SAGE Open Medical Case Reports

SAGE Open Medical Case Reports
Volume 12: 1–7
© The Author(s) 2024
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2050313X241260229
journals.sagepub.com/home/sco

Continued elevation of creatinine and uric acid in a male athlete: A case report

Ali M Alaseem

Abstract

Whey protein and other protein-fortified supplements are frequently consumed as nutritional supplements to aid in muscle hypertrophy and myogenesis. This case presents a 36-year-old athletic male with elevated creatinine and uric acid levels during routine laboratory evaluation. The patient had no history of kidney disease, diabetes, or hypertension. It was revealed that the patient had been regularly consuming whey protein as a dietary supplement for 2 months. Given the potential association between the elevated creatinine and uric acid levels and the use of whey protein, the patient was advised to discontinue the supplement. The patient then switched to protein-fortified milk to mitigate the possible harmful connection between the dietary intake and the laboratory findings. However, despite the dietary change, the increased levels of creatinine and uric acid persisted. This observation suggests that the elevated levels may be attributed to chronic whey protein consumption along with high-protein dietary consumption.

Keywords

Sports medicine, nephrology, creatine, whey protein, creatinine

Date received: 15 April 2024; accepted: 22 May 2024

Introduction

Dietary supplement use among athletes is highly prevalent, with estimates suggesting up to 100% of athletes incorporate them into their routines.[1] The primary purpose of these supplements is to enhance or maintain health and performance. However, a lack of standardized definitions and classifications for these supplements makes it difficult to accurately assess their global use.[1,2] This widespread use, coupled with limited safety data, raises concerns about potential health risks for athletes. In the United States of America, the Dietary Supplement Health and Education Act classifies dietary supplements as food products, exempting manufacturers from pre-market safety and efficacy testing by the U.S. Food and Drug Administration.[3]

Milk protein is predominantly composed of two main components, whey protein (WP) and casein, accounting for approximately 20% and 80%, respectively.[4,5] WP is widely recognized and utilized as a popular protein supplement available in powdered form. It contains essential nutritional elements and functional bioactive compounds that offer significant value.[6] WP is commonly marketed as a dietary supplement to aid in muscle development during resistance training. Due to its fast digestion rate, WP provides a quick supply of amino acids that the muscles can utilize for repairing and rebuilding muscular tissue.[7] While WP has been reported to enhance glycogen storage, antioxidation, and lipid metabolism in relation to aerobic exercises, there are limited studies exploring the beneficial synergistic effects of WP in combination with long-term aerobic exercise training on biochemical profiles in specific tissues. Many studies have highlighted the beneficial effects of WP and its isolates, such as antioxidant properties and the ability to regulate lipid metabolism. It is believed that the bioactive components of WP contribute to its diverse potential health benefits.[4,8,9] A systemic review indicated that WP acts as a beneficial ergogenic aid, positively impacting amino acids, creatinine kinase, and myoglobin levels.[10] However, emerging evidence suggests a potential association between chronic, excessive WP intake and adverse health outcomes, with the kidneys and liver potentially exhibiting increased vulnerability.[11] Individual metabolic variability and the need for more

Department of Pharmacology, College of Medicine, Imam Mohammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia

Corresponding Author:
Ali M Alaseem, Department of Pharmacology, College of Medicine, Imam Mohammad Ibn Saud Islamic University (IMSIU), 7544 Othman Bin Affan Rd, Riyadh 13317, Saudi Arabia.
Email: AMAlaseem@imamu.edu.sa

mechanistic research complicate the interpretation of these observations.

Kidneys play a crucial role in maintaining nutritional homeostasis, and chronic kidney disease (CKD) is a global health burden, affecting nearly 800 million individuals.[12] It is believed that a high-protein diet, typically defined as consuming more than 1.2 g of protein per kilogram of body weight per day, induces significant changes in renal function and renal hemodynamics.[13] High-protein intake increases renal blood flow and glomerular filtration rate, leading to more efficient excretion of protein-derived nitrogenous waste products.[14] Glomerular hyperfiltration, along with increased urinary albumin excretion, can also have detrimental effects on the kidney and other organs over extended period of time.[15,16] High-protein diet may also elevate serum uric acid, potentially exacerbating subclinical CKD in susceptible individuals with pre-existing inflammation and impaired renal hemodynamics such as obese population.[16] This detrimental effect of consuming high protein has been shown in both animal and human studies.[17] In addition, high-protein intake might elevate proteinuria and contribute to transient volume depletion and an increased risk of nephrolithiasis, a marker of potential kidney dysfunction.[17] However, current evidence concludes that high protein is unlikely to harm the kidneys of healthy individuals.[18]

