The Nutritional Management of Patients with Continuous Ambulatory Peritoneal Dialysis

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ABSTRACT

End-stage kidney disease (ESKD) is a severe final phase of chronic kidney disease (CKD). Currently, it is related to high morbidity and mortality rates, making it an important health issue and a catastrophic disease. There is an increase in the death rate, especially when the underlying metabolic disorders are not treated with renal replacement therapy. Continuous ambulatory peritoneal dialysis (CAPD), or continuous dialysis in the peritoneal cavity, is one of the treatment options available in Indonesia as CKD becomes more prevalent each year, in addition to hemodialysis and kidney transplants. Patients with CKD who are on either hemodialysis or CAPD are frequently malnourished. The primary cause of these nutritional and metabolic disorders in uremic patients has decreased appetite, a major disease symptom. It is also observed that the protein levels in the serum and tissues are typically low, although protein and energy intake have been adjusted to meet standard nutritional guidelines. Also, there is reverse epidemiology in CKD patients, where a higher weight gain could result in a lower risk of mortality than non-CKD patients, where a higher weight gain causes an increased risk of death. Assessment and monitoring of nutritional status are necessary to determine mortality and morbidity due to cardiovascular abnormalities and for prevention and management of other complications in CKD patients undergoing CAPD. Lastly, there is currently a scarcity of research on the nutritional status of CAPD patients. Therefore, risk assessment and nutritional management monitoring can help reduce CKD incidence in patients undergoing CAPD.

***Keywords**: CKD, CAPD, nutritional status, malnutrition, inflammation.*

INTRODUCTION

End-stage kidney disease (ESKD) is the final phase of chronic kidney disease (CKD) and remains a unique health issue as a catastrophic disease.[1] Patients with ESKD require routine dialysis or a kidney transplant to survive.[2-4] Indonesian Renal Registry (IRR) shows that in 2018, 66,433 patients were diagnosed with CKD, which is about a twofold increase from what was obtained in 2017.[3,5-7] Meanwhile, data from the CAPD (Continuous Ambulatory Peritoneal Dialysis) Center at Dr. Hasan Sadikin Hospital Bandung, Indonesia, shows that the total number of CKD patients receiving CAPD was around 230 from September 2011 to 2015.[3,8] Meantime, the number of patients undergoing active CAPD continues to rise year after year, though the increase is insignificant according to IRR data. The most recent data obtained in December 2018 showed 2105 active cases of patients with CAPD in Indonesia.[9,10]

Subsequently, malnutrition is common in CKD patients on hemodialysis, particularly if the patient is on active CAPD, and may increase morbidity and mortality. Dialysis patients are at high risk of malnutrition because of uremic symptoms, for instance, anorexia, restricted diet, limited physical activity, inflammation, comorbidities, and metabolic disorders. Additionally, depression, repeated hospitalizations, and low socioeconomic status contribute to CKD patients.[11,12] Protein Energy Wasting (PEW) refers to malnutrition in CKD dialysis patients. Previous research studies reported that approximately 40% – 70% of CKD patients on dialysis were malnourished, ranging from mild to moderate malnutrition. About 10% were severely malnourished.[1,13] Malnutrition affects patients undergoing hemodialysis (HD) and peritoneal dialysis (PD) at a range of 10% to 70% and 18% to 51%, respectively.[3,12]

However, a proper PEW management strategy is essential in CKD patients undergoing CAPD presenting with PEW to optimize nutrition. The assessment of the nutritional status of CKD patients with CAPD is one strategy that is considered to represent a significant role.[13] A proper nutritional assessment could reduce the risk of mortality and morbidity in PEW patients.[14] Meanwhile, since there are no single parameters to diagnose malnutrition, a combination of several biochemical parameters is employed to assess nutritional statuses, such as the Subjective Global Assessment (SGA) score and the Composite Nutritional Index (CNI) score.[15]

Currently, there are several discussions concerning the nutritional management of CAPD patients. Therefore it is necessary to discuss the concept to reduce morbidity and mortality in CAPD patients.

