

A Study on the Effects of Various Dietary Supplement Combinations on Kidney Function Indicators among regular Gym attendees

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Abstract :

This study aimed to evaluate the effects of various commonly used dietary supplements among gym-goers on renal function biomarkers, including urea, creatinine, and uric acid. The study included nine groups, each consisting of seven participants, categorized based on the type of supplements used. Group 1 (G1) served as the control group, composed of individuals who did not consume any supplements. The results revealed statistically significant differences among the groups. Notably, the protein and energy supplement group (G6) exhibited the highest significant increase in blood urea levels in comparison with the control group ($P < 0.001$). Also, the creatine group (G3) showed a marked elevation in both uric acid and creatinine levels relative to other groups ($P < 0.001$). Minor yet significant variations were also observed in other groups, particularly those taking protein, amino acids, and combined supplements. These findings suggest that the use of certain types of supplements, especially combined formulations or high-dose supplements, may lead to noticeable alterations in kidney function markers. Although these changes remained mostly within physiological ranges, they may indicate a substantial metabolic burden on renal function. The study recommends the moderate use of dietary supplements and emphasizes the importance of regular renal function monitoring for individuals who use them.

Keywords: Dietary Supplement, Gym attendees, urea, creatinine, and uric acid.

دراسة تأثير التركيبات المختلفة من المكملات الغذائية على مؤشرات وظائف الكلى في مجموعة من مرتادي الصالات الرياضية

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مستخلص:

هدفت هذه الدراسة إلى تقييم تأثير أنواع مختلفة من المكملات الغذائية والتي تستخدم بصورة شائعة بين مرتادي القاعات الرياضية على مؤشرات وظائف الكلى، بما في ذلك اليوريا، والكرياتينين، وحمض اليوريك. وقد اشتملت الدراسة على تسع مجموعات، تضم كل مجموعة سبعة مشاركين، وزعت حسب نوع المكملات المستخدمة، بينما مثلت المجموعة الأولى (G1) مجموعة السيطرة المكونة من الأفراد غير المستخدمين لأي مكملات.

أظهرت النتائج وجود فروقات معنوية بين المجموعتين، حيث سجلت مجموعة البروتين والطاقة (G6) أعلى ارتفاع معنوي في مستوى اليوريا مقارنة بمجموعة السيطرة ($P < 0.001$). كما أظهرت مجموعة الكرياتينين (G3) ارتفاعاً واضحاً في مستويات حمض اليوريك والكرياتينين مقارنة ببقية المجموعات ($P < 0.001$). كما لوحظ وجود فروقات معنوية طفيفة في بعض المجموعات الأخرى، خصوصاً في مجموعات البروتين، الأحماض الأمينية، والمكملات المركبة.

تشير هذه النتائج إلى أن استخدام بعض أنواع المكملات، لاسيما المكملات المركبة أو المأخوذة بجرعات عالية، قد يؤدي إلى تغيرات ملحوظة في مؤشرات وظائف الكلى، والتي وإن كانت في معظم نتائج الدراسة ضمن النطاقات الفسيولوجية، فإنها قد تشير إلى عبء استقلابي مرتفع على الكلى. توصي الدراسة بأهمية الاستخدام المعتدل للمكملات، وضرورة إجراء تقييم دوري لوظائف الكلى لدى مستخدميها.

الكلمات المفتاحية: المكملات الغذائية، مرتادي الصالات الرياضية، الكرياتينين، اليوريا، حامض اليوريك.

Introduction

Chronic Kidney Disease (CKD) affects 10% of people and can lead to several adverse outcomes, including end-stage renal failure and cardiovascular diseases. Numerous conditions can affect the kidneys, potentially impacting renal blood vessels, glomeruli, renal tubules, and parts of the urinary tract outside the kidneys, such as the ureters and bladder (Vaidya and Aedula, 2024). (CKD) is one of the main causes of mortality in many parts of the world. The most common underlying conditions include tubular diseases, urinary tract infections, urinary tract obstruction, renal calculi, cystic kidney diseases, tumors, and vascular disorders. When these pathological processes progress, they often result in renal failure (Bishop et al., 2005).

In the latest years, fitness centers have grown in popularity, attracting both males and females due to their positive contribution to physical development and overall well-being (Herrington et al., 2022). With this growing popularity, the number of health food stores and supplement shops catering

to the needs of gym-goers has increased (Mousa and Ali, 2021). These supplements have become readily available and are often sold in public places, including within gyms themselves, and it is consumed in large quantities by athletes and fitness enthusiasts. (Rautiainen et al., 2016).

