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Identification of the Dietary Protein Sources and Their Association with Serum Phosphorus Levels among Patients with Kidney Failure

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Abstract

Background: Major dietary protein sources double as major sources of phosphorus with implications on serum phosphorus in kidney failure (KF) patients. **Objectives**: To identify the dietary protein sources of kidney failure patients and its association with their serum phosphorus (SP).**Methods:** Cross-sectional design involving 22 patients with kidney failure ≥ 18 years, recruited from the Renal and Dialysis Unit of the Korle-Bu Teaching Hospital. Sources and amount of protein and phosphorus were determined using quantitative food frequency questionnaire. Serum phosphorus was obtained from patients' hospital records. Correlation between dietary and serum phosphorus was determined. Data were analyzed using SPSS version 21 at a 95% CI at $p \leq 0.05$.**Results:** Mean age was 46.2 ± 2.5 years. Sources of protein and phosphorus were cereals, animal protein (AP) and legumes and nuts (L&N). The highest contribution for both protein and phosphorus was from cereals (65.7% and 63.4%) respectively. There was no significant correlation between all sources of phosphorus with SP (AP r^2 = 0.120, p = 0.595; L&N r^2 = -0.045, p= 0.843; cereals r^2 = 0.117, p = 0.604) howbeit, legumes and nuts showed a negative correlation.**Conclusion**; Main dietary source of both protein and phosphorus was cereals. There was no significant correlation between all sources of phosphorus with serum phosphorus levels. Appropriate medical nutrition therapy by qualified nutritionist/dietitians is recommended for this group to prevent protein energy wasting.

Keywords: kidney failure, protein, phosphorous, protein energy wasting, serum phosphorous.
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1. Introduction

Dietary restrictions are common in the medical nutrition therapy for kidney failure (KF) patients. Nutrient intake, especially protein, potassium, sodium and phosphorus are mostly restricted due to impairment in their metabolism at this stage (Perazella, 2009; Fouque and Pelletier, 2011). A daily protein intake of 0.8g /kg of body weight per day is recommended for chronic kidney disease (CKD) stages 3 to 4 patients (National Kidney Foundation, 2012; Levin and Stevens, 2012). Protein restriction of between 0.6g to 0.75g /kg/d is suggested for KF pre-dialysis patients (D'Alessandro et al., 2016; Gang et al., 2017). Recommendations for patients on maintenance haemodialysis is higher (1.2g /kg/day) due in part, to the demands of the procedure and the associated risk of protein energy wasting (PEW) (National Kidney Foundation, 2019). Protein energy wasting, which is a major risk factor for mortality among this group, is reported in 18% to 75% of patients undergoing maintenance haemodialysis (Fouque et al., 2008). To ensure adequate nourishment at these restricted intakes, KF patients are often advised to choose proteins of high biological value in their meals; those containing all essential amino acids (Joshi et al., 2019). These are mostly proteins from animal sources, such as meat, egg, poultry, fish and milk (Joshi et al., 2019), compared to the relatively lower biological value plant proteins such as legumes, some nuts and seeds.

