Journal of Biological Research

Bollettino della Società Italiana di Biologia Sperimentale

eISSN 2284-0230 - pISSN 1826-883

https://www.pagepressjournals.org/index.php/jbr/index

Publisher's Disclaimer. E-publishing ahead of print is increasingly important for the rapid dissemination of science. The ***Early Access*** service lets users access peer-reviewed articles well before print / regular issue publication, significantly reducing the time it takes for critical findings to reach the research community.

These articles are searchable and citable by their DOI (Digital Object Identifier).

The **Journal of Biological Research** is, therefore, e-publishing PDF files of an early version of manuscripts that undergone a regular peer review and have been accepted for publication, but have not been through the typesetting, pagination and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear on a regular issue of the journal.

E-publishing of this PDF file has been approved by the authors.

J Biol Res 2024 [Online ahead of print]

To cite this Article:

Tasnim T, Saranani S. **Analysis of the effect of brown rice, tuna, cucumber, and pineapple treatment on proteinuria and albuminuria in Wistar Rats strain with chronic kidney disease.** *J Biol Res* doi: 10.4081/jbr.2024.11883

©The Author(s), 2024

Licensee PAGEPress, Italy

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Analysis of the effect of brown rice, tuna, cucumber, and pineapple treatment on proteinuria and albuminuria in Wistar Rats strain with chronic kidney disease

Tasnim Tasnim,[1] Selpirahmawati Saranani[2]

[1]Department of Public Health, Mandala Waluya University; [2]Department of Pharmacy, Mandala Waluya University, Indonesia

Correspondence: Tasnim Tasnim, Department of Public Health, Mandala Waluya University, Jl. Jenderal A.H. Nasution, no.G-37 Kambu, Kendari, Sulawesi Tenggara, 93232, Indonesia.

Tel.: +6282237658472

E-mail: tasnim349@gmail.com

Key words: chronic kidney disease; nutrition therapy; proteins; albumins.

Contribution: study conception and design; analysis and interpretation of results; draft manuscript: TT, SS. Preparation: TT. All authors reviewed the results and approved the final version of the manuscript.

Conflict of interest: the authors declared no potential conflict of interest concerning the research, authorship, and/or publication of this article

Funding: the authors received financial support from the Mandala Waluya Kendari Foundation, Indonesia for the research and authorship.

Ethical approval: this study was approved by the Health Research Ethics Committee of Mandala Waluya University number 012/KEPK/UMW/II/2021.

Acknowledgments: we would like to thank Yayasan Mandala Waluya Kendari for funding this study. We appreciate all participants who took part in this study. Many thanks also go to Mandala Waluya University, which approved this study.

Abstract

This study aims to determine how nutrition therapy with brown rice, tuna fish, pineapple, and cucumber affects proteinuria and albuminuria in male Wistar rats with chronic kidney disease (CKD). In this study, 16 male Wistar rats with CKD were divided into four groups. The result states that the third treatment, consisting of 341 g/kg BW (Body Weight)/day brown rice, 15 g/kg BW/day tuna fish, 2 g/kg BW/day pineapple, and 2 g/kg BW/day cucumber could reduce both proteinuria ($p < 0.01$) and albuminuria ($p < 0.01$) in rats. However, the first (250 g brown rice, 13 g/kg BW/day tuna fish, 1 g/kg BW/day pineapple, 1 g/kg BW/day cucumber) and second treatment (296 g/kg BW/day brown rice, 14 g/kg BW/day tuna fish, 1.5 g/kg BW/day pineapple, 1.5 g/kg BW/day cucumber) could not reduce the levels of proteinuria and albuminuria in rats. In conclusion, giving a balanced diet containing 341 g/kg BW/day of brown rice, 15 g/kg BW/day of tuna fish, 2 g/kg BW/day of pineapple, and 2 g/kg BW/day of cucumber for CKD can maintain body fluid and increase the re-absorption of proteins and albumin. Therefore, the third nutrition formula can be recommended to people with kidney disease after clinical tests on humans.

Introduction

Chronic kidney disease (CKD) is a non-communicable disease that caused 74% of deaths worldwide in 2019.[1] The prevalence of CKD patients in Indonesia has steadily increased; in 2018 it was 0.38% (713,783 patients),[2] with an increase of 0.2% in comparison with 2013. Men had a higher prevalence (0.42%) than women (0.35%), especially at the age of 45 to 74 years. Men often neglect to carry out health checks at health services because of their busy lives compared to women. Insufficient access to control may result in delayed CKD diagnosis and inadequate education in diet.[3]

The etiology of CKD is identified from several causes, such as hypertension, high-fat diet, and environment, and it could also be due to genetic factors.[4,5] Several risk factors for CKD have been identified, such as ethnicity, gender, age, history of cardiovascular disease, smoking, obesity, exposure to heavy metals, excessive consumption of alcohol, use of analgesics, hepatitis C virus, HIV infection, and uncontrolled diabetes mellitus and hypertension.[6,7] CKD is marked by gradually declining kidney function, so the glomerular filtration rate drops to <60 mL/min/1.73 m^2 for 3 months.[8] In this condition, the residue from metabolism products such as proteins, albumin, sodium, potassium, calcium, and phosphorus cannot be discarded from the body. Patients become nauseous, and experience headaches, shortness of breath, and experience edema. Some CKD patients experience depression because they cannot take care of themselves, instead, they have to depend on other people, including their family.[9,10] Patients also feel a lack of freedom in their lives as a result of their dependence on hemodialysis machines.[11]

Patients with CKD lose their appetite and thus become weak.[12] Consequently, their nutritional status deteriorates, necessitating nutrition therapy. However, their diet must address their body's metabolic and liquid needs, such as foods low in protein, sodium, potassium, phosphorus, calcium, and fat.[13] Many types of food have biological value and high fiber content, such as brown rice (*Oryza nivara*), tuna (*Euthynnus affinis)*, pineapple (*Ananas comosus*), and cucumber (*Cucumis sativus*). This type of food also contains low protein and fat, so it is very suitable for chronic kidney sufferers.[14]

The excess of proteins or albumin in the body, for example, causes the body to be unable to filter and reabsorb these substances, resulting in increased intraglomerular pressure and flow, which leads to progressive glomerular damage.[15] Hence, the proteinuria and albuminuria increases. Thus, a healthy diet rich in plant-based foods (including vegetables and fruits) and fish is strongly recommended because it is linked to a lower risk of developing CKD. (16) However, many patients with CKD continue to struggle with adhering to these dietary recommendations.