The use of creatine supplements is widespread among athletes and those who exercise regularly, as it is believed to enhance muscle mass, performance, and recovery.[19] Moreover, a huge body of evidence demonstrates that taking creatine supplements at recommended doses (typically 3–5 g per day) is generally well-tolerated.[20] Skeletal muscle breaks down creatine and phosphocreatine naturally, forming creatinine. Factors like muscle mass, dietary intake, consumption of creatine supplements, and creatine-rich foods can increase both blood and urinary creatinine levels, reaching high levels.[21] Studies suggest short-term rises in creatinine levels are unlikely to indicate a decrease in kidney function.[22] Other factors beyond kidney function, such as medication use, hydration status, and dietary intake, can influence creatinine concentration.[23] However, interpreting blood creatinine levels and estimated creatinine clearance is crucial for assessing kidney health in individuals with high-protein diets or creatine supplements.[24] Elevated uric acid levels, similar to creatinine elevations, are associated with increased risk for kidney impairment, emphasizing the clinical relevance of monitoring uric acid levels for early detection of potential kidney dysfunction.[25] Serum creatinine and uric acid, although commonly used, provide a limited assessment of kidney function. Therefore, the estimated glomerular filtration rate (GFR), which incorporates age, sex, and creatinine, offers a more comprehensive evaluation.[26] Consequently, a comprehensive evaluation of individuals with increased creatinine and uric acid should include eGFR with additional pathological markers of kidney injury and close observation for co-occurring clinical signs and symptoms of renal dysfunction.[23] It is crucial to emphasize the importance of kidney monitoring for individuals with specific dietary preferences or medical conditions.[20,27]

On the other hand, studies have shown that glomerular injury caused by increased intraglomerular pressure and flow can lead to progressive glomerular damage. As a result, adopting a balanced protein diet may be beneficial for managing kidney health and CKD.[13,28,29] The adoption of such diets varies among individuals, and more research is needed to better understand the specific benefits and challenges of implementing balanced-protein diets in the management of CKD. In reality, athletes seek information on dietary supplements from a variety of sources, although the reliability of these sources can vary significantly. These sources may lack the scientific rigor necessary to ensure accurate and unbiased information on supplement efficacy and safety.[1] The current system for monitoring dietary supplement safety is primarily reactive, potentially leading to underestimates of adverse effects. Thus, the health risks associated with chronic supplement use may remain unidentified. The long-term safety of dietary intake necessitates a multifaceted approach that takes into account the potential for interactions with factors such as genetics, metabolism, age, and lifestyle. These factors can significantly influence individual responses to different dietary styles. It prompts further investigation into whether these factors might influence kidney function, particularly for athletes who tend to consume high amounts of protein and creatine. This case report aimed to investigate and assess the potential association between elevated creatinine and uric acid levels observed in an athlete consuming WP and creatine supplements, as well as a chronic high-protein diet, raising concerns about possible kidney function implications.

Case presentation

The patient, a 36-year-old male non-professional athlete, has no history of kidney disease, diabetes, or high blood pressure. The patient reported a healthy lifestyle and regular exercise, focusing on resistance training supplemented by occasional aerobic activities such as treadmill use, five times per week. The patient reported not using any anabolic or androgenic steroids or growth hormones, but acknowledged taking other supplements such as multivitamins and omega-3. A physical examination revealed normal vital signs, with a body mass index within the normal range (25.7 kg/m^2) and a body fat percentage of 7.75%. No history of past surgeries was identified. There is no family history of CKD, and the patient reported no abnormal urine color changes or prior kidney stone episodes. He was found to have an elevated creatinine level of 133 µmol/L. The serum uric acid level was elevated at 487 µmol/L. However, a baseline uric acid value was not available for comparison, limiting the interpretation of this finding (Table 1).