CKD AND MALNUTRITION

PEW is a condition characterized by decreased protein reserves and fat mass levels in the body, associated with morbidity, comorbidity, and a lack of daily activities.[16] International Society of Renal Nutrition and Metabolism (ISRNM) reported that PEW could be classified based on four criteria, which include biochemical indicators (serum albumin, serum prealbumin/transthyretin, and serum cholesterol at values <3.8 g/100ml, <30 mg/100ml, and <100 mg/100ml, respectively), decreased body mass (for instance a marked body mass index (BMI) <23), decreased muscle mass as indicated by muscle wasting or sarcopenia, and decreased upper arm circumference.[17-19] PEW is found in approximately 40% of CKD patients at the start of dialysis therapy and in about 18% – 75% of patients after receiving HD or CAPD.[20,21]

PEW is caused by several CKD mechanisms, including malnutrition, systemic inflammation, comorbidities, hormonal disorders, dialysis procedures, and other complications of the uremic syndrome.[17] Furthermore, it can cause infection, cardiovascular disease, frailty, and depression in the short term, as shown in **Figure 1**.

Uremia in CKD patients results in disrupted protein synthesis, abnormal energy metabolism, increased anaerobic metabolism and decreased fat reserves, and acidosis, which contributes to protein degradation and catabolism of BCAA (branched-chain amino acid). This increases protein and amino acid catabolism while decreasing the conversion to essential amino acids.

Furthermore, several factors contribute to protein loss during dialysis, including inadequate

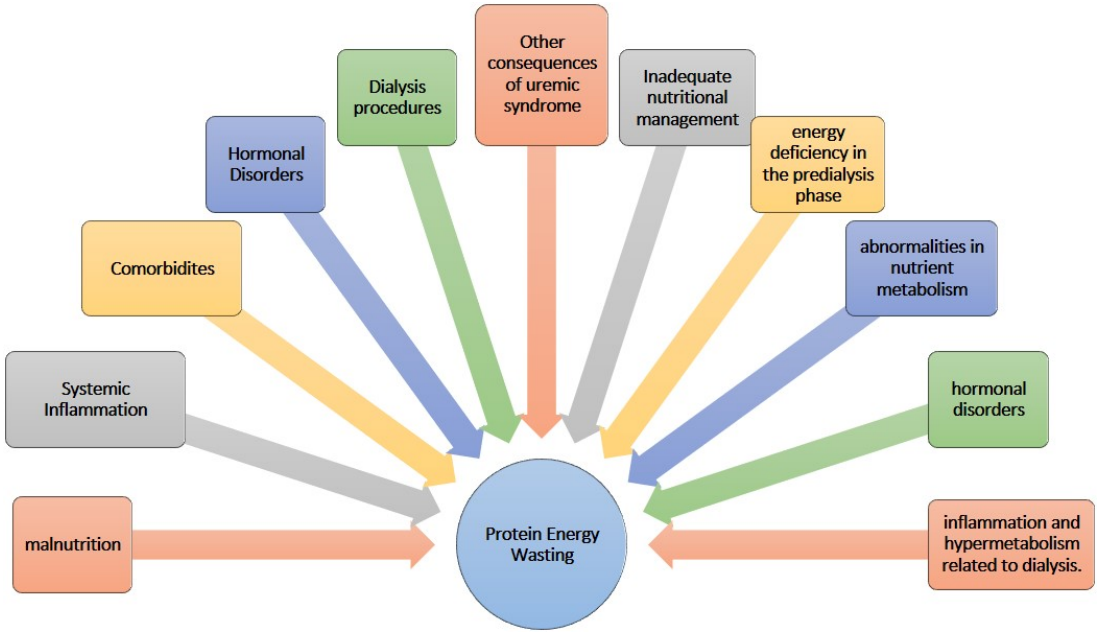

Figure 1. The Protein and Energy Wasting (PEW) concept model on CKD and its direct clinical implications.

nutritional management, energy deficiency in the predialysis phase, abnormalities in nutrient metabolism, hormonal disorders, inflammation, and dialysis-related hypermetabolism. Disorders of glucose metabolism are characterized by insulin resistance caused by an improper breakdown of glucoregulatory peptides in the kidneys, such as insulin, glucagon, and adrenaline, as well as the presence of uremic toxins and acidosis.