Brown rice contains low protein and is a source of energy.[17] Tuna can meet protein needs, is low in fat, and contains omega-3 fatty acids.[18] Cucumbers are rich in antioxidants and anti-carcinogens.[19] Pineapple fruit is also rich in vitamins which are suitable for people with CKD.[20] Based on several previous studies, each of those foodstuffs can improve the nutritional status in patients with chronic diseases, including type 2 diabetes mellitus and cardiovascular diseases.[21] However, the effect of the combination of these four food ingredients on reducing proteinuria and albuminuria in CKD patients still needs to be analyzed. Therefore, it is important to carry out a pre-clinical study about the effect of nutritional therapy with brown rice, tuna fish, pineapple, and cucumber on reducing proteinuria and albuminuria in experimental animals such as rats.

Male Wistar rats are commonly used for metabolic research being more active than Sprague-Dawley rats.[22,23] Thus, this study aimed to determine how nutrition therapy with brown rice, tuna fish, pineapple, and cucumber affects proteinuria and albuminuria in male Wistar rats with CKD.

Materials and Methods

Study design

This experimental study used Wistar strain rats (*Rattus norvegicus*), which were divided into five groups using pretest–posttest control group design. The study analyzed three variant compositions of a balanced nutrition diet and two control groups (negative and positive) (Table 1). The balanced-nutrition diet treatment composition included brown rice (*Oryza nivara*), tuna fish (*Euthynnus affinis*), pineapple (*Ananas comosus*), and cucumber (*Cucumis sativus*). The positive control group received a vitamin-rich supplement (Nutrimax Livomax). The design of the laboratory experimental study is presented in Table 1. The study was conducted from July to September 2021 in the Pharmacology Laboratory at Mandala Waluya University and the Medicine Laboratory at Halo Oleo University, Kendari, Indonesia.

Population and sample size

Male Wistar rats with body weights ranging from 150 to 200 g, and an average age of 12 weeks were utilized in this study. The sample size (16 male Wistar rats) was calculated using the Federer formula for 4 groups. Each group used 4 rats (3.5 rats according to the Federer formula calculation).[24]

$(t-1)(n-1) \geq 10 \rightarrow (5-1)(n-1) \geq 10 \rightarrow 4n-4 \geq 10 \rightarrow 4n \geq 14 \rightarrow \mathbf{n \geq 3.5}$ (rounded up to 4)

Note: n: number of samples; t: number of groups

The rats were housed in experimental animal cages, which were made of plastic with husks and a wire cover on top. The room temperature ranged from 18°C to 26°C, and it was well-ventilated. The *ad libitum* method was used to provide rats with enough food and drink from tap water. Male rats were used as experimental animals in this study because they have a high metabolic activity rate and a high movement rate.[25] Before the intervention, the rats were given up to 125 g/kg BW (Body Weight)/day of meloxicam. Meloxicam is a nonsteroidal anti-inflammatory drug that works by inhibiting the enzyme cyclo-oxygenase 2 (COX-2) and decreasing prostaglandin production, thereby reducing pain and inflammation. Inhibition of prostaglandin biosynthesis causes renal vasoconstriction and increased reabsorption, which results in increased water retention.[26]

Ethical approval

This study was approved by the Health Research Ethics Committee of Mandala Waluya University number 012/KEPK/UMW/II/2021.

Nutritional therapy materials and processes

The nutritional therapy included three variations of the mixed menu, namely brown rice (F_1=250 g/kg BW/day; F_2=296 g/kg BW/day; F_3=341 g/kg BW/day), tuna (F_1=13 g/kg BW/day; F_2=14 g/kg BW/day; F_3=15 g/kg BW/day), pineapple (F_1=1 g/kg BW/day; F_2=1.5 g/kg BW/day; F_3=2 g/kg BW/day), and cucumber (F_1=1 g/kg BW/day; F_2=1.5 g/kg BW/day; F_3=2 g/kg BW/day) (Figure 1). These foodstuffs are widely available in Indonesia. This combination of foodstuffs was compared with commercial supplements, namely Nutrimax Livomax as a positive comparison. Nutrimax Livomax capsule contains calcium ascorbate, red clover, rosemary extract, milk thistle extract, and other components and is recommended for maintaining body health and increasing kidney function.[27]

The nutritional therapy process was conducted on 16 rats with CKD and without CKD divided into 3 intervention groups and 1 control group (Table 1). Each group comprised four rats. The three intervention groups were given nutrition consisting of brown rice, tuna fish, pineapple, and cucumber with different compositions between groups 1, 2, and 3 (Table 1). Determination of food composition was related to the recommended calorie, protein, carbohydrate, fat, and sodium requirements for adults with CKD stages 3–5 without maintenance dialysis. Calories needed for the patients with CKD are approximately 25–35 kcal/kg/day, 0.6–0.8 g protein/kg/day, 55%–60% carbohydrate, <30% fat or <7% saturated fat, and ≤2.3 g/day of sodium.[28] Then, based on the basic needs, they were converted according to the body weight of the rats. The control group was given one capsule/day of Nutrimax Livomax as a standard nutritional therapy. The rats were given food for 15 days according to the formula for each group.