Dietary supplements are defined as a combination of substances that include vitamins, proteins, and minerals, which presented in capsule, tablet, or powder form (Darvishi et al., 2013). They are promoted as an effective means of rapid muscle gain. They are highly absorbable and soluble, for example whey protein being one of the most suitable forms of protein for athletes focused on strength and endurance (Naclerio et al., 2013).

The U.S. Food and Drug Administration defined the dietary supplements as products that contain nutritional ingredients intended for oral consumption to supplement the diet by increasing overall dietary intake (Xu and Sun, 2017). By 2014, over 85,000 different dietary supplements were available in the U.S. market, compared to only 4,000 in 1994. However, as of

2019, the National Institutes of Health Dietary Supplement Label Database included information on only 2,109 out of those 85,000 products (Ulery et al., 2021).

As supplement consumption continues to rise, there is an increasing need for comprehensive education regarding these products. Unfortunately, athletes rarely seek information from reliable sources such as registered dietitians, and educational programs related to supplement use are not universally available—particularly in developing countries—leaving athletes vulnerable to misinformation that may result in health risks and impaired performance (Froiland et al, 2004).

Athletes often experience fatigue during physical training and may continue exercising despite this fatigue, which can result in Delayed Onset Muscle Soreness (DOMS). Ignoring this pain and failing to incorporate sufficient rest may lead to the loss of skeletal muscle mass, muscle damage, and other sports-related injuries (Cleak and Eston, 1992). For this reason it become essential to monitor biomarkers indicative of muscle damage and inflam-

mation resulting from intense training. The most commonly used dietary supplements in gym environments are: Proteins, creatine, amino acids, carbohydrates. Protein is the main supplement which used by bodybuilders to enhance physical performance. It is an essential nutrient for the growth of muscles, bones, hair, and nails. It is composed of amino acids that both athletes and non-athletes need to gain strength, build muscle, fight infection, and regulate fluid movement within the body (Lam et al., 2019). As a result, many athletes use protein such as mass gainers and whey protein to boost their protein intake. These supplements are believed to accelerate muscle growth more effectively than natural animal or plant protein sources (Nasimi et al, 2023).

Creatine is usually used in sports and is known for its benefits in enhancing physical performance and muscle growth. However, there is controversy regarding its potential effects on kidney function (Matczak et al., 2025). Creatine is one of the most studied nutritional supplements and the most widely used among athletes, it became

popular among athletes in the 1990s due to its physiological role in increasing phosphocreatine stores within muscles, which promotes the rapid regeneration of the body's primary energy molecule, adenosine triphosphate (ATP) (Siedlecki et al., 2022). Its benefits include increasing muscle mass, improving physical strength, enhancing performance during high-intensity exercises, and accelerating post-exercise healing (Zhou et al., 2024). There are many concerns about the side effects of creatine supplements, particularly those related to kidney function. One of creatine's metabolites is creatinine, which is excreted by the kidneys, this has raised concerns about the effects of high doses or long-term use of creatine on kidney health. (Gonçalves et al., 2022). As for amino acid, amino acids are the fundamental building blocks of all forms of life, one of them is selenocysteine, which is involved in the synthesis of essential proteins that perform critical functions related to nutrition and sensory perception (Li et al., 2024). They are divided into three main categories: Essential Amino Acids (EAAs), which cannot be synthesized

by the body and become from external sources, and Non-Essential Amino Acids (NEAAs), which can be synthesized endogenously (Hou et al., 2015). Under specific conditions like intense physical activity, lactation, trauma, or illness, the body's demand for certain amino acids may exceed its production capacity. These amino acids are termed Conditionally Essential Amino Acids (CEAAs) (Wu, 2009). Amino acid is common among athletes, because the exercise leads to a temporary decline in muscle strength and muscle damage symptoms such as swelling, stiffness, and discomfort (Owens et al., 2019). This study aimed to demonstrate the effect of different types of dietary supplements taken by gym goers, whether taken alone or with other types, on kidney function indicators.