The patient had been consuming WP as a dietary supplement for a duration of 2 months, averaging 60 g per day, and

Table 1. Serial laboratory monitoring: effects of dietary intervention on kidney function and other blood markers.*

Test type	Test name	Test units	Test value 1 (previous lab result)	Test value 2 (1st follow up)	Test value 3 (2nd follow up)	Reference range*
Complete blood count	Red blood cell	10^{12}/L	5.16	4.84	4.98	4.20–6.20
	Platelets	10^9/L	250	222	205	150–450
	Mean cell volume	fL	87	85	87	81–94
	Hemoglobin	g/L	145.0	132.0	141.0	125.0–180.0
	MCHC*	g/L	323.0	322.0	325.0	310.0–350.0
	Mean cell hemoglobin	pg	28.1	27.3	28.3	27.1–32.5
	MPV*	fL	9.4	9.8	9.4	7.8–11.0
	White blood cell	10^9/L	4.7	3.1	4.1	4.0–11.0
	RDW-CV*	%	12.9	13.2	12.8	11.5–14.1
	Hematocrit	L/L	0.449	0.410	0.434	0.350–0.500
	PDW*	fL	10.5	10.5	9.4	9.0–17.0
Other parameters	Albumin	g/L	49	44	48	35–52
	Bilirubin Total	mcmol/L	6	7	6	2–21
	Alanine Aminotransferase	unit/L	30	20	19	0–41
	Sodium	mmol/L	140	145	139	136–145
	Calcium corrected	mmol/L	2.08	2.24	2.20	2.15–2.50
	Calcium	mmol/L	2.30	2.34	2.40	2.15–2.50
	Phosphorus	mmol/L	0.74	1.13	0.97	0.81–1.45
	Alkaline phosphatase	unit/L	73	76	63	40–129
	Creatinine	μmol /L	**133**	**114**	**113**	59–104
	Potassium	mmol/L	4.3	4.4	4.9	3.5–5.1
	BUN	mmol/L	5.8	6.1	5.7	2.8–8.1
Automated differential	Basophil%	%	0.6	0.6	1.0	0.3–1.3
	Lymphocyte%	%	33.8	52.7	44.9	14.1–45.8
	Eosinophils automated Absolute	10^9/L	0.03	0.06	0.15	0.00–0.40
	IG auto #	10^9/L	0.01	0.01	0.02	⩽0.77
	Monocyte automated percentage	%	9.6	9.6	12.0	3.3–9.2
	Basophils automated absolute	10^9/L	0.03	0.02	0.04	0.00–0.10
	Lymphocyte #	10^9/L	1.59	1.65	1.83	1.10–3.30
	Neutrophil automated absolute	10^9/L	2.61	1.10	1.57	2.00–6.70
	Immature granulocytes percentage	%	0.2	0.3	0.5	⩽7.0
	Neutrophil automated percentage	%	55.4	35.2	38.4	42.9–78.4
	Monocyte#	10^9/L	0.45	0.30	0.49	0.20–0.70
	Eosinophil automated percentage	%	0.6	1.9	3.7	0.3–6.2
Uric acid	Uric acid	μmol /L	Not reported	**487**	Not reported	202–417
Microalbumin/ creatinine urine ratio	Urea microalbumin	mg/L	Not reported	Not reported	8.4	Male: 1.9–33.8
	Microalbumin/creatinine urine ratio	Mg/mmol	Not reported	Not reported	0.3	Male: <1.9
	Urea creatinine	mmol/L	Not reported	Not reported	24.22	3.54–24.60
Glucose Level	Glucose fasting	mmol/L	Not reported	4.5	4.9	4.1–6.1

BUN: blood urea nitrogen; Lipid panel: according to NCEP-recommended lipid levels; MCHC: mean corpuscular hemoglobin concentration; MPV: mean platelet volume; Normal range: referred to lab manual, and reference chart of Prince Sultan Military Medical City (Riyadh, SA); PDW: platelet distribution width; RDW-CV: red cell distribution width-coefficient of variation. Bold highlights uric acid and creatinine readings.
*Collection timepoint (October 2022, May 2023, and August 2023).

Table 2. Serial GFR assessments to evaluate change over time*.