Procedure for collecting and examining urine samples

Before treatment, male rats were put into metabolic cages for 24 hours to collect their urine as pretreatment urine. The volume of accommodated urine was approximately 13–23 mL. Then, the urine samples from each mouse were checked for proteinuria and albuminuria levels using a visible ultraviolet spectrophotometer λ 580 nm: Model of APEL UV-VIS Spectrophotometer, Single Beam PD-3000 UV, made by APEL CO., LTD, Japan and placed in the Medical Laboratory in Halu Oleo University, Kendari, Indonesia. After being treated with nutrition therapy for 15 days, the rats were put in a cage for 24 hours to collect their urine as post-treatment urine, and then proteins and albumin were reexamined with the same instrument.

Data analysis

Data were analyzed using SPSS version 25 descriptively and inferentially. Descriptive analysis described proteinuria and albuminuria before and after intervention in each group. The inferential analysis used a paired t-test and one-way analysis of variance (ANOVA). The paired t-test was used to analyze differences in levels of proteinuria and albuminuria before and after treatment. The significant effect was seen by a p-value of <0.05. One-way ANOVA and continued post hoc test were applied to understand the diversification of the mean between five groups and to identify which diets could reduce proteinuria and albuminuria in rats with CKD. Decreased proteinuria and albuminuria indicate an improvement in kidney function in rats.

Limitation

In previous studies, giving brown rice was stated to be able to reduce weight gain and improve the lipid profile in obese mice and it was stated that it is good for people with chronic diseases.[29] However, this study did not measure the body weight of the mice, so it could not see the effect of the F1, F2, and F3 formulas on the mice's body weight.

Results

Effect of a balanced diet: brown rice, tuna, pineapple, and cucumber on proteinuria

This study has shown that in general, nutritional therapy with a mixed menu of brown rice, tuna fish, pineapple, and cucumber could reduce proteinuria in rats with CKD, especially in the third experiment group ($p<0.001$; Table 2). In the third experiment group (F_3) reduced proteinuria from 11.28 mg/dL ± 1.21 mg/dL to 7.75 mg/dL ± 0.78 mg/dL. The effect of the third food formula was the same as that of the Nutrimax Livomax capsule fed in the positive control group. Nutrimax Livomax reduced the proteinuria from 11.20 mg/dL ± 0.69 mg/dL to 7.04 mg/dL ± 0.71mg/dL ($p<0.001$). However, the percentage of decreased proteinuria in the group fed with the third food formula was slightly lower, when compared to the group given the Nutrimax Livomax capsule, namely 31.29% for the third food formula and 37.14% for the group given the Nutrimax Livomax capsule.

In the first experiment group (F_1), the average proteinuria was the same before and after nutrition therapy ($p = 0.98$). There was one rat only which showed a slight decrease of proteinuria after treatment (15.8%). In the second experiment, the group fed with 296 g/kg BW/day brown rice, 14 g/kg BW/day tuna fish, 1.5 g/kg BW/day pineapple, and 1.5 g/kg BW/day of cucumber (F_2), reduction in proteinuria was also not significant (16.1%; CI 95%: −0.71–4.30; $p = 0.107$). The one-way ANOVA and post hoc test also suggested that the third food formula (F_3) as the mixed menu was effective for rats with CKD (Table 2).

Effect of a balanced diet: brown rice, tuna, pineapple, and cucumber on albuminuria

Overall, the combination diet of brown rice, tuna fish, pineapple, and cucumber could significantly reduce the albuminuria in rats with CKD by 24.0% after 15 days ($p < 0.001$; CI 95%: 0.83 mg/dL –2.82 mg/dL), especially in the second and the third food formula (Table 3). In the second experiment group was fed 296 g/kg BW/day brown rice, 14 g/kg BW/day tuna fish, 1.5 g/kg BW/day pineapple, and 1.5 g/kg BW/day of cucumber (F_2) albuminuria slightly decreased by 16.1% in rats ($p < 0.01$, CI 95%: 0.74 mg/dL – 2.51 mg/dL). In the third experiment group fed with 341 g/kg BW/day brown rice, 15 g/kg BW/day tuna fish, 2 g/kg BW/day pineapple, and 2 g/kg BW/day of cucumber, their albuminuria decreased by 31.5% ($p < 0.003$, CI 95%: 2.09 mg/dL – 4.42 mg/dL). In the control group fed with Nutrimax Livomax capsule, their albuminuria decreased by 47.0% ($p < 0.00$, CI 95%: 4.32 mg/dL– 5.35 mg/dL; Table 3).

Discussion

Effect of balanced diet on proteinuria

The study showed that the third food formula (F_3) consisting of 341 g/kg BW/day brown rice, 15 g/kg BW/day tuna fish, 2 g/kg BW/day pineapple, and 2 g/kg BW/day of cucumber had a significant effect in reducing the proteinuria up to 31.3%. First, every 100 g of brown rice (*Oryza nivara*) contains approximately 76.2 g of carbohydrates, which is lower than white rice (79.9 g of carbohydrates).[30] This is important because the need for carbohydrates should not be too much since it will interfere with the body's metabolic processes, especially in the process of the reabsorption of substances in the proximal tubule.[31] Brown rice contains good-quality fiber and plays a role in the process of water absorption, stimulates peristaltic movement, and prevents constipation, to maintain the glomerular filtration rate. Fiber also functions as a binder of cholesterol in bile, which can lower blood cholesterol levels, and as an emulsifier.[32] Brown rice is also coated with bran which contains many vitamins, including thiamine, niacin, pyridoxine, and minerals, such as phosphorus, manganese, and iron.

Vitamins such as thiamin helped in relieving sensations in the rat's bodies and gave strength to the heart which can supply nutrients.[32] Furthermore, the niacin contained in brown rice can increase the production of enzymes which are members of the prosthetic group, and nicotinamide adenine phosphate which function as endocytosis and receptor mediation so that protein reabsorption can occur through the process of endocytosis. Therefore, giving brown rice can reduce protein levels in rat urine. The browner rice composition given to rats (F3), the more significant the reduction in protein levels in rats' urine compared to the F1 and F2 treatments which contained less brown rice in this study.