Material and methods

Subject and study design:

This study was conducted on Four gyms center in Samarra city, Salah El-Din Governorate, during the period from February 1, 2024, to March 1, 2024. Participants were randomly selected from the local gym. Each par-

participant was asked to complete a questionnaire that included several items such as age, dietary supplements type, duration of supplement intake, and body weight. All of them were male, aged between 18 and 50 years, who regularly attended gyms for periods ranging from one and a half months to eighteen months. Their body weights ranged from 66 to 100 kg. Individuals with a history of liver disease, kidney disease, diabetes, or any other chronic illnesses were excluded from the study. A total of 63 participant were divided into 9 groups, each consisting of 7 participants. This groups includes: The first group (G1) served as control group, which represent the healthy participants : The second group (G2) consisted of participants taking only protein supplements, (G3) consisted of participants taking only creatine supplements, (G4) consisted of participants taking only Amino acid supplements, (G5) consisted of participants taking only Energy supplements, (G6) consisted of participants taking Protein and energy supplements, (G7) consisted of participants taking creatine and energy supplements, (G8), consisted of

participants taking Protein and carbohydrate supplements, (G9) consisted of participants taking Protein, creatine, and amino acid supplements.

Methods:

The concentrations of Urea, Creatinine, and uric acid were determined in sera of all participant in the 9 groups, using standard kits methods provided from: urea kit(BioSystems, Spain), uric acid kit(Biolabo, France), creatinine kit(Spinreact, Spain). The normal ranges for renal indicators according to the manufacturer's recommendations are as follows:

- Blood Urea (BU): 20–45 mg/dL.
- Uric Acid (U.A): 3.4–7.0 mg/dL.
- Creatinine (Cr): 0.7–1.4 mg/dL.

Statistical Analysis:

One-way ANOVA was used to determine the significant differences between the means of the nine study groups for the three study indicators. After confirming the existence of significant differences from the ANOVA test results, and at significance level of $P \leq 0.005$ percent, the Tukey HSD (Honestly Significant Difference) test was performed as a post hoc analysis

to identify specific pairs of groups between which there were significant differences. All statistical analyses were conducted using Graph Pad Prism, version 9.

Results:

This study included nine groups, each consisting of seven participants. The first group served as the control

group, composed of gym attendees who did not use any dietary supplements. The remaining groups were categorized based on the type of supplements used by the participants. Kidney function biomarkers were tested, revealing several significant differences—some subtle and others more pronounced—between the various groups, as shown in Table 1.

Table 1: The Mean±standard deviation of Urea, Uric acid and creatinine in sera of groups under investigation

Parameter / Groups	Urea mg/dl	Uric acid mg/dl	Creatinine mg/dl
G1	32±2.82 d	5.1±0.42 d	0.8±0.14 c
G2	31±4.09 d	5.66±1.58 cd	1.06±0.05 bc
G3	50.5±0.7 b	8.85±0.7 a	1.1±0.14 ab
G4	35.5±0.7 cd	5.1±0.14 d	1.25±0.07 a
G5	39±7.07 c	5.55±2.89 cd	0.95±0.07 cd
G6	61±1.41 a	7.2±0.28 ab	1.05±0.07 bc
G7	36±2.82 cd	5.35±0.07 d	0.95±0.07 cd
G8	50.75±0.35 b	5.35±0.49 d	1.05±0.07 bc
G9	48.5±14.45 bc	6.62±2.14 bc	1.25±0.05 a

Table 1 showed that the level of urea significantly elevated at $p \leq 0.05$ in sera of participant in G3 , G5, G6, G8

and G9, with non-significant difference in G2,G4 and G7 as compare with the control group(G1), Figure 1.

