (77.3)		
V	25 (48.1)	27 (51.9)		
Diabetes Status				
Yes	26 (66.7)	50 (67.6)	0.009	0.923
No	13 (33.3)	24 (32.4)		
Dietary Aspects				
Appetite for the Past Week				
Good	19 (32.8)	39 (67.2)	1.408	0.495
Fair	12 (31.6)	26 (68.4)		
Poor	8 (47.1)	9 (52.9)		
Meal preparation				
By own self	16 (35.6)	29 (64.4)	0.036	0.850
By others	23 (33.8)	45 (66.2)		
Dietary Knowledge Category Score[†]				
Good	15 (24.6)	46 (75.4)	5.775	0.016*
Poor	24 (46.2)	28 (53.8)		

Association was determined with Chi-squared statistics
[†]Total knowledge score was divided by median as per (24)
*p<0.05

DISCUSSION

Our study found that on average, CKD patients had DPI above the dietary protein recommendations while their DEI was way below the recommended level (i.e 30 to 35 kcal/kg/day (32)). Our findings are in parallel with many previous clinical and epidemiological studies of dietary intake among advance CKD patients (37–39). One possible explanation for the higher DPI is the trend of higher DPI of the general population locally and worldwide.

It was reported that the average person around the world consumed more than one-third higher than the average daily adult requirement (40). In Asian countries where the diet is predominantly carbohydrates, the average DPI of the general population although lower than western countries is still 110 – 120% higher than the average daily protein (40). We postulate that as our patients' habitual DPI was high, they might have struggled to change to a lower intake when prescribed, leading to low LPD adherence.

This low LPD adherence rate in our CKD population was very similar to the estimated adherence rate globally, at 31.5% (12). This adherence rate was comparable as well with Malaysian dialysis patients where only 21.0% and 33.0% of PD and HD patients, respectively achieving their protein recommendations (41). Although we could not generalize the findings of our study to the whole Malaysian CKD population, this provides insight that poor dietary adherence rate if not addressed at earlier CKD stages will continue to further worsen during dialysis.

Among the risk factors investigated, four predictors of LPD adherence were found in this study, including longer duration of hospitalization, higher EI, stage IV CKD against stage V CKD, and having a poor dietary knowledge score against a good score. We found that the strongest predictor among the four variables was a higher EI. This is not surprising as DEI and DPI

Table IV: Factors associated with adherence to Low Protein Diet among CKD patients (n=113)

Variables	B	S.E.	Wald	df	p-value	OR	95% CI for OR	
							Lower	Upper
Duration of hospitalization	-0.347	0.176	3.893	1	0.048*	0.707	0.501	0.998
Dietary energy intake[a]	-0.296	0.069	18.334	1	<0.001**	0.744	0.649	0.852
Stage of CKD[b]								
III	-1.102	0.636	3.005	1	0.083	0.332	0.096	1.155
IV	-1.147	0.454	6.371	1	0.012*	0.318	0.130	0.774
V (reference)								
Dietary Knowledge category[c]								
Good	-0.966	0.407	5.634	1	0.018*	0.380	0.171	0.845
Poor (reference)								

B, coefficient; S.E., standard errors of coefficient; df, degree of freedom; OR, odds ratios; CI, confidence interval
Model parameters: pseudo-R^2 = 0.665; Hosmer-Lemeshow test (p=0.739);
[a]Total energy intake per kilogram body weight per day adjusted to ideal body weight (31);
[b]Staging of CKD is based on eGFR estimated with the MDRD equation (48)
[c]Subjects divided into Good and Poor Knowledge grouping at the median as per (24);
*p<0.05; **p<0.001

are strongly correlated in dietary intake studies (5). Furthermore, given that the majority of CKD patients were long term diabetic patients, they tend to control their portion of carbohydrates to attain an optimal blood sugar level (42). This may have led to a higher protein composition in their daily diet.

We observed that CKD stage IV patients were approximately 70% less likely to adhere to LPD as compared to stage V CKD patients. In current clinical settings of Malaysia, most CKD patients referred to a nephrologist are at the later stages of CKD while earlier stages (II to IIIa) patients are still being monitored or managed by the general medical clinic. This is due to the high patient load as compared to the availability of nephrologists particularly in government hospitals (43). Most of these earlier stage patients were not referred to a dietitian for LPD consultation leading to lack of awareness or access to accurate information regarding LPD thus leading to poorer LPD adherence at earlier CKD stages (44).