In malnourished dialysis patients, the inflammatory state is characterized by increased plasma C-reactive protein (CRP) and an imbalance of pro-inflammatory and anti-inflammatory cytokines. Certain signs of malnutrition and inflammation, especially in cases of morbidity induced by cardiovascular disease, can lead to the death of CKD patients undergoing dialysis, accounting for up to 20% of premature mortality in patients with Parkinson's disease. Also, a significant link exists between malnutrition, inflammation, and atherosclerosis in individuals with CKD, known as the MIA (malnutrition, inflammation, and atherosclerosis) syndrome.[22-24] Initial detection of MIA syndrome is critical in identifying patients with high-risk factors, and many markers may be seen in this syndrome.[24-26] Inflammation markers such as CRP, tumor necrosis factor α (TNF-α), vascular endothelial growth factor (VEGF), fibroblast growth factor 23 (FGF23), and transforming growth factor 1 (TGF-1) are thought to play a significant role in the formation of atherosclerosis. **Figure 2** depicts the correlation between malnutrition, inflammation, and atherosclerosis in CKD patients.

NUTRITIONAL STATUS ASSESSMENT OF PD PATIENTS

Nutritional status assessment and monitoring are critical for the diagnosis, prevention, and management of PEW.[27] However, a gold standard for managing nutritional status is not available. Several methods for assessing nutritional status are recommended, including the SGA, the Malnutrition Inflammation Score (MIS), and the Geriatric Nutritional Risk Index (GNRI). Nevertheless, SGA is approved in the routine assessment of the nutritional status of adult dialysis patients by the Kidney Disease/Dialysis Outcomes and Quality Initiative (K/DOQI).[19,24,26-29] Meanwhile, the Indonesian Society of Nephrology (Pernefri) Consensus recommends using the MIS to assess the nutritional status of dialysis patients.[28]

SGA is a nutritional status questionnaire that includes anamnesis, clinical symptoms, and a physical examination component. Furthermore,

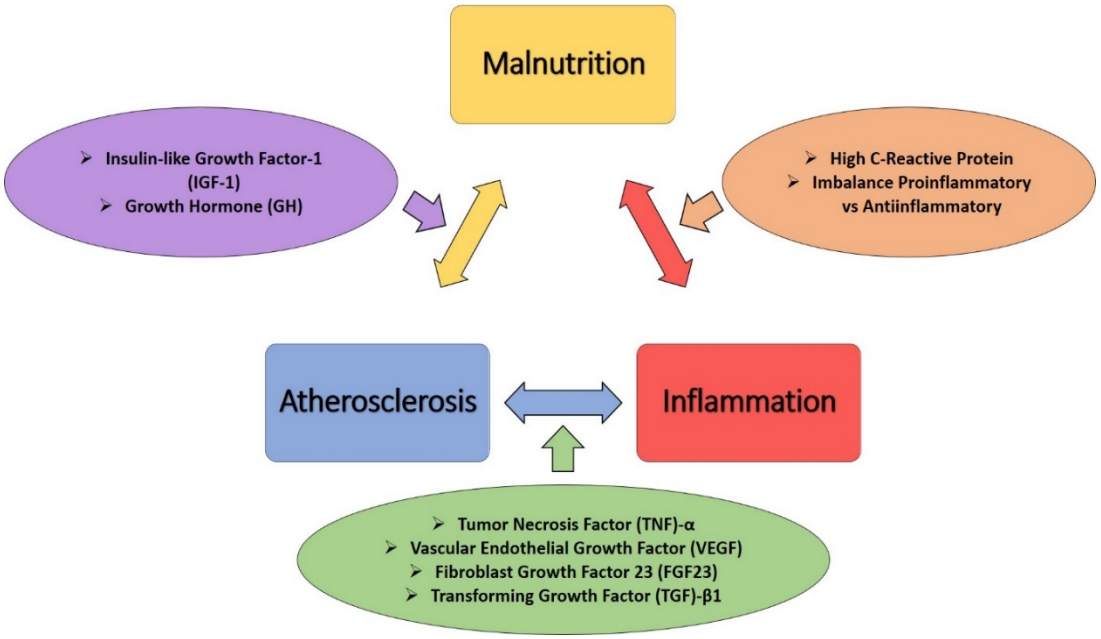

Figure 2. Malnutrition, Inflammation, and Atherosclerosis (MIA) Syndrome.

it is highly reproducible and strongly correlates with the clinical outcome of patients with CKD. The combination of standard anthropometric examination techniques and SGA is effective in detecting malnutrition in CAPD patients.[29] More so, SGA is a validated method for assessing nutritional status in PD patients, which confirmed the increased risk of mortality for PEW patients.[28]

Subsequently, the CNI, which is a combination of SGA, anthropometry, and biochemical examination, is one of the combined nutritional status assessment methods based on existing nutritional classification criteria for the study population.[30-32] Jones et al., found that the comparison between SGA and CNI scores in 72 chronic HD patients indicated malnutrition, which demonstrates that assessing nutritional status using the CNI method yields better results.[21]