Moreover, treatment with 15 g/kg BW/day of tuna (*Euthynnus affinis*) in F3 was also able to reduce an average of 31.3% proteinuria in rats in this study. Every 100 g of tuna contains protein of approximately 20.73–23.2 g.[30,33] Proteins play many roles in body health, including adapting the body to the extracellular environment and maintaining optimal health.[34] Moreover, a protein diet can act synergistically with Angiotensin-converting enzyme inhibitors to suppress proteinuria. The protein content in tuna is also very effective in maintaining the accumulation of waste products from kidney metabolism and can maintain the permeability of the glomerular capillary walls.[35] The ratio between polyunsaturated fatty acids and saturated fatty acids is 2.32 (61.92/26.64). Moreover, it was reported to reduce the production of the classic inflammatory cytokine tumor necrosis factor in rats, so that healing of chronic inflammation occurs.[36] Therefore, by feeding tuna fish, chronic inflammation in rats could be cured which resulted in a decrease of proteins in rats' urine. This means that by feeding tuna, there was an improvement in the rats' kidney function.

Furthermore, pineapples (*Ananas comosus*) contain a lot of vitamin C (0.5 mg/100 g) and minerals such as calcium (0.3 mg/100 g) and phosphorus (0.22 mg/100 g) (30). Thus, pineapples can function as an antioxidant, prevent inflammation, monitor nervous system function, and facilitate bowel movements in rats.[37] Giving 2 g/kg BW/day of pineapple in this study did not disrupt the fluid stability in the mice's bodies, but was able to cure inflammation in mice. This is because pineapple fruit also contains the enzyme bromelain.[38] Pineapple can also increase the function of High-Density Lipoprotein (HDL), namely preventing damage to blood vessel walls due to fat accumulation and keeping the body healthy.[39]

The cucumber mixed into the diet of rats (2 g/kg BW/day) is one of the vegetables that contain lots of phytochemical compounds, such as flavonoids, saponins, phenolics, and steroids. These phytochemical compounds function as antioxidants and antidiabetics.[40] Flavonoids can function as anti-inflammatory, antibacterial analgesic, and anti-constipation.[41] Thus, cucumbers could cure the inflammation in rats, and they could also easily defecate.

Their condition is getting better day by day, including the glomerular filtration membrane, so protein reabsorption occurs, which results in a decrease in proteinuria in rats.

Effect of a balanced diet on albuminuria

This study revealed that the second food formula (F_2) has been able to reduce albuminuria rather than decrease proteinuria. The effect of the third food formula (F_3) was also significant in reducing albuminuria in CKD rats. The decrease in albuminuria is possibly caused by improvements in the glomerular filtration barrier and albumin reabsorption occurs in proximal tubule cells, namely through endocytosis. This condition is likely caused by megalin and cubilin as receptors for endocytosis in the proximal tubule which have begun to function.[42] Thus, albumin can be transferred to lysosomes for degradation, and ultimately there is a decrease in the concentration of albumin in the urine. By giving 296g of brown rice therapy to rats, they provided additional vitamins including niacin, allowing for an increase in enzyme production. The enzymes then supported the endocytosis process in the reabsorption of albumin, so albumin could be degradable. Consequently, albuminuria decreased in rats. Likewise, F3 contains more brown rice (341g) than F2 (296g), therefore the decrease in albuminuria was greater in the F3 therapy group, namely 31.5% compared to the F2 therapy group with a decrease in albuminuria of only 16.1%.

Furthermore, for the composition of pineapple and cucumber, only a small amount was given, namely 1.5 g/kg BW/day each in the F2 therapy group and 2 g/kg BW/day in the F3 therapy group, which probably did not disturb the fluid balance in the rats' bodies but might be able to stabilize the rat's blood. The blood pressure affects sympathetic vasoconstrictor activity in arterioles, including renal arterial afferents. When systolic blood pressure <120 mm Hg and diastolic blood pressure <80 mm Hg are normal,[43] the reflex is reduced and arteriolar vasodilation occurs. This means that the blood entering the glomerulus through the dilated afferent arteriole decreased and declined glomerular blood pressure. Consequently, the glomerulus filtration rate decreased.

Conclusions

The food composition (F_3) of 341 g/kg BW/day brown rice, 15 g/kg BW/day tuna, 2 g/kg BW/day pineapple, and 2 g/kg BW/day of cucumber can provide energy to male Wistar rats with CKD. This food formula was also able to reduce proteinuria and albuminuria in rats with CKD. However, the Food composition (F1) of 250 g/kg BW/day brown rice, 13 g/kg BW/day tuna, 1 g/kg BW/day pineapple, and 1 g/kg BW/day cucumber cannot reduce proteinuria and albuminuria di rats with CKD. Whereas, the food composition (F2) of 296 g/kg BW/day brown rice, 14 g/kg BW/day tuna, 1.5 g/kg BW/day pineapple, and 1.5 g/kg BW/day cucumber can reduce the albuminuria only. Thus, Formula Three (F3) is better than formulas 1 and 2, because it can reduce proteinuria and albuminuria levels, meaning this formula is suitable for therapy for chronic kidney disease sufferers.

To provide a variety of menus for chronic kidney sufferers, it is possible to carry out other research, namely by replacing pineapple with pomegranate in a menu mixture of brown rice, tuna, and cucumber, because pomegranate has also been found to prevent kidney damage.[44] Alternative variations in replacing other food ingredients for a balanced menu for chronic kidney sufferers can also be tested in the future.

References

1. World Health Organization. world Health Statistics 2023: monitoring health for the SDGs, Sustainable Development Goals. Geneva: World Health Organization; 2023.

2. Health Ministry of Republic of Indonesia. Laporan Nasional riset kesehatan dasar 2018 [National report of basic health research 2018] [Internet]. Jakarta: Health Ministry of Republic of Indonesia; 2019. Available from: http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan_Nasional_RKD2018_FINAL.pdf

3. Weldegiorgis M, Woodward M. The impact of hypertension on chronic kidney disease and end-stage renal disease is greater in men than women: a systematic review and meta-analysis. BMC Nephrol 2020;21:1–9.

4. Wanigasuriya K. Update on uncertain etiology of chronic kidney disease in Sri Lanka's North-Central dry zone. MEDICC Rev 2014;16:61–5.