Hyperphosphatemia, which is serum phosphorus levels above the normal range of 2.7 - 4.5 mg/dL (0.87 - 1.45 mmol/L) is common in KF (Cozzolino and Brancaccio, 2007; Noori et al., 2010). It is associated with increased disturbances in bone and mineral metabolism, cardiovascular morbidity and mortality (Moldovan et al., 2016). Especially among patients on dialysis, it is associated with pathogenesis of secondary hyperparathyroidism, renal osteodystrophy and extra skeletal calcification (Cozzolino and Brancaccio, 2007). Three main approaches characterize its management: restricting dietary phosphorus intake, reducing intestinal absorption through the use of phosphate binders or removing phosphorous through renal replacement therapy (dialysis) (Shaman and Kowalski 2016; Friedman, 2005; Nolan and Qunibi, 2005). Dietary restriction is usually at the forefront of ensuring normal serum phosphorous levels, which is mostly difficult to achieve in over 50% of patients. Dietary phosphorus is mostly obtained from organic sources (both plant and animal sources) (Gonzalez-Parra et al., 2012; Chang and Anderson,2017) and inorganic sources: mostly food additives in processed foods and some carbonated drinks (Cupisti and D'Alessandro, 2011). Most organic sources of dietary phosphorous also double as major dietary protein sources. One gram of protein contains 13mg to 15mg of phosphorous, of which 30–70% is absorbed through the intestine (Gonzalez-Parra et al., 2012). A mixed diet on average contains 12mg to 14mg of phosphorous per gram of protein-rich foods (Cupisti and D'Alessandro, 2011; Shinaberger et al., 2008). Animal protein sources especially contain high levels of phosphorus with higher rates of absorption between 40% to 60%, depending on the degree of gastrointestinal vitamin-D-receptor activation. Though equally high in phosphorus, the rate of phosphorus absorption from plant proteins is lower (10%-30%) due to its association with phytate, thereby limiting the ability of the human gastrointestinal tract to absorb it in the absence of phytase, the enzyme needed for its digestion in humans (Moe et al.,2011). Legumes are estimated to have the lowest bioavailability (<40%) while inorganic phosphorus additives have the highest bioavailability (nearly 100% in some studies) (Moe et al., 2011). Plant proteins are therefore recommended in the regulation of serum phosphorous compared to animal proteins (Noori, 2011), notwithstanding the greater risk of protein energy wasting due to their relatively lower biological value.

The prevalence of CKD is feared to rise in Ghana especially with the increasing prevalence of its major risk factors, diabetes and hypertension (Dosoo et al., 2019). Limited information exists on the protein choices made by KF patients in Ghana. The resultant impact of these choices on their health outcomes, primarily their serum phosphorus levels, also remained to be investigated. The contribution of this knowledge to promoting public health and informing dietetic counselling of KF patients, provided the rationale for carrying out this study. The study therefore aimed at identifying the major sources of protein in the diets of patients with KF, their contribution to total daily phosphorus intake and the impact on serum phosphorus levels.

2. Methods

2.1 Study design, setting and participants

The study design was observational cross-sectional. It was carried out at the Renal and Dialysis Unit of the Department of Medicine and Therapeutics, Korle-Bu Teaching Hospital (KBTH), Ghana's main tertiary health facility in the capital, Accra. The study was carried out between January and September of 2017. Participants were KF patients ≥ 18 years, who received care at the study site.

2.2 Sample size and sampling

The estimated minimum required sample size of 7 was calculated using the formular for correlation analysis $\left[\frac{z_{1-\alpha/2}+z_{1-\beta}}{|z'_{r_0}-z'_{r_1}|}\right]^2+3$ described by Kendall et al., (1994) and Draper and Smith, (1998). This was increased to 22 to increase precision and possible non-response. The correlation coefficient (r=0.88) between dietary phosphorus intake and serum phosphorus from a study carried out in the United States (Shinaberger et al., 2008) was used. Other variables used were;

$z_{1-\alpha/2}$ = 1.96, $z_{1-\beta}$= 0.842 and $z' = 0.5\text{I}n\left(\frac{1+r}{1-r}\right)$

Eligible patients in the hospital's register were recruited using systematic sampling. The register contained 200 patients, out of which 72 were eligible. A sampling interval of 3 was determined by dividing the total number of eligible patients by the estimated sample size. The first three eligible patients, identified by numbers, were balloted and patient 2 on the eligible patient's list was picked to become the starting point. Every third eligible patient, beginning from patient number 2, was invited to participate in the study. Only those who consented to participate were included.

2.3 Ethical approval

The study conformed to the 1964 Helsinki declaration and its later amendments. The study protocol was reviewed and approved by the Ethics and Protocol Review Committee of the School of Biochemical and Allied Health Sciences, University of Ghana (SBAHS-ND./10488793/AA/SA/2016-2017). Permission was also sought from the Medical Directorate of the KBTH. Written informed consent was obtained from each participant. Participation was voluntary. Patients were all identified by numbers to ensue confidentiality.