Collection Timepoint	Creatinine (mg/dL)	Estimated GFR (mL/min/1.73 m^2)
1st test	1.33	61.3
2nd test**	1.14	73.7
3rd test***	1.13	74.5

GFR: glomerular filtration rate.
*According to the CKD-EPI 2021 creatinine formula. **2nd visit after 3 months. ***3rd after 5 months as second follow-up.

had also been taking approximately 10 g of creatine per day, before the initial laboratory report. Considering the potential association between the elevated serum creatinine and uric acid levels and the use of WP and creatine, the patient was advised to discontinue the supplements and routinely monitor the renal function. Despite this dietary change and discontinuation of the supplements, the elevated levels of serum creatinine persisted (114 µmol/L) along with an elevated uric acid level of 487 µmol/L (Table 1). This suggests that the elevated creatinine and uric acid levels could not be only related to the WP supplement but could also be attributed to other factors, including high-protein meals.

The patient was also advised to increase fluid intake and adjust protein daily intake. A repeat laboratory evaluation was performed after 5 months, which showed a slight decrease in creatinine levels to 113 µmol/L and remained almost the same (114 µmol /L) after 3 months as the second follow-up (Table 1). The microalbumin/creatinine urine ratio is a diagnostic test utilized to evaluate kidney function and identify early indications of kidney damage. The patient's microalbumin/creatinine urine ratio showed normal values, which differ from the creatinine value. Although there was a slight increase in creatinine levels despite lifestyle modifications, it highlights the interpersonal variations among healthy individuals and underscores the importance of regular laboratory monitoring of kidney function. Serial measurements of GFR revealed values consistently exceeding the CKD threshold (>60 mL/min/1.73 m^2) across all evaluations (Table 2). This pattern suggests preserved kidney function.

Discussion

This case report adds to the growing body of research investigating the potential association between high-protein diets, WP supplements, creatine use, and increased creatinine and uric acid levels. Although the finding of elevated serum creatinine levels does not definitively indicate renal dysfunction, it highlights the necessity for regular monitoring. The eGFR estimates were consistently within the normal range, providing no evidence of CKD and suggesting healthy kidney function. As the use of dietary supplements expands, promoting responsible use and awareness of potential risks becomes increasingly important. The development of kidney injury after using supplements remains controversial. While the evidence concerning potential kidney damage from high-protein diets and creatine supplementation remains inconclusive for healthy individuals, there is a stronger association with anabolic androgenic steroid use and the administration of excessively high doses of vitamins A, D, and E. Thus, the potential for long-term kidney complications and CKD cannot be entirely dismissed. In real-world scenarios, athletes often combine various supplements that might negatively impact the kidneys, further complicating the risk assessment.[30]

Protein is crucial for muscle repair, recovery, and overall performance. Athletes have higher protein requirements than sedentary individuals due to increased demand for protein synthesis and tissue repair. Traditionally, athletes consume protein from animal-based sources like whey, casein, and meat, as well as plant-based sources like soy, pea, and rice. Recent research has shown the potential benefits of specific types of protein, such as WP, for post-workout recovery.[31] On the other hand, healthy individuals typically do not experience negative effects from consuming a high-protein diet, while those with pre-existing kidney conditions should be prudent in their protein intake to safeguard their kidney health.[32] However, a few other reports suggest a possible link between protein supplements and negative impacts on kidney function.[30] A prospective cohort study revealed a strong association between high-protein diets with renal hyperfiltration and a faster rate of renal function decline. This suggests a potentially deleterious impact of high-protein intake on kidney function within the general population.[30,33] It is well established that a high-protein diet can increase the workload of the kidneys, leading to increased creatinine levels. The mechanism behind this is related to the increased production of urea, which is a by-product of protein metabolism. Although the microalbumin/creatinine urine ratio in the patient indicated values within the normal range, extended glomerular hyperfiltration may contribute to the initiation and progression of renal disease by increasing the risk of irreversible nephron injury.