5. Mikolasevic I, Žutelija M, Mavrinac V, Orlic L. Dyslipidemia in patients with chronic kidney disease: etiology and management. Int J Nephrol Renovasc Dis 2017;10:36–45.

6. Kazanciog R. Risk factors for chronic kidney disease: an update. Kidney Int Suppl 2013;3:368–71.

7. Luyckx VA, Tuttle KR, Garcia-Garcia G, et al. Reducing major risk factors for chronic kidney disease. Kidney Int Suppl 2017;7:71–87.

8. Syara A, Suhaimi S, Purma A, et al. Hubungan lama hemodialisis dengan nafsu makan pada pasien gagal ginjal kronik di Unit Hemodialisis Rumah Sakit Grandmed Lubuk Pakam tahun 2019 [The relationship between duration of hemodialysis and appetite in patients with chronic kidney failure at the hemodialysis unit at Grandmed Lubuk Pakam Hospital in 2019]. J Keperawatan dan Fisioter 2020;3:79–86.

9. Simatupang LL. Pengalaman pasien suku Batak Karo dengan gagal ginjal kronis (GGK) dalam menjalani hemodialisa di Murni Teguh Memorial Hospital [The experience of the Karo Batak tribe with chronic kidney disease (CKD) in undergoing hemodialysis at Murni Teguh Memorial Hospital]. Indones Trust Heal J 2018;1:18–25.

10. Nixon A, Wilkinson T, Young H, et al. Symptom burden in people living with frailty and chronic kidney disease. BMC Nephrol 2020;21:1–11.

11. Shouket H, Gringart E, Drake D, Steinwandel U. "Machine-Dependent": The lived experiences of patients receiving hemodialysis in Pakistan. Glob Qual Nurs Res 2022;9:1–13.

12. Sari R, Sugiarto, Probandari A, Hanim D. Hubungan asupan energi, protein, vitamin B6, natrium dan kalium terhadap status gizi pada gagal ginjal kronik dengan hemodialisis [The relationship between energy intake, protein, vitamin B6, natrium and kalium and nutritional stutus in chronic kidney failure with hemodialysis]. J Akad Baiturrahim 2017;6:34–43.

13. Ko GJ, Obi Y, Tortoricci AR, Kalantar-Zadeh, K. Dietary protein intake and chronic kidney disease. Curr Opin Clin Nutr Metab Care 2017;20:77–85.

14. Upadhyay A, Karn SK. Brown rice: Nutritional composition and health benefits. J Food Sci Technol Nepal 2018;10:48–54.

15. Kalantar-Zadeh K, Moore L, Tortorici A, et al. North American experience with low protein diet for non-dialysis-dependent chronic kidney disease. BMC Nephrol 2016;17:90.

16. Adair K, Bowden R. Ameliorating chronic kidney disease using a whole food plant-based diet. Nutrients 2020;12:1–17.

17. Watanabe S, Adachi K, Wakino S, et al. Dietary therapy with low protein "genmai" (brown rice) to improve the gut-kidney axis and reduce CKD progression. Asia Pac J Clin Nutr 2022;31:341–7.

18. Mahaliyana AS, Jinadasa BKKK, Liyanage NPP, et al. Nutritional composition of Skipjack Tuna (*Katsuwonus pelamis*) caught from the oceanic waters around Sri Lanka. Am J Food Nutr 2015;3:106–11.

19. Uthpala TGG, Marapana RAUJ, Lakmini KPC, Wettimuny DC. Nutritional bioactive compounds and health benefits of fresh and processed cucumber (C*ucumis sativus* L.). Sumerianz J Biotechnol 2020;3:75–82.

20. Rompies R, Mayulu N, Nurkolis F, et al. Antioxidant capacity of snack cookies made from mango and pineapple fermentation. Foord Res 2021;5:145–8.

21. Lee YM, Kim SA, Lee IK, et al. Effect of a brown rice vegan diet and conventional diabetic diet on glycemic control of patients with type 2 diabetes: A 12-week randomized clinical trial. PLoS One 2016;11:1–14.

22. Mamikutty N, Thent ZC, Sapri SR, et al. The establishment of metabolic syndrome model by induction of fructose drinking water in male Wistar rats. Biomed Res Int 2014;263897:1–8.

23. Omodanisi IE, Aboua YG, Oguntibeju OO. Assessment of the anti-hyperglycaemic, anti-inflammatory and antioxidant activities of the methanol extract of *Moringa oleifera* in diabetes-induced nephrotoxic male Wistar rats. Molecules 2017;22:1–16.

24. Federer WT. Randomization and sample size in experimentation. In: The Food and Drug Administration Statistics Seminar, Washington, DC. Washington, D.C.: Cornell University; 1966. p. 1–15.

25. Bazzano T, Restel TI, Porfirio LC, et al. Renal biomarkers of male and female Wistar rats (*Rattus norvegicus*) undergoing renal ischemia and reperfusion. Acta Cirúrgica Bras 2015;30:277–88.

26. Burukoglu D, Baycu C, Bektur E. Effects of nonsteroidal anti-inflammatory meloxicam on stomach, kidney, and liver of rats. Toxicol Ind Health. 2016;32(6):980–6.

27. Kawsar A, Alam T, Pandit D, Rahman M, Mia M, Talukdar A, et al. Status of disease prevalence, drugs and antibiotics usage in pond-based aquaculture at Narsingdi district, Bangladesh: A major public health concern and strategic appraisal for mitigation. Heliyon. 2022;8:e09060.

28. Beto JA, Schury KA, Bansal VK. Strategies to promote adherence to nutritional advice in patients with chronic kidney disease: a narrative review and commentary. Int J Nephrol Renovasc Dis 2016;9:21–33.

29. Lim SM, Goh YM, Mohtarrudin N, Loh SP. Germinated brown rice ameliorates obesity in high-fat diet induced obese rats. BMC Complement Altern Med 2016;16:1–11.

