Survey Report

Protein supplementation in dialysis and non-dialysis CKD patients

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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1 INTRODUCTION

Chronic Kidney Disease (CKD) is a medical condition marked by permanent alterations in kidney function and/or structure. It is notable for its irreversible nature and slow, ongoing progression. Additionally, CKD is associated with a higher risk of complications and mortality, particularly from cardiovascular causes [1]. The primary causes of CKD include diabetes, hypertension, chronic glomerulonephritis, chronic pyelonephritis, chronic use of anti-inflammatory medication, autoimmune diseases, polycystic kidney disease, Alport disease, congenital malformations, and prolonged acute renal disease [2].

CKD is very prevalent in the general adult population. Protein-energy malnutrition (PEM) is a prevalent concern in CKD patients, with reported rates ranging from 18-75% in hemodialysis patients and 20-50% in non-dialysis CKD patients [3]. Dietary protein management is crucial in CKD care, with recommendations varying by disease stage. Low-protein diets (0.6-0.8 g/kg/day) are often suggested for non-dialysis CKD stages 3-5 to slow disease progression, while higher protein intakes (1.2-1.4 g/kg/day) are typically recommended for dialysis patients [4]. Plant-based proteins may be preferred due to lower bioavailable phosphorus, but both plant and animal proteins can be part of a balanced renal diet [5].

Protein supplements can play a role in meeting nutritional needs, especially in patients with poor appetite or difficulty consuming adequate protein through diet alone. When selecting supplements, factors such as electrolyte content (particularly potassium, phosphorus, and sodium), fiber content, and the presence of omega-3 fatty acids should be considered. Medium-chain triglycerides (MCTs) may be beneficial due to their easier absorption and metabolism compared to long-chain fatty acids [6]. Patient adherence to dietary interventions can be challenging, influenced by taste, convenience, cost, and perceived benefits. Developing an effective nutritional protocol for CKD patients should involve regular nutritional status assessments, individualized dietary recommendations, monitoring of biochemical parameters and dietary intake, and ongoing patient education and support [7].

Developing a comprehensive nutritional protocol for CKD patients should involve a multidisciplinary approach, including nephrologists, renal dietitians, and other healthcare providers. Regular assessment of nutritional status, adjustment of dietary recommendations based on disease progression and individual patient factors, and ongoing patient education and support are key components of effective nutritional management in CKD

This study employs a questionnaire-based survey conducted among physicians across India to gather insights into their perspectives on the effectiveness of the protein supplementation diets in dialysis and non-dialysis CKD patients. Physician's clinical experiences, patient outcomes, and adherence to treatment protocols are critical factors in assessing the real-world advantages of this protein supplementation diets. By evaluating these perspectives, the study aims to provide valuable data that can inform clinical practice and guide treatment strategies tailored to the Indian CKD patient population.

2 RATIONALE OF THE STUDY

The rationale for this study was to gather comprehensive insights into the prevalence of malnutrition, dietary strategies, protein supplement preferences, patient adherence in managing nutritional consideration of dialysis or non-dialysis CKD among Indian patients. Understanding the current prescribing patterns, supplementation preferences, and perceived nutritional benefits among physicians was aided in optimizing therapeutic strategies and improving patient outcomes.

The purpose of this study was to evaluate the protein supplementation in Indian patients diagnosed with dialysis or non-dialysis CKD. This investigation aimed to understand how clinicians currently manage protein intake and supplementation across different stages of CKD. Ultimately, the insights gained has contributed to enhancing patient care and outcomes in CKD management.

3 STUDY OBJECTIVE

The primary objective of this study was to gather insights from healthcare professionals on current practices, preferences, and challenges in protein supplementation for chronic kidney disease patients, aiming to improve nutritional management strategies and inform product development in Indian patients.

4 METHODS

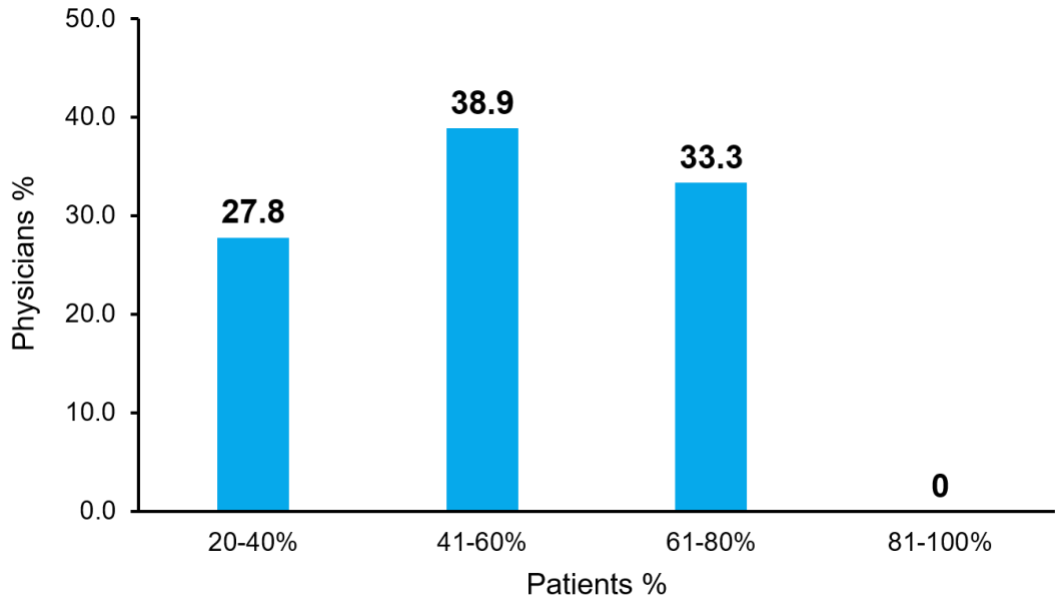
This cross-sectional, questionnaire-based study had involved a sample of 100 Indian physicians who manage patients with hypertension and chronic kidney disease (CKD). The primary aim is to understand physicians' clinical experiences, prescribing practices, and perceptions regarding protein supplementation in dialysis and non-dialysis CKD patients. Physicians will be identified and invited to participate through professional networks and medical associations. Once identified, participants will receive detailed information about the study and their role in it before providing informed consent. The questionnaire will include 15 questions, focusing on their clinical experience, current prescribing practices, and their views on protein supplementation for CKD patients. The survey will be administered electronically, ensuring secure collection and storage of responses. Statistical analysis will follow, employing descriptive statistics to summarize demographic information and response frequencies, and inferential statistics, such as chi-square tests or logistic regression, to explore associations between physician characteristics and their perceptions and prescribing behaviors. The results will be compiled into a comprehensive report and may be disseminated through scientific publications or presentations at conferences, where appropriate. The study will strictly adhere to ethical guidelines as per the Declaration of Helsinki, with ethical approval obtained from an Independent Ethics Committee. Participants will be assured of their right to withdraw at any point without any repercussions, and all responses will be anonymized to maintain confidentiality.