2.4 Data collection

A validated questionnaire was used to obtain socio-demographic information. A validated quantitative food frequency questionnaire (QFFQ) was used to assess patient's usual food intake within a week. The QFFQ listed 94 commonly consumed Ghanaian foods including plant and animal protein sources, carbohydrates, fruits, vegetables as well as beverages. The frequency of intake of each food item within a week was obtained and categorized as never consumed, moderately consumed (consumed once or twice in a week) and frequently consumed (consumed three or more times a week).

With the assistance of food models and household handy measures, patients also estimated the amount of each food item they eat at a sitting. The corresponding weights were determined and their nutrient content computed using MICRODIET nutrient composition database version 3.0; Downlee, United Kingdom. Total daily protein and phosphorus intakes and the foods contributing to them were documented. Estimated glomerular filtration rate, serum phosphorus levels, albumin, urea and creatinine, within the 30 days immediately preceding the study were obtained from patient hospital records.

2.5 Data Analysis

Data was analyzed using SPSS version 21 at a 95% confidence interval. Descriptive statistics (proportions, means ± SE and median with interquartile ranges), were used to analyze data. Normality of all continuous variables were tested before analysis were carried out. Parametric tools such as means ± standard errors and Students' T test were used to analyze and compare means of normally distributed data respectively. For data that were not normally distributed, median with interquartile ranges and Kruskal Wallis Test were used to analyze and compare medians for multiple independent samples respectively. Significance was set at $P \leq 0.05$. Association between phosphorus from the different dietary sources (legumes and nuts, animal proteins, inorganic sources and cereals) and serum phosphorous was determined using Spearman's correlation. Results were summarized into tables.

3. Results

3.1 Demographic, socioeconomic and biochemical information

Table 1 shows a summary of patients' demographic, socioeconomic and biochemical information. The mean age of participants was 46.2 ± 2.5 years. Half of participants were employed and had attained at least a secondary education.

Table 1: **Demographic, socioeconomic and biochemical information of study participants. (Frequency (%)/Mean ± SE)**

Variables	**Total** (*n* = 22)
Gender	
Male	11 (50.0)
Female	11 (50.0)
Marital Status	
Married	12 (54.5)
Other	10 (45.5)
Employment Status	
Employed	11 (50.0)
Unemployed	11 (50.0)
Highest Education	
Primary	11 (50.0)
Secondary	8 (36.4)
Tertiary	3 (13.6)
Age (years)	46.2 ± 2.5
Duration since diagnosis (months)	27 ± 6.2
Urea (mmol/L)	22.2 ± 1.7
Creatinine (μmol/L)	1006.3 ± 202.6
Albumin (g/dL)	3.7 ± 0.1
Serum phosphorus (mmol/L)	1.51 ± 0.05
eGFR (mL/min)	8.7 ± 0.8

3.2 Intake of protein-rich foods by study participants

In Table 2, the frequency of intake of protein-rich foods (animal proteins, legumes and nuts) every week, is shown. Fish, egg and milk were the frequently consumed animal proteins. Chicken was moderately consumed. Over 70% of patients never consumed proteins from legumes or nuts. Cooked beans, roasted groundnut, and groundnut soup were moderately consumed by less than 30% of patients

Table 2: Frequency of consumption of protein-rich foods weekly among participants. Frequency (%)