30. Health Ministry of Republic of Indonesia. Tabel komposisi pangan Indonesia [Indonesian food composition table] [Internet]. Health Ministry of Republic of Indonesia. Jakarta: Health Ministry of Republic of Indonesia; 2020 [cited 2021 Oct 27]. Available from: https://perpustakaan.kemkes.go.id/inlislite3/uploaded_files/dokumen_isi/Monograf/Tabel Komposisi Pangan Indonesia.pdf

31. Park S, Lee S, Kim Y, et al. Causal effects of relative fat, protein, and carbohydrate intake on chronic kidney disease: a Mendelian randomization study. Am J Clin Nutr 2021;113:1023–31.

32. Ho HVT, Jovanovski E, Zurbau A, et al. A systematic review and meta-analysis of randomized controlled trials of the effect of konjac glucomannan, a viscous soluble fiber, on LDL cholesterol and the new lipid targets non-HDL cholesterol and apolipoprotein B1,2. Am J Clin Nutr 2017;105:1239–47.

33. Messina CM, Arena R, Manuguerra S, et al. Valorization of side stream products from sea cage fattened bluefin tuna (*Thunnus thynnus*): Production and *in vitro* bioactivity evaluation of enriched ω-3 polyunsaturated fatty acids. Mar Drugs 2022;20:1–18.

34. Wu G. Dietary protein intake and human health. Food Funct 2016;7:1251–65.

35. Kammoun K, Chaker H, Mahfoudh H, et al. Diet in chronic kidney disease in a Mediterranean African country. BMC Nephrol 2017;18:1–7.

36. Koga N, Ogura J, Yoshida F, et al. Altered polyunsaturated fatty acid levels in relation

to proinflammatory cytokines, fatty acid desaturase genotype, and diet in bipolar disorder. Transl Psychiatry 2019;9:1–9.

37. Ali M, Hashim N, Aziz S, Lasekan O. Pineapple (*Ananas comosus*): A comprehensive review of nutritional values, volatile compounds, health benefits, and potential food products. Food Res Int 2020;137:109675.

38. Muhammad ZA, Tashfeen A. Therapeutic uses of pineapple-extracted bromelain in surgical care - A review. J Pak Med Assoc 2017;67:121–5.

39. Sayago-Ayerdi S, García-Martínez DL, Ramírez-Castillo AC, et al. Tropical fruits and their co-products as bioactive compounds and their health effects: a review. Foods 2021;10:1–26.

40. Landu EA, Dewi NP, Dermiati T. Uji efek antidiabetes ekstrak kulit buah ketimun pada tikus putih jantan yang diinduksi streptocotocin [Test of the antidiabetic effect of cucumber peel extract on male white rats induced by streptocotocin]. Farmakol J Farm 2019;16:177–85.

41. Ferraz CR, Carvalho TT, Manchope MF, et al. Therapeutic potential of flavonoids in pain and inflammation: mechanisms of action, pre-clinical and clinical data, and pharmaceutical development. Molecules 2020;25:1–35.

42. Nusshag C, Stütz A, Hägele S, et al. Glomerular fltration barrier dysfunction in a self-limiting, RNA virus-induced glomerulopathy resembles fndings in idiopathic nephrotic syndromes. Sci Reports 2020;10:1–10.

43. Muntner P, Shimbo D, Carey RM, et al. Measurement of blood pressure in humans: a scientific statement from the American Heart Association. Hypertension 2019;73:e35–66.

44. Radajewska A, Szyller J, Niewiadomska J, et al. *Punica granatum* L. polyphenolic extract as an antioxidant to prevent kidney injury in metabolic syndrome rats. Oxid Med Cell Longev 2023;1–14.

Table 1. Design of the laboratory experimental study with control group design before, during, and after treatment

Group	Before treatment	treatment	After treatment
Experiment 1 (F_1)	X_1	F_1 (250 g/kg BW/day brown rice, 13 g/kg BW/day tuna fish, 1 g/kg BW/day pineapple, 1 g/kg BW/day cucumber)	Y_1
Experiment 2 (F_2)	X_2	F_2 (296 g/kg BW/day brown rice, 14 g/kg BW/day tuna fish, 1.5 g/kg BW/day pineapple, 1.5 g/kg BW/day cucumber)	Y_2
Experiment 3 (F_3)	X_3	F_3 (341 g/kg BW/day brown rice, 15 g/kg BW/day tuna fish, 2 g/kg BW/day pineapple, 2 g/kg BW/day cucumber)	Y_3
Control (P)	X_4	F_4	Y_4

X_1, proteinuria and albuminuria before treatment with food formula 1. F_1, food formula of treatment 1 containing 250 g/kg BW/day brown rice, 13 g/kg BW/day tuna fish, 1g/kg BW/day pineapple, 1 g/kg BW/day cucumber; Y_1, proteinuria and albuminuria after treatment with food formula 1; X_2, proteinuria and albuminuria before treatment with food formula 2; F_2, Food formula of treatment 2 containing 296 g/kg BW/day brown rice, 14 g/kg BW/day tuna fish, 1.5 g/kg BW/day pineapple, 1.5 g/kg BW/day cucumber; Y_2, proteinuria and albuminuria after treatment with food formula 2; X_3, proteinuria and albuminuria before treatment with food formula 3; F_3, Food formula of treatment 3 containing 341 g/kg BW/day brown rice, 15 g/kg BW/day tuna fish, 2 g/kg BW/day pineapple, 2 g/kg BW/day cucumber; Y_3, proteinuria and albuminuria after treatment with food formula 3; X_4, proteinuria and albuminuria before treatment formula 4 of control group; F_4, Food formula of control giving 1 Nutrimax Livomax capsule; Y_4, proteinuria and albuminuria after treatment with food formula 4

Table 2. Proteinuria before and after nutrition therapy in male Wistar rats strain.