5 RESULTS

A total of 108 HCPs participated in the survey. Below is the summary of the responses.

Question 1: In your clinical practice, what is the prevalence of Protein-energy malnutrition (PEM) in haemodialysis patients?

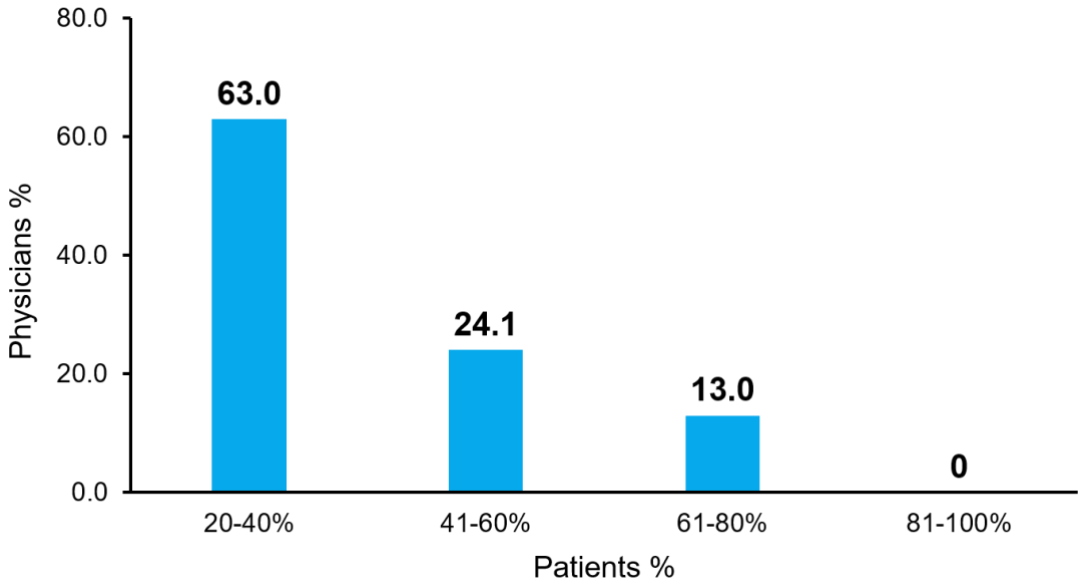
Options	Number of Physicians (N=108)
20-40%	30 (27.8)
41-60%	42 (38.9)
61-80%	36 (33.3)
81-100%	0
Data presented as n (%)	



- Around 38.9% physicians observe that the prevalence of protein-energy malnutrition (PEM) in haemodialysis patients is between 41-60%.
- A significant portion (33.3%) physicians see that the the prevalence of protein-energy malnutrition (PEM) in haemodialysis patients is between 61-80%.
- Approximately 27.8% physicians noted that patients between 20-40% have a revalence of protein-energy malnutrition (PEM) in haemodialysis and no one supported the patients between 81-100%.

Question 2: In your clinical practice, what is the prevalence of Protein-energy malnutrition (PEM) in non-dialysis patients?

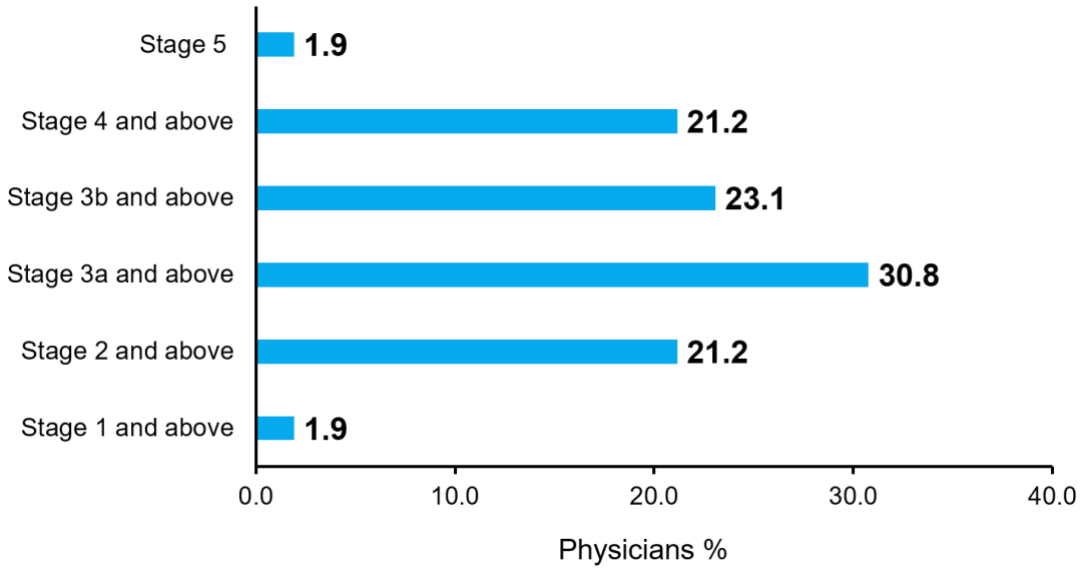
Options	Number of Physicians (N=108)
20-40%	68 (63)
41-60%	26 (24.1)
61-80%	14 (13)
81-100%	0
Data presented as n (%).	



- Majority of physician (63%) agree that the prevalence of protein-energy malnutrition (PEM) in non-dialysis patients is between 20-40%.
- Around 24.1% physicians observe that the prevalence of protein-energy malnutrition (PEM) in non-dialysis patients is between 41-60%.
- Approximately 13% physicians noted that patients between 61-80% have a prevalence of protein-energy malnutrition (PEM) in non-dialysis and no one supported the patients between 81-100%.

Question 3: At what stage of CKD do you prefer using low-protein diet?