Animal protein			
Type of animal protein	**Never**	**Once or twice**	**Thrice or more**
Fried Chicken	18 (81.8)	3 (18.1)	1 (4.5)
Grilled Chicken	15 (68.2)	7 (31.8)	-
Beef	22 (100.0)	-	-
Fried Fish	3 (13.6)	5 (22.7)	14 (63.6)
Grilled Fish	5 (22.7)	4 (18.2)	13 (59)
Fried Egg	13 (59.1)	5 (22.7)	4 (18.1)
Boiled Egg	5 (22.7)	13 (59.1)	4 (18.1)
Wagashie (local fried cheese)	22 (100.0)	-	-
Domedo (grilled offals)	21 (95.5)	1 (4.5)	-
Crabs	19 (86.4)	2 (9.1)	1 (4.5)
Offals	20 (90.9)	2 (9.1)	-
Shrimps	21 (95.5)	-	1 (4.5)
Evaporated Milk	15 (68.2)	4 (18.1)	3 (13.6)
Skimmed Milk	19 (86.4)	-	3 (13.6)
Legumes and nuts			
Type of plant protein	**Never**	**Once or twice**	**Thrice or more**
Cooked Beans	16 (72.7)	6 (27.3)	-
Roasted groundnuts	17 (77.3)	3 (13.6)	2 (9.1)
Roasted Cashew nut	22 (100.0)	-	-
Groundnut soup	17 (77.3)	4 (18.1)	1 (4.5)
Agushie	20 (90.9)	2 (9.1)	-
Soya Beans	20 (90.9)	1 (4.5)	1 (4.5)
Bambara Beans	22 (100.0)	-	-
Neri	22 (100.0)	-	-
Lentils	22 (100.0)		
Tofu	20 (90.1)	1 (4.5)	1 (4.5)

Agushie = Melon seeds

3.3 Intake of cereals among study participants

Table 3 shows the frequency of intake of cereal foods every week. *Banku, Kenkey (*staples prepared from fermented maize dough) and boiled rice were frequently consumed by over 40% of participants. Porridges (*Hausa Koko*-made from polished millet, *Tom brown* -mixed cereal porridge and corn porridge-made from fermented corn dough), oats and *jollof rice* (rice cooked with tomato sauce) were moderately consumed by over 30% of participants.

Table 3: Weekly consumption of cereal foods among participants. Frequency (%)

Type of Cereal food	Never	Once or twice	Thrice or more
Oats	14 (63.6)	7 (31.8)	1 (4.5)
Tom brown	12 (54.5)	8 (36.4)	2 (9.1)
Wheat bread	12 (54.5)	4 (18.2)	6 (27.3)
Wheat	17 (77.3)	4 (18.2)	1 (4.5)
Kenkey	4 (18.2)	9 (40.9)	9 (40.9)
Banku	0 (0)	9 (40.9)	13 (59.1)
Rice balls	18 (81.8)	2 (9.1)	2 (9.1)
Waakye	16 (72.7)	4 (18.2)	2 (9.1)
Sugar bread	20 (91.0)	1 (4.5)	1 (4.5)
Butter bread	14 (63.6)	6 (27.3)	2 (9.1)
Hausa Koko	6 (27.3)	14 (63.6)	2 (9.1)
Tuo zaafi	18 (81.8)	2 (9.1)	2 (9.1)
Corn porridge	11 (50.0)	7 (31.8)	4 (18.2)
Jollof rice	11 (50).0	9 (40.9)	2 (9.1)
Rice porridge	13 (59.1)	5 (22.7)	4 (18.1)
Boiled rice	4 (18.2)	3 (13.6)	15 (68.1)

3.4 Phosphorus and protein intake from the different dietary sources.

The difference between the median phosphorus and protein intakes from the different dietary sources was tested using Kruskal Wallis multiple comparison analysis. Phosphorus intake from the different dietary sources was significantly different (p <0.001). The highest amount was obtained from cereals (666.1 mg) followed by animal protein (263.4 mg) inorganic sources (13.3mg) and legumes and nuts (6.0mg).

Similarly, protein intake from the different dietary sources were significantly different (p<0.001). The highest amount of protein was obtained from cereals (49.6g) followed by animal proteins (19.8g) and legumes and nuts (6.1g), (Table 4)

Table 4: Dietary sources contributing to total daily phosphorus and protein intakes.