WP is a commonly consumed protein supplement, particularly among athletes and bodybuilders, due to its high bioavailability and rapid absorption. Studies in both animals and humans associate whey-protein diets with potential kidney problems. WP intake has been linked to potential kidney and liver damage, particularly at high doses and with chronic use.[11] One possible explanation is that a short-term high-protein diet may indirectly increase the risk of kidney stones by raising urine output and calcium excretion.[34] Another explanation is that protein catabolism generates nitrogenous waste products, primarily urea, and this elevated metabolic burden could potentially lead to glomerular hyperfiltration, ultimately increasing the risk of CKD development.[11] Despite the fact that glomerular hyperfiltration is thought to have a negative impact, a 12-month clinical trial found no significant differences in kidney function markers (serum creatinine and clearance) between high- and low-protein consuming groups.[35] It has been suggested that hyperfiltration can be a normal adaptive mechanism triggered by various physiological conditions and might be misinterpreted as a sign of kidney damage. Therefore, the study concluded that healthy individuals may exhibit renal adaptation to increased protein intake, potentially mitigating these detrimental effects.[36] The specific mechanisms and long-term consequences of this adaptation remain unclear. Thus, the elevated uric acid observed in this report likely reflects increased nitrogenous waste production, a situation potentially exacerbated by the consumption of additional protein sources as part of the daily diet. Other molecular pathological causes and, thereby renal consequences need further studies.

Unlike WP, studies investigating the impact of creatine supplementation on kidney function have shown no clear consensus. This case report describes a patient presenting with borderline eGFR and elevated serum creatinine levels upon initial evaluation. This coincided with the patient's initiation of WP and creatine supplementation. Following dietary counseling, including discontinuation of creatine use, subsequent laboratory tests revealed improvement in both creatinine and eGFR. A recent review comprehensively evaluated the current body of evidence, both pre-clinical and clinical data, to assess the renal safety of creatine supplementation in athletes and bodybuilders without underlying kidney disease. The study indicated that creatine supplementation (5–30 g/day for up to 5 years) did not appear to adversely affect kidney function. However, short-term, high-dose creatine supplementation may increase the production of methylamine and formaldehyde in the urine. However, there is currently no clear evidence linking these metabolites to kidney problems in healthy individuals.[19] In fact, the intramuscular reserves of creatine are subject to a nearly constant, non-enzymatic transformation into creatinine. Creatinine diffuses out of the cells and is subsequently excreted via the kidneys in the urine. Elevated tissue creatinine levels achieved through creatine supplementation directly lead to increased creatinine production.[21] A previous case report showed that short-term, high-dose creatine supplementation did not necessarily impair GFR in a young man with a single kidney.[37] Beyond athletes, clinical trials suggest creatine supplementation is likely safe for men and women with type 2 diabetes and postmenopausal women.[38,39] Pooled results from a meta-analysis and systematic review show that creatine supplementation is likely safe for young adults and patients with chronic renal diseases but did not assess safety and efficacy in elderly populations with chronic renal failure and individuals with co-morbidity.[40]

Limitations

This case report provides a valuable single observation, but intrinsic limitations require cautious interpretation. The results of this case study cannot be generalized to a broader population. In addition, establishing definitive cause-and-effect relationships is often challenging due to the observational nature of this report. Furthermore, there is a lack of long-term follow-up and confirmation through pathological assessment. Similarly, uric acid due to the lack of follow-up data, and thereby caution is needed when extrapolating these findings to different groups. Further monitoring is recommended to definitively assess the persistence or progression of the observed elevation. Given the absence of conclusive evidence, caution is advised when drawing definitive conclusions based solely on the current literature.

Conclusion

This case report emphasizes the need to monitor kidney function in individuals utilizing protein supplements and high-protein diets. While short-term effects may be minimal in those with healthy kidneys, long-term consequences warrant caution and regular monitoring, even for individuals with normal baseline function. In addition, the impact of combined WP and creatine supplementation on kidney function in healthy individuals remains an area of active research. A major challenge in interpreting nutritional intervention trials is the substantial heterogeneity among study protocols, potentially confounding results. When specifically assessing the long-term safety of high-protein intake, it is crucial to consider individual variability arising from factors such as genetics, metabolism, age, and lifestyle choices. It is important to establish educational programs to provide accurate information on the safe use of these supplements. Given the lack of consensus on the long-term health effects of high-protein diets, longitudinal studies investigating a wider range of chronic health outcomes would be informative in determining the full spectrum of potential health consequences of such dietary patterns.

Acknowledgements

I would like to express our heartfelt gratitude to Ms. Maryam Alaseem for her invaluable contribution in reviewing this manuscript.