Bioactive insulin-like growth factor–1 (IGF–1) can be used as a marker in nutritional interventions in CAPD patients. Furthermore, it is secreted in tissues of the body under the influence of growth hormone (GH), where nutrition plays a big role in regulating IGF-1 circulation. For CAPD patients with excess serum albumin and other nutritional status markers, circulating IGF–1 is a sensitive marker for malnutrition. Conversely, decreased IGF–1 bioavailability may perform a role in reduced muscle protein synthesis.[10]

PREVENTION AND THERAPY OF MALNUTRITION IN CKD WITH CAPD

The primary and secondary prevention of malnutrition in patients with CKD and CAPD include optimal and appropriate nutritional intake, physical activity, elimination of the causes of malnutrition, and management of comorbidities. This is dependent on the underlying condition, such as metabolic acidosis, diabetes mellitus, congestive heart failure, and depression. In addition to adequate dialysis, an adequate amount of calories and protein content at a minimum of 35 kcal/kg/day and 1.2 g/kg/day has a significant role in preventing malnutrition in CKD patients. Subsequently, an energy intake of 30 kcal/kg body weight per day is required in older adults with CKD who had sedentary lifestyle.[24,28,33,34,35] Several previous research reported that a daily protein intake (DPI) of 1.0 – 1.2 gr/kg/day is recommended. However, about 0.8 g/kg/day of protein diet combined with 0.4 g/kg/day of keto-analogues is assessed to increase appetite, anthropometry, serum albumin, and decrease serum cholesterol and fasting blood sugar.[12,24]

A good level of discipline from CKD patients on CAPD is required for optimal nutrition

intake, and nutritional counseling has a role in improving the nutritional compliance of CKD patients. Nutritional counseling was also useful in maintaining nutritional status in previous studies, even though it did not significantly improve all nutritional parameters. The K/DOQI recommends intensive nutritional counseling at the beginning of therapy, which is typically scheduled every 1 or 2 months. Subsequently, more frequent counseling is initiated if the nutritional intake is inadequate or PEW has developed.[27] Assessment of nutritional status from laboratory data and nutritional intake of CKD patients with CAPD is recommended once a month and must be reviewed by a renal nutritionist or nutritionist as part of a strategy for optimizing nutritional therapy.[36]

A high protein intake, particularly essential amino acids, performs a vital role in reducing malnutrition and preventing complications, thereby lowering the morbidity and mortality rates of CKD patients undergoing CAPD.[31,32]

The recommended daily diet for CKD patients with CAPD includes protein levels, calories, fiber, potassium, and calcium at 1.2 – 1.3 g/kg, 30 – 35 kCal/ kg, 20 – 30 g, 4.0 g or no restriction at all, and 2.0 g, respectively, as well as cholesterol < 200 mg. Also, it includes phosphorus and magnesium at ranges of 0.8 – 1 g, and 0.2 – 0.3 g, respectively, as well as iron 200 mg, as shown in **Table 1**. Meanwhile, the recommended amount of vitamins in the diet of CAPD patients are vitamin B1 (Thiamin), vitamin B2 (riboflavin), vitamin B3 (niacin), vitamin B6, and vitamin B12 at 1.5 mg, 1.7 mg, 20 mg, 10 mg, and 0.006 mg, respectively, as well as folic acid, pantothenic acid, biotin, and vitamin C at > 1.0 mg, 10 mg, 0.3 mg, and 60 – 100 mg, respectively. Lastly, vitamin D is taken 800 – 2,000 IU (**Table 1**).[37]

Table 1. CAPD Patient Daily Diet Recommendations

Nutrients	**Daily amount of nutrients**
Protein (g/kg)	1.2 – 1.3
Calories (kcal/kg)	30 – 35
Protein (%)	15 – 25
Carbohydrate (%)	50 – 60
Fat (%)	25 – 35
Cholesterol	< 200 mg (0.52 mmol)
Saturated Fat (%)	< 7
Fibre (g)	20 – 30
Sodium	< 2.0 g (< 87 mmol)
Potassium	4.0 g (100 mmol) or no restriction at all
Calcium	2.0 g (50 mmol)
Phosphorus	0.8 – 1.0 g (26 – 32 mmol)
Magnesium	0.2 – 0.3 g (8 – 12 mmol)
Iron	200 mg
Vitamin A	–
B-carotene	–
Retinol	–
Thiamin (mg)	1.5
Riboflavin (mg)	1.7
Vitamin B6 (mg)	10
Vitamin B12 (mg)	0.006
Niacin (mg)	20
Folic acid (mg)	> 1.0
Pantothenic acid (mg)	10
Biotin (mg)	0.3
Vitamin C (mg)	60 – 100
Vitamin E	–
Vitamin D	800 – 2,000 IU