Besides that, it is common for advanced CKD patients to not acknowledge their current detrimental medical conditions (44). This may have led to lesser attention given by patients to manage their CKD including LPD practice. Additionally, it is well reported that before dialysis consideration, the majority of CKD patients prefer to exhaust all available conservative managements, including nutritional strategies which may have led to the higher adherence to LPD among CKD stage V patients (45).

We found that the AD group had a significantly shorter hospitalization duration when compared to the NA group. Although there is lack of literature to explain on this observation, we postulated that AD group would probably be benefited from the retardation of the protein carbamylation and reactive oxygen species production, reducing oxidative stress, inflammation, endothelial dysfunction and ultimately cardiovascular disease risks (4). Furthermore, adhering to LPD intake results in a concurrent reduction of other uremic solutes including indoxyl sulfate and p-cresol sulfate which are nitrogenous based toxic compounds markedly accumulated in CKD patients (4,46). These factors may have resulted in a mutually beneficial relationship between lesser and shorter duration of hospitalization and better LPD adherence.

It is interesting to find that the NA group had a better dietary knowledge score. In an idealistic setting, it is expected that better knowledge leads to improved adherence to treatment (47). However, among the CKD population, reports on dietary knowledge and adherence have shown mixed results. Durose and colleagues (2004) investigated the relationship between dietary knowledge of 71 maintenance HD patients and found that knowledge scores were not predictive of dietary compliance (25). Similar results were seen in the local HD population of 188 respondents, where higher knowledge scores were also not associated with better compliance (26).

Nevertheless, interventional studies on improving dietary knowledge among ESKD patients showed a positive association with renal diet adherence (12). Although the current association of knowledge and LPD adherence were adjusted for possible confounding, this finding suggests multifactorial causes to dietary adherence that were not investigated in this study including changes to taste perception, access to appropriate food for LPD, the ability or time available to prepare low protein meal, and the readiness for patients to make dietary changes (25).

Nevertheless, findings from our study need to be interpreted with the recognition of its shortcomings. First, since this was a cross-sectional study, only associations, but no cause-effect relationships can be established. Second, our LPD adherence was based on the dietary intake estimated with 3DDR. As patients' next clinic follow-up is usually by one to three months, the third-day intake is mostly obtained by phone call. This may lead to misinterpretation of portion size reported by the patients. Furthermore, patients' routine dietary intake may not be represented by three days of dietary records if there were some variations at the period of recruitment.

Additionally, underreporting which is highly prevalent in CKD patients, may introduce errors in our adherence rate (16). However, to compensate for the dietary variance, we used standardized household measurement tools to assist in food portion estimations and dietary data screening for possible misreporters (overreporting and underreporting) and the dietary assessment was done by dietitians. Our misreporting percentages was considerably low at 11.4% as compared to previous reports ranging from 10 to 45% (16). Nevertheless, our DEI data was found in agreement with multiple previous reports of DEI in CKD and ESKD patients (16,37).

Third, our small cohort consisted of patients from a single centre that restricts the study power and generalizability of our findings. Nevertheless, our study population's characteristics were similar to the Malaysian CKD cohort (48) and our DPI data agree with a larger CKD cohort (38) as well as Singaporean CKD populations (39) who reported higher mean DPI than recommendations.

Finally, we did not find an association between sociodemographic or psychosocial factors and dietary adherence, contrasting with previous reports including a recent meta-analysis by Lambert and colleagues (12). It is noteworthy that the majority of reports linking socioeconomic factors with dietary adherence were done on the dialysis population which requires high protein intake as compared to LPD in NDCKD patients

(12). Currently, there is no standard guideline or protocol to measure diet adherence. Most studies used serum renal profile as an objective marker of adherence which can be strongly affected by non-dietary factors such as adherence to prescribed medication, acid-base balance, residual kidney function, and constipation, making them inaccurate and unreliable marker for dietary adherence (12).