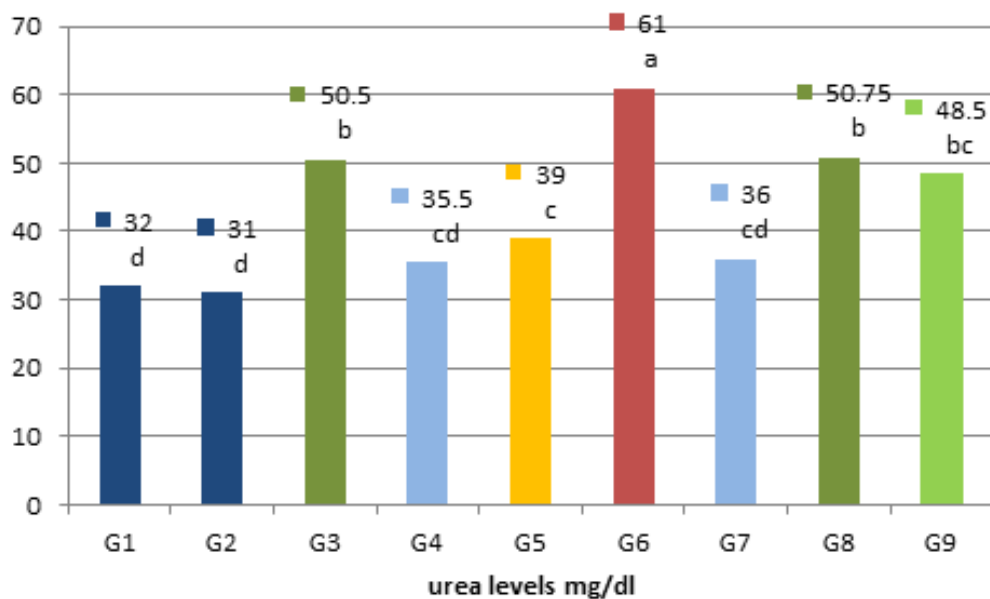


Figure 1: Levels of serum urea in different study groups under investigation.

Table 1 showed that the level of uric acid significantly elevated at $p \leq 0.05$ in sera of participant in G3, G6, G9, with non-significant difference in G2, G4, G5, G7 and G8 as compare with the control group (G1), Figure 2.

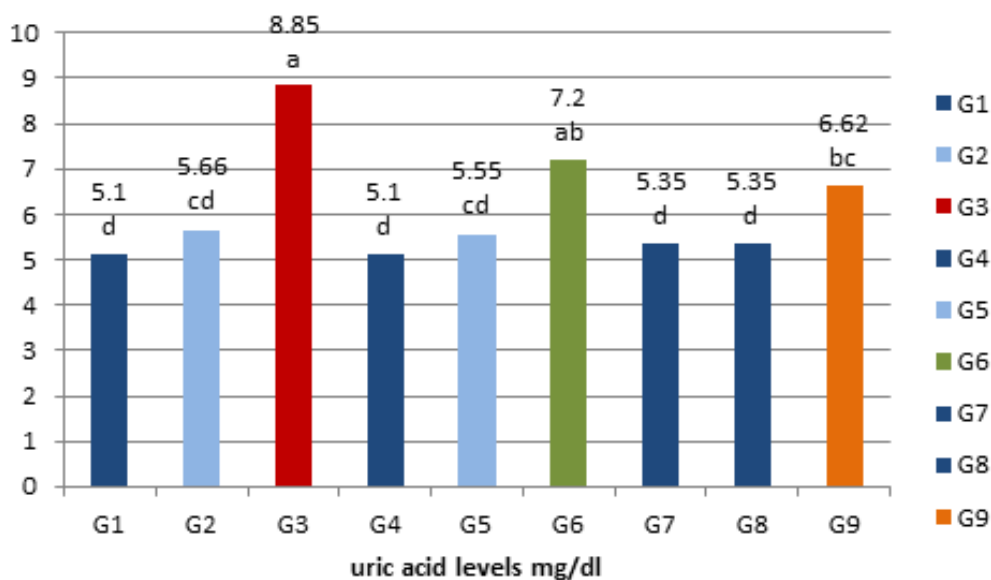


Figure (2): Uric acid levels among the different study groups.

Table 1 showed that the level of creatinine significantly elevated at $p \leq 0.05$ in sera of participant in G3 , G4, G9, with non-significant difference in G2,G5,G6,G7 and G8 as compare with the control group(G1), Figure 3.