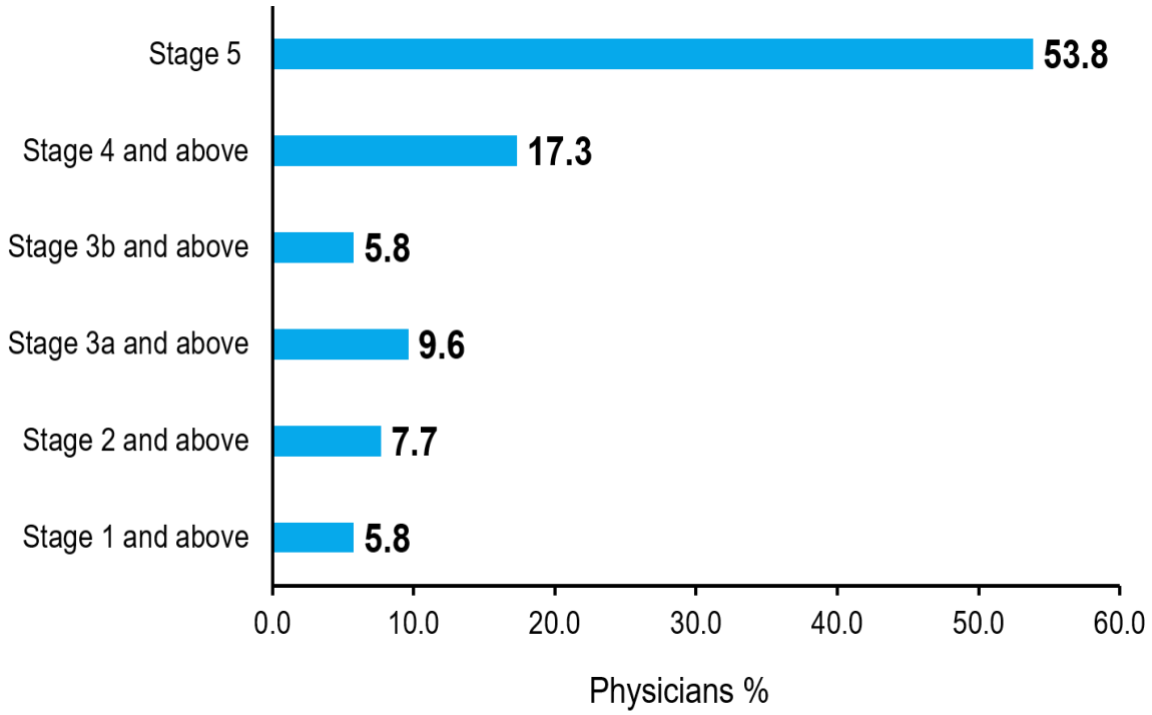
Options	Number of Physicians (N=104)
Stage 1 and above	2 (1.9)
Stage 2 and above	22 (21.2)
Stage 3a and above	32 (30.8)
Stage 3b and above	24 (23.1)
Stage 4 and above	22 (21.2)
Stage 5	2 (1.9)
Data Presented as n (%).	



- Around 30.8% physicians prefer using low-protein diet at stage 3a or above of CKD.
- A significant portion (23.1%) physicians observed patients in stage 3b or above have a preference for low-protein diet in CKD.
- Approximately same portion of physicians (21.2%) have different opinions such as stage 2 and above also stage 4 and above for the preference of low-protein diet.
- Similarly 1.9% of physicians agree for stage 1 and above also stage 5 for the preference of low-protein diet in CKD.

Question 4: At what stage of CKD do you prefer using high-protein diet?

Options	Number of Physicians (N=104)
Stage 1 and above	6 (5.8)
Stage 2 and above	8 (7.7)
Stage 3a and above	10 (9.6)
Stage 3b and above	6 (5.8)
Stage 4 and above	18 (17.3)
Stage 5	56 (53.8)
Data Presented as n (%).	

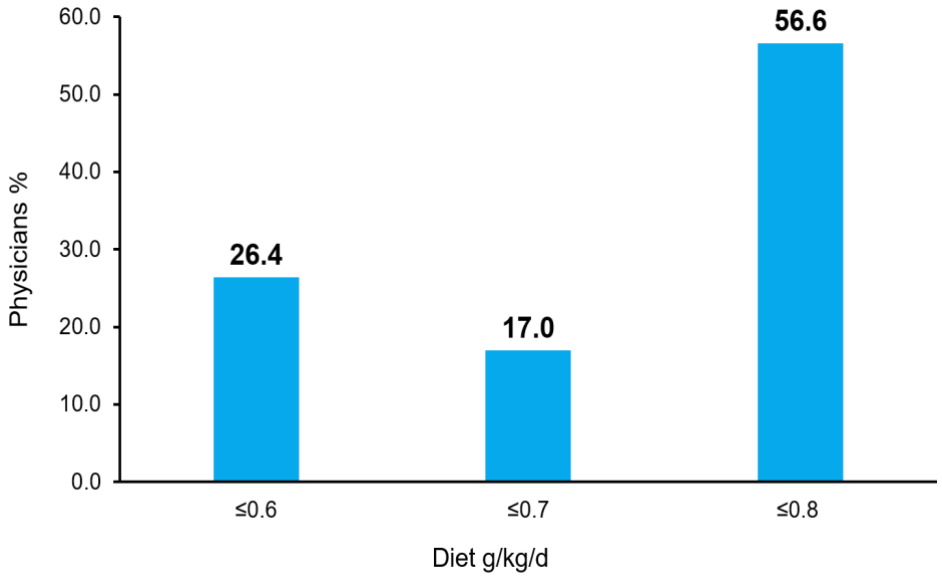


- The majority of physicians (53.8%) prefer using high-protein diet at stage 5 CKD.
- A significant portion (17.3%) physicians observed patients in stage 4 and above have a preference for high-protein diet in CKD.
- Approximately same portion of physicians (5.8%) have different opinions such as stage 3b and above also stage 1 and above for the preference of high-protein diet in CKD.

- Around 9.6% of physicians agree that the preference for high-protein would be patients with stage 3a of CKD or above.
- Small portion of physicians (7.7%) believes stage 2 and above to preferable for high-protein diet with stage 2 and above.

Question 5: What is the recommended level of low protein diet in CKD patients?