Dietary source	Phosphorus intake (mg)	IQR (25^{th}-75^{th} Percentile)	Contribution to daily intake (%)	P-value
Legumes and nuts	6.0	0 - 173.6	5.6	<0.001*
Animal protein	263.4	204.6 - 419.0	27.7	
Cereals	666.1	490.5 -1000.3	63.4	
Inorganic sources	13.3	6.7 - 35.8	3.4	
Total daily intake	**1151.6**	**970.8 – 1689.9**	**100**	
Dietary source	**Protein intake (g)**	**IQR (25^{th}-75^{th} Percentile)**	**Contribution to daily intake (%)**	**P-value**
Legumes and nuts	6.1	4.5 - 8.1	8.1	< 0.001*
Animal protein	19.8	14.6 - 26.3	26.2	
Cereals	49.6	36.7 - 66.1	65.7	
Total daily intake	**75.4**	**55.9 – 100.5**	**100**	

Kruskal Wallis multiple comparison; *Significant at $p \leq 0.05$. IQR= Interquartile range.

3.5 Correlation between phosphorous from different dietary sources and serum phosphorous levels

There was no significant association between phosphorus from all sources with serum phosphorus levels. Phosphorous from legumes and nuts showed a negative correlation with serum phosphorus levels, Table 5.

Table 5: Correlation between phosphorous from different dietary sources and serum phosphorous levels.

Variable		Legumes and nuts	Animal protein	Inorganic sources	Cereals	Total daily phosphorous
S-phosphorous	r^2	-0.045	0.120	0.184	0.117	0.106
	p-value	0.843	0.595	0.413	0.604	0.638

Spearman's correlations: significant at $P \leq 0.05$. S-phosphorus = Serum phosphorus

4. Discussion

The objective of the study was to identify the dietary sources of protein among patients with kidney failure, their contribution to total daily phosphorus intake and their impact on serum phosphorus levels. The highest amount of daily protein intake in patients' diets (49.6 mg) was obtained from cereals (Table 4). Most commonly consumed cereal foods were boiled rice, banku and kenkey (Table 3). Cereal porridge and jollof rice were also moderately consumed. This contradicts findings from other studies where animal proteins contributed the highest amount of protein in patients' diets (Moe et al., 2011). The relatively bigger portion sizes of carbohydrate foods in patient's diets could explain this. The general Ghanaian diet has been described as mostly carbohydrate, with little protein, fruits and vegetables (Heinbuch, 1994; Galbete et al.,2017; Hall, 2009). In the case of participants in this study, the protein portions from animal proteins, legumes and nuts may have been further reduced due to fears that increasing their intake would worsen their condition. Hence, although animal proteins were frequently consumed among participants, it was evident that the quantities consumed were scanty, and therefore did not significantly contribute to daily protein intakes.

Contribution of animal protein to total daily protein was secondary to that of cereals (Table 4). They were obtained mostly from fish, eggs and milk and moderately from chicken (Table 2). Close to two-thirds (63.6% and 59.1%) of study participants frequently consumed fried or grilled fish respectively (Table 2). This was followed by egg (18.1%) and milk (13.6%). Chicken was moderately consumed by 31.8% while beef was never consumed, potentially due to its relatively higher cost (Heinbuch, 1994).

Legumes and nuts contributed the least to daily protein intake (Table 4). Only 9.1% of study participants frequently consumed roasted groundnut while 27.3% moderately consumed cooked beans (Table 2). A possible explanation could be patients' perception that legumes and nuts will not provide adequate protein quality to maintain good health. Protein restriction of between 0.55g/kg - 0.6g/kg and 0.6g/kg - 0.8g/kg per day have been recommended for different categories of adults with chronic kidney disease stages 3 to 5, only with very close clinical supervision (Ikizler et al.,2020). By restricting their intake of protein-rich foods, patients could be increasing their risk of protein energy malnutrition and its associated complications.