Author contribution

A.A. contributed to conceptualization, data curation, formal analysis, investigation, methodology, project administration, writing—original draft, and writing—review & editing.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics statement

This case report was reviewed and approved by the Institutional Review Board committee at IMSIU (Registration: HAPO-01-R-0011, Project Number: 526/2023).

Informed consent

Written informed consent was obtained from the patient for his anonymized information to be published in this article.

ORCID iD

Ali M Alaseem https://orcid.org/0000-0002-2015-9161

References

1. Daher J, Mallick M and El Khoury D. Prevalence of dietary supplement use among athletes worldwide: a scoping review. *Nutrients* 2022; 14(19): 4109.
2. Knapik JJ, Trone DW, Steelman RA, et al. Adverse effects associated with use of specific dietary supplements: the US Military Dietary Supplement Use Study. *Food Chem Toxicol* 2022; 161: 112840.
3. Denham BE. Dietary supplements—regulatory issues and implications for public health. *JAMA* 2011; 306(4): 428–429.
4. Chen W-C, Huang W-C, Chiu C-C, et al. Whey protein improves exercise performance and biochemical profiles in trained mice. *Med Sci Sports Exerc* 2014; 46(8): 1517–1524.
5. Krissansen GW. Emerging health properties of whey proteins and their clinical implications. *J Am Coll Nutr* 2007; 26(6): 713S–23S.
6. Madureira AR, Tavares T, Gomes AMP, et al. Invited review: physiological properties of bioactive peptides obtained from whey proteins. *J Dairy Sci* 2010; 93(2): 437–455.
7. Farup J, Rahbek SK, Vendelbo MH, et al. Whey protein hydrolysate augments tendon and muscle hypertrophy independent of resistance exercise contraction mode. *Scand J Med Sci Sports* 2014; 24(5): 788–798.
8. Morifuji M, Kanda A, Koga J, et al. Post-exercise carbohydrate plus whey protein hydrolysates supplementation increases skeletal muscle glycogen level in rats. *Amino Acids* 2010; 38(4): 1109–1115.
9. Elia D, Stadler K, Horváth V, et al. Effect of soy- and whey protein-isolate supplemented diet on the redox parameters of trained mice. *Eur J Nutr* 2006; 45(5): 259–266.
10. Lam F-C, Khan TM, Faidah H, et al. Effectiveness of whey protein supplements on the serum levels of amino acid, creatinine kinase and myoglobin of athletes: a systematic review and meta-analysis. *Syst Rev* 2019; 8(1): 130.
11. Vasconcelos QDJS, Bachur TPR and Aragão GF. Whey protein supplementation and its potentially adverse effects on health: a systematic review. *Appl Physiol Nutr Metab* 2021; 46(1): 27–33.
12. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. *Kidney Int Suppl* 2022; 12(1): 7–11.
13. Kalantar-Zadeh K, Moore LW, Tortorici AR, et al. North American experience with Low protein diet for Non-dialysis-dependent chronic kidney disease. *BMC Nephrol* 2016; 17(1): 90.
14. Fouque D and Aparicio M. Eleven reasons to control the protein intake of patients with chronic kidney disease. *Nat Clin Pract Nephrol* 2007; 3(7): 383–392.
15. Brenner BM, Meyer TW and Hostetter TH. Dietary protein intake and the progressive nature of kidney disease: the role of hemodynamically mediated glomerular injury in the pathogenesis of progressive glomerular sclerosis in aging, renal ablation, and intrinsic renal disease. *N Engl J Med* 1982; 307(11): 652–659.
16. Schwingshackl L and Hoffmann G. Comparison of high vs. normal/low protein diets on renal function in subjects without chronic kidney disease: a systematic review and meta-analysis. *PLoS One* 2014; 9(5): e97656.
17. Friedman AN. High-protein diets: potential effects on the kidney in renal health and disease. *Am J Kidney Dis* 2004; 44(6): 950–962.
18. Antonio J, Evans C, Ferrando AA, et al. Common questions and misconceptions about protein supplementation: what does the scientific evidence really show? *J Int Soc Sports Nutr* 2024; 21(1): 2341903.
19. Davani-Davari D, Karimzadeh I, Ezzatzadegan-Jahromi S, et al. Potential adverse effects of creatine supplement on the kidney in athletes and bodybuilders. *Iran J Kidney Dis* 2018; 12(5): 253–260.
20. Antonio J, Candow DG, Forbes SC, et al. Common questions and misconceptions about creatine supplementation: what does the scientific evidence really show? *J Int Soc Sports Nutr* 2021; 18(1): 13.
21. Wyss M and Kaddurah-Daouk R. Creatine and creatinine metabolism. *Physiol Rev* 2000; 80(3): 1107–1213.
22. Ronco C, Bellomo R and Kellum JA. Acute kidney injury. *Lancet (London, England)* 2019; 394(10212): 1949–1964.
23. Andreev E, Koopman M and Arisz L. A rise in plasma creatinine that is not a sign of renal failure: which drugs can be responsible? *J Intern Med* 1999; 246(3): 247–252.
24. Pritchard NR and Kalra PA. Renal dysfunction accompanying oral creatine supplements. *Lancet (London, England)* 1998; 351(9111): 1252–1253.
25. Joo HJ, Kim GR, Choi D-W, et al. Uric acid level and kidney function: a cross-sectional study of the Korean national health and nutrition examination survey (2016–2017). *Sci Rep* 2020; 10(1): 21672.
26. Jeong T-D, Hong J, Lee W, et al. Accuracy of the new creatinine-based equations for estimating glomerular filtration rate in Koreans. *Ann Lab Med* 2023; 43(3): 244–252.
27. Persky AM and Rawson ES. Safety of creatine supplementation. *Subcell Biochem* 2007; 46: 275–289.
28. Ko GJ, Obi Y, Tortorici AR, et al. Dietary protein intake and chronic kidney disease. *Curr Opin Clin Nutr Metab Care* 2017; 20(1): 77–85.
29. Bellizzi V. Low-protein diet or nutritional therapy in chronic kidney disease? *Blood Purif* 2013; 36(1): 41–46.
30. Tidmas V, Brazier J, Hawkins J, et al. Nutritional and non-nutritional strategies in bodybuilding: impact on kidney function. *Int J Environ Res Public Health* 2022; 19(7): 4288.
31. Hoffman JR and Falvo MJ. Protein—which is best? *J Sports Sci Med* 2004; 3(3): 118–130.
32. Poortmans JR and Dellalieux O. Do regular high protein diets have potential health risks on kidney function in athletes? *Int J Sport Nutr Exerc Metab* 2000; 10(1): 28–38.