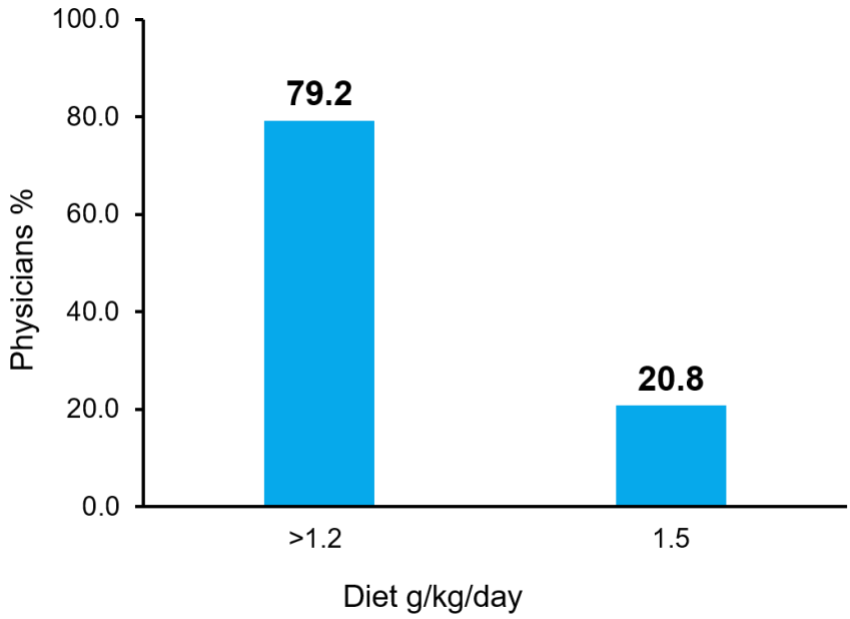
Options	Number of Physicians (N=106)
≤0.6 g/kg/d	28 (26.4)
≤0.7 g/kg/d	18 (17.0)
≤0.8 g/kg/d	60 (56.6)
Data Presented as n (%).	



- According to majority of physicians (56.6%), recommended level of low protein diet in CKD patients should be less than or equal to 0.8 g/kg/d.
- Around 26.4% of physicians observed less than or equal to 0.6 g/kg/d as the recommended level of low protein diet in CKD patients.
- Significant portion of physicians (17%) recommend less than or equal to 0.7 g/kg/d of low protein diet in CKD patients.

Question 6: What is the recommended level of High protein diet in CKD patients?

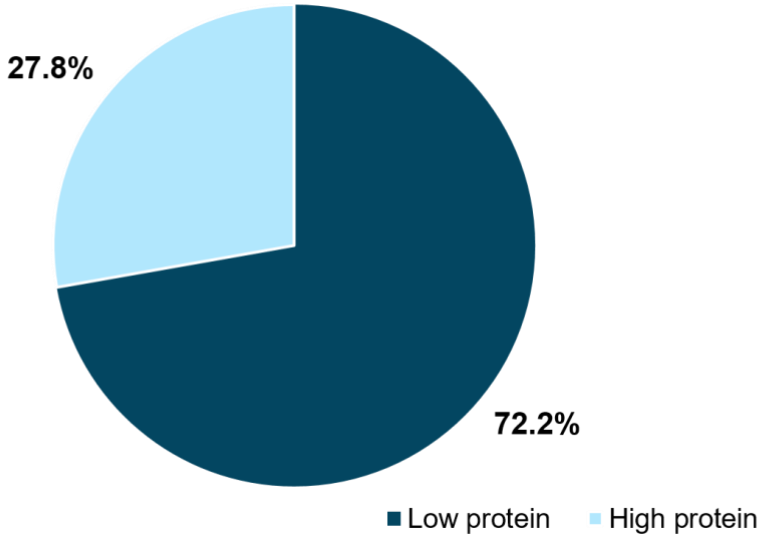
Options	Number of Physicians (N=106)
>1.2 g/kg/day	40 (46.5)
1.5 g/kg/day	17 (19.8)
Data Presented as n (%).	



- Majority of the physicians (79.2%) recommend more than 1.2 g/kg/d of high protein diet and a significant portion (20.8%) recommend 1.5 g/kg/d of high protein diet in CKD patients.

Question 7: Which of the following protein do you prefer in your CKD patients?

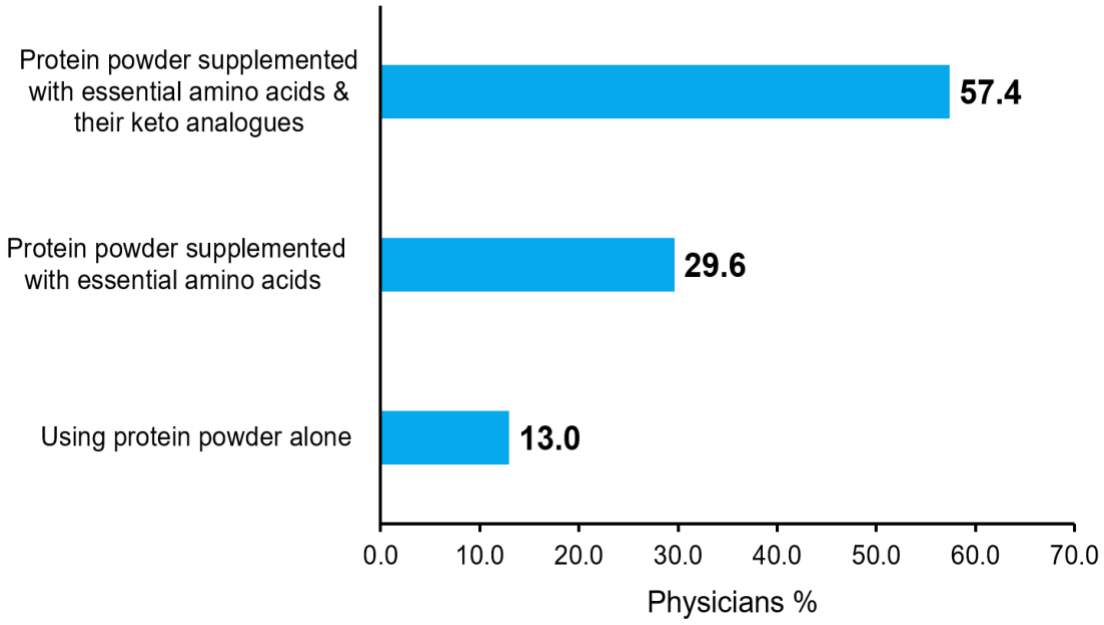
Options	Number of Physicians (N=108)
Low protein	78 (72.2)
High protein	30 (27.8)
Data Presented as n (%).	



- Majority of physicians (72.2%) prefer low protein diet and around 27.8% of physicians prefer high protein diet in patients with CKD.

Question 8: Which of the following is your preferred routine approach in CKD patients?