No.	**Proteinuria (mg/dL)**		**Sig**	**95% CI**		**Mean difference (MD)**				
	Before*	**After***		**Lw**	**Up**	**I**	**J**	**MD (1-j)**	**SE***	**Sig***
Experiment 1 (F_1)*										
1	13.71	11.55	0.98	−5.31	5.25	F1	F2	1.83	1.05	0.66
2	10.11	10.27				F1	F3	3.57	1.05	0.04
3	10.12	10.28				F1	P	4.19	1.05	0.01
4	9.24	11.33								
Mean ± SD	11.02 ± 2.37	11.05 ± 0.68								
Experiment 2 (F_2)*										
1	13.19	9.21	0.107	−0.71	4.30	F2	F1	-1.83	1.05	0.66
2	9.98	8.68				F2	F3	1.74	0.97	0.60
3	11.24	9.60				F2	P	2.36	0.97	0.19
4	10.15	9.90								
Mean ± SD	11.14 ± 1.48	9.35 ± 0.53								
Experiment 3 (F_3)*										
1	9.77	6.71	0.001	2.59	4.48	F3	F1	-3.57	1.05	0.04

2	12.49	8.10				F3	F2	-1.74	0.97	0.60
3	11.98	8.52				F3	P	0.62	0.97	1.00
4	10.89	7.65								
Mean ± SD	11.28 ± 1.21	7.75 ± 0.78								
Control (P)*										
1	10.48	6.56				P	F1	-4.19	1.05	0.01
2	11.22	8.03				P	F2	-2.36	0.97	0.19
3	12.12	6.48	0.004	2.50	5.81	P	F3	-0.62	0.97	1.00
4	10.98	7.09								
Mean ± SD	11.20 ± 0.69	7.04 ± 0.71								
Total:16										
Mean ± SD	**8.38 ± 5.09**	**6.48 ± 4.09**	**0.001**	**0.93**	**2.86**					

The data were obtained from descriptive and paired t-tests of statistical analysis; CI, confidence interval; SD, standard deviation; SE: Standard error; Sig: Significance level between before and after treatment ($p < 0.05$ is significant); Sig: Significance level for differences in values between groups ($p<0.05$ is significant).

Table 3. Albuminuria before and after nutrition therapy in male Wistar rats' strain with chronic kidney failure

No.	**Albuminuria (mg/dL)**		**Sig**	**95% CI**		**Mean difference (MD)**				
	Before*	**After***		**Lw**	**Up**	**I**	**J**	**MD (1-**	**SE***	**Sig***

								j)		
Experiment 1 (F_1)*										
1	10.80	12.00	0.20	−2.67	1.06	F1	F2	2.43	0.46	0.002
2	10.45	10.39				F1	F3	4.06	0.46	0.000
3	10.45	10.39				F1	P	5.65	0.46	0.000
4	8.56	9.84								
Mean ± SD	**9.94 ± 1.21**	**10.74 ± 1.13**								
Experiment 2 (F_2)*										
1	9.23	7.57	0.01	0.74	2.51	F2	F1	- 2.43	0.46	0.002
2	9.56	8.42				F2	F3	1.63	0.43	0.017
3	10.06	8.76				F2	P	3.22	0.43	0.000
4	11.44	9.05								
Mean ± SD	**10.07 ± 0.97**	**8.45 ± 0.64**								
Experiment 3 (F_3)*										
1	10.10	6.19	0.003	2.09	4.42	F3	F1	- 4.06	0.46	0.000
2	11.41	8.04				F3	F2	- 1.63	0.43	0.017
3	9.77	7.56				F3	P	1.59	0.43	0.020
4	10.04	6.51								
Mean ± SD	**10.33 ± 0.73**	**7.08 ± 0.87**								
Control (P)*										
1	10.22	5.61	0.00	4.32	5.35	P	F1	- 5.65	0.46	0.000
2	10.34	5.36				P	F2	- 3.22	0.43	0.000
3	10.20	5.67				P	F3	- 1.59	0.43	0.020
4	10.55	5.30								

Mean ± SD	**10.33 ± 0.16**	**5.48 ± 0.19**								
Total:16										
Mean ± SD	**7.64 ± 4.57**	**5.81 ± 3.86**	0.001	0.83	2.82					

The data were obtained from descriptive and paired t-tests of statistical analysis. CI, confidence interval; SD, standard deviation; Sig: Significance level between before and after treatment ($p < 0.05$ is significant); Sig: Significance level for differences in values between groups ($p<0.05$ is significant).

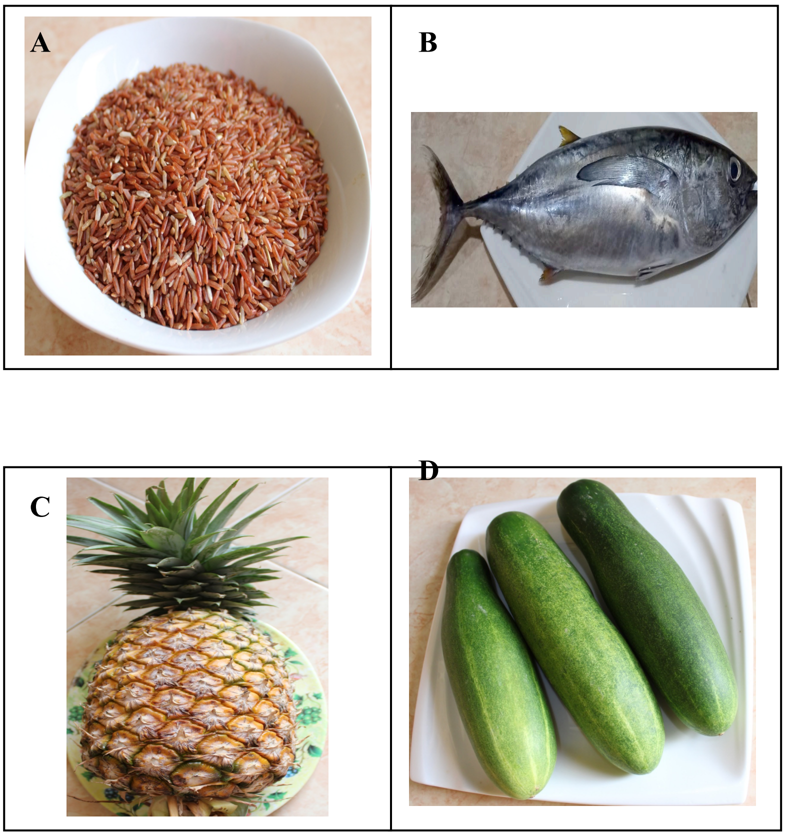

Figure 1. Food that was used as a treatment in this study: (A) Brown rice (*Oryza nivara*), (B) tuna fish (*Euthynnus affinis*), (C) pineapple (*Ananas comosus*), and (D) cucumber (*Cucumis sativus*)