Nevertheless, this study was able to provide data on NDCKD patients such as dietary intake, anthropometry measurements, body composition, and psychological factors, particularly among a multi-ethnic Asian population. Second, our dietary data were analysed with standardized weight calculation for energy and protein requirements and screening for under-reporters which was commonly not reported in previous studies (12). Third, we were able to provide additional evidence that nutritional indices did not differ significantly among patients who are observing lower protein intake (AD groups) as compared to NA patients, further signifies that LPD is nutritionally safe among NDCKD patients.

CONCLUSION

This study found that approximately, only one in three CKD patients in our Nephrology clinic adheres to the recommended DPI. Factors associated with adherence towards LPD recommendation include shorter duration of hospitalization, lower DEI, later staging of CKD, and interestingly, lower dietary knowledge scores.

We suggest a longitudinal study with a larger NDCKD cohort involving multiple centres to provide a better representation of the population and establish cause-effect relationships for these associated factors. As dietary assessments are often time consuming and rely on patients' recall ability, development of a food frequency questionnaire or software may provide an easier method for dietary surveillance over a period of time.

Furthermore, considering that advanced CKD patients (stage V) are more adherent to LPD and higher dietary knowledge does not equate to higher adherence, a future interventional study investigating the effects of cognitive-behavioural approaches or motivational interviewing on LPD adherence in patients with earlier stages of CKD (III-IV) should be conducted.

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REFERENCES

1. Jager KJ, Fraser SDS. The ascending rank of chronic kidney disease in the global burden of disease study. Nephrology Dialysis Transplantation. 2017.
2. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global prevalence of chronic kidney disease - A systematic review and meta-analysis. PLoS ONE. 2016.
3. Bellizzi V, Cupisti A, Locatelli F, Bolasco P, Brunori G, Cancarini G, et al. Low-protein diets for chronic kidney disease patients: The Italian experience. BMC Nephrol [Internet]. 2016;17(1):1–17. Available from: http://dx.doi.org/10.1186/s12882-016-0280-0
4. Kalantar-Zadeh K, Fouque D. Nutritional Management of Chronic Kidney Disease. N Engl J Med. 2017;377(18):1765–76.
5. Rhee CM, Ahmadi SF, Kovesdy CP, Kalantar-Zadeh K. Low-protein diet for conservative management of chronic kidney disease: a systematic review and meta-analysis of controlled trials. J Cachexia Sarcopenia Muscle. 2018;9(2):235–45.
6. Fouque D, Chen J, Chen W, Garneata L, Hwang SJ, Kalantar-Zadeh K, et al. Adherence to ketoacids/essential amino acids-supplemented low protein diets and new indications for patients with chronic kidney disease. BMC Nephrol [Internet]. 2016 [cited 2019 Aug 9];17(1):63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27388899
7. Piccoli GB, Capizzi I, Vigotti FN, Leone F, D'Alessandro C, Giuffrida D, et al. Low protein diets in patients with chronic kidney disease: a bridge between mainstream and complementary-alternative medicines? BMC Nephrol [Internet]. 2016;17(1):1–13. Available from: http://dx.doi.org/10.1186/s12882-016-0275-x
8. MILAS NC, NOWALK MP, AKPELE L, CASTALDO L, COYNE T, DOROSHENKO L, et al. Factors Associated with Adherence to the Dietary Protein Intervention in the Modification of Diet in Renal Disease Study. J Am Diet Assoc. 1995;
9. Cooper BA, Branley P, Bulfone L, Collins JF, Craig JC, Fraenkel MB, et al. A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis. N Engl J Med. 2010;
10. Kurella Tamura M, Covinsky KE, Chertow GM, Yaffe K, Landefeld CS, McCulloch CE. Functional Status of Elderly Adults before and after Initiation of Dialysis. N Engl J Med [Internet]. 2009 Oct 15 [cited 2019 Aug 7];361(16):1539–47. Available from: https://doi.org/10.1056/NEJMoa0904655
11. Kalantar-Zadeh K, Moore LW, Tortorici AR, Chou JA, St-Jules DE, Aoun A, et al. North American experience with Low protein diet for Non-dialysis-dependent chronic kidney disease. BMC Nephrol [Internet]. 2016;17(1):1–11. Available from: http://dx.doi.org/10.1186/s12882-016-0304-9