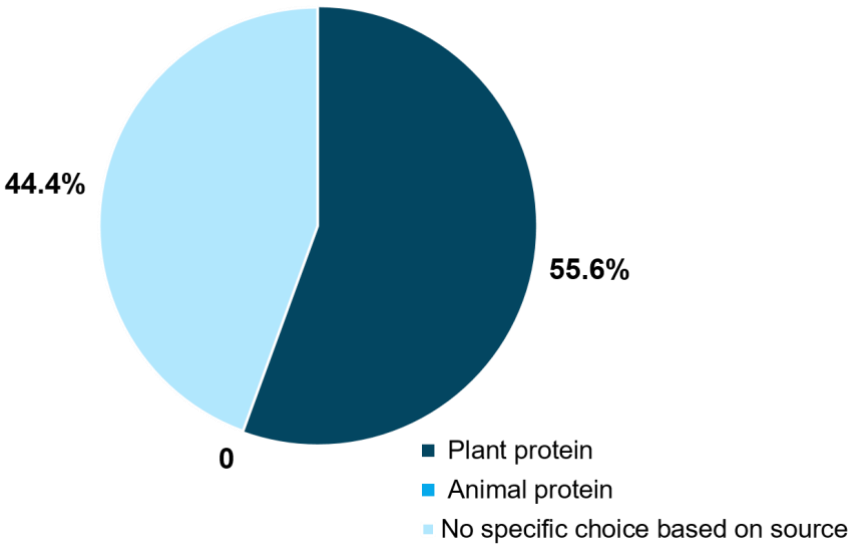
Options	Number of Physicians (N=108)
Using protein powder alone	14 (13)
Protein powder supplemented with essential amino acids	32 (29.6)
Protein powder supplemented with essential amino acids & their keto analogues	52 (57.4)
Data Presented as n (%).	



- Majority of physicians (57.4%) recommend using protein powder supplemented with essential amino acids & their keto analogues as a routine approach in CKD patients.
- Approximately 29.6% physicians advises protein powder supplemented with amino acid as a routine approach in CKD patients.
- Smaller portion of physicians (13%) suggests using protein powder alone as a routine approach in CKD patients.

Question 9: Which of the following type of protein is preferred in CKD patients?

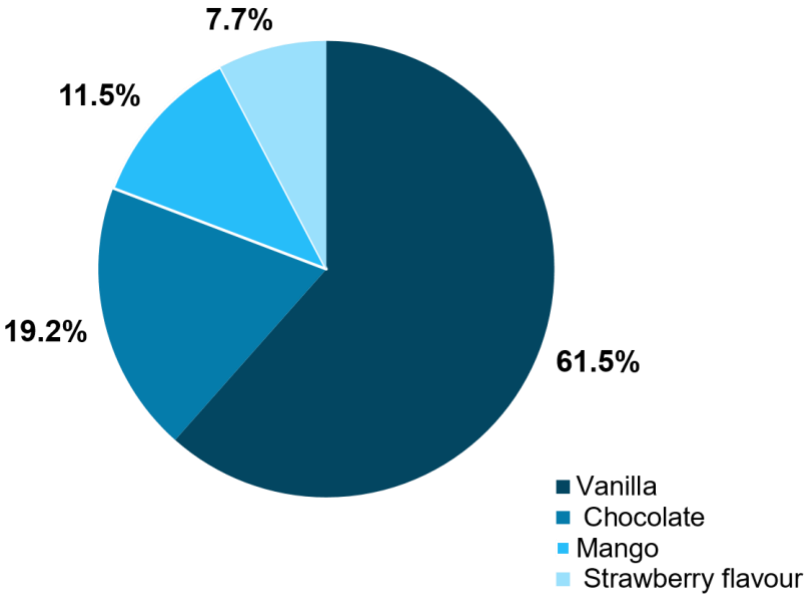
Options	Number of Physicians (N=108)
Plant protein	60 (55.6)
Animal protein	48 (44.4)
No specific choice based on source	0
Data Presented as n (%).	



- Majority of the physicians (55.6%) prefer plant protein and remaining 44.4% of the physicians are in the favor of animal protein for CKD patients.
- No physicians believe in any no specific choice based on the different source.

Question 10: Which type of flavor do you suggest that would be preferred by CKD patients?

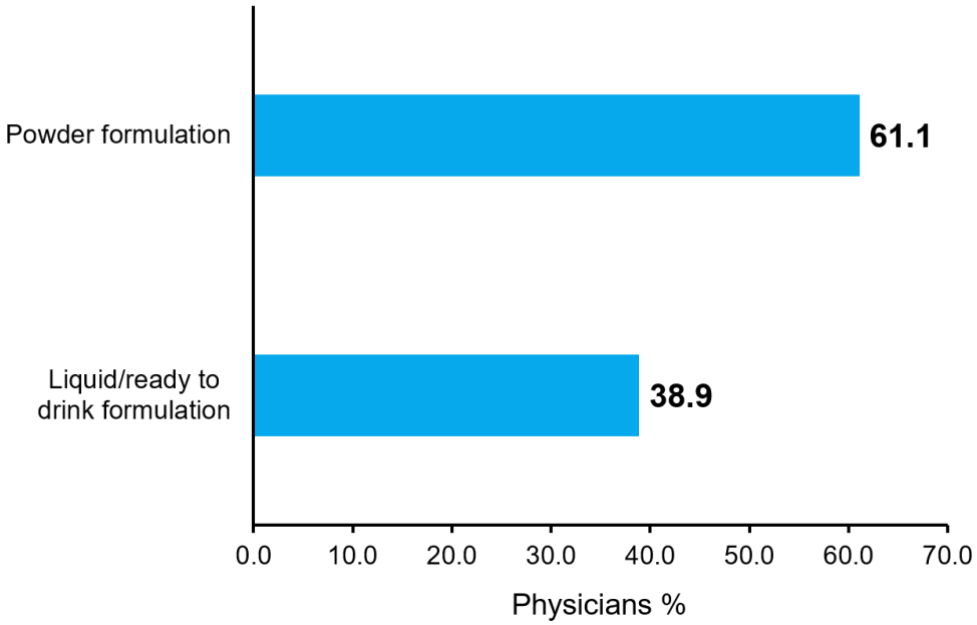
Options	Number of Physicians (N=104)
Vanilla	64 (61.5)
Chocolate	20 (19.2)
Mango	12 (11.5)
Strawberry flavour	8 (7.7)
Data Presented as n (%).	