33. Jhee JH, Kee YK, Park S, et al. High-protein diet with renal hyperfiltration is associated with rapid decline rate of renal function: a community-based prospective cohort study. *Nephrol Dial Transplant* 2020; 35(1): 98–106.
34. Amanzadeh J, Gitomer WL, Zerwekh JE, et al. Effect of high protein diet on stone-forming propensity and bone loss in rats. *Kidney Int* 2003; 64(6): 2142–2149.
35. Li Z, Treyzon L, Chen S, et al. Protein-enriched meal replacements do not adversely affect liver, kidney or bone density: an outpatient randomized controlled trial. *Nutr J* 2010; 9: 72.
36. Martin WF, Armstrong LE and Rodriguez NR. Dietary protein intake and renal function. *Nutr Metab (Lond)* 2005; 2: 25.
37. Gualano B, Ferreira DC, Sapienza MT, et al. Effect of short-term high-dose creatine supplementation on measured GFR in a young man with a single kidney. *Am J Kidney Dis* 2010; 55(3): e7–e9.
38. Gualano B, de Salles Painelli V, Roschel H, et al. Creatine supplementation does not impair kidney function in type 2 diabetic patients: a randomized, double-blind, placebo-controlled, clinical trial. *Eur J Appl Physiol* 2011; 111(5): 749–756.
39. Neves M, Gualano B, Roschel H, et al. Effect of creatine supplementation on measured glomerular filtration rate in postmenopausal women. *Appl Physiol Nutr Metab* 2011; 36(3): 419–422.
40. de Souza E Silva A, Pertille A, Reis Barbosa CG, et al. Effects of creatine supplementation on renal function: a systematic review and meta-analysis. *J Ren Nutr* 2019; 29(6): 480–489.