(Adapted from Daugirdas, 2015)[37]

Metabolic acidosis is a frequent condition in individuals with progressive CKD that affects PEW by enhancing muscle protein catabolism via insulin or insulin growth factor–1 signal suppression and activation of the ubiquitin-proteasome pathway. Furthermore, the oxidation of essential amino acids increases protein requirements in CKD patients on hemodialysis, especially in an acidic state. Metabolic acidosis should be treated with oral sodium bicarbonate supplementation or by increasing the dialysis buffer concentration to about 40 mMol/L lactate. However, the administration of oral bicarbonate supplements improved nutritional status in previous research studies. A randomized clinical trial study of 134 patients with CKD stage 4 showed that increasing serum bicarbonate by 24 mMol/L from protein and energy intake increased arm muscle circumference and serum albumin, slowing the progression of CKD for more than 2 years. In epidemiological studies, a predialysis rate of 22 – 24 mmol/l is recommended in Maintenance Hemodialysis (MHD) patients with PEW to prevent alkalosis after hemodialysis.[31,32,35]

Additionally, peritonitis and other infectious complications must be avoided when CAPD patients receive adequate nutrition. It is also necessary to eliminate nonspecific inflammation and cardiovascular disease therapy in order to treat malnutrition properly.[28,29] The source of inflammation in the intestine can be reduced by preventing dysbiosis through increased dietary fiber proper constipation treatment, and providing enough protein and energy.[36] Some strategies that can be reduce the inflammatory state include optimizing the prescription of PD by increasing the volume state and biocompatible solutions, pharmacological interventions using statins, angiotensin-converting enzyme inhibitors, sevelamer, and also nutritional interventions (antioxidants).[28]

It should be possible to energize the fat-glucose emulsion at the same time. There is a high prevalence of protein-energy malnutrition in CAPD patients.[38] Therefore, severely malnourished CAPD patients should receive more energy than those not malnourished due to the increased catabolism and replacement of their deficient energy reserves.

Table 2 shows the caloric estimates of glucose that will be absorbed from dialysis fluids in CAPD and Continuous Cyclical Peritoneal Dialysis (CCPD) patients. Generally, the total volume of dialysis fluid in CAPD is 2 L, which is utilized during the day and night at a rate of 1.5% and 2.5%, respectively. Also, the calories of glucose absorbed are within the range of 332 – 432. Meanwhile, the volume of dialysis fluid for CCPD is 2 – 3 L, where dialysis is done during the day and night at a rate of 2.5% and 1.5%, respectively. The calories of glucose absorbed in this case range between 144 – 342.[37]

Table 2. Showing The Caloric Estimates of Glucose Absorbed from Dialysis Fluids in CAPD and CCPD Patients

Volume	%D day	%D night	The Calories Absorbed
CAPD			
4 x 2.0 L	1.5% D	2.5% D	332
4 x 2.5 L	1.5% D	7.5% Icodextrin	187
4 x 2.5 L	1.5% D	2.5% D	386
4 x 3.0 L	1.5% D	2.5% D	432
CCPD			
3 x 2.0 & 2.0	2.5% D	1.5% D	299
3 x 2.5 & 2.5	2.5% D	1.5% D	350
3 x 3.0 & 3.0	2.5% D	1.5% D	396
3 x 2.5 & 2.5 + 2.5	both of them 1.5% D	1.5% D	342
3 x 2.5 & Ico	7.5% Icodextrin	1.5% D	144

CAPD: Chronic Ambulatory Peritoneal Dialysis
CCPD: Continuous Cyclical Peritoneal Dialysis
(Adapted from Daugirdas, 2015)[37]

Phosphorus intake in food is an important strategy and plays a vital role in CKD patients' protein nutrition management. Previous epidemiological data show that a combination of reduced phosphorus and raised protein intake produces good results in stabilizing hemodialysis patients. Also, the phosphorus content of specific protein sources and other phosphorus-containing nutrients should be considered in the recommended diet to increase protein intake.[35]