- Majority of the physicians (61.5%) suggest vanilla flavor which is preferred by CKD patients.
- Around 19.2% physicians observed chocolate flavor preferred by CKD patients.
- Approximately, 11.5% and 7.7% of physicians noted mango and strawberry flavor respectively preferred by CKD patients.

Question 11: If there are two protein formulations, having same strength and nutritional value, which type of formulation do you prefer in your patients?

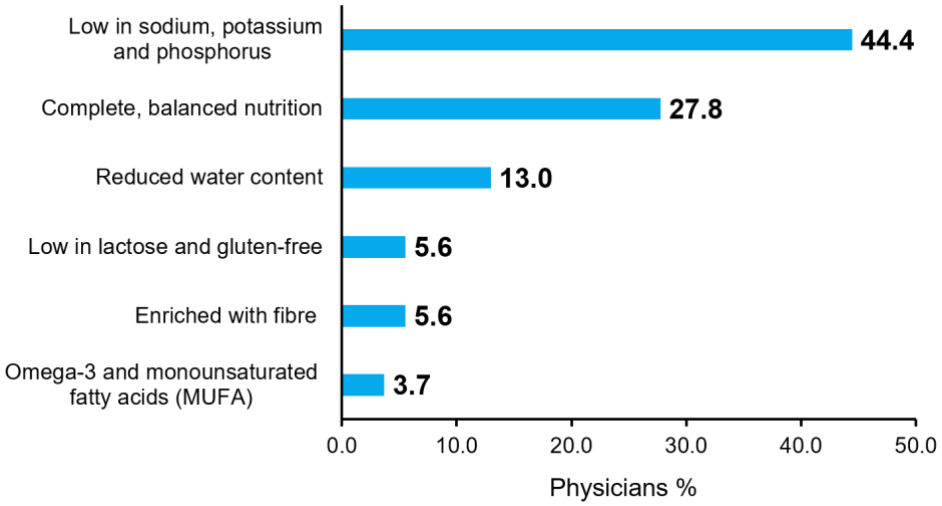
Options	Number of Physicians (N=108)
Powder formulation	66 (61.6)
Liquid/ready to drink formulation	42 (38.9)
Data Presented as n (%).	



- Majority of the physicians (61.1%) will prefer powder formulation having same strength and nutritional value in their patients.
- A significant portion (38.9) of physicians will prefer liquid/ready to drink formulations having same strength and nutritional value in their patients.

Question 12: What according to you are important parameters while selecting a protein supplement for CKD patients? (you can select more than one option)

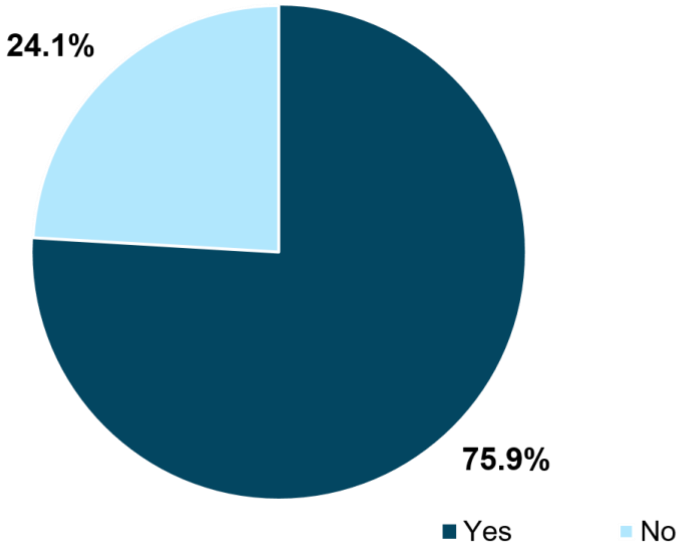
Options	Number of Physicians (N=108)
Complete, balanced nutrition	30 (27.8)
Low in sodium, potassium and phosphorus	48 (44.4)
Omega-3 and monounsaturated fatty acids (MUFA)	4 (3.7)
Reduced water content	14 (13.0)
Low in lactose and gluten-free	6 (5.6)
Enriched with fibre	6 (5.6)
Data Presented as n (%).	



- Approximately 44.4% of physicians believes protein supplement with low in sodium, potassium and phosphorus as an important parameter for CKD patients.
- Around 27.8% of physicians supports complete balanced nutrition in protein supplements as an important parameter for CKD patients.
- Significant portion of physicians (13%) observe reduced water content as important parameter in protein supplements for CKD patients.
- Physicians around 5.6% observed low in lactose and gluten-free and enriched fibre as an important parameter for selection of protein supplements.
- Small portion of physicians (3.7%) consider omega-3 and monounsaturated fatty acids as notable parameter in selection of protein supplements.

Question 13: Does serving size of the protein powder have any impact on patient compliance/adherence?

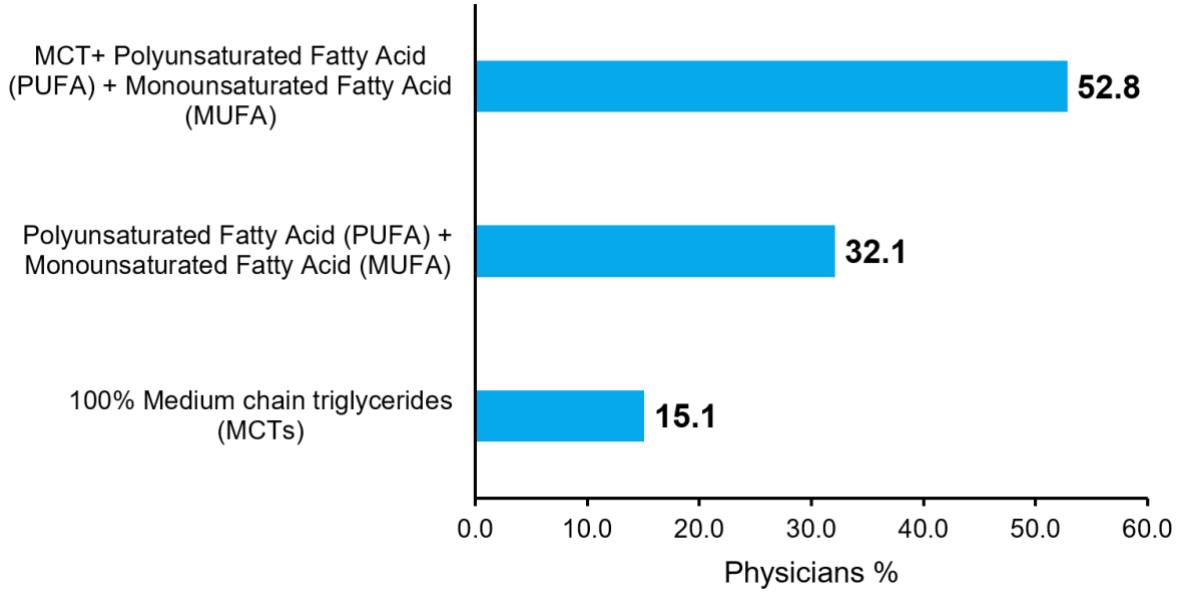
Options	Number of Physicians (N=108)
Yes	82 (75.9)
No	26 (24.1)
Data Presented as n (%).	