12. Lambert K, Mullan J, Mansfield K. An integrative review of the methodology and findings regarding dietary adherence in end stage kidney disease. BMC Nephrol. 2017;18(1):1–20.
13. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3. Heinrich-Heine University - Institute for Experimental Psychology. 2013.
14. Erdfelder E, FAul F, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. Behav Res Methods. 2009;
15. Gibson EL, Held I, Khawnekar D, Rutherford P. Differences in knowledge, stress, sensation seeking, and locus of control linked to dietary adherence in hemodialysis patients. Front Psychol. 2016;7(NOV):1–10.
16. Avesani CM, Kamimura MA, Draibe SA, Cuppari L. Is energy intake underestimated in nondialyzed chronic kidney disease patients? J Ren Nutr. 2005;15(1):159–65.
17. Duan N, Bhaumik DK, Palinkas LA, Hoagwood K. Optimal Design and Purposeful Sampling: Complementary Methodologies for Implementation Research. Adm Policy Ment Heal Ment Heal Serv Res. 2015 Sep 22;42(5):524–32.
18. Norton K, Olds T, Commission AS. Anthropometrica: A Textbook of Body Measurement for Sports and Health Courses [Internet]. UNSW Press; 1996. Available from: https://books.google.com.my/books?id=Bkk8FuB0P4IC
19. Heymsfield B. Heymsfield SB , McManus C , Smith J , Stevens V , Nixon DW . Anthropometric measurement of muscle mass : revised equations for calculating bone-free arm muscle area . Am J Clin Nutr 36 , Anthropometric measurement of muscle mass : revised equations for ca. Am J Clin Nutr. 1982;36(October):680–90.
20. Passauer J, Petrov H, Schleser A, Leicht J, Pucalka K. Evaluation of clinical dry weight assessment in haemodialysis patients using bioimpedance spectroscopy: a cross-sectional study. Nephrol Dial Transplant [Internet]. 2010 Feb [cited 2019 Aug 17];25(2):545–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19808949
21. Fess E, Moran C. Clinical assessment recommendations: American Society of Hand Therapists. Garner: the Society. 1981.
22. Fouque D, Vennegoor M, ter Wee P, Wanner C, Basci A, Canaud B, et al. EBPG guideline on nutrition. Nephrol Dial Transplant [Internet]. 2007 May [cited 2019 Aug 17];22 Suppl 2:ii45-87. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17507426
23. Tee E. Siong, Mohd. Ismail Noor, Mohd Nasir Azudin KI. Nutrient Composition of Malaysia Foods [Internet]. Institute for Medical Research, editor. 1997 [cited 2019 Aug 17]. Available from: http://www.nutriscene.org.my/books/Tee et al 1997 - Nutr Comp of Malaysian Foods.pdf
24. Burrowes JD, Powers SN, Cockram DB, McLeroy SL, Dwyer JT, Cunniff PJ, et al. Use of an appetite and diet assessment tool in the pilot phase of a hemodialysis clinical trial: Mortality and morbidity in hemodialysis study. J Ren Nutr. 1996;6(4):229–32.
25. Durose CL, Holdsworth M, Watson V, Przygrodzka F. Knowledge of dietary restrictions and the medical consequences of noncompliance by patients on hemodialysis are not predictive of dietary compliance. J Am Diet Assoc. 2004;104(1):35–41.
26. Yusop NBM, Mun CY, Shariff ZM, Huat CB. Factors associated with quality of life among hemodialysis patients in Malaysia. PLoS One. 2013 Dec 16;8(12).
27. Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. Proc Natl Acad Sci. 1918 Dec 1;4(12):370–3.
28. Black AE. Critical evaluation of energy intake using the Goldberg cut-off for energy intake:basal metabolic rate. A practical guide to its calculation, use and limitations. Int J Obes. 2000;
29. Hayhurst WSG, Ahmed A. Assessment of physical activity in patients with chronic kidney disease and renal replacement therapy. Springerplus. 2015;
30. Cohen S. PERCEIVED STRESS SCALE [Internet]. 1994. Available from: www.mindgarden.com
31. Wallston KA, Stein MJ, Smith CA. Form C of the MHLC Scales: A Condition-Specific Measure of Locus of Control. Vol. 63, JOURNAL OF PERSONALlTY ASSESSMENT. 1994.
32. Kopple JD. National Kidney Foundation K/DOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure. In: American Journal of Kidney Diseases. W.B. Saunders; 2001.
33. Paes-Barreto JG, Barreto Silva MI, Qureshi AR, Bregman R, Cervante VF, Carrero JJ, et al. Can Renal Nutrition Education Improve Adherence to a Low-Protein Diet in Patients With Stages 3 to 5 Chronic Kidney Disease? J Ren Nutr. 2013;23(3):164–71.
34. Cianciaruso B, Pota A, Pisani A, Torraca S, Annecchini R, Lombardi P, 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(2):636–44.
35. Dolecek TA, Olson MB, Caggiula AW, Dwyer JT, Milas NC, Gillis BP, et al. Registered dietitian time requirements in the Modification of Diet in Renal Disease Study. J Am Diet Assoc [Internet]. 1995 Nov [cited 2019 Aug 17];95(11):1307–12. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7594128
36. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. Source Code Biol Med. 2008;
37. Cuppari L, Ikizler TA. Energy balance in advanced chronic kidney disease and end-stage renal disease. Semin Dial. 2010;23(4):373–7.
38. Moore LW, Byham-Gray LD, Scott Parrott J, Rigassio-Radler D, Mandayam S, Jones SL, et al.