The primary goal of PEW treatment in CKD patients is to maintain metabolic and whole-body homeostasis and body muscle mass. Appropriate protein and energy intake is required in CKD patients with ESKD, where the catabolic signaling state plays a major role. The significance of comorbid conditions like metabolic acidosis in the treatment of PEW cannot be overstated.[32] According to the literature, diabetes mellitus is one of the most frequent comorbidities in CKD patients, and complications of PEW are more common during peritoneal dialysis of diabetic patients than in nondiabetics. Therefore, diabetes management and insulin resistance are critical in regularly preventing body mass loss in patients receiving dialysis. Furthermore, administration of glucose in the range of 80 –330 g is considered quite relevant.[28]

According to several recent studies, if the management of PEW cannot address the loss of protein and energy reserves in CKD patients, additional nutritional supplement therapy can be given orally, intraperitoneally, enterally, and parenterally.[28] For severe PEW, the K/DOQI recommends enteral nutrition through an enteral tube. Moreover, the European Society for Parenteral and Enteral Nutrition recommends adding nutritional supplements, such as intradialytic parenteral nutrition (IDPN), in patients who fail to respond to nutritional counseling and oral nutritional supplements. However, the American Society for Parenteral and Enteral Nutrition does not support this claim since it is not backed up by sufficient evidence.[39] IDPN is an intravenous infusion of vital nutrients given three times weekly during hemodialysis therapy. Furthermore, it comprises 800 – 1200 kcal in glucose, lipid emulsion, and 30 – 60 g protein. This equates to 6 kcal/kg of body weight and 0.30 g/kg protein per day. However, the administration of IDPN has drawbacks, which include an increased risk of metabolic and electrolyte disorders, high cost, and a lack of research data.[39]

Meanwhile, the Otsuka Nutrition Pharmaceutical (ONCE) dialysis formula (ODF) is one of the oral supplements that can be given to CAPD patients. According to one study, the administration of ODF supplements to CAPD patients increased their intake of energy, protein, carbohydrates, fat, fiber, calcium, and magnesium, as well as their body weight, serum albumin, and blood urea nitrogen (BUN) concentrations. Additionally, counseling can help CAPD patients improve their nutritional intake, nutritional status, and quality of life.[40,41]

After attaining the appropriate protein and energy levels, CKD patients with ESKD should be encouraged to engage in mild physical exercise. This is because exercise increases IGF sensitivity and muscle fiber formation, and the expression of follistatin, an anti-inflammatory protein. Previous research in animal models and limited studies on predialysis and dialysis patients have proved that exercise can decrease and prevent muscle loss. Although there are few studies on the role of exercise in stimulating muscle growth, exercise is thought to increase muscle insulin content. Muscle oxidative capacity and the number of satellite cells required for muscle fiber regeneration are raised by the mRNAs (messenger ribonucleic acid) of growth factor 1 and insulin growth factor II. Subsequently, long-term resistance exercise is an anabolic intervention in healthy older adults and people with certain chronic diseases. Still, studies in ESKD patients have not shown consistent long-term improvement.[35] Practically, engaging in physical activity is typically advised to maintain lean body mass and a good protein and nutritional balance.[36]

Recently, about 12 studies have been conducted to evaluate the advantages of oral protein supplements in malnourished PD patients with or without PEW, but no clear value has been found. In one of the studies conducted in Malaysia in 2017, participants were given

Whey protein supplementation (WPS), and the nPCR (normalized protein catabolic rate) was used to measure supplement adherence. This study showed that giving WPS to CAPD patients for six months improved their nutritional status while maintaining good compliance and tolerance to the product. More so, WPS in the powdered form containing about 90 – 94% whey protein isolate and hydrolyzed Whey allows for a complete amino acid supplementation (Ceprolac, Aspen Sari Sdn Bhd). Meanwhile, consuming two sachets of WPS at 15 g per day would add about 27.4 g of protein and 116 kcal to each daily nutritional consumption.[42]

CONCLUSION

The final stage of CKD is ESKD. Patients with CKD who are on dialysis are at a high risk of malnutrition because of the uremic syndrome in a condition referred to as PEW. In addition, the patient's nutritional status is critical in predicting mortality and morbidity due to cardiovascular disorders. It can also lead to considerations for interventions and prevention of other complications in CKD patients with CAPD, as well as assisting in the management of PEW patients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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