- According to majority of the physicians (75.9%) serving size of the protein powder has an impact on patient compliance/adherence and another portion of physicians around 24.1% do not agree with serving size of the protein having any impact on patient compliance/adherence.

Question 14: Which type of fats/lipids should be the component of protein supplement in CKD patients?

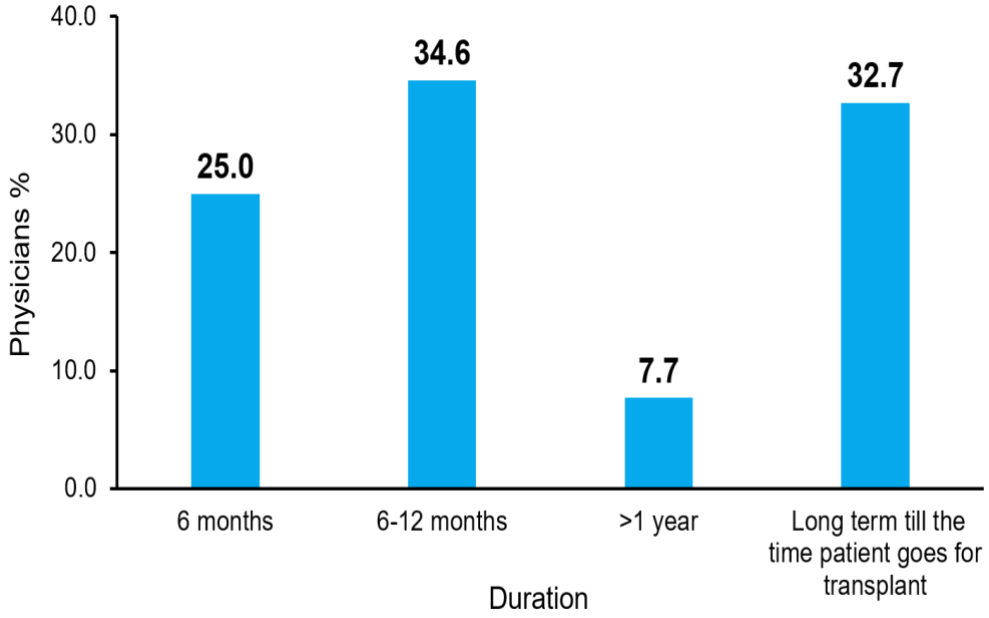
Options	Number of Physicians (N=106)
100% Medium chain triglycerides (MCTs)	16 (15.1)
MCT+ Polyunsaturated Fatty Acid (PUFA) + Monounsaturated Fatty Acid (MUFA)	56 (52.8)
Polyunsaturated Fatty Acid (PUFA) + Monounsaturated Fatty Acid (MUFA)	34 (32.1)
Data Presented as n (%).	



- Majority of the physicians (52.8%) agree that, MCT+ Polyunsaturated Fatty Acid (PUFA) + Monounsaturated Fatty Acid (MUFA) should be the component of protein supplement in CKD patients.
- Significant portion (32.1%) observed Polyunsaturated Fatty Acid (PUFA) + Monounsaturated Fatty Acid (MUFA) to be the component of protein supplement in CKD patients.
- Approximately 15.1% of the physicians consider 100% Medium chain triglycerides (MCTs) to be the component of protein supplement in CKD patients.

Question 15: On an average, how long do CKD patients adhere to the protein powder supplements?

Options	Number of Physicians (N=104)
6 months	26 (25.0)
6-12 months	36 (34.6)
>1 year	8 (7.7)
Long term till the time patient goes for transplant	34 (32.7)
Data presented as n (%).	



- According to 25% of the physicians, duration of 6 months is needed for the patients with CKD taking protein supplements.
- A significant portion (34.6%) of physicians observed duration of 6 to 12 months to get non-dependency on protein supplements in CKD patients.
- Around 32.7% of physicians noted long term adherence to protein supplements till the time CKD patient goes for transplant.
- Small portion of physicians (7.7%) noted that more than 1 year is sufficient for the CKD patients to leave protein supplements.

6 SUMMARY

Approximately 38.9% of physicians observe that the prevalence of protein-energy malnutrition (PEM) in haemodialysis patients is between 41-60%, with 33.3% noting it between 61-80%, and 27.8% between 20-40%. For non-dialysis patients, the majority (63%) see PEM prevalence between 20-40%, 24.1% between 41-60%, and 13% between 61-80%. Regarding dietary preferences, 30.8% of physicians prefer a low-protein diet starting at stage 3a CKD, with similar percentages (21.2%) opting for stages 2 and above or 4 and above. High-protein diets are preferred at stage 5 by 53.8%, with 17.3% starting at stage 4 and above. The recommended low-protein intake for CKD patients is predominantly ≤ 0.8 g/kg/d (56.6%), while high-protein intake is recommended at >1.2 g/kg/d by 79.2%. A majority (72.2%) prefer a low-protein diet, with 27.8% favoring high-protein. Protein powder supplemented with essential amino acids is recommended by 57.4% of physicians. Most (55.6%) prefer plant protein, with 61.5% noting vanilla flavor as preferred by CKD patients. Protein supplements low in sodium, potassium, and phosphorus are important for 44.4% of physicians, with 27.8% emphasizing balanced nutrition. Serving size impacts compliance for 75.9% of physicians. For long-term protein supplement use, 34.6% see a 6-12 month duration to achieve non-dependency