The mean dietary protein intake at different stages of chronic kidney disease is higher than current guidelines. Kidney Int [Internet]. 2013 Apr [cited 2019 Aug 19];83(4):724–32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23302719
39. Teo BW, Toh QC, Xu H, Yang AYT, Lin T, Li J, et al. Dietary Protein Intake in a Multi-ethnic Asian Population of Healthy Participants and Chronic Kidney Disease Patients. Ann Acad Med Singapore [Internet]. 2015 Apr [cited 2019 Aug 19];44(4):145–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26041638
40. Ranganathan J, Vennard D, Waite R, Dumas P, Lipinski B, Searchinger T. (No Title) [Internet]. Available from: http://www.worldresourcesreport.org.
41. Harvinder GS, Chee WSS, Karupaiah T, Sahathevan S, Chinna K, Ghazali A, et al. Comparison of malnutrition prevalence between haemodialysis and continuous ambulatory peritoneal dialysis patients: A cross-sectional study. Malays J Nutr. 2013;19(3):271–83.
42. Lin J, Fung TT, Hu FB, Curhan GC. Association of dietary patterns with albuminuria and kidney function decline in older white women: A subgroup analysis from the nurses health study. Am J Kidney Dis. 2011;
43. Wong HS, Goh BL. 24th Report of the Malaysian Dialysis & Transplant 2016. 2018;
44. Ikizler TA, Franch HA, Kalantar-Zadeh K, ter Wee PM, Wanner C. Time to Revisit the Role of Renal Dietitian in the Dialysis Unit. Journal of Renal Nutrition. 2014.
45. Bolasco P, Kalantar-Zadeh K, Rhee C. Conservative management of chronic kidney disease: how to avoid or defer dialysis. Panminerva Med [Internet]. 2017 [cited 2019 Aug 7];59(2):115. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28290185
46. Liu WC, Tomino Y, Lu KC. Impacts of indoxyl sulfate and p-Cresol sulfate on chronic kidney disease and mitigating effects of AST-120. Vol. 10, Toxins. MDPI AG; 2018.
47. Tomaszek L, Dębska G. Knowledge, compliance with good clinical practices and barriers to effective control of postoperative pain among nurses from hospitals with and without a "Hospital without Pain" certificate. J Clin Nurs. 2018;
48. Hooi LS, Ong LM, Ahmad G, Bavanandan S, Ahmad NA, Naidu BM, et al. A population-based study measuring the prevalence of chronic kidney disease among adults in West Malaysia. Kidney Int [Internet]. 2013;84(5):1034–40. Available from: http://dx.doi.org/10.1038/ki.2013.220
49. Levey AS, De Jong PE, Coresh J, Nahas M El, Astor BC, Matsushita K, et al. The definition, classification, and prognosis of chronic kidney disease: A KDIGO Controversies Conference report. Kidney Int. 2011;