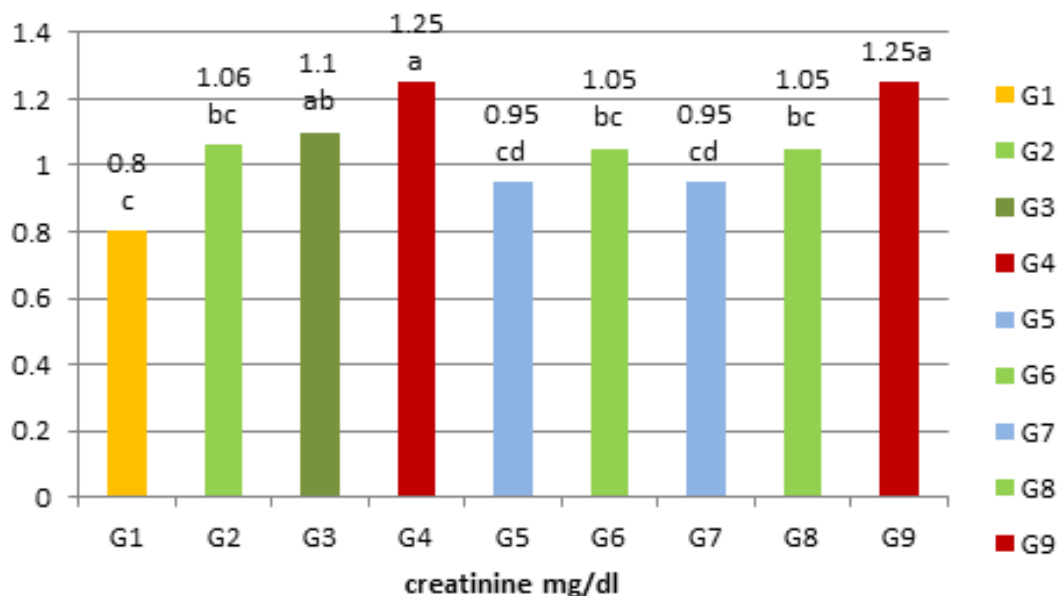


Figure 3: Creatinine levels among the study groups

Discussion:

This study showed that the participants who take both protein and energy supplements G6, showed elevated urea levels, more than the normal values. Protein intake is essential for muscle development, especially resistance training, which stimulates both muscle protein synthesis and breakdown. However, protein synthesis typically outpaces breakdown, resulting in a net increase in muscle pro-

tein mass. (Hartman et al., 2006).

Energy and protein needed increase in individuals who undergo regular training. The increase in blood urea levels in this group can be explained by the metabolic acid load resulting from protein-rich diets. These diets produce acidic metabolites—particularly sulfur-containing anions—which contribute to metabolic acidosis and increased renal acid excretion (Remer, 2001). This acidic nature is attributed to pro-

tein catabolism and produce organic acids during amino acid metabolism. Also, high protein intake stimulates the activity of branched-chain keto acid dehydrogenase (BCAAD), this enzyme responsible for catalyzing the oxidative decarboxylation of BCAAs, thereby facilitating their oxidation and removal of excess amine groups. This excess nitrogen is excreted primarily as urea, which leading to elevated urea levels (Dimou et al., 2022). Studies have also shown that the exercise leads to increased urea concentrations in plasma and urine, and its level remain elevated after exercise (Clauss & Jensen, 2025). Accordingly, the elevated blood urea levels in group 6 can be explained by increased nitrogenous wastes resulting from the metabolism of excess dietary protein, which was also exacerbated by the consumption of energy supplements.

Energy supplements typically contain a combination of compounds that enhance muscle activity, including caffeine, taurine, creatine, B vitamins, sugars, and citrulline malate, a compound that promotes vasodilation and improves blood flow to the muscles.

(Gough et al., 2021; Harty et al., 2018). These supplements are taken to increase alertness, endurance, concentration, and physical performance. These supplement content caffeine range from 70–160 mg per serving, and the high consumption exceeding 600 mg per day has been associated with worsening of chronic kidney disease and the development of other systemic disorders. Caffeine acts as an antagonist at adenosine A_{2A} receptors, which can lead to proteinuria, interstitial nephritis, and stimulation of the enzyme xanthine oxidase, resulting in increased production of uric acid and hydrogen peroxide (H₂O₂), causes that contribute to increased oxidative stress and kidney damage. (Hanna et al., 2024).

The third group showed an increase in uric acid level, which consisted of participants that using creatine supplements, its levels exceeded the normal physiological limit. This increase related with the an increased in oxidative stress which associated with creatine use, and stimulates uric acid production. A study by De Tarso et al. (2012) include 26 handball players divided into three groups: one using creatine

supplementation showed after 32 days that uric acid levels rose significantly from 4.7 to 7.4 mg/dL. This increase was related with a notable reduction in Total Antioxidant Status (TAS), and explain that creatine may promote uric acid generation as part of the oxidative stress response. Also Barros et al. study (2012) reported that after a Wingate test, athletes receiving 20 g/day of creatine for one week exhibited increased uric acid levels. This increase in uric acid plays a vital role in enhancing the Ferric Reducing Antioxidant Power (FRAP), the body use this mechanism to reduce oxidative stress caused from free iron. This means that uric acid is a protective antioxidant response. The using of creatine supplements leads to ATP depletion and an increase in AMP levels. AMP is broken down into inosine, hypoxanthine, xanthine, and finally uric acid via the purine oxidation pathway. This pathway helps restore cellular energy balance and increase uric acid production. (Miller, 2022). As well as, creatine supplements can also cause cellular dehydration if fluid intake is insufficient. Creatine attracts water into muscle cells, reducing the

water content in the kidneys. This affects the kidneys' ability to eliminate uric acid, thus increasing its concentration in the blood. (Pell et al., 2025).