7 DISCUSSION

Physicians observe significant variations in the prevalence of protein-energy malnutrition (PEM) in haemodialysis patients, with 38.9% reporting a prevalence of 41-60% and 33.3% noting it between 61-80%. Interestingly, 27.8% of physicians reported a prevalence of 20-40%, while no one observed prevalence rates of 81-100%. For non-dialysis patients, the majority of physicians (63%) noted a prevalence of 20-40%, with 24.1% observing 41-60%, and 13% indicating 61-80%, again with no reports of prevalence rates between 81-100%. In terms of dietary preferences for CKD patients, 30.8% of physicians recommend a low-protein diet starting at stage 3a, while 23.1% suggest it for stage 3b or above. A similar portion, 21.2%, have differing opinions, recommending a low-protein diet at stage 2 or above, or stage 4 and above. Only a small fraction (1.9%) believe it should start at stage 1 or above, or stage 5. Conversely, for high-protein diets, 53.8% prefer them at stage 5 CKD, with

17.3% favoring stage 4 and above. Additionally, 5.8% recommend high-protein diets for stages 3b and above or stage 1 and above, and 9.6% for stage 3a or above. Regarding the recommended levels of protein intake, 56.6% of physicians suggest a low protein diet of ≤0.8 g/kg/day, 26.4% recommend ≤0.6 g/kg/day, and 17% advocate for ≤0.7 g/kg/day. For high-protein diets, 79.2% recommend >1.2 g/kg/day, and 20.8% suggest 1.5 g/kg/day. Overall, 72.2% of physicians prefer low protein diets for CKD patients, while 27.8% prefer high protein diets.

When it comes to the use of protein supplements, 57.4% recommend those supplemented with essential amino acids and their keto analogues as a routine approach, while 29.6% prefer protein powders with amino acids, and 13% recommend using protein powder alone. Regarding protein sources, 55.6% favor plant proteins, and 44.4% prefer animal proteins, with no physicians indicating no specific preference based on the source.Flavor preferences among CKD patients are also noted, with 61.5% of physicians indicating vanilla as the preferred flavor, followed by 19.2% for chocolate, 11.5% for mango, and 7.7% for strawberry. For protein supplement formulations, 61.1% prefer powder forms, while 38.9% prefer liquid/ready-to-drink formulations.

Regarding important parameters for protein supplements in CKD patients, 44.4% of physicians prioritize low sodium, potassium, and phosphorus content, 27.8% emphasize complete balanced nutrition, and 13% highlight reduced water content. Smaller portions of physicians consider low lactose, gluten-free, enriched fiber (5.6%), and omega-3 and monounsaturated fatty acids (3.7%) as important. Most physicians (75.9%) believe the serving size of protein powder impacts patient compliance, while 24.1% disagree. Finally, when considering the necessary duration for protein supplementation in CKD patients, 25% of physicians suggest six months, 34.6% recommend six to twelve months, 32.7% advocate for long-term adherence until transplant, and 7.7% believe more than one year is sufficient for CKD patients to leave protein supplements.

8 CLINICAL RECOMMENDATIONS

- It is recommended to maintain a balanced protein intake with a focus on high biological value (HBV) proteins. The general recommendation for protein intake in non-dialysis CKD patients is to manage the amount carefully to prevent protein-energy wasting (PEW) while avoiding the risk of accelerating kidney function decline due to excessive protein intake. High biological value proteins should constitute a significant portion of the diet to ensure adequate intake of essential amino acids.
- For patients who are unable to meet their nutritional needs through regular diet, enteral nutrition may be necessary. Guidelines recommend specific formulations designed for renal patients to provide adequate protein without excessive intake of phosphorus, potassium, and sodium.
- Adherence to prescribed daily protein intake can be assessed using urea nitrogen levels. Regular monitoring and adjustment of dietary protein intake based on individual patient needs and clinical conditions are crucial for effective management.
- Continuous monitoring of nutritional status through regular assessments and laboratory tests is essential to adjust dietary plans as needed and to ensure optimal patient outcomes.
- Proper management of protein intake in CKD and ESRD patients is critical to prevent malnutrition, support overall health, and improve quality of life. This requires a comprehensive approach involving dietary planning, nutritional therapy, patient education, and regular monitoring.

9 CONSULTANT OPINION

The prevalence of protein-energy malnutrition (PEM) in haemodialysis patients is noted to be significant, with many physicians observing varying degrees of occurrence. Among non-dialysis patients, the prevalence is also notable but generally lower than in those undergoing haemodialysis. For chronic kidney disease (CKD) patients, dietary preferences differ, with some physicians recommending low-protein diets at earlier stages and others preferring high-protein diets at more advanced stages. The recommended intake levels for low-protein and high-protein diets vary, but there is a general consensus on the importance of protein management.

Protein supplements, especially those enriched with essential amino acids, are widely endorsed, with a preference for plant-based sources over animal-based ones. Important factors in choosing protein supplements include low levels of sodium, potassium, and phosphorus, as well as balanced nutrition. Patient adherence is influenced by the serving size of supplements, and long-term use of protein supplements is recommended by some physicians until a kidney transplant is possible.

10 MARKET OPPORTUNITIES

- There is a strong preference among physicians for low-protein diets, particularly for patients with CKD stages 3a and above. This creates a market opportunity for developing and marketing protein supplements with controlled protein content, tailored for early stages of CKD.
- For patients in stage 5 CKD, there is a clear preference for high-protein diets. Products that cater specifically to advanced CKD stages with higher protein content could meet this demand.
- Vanilla-flavoured protein supplements are most preferred by CKD patients, followed by chocolate, mango, and strawberry. Developing products with these popular flavours could enhance market acceptance.
- There is a significant demand for both powder and liquid/ready-to-drink protein supplements. Offering both types could cater to diverse patient preferences.

- Incorporating MCTs, PUFA, and MUFA in protein supplements aligns with physician recommendations. Developing formulations that include these components could meet the needs of a significant portion of patient.
- The market for long-term adherence products, particularly those that are effective for 6 to 12 months or longer, is significant. This suggests opportunities for developing supplements that cater to both short-term and long-term needs

11 MARKET POSITIONING

- The market for nutritional supplements targeting chronic kidney disease (CKD) is both dynamic and competitive. Key players in this sector are focusing on tailored solutions to meet the specific dietary needs of CKD patients, emphasizing supplements that aid in managing protein-energy wasting and maintaining nutritional balance.
- The emphasis is on providing low-protein and high-quality protein options, adhering to guidelines like those from KDOQI, which recommend precise protein and energy intake levels to optimize patient outcomes.
- Despite the vast market potential, the impact of dietary supplements on kidney disease management remains under evaluation, indicating that ongoing research and adaptation are crucial.
- Companies are also working to enhance patient adherence through strategies that address common dietary challenges and promote consistent use

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