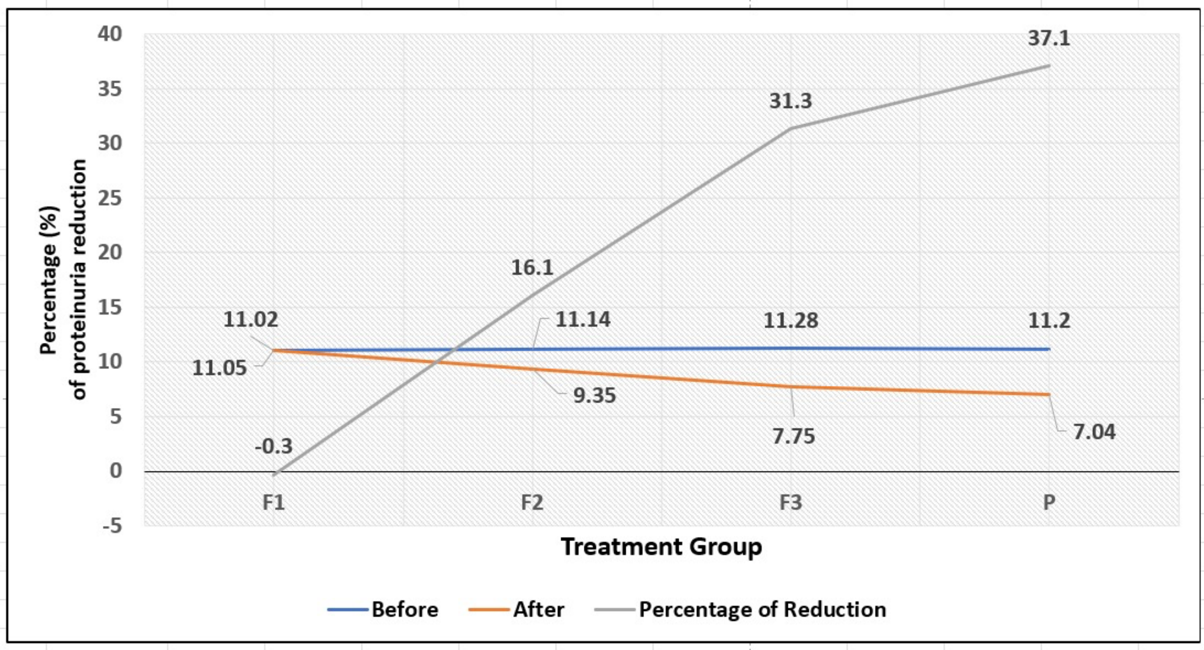

Figure 2. Proteinuria before and after nutrition therapy, and percentage of proteinuria reduction in male Wistar rats' strain.

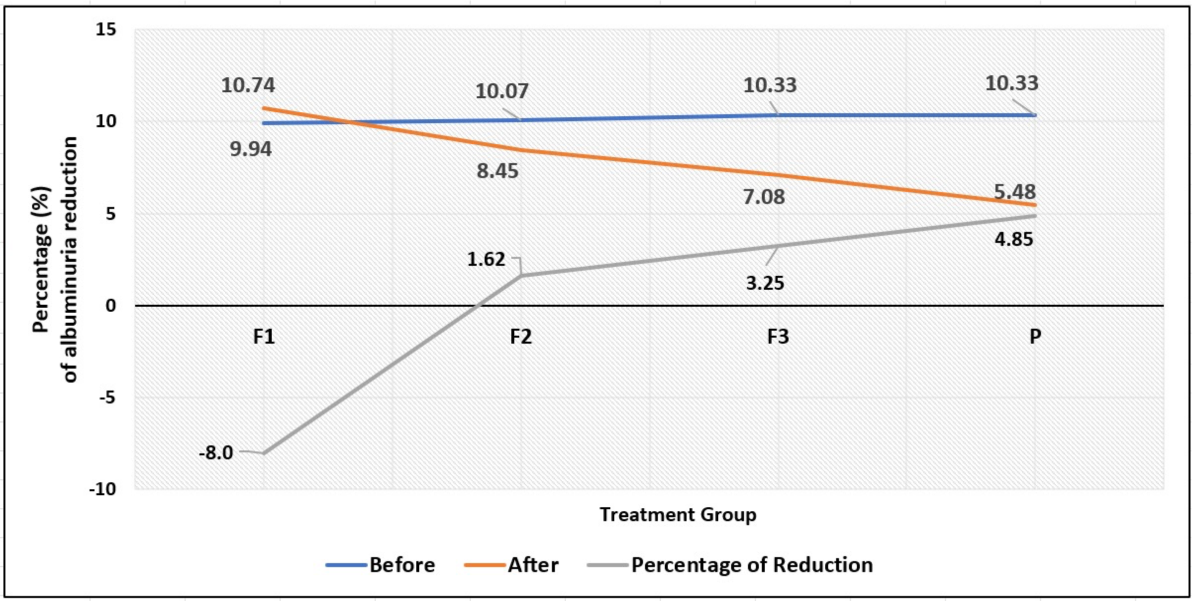

Figure 3. Albuminuria before and after nutrition therapy, and percentage of albuminuria reduction in male Wistar rats' strain.

Submitted: 27 September 2023

Accepted: 19 February 2024

Early access: 7 March 2024