As for G6 who used both protein and energy supplements, also showed a high levels in uric acid. This can be explained by the high nitrogen related with high-protein diets, which cause increased production of nitrogenous wastes such as urea and creatinine, and at last rise in uric acid levels. Proteins are rich in purines especially those of animal origin, which are metabolised into uric acid. According to the study of Xie et al. (2021), individuals consuming various protein supplements subject the renal system to additional stress due to the need to eliminate increased metabolic waste.

A study by Limirio et al. (2021) confirmed that protein intake from animal sources raises uric acid levels more than proteins from plants sources. energy supplements with protein may further increase uric acid because of their high sugar content. A study by Bruun et al. (2015) showed a relationship between sucrose/fructose load and increased uric acid, ATP molecules

are depleted by fructose metabolism, which promotes uric acid production. Chronic consumption of caffeine-containing energy supplements has also been shown to impair kidney and liver function, indirectly impacting uric acid levels. A study by Mihaescu et al. (2024) also showed that long-term consumption of these substance have negatively affects on kidney and liver function, supported the idea that these supplements indirectly contribute to elevated uric acid levels. We conclude that both creatine and the combination of protein and energy supplements are associated with increased uric acid production by several mechanisms, including oxidative stress, enhanced purine metabolism, glycogen-induced ATP depletion, and impaired renal excretion.

Regarding creatinine levels, Group 4 (users of amino acid supplements) and Group 9 (users of a combination of protein, creatine, and amino acids) showed a simple increase in serum creatinine levels. However, these values remained within the normal range. This simple increase is due to the normal metabolic conversion of

creatine to creatinine via a non-enzymatic process. When creatine is taken as a supplement, creatine stores within the muscles increase, leading to an increase in creatinine production as a natural metabolic byproduct. According to Rawson and Volek (2003), this increase in creatinine does not indicate kidney damage, but rather is due to an increase in the presence of creatine within the muscles.

Regarding the increase in creatinine resulting from protein supplementation, proteins are rich in nitrogen, and their metabolism leads to the production of nitrogenous waste products such as urea and creatinine. A study by Park et al. (2021) found that athletes following high-protein diets showed an increase in serum creatinine levels. However, these changes were not associated with any clinical or subclinical indicators of kidney injury.

As for the observed increase in creatinine levels in individuals using amino acid supplements (Groups 4 and 9), there is many physiological explanations exist. Branched-chain amino acids (BCAAs) have been shown to cause temporary elevations in creatinine lev-

els without actual renal damage. One of these factors is renal hyperfiltration, a randomised controlled trial investigating the use of amino acid infusions to prevent acute kidney injury following cardiac surgery reported that amino acid administration improved estimated glomerular filtration rate (eGFR), this reduced the decrease in creatinine levels and increased urine output. These results reflect an increase in glomerular filtration resulting from renal vasodilation, suggesting that amino acids enhance renal blood perfusion, which may temporarily raise creatinine concentrations. (Jappsson et al., 2000).

Another contributing factor is the increased production of nitrogenous wastes resulting from the metabolic conversion of amino acids into energy or lipids. This metabolic pathway leads to the formation of urea and creatinine as end products. This may cause a slight increase in creatinine levels, especially in individuals who consume large amounts of supplements without engaging in sufficient physical training to support effective nutrient utilization. However, despite these increases, no adverse effects on kidney func-

tion were recorded. This is in line with the findings of Williamson and New (2014), who demonstrated that elevated creatinine in such cases is a normal physiological response and not an indicator of kidney dysfunction. These explanations are fully consistent with the results of our current study.

Conclusions:

High-protein diets combined with energy supplements place significant metabolic stress on the kidneys, leading to elevated urea. Creatine supplementation also contributes to increased uric acid levels, without kidney damage. Groups 6 and 3 had the highest significant differences in urea, creatinine, and uric acid levels, which shows the strong effect of combined or high-dose supplements. Protein and amino acid supplements also cause an increase in creatinine levels due to increased production of nitrogenous waste. Although some indicators are elevated, they are within acceptable normal limits and there is no clear indication of kidney damage. Caution should be exercised when using it, especially combined supplements.

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Authors' contributions

The first author (Bashaer Ibrahim Hamdi) was responsible for sample collection, as well as the completion of all experimental procedures. Both authors reviewed and approved the final manuscript.

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