Cereals and other starches are often consumed primarily as a source of carbohydrates. However, every 15g of carbohydrate also contains about 3g of protein (Nutrition Education Materials Online, 2021; American Diabetes Association and the American Dietetic Association, 2021). Cumulatively, the protein from cereals and starches could supersede that of animal proteins or proteins from legumes and nuts if these sources are not consumed in adequate amounts. This seems to be the case with participants in this current study. Thus, although median protein intake by study participants was 75.4g (1.1g/kg body weight per day), which is indicative of high protein intake, it was evident that most of this protein was obtained from cereals, with little from animal proteins (26.2%) and legumes and nuts (8.1%). Protein quality of cereal proteins is regarded as low, due in part, to a lack of balance in amino acid composition (Vasal, 2020). Cereal proteins are deficient primarily in lysine with a secondary deficiency in threonine or tryptophan (Vasal, 2020). When complemented with adequate intake of legumes, the protein quality of cereals is improved and may compare to animal protein (Suri, Tano-Debrah and Shibani, 2014). The observed low intakes of legumes and nuts among study participants therefore compounds the risk of poor-quality protein intake, with a potential to increase the risk of PEW among patients. Encouraging patients to include more legumes in their diet may improve their protein quality while ensuring healthy serum phosphorus profiles.

Total daily phosphorus among study participants was 1151.6 mg. Specific recommendations for dietary phosphorus among patients with kidney failure are currently absent (Ikizler et al., 2020). This follows considerations that factors other than intestinal phosphorus/phosphate absorption, such as exchange with bone and excretion by the kidneys in patients with residual renal function, may be major determinants of serum phosphate levels (Ikizler et al., 2020). Individual needs and clinical judgment are hence recommended (Ikizler et al., 2020). Judging by the current recommended daily phosphorus intake of 700mg per day for apparently healthy adults (Institute of Medicine, 1997), the observed intake among participants could be regarded as high. Animal proteins, which have a relatively higher absorption rate of 40% to 60%, contributed 27.7% of this amount. Legumes and nuts contributed 5.6% while cereals contributed 63.4%. Together plant sources (legumes, nuts and cereals) contributed 69% of total daily phosphorus intake. The rate of phosphorus absorption from plant proteins by the human gastrointestinal tract is lower (10%-30%) due to the absence of the enzyme phytase in the human GIT needed for its digestion (Moe et al., 2011). Inorganic sources of phosphorus from mostly processed foods and sodas, which are known to have the highest intestinal absorption of up to a 100%, contributed a relatively low amount of 3.4% to total daily phosphorus intake among study participants. These proportions may have conferred some benefits to them as their observed serum phosphorus was 1.51 ± 0.05 mmol/L, (Table 1), which falls within the recommended range of (1.13 - 1.78 mmol/L) for patients with kidney failure on haemodialysis or peritoneal dialysis (Clegg and Gallant, 2019).

Phosphorus from animal proteins, legumes and nuts, cereals and inorganic sources showed no significant correlation with serum phosphorus levels. A possible explanation may be due to the other factors contributing to serum phosphorus other than diet, as earlier mentioned (Ikizler et al.,2020). Only phosphorus from legumes and nuts showed a negative correlation with serum phosphorus levels, although not statistically significant (Table 5). This is indicative of a potential beneficial effect of phosphorus from legumes and nuts on serum phosphorus levels. Other studies have reported similar results (Gonzalez-Parra et al., 2020; Moe et al., 2011). A long-term randomized control trial to investigate the effect of legumes and nuts on serum phosphorus levels and nutritional status of kidney failure patients is recommended. This will provide the needed evidence in support or not, the potential for legumes and nuts as the major source of protein for patients with kidney failure.

5. Conclusion

Cereals were the major source of both dietary protein and phosphorus among study participants, potentially due to their relatively higher portion sizes in patients' diets. There was no significant correlation between phosphorus from all sources with serum phosphorus, howbeit, phosphorus from legumes and nuts showed a negative correlation with serum phosphorus. Medical nutrition therapy by qualified nutrition and dietetic professionals is critical for this group of patients to reduce their risk of protein energy malnutrition.

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